

Determinants of Depressive Symptoms at 1 Year Following ICU Discharge in Survivors of ≥ 7 Days of Mechanical Ventilation

Results From the RECOVER Program, a Secondary Analysis of a Prospective Multicenter Cohort Study



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BACKGROUND: Moderate to severe depressive symptoms occur in up to one-third of patients at 1 year following ICU discharge, negatively affecting patient outcomes. This study evaluated patient and caregiver factors associated with the development of these symptoms.

METHODS: This study used the Rehabilitation and Recovery in Patients after Critical Illness and Their Family Caregivers (RECOVER) Program (Phase 1) cohort of 391 patients from 10 medical/surgical university-affiliated ICUs across Canada. We determined the association between patient depressive symptoms (captured by using the Beck Depression Inventory II [BDI-II]), patient characteristics (age, sex, socioeconomic status, Charlson score, and ICU length of stay [LOS]), functional independence measure (FIM) motor subscale score, and caregiver characteristics (Caregiver Assistance Scale and Center for Epidemiologic Studies-Depression Scale) by using linear mixed models at time points 3, 6, and 12 months.

RESULTS: BDI-II data were available for 246 patients. Median age at ICU admission was 56 years (interquartile range, 45-65 years), 143 (58%) were male, and median ICU LOS was 19 days (interquartile range, 13-32 days). During the 12-month follow-up, 67 of 246 (27.2%) patients had a BDI-II score ≥ 20 , indicating moderate to severe depressive symptoms. Mixed models showed worse depressive symptoms in patients with lower FIM motor subscale scores (1.1 BDI-II points per 10 FIM points), lower income status (by 3.7 BDI-II points; $P = .007$), and incomplete secondary education (by 3.8 BDI-II points; $P = .009$); a curvilinear relation with age ($P = .001$) was also reported, with highest BDI-II at ages 45 to 50 years. No associations were found between patient BDI-II and comorbidities ($P = .92$), sex ($P = .25$), ICU LOS ($P = .51$), or caregiver variables (Caregiver Assistance Scale [$P = .28$] and Center for Epidemiologic Studies Depression Scale [$P = .74$]).

ABBREVIATIONS: BDI-II = Beck Depression Inventory II; CAS = Caregiver Assistance Scale; CES-D = Center for Epidemiologic Studies-Depression Scale; FIM = functional independence measure; IQR = interquartile range; LOS = length of stay; RECOVER = Rehabilitation and Recovery in Patients after Critical Illness and Their Family Caregivers

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CONCLUSIONS: Increased functional dependence, lower income, and lower education are associated with increased severity of post-ICU depressive symptoms, whereas age has a curvilinear relation with symptom severity. Knowledge of risk factors may inform surveillance and targeted mental health follow-up. Early mobilization and rehabilitation aiming to improve function may serve to modify mood disorders. CHEST 2019; 156(3):466-476

KEY WORDS: critical care; depression; exercise; health-related quality of life; rehabilitation

Moderate to severe depressive symptoms affect up to one-third of survivors of critical illness at 1 year following ICU discharge.^{1,2} These symptoms have a negative impact on quality of life and the ability to return to work, and they increase the risk of suicide.³⁻⁶

Previously documented determinants of depressive symptoms in ICU survivors include presence of comorbidities, having children aged < 18 years, previous psychological illness, in-ICU agitation, unemployment or sick leave at time of admission, and appearing depressed in the ICU.⁷ However, there is inconsistent support for these associations.^{2,8}

Caregivers may have an important role as a risk modifier for patient depression.⁹ However, caregivers themselves experience significant psychological burden, with high levels of depressive symptoms present in those caring for patients who have been critically ill.^{10,11} It is unknown whether caregiver mental health influences the risk of depressive symptoms in patients.

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There is a need to clearly understand determinants of long-term depressive symptoms in patients following a critical illness. Rehabilitation and Recovery in Patients after Critical Illness and Their Family Caregivers (RECOVER) is a Canadian multicenter collaboration with the Canadian Critical Care Trials Group focused on the creation of a patient- and family-centered practice standard for a continuum of care following critical illness. This group completed a multicenter prospective cohort study (RECOVER Program [Phase 1]), from which we analyzed data to evaluate associations between patient and caregiver factors, collected in the context of this study, and patient depressive symptoms.^{1,11} Our a priori hypotheses were that increased age, female sex, worse postcritical illness functional dependency, lower family income, less education, increased number of comorbidities, and increased caregiver burden and depression were associated with severity of depressive symptoms in patients up to 1 year following critical illness.^{9,11-16}

Patients and Methods

Participants

All included patients and caregivers were identified through the RECOVER Program (Phase 1) database.¹ This multicenter, prospective cohort study was performed between 2007 and 2014 across 10 medical/surgical university-affiliated ICUs in Toronto (5 sites), Hamilton, Ottawa, Montreal, Sherbrooke, and Vancouver, Canada. Eligible patients were screened on day 7 of mechanical ventilation. Included patients were ≥ 16 years of age with dependence on mechanical ventilation in the ICU for ≥ 7 days. Exclusion criteria were current or previously documented neurologic injury precluding questionnaire completion; formal documentation of neuromuscular disease; nonambulatory prior to critical illness; anticipated death or withdrawal of life-sustaining treatment within 48 h of enrollment; previous documented admission for psychiatric illness; significant cognitive impairment; not fluent in English or French; residence > 300 km from referral center; or physician, patient, or substitute decision-maker consent refusal. Patients were evaluated at day 7 and 3, 6, and 12 months following ICU discharge, undergoing an interview, physical examination, and completion of a number of outcome measures.¹ For each patient, 1 caregiver was recruited, if available, and assessed in parallel.¹¹

Outcomes and Independent Variables

Patient variables collected during RECOVER Program (Phase 1) are detailed in the original paper.¹ The current analysis, in line with our a priori hypotheses, focused on age, sex, ICU length of stay (LOS),

TABLE 1] Details of Instruments Used to Assess Patient and Caregiver Independent Variables and Outcomes

| Instrument | Construct Measured | Details of Score |
|---|--|---|
| Acute Physiology and Chronic Health Evaluation II ¹⁷ | Severity of illness | Scored from 0-71 from patient age and 12 physiological variables within 24 h of ICU admission; higher score correlates with increased risk of death |
| Charlson score ¹⁸ | Presence of comorbidities | Originally predicted 1-year survival in medical inpatients with a range of comorbidities; currently used in many patient populations with a score gained from each comorbidity present weighted according to their potential influence on mortality |
| Functional independence measure ¹⁶ | Measurement of disability; indicator of level of dependence in activities of daily living (eg, eating, bathing, toileting, using stairs) | 18 items comprising 13 motor tasks and 5 cognitive tasks rated on a 7-point ordinal scale ranging from complete assistance to total independence; FIM motor subscale score ranges from 13-91, with higher scores indicating greater independence. For example, a score of 13 indicates total assistance is required in all activities of daily living, a score of 52 indicates minimal assistance required, and a score of 91 indicates complete independence |
| Beck Depression Inventory-II ¹⁹ | Severity of depressive symptoms | 21-question multiple-choice self-report inventory. Scores range from 0-63: 0-13 suggests minimal depression; 14-19, mild depression; 20-28, moderate depression; and 29-63, severe depression |
| Caregiver Assistance Scale ^{20,21} | Level of assistance provided by caregiver | 17 activities of daily living and medical care, each scored 0-6. Higher scores indicate more assistance is given by caregiver |
| Center for Epidemiologic Studies-Depression Scale Revised ²² | Depressive symptoms | Score ranges from 0-60; < 16 is considered "normal," scores of 16-21 suggest a risk of clinical depression, and scores > 21 suggest a major depressive episode |

severity of illness (Acute Physiology and Chronic Health Evaluation II score), comorbidities (Charlson score), need for self-care assistance (measured by using the functional independence measure [FIM]), income, and education level. The primary outcome was patient depressive symptoms (as measured by using the Beck Depression Inventory-II [BDI-II]).¹⁶⁻¹⁹

Caregiver variables collected during RECOVER Program (Phase 1) have been previously described.¹¹ For the current analysis, we focused on caregiver burden (measured by using the Caregiving Assistance Scale [CAS]) and caregiver depression (measured by using the Center for Epidemiologic Studies-Depression [CES-D] scale).²⁰⁻²²

Table 1 provides additional details about these instruments.¹⁶⁻²²

Statistical Analysis

Descriptive statistics were calculated for caregiver and patient demographic characteristics and outcomes by using frequencies and proportions for categorical data, and means \pm SD, or medians and interquartile ranges (IQRs), as appropriate, for continuous variables.

We presented boxplots of BDI-II scores at each assessment, and, as a descriptive summary, the percentage of patients with moderate to severe depressive symptoms, defined as a BDI-II score \geq 20. We first determined the strength of associations between patient BDI-II score and the following patient characteristics: age, sex, income, education level, Charlson score, ICU LOS, and FIM motor subscale score at 3, 6, and 12 months. In a second analysis, using the subcohort of patients with a caregiver, we determined the strength of associations between patient BDI-II score and caregiver CAS and CES-D after accounting for patient characteristics at 3, 6, and 12 months. For these analyses, linear mixed regression models with a random intercept per patient were used to account for correlation of observations within a patient. A potential nonlinear relation between FIM, age, or ICU LOS and the BDI-II score was allowed through use of cubic splines. Variables with *P* values > .2 were dropped from this full model, with a reduced model used to estimate effects for remaining variables and produce figures showing the relation between FIM or age with predicted BDI-II, with other predictors at reference values (for categorical variables) or average values (for continuous variables). All analyses were performed by using R statistical software version 3.4.0 (R Foundation for Statistical Computing, 2017; <https://www.R-project.org/>).

Results

Of 391 eligible patients from the RECOVER Program (Phase 1) database, 246 contributed BDI-II data at least once during 12-month follow-up and were included in the study. A total of 179 patients had caregivers who consented to the study. The most common reasons for patient exclusion were

failure to complete the BDI-II questionnaire and death prior to the first BDI-II assessment (Fig 1). The number of patients alive and eligible for follow-up was 244 (99%) at 6 months and 232 (94%) at 1 year. From this cohort, 166 (67.5%) patients completed a BDI-II assessment at 3 months, 170 (69.1%) at 6 months, and 175 (71.1%) at 1 year.

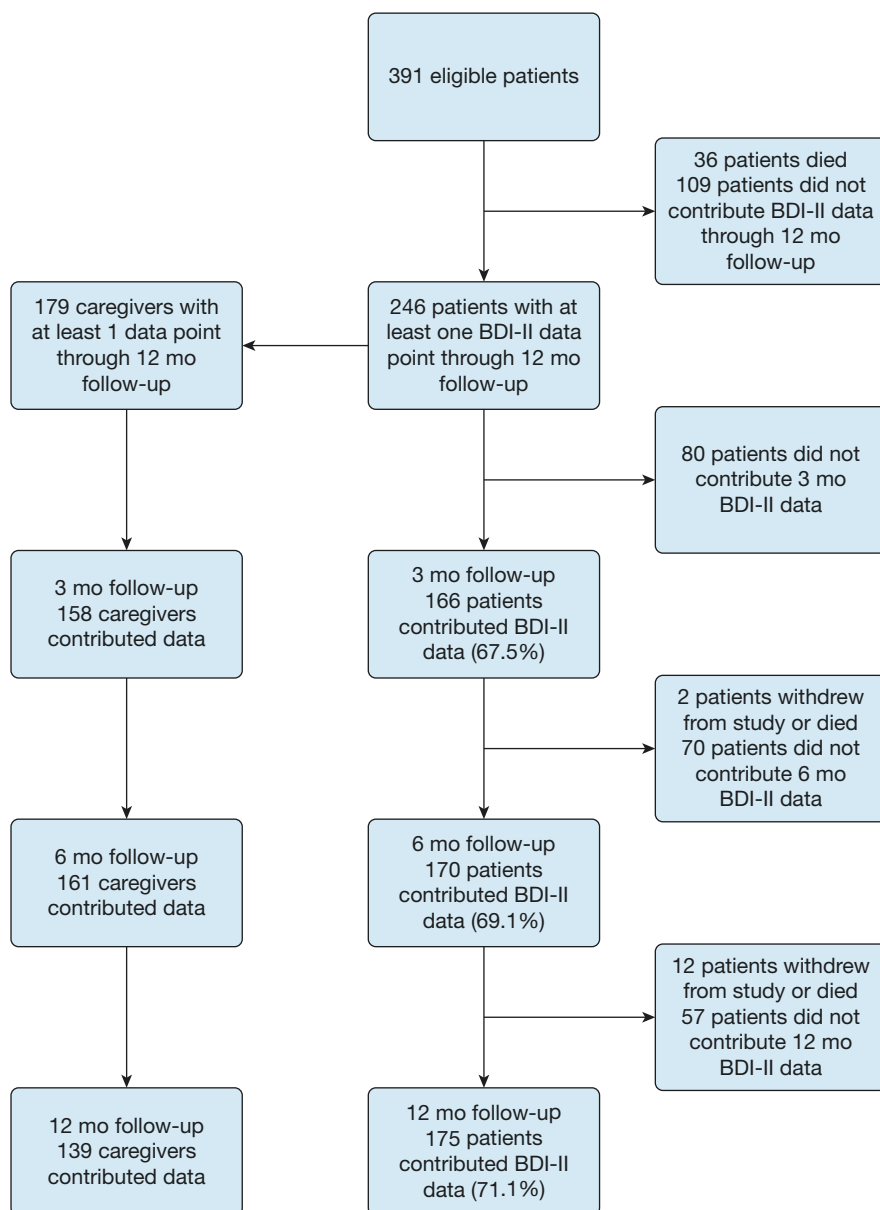


Figure 1 – Consort diagram. Screening and details of the 1-year patient and caregiver follow-up cohorts. The most common reasons for patient exclusion were failure to complete the BDI-II questionnaire and death prior to first BDI-II assessment. The proportion of caregivers who missed evaluation was highest at 12 months (22.3%). The most common reasons for this were death of, or withdrawal of, the corresponding patient within the dyad. BDI-II = Beck Depression Inventory II.

Patient and Caregiver Cohort Characteristics

Patient and caregiver characteristics are summarized in Table 2. Median patient age at ICU admission was 56 years (IQR, 45-65 years), 143 (58%) were male, and median ICU LOS was 19 days (IQR, 13-32 days). The majority of patients (n = 138 [58%]) had completed secondary education. Annual family income in Canadian dollars was less than \$50,000 in 77 patients (31.8%), \$50,000 to \$70,000 in 29 patients (12%), and more than \$70,000 in 71 (29.3%) patients, with 65 (26.9%) patients not reporting. The median Charlson score was 1 (IQR, 0-2), and the mean FIM motor subscale score at day 7 post-ICU was 37.8 ± 24.1. The most common admitting Acute Physiology and Chronic Health Evaluation II diagnostic

groups were respiratory (69 [28.4%]), neurologic (38 [15.6%]), and GI (34 [14.4%]). Median caregiver age was 54 years (IQR, 44.5-63.5 years), 122 (68.2%) were female, and 118 (65.9%) were the spouse of the patient. The majority (103 [57.5%]) were working full- or part-time.

Patient Functional and Neuropsychological Outcomes

Mean patient BDI-II scores were similar at 3-, 6-, and 12-month follow up (12.3 ± 9.0, 11.4 ± 9.8, and 10.7 ± 9.1, respectively). Likewise, the prevalence of moderate to severe depressive symptoms (BDI-II ≥ 20) was similar across time, affecting 28 of 166 (16.9%), 29 of 170 (17.1%), and 31 of 175 (17.7%) patients at 3, 6,

TABLE 2] Patient and Caregiver Characteristics

| Characteristic | Value |
|---|-----------------|
| Patient characteristics (n = 246) | |
| Age (median [IQR]), y | 56 [45,65] |
| Male, No. (%) | 143 (58) |
| Admitting APACHE diagnoses, No. (%) | |
| Respiratory | 69 (28.4) |
| Neurologic | 38 (15.6) |
| GI | 34 (14.4) |
| Trauma | 29 (11.9) |
| Sepsis | 28 (11.5) |
| Other | 44 (18.1) |
| Education, No. (%) | |
| Less than secondary | 100 (42.0) |
| Secondary/some postsecondary | 34 (14.3) |
| Postsecondary | 104 (43.7) |
| Annual family income, No. (%) | |
| < 50,000 | 77 (31.8) |
| 50,000-70,000 | 29 (12.0) |
| > 70,000 | 71 (29.3) |
| Not reported | 65 (26.9) |
| APACHE II (median [IQR]) | 22 [16, 28] |
| Charlson score (median [IQR]) | 1 [0.0, 2.0] |
| ICU LOS (median [IQR]), d | 19 [13, 31.75] |
| Hospital LOS (median [IQR]), d | 42 [26, 71.75] |
| FIM motor subscale score at day 7 (mean ± SD) | 37.8 ± 24.1 |
| Caregiver characteristics (n = 179) | |
| Age (median [IQR]), y | 54 [44.5, 63.5] |
| Female, No. (%) | 122 (68.2) |
| Caring for spouse, No. (%) | 118 (65.9) |
| Completed postsecondary education, No. (%) | 91 (51.1) |
| Annual family income, No. (%) | |
| < 50,000 | 64 (35.8) |
| 50,000-70,000 | 31 (17.3) |
| > 70,000 | 68 (38.0) |
| Not reported | 16 (8.9) |
| Employment status, No. (%) | |
| Working | 103 (57.5) |
| Retired | 48 (26.8) |
| Homemaker or caregiver | 22 (12.3) |

Family income is given in Canadian dollars. APACHE = Acute Physiology and Chronic Health Evaluation; FIM = functional independence measure; IQR = interquartile range; LOS = length of stay.

and 12 months, respectively (Fig 2). Over the 12-month follow-up period, 67 of 246 patients (27.2%) had at least one BDI-II score ≥ 20.

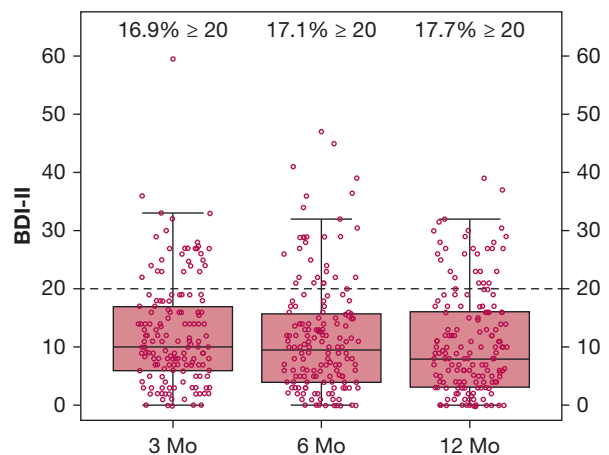


Figure 2 – Patient BDI-II scores at 3-, 6-, and 12-month follow-up. A score ≥ 20 (dotted line) indicates moderate to severe depressive symptoms. For each column, the horizontal line within the box denotes the median value; the bottom and top of the box denote the first and third quartiles, respectively; the upper whisker extends to the highest value that is within (1.5 × interquartile range) of the third quartile; and the lower whisker extends to the lowest value within (1.5 × interquartile range) of the first quartile. Data beyond the ends of the whiskers are outliers and are plotted as points. See Figure 1 legend for expansion of abbreviation.

Mean patient FIM motor subscale scores at day 7 and at 3-, 6-, and 12-month follow-up were 37.8 ± 24.1, 73.5 ± 22.2, 78.9 ± 17.8, and 80.8 ± 15.55, respectively, suggesting across time an overall statistically significant improvement in independence in daily living activities ($P < .001$). However, as detailed in the original article, this recovery was dependent on disability grouping.¹

Caregiver Burden and Depression

Caregiver assessment revealed that many caregivers in our dyads were at risk of, or had, major depressive symptoms. At 3-, 6-, and 12-month follow-up, the number of caregivers with CES-D scores ≥ 16 was 66 of 158 (41.8%), 62 of 161 (38.5%), and 50 of 139 (36%), respectively. Mean CAS scores across time were 40.6 ± 23.4, 32.9 ± 24.6, and 28.3 ± 22.8 at 3-, 6-, and 12-month follow-up, indicating moderate assistance provided at 3 months, decreasing to moderate to minimal assistance at 12 months.

Determinants of Patient Depressive Symptoms

A linear mixed model containing patient FIM, age, income, and education as predictors found a curvilinear relation between patient BDI-II score and age at ICU admission (Fig 3), with the highest BDI-II scores seen in patients aged 45 to 50 years ($P = .001$). Mean BDI-II scores were higher in patients whose annual family income was less than \$50,000 than those with income higher than \$70,000 (by 3.7 BDI-II points; $P = .007$) and

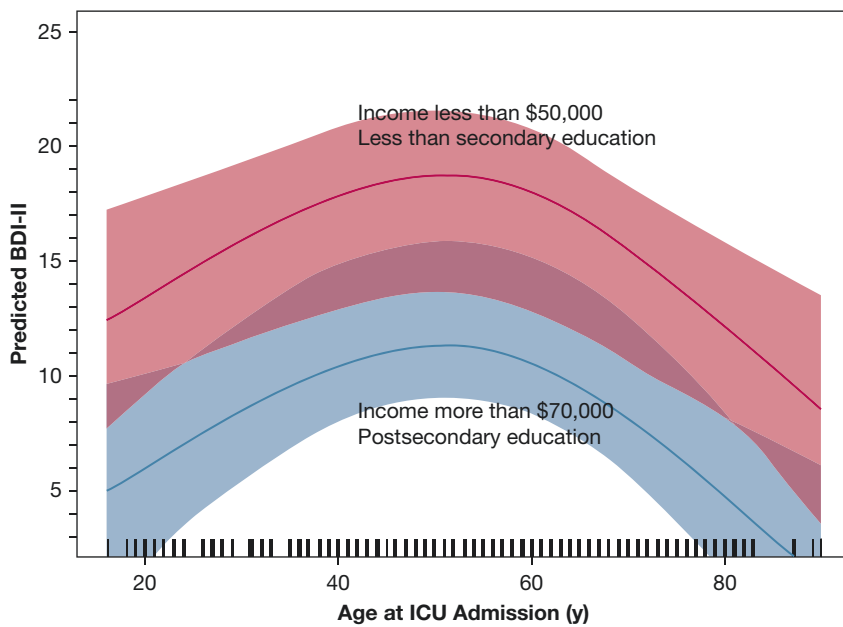


Figure 3 – Predicted BDI-II vs age at ICU admission (FIM motor, 68; ICU LOS, 19 days). In the linear mixed model, there was a curvilinear relationship between depressive symptoms and age, with the highest BDI-II scores associated with age 45 to 50 years. Fitted values from the model and 95% confidence bands are shown for those combinations of income and education leading to the highest and the lowest BDI-II scores. Tick marks on the x-axis show individual values of age at ICU admission. FIM = functional independence measure; LOS = length of stay. See Figure 1 legend for expansion of other abbreviation.

in patients with incomplete secondary education compared with complete postsecondary education (by 3.8 BDI-II points; $P = .009$). The FIM motor subscale score demonstrated a linear association with BDI-II scores (Fig 4) in the linear mixed models, with higher mean BDI-II scores associated with increased functional dependence (by 1.1 BDI points per 10 FIM points). Figure 4 also shows the independent effects of lower income and education level on depressive symptoms.

No remaining patient characteristics had a statistically significant relation with BDI-II (patient sex [$P = .25$]; ICU LOS [$P = .51$]; and Charlson score [$P = .92$]). In the subset of patients with caregiver data, no measured

caregiver variables (CAS [$P = .28$] and CES-D [$P = .74$]) were a significant determinant of patient BDI-II.

Table 3 displays estimates, CIs, and P values from the reduced patient-caregiver model. Table 4 displays results from the final covariate-adjusted patient-only model. These results are also shown graphically by Figures 3 and 4.

Discussion

In this secondary analysis of 246 patients and 179 caregivers from the RECOVER Program (Phase 1) cohort, we determined that patient age, socioeconomic status, and functional outcome were significant

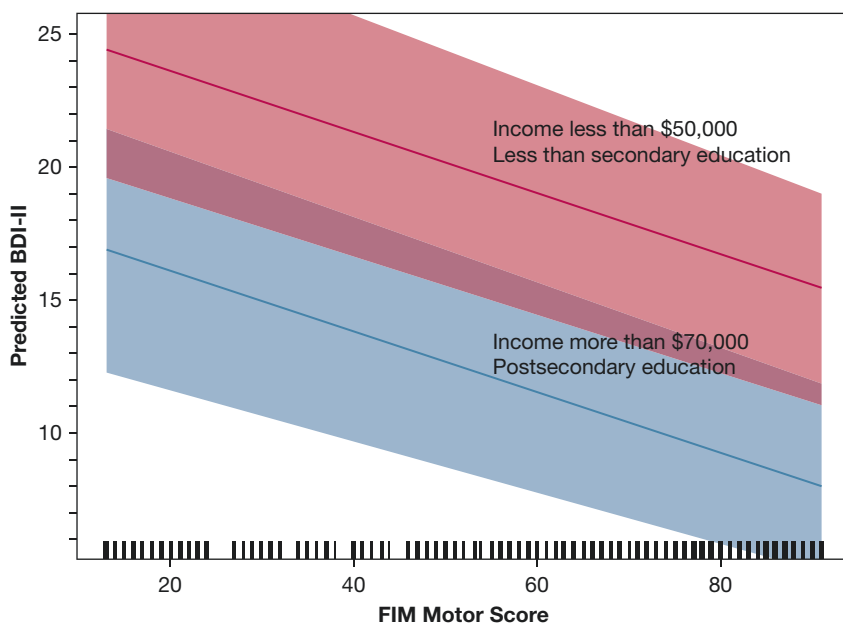


Figure 4 – Predicted BDI-II vs FIM motor (age at ICU admission, 57 y; ICU LOS, 19 days). Lower FIM motor subscale scores were significantly associated with higher patient BDI-II scores. Fitted values from the model and 95% confidence bands are shown for those combinations of income and education leading to the highest and the lowest BDI-II scores. Tick marks on the x-axis show individual values of observed FIM motor subscale scores. See Figure 1 and 3 legends for expansion of other abbreviations.

TABLE 3] Patient and Caregiver Data: Linear Random Effects Model at all Three Time Points With Caregiver Data

| Variable | Dependent Variable BDI-II | |
|---|---|--|
| | Patient-Only Predictors | Patient and Caregiver Predictors |
| Observations | 295 | 295 |
| Intercept | 17.11 (8.90 to 25.31) <i>P</i> = .0001 | 12.58 (3.36 to 21.80) <i>P</i> = .01 |
| Age at ICU admission (spline term 1) | 1.66 (-3.72 to 7.05) <i>P</i> = .55 | 1.38 (-4.04 to 6.79) <i>P</i> = .62 |
| (spline term 2) | 9.85 (-3.65 to 23.34) <i>P</i> = .16 | 11.14 (-2.21 to 24.50) <i>P</i> = .11 |
| (spline term 3) | -6.89 (-14.37 to 0.59) <i>P</i> = .08 | -5.83 (-13.27 to 1.62) <i>P</i> = .13 |
| Education: Secondary/some postsecondary | -0.95 (-4.60 to 2.70) <i>P</i> = .61 | -0.58 (-4.24 to 3.08) <i>P</i> = .76 |
| Postsecondary | -3.64 (-7.05 to -0.24) <i>P</i> = .04 | -3.47 (-6.88 to -0.06) <i>P</i> = .05 |
| Income: \$50,000-\$70,000 | 0.50 (-3.89 to 4.89) <i>P</i> = .83 | 0.70 (-3.63 to 5.04) <i>P</i> = .75 |
| > \$70,000 | -3.93 (-7.21 to -0.66) <i>P</i> = .02 | -3.66 (-6.91 to -0.41) <i>P</i> = .03 |
| Unknown/did not say | -1.65 (-5.09 to 1.79) <i>P</i> = .35 | -1.43 (-4.83 to 1.98) <i>P</i> = .41 |
| FIM motor subtotal score | -0.09 (-0.15 to -0.02) <i>P</i> = .01 | -0.06 (-0.13 to 0.01) <i>P</i> = .07 |
| CAS | | 0.03 (-0.02 to 0.08) <i>P</i> = .28 |
| Caregiver BDI-II | | 0.13 (-0.05 to 0.31) <i>P</i> = .16 |
| CES-D | | -0.02 (-0.16 to 0.11) <i>P</i> = .74 |

Family income is given in Canadian dollars. Cells show estimate, CI, and *P* value. BDI-II = Beck Depression Inventory II; CAS = Caregiver Assistance Scale; CES-D = Center for Epidemiologic Studies-Depression Scale. See Table 1 legend for expansion of other abbreviation.

determinants of depressive symptoms in patients at 1 year following critical illness.

We found that those with greater functional dependence had worse depressive symptoms. The relation between physical function and mental health has been previously described in non-ICU patients, with physical inactivity believed to contribute to depressive symptoms due to augmentation of a proinflammatory state and lower levels of brain-derived neurotrophic factor.²³⁻²⁵ Early physiotherapy during critical illness, in appropriate patients, preserves skeletal muscle cross-sectional fiber area and decreases the odds of weakness on hospital discharge.^{26,27} This strategy may offer potential in reducing chronic functional disability, with its associated psychological sequelae. Physical rehabilitation following critical care is an ongoing area of research, and although

there is current limited evidence supporting the benefits of structured programs, the impact on psychological outcomes offers a new focus of study.²⁸⁻³⁰

When considering depressive symptoms, attributing causality to functional dependence is challenging.³¹ The association between mental health and self-reported physical limitations was previously examined by Ruo et al,³² showing correlation between worse mental health scores and worse self-reported physical functioning following adjustment for measured physical performance identified. The authors postulated that this finding could be attributed to distorted perception of ability to perform activities, leading to overestimation of difficulties, and that those with low mental health scores had low energy or vitality, leading to true limitations not captured in a research study setting. In the current study

TABLE 4] Patient Data: Linear Random Effects Model at All Three Time Points

| Variable | Dependent Variable: BDI-II |
|---|--|
| Observations | 492 |
| Constant | 19.489 (12.819 to 26.160) <i>P</i> = .00000 |
| Ns (age ICU, 3)1 | 1.654 (-2.704 to 6.013) <i>P</i> = .456 |
| Ns (age ICU, 3)2 | 9.165 (-2.107 to 20.436) <i>P</i> = .111 |
| Ns (age ICU, 3)3 | -6.952 (-13.563 to -0.342) <i>P</i> = .040 |
| Education: secondary/ some postsecondary | -1.418 (-4.325 to 1.489) <i>P</i> = .338 |
| Education: postsecondary | -3.781 (-6.578 to -0.984) <i>P</i> = .009 |
| Income (b) \$50,000- \$70,000 | -2.650 (-6.090 to 0.791) <i>P</i> = .131 |
| Income (c) > \$70,000 | -3.657 (-6.300 to -1.014) <i>P</i> = .007 |
| Income (d) unknown/ did not say | -1.560 (-4.263 to 1.143) <i>P</i> = .257 |
| FIM motor score | -0.115 (-0.165 to -0.066) <i>P</i> = .00001 |

Ns = natural spline. See Table 1 and 3 legends for expansion of other abbreviations.

cohort, it is also possible that the reverse is true: that limitations in daily activities following critical illness contribute to worse mental health scores.

We did not have detailed information regarding patients' pre-ICU functional status. However, 51% of the study patients were engaged in full- or part-time employment preadmission, suggesting a reasonable or better functional baseline. Decline in physical function is a significant problem for many critically ill patients.²⁸ Therefore, a significant proportion of our patients likely experienced such deterioration during their critical illness. Although the direction of causality between depressive symptoms and worsening of function is unclear, both are distressing to patients and reduce quality of life. Efforts to prevent and treat these sources of suffering may have a synergistic effect in improving patient outcomes.

The identified curvilinear relation between BDI-II score and age mirrors the general population's overall risk of depression, with those aged 40 to 59 years at highest risk.¹² The reasons postulated for lower risk in older age include increasing self-acceptance, happiness, and a "counting your blessings" phenomenon, contrasted with loss of aspirations in middle age. In addition, those who

are happier live longer, creating survivor bias.³³ Regardless of the etiology, patients in this age range represent an important risk group for development or persistence of depressive symptoms following critical illness.

We identified an association between lower income and education, and worse depressive symptoms. Again, this relation reflects that of the general population, in which financial strain and loss of personal control contribute to the development of depression.^{12,15,34} Individuals with lower socioeconomic status are at higher risk for many diseases, including cardiovascular disease and diabetes mellitus, suggesting health inequalities also contribute.³⁵⁻³⁸

The prevalence of moderate to severe depressive symptoms in the current study cohort was lower than previously described.^{1,2,8} There are several possible explanations. Because this analysis was not a natural history study, patients were offered psychiatric intervention during nonstudy visits as appropriate, which may have reduced depressive symptoms ascertained during later study visits. Selection bias may also have been present, with patients more prone to depression possibly less likely to participate.

Furthermore, preexisting depressive mood is a risk factor for ICU mortality, and therefore some patients with more severe depressive symptoms may have died prior to enrollment.³⁹ Nevertheless, we showed that survivors of critical illness have a higher rate of depressive symptoms than the general population (8% in the Western world).^{12,40} Although evidence is lacking, possible reasons for this higher prevalence in ICU patients include inflammation, sleep disturbance, hypoxemia, experiencing critical illness as a stressful life event, loss of mastery, financial strain, and inactivity.^{24,26,34,41-48} However, the similar prevalence of moderate to severe depressive symptoms in other groups of patients suggests that any significant illness may be an important and common causative factor.^{49,50}

This study represents a rigorous assessment of long-term post-ICU functional and psychiatric outcomes, availing highly granular data but with several limitations. One is the lack of data on depressive symptoms and functional status prior to admission. We cannot definitively conclude whether depressive symptoms following critical illness were incident or prevalent, or whether preadmission psychiatric morbidity was a risk factor. In addition, a large number of patients submitted incomplete BDI-II questionnaires. The investigators concluded, following qualitative

feedback, that the main reasons were reluctance to complain, becoming fatigued during follow-up, and worry over caregivers seeing their answers, which are themes previously recognized.^{51,52} This scenario may account for the lower than expected prevalence of depression in the study cohort. Furthermore, we were unable to examine trajectories of depressive symptoms over time, due to insufficient data, or to examine in-ICU variables of interest, including choice of analgesia and sedation, restraint use, and presence of delirium, due to dataset constraints.⁵³ Lastly, this study was restricted to those being ventilated for ≥ 7 days in university-affiliated ICUs, with many patients being well educated. Thus, our findings may not be generalizable to other critically ill patient populations.

Our study has reaffirmed that critically ill patients have an increased prevalence of depressive symptoms at 1 year following ICU discharge and has identified

important risk factors. This information is beneficial for patient risk stratification and enhancement of tailored care throughout critical illness and recovery.^{27,54-56}

Conclusions

In patients who have been ventilated for ≥ 7 days, approximately one-quarter experience moderate to severe depressive symptoms following ICU discharge. Worse depressive symptoms are associated with increased functional dependence, being aged 45 to 50 years, and less income and education. Further research is needed to identify therapies that minimize the psychiatric morbidity associated with critical illness. In particular, the impact of early mobilization and physical recovery on depressive symptoms should be considered in any further studies examining critical care rehabilitation.

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