INTEGRATED CARE TO PREVENT AND MANAGE CHRONIC DISEASES – BEST PRACTICES IN PUBLIC HEALTH

Prehab Case Study

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Acknowledgements

The authors would like to thank Graciela Martínez-Pallí, Isaac Cano and Josep Roca on behalf of the surgical prehabilitation team at Hospital Clínic of Barcelona (https://surgifit.es/en/about-us/).

This report is part of the series on Best Practices in Public Health and has been produced with the financial and substantive assistance of the European Union.

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Prehab: case study overview

Description: Prehab is a 4-6 week pre-operative intervention for high-risk patients undergoing major elective surgery. It aims to enhance clinical outcomes and patients' functional capacity in order to reduce post-operative morbidity and accelerate recovery through improving aerobic capacity, nutritional balance, and psychological well-being.

It has been implemented and studied since 2013 at the Hospital Clínic of Barcelona (HCB), in the Spanish region of Catalonia, in different variations and for patients undergoing different types of surgery. It is currently being scaled-up in Catalonia and was also transferred to Germany, France, the Netherlands and Poland.

Best practice assessment

OECD Best Practice assessment of Prehab

Criteria	Assessment
Effectiveness	Prehab has been shown to improve aerobic capacity and physical activity, and has the potential to reduce postoperative complications and the use of health care resources; however, results are not yet conclusive
Efficiency	Available economic evaluations indicate that Prehab is likely cost-effective, although robust evidence is lacking
Equity	Prehab can improve outcomes for high-risk surgical patients, which is likely to reduce disparities in health outcomes among surgical patients, although no evidence of its effect on equity is available
Evidence-base	Quality of the evidence of effectiveness of Prehab is strong in many respects, including in study design and methods used However, similar to many other public health interventions, it is difficult to blind participants
Extent of coverage	The coverage of Prehab is still limited to a small proportion of surgery patients that may benefit from the intervention

Enhancement options: Prehab is already aligned with current guidelines for prehabilitation interventions. Modulating exercise intensity and duration of the intervention as well as maximising patient adherence could be ways to *enhance effectiveness* further. Increasing effectiveness would also be a possible avenue to *enhance efficiency*. To *enhance the evidence-base*, larger-scale studies and more granular data are needed to establish the most appropriate prehabilitation protocols for various patient groups. Studies should also report a standardised set of outcomes over longer follow-up periods and assess cost-effectiveness formally. Reporting data relevant for an assessment of equity would be a first step towards *enhancing equity.* The *extent of coverage* could be broadened by increasing capacity for high-risk patients and expanding the range of eligible patient groups.

Transferability: There is need for Prehab in most EU Member States and OECD countries and it may fit reasonably well into the general prevention-related political contexts of these countries. Modularity and scope for personalisation are two characteristics of Prehab that make it transferable. Target contexts need to be evaluated in terms of availability of human and institutional capacity, including digital support, and logistical aspects in hospitals and community settings. A structured implementation plan is a corners stone for integrating Prehab into existing surgical services.

Conclusion: A growing body of evidence underpins the effectiveness of Prehab and evidence is also starting to emerge of its efficiency. The intervention has high transferability potential. It is already being scaled in Catalonia and transferred and scaled in parallel in a number of EU Member States, Canada and the United Kingdom. It could become a routine component of pre-surgical care and has potential for generalisation to other domains of health care beyond surgery. Further efforts need to focus on optimisation of deployment of the service, with a continuous and built-in evaluations.

Intervention description

This section describes the background behind prehabilitation programs followed by the specific prehabilitation program operating in the Spanish region of Catalonia (referred to as *Prehab*).

Background

Complications after surgery are common and represent a significant cause of patient morbidity, contributing to the length of post-operative hospital length of stay (LoS) and hospital costs. For instance, an international cohort study of adults undergoing elective surgery found an incidence of surgical complications before hospital discharge of 19.8% across 19 high-income countries, and that 2.6% of complications resulted in death.[1] Incidence may be as high as 40% or 50% when also including complications that occur post-discharge and for certain types of surgery. For example, a literature review by Tevis and Kennedy (2013[1]) found that, across different studies, incidence of complications within 30 days of surgery ranged from 5.8% to 43.5% in general surgery patients. Another international cohort study of adults undergoing cancer surgery found a 30-day incidence of complications of 31.9%, 43.9% and 47.5% respectively for breast, gastric and colorectal cancer across 31 high-income countries.[2] Surgical complications also account for the majority of adverse events in hospitals, and evidence suggests that some 40% to 50% of adverse events are preventable (de Vries et al., 2008[2]).

[1] See Pearse et al. (2016[50]). Estimate across 19 countries OECD and non-OECD countries classified as high-income: Australia, Austria, Belgium, Canada, Denmark, France, Germany, Greece, Hong Kong, Italy, the Netherlands, New Zealand, Portugal, Romania, Spain, Sweden, Switzerland, the United Kingdom and the United States. The study covered a a total of 27 countries, also including eight low- or middle-income countries: Brazil, China, Indonesia, Malaysia, Nigeria, Russia, South Africa, Uganda.

[2] See Knight et al. (2021[49]). The study covered a total of 82 countries, of which 31 classified as high-income. The list of countries covered was not reported.

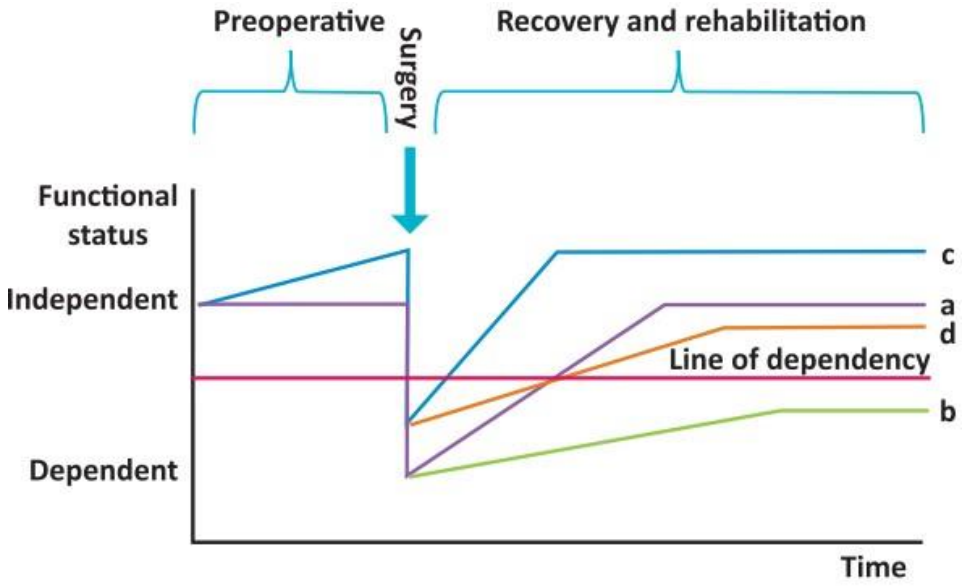
Interventions that prevent surgical complications can therefore be highly effective in terms of a range of patient outcomes. They can also be cost-effective, and indeed have the potential to be cost saving, by reducing hospital LoS or readmissions, and overall costs associated with treating complications.

There are various causes of surgical complications, including patient- and operation-related factors. In recent years, there has been a realisation in surgical practice that favourable patient-related factors, which improve the ability of patients to return to a physically and psychologically healthy state, are a key prerequisite for successful surgery (Scheede-Bergdahl, Minnella and Carli, 2019[3]). Perhaps not surprisingly, many patient-related factors, such as multi-morbidity and age, are significant predictors of the occurrence of complications. For example, a systematic review by Visser et al. (2015[4]) identified 22 patient characteristics as significant risk factors for the occurrence of complications within 30 days of surgery. These included not only older age[3] and the presence of comorbidities, but also being over- or under-weight, poor functional status, smoking and alcohol abuse (ibid.).

Prehabilitation has recently been trialled in patients undergoing various types of surgery, including cardiac and abdominal, for cancer and other types of diseases.[4] Prehabilitation, in general, aims to enhance patients' functional capacity before surgery, with the ultimate goal of improving post-operative outcomes (Banugo and Amoako, 2017[5]; Durrand, Singh and Danjoux, 2019[6]). This is based on the principle that building a functional reserve to withstand the stress of surgery accelerates functional recovery (see Figure 1.1 and Durrand, Singh and Danjoux (2019[6])). During the pre-operative period, patients may be, on the one hand, more motivated than usual to change health-related behaviour but may also lack, on the other hand, confidence to achieve such change, making them receptive to structured behavioural interventions (ibid.). Prehabilitation aims to take advantage of this "window" and is typically delivered as a multi-component intervention addressing patient well-being across three domains: improvement of physical condition, nutritional optimisation, and psychological support to reduce stress and anxiety. Depending on the patient population targeted, it might also comprise additional components, such as medication review, support for smoking cessation and reduction of alcohol intake, or correction of anaemia.[5]

Figure 1.1. The prehabilitation concept

Illustrated by the trajectory of functional status before and after surgery



[3] Using various cut-off ages, but most commonly 65 years (Visser et al., 2015[4]).

[4] See systematic reviews cited in the section about "Effectiveness" below.

[5] For discussions of common components of prehabilitation, see, for example, Banugo and Amoako (2017[5]); Durrand, Singh and Danjoux (2019[6]); López Rodríguez-Arias et al. (2020[56]); and Tew et al. (Tew et al., 2018[7]).

Note: Prehabilitation (trajectory c) aims to shorten the duration of reduced functional status post-surgery and the recovery period experienced by all patients (a). Patients suffering a complication may experience a slower and incomplete recovery threatening longer-term independence (b); prehabilitated patients are better placed to cope with complications (d).
Source: Durrand, Singh and Danjoux (2019[6]), based on Tew et al. (2018[7]).

Prehab in Catalonia

The prehabilitation intervention assessed in this document, referred to below as *Prehab*, is a pre-operative intervention for high-risk patients aged 70 years and above undergoing major elective surgery (Baltaxe et al.[8]). It aims to enhance functional capacity in order to reduce postoperative morbidity and accelerate recovery through improving aerobic capacity, nutritional balance, and psychological well-being. The intervention has been designed in a modular manner, comprising the components listed below, which have been combined in different ways:

1. A motivational interview;
2. Personalised support for increasing physical fitness and promoting physical activity (PA), including:
   a. A plan for increasing PA in daily life, and,
   b. Supervised high-intensity endurance training in selected patients;
3. Personalised nutritional management; and,
4. Psychological support.

These components are integrated into the care pathway as illustrated in Figure 1.2. The intervention has been implemented and studied since 2013 at Hospital Clínic of Barcelona (HCB), in the Spanish region of Catalonia, in different variations and for patients undergoing different types of surgery:

- It was initially trialled between 2013 and 2016 in a randomised controlled trial (RCT) of 144 high-risk patients[6] undergoing major elective abdominal surgery (Barberan-Garcia et al., 2018[9]), providing only component 1 and 2 (motivational interview and supervised and unsupervised PA promotion). All patients in the trial, including those in the control group, received a PA recommendation, nutritional counselling, and advice on smoking cessation and reduction of alcohol intake. The intervention had a mean duration of six weeks, during which patients attended an average of 12 supervised sessions.
- A Prehab Unit was subsequently established at HCB, and its implementation and effectiveness were assessed between 2016 and 2019 in a sample of 327 high-risk patients undergoing digestive, cardiac, thoracic, gynaecologic or urologic surgery, against the same number of matched controls (Barberan-Garcia and Cano, 2020[10]). For logistical reasons, a sub-group of 139 patients in the study only received components 1, 2.a, 3 and 4 of the intervention (i.e. excluding supervised highintensity endurance training), while another sub-group of 188 patients at higher risk because of comorbidities or because of highly aggressive surgery received all components, also including 2.b. Patients were enrolled if the surgical schedule allowed for at least four weeks of Prehab, but the actual median duration of the intervention was 5.5 weeks for non-cardiac surgery patients and 9.1 weeks for patients undergoing cardiac surgery (Risco et al.[11]).

In both studies, all patients including those in the control groups, received 'usual' pre-operative care, including a PA recommendation, nutritional counselling, and advice on smoking cessation and reduction of alcohol intake.

[6] Defined as age 70 years or above or American Society of Anesthesiologists (ASA) score III/IV and Duke Activity Status Index score ≤ 46.

Figure 1.2. Prehab components and process

Source: (Risco et al.[11]).

After a first baseline assessment, patients were assigned either to the program promoting physical activity (PA-based) or to the intervention additionally scheduling hospital-based supervised exercise training sessions twice or three times per week (ET-based). Subsequently, all candidates of the intervention group attended weekly face-to-face sessions during the prehabilitation program. A postintervention evaluation was scheduled before surgery and a final assessment of all cases was done at 30 days after surgery. The care in the control group (usual care) is displayed at the bottom of the figure. *LoS: Length of stay; E.R: Emergency Room*

OECD Best Practices Framework assessment

This section analyses Prehab against the five criteria within OECD's Best Practice Identification Framework – Effectiveness, Efficiency, Equity, Evidence-base and Extent of coverage (see Box 1.1 for a high-level assessment of Prehab). Further details on the OECD Framework can be found in in the document 'Best Practice Project: case study guide'.

Box 1.1. Assessment of Prehab

Effectiveness

- Prehab has shown efficacy in an RCT in terms of improving aerobic capacity and physical activity and reducing the incidence of post-operative complications and hospital re-admissions in high-risk patients undergoing major elective abdominal surgery.
- Effectiveness has also been evaluated in high-risk patients undergoing digestive, cardiac, thoracic, gynaecologic or urologic surgery, which found a reduction in hospital and ICU length of stay (LoS) and a small reduction in post-operative complications, only in adherent patients undergoing highly aggressive types of surgery.

Efficiency

- Available economic evaluations indicate that Prehab and other prehabilitation interventions are likely cost-effective, but formal evidence is lacking.
- The intervention in a randomised controlled trial (RCT) at Hospital Clínic of Barcelona (HCB) had a mean direct cost per patient of EUR 389. Thus, even small decreases in length of hospital LoS, re-interventions or readmissions, which are expensive, could generate savings.

Equity

- Prehab is targeted at high-risk surgical patients, and can improve outcomes in this patient group. Because risk factors for poor surgical outcomes tend to be more prevalent among people in underprivileged population groups, it is likely to reduce disparities in health outcomes among surgical patients. However, no evidence of the effect of Prehab in terms of equity is available. Also, at the population-level, there might be underlying inequities in access to surgery.

Evidence-base

- Prehab has been evaluated in an RCT and a case-control study. The quality of evidence from these studies is strong in many respects related to study design and methods but bias may be introduced an inherent inability to blind participants.
- There is also a broad evidence-base about similar prehabilitation interventions that support the principles of Prehab. However, most of these studies were small and their quality is variable, which may imply that effects are overstated.

Extent of coverage

- Prehab still has limited coverage. Following the initial RCT involving 144 patients, a permanent Prehab unit has been established at HCB with a capacity of 200 patients per year, compared to an estimated 900 patients per year who are suitable for the intervention.
- However, Prehab is being scaled locally and already in the process of being transferred to and scaled in other EU Member States (Germany, France, the Netherlands and Poland) and in Canada and the United Kingdom.

Effectiveness

> *Prehab has been shown to improve aerobic capacity and physical activity, and has the potential to reduce post-operative complications and the use of health care resources, however, results are not yet conclusive*

Prehab has so far been shown to be efficacious in an RCT in terms of improving aerobic capacity and PA, and reducing the incidence of post-operative complications and hospital re-admissions in high-risk patients undergoing major elective abdominal surgery. Effectiveness has also been evaluated for high-risk patients undergoing digestive, cardiac, thoracic, gynaecologic or urologic surgery. Specifically, a case-control study conducted in a real-world setting found small reductions in LoS and post-operative complications among

patients showing high adherence to the program and undergoing highly aggressive surgery (Risco et al.[11]). The RCT and case-control study described above yielded the following results:

- **Aerobic capacity and physical activity**:
  - The RCT of 144 high-risk patients undergoing major **elective** abdominal surgery found an improvement of 135% in endurance time, measured through cardiopulmonary exercise testing, and an improvement of 37 points in the Yale Physical Activity Survey (YPAS) between baseline and the pre-operative endpoint for the intervention group. Conversely, no improvements were observed in the control group (Barberan-Garcia et al., 2018[9]). Although differences were statistically significant, variability across patients was high.
  - The increase in aerobic capacity and PA persisted post-surgery, with a 62% higher endurance time at 30 days in the intervention group vs. the control group, and YPAS scores of 41 vs. 26 and 46 vs. 39 at three and six months post-surgery, respectively.
- **Peri-operative hospital and intensive-care unit length of stay (LoS)**:
  - Barberan-Garcia et al. (2018[9]) estimated that Prehab reduced the number of days patients spent in the intensive care unit (ICU) based on a subgroup analysis of 44 patients in the RCT who were admitted to ICU during their surgery.
  - The case-control study of 328 high-risk patients undergoing digestive, cardiac, thoracic, gynaecologic or urologic surgery found no significant effects for the group as a whole. However, a sub-group analysis including only adherent patients undergoing highly aggressive surgery showed significant reductions of hospital and ICU LoS (Risco et al.[11]).
- **Post-operative complications, hospital readmissions and surgical re-interventions:**
  - Based on data from the RCT, Barberan-Garcia et al. (2018[9]) estimated that Prehab reduced the number of patients who suffered from post-operative complications by 50% (95% confidence interval [CI] 30-80%) – i.e. 62% among patients receiving usual care compared to 31% of patients in the Prehab group. Prehab was also associated with a statistically significant reduction in the mean number of complications per patient. Stratification by type of complication found reductions in cardiovascular complications, fewer infections of uncertain source and a lower incidence of paralytic ileus, a type of intestinal blockage related to nervous and muscular malfunction in the absence of a physical obstruction.
  - At 30 days post-surgery, data from the RCT showed that 18% of all patients in the control group were re-admitted to hospital, compared to only 3% in the intervention group (Barberan-Garcia et al., 2019[12]). Thus, Prehab reduced the risk of re–admission by a factor of six (95% CI 1.4 to 30.0).
  - In the case-control study, only the intervention excluding component 2.b[7] provided to the subgroup of 139 patients was associated with a statistically significant decrease in the incidence of surgical re-interventions, with re-interventions occurring in 1% of patients in the intervention group vs. 7% in the control group (Barberan-Garcia and Cano, 2020[10]). The sub-group analysis including only adherent patients undergoing highly aggressive surgery showed a reduction in post-operative complications in terms of the comprehensive complication index (CCI) (Risco et al.[11])

While the RCT also found an improvement in self-reported physical health, measured in terms of the physical component of the “Short Form 36” health survey (SF-36 PCM), it found no improvement in quality of life or psychological status (Barberan-Garcia et al., 2018[9]). The case-control study found no effect in terms of post-surgery emergency department visits and hospital re-admissions (Barberan-Garcia and Cano, 2020[10]).

[7] Personalised support for increasing physical fitness and promoting PA – specifically, supervised high-intensity endurance training in selected patients.

Evidence from other prehabilitation interventions also suggests that they are effective

These results are partly in line with promising evidence on the effectiveness of prehabilitation interventions before major surgery more broadly. Recent meta-analyses of studies of prehabilitation for patients undergoing abdominal or cardiac surgery, for example, found that various types of prehabilitation interventions, including inspiratory muscle training (IMT) or breathing exercises, aerobic exercise, resistance training, and nutrition supplements and education, were associated with a reduction in postsurgical complications, although there was no effect on mortality.[8]

Effectiveness in terms of other outcomes is less clear. While Katsura et al. (2015[13]) and Hulzebos et al. (2012[14]) found reductions in hospital LoS for cardiac and major abdominal surgery patients receiving IMT, other meta-analyses concluded that there was no effect on LoS. Results are also mixed in terms of aerobic capacity, functional status and health-related quality of life (Hughes et al., 2019[15]; Moran et al., 2016[16]; Katsura et al., 2015[13]; Hulzebos et al., 2012[14]).

It should also be noted that, although surgery patients tend to be elderly, the review by Bruns et al. (2016[17]) is the only one which restricted the patient population to people aged 60 or above, and found no effect on complications following colorectal surgery, despite an improvement in physical condition. None of the other reviews cited above focused on elderly patients or patients considered at high risk because of other factors. Their findings may therefore be of limited relevance to the Prehab intervention assessed in this document (given that Prehab targets high-risk patients aged 70 and over). Another systematic review, which attempted to synthesise evidence of the effectiveness of prehabilitation for frail patients, concluded that robust evidence of clinical effectiveness was lacking; the review found only few and small-scale studies, which showed that prehabilitation programs were feasible for frail patients and increased patient satisfaction (Milder, Pillinger and Kam, 2018[18]).

[8] See Kamarajah et al. (2020[27]); Heger et al. (2020[33]); Hughes et al. (2019[15]); Moran et al. (2016[16]); Katsura et al. (2015[13]); Mans, Reeve and Elkins (2014[57]); and Hulzebos et al. (2012[14]). As a result of study heterogeneity, some recent systematic reviews, including those by Luther et al. (2018[29]), Hijazi, Gondal and Aziz (2017[30]), Bruns et al. (2016[17]) and Thomas et al. (2019[28]) of physical or multi-modal prehabilitation for patients undergoing abdominal surgery, and a review by Piraux, Caty and Reychler (2018[32]) of multi-modal prehabilitation for lung, colorectal, bladder or oesophageal cancer patients undergoing tumour resection, did not pool results from primary studies in metaanalyses; nevertheless, they also concluded cautiously that prehabilitation can reduce post-operative complications.

Efficiency

Available economic evaluations indicate that Prehab is likely cost-effective, although robust evidence is lacking

A cost-consequence analysis based on the RCT of 144 high-risk patients undergoing major elective abdominal surgery found that estimated cost savings at 30 days post-surgery were not statistically significant at the 95%-confidence level but concluded, based on these estimates, that the intervention was at least cost-neutral (Barberan-Garcia et al., 2019[12]). Although the wide confidence intervals around the estimates do not allow for ruling out a true cost increase, it appears rather unlikely that the intervention would have increased costs (Grocott and Ludbrook, 2019[19]). Prehab may therefore be at least costeffective by improving outcomes and having no effects on costs, or might even be cost-saving.

Delivery of the intervention in the RCT had a mean direct cost per patient of EUR 389, of which EUR 230 were for cardiopulmonary exercise testing, EUR 96 for group endurance-exercise training sessions, EUR 41 for the motivational interview, and EUR 22 for provision of the pedometer device to monitor daily PA (Barberan-Garcia et al., 2019[12]).

In the case-control study of 328 high-risk patients undergoing digestive, cardiac, thoracic, gynaecologic or urologic surgery, the sub-group analysis including only adherent patients undergoing highly aggressive types of surgery found a statistically significant mean cost reduction of 32%. Moreover, program completion in patients undergoing highly aggressive surgical procedures was associated with reductions in hospital costs per patient (Risco et al.[11]).

Conclusive evidence of cost-effectiveness from other prehabilitation interventions is still absent

Preliminary results of an ongoing effort to synthesise existing evidence on efficiency also suggest cautiously that prehabilitation interventions are generally cost-effective (Rombey, Eckhardt and Quentin, 2020[20]). However, as has been recognised in prior systematic reviews of effectiveness of prehabilitation,[9] these preliminary results also indicate that formal and conclusive evidence is still limited given: only one formal cost-effectiveness analysis could be identified, there is much heterogeneity across interventions and evaluation methods in available primary studies, there are few RCTs with low risk of bias, and there is no study with a follow-up time exceeding 12 months.[10]

Equity

Prehab can improve outcomes for high-risk surgical patients, which is likely to reduce disparities in health outcomes among surgical patients, although no evidence is available

Although there are no formal evaluations of the effect of Prehab on equity, it can be assumed that the intervention can reduce disparities in health outcomes among surgical patients by targeting high-risk patients and improving outcomes in this patient sub-group. This can also have a positive effect on equity in terms of health outcomes across different socio-economic groups, because population-wide data on socio-economic and health disparities suggest that patients who are at high risk of post-operative

[9] See, for example, Luther et al. (2018[29]); Katsura et al. (2015[13]); Mans, Reeve and Elkins (2014[57]); and Hulzebos (2012[14]).

[10] Based on preliminary results of the systematic review presented at the 19th German Congress for Health Service Research (Rombey, Eckhardt and Quentin, 2020[58]) and personal communication with T. Rombey in June 2021.

complications, and poor health outcomes following surgery more generally, are disproportionately found in population groups that are underprivileged and have high health care needs.

As discussed above, risk factors for post-operative complications include multi-morbidity, being overweight, having poor functional status, smoking and alcohol abuse (Visser et al., 2015[4]). These risk factors tend to be more prevalent among people in underprivileged population groups, such as those with lower levels of education and lower incomes. Prior analyses by the OECD, for example, clearly show that, across OECD countries, overweight and obesity are more prevalent among people with lower levels of education and low incomes (OECD, 2019[21]; OECD, 2019[22]). Across all OECD countries, smoking is more prevalent among population groups with lower levels of education and, in nearly all OECD countries, heavy drinking is also more common among less-educated men.[11] Similarly, people in population groups with lower levels of education are more likely to have two or more chronic diseases,[12] many of which represent co-morbidities that increase the risk of post-operative complications, and are more likely to report poor selfassessed health and limitations in daily activities (OECD, 2019[22]).

It is less clear whether Prehab has a positive effect on equity when considering not only surgical patients but the general population more broadly. This is because only patients who are scheduled to undergo surgery are eligible for the intervention, which does not address potential inequities in access to surgery.

Evidence-base

Prehab has been evaluated in a randomised and an observational study so far

Prehab has been assessed in two main studies so far, a randomised controlled trial (RCT) and a casecontrol study:

- The randomised controlled trial was conducted between 2013 and 2016 at Hospital Clínic de Barcelona (HCB), Catalonia, enrolling 144 high-risk patients undergoing abdominal surgery, all of whom were included in an intention-to-treat analysis.[13] The protocol was published in the United States clinical trials register under record no. NCT02024776 [14] and results published in BarberanGarcia et al. (2018[9]).
- The case-control study was conducted between 2017 and 2019 at HCB, enrolling 327 high-risk patients undergoing digestive, cardiac, thoracic, gynaecologic or urologic surgery, comparing the intervention group of against a propensity score-matched control group. The protocol for implementation of the Prehab, and other community-based interventions, was registered under record number NCT03767387[15] and published in Baltaxe et al. (2019[23]). Preliminary results of the Prehab case-control study are available in Barberan-Garcia and Cano (2020[10]); full results have been submitted for publication (Risco et al.[11]).

[11] See OECD (2019[22]). For women, the pattern is less clear, with many countries reporting higher proportions of heavy drinkers among population groups with high levels of education.

[12] The occurrence of two or more chronic diseases in the same person is referred to as “multi-morbidity”.

[13] Only 110 patients of the 144 enrolled completed the study as planned per the study protocol. However, the ITT and per-protocol analyses yielded similar results.

[14] See https://clinicaltrials.gov/ct2/show/NCT02024776.

[15] See https://clinicaltrials.gov/ct2/show/NCT03767387.

The quality of evidence evaluating the effectiveness of Prehab is strong in many respects

Using the *Quality Assessment Tool for Quantitative Studies* from the Effective Public Health Practice Project, the quality of the evidence from the RCT can be rated as moderate to strong. A "moderate" rating was given in the domain of confounders because a comparison of baseline characteristics of patients revealed some differences between the intervention and control group. For instance, the proportion of male patients was lower in intervention group (68% vs. 80% in the control group), there were more patients in with American Society of Anesthesiologists (ASA) score III or IV in the intervention group (44 vs. 40 in the control group), and the types of surgical interventions, and associated level of surgical aggression, differed between the two groups (see Barberan-Garcia et al. (2018, p. 53[9]) for details). However, it is not clear whether these differences were statistically significant or were likely to bias results. Another "moderate" rating was given in the domain of blinding because patients cannot be blinded to group assignment with this type of intervention. However, outcome assessors were blinded and the informed consent processes were kept separate for the intervention and control groups in the trial so that both groups were unaware of the respective other (Barberan-Garcia et al., 2018[9]).

Evidence from the case-control study can be rated as moderate. The control group was matched to patients in the intervention group using a propensity score, based on variables age, sex, risk-score using ASA and Adjusted Morbidity Groups (GMA) scores, use of healthcare resources during the previous year, and type of surgery. Confounders appear to have been controlled for well through propensity score matching, however, it is unclear whether study drop-out may have introduced bias.

An overview of the quality assessment of evidence from both studies is in Table 1.1.

Table 1.1. Quality of evidence assessment

Assessment category	Question	Score for Barberan-Garcia et al. (2018)	Risco et al. ([11])
Selection bias	Are the individuals selected to participate in the study likely to be representative of the target population?	Very likely	Very likely
	What percentage of selected individuals agreed to participate?	81%	Can't tell
Selection bias score: Moderate			
Study design	Indicate the study design	RCT	Case-control study
	Was the study described as randomised?	Yes	No
	Was the method of randomisation described?	Yes	N.a.
	Was the method of randomisation appropriate?	Yes	N.a.
Study design score: Strong			
Confounders	Were there important differences between groups prior to the intervention?	Yes	No
	What percentage of potential confounders were controlled for?	Can't tell	Can't tell

Confounders score: Moderate			
Blinding	Was the outcome assessor aware of the intervention or exposure status of participants?	Yes	Yes
	Were the study participants aware of the research question or of the intervention or exposure status?	Yes[1]	Yes
Blinding score: Moderate			
Data collection methods	Were data collection tools shown to be valid?	Yes	Yes
	Were data collection tools shown to be reliable?	Yes	Yes
Data collection methods score: Strong			
Withdrawals and dropouts	Were withdrawals and dropouts reported in terms of numbers and/or reasons per group?	Yes	Yes
	Indicate the percentage of participants who completed the study?	60 - 79% [2]	34% [3]
Withdrawals and dropouts score: Strong			

Note: For Barberan-Garcia et al. (2018[9]) note that: 1) two separate informed consent forms were used so that patients in the intervention group were not aware of the existence of the control group and vice versa, however, patients cannot be blinded with respect to the intervention they receive; and 2) although only 110 of 144 patients completed the study per protocol, all 144 were included in an intention-to-treat (ITT) analysis. The ITT analysis produced similar results as the per-protocol analysis. 3) In the case-control study only 112 of 328 patients in the prehabilitation group performed >80% of the sessions and were considered completers.

Sources: Author based on rating methodology by Effective Public Health Practice Project (1998[24]) and Thomas et al. (2004[25]); RCT study information from Barberan-Garcia et al. (2018[9]) and at https://clinicaltrials.gov/ct2/show/NCT02024776; case-control study information from Risco et al. ([11]) and at https://clinicaltrials.gov/ct2/show/NCT03767387.

Evidence from other prehabilitation interventions is of varying quality

In addition, a broad base of studies has been accumulating over the past 10 years about the effectiveness of various types of prehabilitation interventions for abdominal and cardiothoracic surgery, which has been synthesised in systematic reviews (see section on “Effectiveness” above). These reviews concluded that there was much variability in the quality of evidence between studies but that most of the evidence is based on small studies with non-negligible risk of bias, which may imply that effects are overstated. The existing evidence base is also difficult to interpret and generalise because prior studies evaluated varying prehabilitation interventions in settings with different surgical protocols.

Given the nature of the prehabilitation interventions, RCTs generally encounter issues with respect to allocation concealment and blinding of study subjects, healthcare professionals and/or outcome assessors. Beyond this inherent problem, reviews that included RCTs only and applied other restrictive

inclusion criteria, resulting in inclusion of no more than five to 16 original studies,[16] found evidence to be of low to moderate quality, with other issues related to selective reporting of results, the failure to use intention-totreat (ITT) analysis, and the lack of methodological information to fully assess all potential sources of bias. Broader reviews that also included non-randomised studies[17] generally found many of the same issues as with evidence from RCTs. While some of the latter reviews concluded that evidence from non-randomised studies was of fair to good quality, where enough information was available for a formal assessment, information to assess quality was also lacking for a number of non-randomised studies. A review by Milder (2018[18]) of prehabilitation for frail patients undergoing any kind of surgery, on the other hand, concluded that evidence was of low quality.

Extent of coverage

Prehab still has a limited coverage of all high-risk surgery patients, but it is being scaled locally and internationally

Following the initial trial of Prehab at HCB in 144 patients, a permanent Prehab unit was established at Hospital Clínic of Barcelona (HCB). Currently, capacity of the Prehab unit at HCB is at 200 patients per year, while it is estimated that some 900 patients per year are suitable candidates for the intervention. Participation rates, i.e. patients participating vs. patients to whom service is offered, is approximately 85%. However, a marked difference in patient adherence was observed between the RCT (Barberan-Garcia et al., 2018[9]) and the case – control study (Risco et al.[11]) indicating a need for improving various aspects of service delivery and improving adherence.

The sustainability of the service at HCB is being evaluated as part of the deployment and evaluation of a set of population-based interventions to improve integration of care and promote PA in Catalonia (Baltaxe et al., 2019[23]; Barberan-Garcia et al., 2018[26]). In addition to scaling Prehab at HCB in Catalonia, the local study team is already collaborating with hospitals in Germany (Cologne, Heildelberg and Mannheim), France (Grenoble) and Poland (Gdansk) to transfer the intervention.

Policy options to enhance performance

Enhancing effectiveness

Prehab is already aligned with current guidelines for prehabilitation interventions

Prehab has already proven its efficacy in the RCT at HCB and evidence from systematic reviews also strongly suggests that various types of prehabilitation interventions can be effective. Effectiveness hinges upon targeting the patients that can benefit most, designing an effective prehabilitation protocol, with appropriate intensity and duration but which is also sufficiently adapted to the needs of various patient groups as well as individually, and ensuring patient adherence throughout delivery of the intervention.

A comparison of the main features of the Prehab intervention against general recommendations made by recently published guidelines and systematic reviews reveals that virtually all of these recommendations were already applied in the design of Prehab. A guideline for prehabilitation for patients undergoing any

[16] Including reviews by Heger et al. (2020[33]) and Hughes et al. (2019[15]), who reviewed evidence of prehabilitation for patients undergoing major abdominal surgery, and Mans et al. (2014[57]) (cardiothoracic or abdominal surgery).

[17] Including reviews by Bruns et al. (2016[17]) of evidence for colorectal surgery patients; Hijazi, Gondal and Aziz et al. (2017[30]) (abdominal cancer patients); a broad review by Kamarajah et al. (2020[27]), including 61 randomised and non-randomised studies of effectiveness of prehabilitation for patients undergoing major abdominal or cardiothoracic surgery; and Luther et al. (2018[29]) (major abdominal surgery).

type of major surgery is provided by Durrand, Singh and Danjoux (2019[6]). Tew et al. (2018[7]) previously published a guideline for patients awaiting major non-cardiac surgery. In addition, various systematic reviews discuss considerations in the design and delivery of prehabilitation interventions and provide recommendations. The table below summarises the main recommendations and compares them against the features of Prehab.

Table 1.2. Features of Prehab compared to general recommendations for prehabilitation interventions

Based on recently published guidelines and systematic reviews

Recommendation	Sources	Applied in Prehab	Further notes
Screen all major surgery patients for risk factors and prehabilitation need. For at-risk patients, assess physical and psychological status, including comorbidities, lifestyle-related risk factors and potential counter-indications, using well-established measures	Kamarajah (2020[27]); Durand, Singh & Danjou (2019[6]); Tew et al. (2018[7])	Yes	Surgical risk is routinely evaluated in all patients undergoing surgery at HCB during the preoperative visit carried out by an anaesthesiologist. Inclusion criteria are described above. Exclusion criteria are: nonelective surgery; and, no possibility or willingness to attend the appointments. Risk factors depend on the type and invasiveness of surgery but commonly include advanced age, frailty, obesity and underweight, smoking and harmful alcohol use.
Prioritise patients at increased risk of surgical complications or other poor surgical outcomes; take a tiered approach with lower intensity support for patients with lower risk.	Durand, Singh & Danjou (2019[6]); Tew et al. (2018[7])	Yes	Prehab is only provided to high-risk patients.
Adapt prehabilitation protocol and intensity to individual patient characteristics and risk; adapt exercise intensity to achieve 50-70% of heart rate reserve.	Kamarajah (2020[27]); Durand, Singh & Danjou (2019[6])	Yes	Physical exercise can be a combination of aerobic, resistance training and inspiratory muscle training (IMT).
Conduct a motivational / goal setting interview with each patient enrolled.	Kamarajah (2020[27])	Yes	
Provide multi-modal physical exercise (e.g. including aerobic exercise, IMT and resistance training). Combine physical exercise with: • Psychological support; • Nutrition advice and/or supplementation; and, • Support for smoking cessation and reduction of alcohol intake.	Kamarajah (2020[27]); Durand, Singh & Danjou (2019[6]); Thomas et al. (2019[28]); Tew et al. (2018[7]); Luther et al. (2018[29]); Hijazi, Gondal and Aziz (2017[30]); Moran et al. (2016[16]); Gillis and Carli (2015[31])	(Yes)	The intervention for major abdominal surgery trialled in the RCT did not include psychological support, while the intervention for five types of major surgery provided subsequently, and studied in the case-control study, included a weekly mindfulness group session. More specific guidelines are available for nutrition and psychological support, depending on the patient group and individual patient characteristics (see, for example, Kamarajah (2020[27]); Scheede-Bergdahl, Minnella and Carli (2019[3]); Gillis and Carli (2015[31])).

Combine home-based and unsupervised training with supervised training sessions in the hospital- or other healthcare provider-settings.	Piraux, Caty and Reychler (2018[32]); Katsura et al. (2015[13])	(Yes)	One variation of the Prehab intervention only provided unsupervised PA promotion plan but no supervised exercise training.
Provide intervention for at least four weeks prior to surgery, with exercise sessions two to three times per week.	Durand, Singh & Danjou (2019[6]); Kamarajah (2020[27]); Tew et al. (2018[7])	Yes	While most components require several weeks to result in desired effects, smoking cessation can also be beneficial if it occurs shortly before surgery. Exercise frequency varied from one to three weekly sessions in the Prehab intervention.
Monitor patient adherence and goal achievement to reinforce personal objectives, adapt goals as necessary throughout the intervention.	Kamarajah (2020[27]); Durand, Singh & Danjou (2019[6]); Tew et al. (2018[7])	Yes	

Note: Brackets indicate that the recommendation is applied partially, as described in the notes column.
Sources: Guidelines and systematic reviews cited in the table; Barberan-Garcia et al. (2018[9]); Barberan-Garcia and Cano (2020[10]).

Modulating exercise intensity and duration of the intervention as well as maximising patient adherence could be ways to increase effectiveness further

One way of ensuring intervention effectiveness is to use a modular prehabilitation protocol and adapt the intervention to individual patient characteristics. Prehab was tailored to each patient, based on health conditions, social circumstances and logistical access barriers, during the motivational interview (Barberan-Garcia et al., 2018[9]). Modularity of the intervention was an explicit objective in the subsequent establishment of the Prehab unit at HCB (Risco et al.[11]). Although the optimal intensity of exercise sessions is not entirely clear and may well be dependent on individual patient characteristics, it is notable that the frequency of supervised training sessions in the Prehab RCT was relatively low (on average two per week, range one to three) compared to other prehabilitation interventions (Heger et al., 2020[33]).

One avenue for enhancing effectiveness may therefore be to increase the frequency of exercise sessions to achieve even greater improvements in aerobic capacity, in particular for patients who attended fewer than two sessions per week. A minimum of two weekly sessions were delivered in the subsequent Prehab intervention studied in the case-control study (Barberan-Garcia and Cano, 2020[10]). Similarly, effectiveness could potentially be further enhanced by increasing the duration of the intervention, although this requires sufficient time to be available between enrolling patients and the scheduled surgical intervention and is therefore dependent on local clinical workflows. This does imply, however, that potential patients should be identified as early as possible (ibid.). Also, it should be noted that Prehab already met the recommended minimum duration of four weeks (see Table 1.2) and had a mean duration in the RCT of six weeks.

Furthermore, systematic reviews suggest that patient adherence is higher, making interventions more effective, when combining supervised with home-based and unsupervised training (Durrand, Singh and Danjoux, 2019[6]; Piraux, Caty and Reychler, 2018[32]; Katsura et al., 2015[13]). Recent surveys of prehabilitation patients (Waterland et al., 2020[34]; Ferreira et al., 2018[35]) suggest that patients may in fact prefer home-based over supervised exercise but also lend support to the approach of combining supervised with unsupervised exercise. Patients may also prefer group fitness sessions to individual

supervised sessions because the former provide social support (Ferreira et al., 2018[35]). Costs and issues related to transportation were identified as barriers to participation and adherence (Waterland et al., 2020[34]; Ferreira et al., 2018[35]). Despite the somewhat paradoxical results of the Prehab case-control study (Barberan-Garcia and Cano, 2020[10]), it is questionable whether a protocol that only provides an unsupervised PA promotion plan but no supervised exercise training is optimal.

It is clear, however, that patient adherence to the prehabilitation protocol is crucial for the effectiveness of the intervention. The case-control study of Prehab indicated that less than 40% of patients attended more than 80% of the sessions and study results showed a strong relationship between level of adherence and outcomes (Risco et al.[11]). Adherence has also been found to be highly variable in other prehabilitation interventions (see, e.g., Bruns et al. (2016[17])). Guidelines and systematic reviews recommend monitoring patient adherence using self-reported and, if possible, 'objective' measures, and providing feedback regularly and adapting goals to increase effectiveness. Such monitoring and feedback loops help maintain personal motivation, in particular among non-adherent patients (Thomas et al., 2019[28]; Luther et al., 2018[29]; Hijazi, Gondal and Aziz, 2017[30]). In the Prehab intervention, physiotherapists registered and reviewed during the supervised exercise sessions daily step counts and the intensity of non-supervised walks and/or home-based exercises (Risco et al.[11]). The aim of such monitoring was to assess and update patient's PA objective. Technological monitoring support has also been provided during the intervention and is currently still evolving as described in Barberan-Garcia et al. (2021[36]). In the intervention that did not include supervised exercise, a weekly visit at the prehabilitation unit was scheduled for follow-up on and refinement of unsupervised PA objectives (Barberan-Garcia and Cano, 2020[10]).

Enhancing efficiency

Efficiency is a measure of effectiveness in relation to inputs used. Therefore, interventions that increase effectiveness without significant increases in costs, or reduce costs while keeping effectiveness at least constant, have a positive effect on efficiency.

Given the relatively modest direct cost per patient of delivering the Prehab intervention (see "Efficiency") and the fact that inpatient hospital stays tend to be expensive, even small decreases in readmission rates, re-intervention rates as a result of post-operative complications, or hospital LoS or could imply overall cost savings. Even though the intervention may already be cost-effective, efficiency could therefore be further enhanced by increasing effectiveness of the intervention, not only because it would lead to improved health outcomes but also because it could reduce hospital-related costs.

Enhancing equity

As discussed above, it is difficult to assess the effect of Prehab on equity beyond speculation based on characteristic of patients enrolled in the intervention, because no data on socio-economic characteristics of surgery and Prehab patients are reported in available studies. A first step to enhancing equity would therefore be to elicit and report equity-relevant characteristics of Prehab patients to assess whether clinical risk factors used to identify high-risk patients to be enrolled into Prehab are correlated with socio-economic factors deemed relevant for equity and whether Prehab effectively reduces disparities in surgical outcomes across relevant patient sub-groups. Such information could be used to target patients not only based on clinical risk factors but also based on socio-economic status or other relevant characteristics to achieve an explicit objective of reducing health inequalities.

Even if such information were available, it would only allow for an assessment of the effect on equity among surgery patients. There may, however, be underlying disparities in access to surgery, which would not be apparent when studying surgery patients only. An assessment of the effects of an

intervention in terms of equity at the population-level would require, in addition to the above, assessing the need for and access to distinct elective surgery procedures at the population-level and in various population sub-groups deemed relevant for equity, such as groups with varying levels of income and education, as well as ethnicity.

Enhancing the evidence-base

Although, as described above, evidence of the efficacy and effectiveness of prehabilitation has been accumulating in recent years and has been synthesised in systematic reviews and guidelines, a number of uncertainties remain. Also, there is only very limited formal evidence of cost-effectiveness thus far.

> *Larger-scale studies and more granular data are needed to establish the most appropriate prehabilitation protocols for various patient groups and integrate them into clinical practice*

The optimal prehabilitation protocol for various at-risk patient groups is not yet fully established. All systematic reviews cited in the section on "Effectiveness" cautioned that existing evidence is difficult to interpret and generalise because primary studies evaluated varying interventions and may have also been conducted in settings with different surgical protocols. The evidence base for prehabilitation could therefore be enhanced by further standardisation of the intervention and its distinct modules and by reporting more detailed peri-operative patient data and information about the surgical protocols followed. This gap has already been recognised by the team of researchers who evaluated Prehab at HCB (Barberan-Garcia et al., 2019[12]). Effectiveness should be confirmed by larger-scale studies that evaluate different combinations of intervention modules in different patient sub-groups in both experimental and 'real-world' settings (West, Jack and Grocott, 2021[37]). This would help establish a standardised and modular intervention that can be tailored to different patient groups and individual patients (Barberan-Garcia et al., 2019[12]). More detailed peri-operative studies would also facilitate integration of the intervention into existing care delivery pathways (Luther et al., 2018[29]). Although evidence generally supports the intuitively appealing approach of targeting high-risk patients who can be assumed to benefit most from prehabilitation, robust evidence of effectiveness in a number of high-risk patients groups is still sparse; these include, for example, patients with frailty or sarcopenia (Kamarajah et al., 2020[27]; Thomas et al., 2019[28]; Milder, Pillinger and Kam, 2018[18]).

> *Greater standardisation of outcome measures would facilitate pooling of results from individual studies and interpretation of the overall evidence base*

There is also a need for greater standardisation of outcome measures to facilitate pooling of results from individual studies and interpretation of the overall evidence base. Systematic reviews cited above also indicated that there was significant variability across primary studies in the definitions of study endpoints, and a number of reviews did not pool results from primary studies in meta-analyses.[18] The consistent use of widely accepted scales to measure outcomes of interest would facilitate interpretation of the evidence. Suggested measures include, for example, the Clavien-Dindo scale to grade post-surgical complications, the Postoperative Morbidity Survey and the Comprehensive Complications Index for post-surgical morbidity more broadly, the 6-minute walking test (6MWT) for the assessment of functional capacity, and the "Short Form 36" health survey (SF-36) for quality of life (Hijazi, Gondal and Aziz, 2017[30]; Bruns et al., 2016[17]). Finally, studies also need to evaluate effectiveness in terms of longer-term outcomes, including overall mortality (Hijazi, Gondal and Aziz, 2017[30]).

[18] See Note 8.

Formal evidence of cost-effectiveness is still lacking

Few studies have formally evaluated cost-effectiveness so far.[19] Although the cost-consequence analysis by Barbaran-Garcia et al. (2019[12]) suggest that Prehab may be cost-effective, or even cost-saving, it did not consider out-of-hospital costs and did not formally model cost-effectiveness. More definitive health economic analyses with a longer time horizon are therefore needed, considering longer-term outcomes including survival and quality of life, as well as post-discharge costs of medical and non-medical services (Grocott and Ludbrook, 2019[19]).

Enhancing extent of coverage

Coverage of Prehab, and similar variations of prehabilitation interventions for surgery patients, could be enhanced by increasing capacity for enrolling high-risk patients into the intervention within the patient populations for which Prehab has already been implemented and studied; providing 'lighter' interventions to patients with lower risk; and expanding the patient populations to other types of surgery. However, it should be noted that the latter two avenues for enhancing coverage would require additional research to confirm which types of prehabilitation protocols are effective in additional patient populations. This would have to be accompanied by assessments of cost-effectiveness and, ultimately, sufficient financial resources allocated through adequate reimbursement modalities to support routine adoption of prehabilitation interventions with broad coverage.

Increasing capacity for enrolment of high-risk patients is one way of enhancing coverage

A constraint to the coverage of the Prehab intervention implemented at HCB is institutional capacity, including physical and human resources, to screen surgery patients, enrol high-risk patients and deliver the intervention. As described above, the Prehab Unit at HCB has capacity for only about one-sixth of surgery patients currently considered suitable for the intervention. Allocating additional resources to building capacity could therefore be one avenue for enhancing coverage within the existing patient population for which Prehab is suitable. Barberan-Garcia and Cano (2020[10]) report that significant capacity is needed to accommodate the complexity of the intervention and its integration in existing presurgical workflows. This requires coordinating clinical protocols; providing adequate information to patients; training for staff; redefining tasks and roles of staff; community-based logistics and coordination between community and hospital settings; and digital support for patients in the intervention (ibid.).

Lighter prehabilitation interventions could expand coverage to patients with lower risk

Coverage could be further broadened by expanding the eligible patient population beyond high-risk patients and providing 'lighter' interventions to patients with lower risk. Prehab at HCB was initially only provided to patients at high risk of surgical complications, defined by: age >70 years and/or American Society of Anesthesiologists score III or IV, and Duke Activity Status Index score ≤ 46 (Barberan-Garcia et al., 2018[9]; Barberan-Garcia and Cano, 2020[10]). The guideline by Durrand, Singh and Danjoux (2019[6]) for prehabilitation in patients undergoing major surgery suggests a tiered and risk-based approach, as is commonly suggested for a wide range of interventions in prevention and patient management (Figure 1.3). This includes 'lighter' prehabilitation for patients of lower risk, including only general advice about PA and nutrition and unsupervised training sessions. Such an approach would ultimately cover all surgery patients. Along these lines, as of 2020, an ICT-supported and community-based prehabilitation service is being developed in Catalonia.

Prehab could also be expanded to additional types of surgery

Finally, patients undergoing other types of surgery could also be considered as possible target groups. Prehab has so far been implemented and studied at HCB for patients undergoing abdominal, digestive,

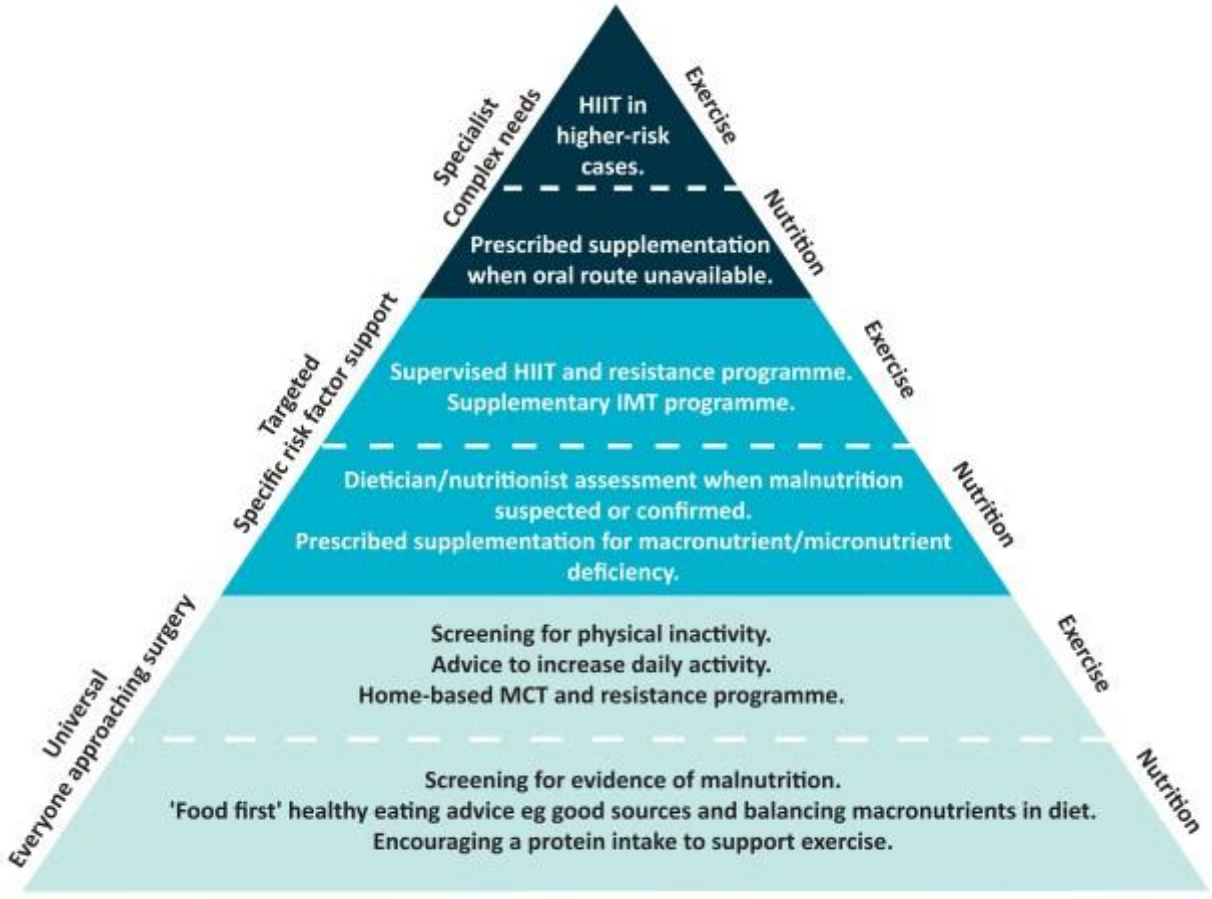
[19] See Note 10.

cardiac, thoracic, gynaecologic or urologic surgery. However, prehabilitation could also be a suitable intervention for patients undergoing other types of surgery, including, for example, joint replacements and peripheral artery surgery, particularly in frail patients (Shinall et al., 2020[38]). It should be noted, however, that the existing literature evaluating the effectiveness of prehabilitation focuses on surgery for cancer and other diseases in the anatomical areas listed above; evidence of the effectiveness of prehabilitation in orthopaedic and other types of surgery patients is less compelling. While prior systematic reviews of prehabilitation in orthopaedic surgery provided conflicting results, results of a review compliant with guidelines by the Cochrane Collaboration have not been published yet (see Punnoose et al. (2019[39])). A recent Cochrane review of exercise-based prehabilitation in patients undergoing lower limb surgery for peripheral arterial disease found no RCTs that met the inclusion criteria of the review (Palmer et al., 2020[40]).

Any expansion of coverage to additional patient populations, however, requires adaptation of the prehabilitation protocol to the modifiable risk factors and other needs present in each group. While the principle of prehabilitation may well be applicable to patients at various levels of risk and undergoing various types of surgery, the current literature is heavily focused on PA- and exercise-based prehabilitation with a view to improving aerobic capacity, inspiratory muscle capacity and broader physical fitness. As such, these prehabilitation intervention appear particularly promising for surgery associated with high pulmonary morbidity (Hughes et al., 2019[15]). Given the gaps in the evidence base even for these types of surgery, discussed above, expanding prehabilitation to additional patient populations may not be straightforward and may require significant additional research.

Figure 1.3. Proposed tiered approach to prehabilitation

Nutritional support and exercise used as examples



Note: HIT = High- intensity interval training; IMT = inspiratory muscle training; MCT = moderate continuous training. Source: Durrand, Singh and Danjoux (2019[6]).

Transferability

This section explores the transferability of Prehab and is broken into three components: 1) an examination of previous transfers and parallel implementations of prehabilitation services in other countries; 2) a high-level transferability assessment using publically available data; and 3) additional considerations for policymakers interested in transferring Prehab.

Lessons from previous transfers

Prehab is in the process of being transferred to Germany, France and Poland and the implementation team at Hospital Clínic of Barcelona (HCB) in Catalonia is part of a network with other centres in Canada, the Netherlands and the United Kingdom that are also scaling prehabilitation. Experience from these parallel implementations and transfers of prehabilitation services suggest that prehabilitation interventions can be transferred to other settings and scaled for various types of surgery patients. Modularity of the intervention and personalisation of services are key attributes that make the intervention transferable and allow for better adaptation to the specificities of the context to which Prehab is being transferred. In addition, the existing experience indicates that transferability can be facilitated by: 1) following a structured implementation methodology in the target setting, in line with the suggestions made in the OECD Guidebook on Best Practices in Public Health, and 2) identifying priority areas for action to achieve synergies with existing surgical services in the target setting.

1. A structured implementation methodology should include an assessment of characteristics and maturity of the target setting, including an identification of barriers and facilitators; formulation of the implementation plan; and the adoption of key performance indicators (KPIs) for continuous monitoring and quality assurance in implementation of the intervention. The methods suggested in the OECD Guidebook can support and facilitate these steps. Based on the implementation of Prehab in Catalonia, at least the following KPIs should be monitored during implementation i) coverage of the service; ii) drop-out rates; iii) adherence rates; iv) hospital LoS; v) 30-day hospital readmissions; and, vi) 30-day surgical reinterventions (see Barberan-Garcia and Cano (2020[10])).

2. Five priority areas for action have been identified in prior implementations of prehabilitation interventions to achieve synergies with existing surgical services: i) increasing efficiency through enhancement of behaviour change interventions, facilitating accessibility of the service for patients, and alignment with surgical agendas; ii) improving digital support for the service as described in Barberan-Garcia et al. (2021[36]); iii) building capacity and simplifying service delivery by strengthening the role of case managers and broadening the roles of physiotherapists and health coachers; iv) enhancing risk assessment and program prescription; and v) developing three types of service profiles for testing (see Table 1.3).

Table 1.3. Proposal of a three-layer service design

Risk	Risk description	Service	Service description
Low	Low surgical aggression, low complexity of associated NCDs (comorbidities)	I	Patient's education and remotely supervised behavioural change
Medium	Major, but not highly aggressive surgeries, in patients with low/medium risk due to age, sedentary lifestyle and/or comorbidities	II	Level I + promotion of daily physical activity and communitybased, partly remotely supervised, physical training
High	Major surgical procedures, including highly aggressive surgeries, in patients showing high risk due to medical/lifestyle factors	III	Level II + initial period with hospital-based face-to-face supervised high-intensity exercise training followed by communitybased physical training

Source: (Baltaxe et al.[8]).

Extensive experience with the implementation of prehabilitation interventions has been made, for example, in the Canadian region of Quebec. A group of clinicians in Montreal pioneered the research and application of prehabilitation in different surgical specialties, providing evidence of the benefits of prehabilitation in terms of increasing perioperative functional capacity (Minnella et al., 2021[41]; Minnella et al., 2018[42]). Exercise-only prehabilitation was implemented in Montreal as early as 2010 for colorectal cancer patients (Carli et al., 2010[43]; Mayo et al., 2011[44]). Further trials including nutritional balance and psychosocial support were subsequently performed showing increased postoperative functional capacity compared to controls or intensive rehabilitation after surgery (Li et al., 2012[45]; Gillis et al., 2014[46]). The benefits of prehabilitation in terms of perioperative functional capacity as well as disease-free survival in colorectal cancer patients were corroborated subsequently (Minnella et al., 2017[47]; Trépanier et al., 2019[48]).

Transferability assessment

Methodological framework

A number of indicators to assess the transferability of Prehab using publicly available data were identified (see Table 1.4. Indicators to assess the transferability of Prehab). Indicators were drawn from international databases and surveys to maximise coverage across OECD Countries and non-OECD EU Member States. Please note that the assessment is intentionally high-level given the availability of public data covering OECD Countries and non-OECD EU Member States. This transferability assessment considers indicators in the sector-specific, political and economic contexts based on data in the public domain.

Population context and need for the intervention

The assessment assumes that the population context, and need for Prehab, is sufficiently similar between EU Member States and OECD Countries that it is not required to compare indicators of population context. The diseases treated with surgery are prevalent in all countries, as are risk factors associated with poor surgical outcomes, such as advanced age, multi-morbidity, overweight and obesity, smoking and harmful alcohol use. Although international studies have found some variation in the incidence of surgical complications between countries (Knight et al., 2021[49]; Pearse et al., 2016[50]), the incidence of complications is high enough everywhere for Prehab to be potentially beneficial.

Population, sector-specific, political and economic context

Indicators to assess the transferability of Prehab in the sector-specific, political and economic contexts, and the rationale for considering these, are listed in the table below.

Table 1.4. Indicators to assess the transferability of Prehab

Indicator	Reasoning	Interpretation
Population context		
Share of the population with access to recreational green space within a 10min walking distance	Could facilitate adherence to PA programme.	↑ value = 'more transferable'
Sector context (PA in health care settings)		
Inclusion of PA and health in curriculum of health professionals	Could indicate that health professionals are knowledgably on the importance of health eating and exercise and feel comfortable providing such advice.	↑ value= 'more transferable'
Programme or scheme to promote counselling on PA by health professionals	Could indicate that health professionals are likely to support a PA intervention like Prehab.	'Yes' = more transferable
Number of physiotherapists per capita	Prehab requires physiotherapists to plan, deliver and monitor the PA plan. A higher density of physiotherapists is an indicator of greater availability of human resources.	↑ value = 'more transferable'
Political context		
Operational strategy/ action plan/ policy to reduce unhealthy eating	Prehab comprises diet advice and may be more successful in countries who prioritise healthy eating.	'Yes' = more transferable
Operational strategy/action plan/policy to reduce physical inactivity	Prehab may be more successful in countries who prioritise PA in the general population.	'Yes' = more transferable
Specific national scheme to promote PA among older adults	Prehab may be more successful in countries who prioritise PA in the elderly population at increased risk of poor surgical outcomes.	'Yes' = more transferable
Economic context		
Spending on secondary care as % of current health expenditure	Prehab is embedded in secondary care and requires hospital resources.	↑ value = 'more transferable'

Source: Eurostat (2021[51]); Poelman (2018[52]); OECD (2021[53]); WHO (2019[54]); WHO Europe (2018[55])

Results

Findings from the data are in Table 1.5 and show that:

- The sector-specific context is variable across OECD countries and EU member states. Only three countries (Belgium, Germany and Sweden) score at least as high as Spain across all four indicators. While in more than two-thirds of countries for which such data are available, the share of the population with access to recreational green space within a 10 minutes' walking distance is at least as high as in Spain (93%), few countries include training about PA and health in the curriculum of health professionals and have implemented a scheme to promote counselling on PA.

The number of physiotherapists per 1,000 population varies widely across countries, from 0.07 in Turkey to 2.51 in Norway; the number is at least as high as in Spain (1.21 per 1,000 population) in 11 of 37 countries for which these data are available.[20]

- Prehab may fit reasonably well into the general prevention-related political contexts of target countries in the OECD and the EU. Survey data suggest that only two countries (Cyprus and Sweden) have neither implemented a strategy to reduce unhealthy diet related to NCDs nor a strategy to reduce physical inactivity; two countries (Greece and New Zealand) report the existence of a strategy related to physical inactivity only among the two. However, promotion of PA among older adults specifically, who are at increased risk of poor surgical outcomes, is less common; 12 of 32 countries for which such survey data are available report that a national scheme to promote PA among older adults has been implemented.

- Not all health care systems of OECD countries and EU member states devote as high a share of current health expenditure to secondary care Spain. Specifically, the share allocated to secondary care is at least as large as in Spain (26%) in only about half of countries (17 of 33 countries for which data are available).

[20] Subject to some limitations to comparability between countries. See OECD Health Statistics 2021: Definitions, Sources and Methods, Physiotherapists (ISCO-08 code: 2264) at http://stats.oecd.org/wbos/fileview2.aspx?IDFile=80130ebd-5f8d-482f-9613-2891b0fc0fcf for details.

Table 1.5. Transferability assessment of Prehab by country (OECD Countries and non-OECD EU Member States)

Country	PA and health in curriculum of professionals	Promotion of counselling on PA by professionals	Practising physiotherapists per capita	Access to recreational green space	Strategy to reduce unhealthy eating	Strategy to reduce physical inactivity	Scheme to promote PA among older adults	Secondary care expenditure % CHE
Spain	**Not implemented**	**Implemented**	**1.21**	**93.3%**	**Yes**	**Yes**	**Implemented**	**25.5%**
Australia			1.07		**Yes**	Yes		30.9%
Austria	Implemented	Implemented	0.45	98.4%	**Yes**	Yes	Implemented	32.2%
Belgium	Implemented	Implemented	2.04	94.9%	**Yes**	Yes	Implemented	27.7%
Bulgaria	Foreseen	Foreseen	0.24		**Yes**	Yes	Foreseen	
Canada			0.65		**Yes**	Yes		16.1%
Chile			1.73		**Yes**	Yes		
Colombia			0.67		**Yes**	Yes		11.3%
Costa Rica					**Yes**	Yes		
Croatia	Not implemented	Implemented	0.83		**Yes**	Yes	Not implemented	20.4%
Cyprus	Not implemented	Not implemented	1.17		**Yes**	No	Not implemented	
Czech Republic	Implemented	Foreseen	0.87	97.7%	**Yes**	Yes	Implemented	24.0%
Denmark	Implemented	Foreseen	1.72	89.2%	**Yes**	Yes	Not implemented	24.9%
Estonia	Implemented	Foreseen	0.41	97.2%	**Yes**	Yes	Implemented	21.8%
Finland	Implemented	Implemented		99.9%	**Yes**	Yes	Implemented	22.2%
France	Implemented	Implemented	1.30	93.0%	**Yes**	Yes	Not implemented	24.7%
Germany	Implemented	Implemented	2.33	95.9%	**Yes**	Yes	Implemented	26.0%
Greece	Not implemented		0.83	93.9%	**Yes**	Yes		42.1%
Hungary	Implemented	Implemented	0.57	91.5%	**Yes**	Yes	Implemented	27.4%
Iceland			1.79	61.3%	**Yes**	Yes		28.3%
Ireland	Foreseen	Foreseen	1.03	94.5%	**Yes**	Yes	Implemented	25.2%
Israel			0.77		**Yes**	Yes		26.5%
Italy	Not implemented	Not implemented	1.10	88.1%	**Yes**	Yes	Not implemented	27.0%

Country	PA and health in curriculum of professionals	Promotion of counselling on PA by professionals	Practising physiotherapists per capita	Access to recreational green space	Strategy to reduce unhealthy eating	Strategy to reduce physical inactivity	Scheme to promote PA among older adults	Secondary care expenditure % CHE
Japan					Yes	Yes		27.1%
Latvia	Implemented	Implemented	0.45	95.2%	Yes	Yes	Foreseen	21.0%
Lithuania	Implemented	Foreseen	1.34	94.8%	Yes	Yes	Not implemented	26.8%
Luxembourg	Not implemented	Not implemented	2.01	98.7%	Yes	Yes	Implemented	24.8%
Malta	Implemented	Foreseen	1.10		Yes	Yes	Not implemented	
Mexico					Yes	Yes		29.5%
Netherlands	Implemented	Not implemented	1.90	97.0%	Yes	Yes	Not implemented	18.8%
New Zealand			1.15		No	Yes		
Norway			2.51	95.4%	Yes	Yes		25.6%
Poland	Implemented	Not implemented	0.70	92.6%	Yes	Yes	Implemented	34.5%
Portugal	Not implemented	Not implemented	0.14	83.3%	Yes	Yes	Not implemented	17.4%
Republic of Korea			0.80		Yes	Yes		
Romania	Implemented	Foreseen	0.11		Yes	Yes	Not implemented	
Slovak Republic	Not implemented	Implemented	0.37	95.6%	Yes	Yes	Not implemented	30.1%
Slovenia	Implemented	Implemented	0.72	93.5%	Yes	Yes	Implemented	26.8%
Sweden	Not implemented	Implemented	1.35	99.1%	No	No	Not implemented	20.0%
Switzerland				97.3%	Yes	Yes		25.8%
Turkey			0.07		Yes	Yes		
United Kingdom	Implemented	Implemented	0.47	91.4%	Yes	Yes	Implemented	22.5%
United States			0.71		Yes	Yes		16.2%

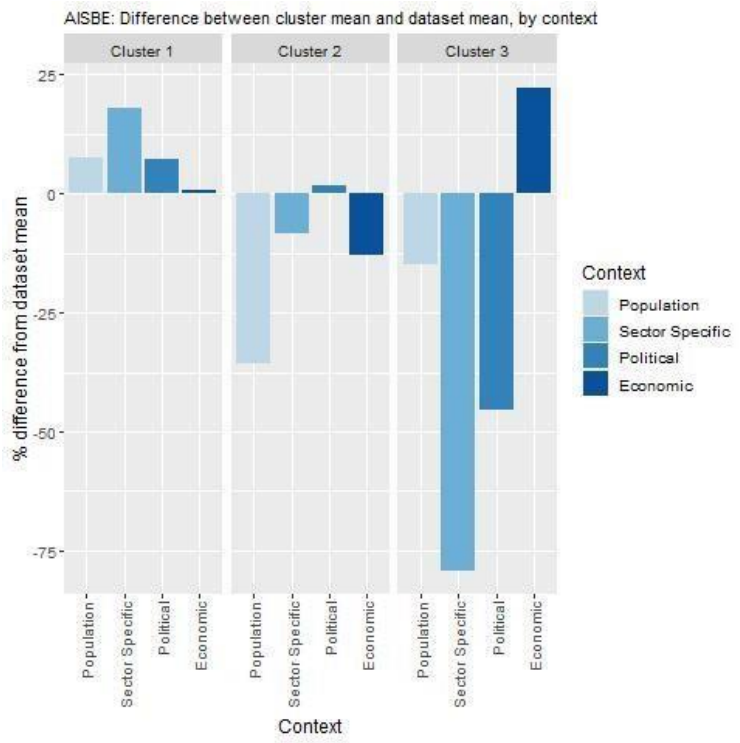
Note: The number of physiotherapists per 1,000 population is subject to some limitations to comparability between countries. See OECD Health Statistics 2021: Definitions, Sources and Methods, Physiotherapists (ISCO-08 code: 2264) at http://stats.oecd.org/wbos/fileview2.aspx?IDFile=80130ebd-5f8d-482f-9613-2891b0fc0fcf for details. Blank cells indicate data is missing. Source: Eurostat (2021[51]); Poelman (2018[52]); OECD (2021[53]); WHO (2019[54]); WHO Europe (2018[55])

To help consolidate findings from the transferability assessment above, countries have been clustered into one of three groups, based on indicators reported in Table 1.4. Countries in clusters with more positive values have the greatest transfer potential. For further details on the methodological approach used, please refer to the 'Best Practice Project: case study guide'.

Key findings from each of the clusters are below with further details in Figure 1.4 and Table 1.6:

- Countries in cluster one have population, sector-specific, political and economic arrangements in place that support that transfer or AISBE. Therefore, these countries are considered good transfer candidates. Cluster one includes the host country of AISBE, Spain.
- Countries in cluster two also have political arrangements in place to support AISBE, however, further research into the intervention's transferability are needed. For example, to assess whether health professionals feel have the appropriate skills and are comfortable providing physical activity advice to patients.
- Countries in cluster three dedicate a relatively high proportion of healthcare spending to secondary care, indicating there could be sufficient funds for AISBE. However, similar to countries in cluster two, further research into the intervention's transferability potential is necessary, particularly in regard to political support and the health profession's readiness.

Figure 1.4. Transferability assessment using clustering



Note: Bar charts show percentage difference between cluster mean and dataset mean, for each indicator.

Source: Eurostat (2021[51]); Poelman (2018[52]); OECD (2021[53]); WHO (2019[54]); WHO Europe (2018[55])

Table 1.6. Countries by cluster

Cluster 1	Cluster 2	Cluster 3
Austria	Australia	Cyprus
Belgium	Canada	Greece
Bulgaria	Colombia	Italy
Croatia	Denmark	Portugal
Czech Republic	Iceland	
Estonia	Lithuania	
Finland	Malta	
France	Romania	
Germany	United States	
Hungary		
Ireland		
Israel		
Latvia		
Luxembourg		
Netherlands		
Norway		
Poland		
Slovak Republic		
Slovenia		
Spain		
Sweden		
Switzerland		
United Kingdom		

Note: Due to high levels of missing data, Chile, Costa Rica, Japan, Mexico, New Zealand, the Republic of Korea and Turkey are not included in the analysis.

New indicators of transferability

The transferability assessment based on publicly available indicators needs to be interpreted with caution because reliable data are not publicly available at the level of detail that is required for a complete assessment of transferability and because there are gaps in available data for some countries. Additional primary indicators to assess transferability are summarised in Box 1.2. While it can be assumed that there is comparable need for prehabilitation in the populations of most in countries, it is important to assess in more detail which types of surgery patients and population groups may suffer from particularly poor surgical outcomes and how access barriers. Also, while in most countries reducing unhealthy diets and physical inactivity, both risk factors for poor surgical outcomes, are priorities for public health policy, more detailed analysis is required to identify compatible and synergistic interventions as well as competing priorities. Finally, significant human and institutional capacity, including digital support, are required to implement prehabilitation successfully within existing surgical services. The number of physiotherapists relative to the population and the amount of resources devoted to prevention and secondary are only very gross measures of capacity. A more detailed analysis of local capacity to implement and scale prehabilitation interventions and integrate them with surgical services is necessary.

Box 1.2. New indicators to assess the transferability of Prehab

In addition to the indicators within the transferability assessment, policy-makers are encouraged to collect data for the following indicators:

Population context

- Which types of surgery patients and population groups are priorities for prehabilitation in the target context?
- What are the main barriers for these priority populations that could keep them from accessing prehabilitation or appropriate surgery services?
- In which settings are the access barriers for these priority populations best overcome?

Sector-specific context (PA in health care settings)

- What, if any, compatible and synergistic interventions exist? (E.g. Other health interventions that promote healthy diets and PA and interventions to improve outcomes in surgical patients.)
- What, if any, competing priorities exist?
- Are the necessary human resources and work force skills available to adapt and deliver the intervention?
- Is the necessary institutional capacity available, including physical premises, to deliver the intervention and integrate it with existing surgical services?
- How can patients, informal caregivers and health professionals be supported by digital technology that supports access to and integration of Prehab with other health services?
- Are information systems available to generate and monitor key performance indicators (KPIs) of the implementation of the intervention?

Political context

- Will the intervention receive political support from key decision-makers in the target setting?
- Will the intervention receive commitments from key decision-makers in the target setting?

Economic context

- What is the cost of implementing the intervention in the target setting? (E.g., How do infrastructure and human resource needs, and the respective costs of these resources, differ between the owner and target settings?)

Source: Authors

Conclusion and next steps

Prehab is pre-operative intervention for high-risk patients undergoing major elective surgery. There is a growing body of evidence underpinning its effectiveness and evidence is also starting to emerge of its efficiency and value-generating potential, through improved and accelerated recovery and a reduced need for surgical re-interventions.

It has been implemented and studied since 2013 at Hospital Clínic of Barcelona (HCB), in the Spanish region of Catalonia, in different variations and for patients undergoing different types of surgery. It is currently being scaled in Catalonia, including in a community-setting, and transferred to Germany, France and Poland. Prehab has also been studied and is being scaled in other EU Member States and non-EU countries such as Canada, the Netherlands and the United Kingdom.

Prehab has high transferability potential, not least because of its modular design and scope for personalisation, which makes it suitable for various settings and a wide range of patient populations. A natural next step would be to make it a mainstream pre-surgical component of the Enhanced Recovery After Surgery of (ERAS) recommendations. The intervention could also become a corner stone of integrated care to manage patients with multi-morbidity. The key components of tri-modal prehabilitation indeed have potential for generalisation to other domains of health care beyond surgery, such as enhanced rehabilitation strategies for chronic patients, prevention of multi-morbidity, oncology patients or prevention of premature births. Further efforts need to focus on optimisation of deployment of the service, with continuous and built-in evaluations of adoption in real-word settings, as recommended by the OECD Guidebook.

Box 1.3. Next steps for policy makers and funding agencies

Next steps for policy makers and funding agencies to enhance Prehab are listed below:

- Support policies outlined in this case study which are designed to improve the effectiveness, efficiency and equity of the Prehab
- Closely follow future evaluations of Prehab and use findings to enhance the performance of Prehab
- Promote findings from the Prehab case study to support efforts to scale-up and transfer this intervention.

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