Depressive symptoms, apathy, and adverse health outcomes in acutely hospitalized older patients

Research to get the ball rolling

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Chapter

5

Trajectories of cognitive-affective depressive symptoms in acutely hospitalized older adults: The hospital-ADL study

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Abstract

Objective: To identify trajectories of cognitive-affective depressive symptoms among acutely hospitalized older patients and whether trajectories are related to prognostic baseline factors and three-month outcomes such as functional decline, falls, unplanned readmissions, and mortality.

Methods: Prospective multicenter cohort of acutely hospitalized patients aged ≥70. Depressive trajectories were based on Group Based Trajectory Modeling, using the Geriatric Depression Scale-15. Outcomes were functional decline, falls, unplanned readmission, and mortality within three months post-discharge.

Results: The analytic sample included 398 patients (mean age = 79.6 years; SD = 6.6). Three distinct depressive symptoms trajectories were identified: minimal (63.6%), mild persistent (25.4%), and severe persistent (11.0%). Unadjusted results showed that, compared to the minimal symptoms group, the mild and severe persistent groups showed a significantly higher risk of functional decline (mild: OR = 3.9, $p < .001$; severe: OR = 3.0, $p = .04$), falls (mild: OR = 2.0, p = .02; severe: OR = 6.0, $p < .001$), and mortality (mild: OR = 2.2, $p = .05$; severe: OR = 3.4, $p = .009$). Patients with mild or severe persistent symptoms were more malnourished, anxious, and functionally limited and had more medical comorbidities at admission.

Conclusion: Nearly 40% of the acutely hospitalized older adults exhibited mild to severe levels of cognitive-affective depressive symptoms. In light of the substantially elevated risk of serious complications and the fact that elevated depressive symptoms was not a transient phenomenon identification of these patients is needed. This further emphasizes the need for acute care hospitals, as a point of engagement with older adults, to develop discharge or screening procedures for managing cognitive-affective depressive symptoms.

Introduction

Depressive symptoms are highly prevalent among hospitalized older adults, whereby studies report that more than one-third display clinically elevated depressive symptoms.[1, 2] Importantly, depression is associated with adverse outcomes, including functional decline,[3, 4] falls,[5, 6] readmissions,[7] and mortality.[4, 7, 8]

The course of depressive symptoms after hospitalization can be transient,[2, 4] increasing, or persistent,[1] and the dynamic course could differentially impact post-hospitalization recovery.[4] For example, Ciro et al[1] found that the vast majority (81%) of acutely hospitalized older patients with severe depressive symptoms during hospitalization were still depressed at three months post-discharge.[1] This is in line with abundant research reporting that elevated late-life depressive symptomatology is often not a transient phenomenon in different settings (e.g., primary care, community based and other clinical samples).[9, 10] Previous research has shown that the first month after acute hospital discharge has been identified as a critical period for recovery among older patients.[11] However, the limited number of longitudinal studies that focused on depressive symptoms during those first critical months post-discharge performed only a single post-hospitalization assessment, making it difficult to infer a time course.[1, 2, 4] Furthermore, perhaps more importantly, previous research distinguished the symptomatology of depression in somatic symptoms (e.g., fatigue and insomnia) and cognitive-affective symptoms (e.g., anhedonia, negative thoughts, and hopelessness).[12] Several recent cardiac studies have shown that somatic symptoms of depression, but not cognitive-affective symptoms are associated with adverse health outcomes.[13-20] However, these studies investigated depressive symptoms by means of measurements involving both somatic symptoms and cognitive-affective symptoms,[1, 4] which may therefore result in confounding, as most somatic depressive symptoms overlap with medical illness symptoms or features of the aging process.[21] Even though somatic symptoms have shown an additional and consistent effect on adverse outcomes, identifying the course of cognitive-affective symptoms solely in the short term has generally not been a focus of study.

A more fine-grained understanding of the course of cognitive-affective depressive symptoms that develop during acute hospitalization and up to three months post-discharge may provide useful information for acute hospital settings in identifying older patients who are vulnerable to severe cognitive-affective depressive symptoms post-hospitalization. Therefore, the aims of the present study were to identify the distinct trajectories of cognitive-affective depressive symptoms from acute hospitalization up to three months post-discharge. Also we investigated whether baseline variables are associated with trajectory group membership, and if such distinct trajectories are associated with short-term adverse outcomes within three months of post-discharge. Therefore, we developed a Group-Based Trajectory Model (GBTM) to fit cognitive-affective depressive symptoms after acute hospitalization and examined how these trajectories correlate with the outcomes.

Materials and methods

Design

The current analysis drew on the Hospital-ADL study, previously described in detail elsewhere.[22] In brief, the Hospital-ADL study is a multicenter prospective cohort study that aims to investigate the cognitive, behavioral, psychosocial, physical, and biological factors that may be associated with adverse outcomes in acutely hospitalized older adults, including functional decline, falls, unplanned readmission and mortality. These adverse outcomes are common among hospitalized older patients[11, 23-29] and also highly associated with depressive symptoms.[3-8] Six hospitals in the Netherlands participated: 1) Amsterdam University Medical Centers (UMC), location Academic Medical Center (AMC), Amsterdam; 2) Isala, Zwolle; 3) Tergooi Hospital, Blaricum; 4) Medical Center (MC) Slotervaart, Amsterdam; 5) BovenIJ Hospital, Amsterdam, and; 6) Meander MC, Amersfoort. Local approval was additionally provided by all six participating hospitals. Data was collected between October 1st, 2015 and June 1st, 2017, and the study was approved by the Institutional Review Board of the Amsterdam UMC location AMC in the Netherlands (Protocol ID: AMC2015_150). The research was performed according to the Dutch Medical Research Involving Human Subjects Act and the principles of the Declaration of Helsinki (1964).

Study sample

A total of 401 participants were recruited from those who were acutely admitted (i.e., unplanned admission, often via the emergency department) at Departments of Internal Medicine, Cardiology, or Geriatrics at one of the six Dutch hospitals. Inclusion criteria were: 1) admitted for ≥48 h; 2) Dutch language proficiency sufficient to complete questionnaires; and 3) a Mini Mental State Examination (MMSE) score of 15 or higher.[30] It is important to note that we were not able to include delirious patients due to the short timeframe of inclusion, i.e., within 48 h after admission. Delirium was often still present at this time point, due to which an MMSE could not be performed or patients scored below 15 points. The Confusion Assessment Method (CAM) was used to identify the presence of delirium.31 Patients were excluded if they: 1) had a life expectancy of three months or less, according to the attending Medical Doctor, or 2) were disabled in all six basic Activities of Daily Livings (ADL), as determined by the Katz-6 ADL index.[32] Due to the fact that this study is part of The Hospital-ADL study aimed to identify predictors of functional decline, this study has decided to exclude participants who were already fully disabled in all six basic ADL at the start of the study.[22]

Procedures

Two researchers (RVS and LR) contacted eligible patients within 48 h of hospital admission. Patients were informed about the objectives and procedures of the study. All participants provided written informed consent before inclusion. A trained geriatric team completed personal interviews at baseline (i.e., within 48 h of admission), at discharge, and at one, two and three months post-discharge. All interviews were performed face-to-face in the hospital or at participants' home or residence, with exception of the interview at two months post-discharge, which took place by telephone.

Measurements

Depressive symptoms. Depressive symptoms were assessed using the Geriatric Depression Scale-15 (GDS-15), which is a short version of the GDS-30,[33] comprising 15 symptom items scored on a binary (yes/no) scale, assessing symptom experience over the preceding week, whereby a score of six or above is considered indicative of clinically relevant depressive symptoms. Regarding the criterion validity, the GDS-15 has a sensitivity of 0.805 and a specificity of 0.750, using worldwide pooled studies.[34] Because the somatic symptoms of depression can also be caused by medical symptoms and may be intrinsic to the aging process, thus artificially inflating depression scores,[34] the GDS-15 was specifically designed to minimize such confounding by excluding somatic symptoms.[35]

Baseline variables. The baseline variables selected for the present analysis were demographic variables (i.e., age, sex, marital status, and living arrangements), admission department, hospital admission diagnosis, comorbidity of chronic conditions, malnutrition, premorbid activities of daily living (ADL) functioning, cognitive impairment, and anxiety at admission. The number and severity of comorbidities were scored with the Charlson Comorbidity Index (CCI),[36] while malnourishment was measured using the Short Nutritional Assessment Questionnaire (SNAQ). The total score of the SNAQ is the sum of the raw scores (range: 0–7), wherein a score of 2 or higher was defined as malnutrition.[37] Premorbid ADL functioning was measured with the Katz-6 ADL index score formulated as two weeks before admission (range: 0–6). The Katz-ADL index score assesses the degree of independence on the following six activities of daily living: bathing, dressing, toileting, use of incontinence materials, transfer from bed to chair, and eating.[32] Higher scores indicate more dependency. Cognitive impairment was measured with the MMSE, a validated 30-point screening of cognitive impairment, whereby a score of 23 or less on the MMSE was defined as cognitive impairment.[30] Finally, anxiety was measured with the State-Trait Anxiety Inventory-6 (STAI-6) on a 4-point Likert scale (range: 6–24, Cronbach's α = 0.79–0.81[38]). The STAI-6 is a short form of the 20-item state scale of the Spielberger State-Trait Anxiety Inventory (STAI),[39] but it maintains results comparable with the full form.[38]

Adverse short-term outcomes. The outcomes selected for the current analysis were functional decline, falls, unplanned readmission, and mortality within three months post-discharge. Functional decline was measured with the Katz-6 ADL index score[32] and defined as the level of basic ADL functioning at three months post-discharge compared to self-reported premorbid ADL functioning (i.e., two weeks before admission) assessed retrospectively during admission. Functional decline was measured as well as the difference between the two following time points: two weeks before hospital admission and three months post-discharge. Only the patients measured at these two time points were included in the analysis. To assess if patients had experienced a fall from discharge to three months post-discharge the following question was asked: *"Have you fallen once in the past month post-hospitalization?"*.[40] Only patients for whom data was available during post-hospitalization were included in the analysis of falls. Any unplanned readmission(s) up to three months postdischarge was registered using medical records, and we also retrieved this information by means of self-reporting at one,

two, and three months post-discharge with the following self-report question: *"Have you been acutely hospitalized in the last one month?"*.[41] Only patients for whom data was available during post-hospitalization were included in the analysis of unplanned readmission. Mortality from admission until three months post-discharge was retrieved from medical records or by means of reports from family members or the general practitioner. Supplementary Figure S1 provides an overview of the different adverse short-term outcomes measurements and sample sizes.

Statistical analyses

This study used Group Based Trajectory Modeling (GBTM), a semiparametric analysis that provides an insightful summary of the longitudinal development of depressive symptoms over time by identifying subgroups with specific developmental patterns.[42] A quadratic development over time was modeled and the Bayesian Information Criterion (BIC) was used to evaluate model fit, which balances model complexity (i.e., the number of parameters) and sample size, with goodness of fit to the sample data. The average posterior probabilities of group membership (≥0.9 is being excellent fit, and ≤0.7 a poor fit) were used to evaluate the adequacy of the final model.[43] Due to the small sample size, model selection included the criterion that each trajectory group had to include at least 10% of participants. We evaluated the appropriate number of trajectories by calculating the estimated log Bayes factor, which compares BIC values between models. To estimate the amount of bias that was introduced due to missing values, we performed sensitivity analysis with the patients with no missing data. Baseline (i.e., admission) characteristics of the total analytic sample and distinct trajectory groups were summarized using descriptive statistics and differences between depressive symptoms trajectories were tested using One-Way ANOVAs and Chi-square tests. The relationship between prognostic baseline covariates and the trajectories of depressive symptoms was assessed with multinomial logistic regression analyses, leading to odds ratios and 95% confidence intervals. The baseline variables were selected on the basis of the previous literature on prognostic factors for depressive symptoms. Finally, for each selected adverse short-term health outcome, multivariable logistic regression analyses were performed to compare depressive symptoms trajectory groups, with and without adjustment for potential confounders. The sample sizes may differ between analyses as we did not measure the adverse health outcomes at the same point in time. Three analyses were performed: 1): crude; 2): adjusted for demographics (i.e., age, sex, education, marital status, and living arrangements); and 3) additionally adjusted for medical comorbidities, malnutrition, ADL functioning, and cognitive functioning at admission. GBTM was performed with PROC TRAJ using SAS software, version 9.3 (SAS Institute Inc., Cary, North Carolina). All other analyses were conducted using IBM SPSS Statistics, version 24.0, Armonk, NY: IBM Corp. Differences were considered statistically significant at $p < .05$ (2-tailed).

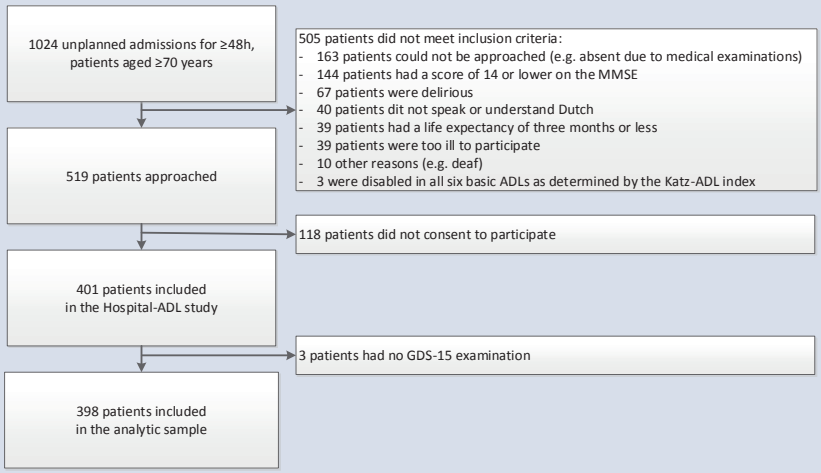

Figure 1. Flow chart of the Hospital-ADL study.
Note: MMSE=Mini Mental State Examination; ADL=Activities of Daily Living; GDS-15=Geriatric Depression Scale-15.

Results

Baseline characteristics

Figure 1 provides an overview of the enrollment of patients. There were 1024 acutely hospitalized patients eligible for participation in this study between October 2015 and February 2017. Of these unplanned admissions, 519 patients met the inclusion criteria and were available to be contacted. A total of 401 agreed to participate, of which 53.6%, 29.4%, and 17.0% were, respectively, patients from the Departments of Internal Medicine, Cardiology, and Geriatrics. Three patients had no GDS-15 data and were excluded from the total sample. Therefore, the analytic sample for the current study included 398 acutely hospitalized patients. Table 1 shows the baseline characteristics of the analytic sample (mean age = 79.6 years (SD = 6.6); 51% men).

Identification of trajectories: minimal, mild, and severe depressive symptoms

On average, the GDS-15 was completed 4.0 times (SD = 1.4; range: 1–5); 70% had four or all five GDS-15 interviews. In total, 1576 GDS-15 observations were available for the trajectory modeling. Although a six-trajectory model showed the lowest BIC value (−3344.4), three of those trajectories had groups containing < 10% of the total sample, as well as the four- and five-trajectory models. Therefore, we selected the three-group trajectory model (BIC = -3389.2). The results of the sensitivity analysis (i.e., a complete case analysis) yielded the same depressive symptoms trajectories as the initial analysis. Figure 2 shows the three distinct depressive symptoms trajectories: 1) minimal (n = 253, 63.6%); 2) persistent mild (n = 101, 25.4%); and 3) persistent severe depressive symptoms (n = 44, 11.0%). In all groups, the average posterior probability of group membership was between

0.85 and 0.95, which is considered a good to excellent fit.42 For the group with persistent severe depressive symptoms, we found a GDS-15 average score (SD) ranging from 9.5 (2.5) at admission to 9.1 (2.9) at three months post-discharge. For the group with persistent mild depressive symptoms, the GDS-15 average score (SD) ranged from 5.6 (1.7) to 4.7 (2.1) and from 2.4 (1.4) to 1.5 (1.4) for the minimal depressive symptoms.

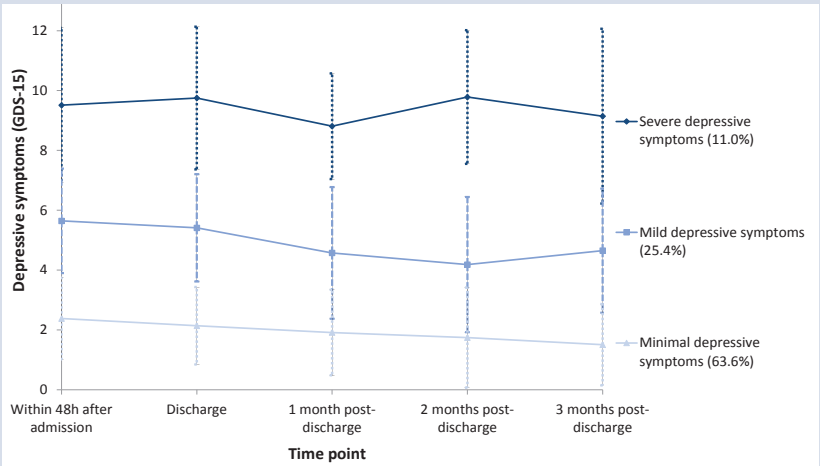

Figure 2. Trajectories, and their associated standard errors, of depressive symptoms from acute hospitalization to three months post-discharge.

Baseline variables associated with trajectory group membership

As shown in Table 1, the three trajectories significantly differ in marital status (p = .005), admission department (p = .001), comorbidity (p < .001), malnutrition (p < .001), premorbid ADL functioning (p < .001), and cognitive impairment (p = .017) at admission. Patient characteristics associated with trajectory group membership are shown in Table 2. The column in Table 2 labeled "Severe vs. Minimal" provides odds ratios estimating the association of baseline prognostic variables with the pattern of depression symptoms, comparing the severe persistent course to the minimal course. Not being married, being admitted to the Department of Geriatrics, reporting more medical comorbidities, being cognitively impaired, and higher anxiety scores were associated with a persistent severe course of depressive symptoms. The column in Table 2 labeled "Mild vs. Minimal" highlights the differences in prognostic factors between the mild persistent and minimal courses. In this regard, being admitted to the Department of Geriatrics, being malnourished, functionally limited, and higher anxiety scores were associated with a persistent mild course of depressive symptoms.

Table 1. Baseline characteristics of analytic sample according to depressive symptoms trajectory.

Characteristics	All patients (N=398)	Minimal (n=253)	Mild (n=101)	Severe (n=44)	Global Test
Age, y, mean (SD)	79.6 (6.6)	79.3 (6.3)	80.5 (7.3)	79.7 (7.0)	.317
Male sex, n (%)	203 (51.0)	138 (54.5)	46 (45.5)	19 (43.2)	.170
Living arrangements, n (%)					.599
Independent	334 (83.9)	216 (85.4)	83 (82.2)	35 (79.5)	
Nursing home	9 (2.3)	5 (2.0)	2 (2.0)	2 (4.5)	
Senior residence	55 (13.8)	32 (12.6)	16 (15.8)	8 (15.9)	
Marital status, n (%)					.005**
Married or living together	206 (51.8)	142 (56.1)	51 (50.5)	13 (29.5)	
Single/divorced/widowed	192 (48.2)	111 (43.9)	50 (49.5)	31 (70.5)	
Hospital sites, n (%)					.363
Amsterdam UMC, AMC	107 (26.9)	67 (26.5)	29 (28.7)	11 (25.0)	
Isala	13 (3.3)	7 (2.8)	5 (5.0)	1 (2.3)	
Tergooi Hospital	79 (19.8)	48 (19.0)	23 (22.8)	8 (18.2)	
MC Slotervaart	56 (14.1)	29 (11.5)	18 (17.8)	9 (20.5)	
BovenIJ Hospital	100 (25.1)	71 (28.1)	20 (19.8)	9 (20.5)	
Meander MC	43 (10.8)	31 (12.3)	6 (5.9)	6 (13.6)	
Admission department, n (%)					.001**
Cardiac	118 (29.6)	85 (33.6)	23 (22.8)	10 (22.7)	
Internal Medicine	213 (53.5)	140 (55.3)	52 (51.5)	21 (47.7)	
Geriatrics	67 (16.8)	28 (11.1)	26 (25.7)	13 (29.5)	
Reasons of hospital admission, n (%)					.075
Infection	58 (14.6)	39 (15.4)	11 (10.9)	8 (18.2)	
Gastrointestinal	45 (11.3)	30 (11.9)	8 (7.9)	7 (15.9)	
Cardiac	121 (30.4)	88 (34.8)	24 (23.8)	9 (20.5)	
Respiratory	74 (18.6)	42 (16.6)	25 (24.8)	7 (15.9)	
Cancer	13 (3.3)	7 (2.8)	5 (5.0)	1 (2.3)	
Electrolyte disturbance	10 (2.5)	6 (2.4)	3 (3.0)	1 (2.3)	
Renal	15 (3.8)	12 (4.7)	3 (3.0)	0 (0.0)	
Other (e.g., malaise, pain, dizziness, and falls)	62 (15.6)	29 (11.5)	22 (21.8)	11 (25.0)	
CCI score, mean (SD)	2.1 (2.0)	1.9 (1.8)	2.5 (2.1)	2.9 (2.2)	<.001***
Malnutrition, n (%)*	153 (38.5)	75 (29.8)	54 (53.5)	24 (54.5)	<.001***
Premorbid ADL functioning, mean (SD)	1.6 (1.7)	1.3 (1.5)	2.0 (1.8)	2.3 (1.9)	<.001***
Cognitive impairment, n (%)†	73 (19.4)	39 (16.1)	20 (21.3)	14 (35.0)	.017*
STAI score, mean (SD)	11.3 (3.0)	10.3 (2.3)	12.5 (2.6)	14.7 (3.5)	<.001***
GDS-15 score, mean (SD)	4.0 (2.9)	2.4 (1.4)	5.6 (1.7)	9.5 (2.6)	<.001***

Note: *Score of 2 or higher on the Short Nutritional Assessment Questionnaire (range, 0–7); †Cognitively impaired if a score of less than 24 on the Mini-Mental State Examination (range, 0–30); SD = standard deviation; UMC = University Medical Centers; AMC = Academic Medical Center; MC = Medical Center; CCI = Charlson Comorbidity Index score; ADL = activities of daily living; STAI = State-Trait Anxiety Inventory; GDS-15 = Geriatric Depression Scale-15; *$p < .05$; **$p < .01$; ***$p < .001$ (reference= minimal).

Associations of trajectories with adverse short-term health outcomes
Functional decline. In total, 46 (16.8%) of the 274 patients experienced functional decline at three months post-discharge, when compared to their pre-admission ADL. The absolute percentage of functional decline was 10.6%, 31.7%, and 26.1% in the groups with minimal, mild, and severe depressive symptoms, respectively. Univariate logistic regression models show that compared with the minimal symptoms group, the mild depressive symptoms group had a significant higher risk of developing functional decline (OR = 3.9, 95% CI = 1.9–7.9, $p < .001$), in addition to the severe patients group (OR = 3.0, 95% CI = 1.0–8.4, $p = .04$). No significant differences were observed between these two groups. Adjusting for baseline variables, only the group with mild depressive symptoms had a significant higher risk of developing functional decline (OR = 3.5, 95% CI = 1.7–7.2, $p = .001$) (see Table 3).

Falls. Of the 267 patients, 31.1% experienced at least one fall three months post-discharge. The absolute percentages of at least one fall three months post-discharge were 26.1%, 41.2%, and 68.0% in the minimal, mild, and severe depressive symptoms groups respectively. Logistic regressions showed that, compared with the minimal symptoms group, the severe patients group (OR = 6.0, 95% CI = 2.4–14.8, $p < .001$) and the mild patients group (OR = 2.0, 95% CI = 1.1–3.6, $p = .02$) had a higher risk of experiencing at least one fall three months post-discharge. The two highest groups were significantly different (OR = 3.0, 95% CI = 1.1–8.0, $p = .03$). Adjusting for confounders, only the group with persistent severe depressive symptoms still had a significantly high risk of falling three months post-discharge (OR = 4.6, 95% CI = 1.6–13.1, $p = .004$) (see Table 3).

Table 2. Multinomial logistic regression of baseline patient characteristics among three trajectories of depressive symptoms generated from the Group Based Trajectory Modeling (N=398).

Characteristics	**Severe vs. Minimal OR [95% CI]**	**Mild vs. Minimal OR [95% CI]**
Marital status (ref: married)	4.8** [1.8–12.3]	1.3 [0.8–2.4]
Admission department (ref: cardiology) Geriatrics Internal Medicine	 4.2** [1.1–16.2] 1.5 [0.5–4.5]	 4.0** [1.6–10.3] 1.5 [0.8–2.9]
Charlson Comorbidity Index (CCI) score	1.4** [1.2–1.7]	1.1* [1.0–1.3]
Malnutrition (ref: malnourished) *	1.8 [0.8–4.4]	2.2** [1.2–3.8]
Premorbid ADL functioning	1.4 [0.9–2.0]	1.5** [1.2–1.9]
Cognitive impairment (ref: cognitive impaired)†	5.7*** [2.2–15.0]	1.7 [0.9–3.4]
State-Trait Anxiety Inventory score	1.9*** [1.6–2.3]	1.4*** [1.3–1.6]

Note: *Score of 2 or higher on the Short Nutritional Assessment Questionnaire (range: 0–7); †Cognitively impaired if a score of less than 24 on the Mini-Mental State Examination (range: 0–30); ADL = activities of daily living; OR = odds ratio; 95% CI = 95% confidence interval; *$p < .05$; **$p < .01$; ***$p < .001$ (reference=minimal).

Table 3. Multivariate logistics regression models for each adverse health outcome within three months post-discharge by depressive symptoms trajectory.

		Model 1_a			Model 2_b			Model 3_c		
Outcome	**Trajectories**	**OR**	**95% CI**	***p***	**OR**	**95% CI**	***p***	**OR**	**95% CI**	***p***
Functional decline	Minimal									
	Mild	3.9	1.9–7.9	<.001	3.5	1.7–7.2	.001	3.1	1.3–7.3	.010
	Severe	3.0	1.0–8.4	.041	2.8	0.9–8.4	.066	1.0	0.2–4.3	.950
Falls	Minimal									
	Mild	2.0	1.1–3.6	.022	1.8	1.0–3.3	.052	1.3	0.6–2.5	.499
	Severe	6.0	2.4–14.8	<.001	6.8	2.6–17.4	<.001	4.4	1.5–12.3	.006
Unplanned readmissions	Minimal									
	Mild	0.9	0.5–1.7	.737	0.9	0.5–1.7	.804	0.6	0.3–1.3	.204
	Severe	1.1	0.4–2.8	.829	1.2	0.5–3.0	.750	1.1	0.4–3.0	.926
Mortality	Minimal									
	Mild	2.2	1.0–4.7	.047	2.2	1.0–4.8	.056	1.3	0.5–3.1	.601
	Severe	3.4	1.3–8.5	.009	3.1	1.2–8.2	.019	1.5	0.5–4.7	.483

Note: OR = odds ratio; 95% CI = 95% confidence interval; *p* = *p*-value; (reference=minimal); a=crude model; b=adjusted for demographics (i.e., age, sex, marital status, and living arrangements); c=additionally adjusted for admission department, hospital admission diagnosis, medical comorbidities, malnutrition, ADL functioning, and cognitive functioning at admission.

Unplanned readmission. Of the 270 patients, 91 (33.7%) had at least one unplanned readmission three months post-discharge. The percentage of unplanned readmission three months post-discharge was 33.5%, 33.3%, and 36.4% in the minimal, mild, and severe depressive symptoms respectively. As shown in Table 3, no significant differences were observed for unplanned readmissions between the three distinct trajectories.

Mortality. Finally, 9.3% (37 out of 397) of the patients passed away within three months post-discharge. The absolute percentage was 6.3%, 12.9%, and 18.6% in the minimal, mild, and severe depressive symptoms groups respectively. Compared with patients in the minimal group, only the group with severe depressive symptoms had a significantly elevated risk of mortality three months post-discharge (OR = 3.4, 1.3–8.5, p = .01). The mild and severe symptoms groups did not differ significantly. Adjusting for confounders, none of the groups showed significant differences in mortality (see Table 3). Significant confounders were marital status (OR = 1.6, 95% CI = 1.0–2.6, p = .05) and comorbidity (OR = 1.2, 95% CI = 1.0–1.5, p = .01).

Discussion

This study, involving 398 acutely hospitalized older patients, aims to identify distinct trajectories of cognitive-affective depressive symptoms from hospitalization up to three months post-discharge, and aims to determine whether these distinct trajectories are associated with adverse short-term outcomes during this time period. Additionally, we examined which baseline variables are associated with trajectory group membership. Three distinct trajectories of cognitive-affective depressive symptoms were identified: 1) minimal; 2) persistent mild, and 3) persistent severe.

A significant and novel aspect of the current study is the sophisticated data analyses, which provided a detailed description of the trajectories of cognitive-affective depressive symptoms, in addition to their prognostic factors and related outcomes. To our knowledge, this is the first study which examined trajectories of cognitive-affective depressive symptoms among acutely hospitalized older patients during hospitalization and in the first critical months post-discharge. Nearly 40% of older patients experienced persistent mild or severe depressive symptoms, and these patterns were unadjusted associated with a substantially higher risk of functional decline, falls, and mortality. No significant differences were observed between the three distinct trajectories for unplanned readmissions. Finally, the two trajectories with more depressive symptoms can be distinguished from the minimal depressive symptoms trajectory by several baseline variables, such as not being married, being admitted to the Department of Geriatrics, having more medical comorbidities, being cognitively impaired, being malnourished, and higher level of anxiety.

Another strength and unique aspect of the current study is measuring trajectories of depressive symptoms by using the Geriatric Depression Scale-15 (GDS-15), which has been specifically developed for use in geriatric populations and purposely excludes somatic symptoms that may be confounded with medical illness or the aging process.[34] Based on results, we suggest that analyses focusing on the relationship between cognitive-affective depressive symptoms and poor outcomes will provide substantial insights that might not

be discovered by studies relying on somatic symptoms. For example, most previous research has found a positive associations between depressive symptoms and readmissions,[20, 44, 45] whereas the cognitive-affective depressive symptoms trajectories identified in the current study were not significantly associated with unplanned readmission. One possible explanation for this discrepancy could be the fact that these prior studies were performed in cardiac patients and measured depressive symptoms with instruments that include somatic measures of depression (e.g., the Center for Epidemiologic Studies Depression Scale (CES-D) or the Beck Depression Inventory (BDI)). Previous research has shown that somatic symptoms are associated with readmission among patients with acute myocardial infarction, while cognitive manifestations are not.[20] Furthermore, sleep quality, loss of appetite, and fatigue can also be symptoms of comorbid illness, which may have resulted in larger effect sizes than those seen in our study.[20, 44, 45]

This study builds on previous research suggesting that elevated late-life depressive symptomatology in different settings (e.g., in primary care, community based care, and other clinical samples) is often not a transient phenomenon.[9, 10] It complements previous research by looking at a persistent cases of cognitive-affective depressive symptoms after hospitalization (i.e., in secondary care). Furthermore, the present work is novel in that persistent mild cognitive-affective depressive symptoms were investigated, and the finding that they are associated with worse outcomes again complements previous research. The group identified as having persistent mild depressive symptoms showed an average score below the cut-off of six, which can be defined as subthreshold or minor depressive symptoms. These symptoms are at least two to three times more prevalent among older adults than major depression, and are associated with adverse short-term health outcomes.[46] The present results are in line with evidence showing that persistent severe depressive symptoms are associated with functional decline, falls and mortality among older patients.[4, 46, 47] Previous research has found that fewer patients with persistent severe depressive symptoms are alive and functionally independent one year post-discharge compared than patients with minimal depressive symptoms.[4] Adjusting for potential baseline factors caused marginal reductions in the effect sizes for functional decline and falls. For mortality, a larger reduction in the effect size was seen, caused by patients having more underlying comorbidities, being unmarried or widowed.

As depressive symptoms can often remain unrecognized in this population,[48, 49] this study examined a broad range of prognostic factors which could be identified as risk factors for each of the three patterns of depressive symptoms patterns after acute hospitalization, such as demographics, department of admission, hospital admission diagnosis, comorbidity of chronic conditions, malnutrition, premorbid activities of daily living (ADL) functioning, cognitive impairment, and anxiety. We found that relative to patients with minimal depressive symptoms, patients with severe persistent depressive symptoms are more likely to be cognitively impaired, to have been admitted to the Department of Geriatrics, to be unmarried, and to have higher levels of medical comorbidity and anxiety. Furthermore, patients with mild persistent depressive symptoms are more likely to be malnourished, to be functionally limited, and to have higher levels of anxiety.

The current study has potential clinical implications. Firstly, the observation that nearly 40% of patients exhibit persistent mild to severe cognitive-affective depressive symptoms and that these symptoms do not appear to improve spontaneously post-discharge further emphasizes the need for acute care hospitals, as a point of engagement with older adults, to develop discharge or screening procedures for management of depressive symptoms. Secondly, GBTM provides an insightful summary into the longitudinal development of depressive symptoms by identifying subgroups with specific developmental patterns. The result that cognitive-affective depressive symptoms do not appear to improve spontaneously over time implies that patients with depressive symptoms during acute hospitalization might need treatment for their depressive symptoms, because, for the average person, they show a persistent course post-discharge. Thirdly, in relation to the prognostic factors for mild and severe cognitive-affective depressive symptoms (i.e., cognitive impairment, unmarried status, medical comorbidities, anxiety, malnourishment, and functional limitations), future research is needed to validate these predictors in further studies which include a clinical diagnosis of depression as an outcome. Finally, in addition to temporal profiling, research could also shift its focus towards identifying distinct symptoms from the cognitive-affective set that are more strongly related to adverse short-term outcomes. For example, previous research has suggested that cognitive-affective depressive symptoms such as apathy and hopelessness predict mortality.[50-54] More refined analyses such as these could provide information about the heterogeneity of depression and the specific cognitive-affective symptoms that predict adverse outcomes among acutely hospitalized patients.

One of the strengths of this study is the sophisticated data analyses which provides acute hospital care settings with guidance for the management of cognitive-affective depressive symptoms. Secondly, participants were assessed free of delirium and severe cognitive impairment at the beginning of the study, which allowed us to examine the trajectory course of depressive symptoms more accurately during and after acute hospitalization. However, some limitations should also be noted as well. Firstly we were not able to include data on the history of depression, treatment of depression, or anti-depressant use because this information was often not included in the hospital records. As a result, we could not control for the potential effect of medication on cognitive-affective depressive symptoms. Future research is warranted on the impact of anti-depressant medication as a predictor in acutely hospitalized older patients. However, given the objectives of this study, the history and treatment of depression has little bearing. In addition, depression was not determined by clinical interview (e.g., DSM5 and ICD-10),[33] and it is therefore not possible to determine what proportion met the formal criterion for major depression. However, whether some patients would have received a clinical diagnosis seemed less relevant to the objectives of the study, as the focus was on the severity of cognitive-affective symptomatology and not on clinical diagnosis per se. Thirdly, the assessment of the outcome could occur concurrently with the trajectory variable. Finally, no formal sample size calculation was conducted, since it does not exist for Group-Based Trajectory Modeling.

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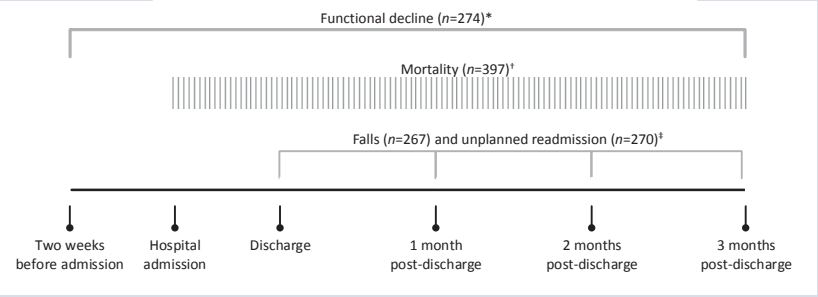
Supplementary Figure S1. Adverse short-term outcomes measurements and sample sizes.



Note: *functional decline was measured with the following formulae: Δfunctional decline = Katz-ADL score two weeks before admission – Katz-ADL score three months post-discharge, whereby scores < 0 were defined as functional decline. Only the patients measured at these two time points were included in the analysis; †mortality from hospital admission until three months post-discharge was retrieved from medical records or by means of reports from family members or the general practitioner; ‡Falls and unplanned readmissions were measured at one, two, and three months post-discharge with the following self-report questions: *"Have you fallen once in the past month post-hospitalization?"* and *"have you been acutely hospitalized in the last one month?"*. Only patients for whom data was available at one of the three time points post-hospitalization were included in the analysis of falls and unplanned readmission.