CYCLE Pilot: Prologue to a multi-centre RCT of early in-bed cycling in the ICU

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Introduction: Survivors of critical illness are at risk of developing long-term physical disability. Early rehabilitation interventions, such as in-bed cycling, may improve functional outcomes. Before embarking on a large randomized controlled trial (RCT) with mechanically ventilated patients, assessment of the feasibility of routine physiotherapy (PT) interventions plus early in-bed cycling (Cycling) versus routine PT alone (Routine) and development of monitoring strategies throughout the hospital stay are of key importance. Given the complex clinical environment, the vulnerability of critically ill patients, and the novelty of an intervention that is rare in present practice, the CYCLE Pilot RCT (NCT02377830) was designed to determine the feasibility of a future large trial.

Objective: To itemize and characterize trial preparation and execution activities during the CYCLE Pilot RCT in participating Intensive Care Units (ICU) and the study Methods Centre.

Methods: In 7 Canadian sites, we retrospectively reviewed timelines to study initiation (e.g., research ethics board (REB) approval, first enrolment), site activities (e.g., start-up visits, protocol education, intervention delivery, outcomes measurement), and additional preparatory activities by the Methods Centre. Data sources included regulatory and Methods Centre documentation (e.g., approvals, communications, meeting agendas, coordinator notes). We report descriptive statistics as counts and proportions, and medians and quartiles (Q1-Q3).

Results: The study was submitted to and approved by 5 individual REBs for implementation in 7 medical-surgical ICUs. Time from REB submission to first enrolment (median, quartiles) was 185 days (146-209) [REB submission to approval was 69 days (28-103), and REB approval to first enrolment was 51 days (28-188)]. From March 2015 to June 2016, we screened 864 patients for eligibility, and randomized 66 patients (7.6%) to Cycling (n=36) or Routine (n=30) study arms. Overall, we screened a median of 12 (11-15) patients for each participant enrolled. Across the 7 ICUs, we provided 11 in-bed cycling training sessions (7 (6-8) hours) and trained 36 physiotherapists to cycle; 21 (58.3%) provided cycling during the trial. We conducted 11 outcome measure training sessions (3 (2-3.5) hours) with 58 therapists and assistants; 35 (60.3%) performed study measurements. Three centres each required an additional training session due to therapist turnover or maternity leaves. We provided 7 training sessions to 15 research coordinators and taught 19 people to conduct data entry; 14 (73.7%) entered data for the study.

Conclusion: Trial planning and execution is multi-faceted and incorporates ethical oversight, patient screening, intervention delivery, and detailed patient tracking for outcomes assessment. Early in-bed cycling research in the ICU requires consideration of site individuality (as demonstrated by the large variation in timelines), intensive training of key professionals in cycling and in research procedures, and establishment of efficient screening methods. The analysis of activities undertaken as a prologue to the CYCLE RCT highlights their scope and magnitude, and may help others interested in evaluating novel ICU rehabilitation interventions to develop

procedures and timelines, train dedicated personnel, and allocate resources to build the foundation for a future large trial.

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