

Functional Effects of Intervening Illnesses and Injuries After Critical Illness in Older Persons

OBJECTIVES: Intervening illnesses and injuries have pronounced deleterious effects on functional status in older persons, but have not been carefully evaluated after critical illness. We set out to evaluate the functional effects of intervening illnesses and injuries in the year after critical illness.

DESIGN: Prospective longitudinal study of 754 nondisabled community-living persons, 70 years old or older.

SETTING: Greater New Haven, CT, from March 1998 to December 2018.

PATIENTS: The analytic sample included 250 ICU admissions from 209 community-living participants who were discharged from the hospital.

INTERVENTIONS: None.

MEASUREMENTS AND MAIN RESULTS: Functional status (13 activities) and exposure to intervening illnesses and injuries leading to hospitalization, emergency department visit, or restricted activity were assessed each month. Comprehensive assessments (for covariates) were completed every 18 months. In the year after critical illness, recovery of pre-morbid function was observed for 169 of the ICU admissions (67.6%), and the mean (SD) number of episodes of functional decline (from 1 mo to the next) was 2.2 (1.6). The adjusted hazard ratios (95% CI) for recovery were 0.18 (0.09–0.39), 0.46 (0.17–1.26), and 0.75 (0.48–1.18) for intervening hospitalizations, emergency department visits, and restricted activity, respectively. For functional decline, the corresponding odds ratios (95% CI) were 2.06 (1.56–2.73), 1.78 (1.12–2.83), and 1.25 (0.92–1.69). The effect sizes for hospitalization and emergency department visit were larger than those for any of the covariates.

CONCLUSIONS: In the year after critical illness, intervening illnesses and injuries leading to hospitalization and emergency department visit are strongly associated with adverse functional outcomes, with effect sizes larger than those of traditional risk factors. To improve functional outcomes, more aggressive efforts will be needed to prevent and manage intervening illnesses and injuries after critical illness.

KEY WORDS: cohort study; critical illness; disability; functional status; hospitalization; risk factor

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In 2015, there were approximately 1.9 million hospitalizations for critical illness among persons 65 or older in the United States (1). This value will increase considerably in the coming years based on projections that the number of persons 65 or older will nearly double from 50.9 million in 2017 to 94.7 million in 2060 (2). One of the most feared complications of critical illness is loss of independence. Prior research has shown that critical illness is a potent precipitant of functional decline and disability in older persons (3–6). In the

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setting of critical illness, the level of disability in daily activities increases in about three-quarter of the cases within the first month (7), and the likelihood of developing severe disability, defined as the need for personal assistance with greater than or equal to 3 essential activities, is increased more than 1,000-fold among previously nondisabled older persons (5).

The capacity to recover after a disabling event, including critical illness, is high (7–9). Among older persons who survive a critical illness, more than half recover to their premorbid level of function within 6 months (7). Increasing evidence, however, suggests that recovery after a disabling event is often followed by recurrent disability and functional decline (8, 10). The factors associated with functional recovery and functional decline after a disabling event are well established and include (among others) older age, frailty, cognitive impairment, multimorbidity, depressive symptoms, sensory impairments, and obesity (7, 11–13). In contrast, far less is known about the functional effects of illnesses/injuries that occur after critical illness. We hypothesized that functional outcomes after critical illness are adversely affected by subsequent illnesses/injuries and that these effects persist after accounting for traditional risk factors.

To test our hypothesis, we used high-quality data from a unique longitudinal study of community-living older persons, which includes monthly assessments of functional status and intervening illnesses/injuries, along with a large array of covariates that were assessed every 18 months for 20 years. Our objective was to evaluate the functional effects of intervening illnesses/injuries in the year after critical illness. The results of this study may provide additional insights on how functional outcomes after critical illness can be improved in community-living older persons.

MATERIALS AND METHODS

Study Population

Participants were members of an ongoing longitudinal study of 754 community-living persons, 70 years or older, who were initially nondisabled in their essential activities of daily living (8, 14). Potential participants were members of a large health plan and were excluded for significant cognitive impairment with no available proxy (15), life expectancy less than 12 months, plans to move out of the area, or inability to speak English.

Enrollment occurred from March 1998 to October 1999, and the participation rate was 75.2%. The study was approved by the Yale Human Investigation Committee, and all participants provided informed consent.

Data Collection

Comprehensive assessments were completed by trained nurse researchers at baseline and every 18 months, whereas telephone interviews were completed monthly by a separate team of researchers through December 2018. For participants who had significant cognitive impairment or were otherwise unavailable, a proxy informant was interviewed using a rigorous protocol (15). In the current study, 18.1% of the monthly interviews were completed by a proxy. Deaths were ascertained from an informant during a subsequent interview and/or by review of local obituaries. Completion of data collection has been high, and attrition has been low (16).

Descriptive Characteristics and Covariates

During the comprehensive assessments, data were collected on demographic characteristics, nine self-reported, physician-diagnosed chronic conditions, body mass index, cognitive status (17), depressive symptoms (18), functional self-efficacy (19), hearing (20), vision (21), and frailty (22). Additional operational details are provided in **Table 1**.

Intervening Events

The intervening illnesses/injuries, that is, events, included hospitalizations, emergency department (ED) visits, and episodes of restricted activity. The primary source of information on hospitalizations and ED visits was linked Medicare claims data, which were available for nearly all hospitalizations and for ED visits among fee-for-service participants (23). For periods when participants had managed Medicare, hospitalizations were ascertained using Medicare Provider and Analysis Review files, whereas information on ED visits and some hospitalizations (i.e., those without a Medicare record) was obtained during the monthly interviews. Participants were asked whether they had visited an ED or stayed overnight in a hospital since the last interview. The accuracy of self-reported hospitalizations, based on an independent review of hospital records, and ED visits, based on Medicare claims

TABLE 1.
Characteristics of Analytic Samples for Critical Illness According to Type of Functional Outcome

Characteristic ^b	Overall ^a	Functional Recovery		<i>p</i>	Functional Decline		<i>p</i>
	<i>n</i> = 250	Yes, <i>n</i> = 169	No, <i>n</i> = 81		Yes, <i>n</i> = 212	No, <i>n</i> = 38	
Age, yr, mean ± SD	82.3 ± 5.7	81.9 ± 5.7	83.1 ± 5.6	0.125	82.2 ± 5.8	82.4 ± 5.4	0.840
Female sex, <i>n</i> (%)	146 (58.4)	98 (58.0)	48 (59.3)	0.848	124 (58.5)	22 (57.9)	0.945
Non-Hispanic White, <i>n</i> (%)	220 (88.0)	146 (86.4)	74 (91.4)	0.258	185 (87.3)	35 (92.1)	0.397
Lives alone, <i>n</i> (%)	98 (39.2)	66 (39.1)	32 (39.5)	0.945	83 (39.2)	15 (39.5)	0.970
Education, yr, mean ± SD	12.0 ± 2.8	12.1 ± 2.9	11.9 ± 2.7	0.621	12.0 ± 2.8	11.9 ± 2.9	0.915
Number of chronic conditions ^c , mean ± SD	2.5 ± 1.3	2.3 ± 1.3	2.7 ± 1.3	0.024	2.5 ± 1.3	2.2 ± 1.3	0.123
Body mass index (kg/m ²), mean ± SD	26.2 ± 5.2	26.4 ± 5.4	25.6 ± 4.9	0.237	26.2 ± 5.3	25.9 ± 5.2	0.777
Cognitive impairment ^d , <i>n</i> (%)	44 (17.6)	26 (15.4)	18 (22.2)	0.184	37 (17.5)	7 (18.4)	0.885
Depressive symptoms ^e , <i>n</i> (%)	43 (17.2)	26 (15.4)	17 (21.0)	0.271	38 (17.9)	5 (13.2)	0.473
Functional self-efficacy ^f , mean ± SD	27.2 ± 8.9	28.5 ± 8.8	24.5 ± 8.6	0.001	27.0 ± 8.7	28.5 ± 9.8	0.353
Hearing impairment ^g , <i>n</i> (%)	80 (32.0)	46 (27.2)	34 (42.0)	0.019	69 (32.6)	11 (29.0)	0.661
Visual impairment ^h , <i>n</i> (%)	116 (46.4)	73 (43.2)	43 (53.1)	0.142	98 (46.2)	18 (47.4)	0.897
Frailty phenotype ⁱ , <i>n</i> (%)				0.015			0.291
Nonfrail	33 (13.2)	28 (16.6)	5 (6.2)		27 (12.7)	6 (15.8)	
Prefrail	109 (43.6)	77 (45.6)	32 (39.5)		89 (42.0)	20 (52.6)	
Frail	108 (43.2)	64 (37.9)	44 (54.3)		96 (45.3)	12 (31.6)	
Number of disabilities ^j , mean ± SD	4.1 ± 3.3	3.6 ± 3.2	5.0 ± 3.3	0.002	4.1 ± 3.2	3.8 ± 4.0	0.600
Mechanical ventilation, <i>n</i> (%)	29 (11.7)	20 (11.8)	9 (11.3)	0.893	24 (11.3)	5 (13.5)	0.701
Length of ICU stay, d, mean ± SD	3.0 ± 4.3	2.8 ± 4.6	3.4 ± 3.6	0.253	2.9 ± 4.5	3.1 ± 2.8	0.841

^aThe 250 observations were contributed by 209 community-living participants, who survived to their first interview after hospital discharge.

^bData on chronic conditions, body mass index, cognitive impairment, depressive symptoms, functional self-efficacy, hearing and visual impairment, and frailty phenotype were collected during the prior comprehensive assessment, whereas data on number of disabilities were collected during the prior monthly interview.

^cIncluded hypertension, myocardial infarction, congestive heart failure, stroke, diabetes mellitus, arthritis, hip fracture, chronic lung disease, and cancer.

^dDefined as score < 24 on Folstein Mini-Mental State Examination.

^eDefined as score ≥ 20 on Center for Epidemiological Studies-Depression Scale.

^fScore on the Modified Self-Efficacy Scale: 0 (low) to 40 (high), where higher scores indicate greater confidence performing activities (19).

^gAssessed using a handheld audioscope, with severe impairment defined as 4 out of 4 tones missed, based on 1,000- and 2,000-Hz measurements for the left and right ears (20).

^hDefined as ≥ 5% when assessed with a Jaeger card and use of corrective lenses, if applicable (7).

ⁱBased on number of frailty criteria met (22).

^jOf 13 possible: four essential, five instrumental, and four mobility.

data, was high, with Kappa = 0.92 (95% CI, 0.90–0.95) and Kappa = 0.80 (0.78–0.82) (24), respectively. For descriptive purposes, the reasons for hospitalizations and ED visits were subsequently grouped into distinct diagnostic categories using revised versions of a previously described protocol (24, 25).

To ascertain less potent intervening events, participants were asked two questions related to restricted activity (14): 1) “Since we last talked on (date of last interview), have you cut down on your usual activities due to an illness, injury, or other problem?” and 2) “Since we last talked on (date of last interview), have you stayed in bed for at least half a day due to an illness, injury, or other problem?” Participants were considered to have restricted activity during a specific month if they answered “Yes” to one or both of the questions. These participants were subsequently asked to identify the reason(s) for their restricted activity using a standardized protocol that included 24 prespecified problems and an open-ended response.

The intervening events were organized into three mutually exclusive hierarchical categories: hospitalization, ED visit without hospitalization, and restricted activity alone (5).

Disability Assessments

Complete details regarding the assessment of disability are provided elsewhere (8, 15). Each month, participants were asked, “At the present time, do you need help from another person to (complete the task)?” for each of four essential activities (bathing, dressing, walking, and transferring), five instrumental activities (shopping, housework, meal preparation, taking medications, and managing finances), and three mobility activities (walk ¼ mile, climb flight of stairs, and lift/carry 10 pounds). For these 12 activities, disability was operationalized as the need for personal assistance. Participants were also asked about a fourth mobility activity, “Have you driven a car during the past month?” Participants who responded “No” (including never drivers) were considered to be “disabled” in driving (26). To address the small amount of missing data on disability (1% of observations), multiple imputation was used with 100 random draws per missing observation (27).

Ascertainment of Critical Illness

As previously described (7), admissions to the ICU were ascertained from two sources. The primary source was

linked Medicare claims data. An ICU admission was defined as any critical care revenue code, including general, specialty, and coronary care units, but excluding psychiatric or intermediate critical care. For periods when participants had managed Medicare, hospitalizations ascertained from the monthly interviews were evaluated for ICU admission through review of the corresponding medical records. Information was also obtained from these two sources on use of mechanical ventilation (7, 28) and length of ICU stay (7).

Functional Outcomes

The two outcomes included functional recovery and functional decline. Functional recovery was defined as the return, within 12 months of the first interview after hospital discharge from critical illness, to a total disability count (out of 13) less than or equal to that from the month immediately prior to the ICU admission (29). Functional decline was defined as an increase in the disability count of one or more essential activities (out of four) or two or more instrumental or mobility activities (out of nine) from 1 month to the next after hospital discharge from critical illness for up to 12 months (30, 31).

Assembly of Analytic Samples

ICU admissions were included through December 2017. Participants could contribute more than one observation to the analysis based on the following criteria: 1) only the first ICU admission within an 18-month interval was eligible, 2) participant was not admitted from a nursing home, 3) participant was not disabled in all 13 activities prior to the critical illness, 4) participant was not discharged from the hospital on hospice, 5) at least one interview was completed after hospital discharge, and 6) participant did not contribute an observation within the prior 12 months. As described in **Figure 1**, the analytic sample included 250 ICU admissions, which were contributed by 209 community-living participants. The reasons for these admissions were grouped into distinct diagnostic categories as described earlier.

Statistical Analysis

The characteristics of the analytic samples, assessed at the start of each 18-month interval, along with information on the ICU admissions, were summarized

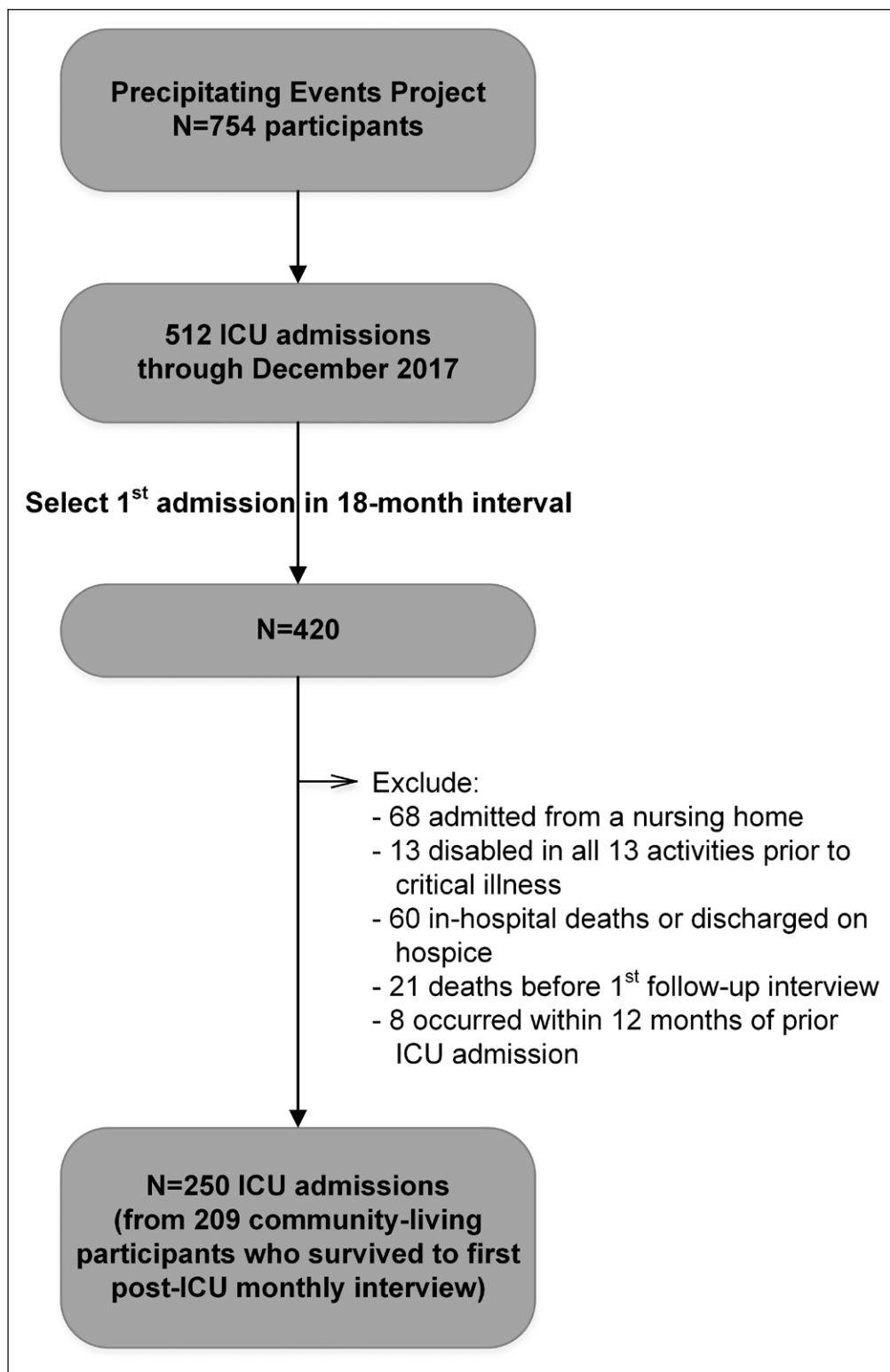


Figure 1. Assembly of Analytic Sample from Parent Cohort. Of the 512 ICU admissions through December 2017, 420 represented the first admission within an 18-mo interval. Of these, 170 were excluded: 68 were admitted from a nursing home, 13 were disabled in all 13 activities, 60 died in the hospital or were discharged on hospice, 21 died before their first interview after hospital discharge, and eight followed a prior ICU admission within 12 mo. The remaining 250 ICU admissions that were contributed by 209 community-living participants formed the final sample.

according to the type of functional outcome. For each outcome, exposure to the intervening events was calculated per 100-person months using an intercept-only Poisson model with generalized estimating equations (GEEs).

A Cox model for recurrent events was used to evaluate the bivariate and multivariable associations between each of the three intervening events and time to functional recovery (32). Participants who had not recovered were censored at time of death, withdrawal from study, or end of 12-month follow-up period. The multivariable model included each of the eight factors that were in a previously published functional recovery model—age, sex, race/ethnicity, body mass index, hearing impairment, visual impairment, functional self-efficacy, and number of disabilities in the month prior to ICU admission (7), along with the number of months to ICU admission from the start of 18-month interval and an indicator for calendar time. Several other factors (Table 1) were evaluated in the multivariable model using backward selection, but only length of ICU stay was retained based on a *p* value of less than 0.20. For each of the intervening events, adjusted hazard

ratios (HRs) and 95% CIs were calculated with the use of a robust sandwich variance estimator for standard errors (32).

Functional decline was evaluated as a recurrent event during the 12-month follow-up period. Months were not included when a further decline in function was not possible. A GEE logistic regression model was used to evaluate the bivariate and multivariable relationships between each of the intervening events and functional decline on a monthly basis (33). Adjusted odds ratios (ORs) and 95% CIs were estimated using the same set of covariates as in the earlier multivariable Cox model. A first-order autoregressive covariance structure was used to account for intercorrelations among repeated observations contributed by the same participants (33).

RESULTS

Table 1 provides the characteristics of the analytic samples. Overall, the mean age was 82.3 years, 58.4% were female, and 88.0% were non-Hispanic White. More than one of six had cognitive impairment, whereas more than four of 10 were frail. The mean number of disabilities was 4.1. About 12% were mechanically ventilated during their critical illness. The characteristics were generally worse among the 81 (32.4%) without recovery than the 169 (67.6%) with recovery. Differences

were less pronounced according to functional decline, and none was statistically significant. As shown in **Supplemental Digital Content 1** (<http://links.lww.com/CCM/G104>), the most common reasons for the ICU hospital admissions were cardiac and infection.

Over the 12-month follow-up period, the mean (SD) time to functional recovery was 3.2 (2.5) months, and the mean (SD) number of subsequent episodes, that is, months, with functional decline was 2.2 (1.6). Of the 541 episodes, 174 (32.2%), 226 (41.8%), and 141 (26.1%) were attributable to decline in essential activities alone, instrumental and/or mobility activities alone, and both.

The overall exposure rates (95% CI) per 100-person months to the intervening hospitalizations, ED visits, and restricted activity were 17.2 (14.3–20.8), 3.8 (2.7–5.2), and 12.1 (9.7–15.1) for the functional recovery analysis and 12.1 (10.3–14.3), 3.1 (2.4–4.0), and 11.5 (9.7–13.6) for the functional decline analysis. As shown in **Table 2**, exposure to intervening hospitalizations was nearly three-fold higher in the absence versus presence of functional recovery. Exposure to intervening ED visits and restricted activity was modestly higher in the absence versus presence of functional recovery, but these differences were not statistically significant. Differences in exposure to the intervening events were less pronounced based on the presence/absence of functional decline, and none of the differences

TABLE 2.
Exposure to Intervening Events in the Year After Critical Illness by Functional Outcome^a

Outcome	Hospitalization	Emergency Department Visit	Restricted Activity
Rate per 100-person months (95% CI)			
Functional recovery			
Yes	9.4 (7.3–12.0)	3.0 (1.8–4.9)	10.5 (7.9–14.0)
No	24.2 (19.2–30.5)	4.6 (3.1–6.7)	13.6 (9.9–18.5)
<i>p</i>	< 0.001	0.172	0.246
Functional decline			
Yes	12.3 (10.4–14.6)	3.2 (2.5–4.1)	11.5 (9.7–13.7)
No	10.8 (6.8–17.3)	2.5 (1.1–5.4)	11.4 (6.9–18.8)
<i>p</i>	0.610	0.523	0.914

^aThe three intervening events are mutually exclusive and hierarchical, as described in the *Materials and Methods* section. The mean (SD) duration of follow-up was 4.8 (3.9) mo for functional recovery and 10.5 (3.2) mo for functional decline.

were statistically significant. The reasons for the intervening hospitalizations, ED visits, and restricted activity are provided in **Supplemental Digital Content 2** (<http://links.lww.com/CCM/G105>), **Supplemental Digital Content 3** (<http://links.lww.com/CCM/G106>), and **Supplemental Digital Content 4** (<http://links.lww.com/CCM/G107>), respectively. For each, the most common reasons were infection and cardiac for hospitalization; cardiac, musculoskeletal, and infection for ED visit; and fatigue and dizziness/unsteadiness on feet for restricted activity. In absolute terms, differences between the no functional recovery and functional decline groups were most pronounced for infection (for hospitalization), cardiac (for ED visit), and problem with memory/difficulty thinking (for restricted activity).

Figure 2 provides the bivariate and multivariable associations between the intervening events and functional outcomes. An intervening hospitalization was strongly and significantly associated with reduced recovery in both bivariate and multivariable analyses,

with an adjusted HR of 0.18. Recovery was also reduced in the setting of an ED visit and restricted activity, respectively, but none of the bivariate or multivariable associations were statistically significant. In the multivariable analyses, the likelihood of functional decline was increased more than two-fold in the setting of a hospitalization, nearly 80% in the setting of an ED visit, and 25% in the setting of restricted activity, although the latter difference was not statistically significant. In the same multivariable model, the effect sizes for hospitalization on both functional outcomes were much larger than those for any of the covariates, including traditional risk factors such as functional self-efficacy and hearing impairment, whereas the effect size for ED visit on functional decline was modestly higher than those for the covariates (**Table 3**).

DISCUSSION

In this prospective study of community-living older ICU survivors, we evaluated the effects of intervening illnesses/injuries on two distinct, but related functional outcomes in the year after hospital discharge from a critical illness. Four main findings warrant comment. First, about a third of participants did not recover their pre-morbid level of function and most experienced at least one subsequent episode of functional decline in the year after their critical illness. Second, intervening illnesses/injuries leading to hospitalization, ED visit, or restricted activity were common in the year after critical illness. Third, in multivariable analyses that included a comprehensive array of demographic, clinical, and geriatric covariates, intervening hospitalizations were significantly associated with a lower likelihood

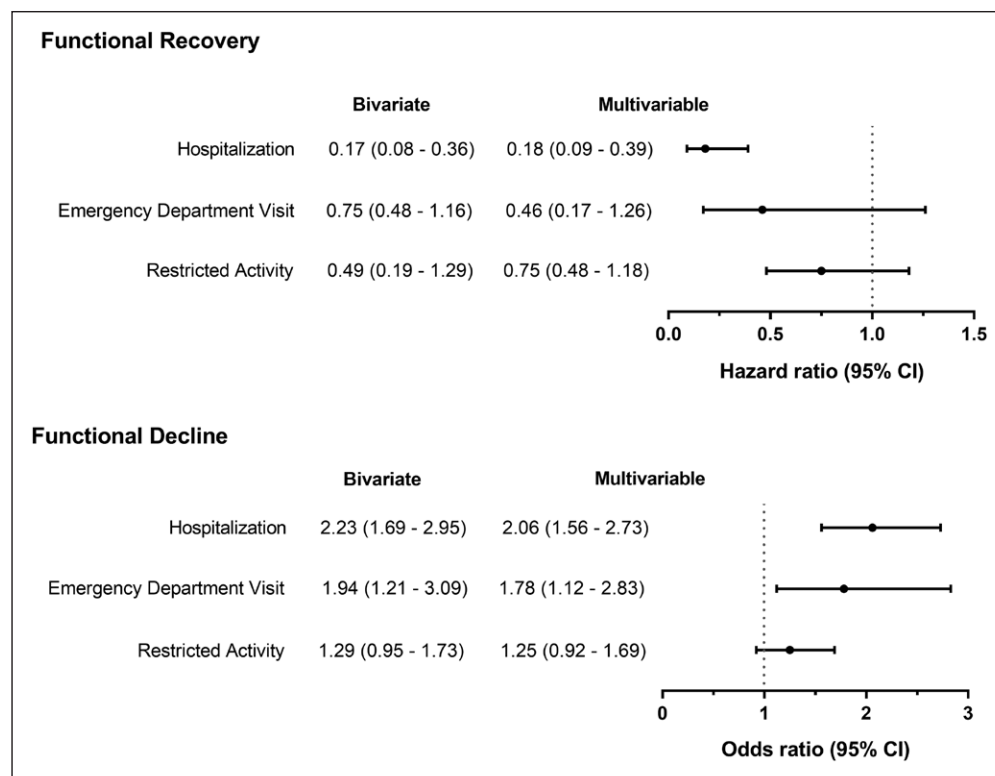


Figure 2. Bivariate and multivariable associations between the intervening events and functional outcomes. Each of the models included the three intervening events, which were mutually exclusive and hierarchical, as described in the *Materials and Methods* section. The multivariable models also included age, sex, race/ethnicity, body mass index, functional self-efficacy, hearing impairment, visual impairment, number of disabilities in the month prior to critical illness, length of ICU stay, number of months to ICU admission from start of 18-mo interval, and number of the specific 18-mo interval (to account for calendar time).

TABLE 3.
Multivariable Associations Between Covariates and Functional Outcomes^a

Covariate ^b	Functional Recovery	Functional Decline
	Hazard Ratio (95% CI)	OR (95% CI)
Age per year	1.00 (0.97–1.03)	1.00 (0.98–1.02)
Female sex	0.96 (0.73–1.27)	0.84 (0.68–1.04)
Non-Hispanic White	0.98 (0.66–1.47)	1.02 (0.75–1.38)
Body mass index, kg/m ²	1.02 (1.00–1.05)	0.98 (0.96–1.00)
Functional self-efficacy ^c	1.04 (1.02–1.06)	0.98 (0.97–0.99)
Hearing impairment ^d	0.72 (0.52–0.99)	1.02 (0.82–1.30)
Visual impairment ^e	1.00 (1.00–1.01)	0.79 (0.64–0.98)
Disabilities ^f , per each number	1.04 (0.98–1.10)	1.03 (0.99–1.07)
Length of ICU stay, per day	0.97 (0.93–1.01)	0.99 (0.97–1.01)

OR = odds ratio.

^aThe results are from the same multivariable models that are described in Figure 2. The models included the three intervening events, which were mutually exclusive and hierarchical, and also adjusted for number of months to ICU admission from start of 18-month interval, and number of the specific 18-mo interval (to account for calendar time). The 250 observations were contributed by 209 community-living participants.

^bData on body mass index, functional self-efficacy, hearing impairment, and visual impairment were collected during the prior comprehensive assessment, whereas data on number of disabilities were collected during the prior monthly interview.

^cPer point on scale from 0 to 40, where higher scores indicate greater confidence performing activities.

^dAssessed using a handheld audioscope, with severe impairment defined as 4 out of 4 tones missed, based on 1,000- and 2,000-Hz measurements for the left and right ears.

^eDefined as > 26% when assessed with a Jaeger card and use of corrective lenses, if applicable.

^fOf 13 possible: four essential, five instrumental, and four mobility.

of functional recovery, whereas intervening hospitalizations and ED visits were each significantly associated with a higher likelihood of subsequent functional decline. Finally, the magnitude of these associations was larger than that of the covariates, including traditional risk factors. These findings suggest that attention to intervening illnesses/injuries will be necessary to improve functional outcomes after critical illness in community-living older persons.

Prior studies of functional outcomes after critical illness have largely focused on factors available at the time of hospital discharge (7, 13, 34–36). Although several of these factors were evaluated in the current study, their effect on the two functional outcomes was generally much smaller than that of the intervening hospitalizations and ED visits. Because the rate of hospitalization after critical illness was higher than that of ED visit without hospitalization, strategies for improving functional outcomes after critical illness might focus most

intently on intervening hospitalizations, including minimizing preventable illnesses/injuries leading to hospitalization (37–41), decreasing the adverse functional consequences of hospitalization (42–46), bolstering restorative therapies after hospitalization (47, 48), and substituting hospital-at-home for traditional inpatient care (49). However, because the reasons for intervening hospitalizations were quite varied, with no single diagnostic category comprising more than 30% of the reasons, interventions delivered during or after these hospitalizations may have the greatest opportunity for success. Although only a minority of hospitalizations occurred within the first month of discharge after critical illness (24.6% for functional recovery and 15.4% for functional decline), facilitating safe and effective discharges, perhaps coupled with follow-up in a post-ICU clinic (50), may improve short- and long-term functional outcomes. Unfortunately, information was not available in the current study on posthospital outpatient care.

A unique feature of our study is the availability of data from monthly interviews, which allowed us to determine changes in functional status more accurately and ascertain exposure to intervening illnesses/injuries more completely. The frequency of our assessments increases the likelihood that the intervening events preceded the functional outcomes, thereby strengthening temporal precedence and supporting causal associations (25). Other strengths include assessment of a comprehensive set of essential, instrumental, and mobility activities, which allowed us to more precisely determine recovery of premorbid function and ascertain clinically meaningful declines in functional status; the availability of detailed data on a large array of demographic, clinical, and geriatric factors, which were reassessed every 18 months; and complete ascertainment of ICU admissions, using several different sources of information.

Our findings should be interpreted in the context of several potential limitations. First, information was not available on ICU-specific factors that cannot be reliably drawn from administrative data, such as delirium and severity of illness. To address this issue partially, the multivariable models included ICU length of stay and use of mechanical ventilation. Second, as evidenced by the wide CIs, power was limited to detect statistically significant differences for associations that are likely clinically meaningful, such as the 54% reduction in functional recovery in the setting of an ED visit. Third, because this was an observational study, the reported associations cannot be construed as causal. Even if the associations were causal, whether functional outcomes could be improved through currently available interventions is uncertain. Fourth, because our participants were members of a single health plan in a small urban area, our findings may not be generalizable to older persons in other settings. Generalizability, however, depends not only on the choice of the study sample but also on the stability of the sample over time (51). One of the great strengths of our study is the low attrition rate. The generalizability of our findings is also enhanced by our high participation rate, which was greater than 75%.

CONCLUSIONS

Intervening illnesses/injuries are common in the year after critical illness and those leading to hospitalization and ED visit are strongly associated with adverse

functional outcomes, with effect sizes larger than those of traditional risk factors. To improve functional outcomes among older persons, more aggressive efforts will be needed to prevent and manage intervening illnesses/injuries after critical illness.

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REFERENCES

1. Weissman GE, Kerlin MP, Yuan Y, et al: Population trends in intensive care unit admissions in the United States among Medicare beneficiaries, 2006-2015. *Ann Intern Med* 2019; 170:213-215
2. Administration on Aging, Administration for Community Living, U.S. Department of Health and Human Services: 2018 Profile of Older Americans, 2018. Available at: <https://acl.gov/sites/default/files/Aging%20and%20Disability%20in%20America/2018OlderAmericansProfile.pdf>. Accessed January 4, 2021

3. Ferrante LE, Pisani MA, Murphy TE, et al: The association of frailty with post-ICU disability, nursing home admission, and mortality: A longitudinal study. *Chest* 2018; 153:1378–1386
4. Ferrante LE, Pisani MA, Murphy TE, et al: Functional trajectories among older persons before and after critical illness. *JAMA Intern Med* 2015; 175:523–529
5. Gill TM, Han L, Gahbauer EA, et al: Risk factors and precipitants of severe disability among community-living older persons. *JAMA Netw Open* 2020; 3:e206021
6. Brummel NE, Balas MC, Morandi A, et al: Understanding and reducing disability in older adults following critical illness. *Crit Care Med* 2015; 43:1265–1275
7. Ferrante LE, Pisani MA, Murphy TE, et al: Factors associated with functional recovery among older intensive care unit survivors. *Am J Respir Crit Care Med* 2016; 194:299–307
8. Hardy SE, Gill TM: Recovery from disability among community-dwelling older persons. *JAMA* 2004; 291:1596–1602
9. Loyd C, Beasley TM, Miltner RS, et al: Trajectories of community mobility recovery after hospitalization in older adults. *J Am Geriatr Soc* 2018; 66:1399–1403
10. Prvu Bettger JA, Coster WJ, Latham NK, et al: Analyzing change in recovery patterns in the year after acute hospitalization. *Arch Phys Med Rehabil* 2008; 89:1267–1275
11. Stuck AE, Walthert JM, Nikolaus T, et al: Risk factors for functional status decline in community-living elderly people: A systematic literature review. *Soc Sci Med* 1999; 48:445–469
12. Hardy SE, Gill TM: Factors associated with recovery of independence among newly disabled older persons. *Arch Intern Med* 2005; 165:106–112
13. Ferrante LE, Murphy TE, Leo-Summers LS, et al: The combined effects of frailty and cognitive impairment on post-ICU disability among older ICU survivors. *Am J Respir Crit Care Med* 2019; 200:107–110
14. Gill TM, Desai MM, Gahbauer EA, et al: Restricted activity among community-living older persons: Incidence, precipitants, and health care utilization. *Ann Intern Med* 2001; 135:313–321
15. Gill TM, Hardy SE, Williams CS: Underestimation of disability in community-living older persons. *J Am Geriatr Soc* 2002; 50:1492–1497
16. Gill TM, Han L, Gahbauer EA, et al: Cohort profile: The precipitating events project (PEP study). *J Nutr Health Aging* 2020; 24:438–444
17. Folstein MF, Folstein SE, McHugh PR: "Mini-mental state." A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 1975; 12:189–198
18. Kohout FJ, Berkman LF, Evans DA, et al: Two shorter forms of the CES-D (Center for Epidemiological Studies Depression) depression symptoms index. *J Aging Health* 1993; 5:179–193
19. Reid MC, Williams CS, Gill TM: The relationship between psychological factors and disabling musculoskeletal pain in community-dwelling older persons. *J Am Geriatr Soc* 2003; 51:1092–1098
20. Lichtenstein MJ, Bess FH, Logan SA: Validation of screening tools for identifying hearing-impaired elderly in primary care. *JAMA* 1988; 259:2875–2878
21. Spaeth EB, Fralick FB, Hughes WF: Estimates of loss of visual efficiency. *Arch Ophthalmol* 1955; 54:462–468
22. Fried LP, Tangen CM, Walston J, et al; Cardiovascular Health Study Collaborative Research Group: Frailty in older adults: Evidence for a phenotype. *J Gerontol A Biol Sci Med Sci* 2001; 56:M146–M156
23. Gill TM: Disentangling the disabling process: Insights from the precipitating events project. *Gerontologist* 2014; 54:533–549
24. Nagurney JM, Fleischman W, Han L, et al: Emergency department visits without hospitalization are associated with functional decline in older persons. *Ann Emerg Med* 2017; 69:426–433
25. Gill TM, Allore HG, Holford TR, et al: Hospitalization, restricted activity, and the development of disability among older persons. *JAMA* 2004; 292:2115–2124
26. Gill TM, Gahbauer EA, Murphy TE, et al: Risk factors and precipitants of long-term disability in community mobility: A cohort study of older persons. *Ann Intern Med* 2012; 156:131–140
27. Gill TM, Guo Z, Allore HG: Subtypes of disability in older persons over the course of nearly 8 years. *J Am Geriatr Soc* 2008; 56:436–443
28. Sjoding MW, Prescott HC, Wunsch H, et al: Longitudinal changes in ICU admissions among elderly patients in the United States. *Crit Care Med* 2016; 44:1353–1360
29. Becher RD, Murphy TE, Gahbauer EA, et al: Factors associated with functional recovery among older survivors of major surgery. *Ann Surg* 2020; 272:92–98
30. Kempen GI, Myers AM, Powell LE: Hierarchical structure in ADL and IADL: Analytical assumptions and applications for clinicians and researchers. *J Clin Epidemiol* 1995; 48:1299–1305
31. Finch M, Kane RL, Philp I: Developing a new metric for ADLs. *J Am Geriatr Soc* 1995; 43:877–884
32. Therneau TM, Grambsch PM: *Modeling Survival Data: Extending the Cox Model*. New York, NY, Springer, 2000
33. Diggle PJ, Heagerty PJ, Liang KY, et al: *Analysis of Longitudinal Data*. Second Edition. New York, NY, Oxford University Press, 2002
34. Neuman MD, Eckenhoff RG: Functional outcomes after critical illness in the elderly. *Crit Care Med* 2015; 43:1340–1341
35. Baldwin MR: Measuring and predicting long-term outcomes in older survivors of critical illness. *Minerva Anesthesiol* 2015; 81:650–661
36. Herridge MS, Chu LM, Matte A, et al; RECOVER Program Investigators (Phase 1: Towards RECOVER); Canadian Critical Care Trials Group: The RECOVER program: Disability risk groups and 1-year outcome after 7 or more days of mechanical ventilation. *Am J Respir Crit Care Med* 2016; 194:831–844
37. Tinetti ME: Clinical practice. Preventing falls in elderly persons. *N Engl J Med* 2003; 348:42–49

38. Straus SE, Majumdar SR, McAlister FA: New evidence for stroke prevention: Clinical applications. *JAMA* 2002; 288:1396–1398
39. Kim DK, Hunter P; Advisory Committee on Immunization Practices: Recommended adult immunization schedule, United States, 2019. *Ann Intern Med* 2019; 170:182–192
40. Kastner M, Cardoso R, Lai Y, et al: Effectiveness of interventions for managing multiple high-burden chronic diseases in older adults: A systematic review and meta-analysis. *CMAJ* 2018; 190:E1004–E1012
41. Pritchard C, Ness A, Symonds N, et al: Effectiveness of hospital avoidance interventions among elderly patients: A systematic review. *CJEM* 2020; 22:504–513
42. Rich MW: Heart failure in the 21st century: A cardiogeriatric syndrome. *J Gerontol A Biol Sci Med Sci* 2001; 56: M88–M96
43. Landefeld CS, Palmer RM, Kresevic DM, et al: A randomized trial of care in a hospital medical unit especially designed to improve the functional outcomes of acutely ill older patients. *N Engl J Med* 1995; 332:1338–1344
44. Cohen HJ, Feussner JR, Weinberger M, et al: A controlled trial of inpatient and outpatient geriatric evaluation and management. *N Engl J Med* 2002; 346:905–912
45. Inouye SK: Delirium in older persons. *N Engl J Med* 2006; 354:1157–1165
46. Detsky AS, Krumholz HM: Reducing the trauma of hospitalization. *JAMA* 2014; 311:2169–2170
47. Tinetti ME, Baker D, Gallo WT, et al: Evaluation of restorative care vs usual care for older adults receiving an acute episode of home care. *JAMA* 2002; 287:2098–2105
48. Hoenig H, Nusbaum N, Brummel-Smith K: Geriatric rehabilitation: State of the art. *J Am Geriatr Soc* 1997; 45:1371–1381
49. Federman AD, Soones T, DeCherrie LV, et al: Association of a bundled hospital-at-home and 30-day postacute transitional care program with clinical outcomes and patient experiences. *JAMA Intern Med* 2018; 178:1033–1040
50. Kuehn BM: Clinics aim to improve post-ICU recovery. *JAMA* 2019; 321:1036–1038
51. Szklo M: Population-based cohort studies. *Epidemiol Rev* 1998; 20:81–90