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PUBMED: ((family[Title/Abstract] OR families[Title/Abstract] OR next of kin[Title/Abstract] OR relative*[Title/Abstract] OR spouse*[Title/Abstract] OR loved one*[Title/Abstract] OR caregiver*[Title/Abstract]) AND (post-traumatic stress disorder[Title/Abstract] OR PTSD[Title/Abstract] OR posttraumatic stress disorder[Title/Abstract] OR depression[Title/Abstract] OR anxiety[Title/Abstract] OR post-intensive care syndrome[Title/Abstract] OR burden[Title/Abstract] OR complicated grief[Title/Abstract])) AND (intensive care[Title/Abstract] OR ICU[Title/Abstract] OR critical care[Title/Abstract] OR critically ill[Title/Abstract])

MEDICAL SUBJECT HEADINGS: (((("Stress, Psychological"[Mesh] AND "Anxiety"[Mesh]) OR "Depression"[Mesh]) OR "Stress Disorders, Post-Traumatic"[Mesh]) AND "Critical Care"[Mesh]) AND "Family"[Mesh]

EMBASE: (family:ti,ab,kw OR families:ti,ab,kw OR 'next of kin':ti,ab,kw OR relative*:ti,ab,kw OR spouse*:ti,ab,kw OR 'loved one*':ti,ab,kw OR caregiver*:ti,ab,kw) AND ('post-traumatic stress disorder':ti,ab,kw OR 'posttraumatic stress disorder':ti,ab,kw OR depression:ti,ab,kw OR anxiety:ti,ab,kw OR 'post-intensive care syndrome':ti,ab,kw OR burden:ti,ab,kw OR 'complicated grief':ti,ab,kw) AND ('intensive care':ti,ab,kw OR 'critical care':ti,ab,kw OR 'critically ill':ti,ab,kw)

SCOPUS: (TITLE-ABS-KEY (family OR families OR next AND of AND kin OR relative* OR spouse* OR loved AND one* OR caregiver*) AND TITLE-ABS-KEY (post-traumatic AND stress AND disorder OR posttraumatic AND stress AND disorder OR depression OR anxiety OR post-intensive AND care AND syndrome OR burden OR complicated AND grief) AND TITLE-ABS-KEY (intensive AND care OR critical AND care OR critically AND ill))

COCHRANE LIBRARY: family OR families OR next of kin OR relative* OR spouse* OR loved one* OR caregiver* in Title Abstract Keyword AND post-traumatic stress disorder OR posttraumatic stress disorder OR depression OR anxiety OR post-intensive care syndrome OR burden OR complicated grief in Title Abstract Keyword AND intensive care OR critical care OR critically ill in Title Abstract Keyword - in Cochrane Reviews, Trials, Special Collections (Word variations have been searched)

CLINICALTRIALS.GOV: family | post-intensive care syndrome

Table 1. Anxiety: 18 studies.

Author (year)	Study type	Population characteristics of patients who were hospitalized in the ICU	Population characteristics of relatives of patients	Mental health assessment tools	Time-point of mental health assessment of relatives	Loss-to-follow-up	Prevalence of anxiety	Statistically significant risk factors for anxiety
Naef et al. (2021) [20] Switzerland	Prospective Cohort	193 patients hospitalized in surgical-transplant ICU for 24h or longer -mean age 60.84 years -42.5% female -median ICU LOS 5 days -19.7% died in ICU	214 relatives -mean age 53.95 years -69.2% female -45.3% spouse, 26.6% child, 13.1% parent -48.6% university	HADS-A anxiety >7	0-4 weeks and >4 weeks after ICU discharge 50% of relatives returned questionnaire up to 4 weeks after ICU discharge, 50% >4 weeks	50%	38.9%	Multivariable analysis -none

Meyers et. al. (2020) Neurocritical care [21] USA	Prospective cohort	Patients admitted to neuro-ICU Exclusion: severe aphasia or cognitive impairment (unable to answer questions), anticipated death 102 individuals -mean age 52 years -47% female	Primary caregivers 103 individuals: -mean age 53 years -63% female - 66% spouse 13% parent, 13% child, 5% sibling -89% white -80% college	HADS-A anxiety >7	3 and 6 months after ICU discharge	3 months: 23% 6 months: 29%	3 months: 36% 6 months: 32%	Univariate analysis -prior mental health history -relative's anxiety during ICU, patient's anxiety
Lester et al. (2020) [22] USA	Prospective cohort	Patients in the Neuro-ICU	Only primary caregivers were included in the study. 96 individuals: - mean age 53.3 years - 61.4% female - 69.8% spouses - 53.1% higher education - 87.3% white, 12.7% non-white	HADS-A	3 months and 6 months after hospitalization	3 months: 14.6% 6 months: 19.8%	N/A	ANCOVA model: - anxiety at baseline
Tang et al. (2020) [23] Taiwan	Prospective cohort	Patients identified as high risk for dying (APACHE II score ≥ 20) or ICU-care goal as palliative Exclusion: death within 3 days of ICU admission, discharged alive 278 individuals: - mean age 66.1 years - 36.3% female - mean APACHE II score 32.61 - mean SOFA score 14.73 - median ICU LOS 21.4 days	Relatives of patients who died in ICU, surrogate decision-makers 278 individuals: - mean age 49.8 years -59% female - 82% > high school - 29.1% spouse, 53.6% child	HADS-A (severe anxiety symptoms ≥ 8)	1 month, 3 and 6 months after patient's death	1 month: 0% 3 months: 7.9% 6 months: 24.1%	1 month: 21.94% 3 months: 8.59% 6 months: 3.32%	Multivariable logistic regression: -severe anxiety symptoms at 1 month after patient's death (OR=28.168), - physician-surrogate prognostic communication (OR=297.169)

Metzger et al. (2019) [24] Switzerland	Prospective cohort	<p>Patients with out-of-hospital cardiac arrest admitted to the ICU</p> <p>101 individuals: - mean age 65.4 years - 24% female - 90-day mortality: 51%</p>	<p>Relatives who served as surrogate decision-makers.</p> <p>101 individuals: - mean age 55.1 years - 72 % female - 59% spouse, 25% children, 2% parent - 63% higher education</p>	HADS-A (anxiety defined as ≥ 11 points)	3 months after ICU hospitalization	28.3%	12.9%	<p>Stratified analysis (adjusted for age and gender)</p> <p>-unemployment (OR=10.41; 95%CI=1.18-92.35) -subsequent depression (OR=9.36; 95%CI=2.30-38.11)</p>
Lee et al. (2019) [25] USA	Prospective cohort	<p>Patients with ARDS hospitalized in the ICU who: - survived ICU discharge - were not pregnant - were not incarcerated - whose initial diagnosis wasn't head trauma or stroke</p> <p>120 individuals: - mean age 54,8 (SD 15.7) - 38% female - mean APACHE II score 23.2 (SD 7.7) - median ICU LOS 13 days (IQR 8-21.5)</p>	<p>Relatives most involved in patients ICU and post-ICU care or their legal next-of-kins</p> <p>162 individuals: - mean age 51,5 (SD 14.7) - 73% female - 34% with higher education - 62% employed, 15% unemployed, 16% retired, 7% disabled - 40% spouse, 21% child, 16% parent</p>	GAD-7 anxiety defined as ≥ 10	median of 5.9 months after patient discharge (IQR 5.0-7.0)	0%	18% (95% CI 13-25%)	<p>Multivariable logistic regression</p> <p>-preexisting mental health disorder during the year prior (OR=3.67; 95%CI=1.39-9.68)</p>
Fumis et al. (2019) [26] Brazil	Prospective cohort	<p>Chronically critically ill patients who have spent at least 8 days of MV/ experienced sepsis/stroke/traumatic brain injury:</p> <p>186 individuals: - median age ~65 years - 63.4% female - median SOFA score ~ 5 points - median ICU LOS: 16 days</p>	<p>186 individuals: - median age ~45 years - 76% female - 71.5% spouses - 51% higher education - 84% employed</p>	HADS-A	1 month and 3 months after ICU hospitalization	59% at first month and 75% at 3 months after ICU hospitalization	<p>1 month: 19.5%</p> <p>3 months: 25%</p>	<p>Multivariable logistic regression:</p> <p>-atheism (OR=2.1; 95%CI 1.1-3.97) -lack of previous ICU experience (OR=2.45; 95%CI=1.22-4.95)</p>

		- death during hospitalization: 35%						
Oliveira et al. (2018) [27] Brazil	Prospective cohort	<p>Patients hospitalized in ICU for >48h - unit with private rooms where family member can stay with patient for 24h per day</p> <p>Exclusion: psychiatric disorders, severe neurologic disease, illness too severe to answer</p> <p>118 individuals - mean age 58.8 - 18.6% female - median SAPS III 45.6 - median SOFA score 1.5 mean ICU LOS 5.63 days</p>	<p>118 spouses Exclusion: psychiatric disorders (anxiety, depression)</p> <p>- mean age 54.8 - 81.4% female -71.2% college -72.9% catholic</p>	HADS-A anxiety >10/21 points	1 month and 3 months after ICU discharge	30 days: 12.7% 90 days: 20.3%	1 month: 10.7% 3 months: 7.4%	Multivariate analysis -female sex
Beesley (2018) [28] USA	Prospective cohort	<p>Patients with APACHE II score on admission > 15 points</p> <p>99 individuals: -mean age 60 years -51% female -mean admission APACHE II score: 30 points -median ICU LOS: 3.3 days -21% died during the ICU stay</p>	<p>Relatives with no previous history of PTSD, dementia or schizophrenia</p> <p>99 individuals: -mean age 54 years -64% female -53% spouse, 11% parent and 26% child -48% higher education</p>	HADS-A (anxiety defined as ≥8 points)	3 months after ICU hospitalization	7.1%	32%	Multivariable analysis: -History of anxiety (OR=6.70; 95%CI=1.89-26.69) -Cortisol awakening response (OR=1.10; 95%CI=1.03-1.18)

<p>Petrinec et al. (2017) [29] USA</p>	<p>Prospective cohort</p>	<p>Patient who were hospitalized in the ICU who were mechanically ventilated or their predicted ICU stay was greater than 5 days</p> <p>48 individuals: - median age 62.5 years - 39,6% female - median admission SAPS II score: 42.7 points - 50% died till 60 days post enrollment</p>	<p>Family decision-makers who:</p> <p>48 individuals: - median age 56.3 years - 79.2 % female - 33.3% spouse, 35.4% children, 14.6% parent</p>	<p>HADS-A Anxiety defined as score ≥ 11 is</p>	<p>T1 = days 3-5 after discharge or death T2 = 30 days after discharge or death T3 = 60 days after discharge or death</p>	<p>T2 - 20,8% T3 - 25%</p>	<p>T1 = 45,8% T2 = 34,2% T3 = 30,6%</p>	<p>Multiple linear regression</p> <p>T1: - previous history of psychiatric symptoms</p> <p>T2: - previous history of psychiatric symptoms -avoidant coping mechanism</p> <p>T3: - previous history of psychiatric symptoms -emotion-focused coping mechanism</p>
<p>Matt et al. (2017) [30] Germany</p>	<p>Prospective cohort</p>	<p>Severe septic patients were included in the study</p> <p>143 individuals: - median age 67 years - 49.7% female - median SOFA score at admission: 14 points - median ICU LOS: 10.7 days - 45.4% 90-day mortality</p>	<p>143 individuals: - median age 54 years - 73.4% female - 42.7% spouses, 39.2% children - 33.1% higher education</p>	<p>HADS-A (anxiety defined as >7 points)</p>	<p>3 months after hospitalization</p>	<p>0%</p>	<p>39%</p>	<p>Multivariable linear regression:</p> <p>- female sex of a relative (B=+0.63) - stressors identified via qualitative analysis (B=+0.52)</p>
<p>McPeake et al. (2016) [31] UK</p>	<p>Prospective cohort</p>	<p>36 patients, mechanically ventilated for at least 72h - median ICU LOS 14.5 days - median APACHE II score 23.5 - single center in the area of high deprivation</p>	<p>36 caregivers: - median age 57.5 years - 64% female - 67% spouses, 25% parent, 5.5% children, 2.5% sibling</p>	<p>HADS-A (anxiety >7)</p>	<p>4 weeks - 3 years after discharge</p>	<p>0%</p>	<p>69%</p>	<p>Linear regression</p> <p>-caregiver strain</p>

Hartog et al. (2015) [32] Germany	Prospective cohort	<p>Patients with severe sepsis receiving end-of-life care.</p> <p>145 individuals: -mean age 72 years -35.2% female -mean admission SOFA score: 10 points -median ICU LOS: 241 days -81.4% died during the ICU stay</p>	<p>Relatives with the main decision-making role.</p> <p>84 individuals: -mean age 57 years -73.8% female -41.7% spouse, 3.6% parent and 41.7% child -34.5% higher education</p>	HADS (anxiety defined as > 7 points)	3 months after ICU hospitalization	N/A	48%	<p>Multiple linear regression:</p> <p>-lower satisfaction with communication and care</p>
de Miranda et al. (2011) [33] France	Prospective cohort	<p>Patients with COPD exacerbation. Patients who died during hospitalization were excluded.</p> <p>126 individuals: -median age 67 years</p>	<p>102 relatives: -54% spouses -37% caregivers</p>	HADS-A (anxiety defined as ≥8 points)	3 months after ICU hospitalization	53.9 %	<p>3 months: 40.4%</p>	<p>Multivariable analysis:</p> <p>3 months: -None</p>
Pillai et al. (2010) India [34]	Prospective cohort	<p>Patients hospitalized for at least 5 days</p>	<p>178 individuals: -average age 36 yrs (18-67) - 45,8% female - 31,3% spouse, 28,9% child - 32,5% higher education</p>	<p>HADS</p> <p>(Sum of the score greater than 11 was considered as severe)</p>	Follow-up at 2 months post-ICU discharge or death	40%	48%	<p>Univariable analysis:</p> <p>- lower education levels - trauma admission</p>

Anderson et al. (2008) [35] USA	Prospective cohort	Patients who were anticipated to be in the ICU for more than 2 days and were unable to make medical decisions	50 individuals: -mean age 54 years -84% female -36% spouse, 26% parent and 12% child -96% christian -34% higher education	HADS-A (anxiety defined as ≥ 8 points)	1 month and 6 months after ICU hospitalization	1 month: 22% 6 months: 32%	1 month: 21% 6 months: 15%	Univariable analysis: 1 month: -Younger age of a relative 6 months: - None
Azoulay (2022) [66]	Prospective cohort	Patients who were hospitalized due to ARDS of COVID-19 origin or of different cause. 307 individuals: median age 61 years -34% female -COVID-19 ARDS 59% -ECMO 3% -mortality 26%	602 family members: -median age 51 years -72% female -48% spouses -8.9% unemployed	HADS-A (anxiety defined as ≥ 7 points)	3 months after ICU hospitalization	14%	37%	Death was associated with higher anxiety prevalence Multivariable analysis: -patient was a COVID-19 patient -family member is female -younger family member -lower level of social support
McPeake et al. (2022) [70]	Prospective cohort	Patients discharged from the ICU. 170 patients: -median age ~61 years -female 46.5% -median APACHE II 19 points	Primary caregivers. 170 individuals: -median age ~58 years -female 64.6% -spouse 70.6% -child 17% -parent 6.5%	HADS-A (anxiety defined as ≥ 7 points)	12 months after ICU hospitalization	40%	Unclear	Multivariable analysis: -pre-ICU mental health disease in critically-ill patient -younger caregiver age

Legend: ICU: intensive care unit; HADS-A: Hospital Anxiety and Depression scale-subscale for anxiety; APACHE II: Acute Physiology and Chronic Health Evaluation II; SOFA: Sequential Organ Failure Assessment score; SAPS II: Simplified Acute Physiology Score II; LOS: length of stay; ARDS: acute respiratory distress syndrome; VV-ECMO: veno-venous extracorporeal membrane oxygenation; GAD-7: Generalized Anxiety Disorder-7; MV: mechanical ventilation; PTSD: post-traumatic stress disorder

Table 2. Depression: 27 studies

Author (year)	Study type	Population characteristics of patients who were hospitalized in the ICU (+ inclusion and exclusion criteria)	Population characteristics of relatives of patients	Mental health assessment tools	Time-point of mental health assessment of relatives	Loss-to-follow-up	Prevalence of depression	Statistically significant risk factors for depression
Naef et al. (2021) [20]	Prospective Cohort	193 patients hospitalized in surgical-transplant ICU for 24h or longer -mean age 60.84 years -42.5% female -median ICU LOS 5 days -19.7% died in ICU	214 relatives -mean age 53.95 years -69.2% female -45.3% spouse, 26.6% child, 13.1% parent -48.6% university -	HADS-D depression >7	0-4 weeks and >4 weeks after ICU discharge 50% of relatives returned questionnaire up to 4 weeks after ICU discharge, 50% >4 weeks	50%	22.4%	Multivariable analysis -patient's death (B=3.186, CI 1.54-4.83)
Meyers et al. (2020) [36] USA	Prospective cohort	Patients hospitalized in the Neuro-ICU 102 individuals -cognitively intact (excludes most critically ill patients) - mean age 52 years - 47% female	103 caregivers - mean age 53 years - 63% female - 66 % spouse, 13% child, 13% parent, 5% sibling - 82% some college or more - 89% white	HADS-D (depression when score ≥8)	3 and 6 months after hospital discharge	Baseline 6% 3 months 23% 6 months 29%	3 months 19% 6 months 20%	Univariate analysis -no college education Bivariate analysis -baseline depressive symptoms, - patient's depressive symptoms
Tang et al. (2020) [23]	Prospective cohort	Patients identified as high risk for dying (APACHE II score ≥20) or ICU-care goal as palliative Exclusion: death within 3 days of ICU admission, discharged alive 278 individuals: - mean age 66.1 years - 36.3% female - mean APACHE II score 32.61 - mean SOFA score 14.73 - median ICU LOS 21.4 days	Relatives of patients who died in ICU, surrogate decision-makers 278 individuals: - mean age 49.8 years -59% female - 82% > high school - 29.1% spouse, 53.6% child	HADS-D (Depressive symptoms ≥ 8)	1 month, 3 months and 6 months after patient's death	3 months 7.9% 6 months 24.1%	1 month 42.09% 3 months 20.70% 6 months 11.37%	Multivariable logistic regression: -severe anxiety symptoms at 1 month after patient's death (OR=6.36), -severe depressive symptoms at 1 month after patient's death (OR=5.778), -family meetings conducted (OR=5.916)
Metzger et al. (2019) [24]	Prospective cohort	Patients with out-of-hospital cardiac arrest admitted to the ICU 101 individuals: - mean age 65.4 years - 24% female	Relatives who served as surrogate decision-makers. 101 individuals: - mean age 55.1 years - 72 % female	HADS-D (depression defined as ≥ 9 points)	3 months after ICU hospitalization	28.3%	16.8%	Stratified analysis (adjusted for age and gender) -relatives who witnessed CPR by medical team

		- 90-day mortality: 51%	- 59% spouse, 25% children, 2% parent -XXX higher education					(OR=6.71; 95%CI=1.27-35.34) -poor neurological outcome (OR=7.07; 95%CI=1.74-28.67) -death of a patient (OR=4.01; 95%CI=1.12-14.36) -subsequent anxiety (OR=9.33; 95%CI=2.28-38.24) -use of psychotropic drugs (OR=4.68; 95%CI=1.38-15.82)
Lee et al. (2019) [25]	Prospective cohort	Patients with ARDS hospitalized in the ICU who: - survived ICU discharge - were not pregnant - were not incarcerated - whose initial diagnosis wasn't head trauma or stroke 120 individuals: - mean age 54,8 (SD 15.7) - 38% female - mean APACHE II score 23.2 (SD 7.7) - median ICU LOS 13 days (IQR 8-21.5)	Relatives most involved in patients ICU and post-ICU care or their legal next-of-kins 162 individuals: - mean age 51,5 (SD 14.7) -73% female - 34% with higher ED - 62% employed, 15% unemployed, 16% retired, 7% disabled - 40% spouse, 21% child, 16% parent	PHQ-9 depression defined as ≥ 10	median of 5.9 months after patient discharge (IQR 5.0-7.0)	0%	21% (95% CI 15-29%)	Multivariable logistic regression -preexisting mental health disorder during the year prior (OR=4.11; 95%CI=1.80-9.34)
Fumis et al. (2019) [26]	Prospective cohort	Chronically critically ill patients who have spent at least 8 days of MV/ experienced sepsis/stroke/traumatic brain injury: 186 individuals: -median age ~65 years -63.4% female -median SOFA score ~ 5 points	186 individuals: -median age ~45 years -76% female -35.4% spouses, 43% children -51% higher education -84% employed	HADS-D	1 month and 3 months after ICU hospitalization	59% at first month and 75% at 3 months after ICU hospitalization	1 month: 19.5% 3 months: 25%	Multivariable logistic regression: -higher education (OR=8.4; 95%CI=2.7-26.5) -cohabitation with a patient (OR=8.82; 95%CI=2.48-31.39)

		<p>- median ICU LOS: 16 days</p> <p>- death during hospitalization: 35%</p>						
Oliveira et al. (2018) [27]	Prospective cohort	<p>Patients hospitalized in ICU for >48h - unit with private rooms where family member can stay with patient for 24h per day</p> <p>Exclusion: psychiatric disorders, severe neurologic disease, illness too severe to answer</p> <p>118 individuals</p> <ul style="list-style-type: none"> - mean age 58.8 - 18.6% female - median SAPS III 45.6 - median SOFA score 1.5 mean ICU LOS 5.63 days 	<p>118 spouses</p> <p>Exclusion: psychiatric disorders (anxiety, depression)</p> <ul style="list-style-type: none"> - mean age 54.8 - 81.4% female -71.2% college -72.9% catholic 	HADS-D depression >10/21 points	1 month and 3 months after ICU discharge	<p>1 month: 12.7%</p> <p>3 month: 20.3%</p>	<p>1 month: 5.8%</p> <p>3 month: 5.3%</p>	Multivariate analysis -female sex
Kentish-Barnes et al. (2017) [37]	Randomized controlled trial	<p>Patients who stayed in the ICU for more than 2 days and died during hospitalization.</p> <p>242 individuals:</p> <ul style="list-style-type: none"> - median age 61 years - 35.1% female 	<p>Relatives designated as healthcare proxy.</p> <p>208 individuals:</p> <ul style="list-style-type: none"> - median age 57 years - 69.7 % female - 35.5% spouse, 39.9% children 	HADS-D (depression defined as score ≥8 points)	1 month and 6 months after ICU hospitalization.	6 months: 10%	<p>1 month: 49.3%</p> <p>6 months: 30.7%</p>	<p>Multivariable analysis:</p> <p>1 month:</p> <ul style="list-style-type: none"> -being a spouse (OR=5.16; 95%CI=2.61-10.18) -female sex of a relative (OR=2.3; 95%CI=1.14-4.65) <p>6 months:</p> <ul style="list-style-type: none"> -age of a patient; per age (OR=0.96; 95%CI=0.93-0.99) -being a spouse (OR=4.89; 95%CI=2.07-11.54) -relative living alone (OR=3.85; 95%CI=1.59-9.30)
Petrinec et al. (2017)	Prospective cohort	Patient who were hospitalized in the ICU who were mechanically ventilated or their predicted ICU stay was greater	Family decision-makers who: 48 individuals:	HADS-D (depression defined as score ≥11 points)	T1 = days 3-5 after ICU hospitalization T2 = 30 days after ICU	T1 - 0% T2 - 20,8% T3 - 25%	T1 = 14.6% T2 = 21.1% T3 = 25%	Multiple linear regression

[29]		<p>than 5 days</p> <p>48 individuals: - median age 62.5 years - 39,6% female</p> <p>- median admission SAPS II score: 42.7 points - 50% died till 60 days post enrollment</p>	<p>- median age 56.3 years - 79.2 % female</p> <p>- 33.3% spouse, 35.4 child, 14.6% parent</p>		<p>hospitalization T3 = 60 days after ICU hospitalization</p>			<p>T2: - previous history of psychiatric symptoms</p> <p>T3: - previous history of psychiatric symptoms</p>
Matt et al. (2017) [30]	Prospective cohort	<p>Severe septic patients were included in the study</p> <p>143 individuals: - median age 67 years - 49.7% female</p> <p>- median SOFA score at admission: 14 pointes - median ICU LOS: 10.7 days - 45.4% 90-day mortality</p>	<p>143 individuals: - median age 54 years - 73.4% female</p> <p>- 42.7% spouses, 39.2% children - 33.1% higher education</p>	<p>HADS-D (anxiety defined as >7 points)</p>	<p>3 months after hospitalization</p>	<p>0%</p>	<p>39%</p>	<p>Multivariable linear regression:</p> <p>- female sex of a relative (B=+0.46) - being a spouse (B=+0.49) - low quality of life of a patient (B=+0.61) - death of a patient (B=+0.41)</p>
McPeake et al. (2016) [31]	Prospective cohort	<p>36 patients, mechanically ventilated for at least 72h - median ICU LOS 14.5 days - median APACHE II score 23.5 - single center in the area of high deprivation</p>	<p>36 caregivers: - median age 57.5 years - 64% female</p> <p>- 67% spouses, 25% parent, 5.5% children, 2.5% sibling</p>	<p>HADS (depression \geq 8)</p>	<p>4 weeks - 3 years after discharge</p>	<p>0%</p>	<p>55%</p>	<p>Univariate analysis</p> <p>-caregiver strain</p>
Warren et al. (2016) [38]	Prospective cohort	<p>Patients admitted to ICU for at least 48h with an expected survival >96h Two groups - non-TBI and TBI (moderate to severe TBI = loss of consciousness for 30min.)</p>	<p>100 relatives, caregivers</p> <p>-mean age 49.2 years -73% female -24% spouse, 27% parents, 18% child, 6% sibling -45% white -46% college -48.7% family of patients with TBI</p>	<p>PHQ-8 (depression \geq10)</p>	<p>3 months after ICU hospitalization</p>	<p>0%</p>	<p>20%</p>	<p>Univariable analysis:</p> <p>-significant decrease in depressive symptoms for 3 months (21%) in non-TBI group (p=0.0027), no significant decrease in the TBI group</p> <p>TBI group had less improvement in depression at 3 months</p>
Hartog et al. (2015) [32]	Prospective cohort	<p>Patients with severe sepsis receiving end-of-life care.</p>	<p>Relatives with the main decision-making role.</p>	<p>HADS-D (depression defined as > 7 points)</p>	<p>3 months after ICU hospitalization</p>	<p>N/A</p>	<p>33%</p>	<p>Multiple linear regression:</p>

		<p>145 individuals: -mean age 72 years -35.2% female -mean admission SOFA score: 10 points -median ICU LOS: 241 days -81.4% died during the ICU stay</p>	<p>84 individuals: -mean age 57 years -73.8% female -41.7% spouse, 3.6% parent and 41.7% child -34.5% higher education</p>					-being a spouse
Downey et al. (2015) [39] Canada	Randomized controlled trial	<p>Mechanically ventilated patients with estimated mortality of $\geq 30\%$ (SOFA score)</p> <p>131 individuals: -mean age 55 years -38.2% female -28.2% died during ICU hospitalization</p>	<p>193 individuals: -mean age 51.1 years -67.9% female -30.6% spouses, 26.9 children, 17.6 parent -the majority of relatives graduated from college</p>	PHQ-2	3 months and 6 months after ICU hospitalization	64.7%	N/A	<p>Path model:</p> <p>3 months and 6 months:</p> <p>-younger age of a patient -depression of a relative during hospitalization -being a spouse -death of a patient in the ICU</p>
Davydov et al. (2013) [40] USA	Prospective cohort	<p>Patients with severe sepsis</p> <p>1212 individuals: -mean age 73.4 years -34.8% female -mean ICU LOS 12.1 days -21.9% died</p>	<p>Only spouses were included in the study</p> <p>1212 individuals: -mean age 71.3 years -65.3% female -100% spouse -82% religious -13.8% higher education</p>	CES-D (depression defined when ≥ 4 points)	A maximum of 2 years after ICU hospitalization (median 1 year)	7%	34%	<p>Multivariable analysis:</p> <p>-female sex of a spouse (OR=3.74; 95% CI=2.20-6.37); the association persisted after controlling for the death of a patient -disability of patients after hospitalization (OR=1.35; 95% CI=1.12-1.64)</p>
Choi et al. (2013) [41]	Prospective cohort	<p>Patients who required MV for ≥ 4 consecutive days and survived the ICU</p> <p>47 individuals: -mean age 55.5 years -34% female -mean admission APACHE II score: 21.6 points -mean ICU LOS 22.9 days</p>	<p>Only primary caregivers were included in the study</p> <p>50 individuals: -mean age 52.3 years -74% female -58% spouse, 18% parent -82% religious -mean years of education 14.5 years</p>	Shortened CES-D (depression defined when ≥ 8 points)	2 months after ICU hospitalization	38%	2 months: 56%	<p>Univariable analysis:</p> <p>2 months:</p> <p>-Difficult financial situation -Relative who lived with a patient prior to an ICU hospitalization -Unemployment -Limited activity of a patient prior to an ICU hospitalization</p>

de Miranda et al. (2011) [33]	Prospective cohort	Patients with COPD exacerbation. Patients who died during hospitalization were excluded. 126 individuals: -median age 67 years	102 relatives: -54% spouses -37% caregivers	HADS-D (depression defined as ≥ 8 points)	3 months after ICU hospitalization	53.9%	3 months: 14.9%	Univariable analysis: 3 months: -None
Gries et al. (2010) [42]	Randomized controlled trial	Patients who died during the ICU hospitalization	226 individuals: -mean age 59.7 years -74.8% female -48.7% spouse, 36.7% child -37.2% higher education	PHQ-8 (depression defined as > 10 points)	At least 6 months after ICU hospitalization	18%	18.4%	Multivariable linear regression: -female sex of a relative ($\beta=1.97$) -education ($\beta=-1.1$) -years of association with a patient ($\beta=-0.051$) -Mood/emotions drugs taken by relatives prior to the ICU hospitalization ($\beta=+3.6$) -psychiatric counseling prior to the ICU hospitalization ($\beta=+3.5$) -neurologic counseling prior to the ICU hospitalization ($\beta=+3.2$)
Douglas et al. (2010) [43] USA	Prospective cohort	Patients who were mechanically ventilated for at least 3 days and survived the ICU hospitalization. 370 individuals: -mean age 55.3 years -44.1% female -mean ICU LOS 15.2 days	Only primary caregivers were included in the study 370 individuals: -mean age 52.7 years -70.5% female -38% spouse, 26.7% child, 21.4% parent -22.62% higher education -68% white, 32% non-white	CES-D (depression defined as > 15 points)	2 months after ICU hospitalization	25%	2 months: 43.3%	Multivariable linear regression: 2 months: -female sex of a relative ($\beta=+ 4.18$) -CES-D during hospitalization of a relative ($\beta= +0.35$) -worse condition of a patient during hospitalization -institutional residency 2 months after discharge
Van Pelt et al. (2010)	Prospective cohort	48 patients, mechanically ventilated for at least 48h, survived at least 2 months Exclusion: organ transplantation,	48 caregivers -mean age 52.8 years	CES-D (depression ≥ 16)	2, 6 and 12 months after initiation of mechanical ventilation	Unclear	2 months 37.5% 6 months	Multivariable linear regression:

[44]		chronically ventilator dependent prior to admission, intubated >24h in an outside hospital -mean age 52.5 years -33.3% female -median APACHE III score: 52 -median ICU LOS 13 days	-81.2% female -47.9% spouse, 37.5% family members, 14.6% not family -91.7% white -87.5% education >=12th grade				29.2% 12 months 29.2%	2 months patient's male gender (B=-1.66), 12 months patient's male gender (B=-1.02), tracheostomy (B=1.26)
Anderson et al. (2008) [35]	Prospective cohort	Patients who were anticipated to be in the ICU for more that 2 days and were unable to make medical decisions	50 individuals: -mean age 54 years -84% female -36% spouse, 26% parent and 12% child -96% christian -34% higher education	HADS-D	1 month and 6 months after ICU hospitalization	1 month: 22% 6 months: 32%	1 month: 8% 6 months: 6%	Univariable analysis: 1 month: - younger age of relatives 6 months: -None
Van Pelt et al. (2007) [45] USA	Prospective cohort	169 patients, mechanically ventilated for at least 48h, survived at least 2 months -mean age 56.6 years -40.2% female -median APACHE III score: 56 -median ICU LOS 14 days -median MV duration 9 days	169 caregivers -mean age 54.6 years -75.7% female -52.7% spouse, 35.5% family members, 11.8% not family -91.1% white -88.8% education >=12th grade -41.4% family of patients with pre-ICU functional dependency	CES-D (depression >=16)	2, 6 and 12 months after initiation of mechanical ventilation	Unclear	2 months 33.9% 6 months 30.8% 12 months 22.8%	Multivariate analysis: -older patient -using paid assistance
Douglas et al. (2005) [46] USA	Randomized controlled trial	Patients who were mechanically ventilated for at least 3 days and survived the ICU hospitalization. 290 individuals: -mean age 60.7 years -55.8% female -mean ICU LOS 17.6 days	Only primary caregivers were included in the study 290 individuals: -mean age 53 years -72% female -42% spouse, 32% child -22.62% higher education -65% white, 35% non-white	CES-D (depression defined as > 15 points)	2 months after ICU hospitalization	23.5%	2 months: 31.1%	Multivariable logistic regression: 2 months: -depression of a relative during hospitalization
Im et al. (2004) [47] USA	Prospective cohort study	Patients who underwent ≥ 48 hours of mechanical ventilation. 115 individuals: -mean age 54.1 years -38.3% female	Only primary caregivers were included in the study. 115 individuals: -mean age 52.9 years -76.5% female	CES-D (depression defined as ≥ 16 points)	2 months after ICU hospitalization	34.7%	33.9%	Multiple linear regression: -more hours spent daily helping with patient's activity of daily living and

			-52.2% spouse, 19.1% parent and 18.3% children -44.3% completed high school or more -90.4% white, 9.6% non-white -28.6% employed					instrumental activities of daily living
Cleiren et al.(2002) [48]	Cross-sectional	Patients who died in the ICU due to brain injury -mean age 44 years	Relatives of first degree: 95 individuals: -mean age 47 years -65% female -78% spouse or parent	BDI-13 Depression	6.1 months (the mean) after ICU death	N/A	N/A	Univariable analysis: -female sex of a relative - being a spouse or a parent
Azoulay (2022) [66]	Prospective cohort	Patients who were hospitalized due to ARDS of COVID-19 origin or of different cause. 307 individuals: median age 61 years -34% female -COVID-19 ARDS 59% -ECMO 3% -mortality 26%	602 family members: -median age 51 years -72% female -48% spouses -8.9% unemployed	HADS-D (anxiety defined as ≥7 points)	3 months after ICU hospitalization	14%	25.6%	Death was associated with higher depression prevalence Multivariable analysis: -patient was a COVID-19 patient -family member is female -younger family member -lower level of social support
McPeake et al. (2022) [70]	Prospective cohort	Patients discharged from the ICU. 170 patients: -median age ~61 years -female 46.5% -median APACHE II 19 points	Primary caregivers. 170 individuals: -median age ~58 years -female 64.6% -spouse 70.6% -child 17% -parent 6.5%	HADS-D (anxiety defined as ≥7 points)	12 months after ICU hospitalization	40%	~24.5%	Multivariable analysis: -pre-ICU mental health disease in critically-ill patient -younger caregiver age

Legend: ICU: intensive care unit; HADS-D: Hospital Anxiety and Depression scale-subscale for depression; CES-D: Center for Epidemiologic Studies Depression Scale; BDI-13: Beck Depression Inventory-13; PHQ:Patient Health Questionnaire depression scale; APACHE II: Acute Physiology and Chronic Health Evaluation II; SOFA: Sequential Organ Failure Assessment score; SAPS II: Simplified Acute Physiology Score II; LOS: length of stay; ARDS: acute respiratory distress syndrome; VV-ECMO: veno-venous extracorporeal membrane oxygenation; MV: mechanical ventilation; PTSD: post-traumatic stress disorder; TBI: Traumatic Brain Injury;

Table 3. PTSD: 27 studies

Author (year)	Study type	Population characteristics of patients who were hospitalized in the ICU (+ inclusion and exclusion criteria)	Population characteristics of relatives of patients	Mental health assessment tools	Time-point of mental health assessment of relatives	Loss-to-follow-up	Prevalence of PTSD	Statistically significant risk factors for PTSD
Naef et al. (2021) [20]	Prospective Cohort	193 patients hospitalized in surgical-transplant ICU for 24h or longer -mean age 60.84 years -42.5% female -median ICU LOS 5 days -19.7% died in ICU	214 relatives -mean age 53.95 years -69.2% female -45.3% spouse, 26.6% child, 13.1% parent -48.6% university -	IES-R-6 (PTSD>9; corresponds to the value of 30 in IES-R)	0-4 weeks and 4-12 weeks after ICU discharge 50% of relatives returned questionnaire up to 4 weeks after ICU discharge, 50% >4 weeks	50%	67.6%	Multivariable analysis -patient's death (B=3.096, CI 1.31-4.88)
Lee et al. (2019) [25]	Prospective cohort	Patients with ARDS hospitalized in the ICU who: - survived ICU discharge -were not pregnant - were not incarcerated - whose initial diagnosis wasn't head trauma nor stroke 120 individuals: - mean age 54,8 (SD 15.7) - 38% female - mean APACHE II score 23.2 (SD 7.7) - median ICU LOS 13 days (IQR 8-21.5)	Relatives most involved in patients ICU and post-ICU care or their legal next-of-kins 162 individuals: - mean age 51,5 (SD 14.7) -73% female - 34% with higher ED - 62% employed, 15% unemployed, 16% retired, 7% disabled - 40% spouse, 21% child, 16% parent	PCL-C PTSD defined as ≥ 35 points	median of 5.9 months after patient discharge (IQR 5.0-7.0)	0%	31%	Multivariable logistic regression -preexisting mental health disorder during the year prior (OR=3.22; 95%CI=1.42-7.31) -recent serious physical illness (OR=3.07; 95%CI=1.40-6.75) -female gender of the relative (OR=5.18; 95%CI=1.74-15.4) - no comorbidities prior to ARDS admission in patient (OR=2.25; 95%CI=1.06-4.77)
Oliveira et al. (2018) [27]	Prospective cohort	Patients hospitalized in ICU for >48h - unit with private rooms where family member can stay with patient for 24h per day Exclusion: psychiatric disorders, severe neurologic disease, illness too severe to answer 118 individuals - mean age 58.8 - 18.6% female - median SAPS III 45.6	118 spouses Exclusion: psychiatric disorders (anxiety, depression) - mean age 54.8 - 81.4% female -71.2% college -72.9% catholic	IES (PTSD >30)	1 month and 3 months after ICU discharge	1 month: 12.7% 3 months: 20.3%	N/A	Multivariable analysis: -None

		-median SOFA score 1.5 mean ICU LOS 5.63 days						
Wendlandt et al. (2018) [49] USA	Randomized controlled trial	224 patients with CCI, >=21 years, at least 7 days of mechanical ventilation. Exclusion: ventilated for >7 days at an outside hospital, chronic neuromuscular disease, trauma, burns. - mean age 59 years -49% female -mean hospital LOS before enrollment 13 days -RASS at enrollment: 44% unresponsive, 38% arousable, 18% awake -mean 1-yr mortality as predicted by ProVent score 62%	306 relatives served as a surrogate decision-makers -mean age 51 years -71% female -33% spouse, 13% parent, 36% child, 12% sibling -90% christian -63% white -68% living with patient -72% higher education	IES-R (PTSD>= 33)	90 days after enrollment (enrollment about 10th day of MV)	16%	30%	Multivariable linear regression -relative's HADS score (measured on day 10 +/- 3.4 of mechanical ventilation), ($\beta = +1.02$, CI=0.73-1.3) -patient's unresponsiveness (RASS score -5 or -4), ($\beta = +8.39$, CI=0.83-15.95)
Choi et al (2018) [50]	Prospective cohort	99 Neuro-ICU patients who survived the hospitalization	Only primary caregivers were included in the study: 99 individuals: -mean age 53.3 years -62.2% female -65.7% spouse, 15.2% parent, 15.2 child -98% christian -80.6% higher education -57.7% employed	PCL-S (cut-off point not specified by the authors)	3 months and 6 months after ICU hospitalization	38%	3 months: 18% 6 months: 22%	Multivariable linear regression: - caregiver anxiety during ICU hospitalization ($\beta = +0.44$) - bond with the patient ($\beta = -0.08$)
Schoeman et al. (2017) [51]	Prospective cohort	Patients who stayed in the ICU for > 48h 60 individuals: - mean APACHE II 20.61 (+/- 8.33) - mean SAPS 39.73 (+/- 13.84) - mean ICU LOS 11.85 (+/- 8.40) - 20% died till 90 day follow-up	Relatives of patients that were considered highest in hierarchy for substitute decision making 60 individuals: - mean age 54.35 (+/- 20.39) yrs - 75%	IES-R (PTSD defined as > 33 points)	3 months from the enrollment (enrollment on day 3 of patient's admission)	0%	baseline - 33.33% at follow-up - 15%	Univariate linear regression: -unemployment

			spouses/partners, 18.33% parent, 3.33% children - 25% female 80% received social worker support - 51.67% employed					
Kentish-Barnes et al. (2017) [37]	Randomized controlled trial	Patients who stayed in the ICU for more than 2 days and died during hospitalization. 242 individuals: - median age 61 years - 35.1% female	Relatives designated as healthcare proxy. 208 individuals: - median age 57 years - 69.7 % female - 35.5% spouse, 39.9% children	IES-revised (PTSD defined as score >26 points)	6 months after ICU hospitalization.	6 months: 10%	44.8%	Multivariable analysis: -age of a patient; per 1 year (OR=0.96; 95%CI=0.94-0.99) -being a spouse (OR=5.61; 95%CI=2.59-12.11)
Petrinec et al. (2017) [29]	Prospective cohort	Patient who were hospitalized in the ICU who were mechanically ventilated or their predicted ICU stay was greater than 5 days 48 individuals: - median age 62.5 years - 39.6% female - median admission SAPS II score: 42.7 points - 50% died till 60 days post enrollment	Family decision-makers who: 48 individuals: - median age 56.3 years - 79.2 % female - 33.3% spouse, 35.4 child, 14.6% parent	PCL-5 PTSD suggested with score ≥ 38	T1 = days 3-5 after after ICU hospitalization T2 = 30 days after after ICU hospitalization T3 = 60 days after after ICU hospitalization	T2 - 20,8% T3 - 25%	T1 = 0 T2 = 7,9% T3 = 11.1%	Multiple linear regression T2: -avoidant coping mechanism - previous history of psychological symptoms T3: - avoidant coping mechanism - previous history of psychological symptoms -emotion-focused coping mechanism
Matt et al. (2017) [30]	Prospective cohort	Severe septic patients were included in the study 143 individuals: - median age 67 years - 49.7% female - median SOFA score at admission: 14 pointes - median ICU LOS: 10.7 days - 45.4% 90-day mortality	143 individuals: - median age 54 years - 73.4% female - 42.7% spouses, 39.2% children - 33.1% higher education	IES (PTSD defined as >32 points)	3 months after hospitalization	0%	39%	Multivariable linear regression: - female sex of a relative (B=+0.4) - stressors identified via qualitative analysis (B=+0.55)
Trevick et al. (2017) [52]	Prospective cohort	17 patients hospitalized in neuro-ICU, with advanced illness, who fulfilled criteria for a palliative	30 decision makers -median age 49 years -63.3% female	IES-R	1 month and 6 months after enrollment	1 month 13.3% 6 months	1 month 7.7% 6 months	Univariate analysis -daily visits, -persistent perceived pain

		care consult	-76.7% white -80% christian -13.3% spouse, 6.7% parents, 36.7% child, 16.7% sibling -88.5% college			23.3%	17%	
Wintermann et al. (2016) [53]	Cross-sectional	Patients with CCI hospitalized for a minimum of 6 days, transferred to post-acute rehabilitation, diagnosed with CIP or CIM, aged 18- 72 years, negative evaluation of the CAM-ICU. Exclusion: not alert, cognitively impaired, limited ability to communicate 83 individuals: -median age 61.7 years -26.5% female -median ICU LOS 66 days -median duration of mechanical ventilation 50 days -26% died	83 Relatives -median age 59.9 years -72.3% female -71.1% spouse, 6% parent, 18% child, 4.8% sibling - 65.1% >=10 years of education	PTSS-10 (PTSD>35),	Median 4.8 months after transfer from ICU to post-acute rehabilitation (72.3% about 3 months, 27.7% about 6 months)	42.6%	15.7%	Multivariable stepwise regression: -longer time following ICU discharge (B=0.262, CI=0.061-0.476) -diagnosis of post-ICU PTSD in CCI patient (B=0.254, CI = 0.089-1.102)
Warren et al. (2016) [38]	Prospective cohort	Patients admitted for at least 48h with an expected survival >96h Two groups - non-TBI and TBI (moderate to severe TBI = loss of consciousness for 30min.)	100 relatives -mean age 49.2 years -73% female -24% spouse, 27% parents, 18% child, 6% sibling -45% white -46% college -48.7% family of patients with TBI	PC-PTSD (PTSD risk >= 3)	during patient's admission and 3 months after ICU hospitalization	0%	during admission: 24.3% 3 months: 17%	Univariable analysis: -significant decrease in PC-PTSD scores for 3 months 17%) in non-TBI group (p=0.0196), no significant decrease in the TBI group TBI group had less improvement in PTS symptoms at 3 months
McPeake et al. (2016) [31]	Prospective cohort	36 patients, mechanically ventilated for at least 72h -median ICU LOS 14.5 days -median APACHE II score 23.5 -single center in the area of high deprivation -patients who decided to take	36 caregivers: - median age 57.5 years - 64% female - 67% spouses, 25% parent, 5.5% children, 2.5% sibling	IES-R (PTSD ≥33)	4 weeks - 3 years after discharge	0%	53%	Univariate analysis: -caregiver's strain

		part in 5-week rehabilitation course for patients and caregivers						
Kentish-Barnes et al. (2015) [54]	Prospective cohort	Patients who died in the ICU after 48 hours of hospitalization. 475 individuals	Only relatives who served as surrogates were included in the study. 475 individuals	IES-revised (PTSD defined when > 32 points)	6 months after ICU hospitalization	40.6%	43.6%	Multivariable logistic regression: -patient died while intubated -female sex of a relative -relative living alone -no chance to say the final goodbye -presence at the time of patients death -patient did not breathe peacefully
Hartog et al. (2015) [32]	Prospective cohort	Patients with severe sepsis receiving end-of-life care. 145 individuals: -mean age 72 years -35.2% female -mean admission SOFA score: 10 points -median ICU LOS: 241 days -81.4% died during the ICU stay	Relatives with the main decision-making role. 84 individuals: -mean age 57 years -73.8% female -41.7% spouse, 3.6% parent and 41.7% child -34.5% higher education	IES (PTSD defined as > 32 points)	3 months after ICU hospitalization	N/A	51%	Multiple linear regression: -being a spouse -female sex of a relative
Andersen et al. (2015) [55]	Prospective cohort	Patients who were anticipated to be hospitalized in the ICU more than 2 days. 74 individuals: -mean age 59.9 years -50% female -mean admission APACHE II score: 17.8 points -mean ICU LOS 9.4 days -26% died	51 individuals: -mean age 47 years -68.6% female -41% son, 25% spouse -98% christian -49% completed high school	PCL-S	2 months after ICU hospitalization	Unclear	2 months: 22.89%	Univariable analysis: 2 months: -higher patient's APACHE II score -longer ICU LOS -female sex of a relative -lower educational level of a relative -anxiety of a relative at admission of a patient
Fumis (2015) [56]	Prospective cohort	Patients who stayed in the ICU for more than 48 hours. Patients with severe neurologic diseases were excluded from the analysis. 184 individuals: -mean age 59.3 years	Only primary caregivers were included in the study. 184 individuals: -mean age 51.8 years -79% female	IES (PTSD defined when > 30 points)	1 month after ICU hospitalization	21%	1 month: 2.5%	Multivariable linear regression: -Age of a patient ($\beta=-0.123$) -Death of a patient ($\beta= +13.559$) -Anxiety and depression of a relative during an ICU hospitalization ($\beta=$

		-36,4% female -mean SOFA score: 2.38 points -mean ICU LOS: 5.5 days	-64.1% spouses, 25% children -69% religious -74.5% higher education					+13.574)
Zimmerli et al. (2014) [57]	Cross-sectional	Patients admitted to the ICU for treatment of OHCA 101 individuals: -mean age 63.4 years -33% female -mean admission APACHE II score 24 -mean SAPS II score 61.19 -mean ICU LOS 5.83 days -56% died	Relatives served as a surrogate decision-makers: 101 individuals: -mean age 58.1 years -70% female -71% spouse, 3% parent, 4% sibling, 17% child -91% higher education (college), 9% high school -6% changed work due to patient's OHCA	IES-R (PTSD >0*) *IES-r score was calculated: "-0.02 x intrusion subscale + 0.07 x avoidance subscale + 0.15 x hyperarousal subscale - 4.36"	Mean time since OHCA = 2.6 years	0%	40%	Multivariate logistic regression: -female sex of the relative (OR 2.97 CI=1.1-8.0) -history of the depression (OR 3.43 CI= 1.02-11.61) -therapeutic measures perceived as insufficient (OR 18.40 CI= 1.52-224.22)
Sundararajan et al. (2014) [58]	Prospective cohort	63 patients admitted to ICU for >48h - mean age 51.54 - 28.57% female - mean SAPS II 39.78 -mean APACHE II 19.86 -median LOS 7.79 days	63 caregivers - 73% spouses, 12.69% parent, 7.94% children, 6.35% sibling -42.85% high school, 55.5% more	IES-R (PTSD >26)	3 months after ICU discharge	21.3%	41.27%	Logarithmic binomial regression: -anxiety (HADS score) (RR 1.07 CI 1.00-1.14)
Dithole et al. (2013) [59]	Prospective cohort	Patients who were mechanically ventilated and were hospitalized for at least 3 days. All patients survived the ICU hospitalization 28 individuals.	Only spouses were included in the analysis: 28 individuals: -median age 35 years -60% female -35.7% higher education -71.4% employed	PCL-S (PTSD defined when ≥43 points)	6 months after ICU hospitalization	N/A	6 months: 57.1%	Univariable analysis: -female sex of a relative
de Miranda et al.	Prospective	Patients with COPD	102 relatives:	IES-R	3 months after ICU	54%	3 months:	Multivariable analysis:

(2011) [33]	cohort	exacerbation. Patients who died during hospitalization were excluded. 126 individuals: -median age 67 years -pre-ICU FEV: 32.5%	-54% spouses -37% caregivers	(PTSD defined when ≥ 22 points)	hospitalization		29.8%	3 months: -large ICU (>12 beds) (OR=6.00; 95% CI=1.15-31.3) -symptoms of depression at discharge (per point of HADS: OR=1.27; 95% CI=1.04-1.54) -worse PDEQ score at ICU discharge (per point of PDEQ score: OR=1.11; 95% CI=1.05-1.22) <i>PDEQ= Peritraumatic Dissociative Experiences Questionnaire</i>
Gries et al. (2010) [42]	Randomized controlled trial	Patients who died during the ICU hospitalization	226 individuals: -mean age 59.7 years -74.8% female -48.7% spouse, 36.7% child -37.2% higher education	PCL-C (PTSD defined when at least: 1 intrusive, 3 avoidant and 2 arousal symptoms)	At least 6 months after ICU hospitalization	18%	14%	Multivariable linear regression: -female sex of a relative ($\beta=3.9$) -years of association with a patient ($\beta=-0.175$) -Mood/emotions drugs taken by relatives prior to the ICU hospitalization ($\beta=+3.6$) -psychiatric counseling prior to the ICU hospitalization ($\beta=+3.5$)
Pillai et al. (2010) [34]	Prospective cohort	Patients hospitalized for at least 5 days	178 individuals: -average age 36 yrs (18-67) - 45,8% female - 31,3% spouse, 28,9% child - 32,5% higher education	IES-R (Sum of the score greater than 26 was considered as severe)	First assessment after the patient had been in the ICU for 5 days Follow-up at 2 months post-ICU discharge or death	40%	35%	Univariable analysis: -HADS score at admission greater than 11
Anderson et al. (2008) [35]	Prospective cohort	Patients who were anticipated to be in the ICU for more that 2 days and were unable to make medical decisions	50 individuals: -mean age 54 years -84% female -36% spouse, 26% parent and 12% child -96% christian -34% higher education	IES	6 months after ICU hospitalization	6 months: 32%	6 month: 35%	Univariable analysis: 6 months: None

Azoulay et al. (2005) [60]	Prospective cohort	<p>Patients who were hospitalized for more than 2 days.</p> <p>284 individuals: -mean age 59 years -44.4% female -mean admission APACHE II score: 40 points -19.7% died</p>	<p>Relatives with highest hierarchy for surrogate decision making:</p> <p>284 individuals: -mean age 51 years -67.6% female -48%% spouses, 13% children, 23.9% parents</p>	IES (PTSD defined when >30 points)	3 months after ICU hospitalization	38.2%	3 months: 33.1%	<p>Multivariable linear regression:</p> <p>3 months:</p> <ul style="list-style-type: none"> -Cancer of a patient ($\beta= +4.49$) -APACHE II score ($\beta= +0.08$) -Death of a patient ($\beta= +6.19$) -Children of patients ($\beta=+ 6.33$) -female sex of a relative ($\beta=+6.29$) -Relatives who felt the information from medical team was incomplete ($\beta=+5.53$) -Involvement of family members in everyday decisions ($\beta=+5.86$)
Jones et al. (2004) [61]	Randomized controlled trial	<p>Patients hospitalized in the ICU > 48 hours, were admitted emergently and were ventilated.</p> <p>104 individuals: -median age 56.5 years -median admission APACHE II score: 16.5 points -median ICU LOS: 13 days -81.4% died during the ICU stay</p>	<p>Relatives most closely involved in the patient's care</p> <p>104 individuals: -mean age 57 years -73.8% female -41.7% spouse, 3.6% parent and 41.7% child -34.5% higher education</p>	IES (PTSD defined as > 19 points)	6 months after ICU hospitalization	19%	49%	<p>Correlation:</p> <ul style="list-style-type: none"> - higher HAD-anxiety score in patients at recruitment ($\rho=0.21$) - higher HAD-anxiety score in patients at 6 months ($\rho=0.32$) -higher HAD-depression score in patients at 6 months ($\rho=0.23$) -higher IES score in patients at 6 months ($\rho=0.40$)
Cleiren et al.(2002) [48]	Cross-sectional	<p>Patients who died in the ICU due to brain injury</p> <p>-mean age 44 years</p>	<p>Relatives of first degree:</p> <p>95 individuals: -mean age 47 years -65% female -78% spouse or parent</p>	IES-Intrusions IES-Avoidance	6.1 months (the mean) after ICU death	N/A	N/A	<p>Univariable analysis:</p> <p>IES-Intrusions:</p> <ul style="list-style-type: none"> -female sex of a relative -spouse or parent relative <p>IES-Avoidance:</p> <ul style="list-style-type: none"> -none
Azoulay (2022) [66]	Prospective cohort	<p>Patients who were hospitalized due to ARDS of COVID-19 origin or of different cause.</p> <p>307 individuals: median age 61 years</p>	<p>602 family members:</p> <p>-median age 51 years -72% female -48% spouses -8.9% unemployed</p>	IES-R (cut-off 22 points)	3 months after ICU hospitalization	14%	27.6%	<p>Death was associated with higher PTSD prevalence</p> <p>Multivariable analysis:</p> <ul style="list-style-type: none"> -patient was a COVID-19 patient

		-34% female -COVID-19 ARDS 59% -ECMO 3% -mortality 26%						-family member is female -younger family member -lower level of social support
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Legend: ICU: intensive care unit; IES: Impact of Events Scale; IES-R: Impact of Events Scale-Revised; PCL-C: PTSD Checklist for DSM-IV (civilian); PCL-S: PTSD Checklist for DSM-IV (specific); PCL-5: PTSD Checklist for DSM-V; PTSS: PTSD Symptom Scale; PC-PTSD: Primary Care PTSD Screen for DSM-V; TSQ: Trauma Screening Questionnaire; APACHE II: Acute Physiology and Chronic Health Evaluation II; SOFA: Sequential Organ Failure Assessment score; SAPS II: Simplified Acute Physiology Score II; LOS: length of stay; ARDS: acute respiratory distress syndrome; VV-ECMO: veno-venous extracorporeal membrane oxygenation; MV: mechanical ventilation; PTSD: post-traumatic stress disorder; TBI: Traumatic Brain Injury;

Table 4. Complicated grief studies (*n* = 5)

Author (year)	Study type	Population characteristics of patients who were hospitalized in the ICU (+ inclusion and exclusion criteria)	Population characteristics of relatives of patients	Mental health assessment tools	Time-point of mental health assessment of relatives	Loss-to-follow-up	Prevalence of Complicated grief	Risk factors for complicated grief
Kentish-Barnes et al. (2018) [62]	Prospective cohort	Brain-dead patients who were eligible for organ donation	117 individuals: -median age ~52 years -42% female -41% spouses, 27.3% children, 12.8% parents -66% employed	ICG (complicated grief defined as > 25 points)	9 months after patient's death	42%	47.7%	Univariable analysis: -Not understanding the concept of brain death
Trevick et al. (2017) [52]	Prospective cohort	17 patients hospitalized in neuro-ICU, with advanced illness, who fulfilled criteria for a palliative care consult -mean age 66.6 years -mean ICU LOS 9.5 days	30 decision makers -median age 49 years -63.3% female -80% christian -13.3% spouse, 6.7% parents, 36.7% child, -88.5% higher education -76.7% white, 23.3% non-white	ICG-R (complicated grief defined as ≥36 points)	6 months after enrollment	23.3%	21.7%	-None
Kentish-Barnes et al. (2017) [37]	Randomized controlled trial	Patients who stayed in the ICU for more than 2 days and died during hospitalization. 242 individuals: - median age 61 years - 35.1% female	Relatives designated as healthcare proxy. 208 individuals: - median age 57 years - 69.7 % female - 35.5% spouse, 39.9% children	ICG (complicated grief defined as score ≥25 points)	6 months after ICU hospitalization.	6 months: 10%	32.4%	Multivariable analysis: -age of a patient; per 1 year (OR=0.95; 95%CI=0.93-0.98) -being a spouse (OR=3.44; 95%CI=1.47-8.05) -relative living alone (OR=4.33; 95%CI=1.81-10.38)
Kentish-Barnes et al. (2015) [54]	Prospective cohort	Patients who died in the ICU after 48 hours of hospitalization. 475 individuals	Only relatives who served as surrogates were included in the study. 475 individuals	ICG (Complicated grief defined as > 25 points)	6 months after ICU hospitalization	40.6%	52.1%	Multivariable logistic regression: -intensivist board certification before 2009 (OR=3.82; 95%CI=1.57-9.34) -patient died while intubated (OR=2.12; 95%CI=1.16-3.89) -female sex of a relative (OR=3.07; 95%CI=1.62-5.80) -relative living alone (OR=1.97;

								<p>95%CI=1.10-3.51) -unsatisfactory communication with the medical staff (OR=3.27; 95%CI=1.42-7.50) -patient's refusal to treatment (OR=0.24; 95%CI=0.08-0.69) -no chance to say the final goodbye (OR=2.47; 95%CI=1.30-4.68) -presence at the time of patients death (OR=2.91; 95%CI=1.62-5.21)</p>
Anderson et al. (2008) [35]	Prospective cohort	Patients who were anticipated to be in the ICU for more than 2 days and were unable to make medical decisions.	<p>50 individuals: -mean age 54 years -84% female -36% spouse, 26% parent and 12% child -96% christian -34% higher education</p>	ICG	6 months after ICU hospitalization	32%	6 month: Out of 13 bereaved relatives, 46% of participants were diagnosed with complicated grief	<p>Univariable analysis:</p> <p>6 months: - None</p>

Legend: ICU: intensive care unit; LOS: length of stay; ICG: Inventory of Complicated Grief; ICG-R: Inventory of Complicated Grief-revised;

Table 5. Other studies (*n* = 12)

Author and year [X]	Study type	Population characteristics of patients who were hospitalized in the ICU (+ inclusion and exclusion criteria)	Population characteristics of relatives of patients	Mental health area	Mental health assessment tools	Time-point of mental health assessment of relatives	Loss-to-follow-up	Prevalence of PICS-F	Risk factors for PICS-F
Vallet et al. (2019) [63]	Prospective cohort (nested within randomized-controlled trial)	Patients ≥ 75 years who survived the ICU with preserved functional and nutritional status and without cancer. 191 individuals: -median age 86 years -61.3% female -median admission SAPS III score: 62 points	Only primary caregivers were included in the study. 191 individuals	Caregiver burden	ZBI (Caregiver burden defined as ≥21 points)	6 months after ICU hospitalization	Unclear	37%	Multivariable logistic regression: -ADL of a patient; per 1 point decrease (OR=1.46; 95%CI=1.2-1.8)
McPeake et al. (2016) [31]	Prospective cohort	36 patients, mechanically ventilated for at least 72h -median ICU LOS 14.5 days -median APACHE II score 23.5 -single center in the area of high deprivation	36 caregivers: - median age 57.5 years - 64% female - 67% spouses, 25% parent, 5.5% children, 2.5% sibling	Caregiver strain, insomnia	CSI (>=7 high level of stress) ISI (15-28 clinical insomnia)	4 weeks - 3 years after discharge	0%	caregiver strain: 53% insomnia: 33%	Univariate analysis -Strain: poor QOL in the patient Linear regression -Insomnia: anxiety
Myhren et al. (2010) [64]	Cross-sectional study	Patients aged 18-75 years old, who stayed at least 24 h in the ICU: 255 individuals: - mean age 47.9 (SD 15.7) - 37.3 % female - 84.7% mechanically ventilated - mean duration of MV 11.0 (CI 9.3-12.7) - mean SAPS-II 29.6 (CI 28.8-30.5) - mean LOS ICU 12.0 (10.03-13.8)	The closest / most representative relatives 354 individuals: - mean age 50.3 (SD 12.2) - 70.1% female - 38.1% had higher education - 17.8% unemployed - 50.2% spouse/partner, 25.5% child, 14.7% parent	Psychological distress	Previously-developed questionnaire validated against HADS and IES.	4 weeks post-ICU discharge	62.14%	N/A	Multivariate linear regression: -unemployment status -more environmental strain -less hope for the situation to get better - absence from work - patient still in hospital/institution at the time of evaluation
Van Pelt et al. (2010)	Prospective cohort	48 patients, mechanically ventilated for at least 48h, survived 2 months	48 caregivers	Lifestyle disruption	ARS	2, 6 and 12 months after initiation of	Unclear	N/A	Multivariable linear regression:

[44]		<p>Exclusion: organ transplantation, chronically ventilator dependent prior to admission, intubated >24h in an outside hospital</p> <p>-mean age 52.5 years -33.3% female -median APACHE III score: 52 -median ICU LOS 13 days -mean duration of MV 10 days</p>	<p>-mean age 52.8 years -81.2% female -47.9% spouse, 37.5% family members, 14.6% not family -91.7% white -87.5% education >=12th grade</p>			mechanical ventilation			<p>2 months: -patient's male gender (B=-7.29) , -patient's education >=12th grade (B=7.09)</p> <p>12 months: -patient's male gender (B=-0.73), -tracheostomy (B=0.56) - post -ICU functional dependency (B=0.73)</p>
Siegel et al. (2008) [65]	Cross-sectional study	<p>Patients who died in the ICU</p> <p>41 individuals: - mean age 72 (SD 14) - 44% female - mean ICU LOS: 3 days - 83% mechanically ventilated - mean time since death - 8 months -main illness - cancer (29%)</p>	<p>Relatives of patients who died in the ICU 3-12 months prior to enrollment, who served as the patient's primary surrogate decision maker.</p> <p>41 individuals: - mean age 57 (SD 14) - 73% female - 14% religious (42% of those catholic) - 17% had prior mental disorders</p>	Composite outcome of: depression, anxiety, panic & complicated grief	3-12 months from the patient's death	0%	20%	34%	<p>Bivariate analysis</p> <p>- being a spouse (compared to other relatives) - suffering from an additional stressor - the patient's sickness duration < 5 years - failure to find the physician comforting</p>
Van Pelt et al. (2007) [45]	Prospective cohort	<p>169 patients, mechanically ventilated for at least 48h, survived at least 2 months</p> <p>-mean age 56.6 years -40.2% female -median APACHE III score: 56 -median ICU LOS 14 days</p>	<p>169 caregivers</p> <p>-mean age 54.6 years -75.7% female -52.7% spouse, 35.5% family members, 11.8% not family -91.1% white -88.8% education</p>	Lifestyle disruption	ARS AND proportion of caregivers that stopped working in order to provide care	2, 6 and 12 months after initiation of mechanical ventilation	Unclear	<p>% of caregivers who stopped working to provide care</p> <p>2 months 13% 6 months 10.3% 12 months</p>	<p>Univariate analysis:</p> <p>2 months and 12 month -none</p> <p>6 months -pre-ICU functional dependency</p>

			>=12th grade -41.4% family of patients with pre-ICU functional dependency					14.1%	
Douglas et al. (2005) [46]	Randomized controlled trial	Patients who were mechanically ventilated for at least 3 days and survived the ICU hospitalization. 290 individuals: -mean age 60.7 years -55.8% female -mean ICU LOS 17.6 days	Only primary caregivers were included in the study 290 individuals: -mean age 53 years -72% female -42% spouse, 32% child -22.62% higher education -65% white, 35% non-white	Caregiver burden	Caregiver reaction assessment	2 months after ICU hospitalization	23.5%	N/A	Univariable analysis: 2 months: -children as caregivers reported lack of family support -institutional residency 2 months after discharge
Fu et al. (2021) [67]	Cross-sectional	Patients discharged from the ICU. 522 individuals: ->65 years 50.5% -female 50.4%	Only primary caregivers were included in the study. 554 individuals: ->65 years 46.2% -Spouse 79.8% -female 50.9% -unemployment 53.6%	Caregiver burden	ZBI	Unclear	5.8%	Unclear	Multivariate analysis: -younger family member -higher education of a family member -Being other than a spouse -Higher caregiving time each day -older patient -poor health of a patient -prior chronic disease of patient -worse economic situation -not being covered by a medical aid system
Heesakkers et al. (2022) [68]	Prospective cohort	COVID-19 Patients discharged from the ICU. 166 patients: -mean age 61.1 years -female 25.2% -mean APACHE IV score 59.6	Family members. 166 individuals: -mean age 57.8 years -female 78.9% -spouse 86.1% -higher education	Composite outcome of PTSD, depression and anxiety	HADS-A (above or equal 8 points) HADS-D (above or equal 8 points) IED-6 (each question with above or equal 1.75 cut-off point)	3 months and 12 months after ICU discharge	3 months: -anxiety 31.6% -depression 28.3% -PTSD 29.2%	3 months: 34.6% 12 months: 39.8%	Multivariate analysis: -prior mental health disorders in family

		-median ICU LOS 20 days	28.8%				12 months: -anxiety 29.0% -depression 22.8% -PTSD 20.2%		
Milton et al. (2021) [69]	Prospective cohort	Patients discharged from the ICU: 62 patients: -median age 64 years -female 18% -median APACHE II 18 points -ICU LOS 3 days	Primary caregivers: 62 individuals: -median age 63 years -female 81% -spouse 92% -parent 3% -child 3%	Caregiver burden	CBS	3 months after ICU discharge	11%	Unclear	Adjusted analysis: -worse ICU outcome of a patient
McPeake et al. (2022) [70]	Prospective cohort	Patients discharged from the ICU. 170 patients: -median age ~61 years -female 46.5% -median APACHE II 19 points	Primary caregivers. 170 individuals: -median age ~58 years -female 64.6% -spouse 70.6% -child 17% -parent 6.5%	Caregiver strain and Insomnia	Caregiver strain: CSI (above or equal to 7 points) Insomnia (ISI above 7 points)	12 months after ICU hospitalization	Caregiver strain ~ 24.5% Insomnia ~ 49.5%	40%	Multivariable analysis: -pre-ICU mental health disease in critically-ill patient -younger caregiver age

Legend: ICU: intensive care unit; ZBI: Zarit Burden Interview; CSI: Caregiver Strain Index; ISI: insomnia severity index; CBS: Caregiver burden scale; APACHE II: Acute Physiology and Chronic Health Evaluation II; SOFA: Sequential Organ Failure Assessment score; SAPS II: Simplified Acute Physiology Score II; LOS: length of stay; ARS: Activity Restriction Scale