Original Investigation

# Increased Hospital-Based Physical Rehabilitation and Information Provision After Intensive Care Unit Discharge
## The RECOVER Randomized Clinical Trial

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**IMPORTANCE** Critical illness results in disability and reduced health-related quality of life (HRQOL), but the optimum timing and components of rehabilitation are uncertain.

**OBJECTIVE** To evaluate the effect of increasing physical and nutritional rehabilitation plus information delivered during the post–intensive care unit (ICU) acute hospital stay by dedicated rehabilitation assistants on subsequent mobility, HRQOL, and prevalent disabilities.

**DESIGN, SETTING, AND PARTICIPANTS** A parallel group, randomized clinical trial with blinded outcome assessment at 2 hospitals in Edinburgh, Scotland, of 240 patients discharged from the ICU between December 1, 2010, and January 31, 2013, who required at least 48 hours of mechanical ventilation. Analysis for the primary outcome and other 3-month outcomes was performed between June and August 2013; for the 6- and 12-month outcomes and the health economic evaluation, between March and April 2014.

**INTERVENTIONS** During the post-ICU hospital stay, both groups received physiotherapy and dietetic, occupational, and speech/language therapy, but patients in the intervention group received rehabilitation that typically increased the frequency of mobility and exercise therapies 2- to 3-fold, increased dietetic assessment and treatment, used individualized goal setting, and provided greater illness-specific information. Intervention group therapy was coordinated and delivered by a dedicated rehabilitation practitioner.

**MAIN OUTCOMES AND MEASURES** The Rivermead Mobility Index (RMI) (range 0-15) at 3 months; higher scores indicate greater mobility. Secondary outcomes included HRQOL, psychological outcomes, self-reported symptoms, patient experience, and cost-effectiveness during a 12-month follow-up (completed in February 2014).

**RESULTS** Median RMI at randomization was 3 (interquartile range [IQR], 1-6) and at 3 months was 13 (IQR, 10-14) for the intervention and usual care groups (mean difference, −0.2 [95% CI, −1.3 to 0.9; $P = .71$]). The HRQOL scores were unchanged by the intervention (mean difference in the Physical Component Summary score, −0.1 [95% CI, −3.3 to 3.1; $P = .96$]; and in the Mental Component Summary score, 0.2 [95% CI, −3.4 to 3.8; $P = .91$]). No differences were found for self-reported symptoms of fatigue, pain, appetite, joint stiffness, or breathlessness. Levels of anxiety, depression, and posttraumatic stress were similar, as were hand grip strength and the timed Up & Go test. No differences were found at the 6- or 12-month follow-up for any outcome measures. However, patients in the intervention group reported greater satisfaction with physiotherapy, nutritional support, coordination of care, and information provision.

**CONCLUSIONS AND RELEVANCE** Post-ICU hospital-based rehabilitation, including increased physical and nutritional therapy plus information provision, did not improve physical recovery or HRQOL, but improved patient satisfaction with many aspects of recovery.

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Patients surviving critical illness frequently experience disabilities, poor health-related quality of life (HRQOL), and reduced ability to undertake activities of daily living.[1,2] Observational studies indicate high levels of fatigue, muscle weakness, and other symptoms that may contribute to delayed recovery.[1,3] Cognitive impairment, depression, anxiety, and posttraumatic stress are also prevalent.[4-6] Although patients are often older or have preexisting comorbidity,[7] many were previously fit and of working age. The long-term costs of critical illness at individual, family, and societal levels are high.[8,9]

Regular assessment and individualized rehabilitation have been recommended from the time of intensive care unit (ICU) admission until at least 2 to 3 months after hospital discharge[10]; in the United Kingdom, this assessment and rehabilitation constitute a national quality standard.[11] However, less than 30% of UK health care organizations provide any formal post-ICU rehabilitation service,[12] and few data exist for other health care systems. The optimum organization, timing, and key components of rehabilitation after ICU discharge are uncertain.[10,13] Published research suggests that early mobilization during ICU care is effective,[14] but post-ICU self-directed exercise programs,[15] protocol-based exercise rehabilitation,[16] and post-hospital discharge follow-up clinics[17] did not generate measurable benefits. One trial found improved physical outcomes with the supported use of a rehabilitation manual at 3 months.[18]

Interventions designed to meet a range of patient needs concurrently, from ICU discharge through the remainder of the hospital stay when patients often become dispersed across different wards and specialties, have not been evaluated. The RECOVER (Evaluation of a Rehabilitation Complex Intervention for Patients Following Intensive Care Discharge) Collaboration[19-22] undertook a program of work, including research with patients discharged from the ICU, to identify rehabilitation requirements during the early post-ICU period, with the primary focus on physical rehabilitation and provision of information. We developed a model for supplementing existing therapy with a dedicated multiskilled rehabilitation assistant (RA) and herein report the effect of this rehabilitation strategy on physical and psychological outcomes, HRQOL, and patient satisfaction. We also report the cost-effectiveness of the intervention during the 12 months after randomization.

## Methods

We undertook a prospective, parallel-group, randomized clinical trial with blinded outcome assessment at 2 hospitals in Edinburgh, Scotland. These hospitals housed 34 of 39 regionally funded medical and surgical ICU beds (cardiac and pediatric services were managed separately). During the ICU stay, all patients received daily review of sedation, with reduction when appropriate. As routine care, physiotherapists in both ICUs provided respiratory assessment and treatment within 24 hours of admission to the ICU, which was ongoing throughout the ICU stay. The ICU team assessed rehabilitation needs and provided treatment as indicated, including exercises and early mobilization. The trial protocol and analysis plan have been published previously[19] and can be found in Supplement 1. Patients receiving a minimum of 48 hours of mechanical ventilation were eligible for the study when declared fit for ICU discharge by the responsible physician. Exclusion criteria consisted of a primary neurologic diagnosis, palliative care, current or planned home ventilation, being younger than 18 years, and discharge to a nonstudy hospital (**Figure 1**). This study was approved by the Scotland A Research Ethics committee. Participants or their surrogate decision makers provided written informed consent.

### Intervention and Usual Care Practices

The target intervention period was the acute period from ICU discharge through a hospital stay of no longer than 3 months, when the primary outcome was assessed. In the United Kingdom, ICU discharge typically occurs within 2 to 3 days of discontinuing mechanical ventilation, and patients become dispersed across specialty ward areas according to the referring specialist service or the service considered most appropriate for post-ICU specialist care, with clinical responsibility transitioning to ward-based medical, nursing, and allied health professional teams. For both trial groups, the focus of rehabilitation was to maximize the rate and degree of physical recovery and to achieve a level of mobility and self-care that enabled hospital discharge. Pretrial work indicated that variation in patient disability meant that compliance with highly protocol-driven exercise, nutrition, and other therapy was poor at this stage of recovery. Patients therefore received individualized therapies, which were regularly reviewed and modified according to progress. The trial aimed to investigate whether a strategy that increased mobility, exercise, nutrition, and other relevant therapies was more effective than the existing practice. Key differences were greater coordination, intensity, and frequency of individual rehabilitation therapies. Enhanced provision of information was identified as an unmet patient need and was included as part of the intervention strategy, with the hypothesis that it might support short- and longer-term self-management and psychological morbidity.

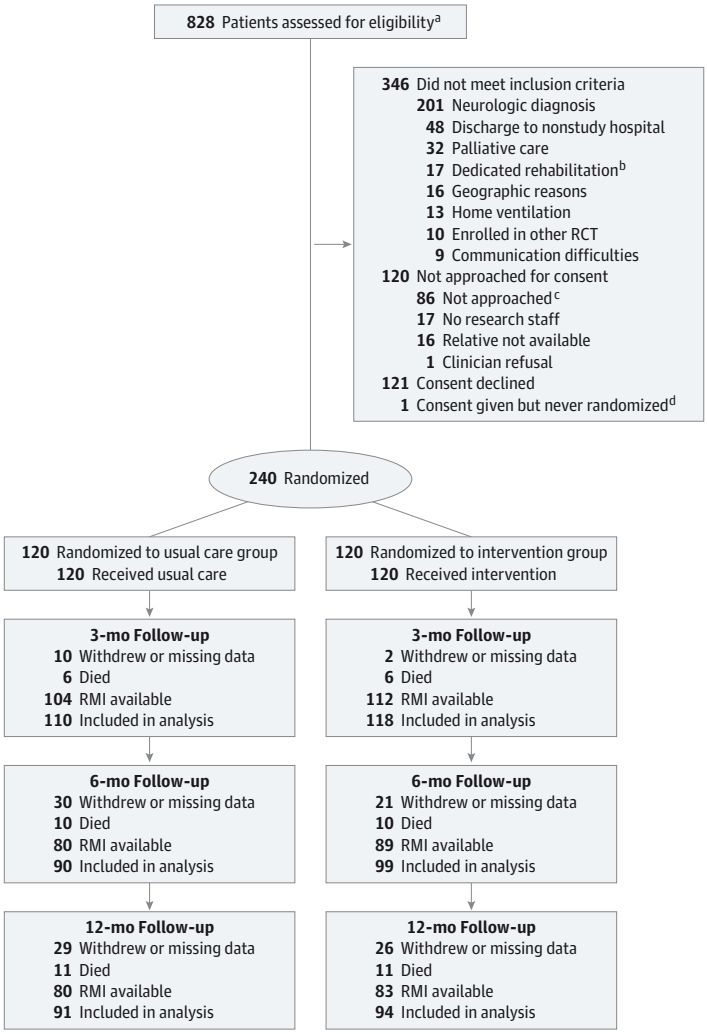
#### Usual Care Group

For the usual care group, we aimed to deliver rehabilitation currently typical in UK hospitals after ICU discharge. This care was provided by ward-based multidisciplinary teams (principally physiotherapy [PT], dietetics, speech/language therapy [SLT], and occupational therapy [OT]); the frequency and intensity of therapy was not controlled by the trial protocol to ensure that it represented current practice. All patients received a self-help ICU rehabilitation manual previously associated with improved physical recovery and recommended in UK guidelines.[18] Pretrial work had benchmarked the frequency and intensity of usual care treatment in the participating hospitals.[21]

#### Intervention Group

For the intervention group, we aimed to deliver higher levels of mobilization, exercise, and relevant dietetic therapy, OT, and SLT compared with usual care. The intervention strategy was

Figure 1. CONSORT Diagram for the Trial




RCT indicates randomized controlled trial; RMI, Rivermead Mobility Index (range, 0-15, with lower scores indicating poorer physical function).

[a] Of 3849 admissions to the 2 intensive care units (ICUs) during the recruitment period, 1055 required 48 hours or more of mechanical ventilation; of these, 828 were discharged from the ICU (227 deaths in the ICU).

[b] Included 14 patients undergoing liver transplant and 3 patients with cardiac rehabilitation.

[c] The reasons for not approaching 86 patients included no rehabilitation assistant available owing to change in staff or leave (n = 49); patients were about to be discharged from the hospital (n = 27); patients were prisoners (n = 4); palliative care was imminent at the time of approach (n = 3); intervention was not feasible (n = 1); the patient refused treatment (n = 1); and the patient hired a private physiotherapist (n = 1).

[d] One patient consented but the clinical team then made a decision to discharge him or her from the hospital, so the patient was not randomized.

developed before the trial using qualitative research with patients, literature review, multidisciplinary expert input, and piloting; Medical Research Council guidance for developing complex interventions was followed.[20] As with the usual care group, treatment was provided by ward-based therapists but was supplemented by 3 multiskilled dedicated RAs working under the supervision of senior therapists. The RAs received pretrial competency-based training in PT, dietetics, SLT, OT, and psychological support relevant to patients discharged from the ICU.[20] The RAs assessed patients daily and delivered a wide range of treatments on weekdays, with individualized therapy across all therapy domains aimed at promoting physical recovery and self-care. Prespecified screening and trigger tools were used to involve relevant senior specialist staff as required (especially for OT and SLT). Wherever possible, individualized rehabilitation goals were regularly agreed upon with patients to assist motivation and mark achievement. The RAs worked across all hospital wards, contributed to hospital discharge planning, and sent an individual patient status report to the patient's general practitioner. The RA role was developed and extensively piloted before the study[21,22] and funded specifically for the trial. The RAs tried to contact all patients at least once after hospital discharge to check their status, and patients were given mobile telephone numbers to contact their nominated RA for advice/support. In addition, prespecified strategies were used to provide information to patients in the intervention group and their families, coordinated by the RAs. First, they were offered a meeting with an ICU consultant to discuss their illness and care; second, they received a lay summary of key events that occurred during their ICU stay; third, they were offered a visit to the ICU before hospital discharge; and fourth, RAs reinforced information whenever relevant when treating patients. Predefined topic guides were used to structure these strategies.[20]

## Randomization and Blinding

Randomization was undertaken by research staff by remote telephone-based randomization service. Randomization was by minimization with a random element using the following predefined factors: age (>65 vs ≤65 years), disability at study

entry (Rivermead Mobility Index [RMI][23] of 0-5 vs 6-10 vs 11-15), nutritional status at randomization (using the physical component of the Subjective Global Assessment tool[24]; malnourished vs well-nourished), the presence/absence of delirium (using the Confusion Assessment Method for the ICU tool[25]; delirium vs no delirium), and the ward destination (surgical vs medical). Group allocation was not formally communicated to clinical staff providing cointerventions or to patients, but formal blinding was not possible.

### Process Evaluation

A detailed process evaluation was undertaken to describe the rehabilitation treatments received using a taxonomy developed before the trial.[20] Data were collected from patient records of both groups by research staff at weekly intervals. Because the hospital length of stay was skewed, we calculated treatment frequency per week and for the overall hospital stay for major mobility/exercise and dietetic interventions. For mobilization/exercise treatments, we also calculated a summary statistic for the mean proportion of post-ICU hospital days on which each treatment type was delivered. Treatment type by specialty (PT, dietetics, OT, and SLT) delivered each week was summarized to describe rehabilitation by specialty. Delivery of the information-giving strategy was recorded for each element.

### Outcomes

Our primary outcome was the RMI[23] at 3 months after randomization. This hierarchical mobility index (range, 0-15, with higher values representing better physical function) captures function ranging from bedridden to ability to run using 15 discrete items (14 self-reported and 1 observed). We chose this measure because it has good validity, reliability, and responsiveness in stroke research and is unaffected by environmental influences.[26] The RMI also performed well in our pilot study[21] and was simple to administer, which made adjustment for baseline function and long-term follow-up feasible (for a detailed description of the RMI scoring system, see eTable 4 in Supplement 2). To acknowledge the range of health and disability issues that contribute to the post-ICU syndrome, we measured a range of secondary outcomes. Hospital outcomes included post-ICU length of stay, readmission to the ICU, hospital survival, and RMI before hospital discharge. Patient-reported outcome measures at 3, 6, and 12 months after randomization included the Physical and the Mental Component Summary scores of the 12-Item Short Form Health Survey (HRQOL; range, 0-100; typical population mean, 50, with higher values representing better health),[27] the Hospital Anxiety and Depression Scale (anxiety and depressive symptoms; each subscale range, 0-21, with higher values representing worse symptoms),[28] the Davidson Trauma Scale (traumatic symptoms; range, 0-136, with higher scores representing worse symptoms),[29] and 5 self-reported symptom scores using visual analog scales for fatigue, breathlessness, appetite, pain, and joint stiffness (range, 0 [no symptoms] to 10 [worst symptoms]). In addition to comparing scores as continuous measures, we prespecified a Hospital Anxiety and Depression Scale score of at least 8 and a Davidson Trauma Scale score of at least 27 as indicative of significant symptoms. At 3 months, patient experience was assessed using a satisfaction questionnaire for 9 aspects of care identified as important by patients discharged from the ICU in pretrial qualitative research.[30] At 3 months, muscle strength was measured using hand grip dynamometry, and mobility was measured using the 2-m timed Up & Go test.[31] Three-month assessments were undertaken face to face (at the patient's home or the hospital research facility) or by telephone when face-to-face follow-up was impossible by research staff blinded to group allocation. Later assessments were undertaken by postal follow-up.

### Study Size

In our pilot study, mean (SD) RMI at 3 months was 10 (4.3).[21] We predefined a minimum clinically important difference in the RMI of 2 points at 3 months between the groups, adjusted for the randomization RMI. To detect this difference we required 100 patients eligible for evaluation per group (80% power; 5% significance level). We assumed a 12% death rate during the intervention period and a 5% loss to follow-up, resulting in a sample size of 240 patients.

### Statistical Analysis

We used analysis of covariance to compare the primary and most secondary outcomes with adjustment for minimization variables. For patients who died, an RMI score of 0 was imputed. Unless stated, only adjusted analyses are presented. We used Mann-Whitney tests to compare visual analog scale responses for symptoms, patient satisfaction, and the 2-m timed Up & Go test results. We performed prespecified subgroup analyses for the RMI at 3 months for the following randomization variables: 65 years or younger vs older than 65 years; RMI of 0 to 5 vs 6 to 15 (groups with RMI of 6-10 and 11-15 were combined in this subgroup analysis because only 1 patient had a baseline RMI of 11-15 [usual care group]); and moderate/severe vs no/mild nutritional abnormality.

We undertook a cost-utility analysis from a National Health Service perspective according to the trial protocol, with costs limited to secondary care,[19] based on data from randomization to 12 months of follow-up. Costs are presented in US dollars (pounds sterling).

For process measures, medians (interquartile range [IQR]) and proportions (SEM) were used to describe treatments received by each group. Because these were not outcome measures, no statistical comparison between groups was reported.

## Results

Patients were recruited from December 1, 2010, through January 31, 2013. Analysis for the primary outcome and other 3-month outcomes was started in June 2013 and completed in August 2013. Analysis for the 6- and 12-month outcomes and the health economic evaluation took place from March through April 2014. Follow-up was completed in February 2014. Participants included 240 of 482 potentially eligible patients (49.8%). At 3 months, 12 patients had died (6 per group); pri-

mary outcome data were complete for 118 of the 120 patients in the intervention group (98.3%) and 110 of the 120 patients in the usual care group (91.7%). The trial CONSORT diagram is shown in Figure 1. Characteristics at randomization were similar between groups, indicating significant preexisting comorbidity and severe critical illness during the ICU stay (**Table 1**). The RMI scores at randomization indicated severe functional impairment (median score, 3 for both groups).

## Process Evaluation

A high proportion (>90%) of patients in both groups received some PT after discharge from the ICU, but the intervention group received all mobility/exercise treatment at a frequency of 2 to 3 times higher during their hospital stays (**Table 2**), and exercise/mobility was provided on 2 to 3 times more hospital days to the intervention group (eTable 1 in Supplement 2). The combined effect of all treatment types indicated substantially increased mobility/exercise therapy for the intervention group. More patients in the intervention group received dietetic review (95.0% vs 66.7%), and rates of monitoring nutritional requirements and intake were higher (Table 2). The use of trigger tools resulted in higher rates of OT for the intervention group (43.3% vs 32.5%), although similar proportions received SLT (19.2% vs 15.8%). Differences in PT, dietetic treatment, and OT persisted throughout the hospital stay as the in-patient cohort became progressively smaller (eTable 2 in Supplement 2). Individual goal setting was undertaken for more than 50% of weeks in the hospital for the intervention group but was not part of usual care (eTable 2 in Supplement 2). The information provision strategy resulted in much greater provision of information during the hospital stay (Table 2).

## Study Outcomes

Outcomes to 3 months are shown in **Table 3**; 6- and 12-month data are presented in eTable 3 in Supplement 2. The mean (SD) change in RMI from baseline to 3 months was 7.7 (4.8) for the usual care group and 7.9 (4.3) for the intervention group, resulting in a median RMI at 3 months of 13 (IQR, 10-14) for both groups. The adjusted mean difference was −0.2 (95% CI, −1.3 to 0.9; $P$ = .71). The trajectory of recovery in the RMI was similar for both groups during the 12-month postrandomization follow-up (Table 3; eTable 3 and eFigure 1 in Supplement 2), and individual RMI components were similar (eTable 4 in Supplement 2). We found no difference in the post-ICU hospital stay. Seven ICU readmissions occurred in the usual care group vs 1 in the intervention group. We found no differences in HRQOL, anxiety and depressive symptoms, posttraumatic symptoms, or any of the physical symptom scores between the groups at 3, 6, or 12 months (Table 3; eFigure 1 and eTable 3 in Supplement 2). However, these findings indicated substantially reduced HRQOL (especially for physical function), high rates of significant psychological symptoms, and prevalent physical symptoms (especially fatigue, pain, and joint stiffness). Scores tended to remain static for 3 to 12 months, notably in relation to HRQOL. Patients in the intervention group reported higher satisfaction across 6 of the 9 recovery domains, with statistically significant differences in relation to

**Table 1. Participant Characteristics at Randomization**

| Characteristic | Treatment Group | |
|---|---|---|
| | Usual Care (n = 120) | Intervention (n = 120) |
| Male sex, No. (%) | 70 (58.3) | 67 (55.8) |
| Age, median (IQR), y | 62 (53-69) | 62 (51-71) |
| Functional Comorbidity Index, median (IQR)[a] | 2 (1-4) | 2 (1-4) |
| Patients classified as social class 4 or 5 (deprivation), No. (%)[b] | 52 (43.3) | 54 (45.0) |
| Time from hospital to ICU admission, median (IQR), d | 1 (0-2) | 1 (0-2) |
| ICU admission diagnosis category, No. of patients | | |
| Cardiovascular | 35 | 35 |
| Respiratory | 43 | 41 |
| Gastrointestinal tract | 29 | 30 |
| Renal diagnosis | 1 | 2 |
| Trauma | 3 | 5 |
| Neurologic | 6 | 6 |
| Miscellaneous diagnoses | 3 | 1 |
| APACHE II score, median (IQR) | 19 (15-26) | 20 (17-24) |
| Duration of ventilation in ICU, median (IQR), d | 8 (4-15) | 9 (5-16) |
| Requirement, No. (%) | | |
| Vasopressor/inotropic support in ICU | 89 (74.2) | 89 (74.2) |
| Renal replacement therapy in ICU | 32 (26.7) | 32 (26.7) |
| Time in ICU before randomization, median (IQR), d | 11 (6-18) | 11 (6-18) |
| Status at randomization | | |
| RMI, median (IQR)[c] | 3 (1-7) | 3 (1-6) |
| Moderate to severe malnourishment, No. (%) | 65 (54.2) | 68 (56.7) |
| Delirium at randomization, No. (%) | 19 (15.8) | 16 (13.3) |
| Ward destination, No. (%) | | |
| Medical | 70 (58.3) | 66 (55.0) |
| Surgical | 50 (41.7) | 54 (45.0) |
| SOFA score at randomization, median (IQR)[d] | 2 (2-4) | 3 (2-4) |
| Time from ICU discharge to randomization, median (IQR), d | 2 (1-4) | 2 (1-4) |

Abbreviations: APACHE II, Acute Physiology and Chronic Health Evaluation; ICU, intensive care unit; IQR, interquartile range; RMI, Rivermead Mobility Index; SOFA, Sequential Organ Failure Assessment.

[a] Indicates a measure of chronic disease, which is strongly associated with physical health-related qualify of life (HRQOL). It has 18 disease domains, each scoring 0 or 1, with the total score ranging from 0 to 18, with higher scores indicating more comorbidities (correlated with poorer HRQOL).[32]

[b] Deprivation was derived from the patient postcode (zip code), which has been mapped to social deprivation as part of the Scottish Index of Multiple Deprivation, a government-funded national resource. These were grouped into 5 quintiles, where 5 indicates the highest level of social deprivation (http://www.gov.scot/Topics/Statistics/SIMD).

[c] Scores range from 0 to 15, with lower scores indicating poorer physical function. For full description of the RMI categories, see eTable 4 in Supplement 2.

[d] Indicates a categoric measure of organ dysfunction in critically ill patients. Six categories (cardiovascular, respiratory, renal, hepatic, hematologic, and neurologic) are graded 0 (no dysfunction) to 4 (severe dysfunction). Total SOFA ranges from 0 to 24.[33]

Table 2. Comparison of Major Treatments Received During the Intervention Period According to the Predefined Key Elements of the Rehabilitation Intervention

| Stage of Patient Journey | Treatment Group | |
|---|---|---|
| | Usual Care (n = 120) | Intervention (n = 120) |
| **ICU Discharge** | | |
| Provision of ICU recovery manual, No. (%) | 120 (100) | 120 (100) |
| Structured discussion with ICU consultant, No. (%) | 0 | 68 (56.7) |
| Provision of lay summary of illness, No. (%) | 0 | 114 (95.0) |
| **Ward-Based Rehabilitation** | | |
| Patients receiving therapy types at least once during ward stay, No. (%) | | |
| PT | 111 (92.5) | 118 (98.3) |
| Dietetics | 80 (66.7) | 114 (95.0) |
| OT | 39 (32.5) | 52 (43.3) |
| SLT | 19 (15.8) | 23 (19.2) |
| Hospital treatment, median rate per week (IQR) [range] | | |
| Transfers | 1 (0-2) [0-6] | 2 (1-4) [0-14] |
| Walking | 2 (1-3) [0-7] | 4 (2-6) [0-21] |
| Exercises | 0 (0-1) [0-5] | 2 (1-4) [0-14] |
| Balance work | 0 (0-0) [0-5] | 1 (0-2) [0-7] |
| Stairs | 0 (0-1) [0-3] | 1 (0-1) [0-7] |
| Mobility advice | 0 (0-1) [0-7] | 1 (0-2) [0-7] |
| Calorie and protein requirement calculated | 0 (0-0) [0-2] | 0 (0-1) [0-7] |
| Actual calorie and protein intake calculated | 0 (0-0) [0-3] | 3 (2-4) [0-14] |
| Total No. of treatments during hospital stay, median (IQR) [range] | | |
| Transfers | 2 (0-5) [0-23] | 4 (1-8) [0-39] |
| Walking | 3 (1-6) [0-22] | 6 (3-12) [0-48] |
| Exercises | 0 (0-2) [0-33] | 4 (2-9) [0-70] |
| Balance work | 0 (0-0) [0-23] | 1 (0-3) [0-23] |
| Stairs | 0 (0-1) [0-7] | 1 (0-2) [0-21] |
| Mobility advice | 0 (0-1) [0-10] | 1 (0-3) [0-22] |
| Calorie and protein requirement calculated | 0 (0-1) [0-9] | 1 (0-2) [0-10] |
| Actual calorie and protein intake calculated | 0 (0-1) [0-8] | 5 (2-11) [0-54] |
| Hospital discharge, No. (%) | | |
| Offered ICU visit before hospital discharge | 0 | 90 (75.0) |
| Visited ICU | 2 (1.7) | 17 (14.2) |
| Structured status summary sent to general practitioner/family physician | 0 | 116 (96.7) |
| **After Hospital Discharge** | | |
| Follow-up contact with study rehabilitation team, No. (%) | 0 | 90 (75.0) |
| No. of contacts, median (IQR) | 0 | 2 (1-2) |

Abbreviations: ICU, intensive care unit; IQR, interquartile range; OT, occupational therapy; PT, physiotherapy; SLT, speech/language therapy.

PT, eating/nutritional support, organization/coordination of care, and information provision (**Figure 2**).

For the predefined subgroups, no significant differences in the RMI at 3 months were found for those 65 years or younger vs older than 65 years (mean difference, 0.1 [95% CI, −1.3 to 1.4] vs −0.3 [95% CI, −2.1 to 1.5]); baseline RMI of 0 to 5 (mean difference, 0.05 [95% CI, −1.4 to 1.5]) vs 6 to 15 (mean difference, −0.7 [95% CI, −2.4 to 0.9]); or baseline moderate/severe (mean difference, −1.1 [95% CI, −2.6 to 0.4]) vs no/mild (mean difference, 0.8 [95% CI, −0.8 to 2.4]) malnutrition. No serious adverse events were attributed to the study intervention.

Mean postrandomization secondary health care costs through 12 months were similar for the intervention ($81 000 [£49 000]; range, $12 000-$412 000 [£7000-£249 000]) and usual care ($81 000 [£49 000]; range, $17 000-$502 000 [£10 000-£304 000]) groups (see also eTable 5 in Supplement 2). In generalized linear regression models accounting for the skewed cost distribution and estimations of additional costs associated with intervention delivery, the point estimate found the intervention led to a nonsignificant additional $3000 (£2000) cost (95% CI, −$7000 to $13 000 [−£4000 to £8000]; see eTable 6 in Supplement 2). We found no difference in mean (SD) quality-adjusted life-years between the intervention (0.54 [0.20]) and usual care (0.54 [0.18]) groups (difference, 0.00 [95% CI, −0.04 to 0.04]). Based on the RA salaries alone, the additional cost of providing this service was approximately $1100 (£700) per patient treated. The point estimate of the incremental cost-effectiveness ratio lay in the northwest quadrant (see eFigure 2 in Supplement 2), indicating that the intervention was not cost-effective. More detailed analysis is available in the eAppendix of Supplement 2.

## Discussion

We compared the effectiveness of rehabilitation that primarily increased the frequency of mobilization and exercise therapy, dietetic management, and provision of information to existing care between the discharges from the ICU and hospital. Although the frequency of therapy episodes increased 2- to 3-fold across multiple domains and monitoring of nutrition increased, patient recovery of mobility, physical function, HRQOL, and self-reported symptoms were no different from those of the usual care group at 3 months or during the 12-month follow-up. Health care costs were similar, and the intervention generated no benefit based on quality-adjusted life-years. However, at the 3-month assessment, patients appeared more satisfied with many aspects of care.

We excluded the predefined minimum clinically important difference in the RMI at 3 months. Twenty-five percent of patients achieved RMI scores of 14 of 15, which suggests a ceiling effect that could have reduced the responsiveness of this measure. However, groups also had similar RMIs at hospital discharge, suggesting that the RMI was not altered by the intervention. The similar muscle strength and mobility measures at 3 months further support this conclusion. The Physical Component Summary scores were also similar throughout follow-up, and the precision of the intergroup differences made a variation of more than 3 points (equivalent to an effect size of approximately 0.25) unlikely, which excludes even small clinical differences with this HRQOL measure.[34] The

Table 3. Primary and Secondary Outcome Measures

| Outcome (No. of Patients With Evaluable Data in Usual Care/Intervention Groups) | Treatment Group | | Difference Scores, Mean (95% CI) | *P* Value |
|---|---|---|---|---|
| | Usual Care | Intervention | | |
| RMI at 3 mo (110/118)[a] | 13 (10 to 14) | 13 (10 to 14) | −0.2 (−1.3 to 0.9)[b] | .71 |
| **Hospital Discharge Outcome** | | | | |
| Post-ICU hospital length of stay, d (119/119)[c] | 10 (6 to 23) | 11 (6 to 22) | 0 (−2 to 2)[b] | .90 |
| RMI (84/83)[d] | 8 (5 to 10) | 8 (6 to 11) | −0.7 (−1.7 to 0.4)[b] | .20 |
| Handgrip strength, kg (82/82)[e] | 15.0 (9.7 to 22.6) | 14.7 (10.0 to 22.0) | 1.1 (−1.3 to 3.6)[b] | .36 |
| VAS symptom score, median (IQR) (83/80) [f] | | | | |
| Breathlessness | 2.8 (1.1 to 5.3) | 2.5 (1.0 to 5.0) | 0.2 (−0.5 to 1.0) | .49 |
| Fatigue | 5.0 (3.2 to 6.7) | 5.1 (2.7 to 7.2) | 0.0 (−0.9 to 0.9) | .96 |
| Appetite | 4.1 (1.7 to 6.7) | 5.0 (1.9 to 7.6) | −0.4 (−1.6 to 0.4) | .33 |
| Pain | 2.6 (0.7 to 5.2) | 2.3 (0.8 to 4.7) | 0.0 (−0.6 to 0.8) | .89 |
| Joint stiffness | 3.6 (1.1 to 6.2) | 3.3 (1.1 to 4.9) | 0.5 (−0.3 to 1.5) | .21 |
| Destination, % (116/118)[g] | | | | |
| Own residence | 72 | 76 | NA | NA |
| Rehabilitation hospital/facility | 13 | 13 | NA | NA |
| Other acute care nonstudy hospital | 7 | 6 | NA | NA |
| Other | 6 | 3 | NA | NA |
| Died | 2 | 2 | NA | NA |
| **3-mo Outcome** | | | | |
| Death, No. (%) (110/118)[h] | 6 (5) | 6 (5) | | >.99 |
| SF-12 PCS score, median (IQR) (96/101)[i] | 35 (26 to 44) | 34 (26 to 44) | −0.1 (−3.3 to 3.1)[b] | .96 |
| SF-12 MCS score, median (IQR) (96/101)[i] | 47 (33 to 56) | 45 (34 to 54) | 0.2 (−3.4 to 3.8)[b] | .91 |
| HADS Anxiety score (87/98)[j] | | | | |
| Median (IQR) | 6 (3 to 10) | 7 (3 to 11) | 0.2 (−1.6 to 1.4)[b] | .73 |
| ≥8, % | 36 | 46 | | |
| HADS Depression score (87/98)[j] | | | | |
| Median (IQR) | 7 (4 to 10) | 7 (4 to 9) | 0.5 (−0.7 to 1.6)[b] | .44 |
| ≥8, % | 45 | 37 | | |
| DTS score (78/82)[k] | | | | |
| Median (IQR) | 10 (2 to 22) | 11 (0 to 31) | 0 (−4 to 3)[b] | .83 |
| ≥27, % | 23 | 29 | | |
| 2-m Timed Up & Go test score, median (IQR), s (84/91)[l] | 10.3 (7.4 to 14.2) | 10.4 (8.0 to 13.3) | 0.1 (−1.2 to 1.6)[b] | .86 |
| Hand grip strength, median (IQR), kg (89/98)[m] | 19.7 (13.0 to 28.2) | 17.9 (13.4 to 24.7) | 1.6 (−1.0 to 4.2)[b] | .23 |
| VAS symptom score, median (IQR) (89/99)[n] | | | | |
| Breathlessness | 2.9 (0.9 to 5.1) | 2.8 (1.1 to 5.0) | 0.0 (−0.8 to 0.6) | .86 |
| Fatigue | 5.0 (3.0 to 6.8) | 4.9 (2.3 to 7.3) | 0.0 (−0.8 to 0.8) | .96 |
| Appetite | 2.9 (1.1 to 4.8) | 3.0 (1.0 to 6.1) | −0.3 (−1.1 to 0.4) | .34 |
| Pain | 4.1 (0.5 to 5.9) | 3.3 (1.0 to 5.2) | 0.1 (−0.6 to 0.9) | .77 |
| Joint stiffness | 4.2 (1.6 to 6.5) | 3.6 (1.3 to 7.2) | 0.1 (−0.7 to 1.0) | .81 |

Abbreviations: DTS, Davidson Trauma Scale; HADS, Hospital Anxiety and Depression Scale; ICU, intensive care unit; IQR, interquartile range; NA, not applicable; RMI, Rivermead Mobility Index; SF-12 MCS, 12-Item Short Form Health Survey Mental Component Summary; SF-12 PCS, SF-12 Physical Component Summary; VAS, visual analog scale.

[a] Five patients withdrew; 7 were missing data.

[b] Adjusted for age group and baseline Subjective Global Assessment nutrition status, presence of delirium, and ward destination.

[c] Two patients withdrew after randomization.

[d] Seventy-two patients were discharged with only baseline data; 3 were missing data.

[e] Seventy-two patients were discharged before first assessment; 4 were missing data.

[f] Seventy-two patients were discharged before first assessment; 5 were missing data. Zero centimeters indicates no symptoms; 10 cm, worst symptoms (for appetite, 0 cm indicates best appetite; 10 cm, worst appetite).

[g] Six patients were missing data.

[h] Twelve patients were missing data regarding survival status.

[i] Twelve patients died; 15 withdrew at 3 months; and 16 declined, could not be contacted, or did not participate for other reasons.

[j] Twelve patients died; 15 withdrew before the 3-month follow-up; and 28 had missing scores due to loss to follow-up or declined to complete the questionnaire.

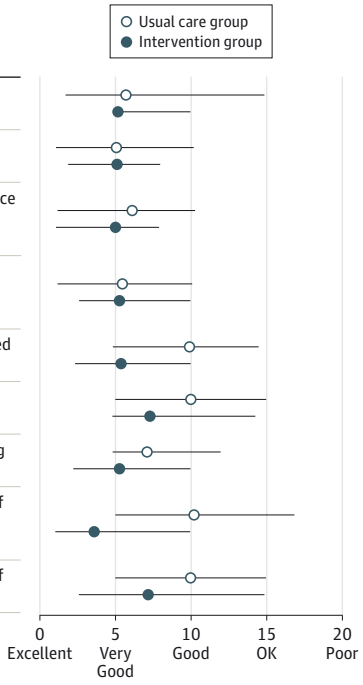
[k] Twelve patients died; 15 patients withdrew before the 3-month follow-up; and 53 had missing scores due to loss to follow-up or declined to complete the questionnaire.

[l] Twelve patients died; 15 withdrew before the 3-month follow-up; and 38 had missing scores due to loss to follow-up or declined to complete the questionnaire.

[m] Twelve patients died; 15 withdrew before the 3-month follow-up; and 26 had missing scores.

[n] Twelve patients died; 15 withdrew; and 25 had missing scores due to loss to follow-up or declined to complete the questionnaire.

Figure 2. Summary of Responses to Satisfaction Questionnaire




| Satisfaction Domain | Excellent Anchor Quotation | Poor Anchor Quotation | *P* Value |
|---|---|---|---|
| Transfer from ICU to the ward | "The ICU staff prepared me well for going to the ward." | "No one told me what was happening or what the wards would be like." | .48 |
| Ward staff's understanding of your time in intensive care | "They really understood and cared about what I'd been through." | "No one had a clue about what had happened to me." | .85 |
| Exercises to get you moving/back on your feet | "I had all the help, support, and advice I needed to get me moving/back on my feet." | "I had little or no help, support, or advice, and my recovery suffered as a result." | .04 |
| Help, support, and advice with being independent | "I had all the help, support, and advice I needed to get my independence back." | "I had little or no help, support, or advice, and I really struggled to get my independence back." | .79 |
| Help with eating and nutrition | "I had all the help and advice I needed with eating and nutrition." | "No one seemed to notice or care if I was able to eat ok." | .04 |
| Being involved in decisions about your care | "I was always asked about what was best for me, and I felt listened to." | "No one asked about what was best for me, and I felt invisible." | .23 |
| Organization and coordination of care | "Everyone knew what was happening and worked together well." | "No one seemed to know what was happening. It was totally disorganized." | .04 |
| Information about what happened in intensive care | "I was given a clear understanding of how I ended up in intensive care and what happened to me." | "No one told me anything about how I ended up in intensive care or about what happened to me." | <.01 |
| Knowing what to expect after you got home | "I was given a clear understanding of what being at home might be like." | "No one told me anything about what being at home might be like." | .49 |

Data markers indicate median values; error bars, interquartile ranges. A 0- to 20-cm Likert scale was used with the gradations indicated on the x-axis. The title for each satisfaction domain was shown with the anchor quotations placed at each end of the domain to guide patient responses. Each domain was presented to patients on a separate page. *P* values for all comparisons between the intervention and usual care groups for each domain are shown are shown (Mann-Whitney test). ICU indicates intensive care unit.

36-item Short Form Health Survey, from which the 12-item version is derived, correlates with physical function measures in patients discharged from the ICU, indicating consistency with the mobility outcomes.[35] We found no effect on a range of patient-reported symptoms.

Our findings differ from those of trials of interventions starting and primarily delivered during ICU treatment, where increasing mobilization appears to improve physical recovery.[14] Our findings also differ from those of trials in noncritical care patient cohorts (mainly stroke and orthopedic) in whom increased physical rehabilitation improves a range of outcomes and reduces hospital stay.[36] Typically, these studies found benefit from approximately 20 minutes of additional therapy per day, which is substantially less than the mean amount delivered in our trial. However, our findings are consistent with those of previously published exercise-based trials delivered at different points after ICU discharge.[15,16]

Several factors may explain the ineffectiveness of our intervention compared with usual care. Loss of muscle mass and function start early during critical illness and frequently result in a neuromyopathy.[37] By ICU discharge when our intervention started, established neuromuscular lesions may limit the impact of rehabilitation, such that an increase of frequency and intensity lacks efficacy. Persisting inflammation could further impair muscle recovery, supporting the hypothesis that some patients do not respond to physical rehabilitation after ICU discharge owing to established and ongoing neuromuscular dysfunction.[38] Although we individualized therapy and goal setting, patients had limited ability and functional reserve to participate in and comply with treatments. We cannot exclude an effect from a more intense training program, but believe compliance would be significantly limited by symptoms. The usual care group in our trial received rehabilitation therapy across all domains, and the differences between groups may have been insufficient or the therapy received with usual care may have been sufficient to maximize the recovery trajectory for most patients. All patients in our study received PT and mobilization efforts before randomization during ICU care, which could have decreased the importance of post-ICU therapy. Our negative findings, considered alongside the generally positive findings in ICU-based mobilization trials,[14] are consistent with greater benefit from early ICU-based therapy. These data suggest resources and effort to increase rehabilitation should be weighted toward the early ICU-based period.

Despite the lack of effect on physical and HRQOL outcomes, patients in the intervention group reported greater satisfaction, with high value placed on access to information, PT, nutritional advice, and the coordination of care. Satisfaction with greater information was particularly high, consistent with published qualitative studies with critical care survivors.[39] These data suggest that the way rehabilitation was delivered addressed unmet patient needs anticipated during pretrial work[30] and illustrates how improvements in care that matter to patients can occur without measureable effects on biomedical outcomes. These findings are consistent with qualitative

data in other rehabilitation settings.[40] Although overall costs and quality-adjusted life-years during the 12 months were similar, indicating no incremental cost-effectiveness, our novel service model could provide adequate rehabilitation, a better patient experience, and greater quality of care at a similar cost to current practice.

Our trial was not primarily designed to affect psychological outcomes. We confirmed the high prevalence of anxiety, depression, and posttraumatic stress symptoms among ICU survivors,[5,6] and persistence during the 12-month follow-up was striking, especially for traumatic symptoms. The effectiveness of information provision as psychological therapy is uncertain, but patient diaries show promise.[41] However, we found no improvement in psychological outcomes from our information strategy, highlighting the need for trials of psychological interventions after critical illness.

Our study has several limitations. We could not formally blind participants or clinicians to group randomization, but we minimized bias by restricting RAs to the intervention group and blinding outcome assessors. The post-ICU hospital stay was relatively short for many patients, who were frequently discharged despite significant mobility impairment. This duration of stay reflected current practice but could have decreased the potential treatment effect. We cannot exclude a benefit from a longer period of supervised treatment. Although predefined subgroup analyses found no treatment effects, we cannot exclude important effects within other patient subgroups. Research is needed to better define ICU phenotypes in relation to the recovery trajectory and to include these definitions in future trial designs. In addition, despite including outcomes that assessed symptoms, functioning, relevant health status, and HRQOL, we might have missed clinically important effects that might have been captured by other measures.

## Conclusions

Increasing the frequency and intensity of mobility, exercise, dietetic, and related therapies for patients discharged from the ICU during the post-ICU hospital stay and greater provision of information did not improve measures of physical function or HRQOL compared with the usual practices. However, the intervention improved patient satisfaction with many aspects of recovery.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