

## **Early rehabilitative activities in intensive care patients: systematic early versus later or no rehabilitative activities in the intensive care unit**

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### Scoping Document / Study Protocol

Authors: Michaela Barbier, Yuki Tomonaga, Matthias Schwenkglenks, Henock Yebyo, Dominik Menges, Milo Puhan

Considering inputs by ICU expert group (Philippe Eckert, Marie-Madlen Jeitzinger, Bara Ricou, Conrad Wesch)

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## Rationale

Intensive care unit (ICU) stays of more than one week (or perhaps even shorter) are associated with functional impairment and decreased quality of life after discharge, attributed to muscle weakness, disuse atrophy, delirium, and fatigue. In the most extreme, there may be acute onset of severe neuromuscular disorder and/or multi-organ failure.<sup>1-3</sup> Patients often take months to recover and regain full functionality in daily and professional life. Moreover, ICU survivors may have suboptimal quality of life after discharge due to decreased capacity to perform vigorous exercise and may have long-term cognitive impairment. In addition there may be an increased risk of death, health care utilization, and higher costs.<sup>3-6</sup>

There is evidence that rehabilitative activities initiated on the ICU reduce the risk of occurrence of the outcomes mentioned above.<sup>7-10</sup> It is current practice in many hospitals in Switzerland to initiate rehabilitative activities in the ICU, in particular in patients whose ICU stay is expected to be longer than a week. According to the Swiss Statistics on Health Insurance published by the Swiss Federal Office of Public Health, there were 11,369 patients in 2015 who received more than 24 hours of mechanical ventilation (divided among 70 acute-care hospitals, with a mean of 162 cases per hospital).<sup>11</sup> According to expert opinion, approximately 2,000 of these patients may be eligible for early rehabilitative activities during their ICU stay. A cross sectional survey, conducted by Sibila et al. in 35 ICUs that provide mechanical ventilation in Switzerland, showed that 33% of 161 adult patients admitted to ICU had active mobilization and 33% did not have any active or passive mobilization. Patients with endotracheal intubation were substantially less likely to receive active mobilization (4%) than those with tracheostomy or noninvasive ventilation.<sup>12</sup>

While rehabilitative activities are considered important overall and widely implemented in Switzerland, it is currently not clear in whom, when and how systematic early rehabilitative interventions should be initiated.<sup>2</sup> Some evidence suggests that early rehabilitative activities may reduce the time to wean from mechanical ventilation compared to usual care, and thus improve physical functionality<sup>9</sup> or prevent ICU-acquired weakness,<sup>13,14</sup> yet other authors found no effect.<sup>2</sup> Arguments for systematic early rehabilitative activities in all eligible patients (i.e., all but those contraindicated) are the early countering and prevention of muscle loss and dysfunction, as well as reduction of consequences post ICU or hospital discharge. However, rehabilitative activities that are started at individually tailored points in time and, on average, delayed activities may be associated with less complications and lower immediate costs (most importantly, due to fewer patients receiving early rehabilitative activities if the decision is taken later). It is also common practice because critical patients are sometimes viewed as 'too sick' to tolerate mobilization in the early phase of their ICU stay.<sup>15</sup> Moreover, while serious harmful effects are not expected, it is important to assess safety of within-ICU rehabilitative activities because mobilizing critically ill patients (i.e., patients with support monitors, artificial airways and multiple catheters) may not be without risk. Possible risks include dislodging of supportive equipment, pain due to reinsertion of catheters, related infections and physiological derangements and injury.

## **Pre-systematic search and review: what evidence exists on rehabilitative activities in ICU and specifically on systematic early rehabilitative activities for all patients versus later or no rehabilitative activities?**

As part of the scoping process, we performed a limited search and found that a number of studies exist on rehabilitative activities in ICU. Most of them had quite small sample sizes, were affected by some methodological limitations and used different interventions and outcome measures.<sup>1,3-5,7,9,13,14,16</sup> Some of the studies showed that rehabilitative activities in the ICU (in some cases compared to standard care with physical mobilization as ordered by a care team; in other cases compared to minimum level of physiotherapy or less intensity and volume) in critically ill patients improved quality of life, physical functions (such as peripheral muscle strength, respiratory muscle strength), and shortened length of stay in hospital/ICU.<sup>17-20</sup> However, these studies mostly examined rehabilitation interventions tailored according to individual patient impairment and usually were delayed or late rehabilitative activities. Most studies did not assess the impact of time to first mobilization or rehabilitative activities, doses and frequencies.

We analyzed four trials that tested early rehabilitative activities compared to standard care (that involved physical mobilization as prescribed by a care team). These had heterogeneous effects (i.e., some of them reported positive outcomes, others none). For example, Schweickert et al. showed that early rehabilitative activities were associated with faster return to independent functional status, shorter time in delirium, and more ventilation-free days.<sup>18</sup> Hanekom et al. showed that patients with early rehabilitative activities were more likely to have early hospital discharge.<sup>21</sup> Morris et al. reported more comprehensive outcome measures. They showed marginally improved functional performance with early rehabilitation, but no effects on length of stay, length of ventilation or ICU care, handgrip after 6 months and hand dynamometer strength, and cognitive function.<sup>22</sup> Brummel et al. did not show better outcomes for patients with early rehabilitative activities.<sup>23</sup>

We identified three most recent systematic reviews that assessed early rehabilitative activities. Castro-Avila et al. reported no significant effect of early rehabilitative activities on functional performance and quality of life, except for an improvement in walking without assistance.<sup>2</sup> The systematic review defined early rehabilitative activities as those started within seven days of admission to ICU, which may be sometimes too delayed to prevent functional problems that could occur within few days after ICU admission. The other relevant systematic reviews by Fuke et al. and Doiron et al. have been published in May 2018.<sup>24,25</sup> Fuke et al. identified significant improvements in short-term physical-related outcomes. They did not identify short-term effects on cognition, mood or long-term effects on quality of life (EQ-5D, physical functioning). The six trials they could include were small and data were generally sparse. Doiron et al. included 4 trials and concluded that the available evidence was too sparse and affected by risks of bias to draw firm conclusions.

We plan a Health Technology Assessment (HTA) that focuses on systematic early start of clearly defined rehabilitative activities (no later than 7 days after admission) and a comparison intervention of later or no rehabilitative activities, in the ICU setting. As a starting point for identifying studies our review will consider the results of the most recent high quality systematic reviews on the topic. Of note, our review may have a challenge to generate robust conclusions due to heterogeneity of interventions and outcomes, as well as limited number of eligible studies. We will strive to generate and include

contextual information for Switzerland to provide a basis for locally relevant recommendations, to the extent possible.

## **Objective of the Health Technology Assessment**

To determine the effectiveness, safety, cost-effectiveness, and budget impact of systematic early rehabilitative activities (started no later than 7 days after admission) in all ICU patients requiring ventilation support anytime during their ICU stay, having no contraindications, and not belonging to groups with special characteristics, versus later or no rehabilitative activities in the ICU. (Details on operationalization are provided in the PICO, below.) To generate contextual information for Switzerland.

Research questions raised by the Swiss Federal Office of Public Health (SFOPH) regarding the current use and appropriateness of early rehabilitative activities in extended ICU stays will be covered to the extent possible.

## **Patients, intervention, comparator, and outcomes (PICO)**

### **Population**

The review will include adult patients ( $\geq 18$  years) requiring ventilation support (i.e., intubation-based mechanical ventilation or mask-based positive airway pressure ventilation) at study inclusion or before study inclusion during the same ICU stay. We will exclude burn patients, patients with pre-existing neurological illness (such as brain trauma, neurosurgery, neuromuscular diseases, stroke, multiple sclerosis, brain tumor, spinal cord injury, patients with para- and tetraplegia), transplant patients, and other patient groups with contraindications for rehabilitative activities.

### **Intervention**

Systematic early rehabilitative activities after the stabilization phase in the ICU systematic early rehabilitative activities (started no later than 7 days after admission) in all patients who meet the inclusion criteria. Rehabilitative activities include physiotherapy, or similar activities performed by nursing staff or physiotherapists, that target muscle activation (including predominantly active range of muscle activation and training, active side to side turning, active and passive cycling in bed, exercises in bed, sitting on the edge of the bed, transferring from bed to a chair, ambulation, tilt table, active resistance exercises, contracture prophylaxis) or electrical muscle stimulation. It may also include ergotherapy, speech therapy, and psychological support as well as diary keeping (i.e., relatives or staff keep a log of the patient's history and activities while in ICU, which may help him/her to reconstruct ICU experience and prevent post-traumatic stress disorder).

## Comparator

The comparator can be either similar to the intervention (or involve a passive and active range of motions as they occur during standard medical or nursing care), but characterized by a later start of rehabilitative activities, or no intervention. We will not consider interventions to prevent pressure ulcers (e.g. changing position in bed) or to prevent joint stiffness (i.e., joint mobilization but without the goal of activating skeletal muscles) as rehabilitative activities. Approaches where only such interventions are used, would thus be classified as 'no intervention'. Both in the clinical and health economic parts, subgroup analyses may treat comparators of later rehabilitative activities or no intervention separately.

## Outcomes

### *Primary outcomes*

**Muscle strength:** hand-held dynamometry, ICU acquired weakness manual muscle testing such as using the Medical Research Council (MRC) Muscle Scale.

**Functional mobility:** Barthel index, Functional Independence Measure (FIM), Katz activities of daily living, physical function in the ICU tests (PFIT), time to mobility milestones (e.g. time to independence from assistance, time to discharge, time to first out of bed, time to standing, distance walked without assistance, 6-minute or other walking tests, time-up-and go, time to work), ventilator-free days for a given, defined time period in the ICU (e.g. 28 or 60 days).

Results on primary outcomes will be included on the GRADE summary of findings (SoF) tables.

### *Secondary outcomes*

**Quality of life:** health-related quality of life (generic or disease-specific) at discharge from ICU, discharge from hospital, after 6 months and after one year. If available, long-term quality of life and risk of mortality will also be included.

**Cognitive function and mental health:** any instruments used by eligible studies.

**Organ failure:** sequential Organ Failure Assessment.

### *Safety outcomes*

**Events during rehabilitative activities and sequelae:** accidents and fractures (during rehabilitative activities, outside rehabilitative activities), dislodging of catheters, loss of muscle tone, hypotension, pain due to insertion and reinsertion of catheters.

### *Health economic outcomes*

**Main health-economic outcomes:** costs (direct medical, indirect); quality-adjusted life years (QALYs); cost per QALY gained.

**Indicators of medical resource use with cost implications:** duration of mechanical ventilation, length of ICU stays, sedative and analgesic use, length of hospital stay, type of care at discharge, duration of rehabilitation after hospital discharge, time to return to work.

## **Part I. Systematic review of effectiveness and safety of systematic early versus later rehabilitative activities**

### **General methods**

The research protocol will follow the PRISMA-P guidelines for systematic reviews,<sup>26</sup> and will be registered on PROSPERO.

### **Types of studies to be included**

We will primarily consider randomized controlled trials (RCTs) that fulfill the above PICO. Observational studies are important to anchor the effect estimates from RCTs in terms of absolute effects and for cost-effectiveness and budget impact analyses. However, we found only five observational studies during the scoping process, which all were of rather small sample sizes ( $n < 200$ ).<sup>17,27-30</sup> We will not include observational studies in the literature searches since it is unlikely to find large studies with our comparison of interest. But we will contact experts and researchers in this field to identify potential studies or dataset, studies that would help to provide important information on the course of recovery and prognosis.

### **Information sources and search strategy**

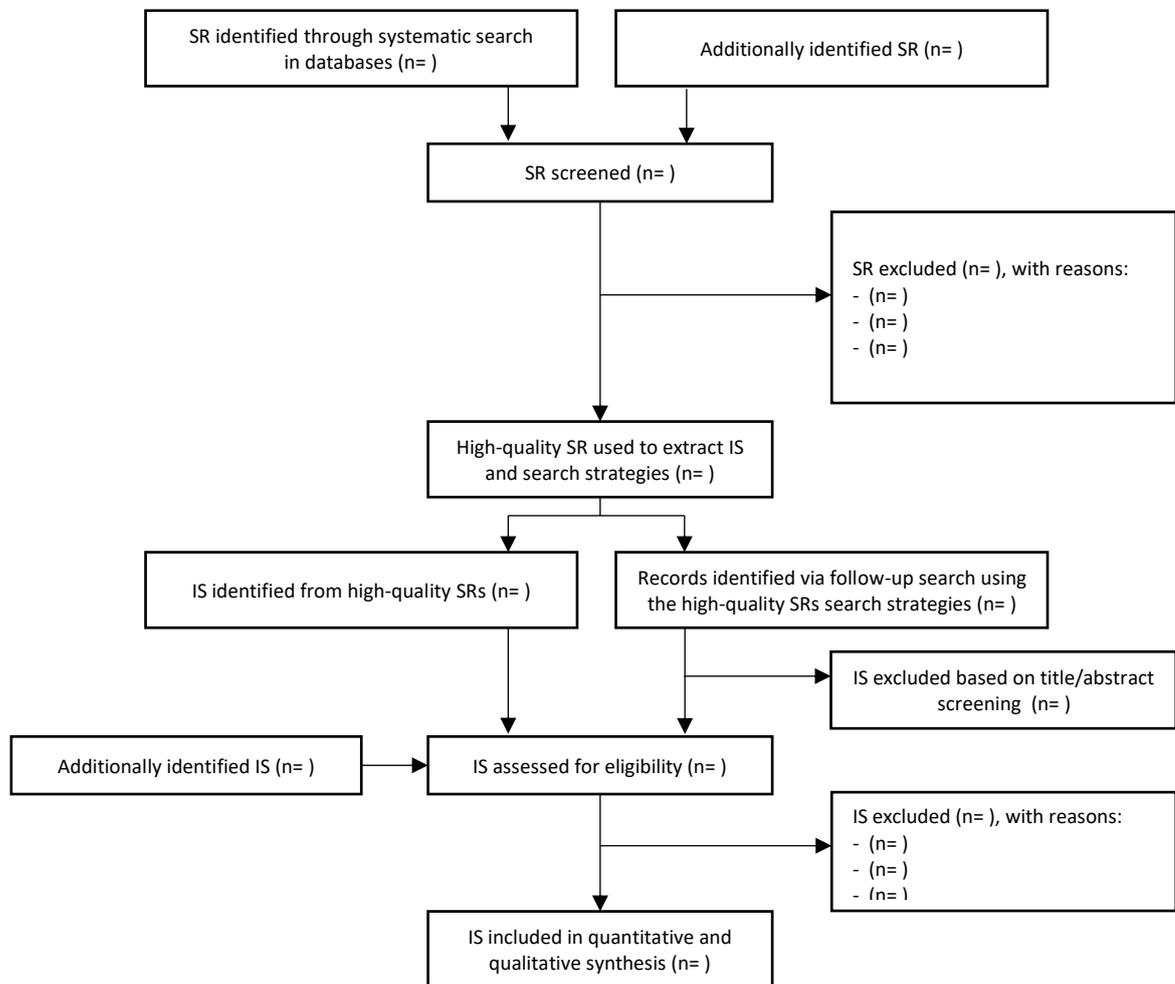
The number of published studies on rehabilitative activities in the ICU appears to be limited and we expect them to be captured entirely by the literature searches of the most recent high quality systematic reviews. Hence, we will perform two-stage systematic searches; i.e., selection of high-quality systematic reviews on early rehabilitation, and selection of individual studies included in the systematic reviews as well as further follow-up searches from other sources.

In the first stage, we will conduct a systematic search in the Medline (PubMed) and Cochrane Library databases for systematic reviews on early rehabilitative activities in ICU patients published in the last 3 years (2015-2018). Search terms will be of 'intensive care', 'critical ill', 'critical illness', 'critical care', 'intensive care', 'mechanical ventilation', 'mechanical ventilated', 'postoperative care', 'physical therapy', 'mobility intervention', 'muscle training', 'physiotherapy', 'mobilization', 'rehabilitation', 'exercise', 'ICU acquired weakness' and 'postintensive care syndrome'. In the second stage, we will pool all publications identified by the high-quality systematic reviews (both in- and excluded studies). Additionally, we will complement the resulting reference list by performing a systematic follow-up search using search strategies used in those selected reviews (mainly focusing on strategies that considered Medline, Embase, and Cochrane Central Register of Controlled Trials) for the timeframe since the last search was performed in the respective review until the date of the follow-up search. The results of this search will then be screened on title and abstract to identify further publications potentially relevant to our review. Additionally, unpublished data will be searched and considered. We will include studies that are published in English, German, French or Italian.

### **Selection process and data management**

Two independent reviewers will screen the titles and abstracts from the search results to identify eligible systematic reviews. Eligible systematic reviews will then be analyzed in full-text and their quality will be evaluated using the AMSTAR 2 checklist,<sup>31</sup> based on which we will consider the further identification of individual studies. In cases of disagreements between the two reviewers in screening, eligibility assessment or quality appraisal, a third reviewer will be invited to resolve the discrepancy by consensus. Eligible systematic reviews judged of high quality (i.e., reviews with no or maximum one non-critical weakness) will then be considered as a basis for the further identification of individual

studies. In the selection of individual studies, two independent reviewers and one mediator will be involved in the assessment of potential individual studies and selection of full-texts based on our eligibility criteria specified above (PICO) as well as study type. Whenever a full article is not available, we will contact authors by email. An Excel spreadsheet will be produced and stored containing all results from eligibility assessment and data extraction.



**Fig 1. Study selection process** (SR= Systematic Reviews; IS= Individual Studies)

### Data collection and data items

We will prepare a data extraction form comprising pertinent attributes, including characteristics of study participants, intervention and control, measured outcomes, type of statistic used for measuring outcome, time to initiate rehabilitative activities, study design, setting, aspect of the methodological quality, and sample size. The data extraction will be performed by two independent reviewers, with the involvement of a third reviewer in case of disagreements. Additionally, we will seek for individual patient data on rehabilitative activities in Switzerland or beyond.

**Risk of bias (methodological quality) assessment**

We will assess the study-level risk of bias using the Cochrane criteria based on parameters such as blinding, random sequence generation, allocation concealment, masking of outcome assessment, differential loss to follow-up and other biases for the RCTs.<sup>32</sup>

**Data synthesis**

We will provide a narrative analysis per outcome or group of outcomes (i.e., muscle strength, functional mobility, and health-related quality of life) and, where appropriate, conduct a meta-analysis to summarize and synthesize the effects of intervention versus comparator strategies. We will use relative treatment effects or standardized mean differences (such as for the Barthel index, Katz activities of daily living, PFIT, 6-min walk etc.) to estimate the overall effect.

**Subgroup analysis**

Results may be grouped based on type and nature of the intervention. Furthermore, as the patients' health state and comorbid conditions prior ICU admission may have an impact on the result of rehabilitative activities, we may also consider different patient subgroups to the extent possible based on the available data. If feasible, we will attempt to perform subgroup analyses for the following subgroups used by Herridge et al.:<sup>33</sup> (a) young patients, short length of stay (LOS): age <42 years, LOS <2 weeks; (b) mixed-age patients, variable LOS: age >42 years, LOS <2 weeks and age <45 years, LOS >2 weeks; (c) older patients, long LOS: age 46-66 years, LOS >2 weeks; (d) oldest patients, long LOS: age >66 years, LOS >2 weeks.

**Meta-bias**

Publication bias will be visually explored using funnel plots and assessed using Egger's test or Peter's test, depending on the statistic used to measure the outcome.

**Confidence in cumulative evidence**

We will assess the quality or confidence of the estimates for the primary outcomes (i.e., muscle strength and functional mobility) using the standard Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach based on the five domains of risk of bias,<sup>34</sup> inconsistency,<sup>35</sup> indirectness,<sup>36</sup> imprecision,<sup>37</sup> and publication bias.<sup>38</sup>

## Part II. Health-economic assessment of systematic early versus later rehabilitative activities

### Health economic literature research

As part of the scoping process we performed a first health economic literature search in PubMed to identify potentially relevant studies (e.g. cost-effectiveness, cost-utility, or costs studies). We added the economic search strings listed below to the search terms used for the clinical systematic review part. Future updates of the economic search will consider changes to the searches for the clinical systematic review part, if any.

(Afford\$[tiab] OR "Budget\$[tiab] OR "Capital expenditure\$[tiab] OR "cost\$[tiab] OR "cost-benefit\$[tiab] OR "Cost-consequence\$[tiab] OR "Cost-effectiveness\$[tiab] OR "Cost-minimization\$[tiab] OR "Cost-utility\$[tiab] OR "Economic\$[tiab] OR "Economic-evaluation\$[tiab] OR "Expenditure\$[tiab] OR "Fee\$[tiab] OR "Finance\$[tiab] OR "Financial\$[tiab] OR "Financing\$[tiab] OR "Health expenditure\$[tiab] OR "Health resource allocation\$[tiab] OR "Health resource utilization\$[tiab] OR "Health-economic\$[tiab] OR "Medical savings accounts\$[tiab] OR "Monetary\$[tiab] OR "Pharmaco-economic analyses\$[tiab] OR "Pharmaco-economic analysis\$[tiab] OR "Pharmacoeconomic\$[tiab] OR "Pharmacoeconomic-analyses\$[tiab] OR "Pharmacoeconomic-analysis\$[tiab] OR "Price\$[tiab] OR "Socioeconomic\$).

The Pubmed search resulted in 304 hits. After a first round of reviews based on title alone, 24 references published between 2003 and 2018 were selected as possibly relevant. A further review of the abstracts or their full text resulted in 11 potentially relevant articles (see appendix).

### Approach to health economic assessment

During the pre-review of the potentially relevant articles, no relevant cost-effectiveness studies were found. Only 11 studies investigating or mentioning the costs of rehabilitative activities for patients in ICU were identified.<sup>25,32-41</sup> Further review of the 11 cost studies showed that most of them did not include a cost comparison of intervention and comparator as planned in this assessment. Only two studies were considered potentially relevant:

- **Corcoran et al.** Early rehabilitation in the medical and surgical intensive care units for patients with and without mechanical ventilation: an interprofessional performance improvement project. *PM R* 2017;<sup>48</sup> the Performance Improvement Project (PIP) project examined early mobility and increased intensity of therapy services on patients in the ICU with and without mechanical ventilation. It was based on a prospective data collection in 2014 (PIP) compared with a historical patient population in 2012 (pre-PIP). Inclusion criteria for patients in the early mobilization group were admission to ICU within 3 days of hospital admission and receiving physical therapy and occupational therapist orders within 3 days of admission into the ICU. The historical comparator group received usual care including physical therapy. Rehabilitation therapy services increased from 2012 to 2014 by approximately 60 minutes per patient. The average ICU LOS decreased by almost 20% from 4.6 days (pre-PIP) to 3.7 days (PIP) ( $p = 0.05$ ). A decrease of over 40% was observed in the floor bed average LOS from 6.0 days (pre-PIP) to 3.4 days (PIP) ( $p < 0.01$ ). An increased percentage of PIP patients, 40.5%, were discharged home without services compared with 18.2% in the pre-PIP phase ( $p < 0.01$ ). Average cost per day in the ICU and floor bed decreased in the PIP group.

- **Morris et al.** Early intensive care unit mobility therapy in the treatment of acute respiratory failure. Crit Care Med 2008:<sup>43</sup> the authors conducted a prospective cohort study in a university medical ICU. They assessed for ICU patients with acute respiratory failure requiring mechanical ventilation on admission whether a mobility protocol would increase the proportion of patients receiving physical therapy vs. usual care. In the Protocol group, physical therapy was initiated by the protocol's automatic physician's order; whereas, in the Usual Care group, physical therapy was initiated based on a physician's patient-specific order. The primary outcome was the proportion of patients receiving physical therapy in patients surviving to hospital discharge. Baseline characteristics were similar between groups. Outcome data are reflective of survivors. More Protocol patients received at least one physical therapy session than did Usual Care patients (80% vs. 47%,  $p < 0.001$ ). Protocol patients were out of bed earlier (5 vs. 11 days,  $p < 0.001$ ), had therapy initiated more frequently in the intensive care unit (91% vs. 13%,  $p < 0.001$ ), and had similar low complication rates compared with Usual Care. For Protocol patients, intensive care unit length of stay was 5.5 vs. 6.9 days for Usual Care ( $p = 0.025$ ); hospital length of stay for Protocol patients was 11.2 vs. 14.5 days for Usual Care ( $p = 0.006$ ). There were no untoward events during an intensive care unit Mobility session and no cost difference between the two arms, considering Mobility Team costs. The average direct inpatient costs for the Protocol group inclusive of the Mobility Team salaries were USD 44,302 per patient for the Usual Care group and USD 41,142 per patient for the Protocol group,  $p = 0.262$ .

The following approach will be pursued:

- In a full systematic literature search we will identify Swiss and international literature on the costs and cost-effectiveness of systematic early versus later (possibly more individualized) or no rehabilitative activities for ICU patients eligible according to the PICO. The identified economic studies will be critically assessed. As one tool, the "Consolidated health economic evaluation reporting standards" (CHEERS) checklist will be used.<sup>49</sup> Plausibility of the results and the transferability of international results to Switzerland be critically considered. Results will be summarized in tabular and/or graphical formats and synthesized narratively.
- We will characterize the current practice variation and cost structure in Swiss ICUs (closely related to Part III; see below).
- Due to the lack of available cost-effectiveness studies, we would ideally perform a *de novo* cost-effectiveness analysis for Switzerland. This analysis would adopt a lifelong time horizon if possible, although limited data would probably force a shorter time horizon. In case a cost-effectiveness analysis is not sensibly feasible given the available data, we will develop a cost or cost-minimization model. The model will be suitable to accommodate new evidence as it arises and link different levels of effectiveness of systematic early rehabilitative activities to cost impact and economic performance.
- The expenditure for systematic early versus later (possibly more individualized) or no rehabilitative activities and the impact on the Swiss healthcare system will also be investigated in a budget impact analysis, considering the available/to be generated contextual information for Switzerland. The current use and status of within-ICU rehabilitative activities in Switzerland will be used as a reference point (closely related to Part III; see below).

**Perspective**

Costs will be assessed from a health insurance law (KVG) perspective as well as from a societal perspective.

**Additional data sources**

In addition to the published literature, the following sources of information may be used for the cost and budget impact analyses:

Swiss Hospital Statistics 2015 (and 2016, if available): patients will be identified through relevant treatments (e.g. CHOP codes suggesting intubation and mechanical ventilation) and diagnostic codes (i.e. ICD-10 codes according to the inclusion criteria).

Diagnosis-related case cost statistics (Statistik diagnosebezogener Fallkosten) of the Swiss Federal Office of Statistics: this statistic may be used to estimate the hospitalization cost per patient according to their SwissDRG (i.e. according to their diagnoses and treatment combinations received).

Database of the Inselspital Bern: Inselspital Bern has been collecting information in ICU-patients for a couple of years. According to the leading physician, Prof. Dr. med. Joerg Schefold, a considerable amount of the important variables should be available (e.g. duration of ICU stays, timepoint for rehabilitative activities, or functional performance). This information will be fundamental for the creation of a Swiss model. We will assess possibilities to make use of these data in cooperation with the responsible at Inselspital Bern, where a submission to the responsible ethic committee is currently in preparation.

A master thesis in economics, currently conducted under the supervision of Prof. Stefan Felder (University of Basel) and Prof. Matthias Schwenkglens (Universities of Basel and Zürich), may provide additional insights into the current practice of within-ICU rehabilitative activities in Switzerland and perceived issues that could be fruitful for this HTA.

Further sources may be identified and added at a later point in time.

### **Part III. Study on the Service Supply Situation**

A survey will be performed to describe current approaches, practice variation etc. in Swiss ICUs. This should also generate data for health economic assessment (e.g. work time requirements for rehabilitative activities, staff categories involved, staff costs per unit of time). Completion of some elements of the health economic part will require results of the survey as a basis.

A draft questionnaire has been prepared by the ICU expert group and is currently being amended by the assessment team.

The survey will be conducted by the Swiss Society of Intensive Care Medicine, targeting all recognized Swiss ICUs, and analyzed by the assessment team.

While work on the questionnaire is ongoing, we expect to cover at least the following aspects:

- Service supply situation regarding early rehabilitative activities in Switzerland
  - Models of applied early rehabilitation in Switzerland
  - Degree and variability of use of early rehabilitation in Switzerland
  - Regional differences
  - Differences relating to hospital type and ICU characteristics
  - Differences driven by patient characteristics (possibly subgroup analyses)
- Use of resources for early rehabilitation, e.g. staff time requirements
- Use of evaluation of early rehabilitation outcomes and related approaches
- Statements on causes of possible differences in service supply

The availability of additional data sources (e.g. at the Swiss Federal Statistical Office or OBSAN) will be checked. If any such sources exist, they will be considered.

### Current planned timetable: scoping to finalizing the HTA

Date	Milestone	Actors
<b>Scoping</b>		
05.06.2018	Kick-off with Stakeholder / Input for Scope	Assessment Team, Stakeholder, scientific secretariat
15.06.2018	Mandate for Scoping	Swiss Medical Board
25.07.2018	Draft of Scoping Document	Assessment Team clinical experts;
25.08.2018	Stakeholder Review pf draft document	Stakeholder
14.09.2018	Adjustments in Scoping-Document	Assessment Team
15.11.2018	Additional Consultation with ICU-Experts following the Stakeholder Consultation	Assessment Team, Clinical Experts
10.12.2018	Adjustments on Scoping Document	Assessment Team
10.01.2018	Review FOPH	SMB / FOPH
15.01.2019	Mandate to start Assessment	SMB
<b>Assessment</b>		
15.06.2019	Systematic Review for medical effectiveness	Assessment Team
	Health Economic Analysis	Assessment Team
30.06.2019	Prepare Draft of Assessment Report	Assessment Team
31.07.2019	External Review of Assessment-Report	external Reviewers
31.08.2019	Final Assessment-Report	Assessment Team
20.09.2019	Stakeholder-Consultation	FOPH / Stakeholder
	Translation Executive Summary (G/F)	Assessment Team
31.10.2019	Submission of Assessment Report	Assessment Team
<b>Analyses Service Supply Situation</b>		
15.09.2018	Development Survey Questions, Phase 1	ICU-Experts Assessment Team
20.12.2018	Development Survey Questions, Phase 2	Assessment Team
28.02.2019	Review Survey, Translation an Piloting	ICU-Experts, SGI, Assessment Team
30.04.2019	Conduct the Survey	SGI
30.06.2019	Evaluate the Survey	Assessment Team
31.08.2019	Draft Report on service supply situation	Assessment Team
30.09.2019	Review report service supply situation	ICU-Experts, FOPH
22.10.2019	Stakeholder Consultation	Stakeholder
15.11.2019	Final Report on service supply situation	Assessment Team
<b>Acknowledgement and Recommendations</b>		
20.09.2019	Discussion and Draft Report	Appraisal Committee
31.01.2020	Final Report	Appraisal Committee / SMB

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