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Exercise interventions are delayed in critically ill patients: a historical cohort study in an Australian tertiary intensive care unit

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Authors' contributions

MRN, LJC, SMM, LMA, JW contributed to study conception, design, analysis plan, data management, appraisal and editing. AGB contributed to study analysis plan, appraisal and editing. All authors read and approved the final manuscript.

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1 **Exercise interventions are delayed in critically ill patients: a cohort study in an Australian**
2 **tertiary intensive care unit**

3
4 **Abstract:**

5 **Objectives:** This study aims to (i) describe the time to exercise commencement (sitting and upright
6 activities) relative to ICU admission and relative to achievement of initial neurological, respiratory and
7 cardiovascular stability; (ii) examine factors associated with whether sitting and upright activities
8 occurred in ICU; and (iii) examine factors associated with time taken to commence these activities
9 after stability has been achieved.

10 **Design:** Five-year historical cohort study.

11 **Setting:** An Australian tertiary mixed medical, surgical, trauma ICU.

12 **Participants:** The cohort (n=3222, mean(SD) age 54(18) years, 67% male) included consecutive ICU
13 patients with length of stay over 48 hours admitted to a tertiary ICU who achieved stability.

14 **Main outcome measures:** Time from stability to patients first completed sitting and upright activities
15 was calculated. Logistic regression (and Cox proportional hazard models) examined whether sitting
16 and upright activities in ICU occurred (and time to these events).

17 **Interventions:** None.

18 **Results:** For patients who completed exercise interventions (n=1845/3222, 57%), this commenced a
19 median (IQR) 2.3(1.3 to 4.4) days after stability for upright activities and 2.7(1.5 to 5.7) days for
20 sitting. A large proportion of patients did not complete exercise interventions despite achieving
21 stability (n=1377/3222, 43%). Elective surgical admissions, lower illness severity and older age were
22 associated with completion (and earlier completion) of sitting and upright activity ($p<0.01$).

23 **Conclusions:** Many stable patients did not commence sitting or upright activity in ICU despite known
24 benefits, or commencement was somewhat delayed. Opportunities may exist to improve patient
25 outcomes through timely implementation of exercise-based interventions.

26 **Keywords:** Critical illness; Intensive care units; Rehabilitation; Physical therapy (specialty); Cohort
27 studies; Early ambulation

28 **Background:**

29 Survival rates for patients who have been admitted to intensive care units (ICUs) are improving[1, 2].
30 However, the number of patients surviving with persistent physical, cognitive and mental health
31 deficits is increasing[1, 3]. Additionally, survivors' health-related quality of life is adversely affected[1,
32 4] and 60% remain unemployed at 6 months after ICU admission due to poor health[5].

33

34 Acute muscle loss is likely to be associated with persistent poor functional outcomes and health-
35 related quality of life. Muscle atrophy is rapid and pronounced in patients with multi-organ failure[6].

36 Active exercise leads to greater muscle strength at ICU discharge, greater probability of walking
37 without assistance at hospital discharge and improved survival at 6 months post ICU admission[7].

38 Early exercise is safe and feasible with adverse events (typically minor) reported in less than three
39 percent of interventions[8]

40 The proportion of critically ill patients admitted to an ICU for over 48 hours that participate in exercise
41 interventions whilst in the ICU is often low, with point prevalence studies reporting 24–50%
42 completing any form of exercise[9-12].

43 The duration that critically ill patients remain in bed prior to commencing exercise is inconsistent.

44 Intervention studies have reported the median time to sitting out of bed (SOOB) to range between 1.7
45 and 8.5 days[13-16]. There is also inconsistency in the literature regarding the proportion of patients
46 who participate in active out of bed exercise in ICU settings, which has ranged from 40% to 73%[17,
47 18]. The duration of bed rest in the ICU has been the only risk factor reported to have consistently
48 been associated with persistent muscle weakness[4]. Consequently, longer duration of bed rest in
49 ICU settings may adversely affect survivors' ability to function, maintain employment and their health-
50 related quality of life after their critical illness.

51

52 Previous studies examining exercise practices have been limited to point prevalence studies with
53 limited study days examined, interventional studies that are likely to report a greater incidence of
54 activity compared to usual practice, or observational studies with relatively small sample sizes. No

55 studies have yet considered the time to commence activity in ICU relative to the time when a patient
56 could safely commence activity. The present study sought to address these issues by examining a
57 large historical cohort of consecutively admitted critically ill patients who required more than 48 hours
58 length of stay within a tertiary ICU. The aims of this study were to:

- 59 (i) describe the time to exercise commencement (sitting and upright activities) relative to ICU
60 admission;
- 61 (ii) describe the time to exercise commencement relative to achievement of initial neurological,
62 respiratory and cardiovascular stability;
- 63 (iii) examine factors associated with whether sitting and upright activities occurred in ICU; and
- 64 (iv) examine factors associated with time taken to commence these activities after neurological,
65 respiratory and cardiovascular stability had been achieved.

66

67 **Methods**

68 **Study Setting**

69 An historical observational cohort study was conducted at a 25-bed adult mixed medical, surgical,
70 trauma ICU in an Australian metropolitan tertiary hospital. The ICU has approximately 2200
71 admissions per year including 1200 elective surgical, 300 emergency surgical and 700 medical
72 patients. Adult patients from all specialities including liver transplant and spinal cord injury, but
73 excluding maternity and burns are admitted. Cardiology patients are cared for in a separate Coronary
74 Care Unit, unless there is a requirement for invasive ventilation.

75

76 **Usual practice**

77 There is typically a 1:1 nurse: patient ratio and equivalent to 3.5 physiotherapists for the ICU Monday
78 to Friday and 2 physiotherapists on weekends, an additional physiotherapist is available on-call if
79 respiratory interventions are required overnight. Physiotherapists lead the daily assessment of a
80 patients' ability to participate in an exercise intervention. Other clinicians are consulted regarding
81 concerns or planned procedures that may affect the treatment plan. A pre-specified mobilisation
82 protocol has not been implemented at the study site. Unless contraindications exist, there is an
83 expectation that elective surgery patients are mobilised within ICU prior to discharge to the ward.

84 Ventilated patients rarely complete upright activities, but occasionally perform sitting activities such as
85 sitting on the edge of the bed or passive slide transfer to sit out of bed.

86

87 **Ethics**

88 Ethical approval for the study was obtained from the Metro South Human Research Ethics Committee
89 (HREC/12/QPAH/009) and from the Queensland University of Technology University Human
90 Research Ethics Committee (1400000587). These ethical approvals included approval of a waiver of
91 individual consent as this study used routinely recorded information and there was no undue risk to
92 patients' rights or welfare. Public Health Act approval (RD005370) was obtained for the release of
93 Confidential Information for the purposes of research under the provision of Section 280 of the state
94 Public Health Act 2005 for the jurisdiction where the research was conducted.

95

96 **Clinical Data**

97 Data pertaining to all patients admitted over a 5-year period for more than 48 hours to the study ICU
98 was retrieved by the ICU Computer Information Systems (CIS) Administrator (RH) using Structured
99 Query Language (SQL) queries from an intensive care electronic medical records database (Phillips
100 Medical Systems, IntelliVue Clinical Information Portfolio; ICIP Release D.03.03, Eindhoven, The
101 Netherlands). Regular manual checks of individual cases were conducted (by comparing query output
102 with a manual review of clinical records) were conducted during the development of the SQL queries
103 by the lead investigator (MN) and ICU CIS Administrator (RH) to ensure the accuracy of the queries.
104 Patients' characteristics recorded included gender, age, admission classification (medical, elective
105 surgical and emergency surgical), admission diagnosis, and APACHE III scores. Data pertaining to
106 neurological and physiological parameters, ventilation times, ICU and hospital length of stay,
107 discharge destination, and death in ICU or hospital were also recorded.

108 The time taken for patients to achieve neurological, respiratory and cardiovascular stability whilst in
109 ICU was calculated. Patients were deemed to have achieved stability at the first time point since
110 admission to ICU when their observations were recorded to be within the ranges specified in Table 1.
111 These definitions were based on safety criteria for active mobilisation of critically ill adults[19] and
112 were defined at study inception, prior to data extraction. These definitions are consistent with

113 published expert consensus recommendations for the mobilisation of mechanically ventilated
114 adults[20].

115

116 ICU electronic medical records were searched by lead investigator (MN) to calculate the time to initial
117 sitting and upright activity using electronic keywords (Supplementary Table 1). Initial sitting was
118 defined as the first time a patient was transferred to another surface or completed a sitting balance
119 activity. These activities represent a score on the ICU Mobility Scale of 2 and 3, respectively[21].

120 Sitting activity did not include sitting up in bed with the bed repositioned into a chair position. The time
121 of initial 'upright activity' was also calculated. Initial upright activity was defined as mobilisation
122 activities including; standing with the assistance of a tilt table, standing, marching on the spot, stand
123 transfer to a seated position or ambulation. These upright activities represent a score on the ICU
124 Mobility Scale from 4 to 10[21].

125

126 **Minimising potential sources of bias**

127 Selection bias was minimised by analysing all ICU admissions that had a length of stay of over 48
128 hours over a 5-year period. To minimise information bias, the principal investigator (MN) individually
129 scrutinised medical records to verify that the activity occurred rather than noting a planned
130 intervention not yet completed. Co-investigator (LA) manually checked a series of 100 consecutive
131 records for accuracy plus additional checks at random. These manual checks concurred with the
132 findings of the recorded time to activity (or whether activity had not occurred). Because this study was
133 dependent on routinely recorded clinical records, it is possible that inadvertent omissions or
134 documentation errors occurred when clinicians recorded their clinical notes which was not able to be
135 verified for this historical cohort. As the ICU and acute hospital discharge destination is known for all
136 patients there was no losses to follow-up.

137

138 **Statistical analysis**

139 Descriptive statistics were used to describe patient and clinical characteristics. Logistic regression
140 models were used to examine patient and clinical factors associated with whether patients i)
141 completed sitting activity ii) completed upright activity in ICU. Cox proportional hazards models were
142 used to examine factors associated with time to i) first completed sitting activity, and ii) first completed

143 an upright activity after neurological, respiratory and cardiovascular stability was achieved. Potential
144 explanatory factors included in these models were admission category (medical, elective surgical,
145 emergency surgical), illness severity (APACHEIII), age, sex, duration of mechanical ventilation, and
146 whether patients received haemodialysis. To adjust for potential clustering attributable to repeat ICU
147 admissions by the same patient, standard error adjustments for cluster-correlated data were
148 applied[22].

149

150 **Results**

151 There were 11445 patients admitted to ICU over a period of 60 months, of which 3434/11445 (30.0%)
152 had an ICU length of stay longer than 48 hours. A total of 212/3434 (6%) patients (Supplementary
153 Table 3) did not achieve stability. Patients who did not achieve stability were excluded from further
154 analysis. The remaining 3222 ICU admissions (from 2983 unique patients) where stability was
155 achieved were included in further analysis (Figure 1). Patients were predominantly male (67%), had a
156 mean (SD) age of 54 (18) years, the majority were admitted for medical reasons (65%) and stayed in
157 ICU a median (IQR) of 4.9 (3.0 to 9.5) days. During their ICU admission, 1377/3222 (43%) patients
158 achieved stability but did not complete sitting or upright activities (Table 2). Most patients completed
159 sitting activities (57%), but less than half completed upright activities (45%). Three patients completed
160 activity prior to achieving stability and six patients completed activity but never achieved stability
161 (Table 3).

162

163 *Factors associated with participation in activity*

164 Findings from the logistic regressions examining factors associated with whether or not i) sitting
165 activity or ii) upright activity from when patients had achieved stability was completed are in Table 4.
166 Older patients were more likely to complete sitting activity (OR per 10 years 1.10; 95% CI, 1.05 to
167 1.15) and upright activities (OR 1.10; 95% CI, 1.05 to 1.15). A higher severity of illness was
168 significantly associated with not completing both sitting (OR per 10 APACHE III 0.92, 95% CI, 0.89 to
169 0.96) and upright activity (OR 0.92, 95% CI, 0.89 to 0.95). Elective surgical admissions to ICU were
170 more likely to participate in sitting activities (OR 1.76, 95% CI, 1.40 to 2.21) and upright activities (OR
171 1.59, 95% CI, 1.29 to 1.97) in comparison to medical admissions. In contrast, emergency surgical
172 admissions were less likely to participate with sitting activities (OR 0.64, 95% CI, 0.53 to 0.76) and

173 upright activities (OR 0.68, 95% CI, 0.57 to 0.81). Longer mechanical ventilation time was positively
174 associated with completing sitting activities (OR per day 1.04, 95% CI, 1.02 to 1.06) but not
175 associated with upright activity. There was no association between patients' receiving dialysis and
176 completing sitting activities or upright activities.

177

178 *Factors associated with time to commence activity following achievement of stability*

179 Findings from the time-to-event analyses are in Table 5. Older age was associated with shorter time
180 to achieve initial sitting activity (HR per 10 years 1.05; 95% CI, 1.02 to 1.08) and upright activity (HR
181 1.05; 95% CI 1.01 to 1.08). A higher severity of illness delayed the time to commence sitting activities
182 (HR per 10 APACHE III 0.95; 95% CI 0.93 to 0.97) and upright activities (HR 0.93; 95% CI 0.91 to
183 0.96). Following achievement of stability, patients admitted to ICU following an elective surgical
184 procedure commenced initial sitting activities (HR 1.68; 95% CI 1.47 to 1.92) and upright activities
185 (HR 1.62; 95% CI 1.41 to 1.87) earlier than patients with medical admissions. In contrast, patients
186 admitted to ICU for an emergency surgical procedure were slower to commence initial sitting (HR
187 0.71, 95% CI 0.62 to 0.80) and upright activity tasks (HR 0.73, 95% CI 0.63 to 0.85). Longer
188 mechanical ventilation duration was associated with a longer time until commencement of sitting
189 activities (HR per day 0.92, 95% CI, 0.90 to 0.94) and upright activities (HR 0.88; 95% CI, 0.87 to
190 0.91). Receiving dialysis was also associated with a longer time from achievement of stability to
191 commence sitting activities (HR 0.63, 95% CI, 0.53 to 0.74) and upright activities (HR 0.67, 95% CI
192 0.56-0.82).

193

194 **Discussion:**

195 *Main findings*

196 This study found that 43% of critically ill patients with an ICU length of stay of over 48 hours who
197 achieve neurological, respiratory and cardiovascular stability, did not complete any sitting or upright
198 activities for the duration of their ICU admission. For those patients who did participate in exercise
199 interventions, commencement of activity may have been delayed as it did not occur until a median of
200 more than two days after patients were considered to have achieved stability. This occurred despite
201 published safety considerations[19] indicating that exercise interventions could have commenced
202 considerably earlier than they did in many of these patients.

203

204 *Comparison to prior research*

205 In the current study, patients who had an ICU length of stay greater than 48 hours commenced
206 activity approximately 3½ days after admission, with slightly more than half of patients completing
207 sitting activities and slightly less than half of patients completing upright activities. This is consistent
208 with the growing body of literature where reports of between 24% and 73% of patients completed
209 exercise interventions within the ICU[9-12, 17, 18, 23-25] and have noted that less than 5% of
210 mechanically ventilated patients completed upright activities [9-12, 26]. A recent prospective study
211 reported that 73% of patients were mobilised during their ICU admission, this proportion may
212 represent something of an upper limit of what is feasible with critically ill patients[17]. Early
213 interventional studies in the United States report a range of times to commence sitting typically
214 between 3 and 9 days[15, 16]. The interval between admission and time of activity reported in the
215 present study is consistent with other reports including a binational observational cohort study where
216 time to mobilisation was 2 days in Australia and 3½ days in Scotland[18], and a historical cohort study
217 from Australia where the time to both sitting and upright activity was 3 days[25]. A 12-centre
218 Australian and New Zealand study reported the time to commence sitting and standing activities was
219 7 days[27]. However, this study only enrolled patients who were expected to be mechanically
220 ventilated for more than 48 hours from enrolment, potentially contributing to the delay to commence
221 activities[27]. To date, no prior studies have considered the timing of activity commencement relative
222 to the achievement of neurological, cardiovascular and cardiorespiratory stability which renders the
223 current study something of an innovation, albeit caveats are warranted given that pre-specified
224 physiological indicators of stability are not intended to reflect the full gamete of complex clinical
225 reasoning that may precede mobility-related decision making in ICU settings. Given the large sample
226 size this study has also assisted in defining usual care of ICU patients who are admitted for over 48
227 hours within an Australian setting. This is one step toward the establishment of benchmarks related to
228 mobilisation activities among patient who are critically ill that may assist individual facilities to interpret
229 their own practice[28].

230

231 The definition of 'stability' utilised in this study is consistent with an expert consensus on the
232 mobilisation of mechanically ventilated patient publication that was published during the study
233 period[20]. The adverse event rate of exercise interventions with critically ill patients is less than 3%

234 with most adverse events being minor and transient[8]. To date no consensus has been achieved to
235 describe the doses of vasoactive medications that patients could simultaneously receive whilst safely
236 participating in exercise interventions[20]. A recent single centre study reported that cardiothoracic
237 patients were safely able to commence exercise rehabilitation interventions whilst receiving
238 vasoactive medications, with a less than 2% minor adverse event rate[29]. Consequently, the
239 'stability' definitions utilised could be interpreted as conservative. As bed rest is the only risk factor
240 associated with prolonged weakness[4], determining which patients receiving vasoactive medications
241 can safely exercise remains a priority for future research.

242
243 Several studies that have incorporated exercise protocols have demonstrated reductions in time to
244 commence exercise interventions and decreased ventilation and ICU length of stay with critically ill
245 patients[13, 14, 24, 30, 31]. A protocolised approach to early exercise has been recommended by
246 The American Thoracic Society guidelines for the liberation of mechanical ventilation[32]. Patients did
247 not follow an exercise protocol at the study site, however there was a local expectation at the
248 participating facility that elective surgical short stay patients ambulate prior to ICU discharge. These
249 short-stay patients were excluded from the present study to enable the analysis to focus on patients
250 who are at a higher risk of deconditioning. Consequently, the excluded patients were predominately
251 elective surgical patients (66%) (Figure 1). This study has extended the field by highlighting the extent
252 to which higher severity of illness, receiving dialysis, mechanical ventilation time and admission type
253 (e.g., emergency surgical admission) to ICU may contribute to delay until patients complete
254 rehabilitation activities. Effective strategies for reducing the duration of bed rest are likely to represent
255 opportunities to improve patient outcomes. The implementation of an exercise protocol may reduce
256 delays to commence exercise interventions. However, despite recommendations to follow a
257 protocolised approach to implement early activity[32], there is no consensus on exercise dose
258 prescription in terms of frequency, volume and intensity with critically ill patients[33-35] therefore this
259 remains a priority for further research.

260
261 Receiving dialysis had a substantial negative association with time to commence exercise
262 interventions. Whilst prior studies have noted that it is safe and feasible for patients receiving dialysis
263 to complete exercise[36, 37], clinicians in real-world clinical practice maybe somewhat reluctant, or

264 find it pragmatically challenging, to commence sitting out of bed or upright activities with their patients
265 who are receiving dialysis in comparison to patients who do not require dialysis. Investigation of
266 pragmatic strategies to facilitate mobility activities among patients receiving dialysis are also a priority
267 for further research.

268

269 The present study made use of electronic clinical records. Electronic medical records are being
270 incorporated into standard clinical care internationally and providing new opportunities advancing the
271 quality, safety and effectiveness of clinical care[38]. Additionally, de-identified critical care databases
272 such as the Medical Information Mart for Intensive Care III (MIMIC-III) and Australian and New
273 Zealand Intensive Care Society Centre for Outcome and Resource Evaluation (ANZICS CORE) are
274 enabling researchers to access clinical data from large cohorts of patients[38] and evaluate the
275 performance of ICUs relative to each other[39]. The ongoing advancement in digitisation of hospital
276 systems is likely to enable others to analyse and report their mobilisation practices, which could
277 enable comparisons between similar ICUs and promote quality improvement activities within critical
278 care settings.

279

280 *Strengths and limitations*

281 Strengths of this investigation include that it was the largest sample to date in which exercise
282 practices and factors associated with the commencement of exercise interventions were examined.

283 Furthermore, this was the first investigation to have considered the duration of bed rest of critically ill
284 patients' following the achievement of neurological, respiratory and cardiovascular stability.

285 Limitations of this investigation are that it was limited to routinely collected data in a single centre
286 mixed medical, surgical, trauma ICU and times analysed were based on routinely collected
287 observations. It is important to note, that the physiological parameters used in this study were likely to
288 be a conservative indicator of patients' having reached a point of physiological stability. However, it is
289 unlikely that any set of physiological parameters could entirely reflect or substitute for contextualised
290 clinical decision making. Nonetheless, these indicators were useful for highlighting that many patients
291 were likely to have been physiologically stable for some time before they were mobilised. It is worth
292 noting that following the achievement of initial stability patients' may not remain stable or may have
293 achieved 'stability' at times when staffing was not sufficient to enable an exercise intervention to be

294 completed and this may have influenced their time until exercise commencement. Most patients who
295 did not complete exercise interventions survived acute-hospitalisation (76%). This indicates that
296 patients were likely to achieve 'stability' and continued to recover. Consequently, it is likely that
297 patients were well enough to participate in some form of exercise whilst in ICU. Results may not be
298 generalisable to dissimilar ICUs or to short-stay post-elective surgery ICU admissions which were
299 intentionally excluded from this investigation. However, this study demonstrated agreement with
300 previous international publications in terms of the proportion of patients who completed exercise
301 interventions whilst in ICU and the duration from ICU admission to commence exercise interventions.
302 It should be noted that the present study did not set-out to define cause and effect relationships
303 related to the timing of activity commencement in ICU. Furthermore, barriers to the implementation of
304 exercise interventions are diverse and include patient, clinician and health care system factors[40].
305 However, the barriers to early activity commencement were not routinely reported and therefore could
306 not be analysed for this cohort.

307

308 *Future research*

309 This study has identified that patients either do not complete exercise interventions whilst admitted to
310 the ICU, or the interventions are delayed following achievement of stability. Future prospective work is
311 required to confirm or refute these findings and to examine if barriers exist that could be addressed to
312 optimise the timing of the implementation of exercise interventions with critically ill patients. In addition
313 to research regarding intervention timing, effectiveness and implementation, clinical practice may be
314 further informed by research examining potential physiological mechanisms and biomarkers that may
315 help guide personalised exercise prescription among critically ill patients.

316

317 **Conclusion:**

318 Critically ill patients who spent more than 48 hours in ICU often did not complete exercise
319 interventions whilst in ICU, and the commencement of exercise was somewhat delayed despite most
320 patients achieving neurological, respiratory and cardiovascular stability relatively early in their ICU
321 admission. A range of patient and clinical factors associated with time-to-commencement of sitting
322 and upright activity were identified that may help inform the development of clinical practice protocols
323 to help reduce unnecessary delays in these activities among critically ill patients.

324

325

326 **Ethical Approval:** Ethical approval for the study was obtained from the Metro South Human
327 Research Ethics Committee (HREC/12/QPAH/009) and from the Queensland University of
328 Technology University Human Research Ethics Committee (1400000587).

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332

333 **Conflicts of interest:** None to declare

334

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338

339

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341

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455

Table 1: Definition of patient physiological stability used for the present study examining early exercise interventions in intensive care

| Physiological variable | Variable range |
|-----------------------------------|--|
| Neurological stability | |
| Glasgow Coma Scale | M6 (able to follow commands) E4 (eyes open) |
| Richmond Agitation-Sedation Score | -1 to +1 |
| Respiratory stability | |
| Fraction of inspired oxygen | 0.6 or less |
| Positive end expiratory pressure | 10 cmH ₂ O or less |
| Respiratory rate | 30 breaths per minute or less |
| Pulse oximetry oxygen saturations | 90% or greater |
| Cardiovascular stability | |
| Heart rate | 60–120 beats per minute |
| Mean arterial blood pressure | 65–110 mmHg |
| Vasoactive medication infusions* | Absence of vasoactive medications |

*noradrenaline, dopamine, adrenaline, vasopressin, milrinone, glyceryl trinitrate, sodium nitroprusside.

Table 2. Patient characteristics and outcomes for patient admissions where stability was achieved

| Variable | Cohort, n= 3222 ^a (100%) | Participated in exercise interventions ^b , n= 1845 (57%) | Did not participate in exercise interventions, n= 1377 (43%) |
|---|--|--|--|
| Age in years, mean (SD) | 53.5 (17.6) | 54.4 (17.1) | 52.3 (18.2) |
| Males, n (%) | 2169 (67%) | 1247 (68%) | 922 (67%) |
| Received dialysis, n (%) | 293 (9%) | 159 (9%) | 134 (10%) |
| Admission type, n (%) | | | |
| Medical (non-surgical) | 2096 (65%) | 1193 (65%) | 903 (66%) |
| Trauma | 455 (14%) | 211 (11%) | 244 (18%) |
| Cardiac | 421 (13%) | 223 (12%) | 198 (14%) |
| Sepsis | 343 (11%) | 219 (12%) | 124 (9%) |
| Neurological | 302 (9%) | 150 (8%) | 152 (11%) |
| Respiratory | 296 (9%) | 206 (11%) | 90 (7%) |
| Abdominal | 139 (4%) | 82 (4%) | 57 (4%) |
| Other | 140 (4%) | 102 (6%) | 38 (3%) |
| Emergency surgical | 652 (20%) | 311 (17%) | 341 (25%) |
| Trauma surgery | 254 (8%) | 86 (5%) | 168 (12%) |
| Cardiac and vascular surgery | 125 (4%) | 83 (4%) | 42 (3%) |
| Abdominal surgery | 120 (4%) | 74 (4%) | 46 (3%) |
| Neurological surgery | 80 (2%) | 28 (2%) | 52 (4%) |
| Other emergency surgery | 73 (2%) | 40 (2%) | 33 (2%) |
| Elective surgical | 474 (15%) | 341 (19%) | 133 (10%) |
| Cardiac and vascular surgery | 281 (9%) | 219 (12%) | 62 (5%) |
| Cancer related surgery | 50 (2%) | 34 (2%) | 16 (1%) |
| Liver transplant | 49 (2%) | 39 (2%) | 10 (1%) |
| Neurological surgery | 45 (1%) | 19 (1%) | 26 (2%) |
| Other elective surgery | 49 (2%) | 30 (2%) | 19 (1%) |
| APACHE III score, median (IQR) | 57 (42, 75) | 56 (42, 73) | 59 (42, 77) |
| Required MV, n (%) | 2969 (92%) | 1711 (93%) | 1258 (91%) |
| Length of MV, days, median (IQR) ^c | 1.5 (0.5, 3.6) | 1.6 (0.6, 3.8) | 1.5 (0.5, 3.3) |

| | | | |
|--|-------------------|-------------------|-------------------|
| ICU length of stay ^d , days, median (IQR) | 4.9 (3.0, 9.5) | 4.9 (3.0, 9.9) | 4.8 (3.0, 9.1) |
| Hospital stay ^e , days, median (IQR) | 19.9 (11.3, 34.6) | 17.4 (10.5, 31.2) | 24.4 (13.7, 39.6) |
| ICU discharge destination, n (%) | | | |
| Acute hospital ward | 2979 (93%) | 1809 (98%) | 1170 (85%) |
| Died in ICU | 200 (6%) | 10 (1%) | 190 (14%) |
| Transferred to other acute hospital | 24 (1%) | 12 (1%) | 12 (1%) |
| Home | 16 (1%) | 11 (1%) | 5 (<1%) |
| Transferred to rehabilitation facility | 3 (<1%) | 3 (<1%) | 0 (0%) |
| Acute hospital discharge destination, n (%) | | | |
| Home | 1888 (59%) | 1274 (69%) | 614 (45%) |
| Died in Hospital | 421 (13%) | 92 (5%) | 329 (24%) |
| Transferred to a rehabilitation facility | 630 (20%) | 313 (17%) | 317 (23%) |
| Other acute hospital | 282 (9%) | 166 (9%) | 116 (8%) |
| Palliative care hospital | 1 (<1%) | 0 (0%) | 1 (<1%) |

^a 2983 unique individuals representing 3222 ICU admissions during study period

^b Participated in exercise: completed either sitting activity or upright activity (or both) in ICU

^c Calculated for those who were invasively mechanically ventilated

^d Length of stay for patients who survived ICU admission

^e Length of stay for patients who survived acute hospital admission

SD, standard deviation, n, number; APACHE III = Acute Physiology and Chronic Health Evaluation III severity of illness score (0-299); IQR, interquartile range; MV, mechanical ventilation; ICU, intensive care unit.

Table 3: Description of whether sitting and upright activity occurred in patients who achieved physiological stability, and time to these activities (n = 3222)

| Outcome | Sitting activity | Upright activity |
|--|------------------|------------------|
| Completed activity after achieving stability, n (% of admissions ^a) | 1842 (57.2%) | 1454 (45.1%) |
| Time from stability to first complete activity, days, median (IQR) | 2.7 (1.5, 5.7) | 2.3 (1.3, 4.4) |
| Time from ICU admit to first complete activity, days, median (IQR) | 3.6 (2.0, 7.7) | 3.3 (2.0, 6.7) |
| Achieved stability but not activity, n (% of admissions ^a) | 1377 (42.7%) | 1768 (54.9%) |
| Completed activity prior to achieving stability, n (% of admissions ^a) | 3 (0.1%) | 1 (<0.1%) |
| Completed activity but never achieved stability, n (% of admissions ^b) | 6 (0.2%) | 6 (0.2%) |

^a cohort of patients who achieved physiological stability

^b all admissions

ICU, intensive care unit, IQR, interquartile range; n, number.

Table 4: Findings from the logistic regression examining patient and clinical factors associated with whether i) sitting activity, and ii) 'upright activity' occurred in ICU for patients who achieved stability n=3222

| Activity achieved | Independent variables | Odds ratio | 95% CI | p-value |
|-------------------------------------|------------------------------|-------------|-------------|---------|
| i) Achieved sitting activity in ICU | Age (per 10 years) | 1.10 | (1.05-1.15) | <0.001 |
| | Male | 1.00 | (0.86-1.16) | 0.99 |
| | APACHE III (per 10) | 0.92 | (0.89-0.96) | <0.001 |
| | Admission type | | | |
| | Medical admission | Referent | | |
| | Elective surgical admission | 1.76 | (1.40-2.21) | <0.001 |
| | Emergency surgical admission | 0.64 | (0.53-0.76) | <0.001 |
| | MV time (days) | 1.04 | (1.02-1.06) | <0.001 |
| Received dialysis | 0.96 | (0.74-1.25) | 0.76 | |
| i) Achieved upright activity in ICU | Age (per 10 years) | 1.10 | (1.05-1.15) | <0.001 |
| | Male | 1.03 | (0.89-1.20) | 0.69 |
| | APACHE III (per 10) | 0.92 | (0.89-0.95) | <0.001 |
| | Admission type | | | |
| | Medical admission | Referent | | |
| | Elective surgical admission | 1.59 | (1.29-1.97) | <0.001 |
| | Emergency surgical admission | 0.68 | (0.57-0.81) | <0.001 |
| | MV time (days) | 0.99 | (0.97-1.01) | 0.29 |
| Received dialysis | 1.00 | (0.77-1.31) | 0.97 | |

CI, confidence interval; p, probability; APACHE III = Acute Physiology and Chronic Health Evaluation III severity of illness score; MV, mechanical ventilation; ICU, intensive care unit.

Table 5: Hazard Ratios from a Cox regression examining the factors associated with time to commencement of sitting activity and upright activity in ICU since stability

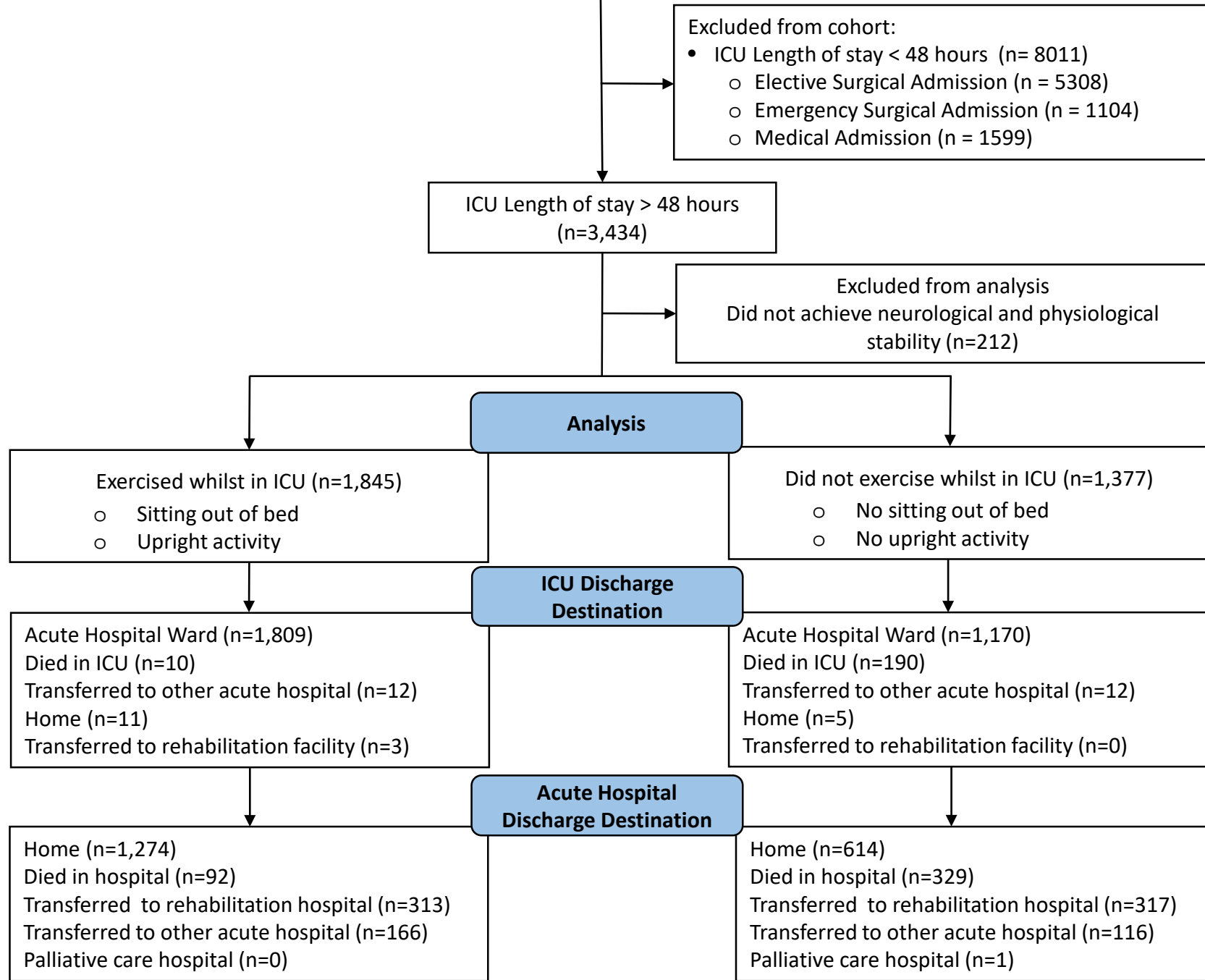
| Time to activity | Independent variables | Hazard ratio ^a | 95% CI | p-value |
|---|--|---------------------------|-------------|-------------|
| i) Time to sitting activity ^b in ICU since stability | Age (per 10 years) | 1.05 | (1.02-1.08) | <0.01 |
| | Male | 0.97 | (0.88-1.07) | 0.54 |
| | APACHE III (per 10) | 0.95 | (0.93-0.97) | <0.001 |
| | Admission type | | | |
| | Medical admission | Referent | | |
| | Elective surgical admission | 1.68 | (1.47-1.92) | <0.001 |
| | Emergency surgical admission | 0.71 | (0.62-0.80) | <0.001 |
| | MV time (days) | 0.92 | (0.90-0.94) | <0.001 |
| | Received dialysis | 0.63 | (0.53-0.74) | <0.001 |
| | ii) Time to upright activity ^c in ICU since stability | Age (per 10 years) | 1.05 | (1.01-1.08) |
| Male | | 1.00 | (0.89-1.11) | 0.95 |
| APACHE III (per 10) | | 0.93 | (0.91-0.96) | <0.001 |
| Admission type | | | | |
| Medical admission | | Referent | | |
| Elective surgical admission | | 1.62 | (1.41-1.87) | <0.001 |
| Emergency surgical admission | | 0.73 | (0.63-0.85) | <0.001 |
| MV time (days) | | 0.88 | (0.87-0.91) | <0.001 |
| Received dialysis | | 0.67 | (0.56-0.82) | <0.001 |

CI, confidence interval; p, probability; APACHE III = Acute Physiology and Chronic Health Evaluation III severity of illness; MV, mechanical ventilation; ICU, intensive care unit.,

^aHazard ratio greater than 1.0 indicates a shorter time to event.

^bn=3219 (3434 observations, 212 patients did not achieve stability and 3 individuals completed activity without achieving stability excluded from analysis)

^cn=3221 (3434 observations, 212 patients did not achieve stability and 1 individual completed activity without achieving stability excluded from analysis)



Supplementary Table 1: Keywords used to search electronic medical records for exercise interventions

| Inclusion | Keywords |
|------------------|--|
| Sitting Activity | edge, lie to sit, oxford chair, patslide, sit* (sit out of bed, sitting balance, sitting out, sitting over), SOEOB, SOOB. |
| Upright Activity | FASF, mob* (mobile, mobilise, mobility), MOS, on spot, rollator, stand, spot, step, stood, "sit to stand", STS, tilt, table, walk. |
| Excluding | plan, P:, P/, chair position, nil, not, unable, sit up |

SOEOB; sit on edge of bed, SOOB; sitting out of bed, FASF; forearm support frame, MOS; march on spot, STS; sit to stand P: plan, P/; plan.

Supplementary Table 2: Description of outcomes for patients relative to achieving physiological stability (n = 3434)

| Outcome | Cohort (n = 3434) |
|---|-------------------|
| Achieved physiological stability, n (% of admissions) | 3222 (93.8%) |
| Did not achieve physiological stability, n (% of admissions) | 212 (6.2%) |
| Time from ICU admission to achieve stability, median (IQR) | 0.6 (0.2,1.5) |
| Acute Hospital Mortality of patients who achieved stability, n (% of admissions ^a) | 395 (12.3%) |
| Acute Hospital Mortality of patients who did not achieve stability, n (% of admissions ^b) | 186 (87.7%) |

^a cohort of patients who achieved physiological stability

^b cohort of patients who did not achieve physiological stability
ICU, intensive care unit; IQR, interquartile range; n, number.

Supplementary Table 3. Patient characteristics and outcomes for patient admissions where stability was not achieved

| Variable | Cohort, n= 212 ^a (100%) |
|---|------------------------------------|
| Age in years, mean (SD) | 54.2 (17.5) |
| Males, n (%) | 139 (65.6%) |
| Received dialysis, n (%) | 25 (11.8%) |
| Admission type, n (%) | |
| Medical | 140 (66.0%) |
| Elective surgical | 40 (18.9%) |
| Emergency surgical | 32 (15.1%) |
| APACHE III score, median (IQR) | 56 (42, 73) |
| Required MV, n (%) | 173, (81.6%) |
| Length of MV, days, median (IQR) ^b | 1.0 (0.2, 2.7) |
| ICU length of stay, days, median (IQR) | 3.9 (2.8, 6.9) |
| Hospital stay, days, median (IQR) | 5.0 (3.2, 8.7) |
| ICU discharge destination, n (%) | |
| Acute hospital ward | 54 (25.5%) |
| Died in ICU | 157 (74.1%) |
| Transferred to other acute hospital | 1 (0.5%) |
| Home | 0 (0%) |
| Transferred to rehabilitation facility | 0 (0%) |
| Acute hospital discharge destination, n (%) | |
| Home | 12 (5.7%) |
| Died in Hospital | 186 (87.7%) |
| Transferred to a rehabilitation facility | 4 (1.9%) |
| Other acute hospital | 10 (4.7%) |

^a 208 unique individuals representing 212 ICU admissions during study period

^b Calculated for those who were invasively mechanically ventilated

SD, standard deviation, n, number; APACHE III = Acute Physiology and Chronic Health Evaluation III severity of illness score (0-299); IQR, interquartile range; MV, mechanical ventilation; ICU, intensive care unit.