

Supplemental Online Content

Azoulay E, Resche-Rigon M, Megarbane B, et al. Association of COVID-19 acute respiratory distress syndrome with symptoms of posttraumatic stress disorder in family members after ICU discharge. *JAMA*. doi:10.1001/jama.2022.2017

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This supplemental material has been provided by the authors to give readers additional information about their work.

eTable 1. Main Characteristics of the 23 Participating ICUs

| ICU characteristics Number (%) or Median [IQR] | Before the pandemic | During the pandemic |
|---|------------------------|------------------------|
| University-affiliated hospitals | 16 (70) | 16 (70) |
| Number of beds (baseline / during the pandemic) | 20 [15-25] | 32 [26/37] |
| Number of nurses (baseline / during the pandemic) | 48 [38-57] | 69 55-83] |
| Patient to nurse ratio | 2.5 (2.5-2.5) | 2.5 (2.5-2.5) |
| Number of nursing assistants (baseline / during the pandemic) | 30 [22-35] | 42 [30-52] |
| Number of senior physicians (baseline / during the pandemic) | 10 [8-12] | 13 [11-15] |
| Number of residents (baseline / during the pandemic) | 8 [7-11] | 12 [10-15] |
| Ranking by ICU head (0 never-10 always): | | |
| Nurses participate in clinical rounds | 8 [5-9] | |
| Nurses can initiate an end-of-life discussion | 8 [7-9] | |
| Palliative care service used for end-of-life care | 9 [7-10] | |
| Psychologist available | 16 (70) | |
| Nurses take part in family information | 22 (96) | |
| Visitation policies before the COVID-19 pandemic | | |
| Visiting hours per day | | |
| Open visitation policies | 13 (57%) | |
| >12 hours per day | 10 (43%) | |
| Numbers of visitors allowed at the same time in the room | 2 (2-2) | |
| Presence of navigators | 0 | |
| Social worker available for the family members | 23 (100%) | |
| Chaplaincy available | 23 (100%) | |
| Total COVID-19 patients managed | | 478 [350-780] |
| Number of professionals who contracted COVID-19 | | 108 / 1736 (6.2) |
| Communication was modified for COVID-19 families | | 22 (96) |
| - <i>Routine telephone call set up by one of the clinicians^a</i> | | 19 (83) |
| - <i>Videoconferences set up with family and clinicians^a</i> | | 6 (26) |
| - <i>Clinicians wrote their name on their PPE</i> | | 4 (17) |
| - <i>ICU visits allowed</i> | | |
| - <i>* no ICU visit allowed</i> | | 0 |
| - <i>* for one person only</i> | | 16 (70) |
| - <i>* for a limited time</i> | | 15 (65) |
| - <i>* unrestricted visits</i> | | 7 (30) |
| - <i>* unrestricted visits for relatives of dying patients</i> | | 19 (83%) |
| - <i>* relatives declined ICU visits</i> | | 12 (52) |

^aphysicians and nurses

φ in the eight ICUs who allowed family members to visit the patient

eTable 2. Assessment of the 135 Bereaved Relatives on Day 90 After ICU Discharge

| N (%) or Median [interquartile range] | COVID-19 N=78 | Non-COVID-19 N=57 |
|--|------------------|----------------------|
| Primary endpoint | | |
| Impact of Event Scale - Revised | 27 [19-39] | 18 [8-27] |
| <i>Proportion of bereaved relatives with PTSD-related symptoms (IES-R>22)</i> | 48/76 (63%) | 22/56 (39%) |
| Secondary endpoint | | |
| HADS anxiety subscale | 8 [3-12] | 4 [2-7] |
| <i>Proportion of bereaved relatives with symptoms of anxiety (subscale≥7)</i> | 43 (55%) | 18 (32%) |
| HADS depression subscale | 7 [3-12] | 4 [1-6] |
| <i>Proportion of bereaved relatives with symptoms of depression (subscale≥7)</i> | 41/75 (55%) | 11/55 (20%) |
| | | |

eTable 3. Characteristics of Patients Who Provided Informed Consent

| N (%) or Median [interquartile range] | COVID-19 N=178 | Non-COVID-19 N=129 | P value |
|--|---------------------------|-------------------------------|--------------------|
| Male sex | 135 (76%) | 68 (53%) | <.001 |
| Female sex | 53 (24%) | 61 (47%) | |
| Age | 60 [50-68] | 62 (48-72) | .56 |
| Comorbidities | | | |
| Hypertension | 74/177 (42%) | 43/128 (34%) | .15 |
| Diabetes | 43/176 (24%) | 27/127 (21%) | .58 |
| Cardiovascular disease | 26/176 (15%) | 30/128 (23%) | .07 |
| Hematologic malignancy | 15/176 (9%) | 31/128 (24%) | <.001 |
| Solid organ transplant | 4/176 (2%) | 11/128 (9%) | .015 |
| Other immunocompromised patients | 10/176 (6%) | 28/127 (22%) | <.001 |
| Respiratory rate | 28 [23-32] | 28 [20-33] | .14 |
| PaO₂ / FiO₂ ratio | 99 [84;150] | 125 [81-219] | .13 |
| Need for high flow nasal oxygen within 24 h of ICU admission | 65/177 (37%) | 59/128 (45%) | .12 |
| Need for noninvasive mechanical ventilation | 69/176 (39%) | 53/126 (42%) | .55 |
| Need for endotracheal mechanical ventilation within 24 h of ICU admission | 127/177 (72%) | 58 (46%) | <.001 |
| Need for prone positioning | 100 (56%) | 14/126 (11%) | <.001 |
| Extracorporeal membrane oxygenation | 6/177 (3%) | 4/127 (3%) | >.99 |
| Duration of invasive mechanical ventilation | 15 [11-20] | 8 [4-11] | <.001 |
| Need for vasopressors | 70/174 (40%) | 39/128 (30%) | .09 |
| Acute kidney injury ^Y | 50/176 (28%) | 38/126 (30%) | .80 |
| Renal replacement therapy | 18/176 (10%) | 7 (5%) | .15 |
| Neurological disturbances at ICU admission ^φ | 18/175 (10%) | 29/128 (23%) | .004 |
| | | | |

^φ Neurological disturbances include encephalopathy, dizziness, stroke, movement disorders, motor and sensory deficits, ataxia, and seizures

^Y Acute kidney injury was defined as an increase in serum creatinine by ≥ 0.3 mg/dl (>26.5 $\mu\text{mol/l}$) observed within 48 hours; or an Increase in serum creatinine to ≥ 1.5 times baseline; or Urine volume <0.5 ml/kg/h for 6 hours

eTable 4. Assessment of the Patients on Day 90 After ICU Discharge

| N (%) or Median (interquartile ranges) | COVID-19 N=178 | Non-COVID-19 N=129 | <i>P</i> value |
|---|---------------------------|-------------------------------|---------------------------|
| Cannot remember the time of ICU admission | 77/157 (49%) | 46/110 (42%) | .26 |
| Report having been sedated in the ICU | 116/155 (75%) | 56/107 (52%) | <.001 |
| Rating (0 poor-10 excellent) of quality of information | 8 [6-9] | 8 [6-10] | .32 |
| Rating (0 poor-10 excellent) of clinicians^a behaviors | 9 [8-10] | 10 [8-10] | .79 |
| Report clinicians^a were wearing personal protective equipment | 126/156 (81%) | 48/109 (44%) | <.001 |
| Did not receive any family visit in the ICU | 109/157 (69%) | 10/109 (9%) | <.001 |
| Remote communication with family while in the ICU | 87/156 (56%) | 62/102 (61%) | .44 |
| Over the phone | 67 (43%) | 58 (57%) | |
| Using videoconferencing | 16 (10%) | 2 (2%) | |
| Other | 4 (3%) | 2 (2%) | |
| No remote communication | 69 (44%) | 40 (39%) | |
| Felt lonely (0 not at all - 10 very much so) during the ICU stay | 5 [1-8] | 2 [1-5] | .004 |
| Felt distressed (0 not at all - 10 very much so) during the ICU stay | 5 [1-8] | 5 [1-8] | .86 |
| Rating (0 poor-10 excellent) of symptom control | 9 [8-10] | 10 [8-10] | .29 |
| Felt they were shunned by ICU clinicians | 1 [1-3] | 1 [1-1] | .002 |
| Unemployed | 20/155 (13%) | 10/108 (9%) | .43 |
| Rating of own social support | 10 [9-10] | 10 [8-10] | .24 |
| Psychotropic drug intake | 23/156 (15%) | 20/108 (19%) | .50 |

^aphysicians and nurses

eTable 5. Day 90 Outcomes in 307 Surviving Patients

| N (%) or Median [interquartile range] | COVID-19 | Non-COVID-19 | P value |
|--|------------------|---------------------|----------------|
| Patients | N=178 | N=129 | |
| Impact of Event Scale - Revised | 8 [3-19] | 7 [3-18] | .59 |
| <i>Proportion of patients with PTSD-related symptoms (IES-R>22)</i> | 30/150 (20%) | 16/105 (15%) | .24 |
| | | | |
| HADS anxiety subscale | 3 [1-6] | 5 [2-8] | .01 |
| <i>Proportion of patients with symptoms of anxiety (subscale≥7)</i> | 38/154 (25%) | 38/108 (35%) | .07 |
| HADS depression subscale | 2 [1-6] | 3 [1-6] | .25 |
| <i>Proportion of patients with symptoms of depression (subscale≥7)</i> | 32/148 (22%) | 26/107 (24%) | .65 |
| Quality of life (SF-36) | | | |
| <i>Mental health component</i> | 54.7 [46.7-60.3] | 53.3 [43.3-58.0] | .20 |
| <i>Physical health component</i> | 41.7 [31.9-49.8] | 39.3 [24.8-48.7] | .14 |
| | | | |

The presence of PTSD-related symptoms was defined by the proportion of patients with an IES-R>22

eTable 6. Multivariable Analysis: Independent Determinants of Symptoms of Anxiety and Depression in the Family Members

| Odds Ratio associated with | | Odds Ratio for Anxiety (95% Confidence Interval) | Odds Ratio for Depression (95% Confidence Interval) |
|---|--------|---|--|
| | | | |
| Family member of a COVID-19 patient | No | 1 | 1 |
| | Yes | 1.29 (0.87-1.92) | 1.89 (1.19-2.99) |
| Sex | Female | 1 | 1 |
| | Male | 0.52 (0.33-0.80) | 0.64 (0.39-1.06) |
| Age (per 10-year increase) | | 0.85 (0.75-0.97) | 0.89 (0.76-1.03) |
| Level of social support (0 extremely limited-10 extremely effective) (per additional point) | | 0.81 (0.74-0.89) | 0.80 (0.73-0.88) |
| | | | |

Hosmer and Lemeshow goodness of fit (GOF) test, P=.51 for anxiety and P=.99 for depression.

A sensitivity analysis that took into account a center effect and another analysis that used a set of data after imputation of missing variables found similar results.

Variables considered for the LASSO step included sex, age, marital status, profession, and social support.

eTable 7. Day 90 Outcomes in 517 Family Members of COVID-19 and Non-COVID-19 Patients After Multiple Imputation

| N (%) or Median [interquartile range] | Proportion differences (95% CI) | P value |
|---|--|----------------|
| Family Members | | P value |
| Primary endpoint | | |
| <i>Proportion of relatives with PTSD-related symptoms (IES-R>22)</i> | 16% (9.0-23.0) | <.001 |
| Secondary endpoint | | |
| <i>Proportion of relatives with symptoms of anxiety</i> | 9% (0-16) | .06 |
| <i>Proportion of relatives with symptoms of depression</i> | 13% (6-20) | <.001 |
| | | |

eTable 8. Independent Determinants of PTSD-Related Symptoms in Family Members Including Center Effect

| Odds Ratio associated with | | Odds Ratio (95% Confidence Interval) |
|---|--------|---|
| | | |
| Family member of a COVID-19 patient (as compared to a non-COVID-19 patient) | No | 1 |
| | Yes | 1.94 (1.19-3.14) |
| Male sex | Female | 1 |
| | Male | 0.39 (0.23-0.67) |
| Age (per 10-year increase) | | 0.83 (0.71-0.97) |
| Level of social support (0 extremely limited-10 extremely effective) (per additional point) | | 0.82 (0.74-0.90) |
| | | |

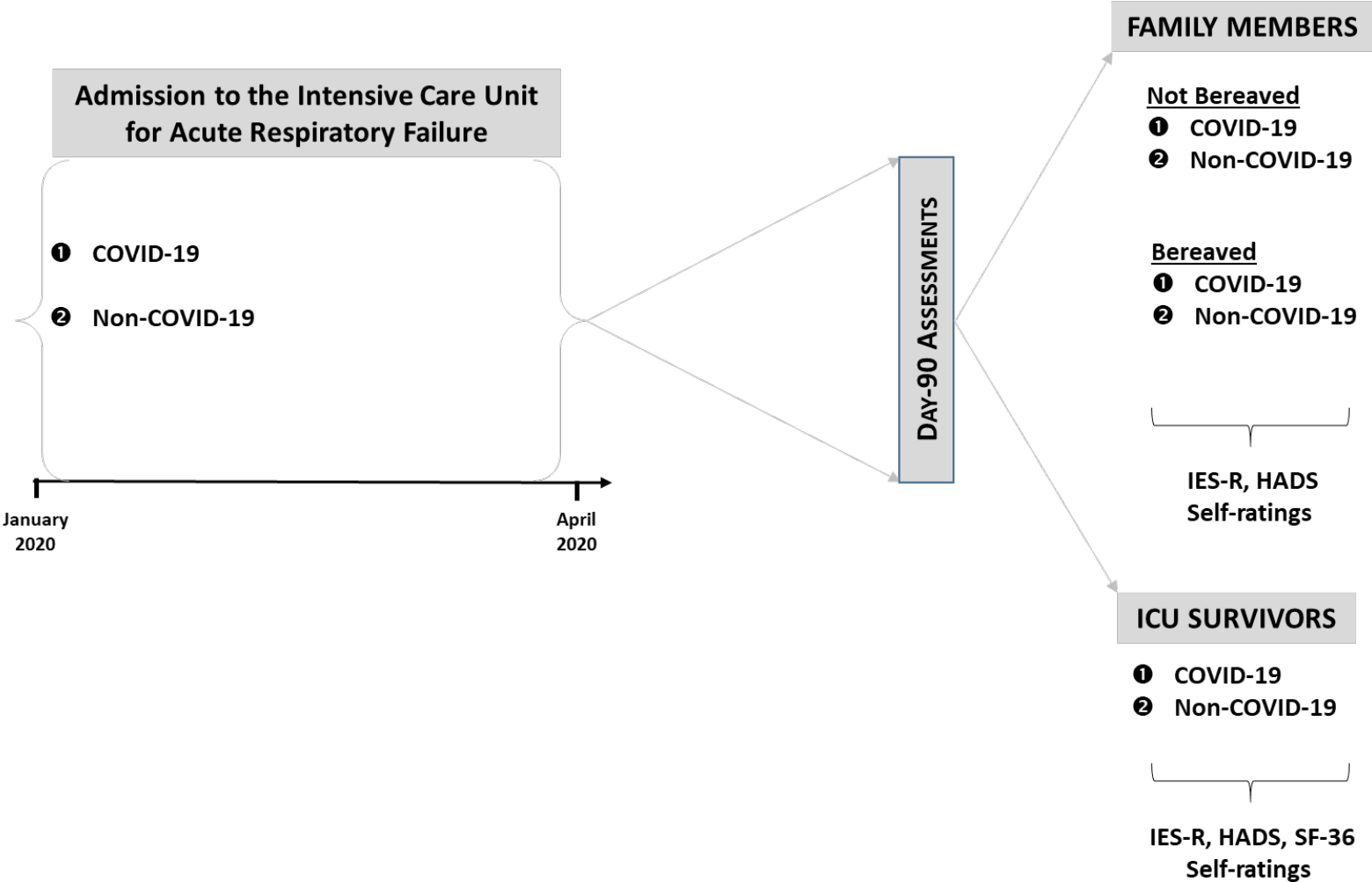
eTable 9. Independent Determinants of PTSD-Related Symptoms in Family Members After Multiple Imputation

| Odds Ratio associated with | | Odds Ratio (95% Confidence Interval) |
|--|---------------|---|
| Family member of a COVID-19 patient (as compared to a non-COVID-19 patient) | No | 1 |
| | Yes | 2.12 (1.37-3.27) |
| Male sex | Female | 1 |
| | Male | 0.37 (0.22-0.62) |
| Age (per 10-year increase) | | 0.85 (0.73-0.98) |
| Level of social support (0 extremely limited-10 extremely effective) (per additional point) | | 0.82 (0.75-0.90) |
| | | |

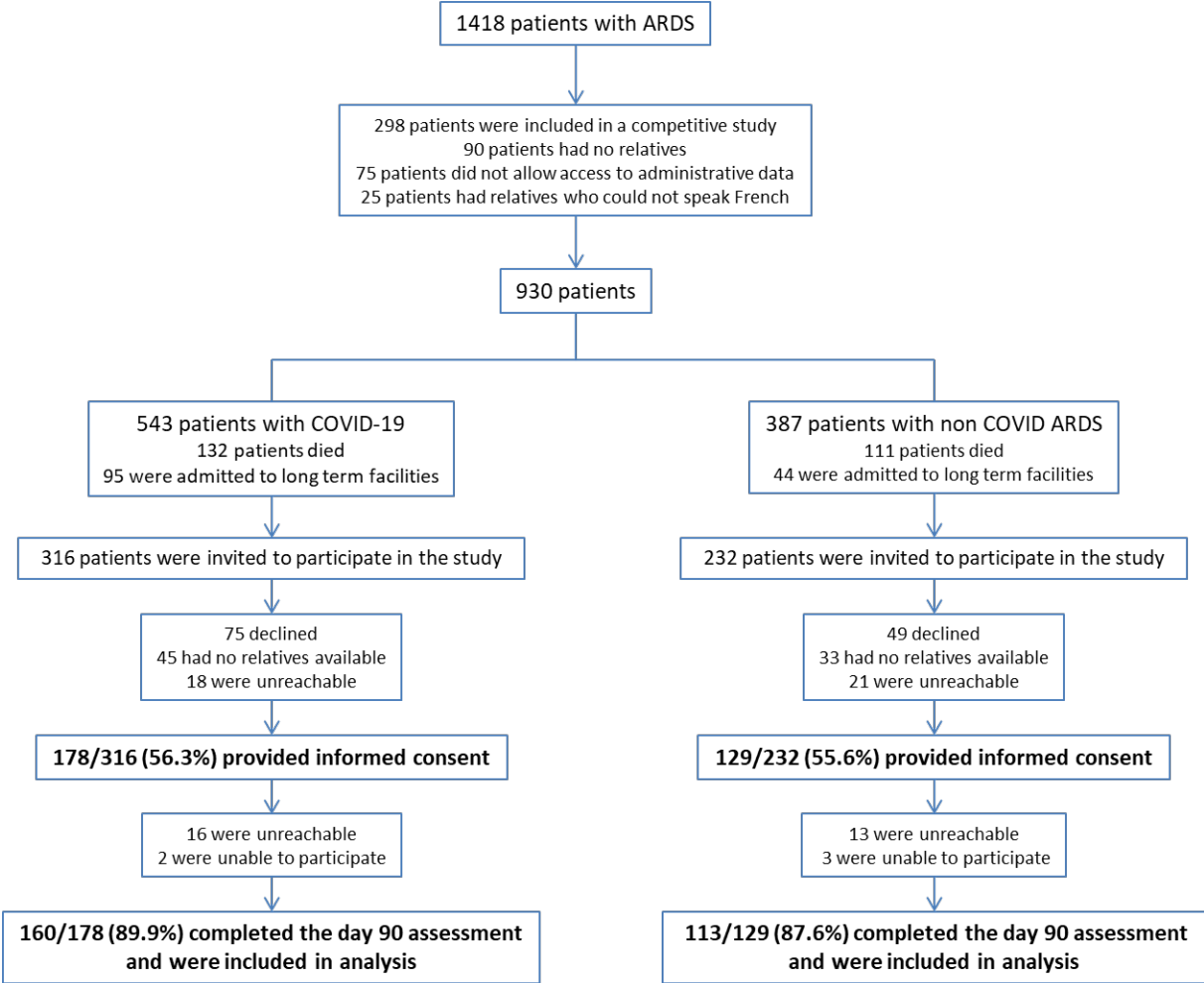
eTable 10. Independent Determinants of PTSD-Related Symptoms Defined by Score Greater Than 26

| Odds Ratio associated with | | Odds Ratio (95% Confidence Interval) |
|---|--------|---|
| Family member of a COVID-19 patient (as compared to a non-COVID-19 patient) | No | 1 |
| | Yes | 2.05 (1.23-3.40) |
| Male sex | Female | 1 |
| | Male | 0.31 (0.17-0.59) |
| Age (per 10-year increase) | | 0.79 (0.67-0.93) |
| Level of social support (0 extremely limited-10 extremely effective) (per additional point) | | 0.81 (0.73-0.90) |
| | | |

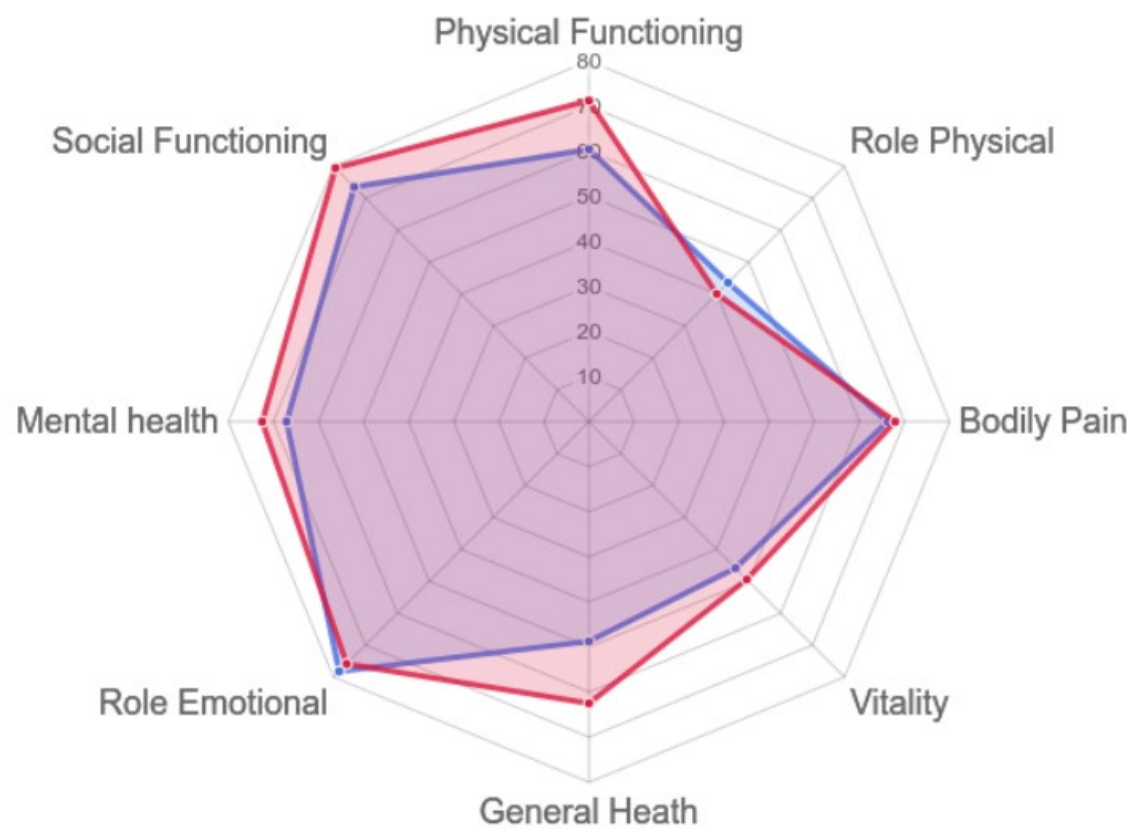
eFigure 1. Study Design



eFigure 2. Patients' Flow Diagram



eFigure 3. Health-Related Quality of Life in Patients Who Were Alive at 90 Days



The 8 domains were assessed using the SF-36 instrument during a telephone interview 90 days after ICU discharge in patients with COVID-19 (red) or non-COVID-19 (blue) ARDS.

eFigure 4. Mental (Left) and Physical (Right) Components Scores of the SF-36 in Patients With COVID-19 (Red) vs Non-COVID-19 (Blue) ARDS 90 Days After ICU Discharge

