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# Posttraumatic Stress Disorder Symptom Trajectories in ICU Family Caregivers

**OBJECTIVES:** To use latent class growth analysis to identify posttraumatic stress disorder symptom trajectories in ICU family caregivers.

**DESIGN:** Prospective cohort study.

**SETTING:** The medical ICU at a tertiary-care center in the United States.

**PARTICIPANTS:** Adult patients experiencing acute cardiorespiratory failure (defined as requiring at least one of the following: 1) vasopressors, 2) noninvasive positive pressure ventilation, 3) high-flow nasal cannula, or 4) mechanical ventilation) were enrolled in a pair with their primary family caregivers.

**MEASUREMENTS AND MAIN RESULTS:** Participants were enrolled within the first 48 hours of ICU admission. Family caregiver posttraumatic stress disorder symptoms were measured using the Impact of Events Scale-Revised at four time points: at enrollment, shortly after ICU discharge, and at 3 and 6 months after ICU discharge. The data were examined using latent class growth analysis to identify posttraumatic stress disorder symptom trajectories. Two distinct symptom trajectories were identified: a persistently high trajectory, characterized by high posttraumatic stress disorder symptoms at initial assessment, which remained elevated over time, and a persistently low trajectory, characterized by low posttraumatic stress disorder symptoms at initial assessment, which remained low over time. Approximately two-thirds of caregivers belonged to the persistently high trajectory, and one-third of caregivers belonged to the persistently low trajectory.

**CONCLUSIONS:** Using latent class growth analysis to measure 6-month ICU family caregiver posttraumatic stress disorder symptom trajectories, we identified two distinct trajectories (persistently low and persistently high). A larger cohort study is warranted to further delineate posttraumatic stress disorder trajectories in this population, with the ultimate goal of targeting high-risk caregivers for interventions to reduce psychological distress and improve long-term caregiver outcomes.

**KEY WORDS:** acute cardiorespiratory failure; family caregivers; intensive care unit; latent class growth analysis; posttraumatic stress disorder

Family members are integral to the care of patients admitted to the ICU. Serving as advocates and surrogate decision makers (1), ICU family caregivers experience a variety of negative emotions, including helplessness, uncertainty, and the stress of a loved one's severe disability or death (2). Psychological distress is common, with over 50% of family caregivers displaying clinically significant symptoms of posttraumatic stress disorder (PTSD) when assessed 1 month after a loved one's ICU admission (3).

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Methods to enhance emotional support and reduce psychologic distress among ICU family caregivers have been identified as key research priorities by the Society of Critical Care Medicine and other leaders in ICU outcomes research (4–6). Interventions to improve caregiver distress, which have focused primarily on enhanced communication and emotional support during the ICU stay, have shown limited success (7–12). To be effective, interventions may require further targeting to caregivers who are at highest risk for clinically significant psychologic distress and, thus, are most likely to respond to intervention (13, 14). Research in other populations has shown that traumatized individuals display different trajectories of PTSD symptoms over time (including persistently low, improving, worsening, and persistently high over time) and that symptom trajectories differ with respect to predictors, outcomes, and response to intervention (15–19). For example, among people meeting criteria for PTSD in an emergency department, three distinct PTSD symptom trajectories were identified over a 15-month follow-up period: rapid decline in symptoms, slow decline in symptoms, and persistent elevations in symptoms. Individuals in the slow decline trajectory showed a positive response to cognitive behavioral therapy (CBT) with faster resolution of symptoms, whereas individuals in the other two trajectories did not show response to CBT (20). PTSD symptoms are common for ICU family caregivers, yet their symptom trajectories have not been defined (21).

We enrolled a cohort of ICU family caregivers of patients experiencing acute cardiorespiratory failure and followed them longitudinally over the 6 months after ICU discharge in a pilot study to identify family caregiver PTSD trajectories. We hypothesized that latent class growth analysis (LCGA) would identify multiple distinct trajectories, including improving, worsening, persistently low, and persistently high over time (17).

## MATERIALS AND METHODS

### Setting and Sample

In a single medical ICU in an academic 903-bed hospital, we enrolled a cohort of adult patients with acute cardiorespiratory failure and their primary family caregiver within the first 48 hours of ICU admission. Patients were eligible if they had one of the following

conditions: 1) mechanical ventilation through an endotracheal tube for greater than 12 hours, 2) high-flow nasal cannula (HFNC) for greater than 4 hours, 3) noninvasive positive pressure ventilation (NIPPV) for an etiology other than known sleep disordered breathing for greater than 4 hours, or 4) hypotension requiring vasopressors or inotropes for greater than 1 hour (22). Patients who were intubated in anticipation of a procedure with intent to extubate immediately afterward or solely for airway protection in the setting of intoxication were excluded as true underlying cardiorespiratory dysfunction is often absent in these cases. The primary caregiver was defined as the unpaid individual who provided the most physical, emotional, or financial support prior to ICU admission (neither cohabitation or legal relationship was required) (23). Patients with decision-making capacity were asked to define the primary family caregiver. For patients without capacity, caregivers were identified via discussion with individuals at the bedside and/or telephone contacts. We only enrolled patients who were experiencing a first-time ICU admission during the hospitalization. Caregivers of deceased patients were retained in the study cohort. Patients and caregivers were required to have English language proficiency. The study protocol was approved by the Institutional Review Board at The University of North Carolina at Chapel Hill (19-0820).

### Measures and Data Collection Procedures

The primary outcome of the study was a family caregiver PTSD symptom trajectory. Caregiver PTSD symptoms were measured at four time points over a 6-month period using the Impact of Events Scale-Revised (IES-R), a validated instrument that has been used (in original form) to evaluate the experience of families of ICU survivors and nonsurvivors (7, 24, 25). The principal investigator collected all study data using the following procedures: a baseline caregiver interview, including initial PTSD symptom assessment, occurred within the first 48 hours of ICU admission. The initial assessment was conducted either in person or by phone or e-mail, depending on caregiver preference and availability. This initial data collection included sociodemographics, medical and psychiatric comorbidities for both patient and caregiver, and prehospital functional status and acute comorbidities for the patient. Data were obtained through a combination of caregiver interview,

patient interview (for patients who were able to participate), and medical record abstraction. For caregivers with symptom scores consistent with clinically significant psychologic distress—score greater than or equal to 11 on either subscale of the Hospital Anxiety and Depression Scale (HADS) at baseline or IES-R greater than or equal to 33 at any point—the corresponding portion of the Mini International Neuropsychiatric Interview (MINI) was administered (26). The purpose of this additional assessment was to evaluate for a pre-existing diagnosis of anxiety, depression, or PTSD. The MINI is a short validated interview, developed jointly by psychiatrists and clinicians in the United States and Europe, for Diagnostic and Statistical Manual of Mental Disorders-IV and *International Classification of Diseases*, 10th Edition psychiatric disorders (26). Patient functional status was assessed using the Functional Independence Measure (FIM), an 18-item measure of physical, psychologic, and social function used to assess a patient's level of disability (27). The second caregiver PTSD symptom assessment occurred at the time of ICU discharge; if the patient died in the ICU, this assessment was delayed by 4–6 weeks as a courtesy to the family caregiver. The third caregiver PTSD symptom assessment occurred at 3 months. The fourth caregiver PTSD symptom assessment occurred at 6 months, along with reassessment of the patient's physical function using the FIM.

### Statistical Analysis

Patient and caregiver characteristics were analyzed using mean and SD for continuous variables or median and interquartile range for countable continuous variables. Categorical variables were calculated as proportions. For this pilot study, we chose a convenience sample of 30 patients and their primary caregivers. To measure PTSD symptom trajectories in this population, we performed an LCGA. LCGA is a statistical modeling technique often used in behavioral research, which aims to uncover unobserved heterogeneity in a group of individuals and to identify meaningful subgroups who display similar responses to particular variables (28). Our LCGA modeling began with three single-class unconditional growth models (models without covariates): one with a constant (flat) trajectory, second with a linear trajectory, and the last one with a quadratic trajectory of PTSD symptom IES-R scores. These models were compared by assessing relative fit with Bayesian information

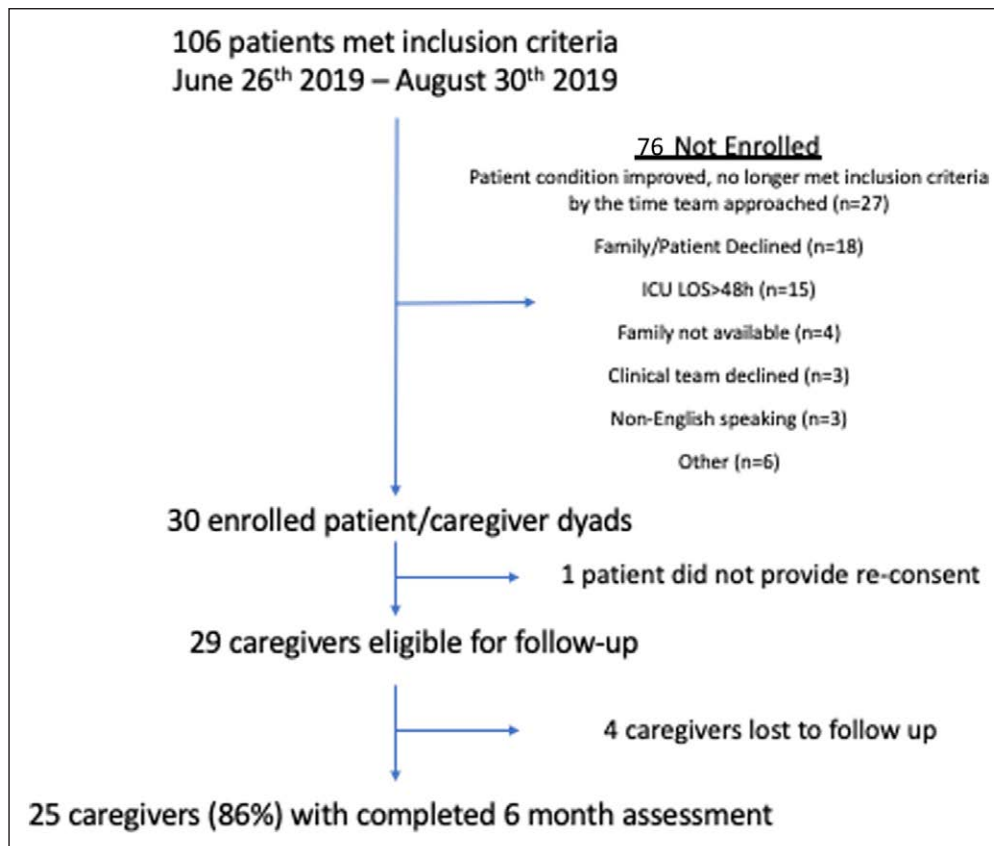
criteria (BIC), which penalize models that are more complex when they fail to provide a better fit to the data. The lower the BIC, the better the fit of the model to the data with less problem of overfitting; or simply put, the closer it is to the true model (true IES-R score trajectory in ICU family caregivers). The single-class model with the lowest BIC of these three models was selected. Next, we looked at two- to five-class unconditional LCGA models until the model with the lowest BIC was identified. Finally, this LCGA was extended to include predictors of class membership in a conditional model where we selected covariates based on conceptual relevance. The final model solution was determined by a combination of fit statistics, conceptual rationale, and interpretability.

## RESULTS

Study subjects were screened and enrolled between June 26, 2019, and August 30, 2019. Of 106 patients who met inclusion criteria, 76 were excluded, as shown in **Figure 1**. The most common reasons for exclusion were a patient no longer meeting criteria by the time morning screening was performed (e.g., admitted overnight and started on vasopressors that were then weaned by the following morning) or caregiver declining participation. A total of 30 patient patients and their primary caregivers were enrolled over an 8-week period. Initial PTSD symptom assessment occurred at an average of 20.3 (SD, 12.9) hours following ICU admission. One patient did not provide consent following liberation from mechanical ventilation, leaving 29 eligible dyads for follow-up. Four caregivers were not able to be reached after hospital discharge, and thus, no follow-up data were collected. Thus, 25 of 29 caregivers had complete 6-month assessment for an 86% retention rate.

### Baseline Characteristics

As described in **Table 1**, the mean age of enrolled caregivers was 57 years, and 22 (76%) were women. Nearly half (14, 48%) were the spouse of the patient, and 20 (69%) caregivers lived with the patient prior to hospital admission. Sixteen (55%) were employed full time at study enrollment, and 10 (34%) were retired. Nearly one quarter of caregivers (24%) had previously changed their employment status due to caregiving responsibilities. In terms of prior psychiatric diagnoses, eight caregivers (30%) had a history of depression,



**Figure 1.** Flow diagram. LOS = length of stay.

six (22%) had a history of anxiety, and three (11%) had a history of PTSD. The mean caregiver IES-R score at the time of enrollment was 22.8, approaching the threshold for clinically concerning symptoms (29).

The mean age of enrolled patients was 65 years, and 11 patients (38%) were women. Prior to study ICU admission, 25 of patients (86%) were living at home (Table 2). Mean baseline FIM score was 112, indicating high baseline physical and cognitive functional status. Eighteen of these patients (62%) were admitted to the ICU with acute respiratory failure requiring mechanical ventilation, HFNC, or NIPPV, and 11 (38%) were admitted with shock requiring vasopressors. Just over half (15, 52%) were delirious at the time of enrollment.

### Patient Outcomes

Mean ICU length of stay was 6 days, and mean hospital length of stay was 20 days. Two patients (7%) received a tracheostomy. Eight patients (28%) died in the ICU; of the surviving patients, eight (28%) were able to be discharged home, one patient (3%) was discharged to a long-term acute care hospital, and 12 patients (41%) were discharged to a skilled nursing facility.

By 6 months, a total of 17 patients (59%) had died. The mean FIM score at 6 months for survivors was 116, indicating good functional status.

### Latent Class Growth Analysis Results

Comparing the best single-, two-, and three-class unconditional models, we selected the best two-class unconditional LCGA model, since it has the lowest BIC (749.12) of the three models (Table s1, <http://links.lww.com/CCX/A598>). We identified two distinct PTSD symptom trajectories: persistently low and persistently high (Fig. 2). Approximately two-thirds of caregivers belonged to the persistently high tra-

jectory, which was characterized by high PTSD symptoms at initial assessment that remained elevated over time. Approximately one-third of caregivers belonged to the persistently low trajectory and did not demonstrate elevated PTSD symptoms at any point over the 6-month assessment period. 95% CIs for the two trajectories are also shown in Figure 2. The resulting parameter estimates, SEs, and *p* values based on the final model are presented in Table s2 (<http://links.lww.com/CCX/A598>). We then examined the potential predictors of latent class trajectory membership. Because of the small sample size, we selected three: caregiver age at enrollment, caregiver anxiety and depression symptoms at enrollment as measured by the HADS score, and patient severity of illness, as measured by the APACHE score. None of these predictors were significantly associated with trajectory membership (Table s3, <http://links.lww.com/CCX/A598>).

## DISCUSSION

Findings from this pilot cohort study indicate that at least two distinct trajectories of PTSD symptoms in primary caregivers of patients present with acute



**TABLE 1.**  
**Caregiver Demographics**

| Characteristic  | Caregivers<br>(n = 29) |
|---|------------------------|
| Age, mean (sd), yr  | 56.8 (18.0)            |
| Female, n (%)   | 22 (76)                |
| Race, n (%)   |                        |
| American Indian/Alaska Native   | 2 (7)                  |
| African American  | 8 (27)                 |
| Caucasian   | 18 (62)                |
| Prefer not to say   | 1 (4)                  |
| Hispanic or Latino ethnicity  | 1 (4)                  |
| Employment status, n (%)  |                        |
| Employed  | 16 (55)                |
| Unemployed (but not disabled)   | 1 (4)                  |
| Retired   | 10 (34)                |
| Student   | 2 (7)                  |
| Relationship to patient, n (%)  |                        |
| Spouse/partner  | 14 (48)                |
| Child   | 9 (31)                 |
| Parent  | 2 (7)                  |
| Other relative  | 3 (10)                 |
| Nonrelative   | 1 (4)                  |
| Length of time providing care for patient, n (%)                        |                        |
| <6 mo   | 7 (24)                 |
| 6–11 mo   | 2 (7)                  |
| 1–3 yr  | 4 (14)                 |
| 3–5 yr  | 3 (10)                 |
| >5 yr   | 13 (45)                |
| Lives with patient, n (%)   | 20 (69)                |
| Ever had to change employment due to caregiving responsibilities, n (%) |                        |
| No change   | 22 (76)                |
| Early retirement  | 2 (7)                  |
| Family/medical leave  | 1 (4)                  |
| Leave of absence  | 2 (7)                  |
| Reduced work hours  | 1 (3)                  |
| Other   | 1 (3)                  |

*(Continued)***TABLE 1. (Continued).**  
**Caregiver Demographics**

| Characteristic   | Caregivers<br>(n = 29) |
|--|------------------------|
| Self-reported previous diagnosis of depression, n (%)                    | 8 (30)                 |
| Self-reported previous diagnosis of anxiety, n (%)                       | 6 (22)                 |
| Self-reported previous diagnosis of posttraumatic stress disorder, n (%) | 3 (11)                 |
| Mean Impact of Events Scale-Revised, mean (sd)                           | 22.8 (16.7)            |
| Mean HADS, depression, mean (sd)   | 5.1 (3.9)              |
| Mean HADS, anxiety, mean (sd)  | 8.5 (4.9)              |

HADS = Hospital Anxiety and Depression Scale.

critical illness. This finding offers proof-of-concept for the existence of PTSD trajectories in this population. It also indicates the importance a larger cohort study that will offer greater power to detect additional trajectories and predictors of trajectory membership.

The use of LCGA to measure PTSD symptom trajectories in ICU family caregivers is a novel approach toward understanding psychologic distress in this population. Although prior studies in this population have measured PTSD symptoms at multiple time points, they have reported only change in mean symptom score rather than distinct symptom trajectories (3, 30, 31). Research in noncaregiver populations has demonstrated that the development of PTSD symptoms varies widely among individuals exposed to a similar trauma, and trajectory analysis can capture important PTSD symptom patterns that would be missed by mean scores alone (15). For example, latent class LCGA has been used to identify subgroups of individuals within a cohort who display persistently elevated or even worsening symptoms over time (17, 32), which could have implications for future treatment strategies. A telephone- and web-based coping skill training program developed by Cox et al (8) did not improve psychologic distress for a cohort of ICU caregivers, but a subgroup analysis did find that the intervention was associated with improved psychologic distress among participants with the highest early levels of distress. This suggests that using techniques such as LCGA to identify subgroups of caregivers with high-risk

**TABLE 2.**  
**Patient Demographics**

| Characteristics   | Patients<br>(n = 29) |
|---|----------------------|
| Age, mean (SD), yr  | 64.9 (16.3)          |
| Female, n (%)   | 11 (38)              |
| Race, n (%)   |                      |
| African American  | 9 (31)               |
| Caucasian   | 20 (69)              |
| Hispanic or Latino ethnicity                                    | 0 (0)                |
| Insurance status, n (%)   |                      |
| Commercial  | 10 (34)              |
| Medicare  | 11 (38)              |
| Medicaid  | 4 (14)               |
| None  | 3 (10)               |
| Other   | 1 (4)                |
| Functional Independence Measure,<br>mean (SD)                   | 112 (18.6)           |
| Motor subtotal  | 79.3 (16.0)          |
| Cognitive subtotal  | 32.7 (4.0)           |
| Patient location prehospitalization, n (%)                      |                      |
| Home  | 25 (86)              |
| Nursing home  | 3 (10)               |
| Outside hospital  | 1 (4)                |
| Acute Physiology and Chronic Health<br>Evaluation II, mean (SD) | 24.7 (7.5)           |
| Code status at ICU admission, n (%)                             |                      |
| Full code   | 25 (86)              |
| Do not resuscitate/do not intubate                              | 4 (14)               |
| Primary ICU admission diagnosis, n (%)                          |                      |
| Acute respiratory failure                                       | 18 (62)              |
| Shock   | 11 (38)              |
| Select chronic comorbidities, n (%)                             |                      |
| Cancer  | 13 (49)              |
| Liver disease   | 5 (17)               |
| End-stage renal disease   | 1 (4)                |
| Pulmonary disease requiring home oxygen                         | 4 (14)               |
| Substance abuse   | 8 (28)               |
| Dementia  | 1 (3)                |
| Stroke  | 3 (10)               |

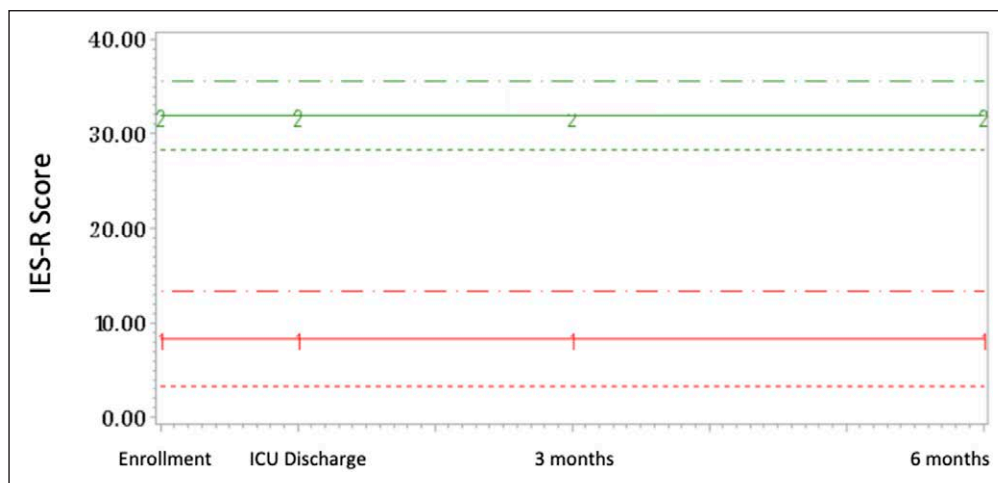
*(Continued)***TABLE 2. (Continued).**  
**Patient Demographics**

| Characteristics   | Patients<br>(n = 29) |
|---|----------------------|
| Previous diagnosis of depression, n (%)                       | 7 (24)               |
| Previous diagnosis of anxiety, n (%)                          | 10 (34)              |
| Previous diagnosis of posttraumatic stress<br>disorder, n (%) | 1 (3)                |
| RASS at enrollment, n (%)                                     |                      |
| −5 or −4 (unresponsive)                                       | 2 (7)                |
| −3 to −1 (arousable)  | 13 (45)              |
| 0 and above (awake)   | 14 (48)              |
| Confusion assessment method for the ICU at enrollment, n (%)  |                      |
| Negative  | 12 (41)              |
| Positive  | 15 (52)              |
| Unable to assess (RASS −5 or −4)                              | 2 (7)                |

RASS = Richmond agitation-sedation scale.

patterns of psychologic distress could allow for future interventions to be targeted toward the caregivers who are most likely to benefit. Furthermore, LCGA has been used to distinguish individuals whose PTSD symptoms initially rise but then resolve over time (i.e., a “recovery” trajectory) from individuals who display persistently low PTSD symptoms (i.e., a “resilience” trajectory). This type of distinction is crucial, because although individuals displaying a recovery pattern may benefit from emotional support interventions, those in the resilience trajectory are unlikely to respond and might actually experience increased burden and harm (33). Accordingly, measuring PTSD symptom trajectories in ICU family caregivers may allow for future interventions to not only confer the greatest benefit but also avoid causing increased distress. Studies in other populations, such as geriatric patients or individuals with dementia, have found that caregiver distress is associated with worse patient health (34–36). These findings suggesting that early targeting of caregivers with symptoms of PTSD could have implications for patient outcomes as well.

Our study has several limitations. The LCGA findings should be interpreted with caution given the small sample size and pilot nature of our study. However, a planned larger cohort study will offer additional power to identify more reliably PTSD symptom trajectories as well as trajectory predictors. Importantly, this larger study



**Figure 2.** Group trajectory plot of family caregiver posttraumatic stress disorder symptom trajectories. IES-R = Impact of Events Scale-Revised.

will include a qualitative component to gain a richer understanding of contributors to caregiver distress. The fact that we enrolled only medical ICU patients from a single center may limit generalizability to other populations.

The results of this pilot study highlight several important lessons to be applied to cohort studies of behavioral symptom trajectories in caregivers of critically ill patients. First, we found that many caregivers will display clinically significant symptoms of PTSD within the first 48 hours of ICU admission. Previous interventions to reduce caregiver psychologic distress have generally taken place either later in the ICU stay or after ICU discharge (7, 8), but our findings suggest that stressors occur early in the ICU stay or potentially even prior to ICU admission. The findings in this study will contribute to the design of a large cohort study designed to measure 6-month PTSD symptom trajectories in a larger population to understand better the evolution of distress over time, to gain additional information about risk factors for PTSD in ICU caregivers, and to measure the association between caregiver PTSD and patient health outcomes. The study will use a mixed-method design, with caregivers displaying persistent or worsening PTSD symptom trajectories participating in focus groups in order to obtain a nuanced understanding of how stressors before, during, and after the ICU stay contribute to psychologic distress so that targets for intervention can be identified. Second, the results of our analysis show that PTSD symptom level at the time of enrollment is predictive of PTSD symptom at all subsequent time points. The finding of a fixed PTSD symptom trajectory for at least some caregivers suggests that factors not

specifically attributable to a loved one's ICU stay could play an important role in PTSD trajectory membership. Evidence from studies in other populations suggests that these factors include underlying personality traits, previously diagnosed mental health disorders, or social determinants of health. Finally, the 6-month mortality of our cohort was greater than 50%, which was higher than anticipated. We will

stratify future analyses to understand whether caregiver PTSD symptom trajectories differ based on patient vital status.

## CONCLUSIONS

LCGA to measure 6-month ICU family caregiver PTSD symptom trajectories identifies at least two distinct trajectories (persistently low and persistently high). A larger cohort study is warranted to further delineate PTSD trajectories in this population, with the ultimate goal of targeting high-risk caregivers for interventions to reduce psychologic distress and improve long-term caregiver outcomes.

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