

# Delirium as a Determinant of Long-Term Cognitive Dysfunction in the Context of Post-intensive Care Syndrome: A Prospective Study in a Latin American Environment

Review began 02/07/2025

Review ended 03/02/2025

Published 03/14/2025

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DOI: 10.7759/cureus.80578

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## Abstract

### Introduction

Cognitive dysfunction represents a major healthcare concern in the 21st century. Prolonged cognitive dysfunction and concomitant psychological and physical disorders in patients admitted to the intensive care unit (ICU) are components of the post-ICU syndrome (PICS). Notwithstanding the numerous published studies in this area, our work is the first to explore the relationship between PICS and delirium in the ICU in Uruguay. This research underscores the significance and potential of our study, which we believe will make a substantial contribution to this field of research in Latin America.

### Objectives

The incidence rates of the cognitive, psychological, and physical sequelae constituting PICS were evaluated, and the relationships between these disorders and delirium in the ICU were studied.

### Methods

This was a prospective cohort study in which patients were followed up for one year after admission to the ICU of Hospital Pasteur between 03/01/2017 and 05/31/2017. The pre-ICU condition of each patient was considered in the analysis. An initial telephone interview was conducted using the following scales: the Hamilton scale was used to assess anxiety, the Pfeiffer scale was used to assess cognitive impairment, and the Barthel scale was used to assess activities of daily living (ADLs). In a second face-to-face interview, the Mini-Mental State Examination (MMSE) and the Beck Depression Scale II (BDS-II) were used.

### Results

Forty-three patients were divided into two groups: 15 (34%) with delirium in the ICU and 28 (66%) without delirium. The association of delirium with different sequelae was evaluated using the corresponding scales: Pfeiffer scale: Cognitive impairment was observed in 7/13 patients (53%) in the delirium group vs. 0/29 patients (0%) in the non-delirious group ( $p = 0.001$ ); MMSE score: Deterioration was observed in 6/7 patients (86%) in the delirium group vs. 1/7 patients (14%) in the non-delirious group ( $p = 0.007$ ). Cognitive impairment was found in 3/6 patients (50%) who presented with delirium in the ICU, while 1/8 patients (13%) who did not present with delirium experienced cognitive impairment ( $p = 0.036$ ); Hamilton scale: Anxiety was found in 8/15 patients (57%) in the delirium group and 20/29 patients (68%) in the non-delirious group; BDS-II: Depression was found in 12/12 patients (100%) in the delirium group vs. 27/29 patients (93%) in the non-delirious group ( $p = 0.57$ ). Barthel scale: Dependence on others for ADLs was observed in 3/15 patients (20%) in the delirium group vs. 4/29 patients (14%) in the non-delirious group ( $p = 0.23$ ).

### Conclusions

Cognitive impairment was observed to be associated with delirium in the ICU, opening new avenues for research and possible treatment options. Although dependence on activities of daily living (ADLs) was more common in the delirium group, the difference between the two groups was not significant, highlighting the need for further research to understand the whole picture. Rates of anxiety and depression after ICU stay were also similar between the two groups, providing a baseline for comparison and informing future studies. The study highlights the urgent need for delirium-specific interventions in the ICU to address cognitive dysfunction and improve long-term outcomes in critically ill patients.

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#### How to cite this article

Mesa P, Kotfis K, Lecor C, et al. (March 14, 2025) Delirium as a Determinant of Long-Term Cognitive Dysfunction in the Context of Post-intensive Care Syndrome: A Prospective Study in a Latin American Environment. *Cureus* 17(3): e80578. DOI 10.7759/cureus.80578

**Categories:** Neurology, Emergency Medicine, Anesthesiology

**Keywords:** cam-icu, cognitive, cognitive impairment, delirium, medical intensive care unit (micu), physical sequelae, post intensive care, psychological

## Introduction

Cognitive dysfunction is one of the most important health concerns of the 21st century. Long-term cognitive dysfunction is common in patients admitted to the intensive care unit (ICU), and together with psychological and physical disorders, it is part of post-intensive care unit syndrome (PICS). PICS is an entity that was first described in 2010 by the Critical Care Medicine Society [1]. It encompasses a set of physical, cognitive, and psychological sequelae that patients may experience after discharge from the ICU.

These sequelae lead to impaired quality of life and influence the long-term prognosis of critically ill patients. This syndrome affects many patients discharged from the ICU [1], causing negative impacts on the quality of life for both the survivors and their relatives and generating substantial healthcare costs. The complications associated with PICS can persist for a long time, and patients must be monitored for signs of these sequelae from the time of admission to the ICU. To optimize the care of ICU survivors, it is important to identify during the ICU stay which patients have factors that may increase the risk of developing PICS.

There is a relationship between brain injury and the development of PICS, especially with respect to the cognitive aspects of PICS [1,2]. The most frequently observed forms of acute brain dysfunction in critically ill patients are delirium and coma [2,3]. Delirium is characterized by acute changes in attention and cognition and has a high incidence in ICU patients. Compared to patients who do not experience delirium, patients with delirium in the ICU have higher mortality rates, a longer duration of invasive mechanical ventilation (IMV), longer stays in the ICU, longer hospital stays, and greater long-term cognitive decline [4].

Early interventions can decrease the risk and duration of delirium in the ICU and represent one type of factor that healthcare professionals can influence to prevent long-term cognitive impairment and other aspects of PICS [2,3]. In Uruguay, a prospective cohort study showed that delirium occurred in 80% of patients subjected to IMV [5].

The objectives of the present study were to evaluate the incidence rates of the cognitive, psychological, and physical disorders that comprise PICS and to study the relationship between the development of delirium during the ICU stay and the development of these disorders.

## Materials And Methods

### Study population and environment

This descriptive, prospective cohort study followed patients who were admitted to the ICU of Pasteur Hospital between March 1 and May 31, 2017, for one year. The setting was the ICU of Hospital Pasteur in Montevideo, Uruguay. This multipurpose ICU has 25 beds and provides care to both medical and surgical patients.

All surviving patients 12 months after discharge from the ICU who were older than 18 years, who had been admitted to the ICU for at least 24 hours, and who had been assessed with a tool for diagnosing delirium, namely, the confusion assessment method for the intensive care unit (CAM-ICU), were eligible for inclusion, regardless of whether they required IMV [6,7].

Patients with a known and documented diagnosis of neurological pathology were excluded, as were those with severe neuropsychiatric disorders that prevented the communication necessary for the CAM-ICU. The CAM-ICU is less reliable in patients with neurological disorders [8].

All patients who had a sustained Richmond Agitation-Sedation Scale (RASS) score of -4 or -5, that is, those who remained in a coma for their whole stay in the ICU, were excluded because delirium could not be assessed in these patients.

To determine which subjects were alive one year after admission to the ICU, the medical records system of the hospital was consulted, and patients who could not be traced were excluded.

### Recorded clinical characteristics

The following characteristics of the patients were recorded during their stay in the ICU: age, sex, personal history, comorbidities, disease severity indicated by the Acute Physiology and Chronic Health Disease Classification System II (APACHE II) score, whether they received IMV, type of medical or surgical pathology, number of days in the ICU, number of days in the hospital, number of days of analgesia and sedation, and diagnosis of delirium (yes/no). The patient's condition before admission to the ICU was recorded.

The population was divided into two groups: those who presented delirium during their stay in the ICU and

those who did not. The influence of delirium on the development of cognitive disorders was evaluated separately for the psychological and physical aspects of PICS. This study was carried out by an interdisciplinary team composed of medical psychology graduates and psychiatrists from the Department of Mental Health of Hospital Pasteur, members of the ICU of Hospital Pasteur, nursing assistants and graduates, resident physicians, and coordinators.

### **Delirium diagnosis**

We used a validated Spanish language version of the CAM-ICU [6,7] as a diagnostic tool. Delirium was diagnosed when the result obtained with the CAM-ICU was positive.

The presence of delirium was evaluated using the CAM-ICU twice a day during the morning and afternoon shifts by the corresponding nurses and/or resident physicians. Delirium during the ICU stay was defined as at least one positive result on the CAM-ICU [6,7].

### **Evaluation of the components of PICS**

We defined PICS using measures established for the evaluation of cognitive impairment, psychological disorders (depression and anxiety), and physical debilitation, as follows.

#### *Cognitive Impairment*

We used the Pfeiffer scale to assess cognitive impairment and the Mini-Mental State Examination (MMSE) to assess cognitive status.

**Pfeiffer scale:** This scale was developed specifically to detect cognitive impairment in patients older than 18. It consists of 10 questions that assess several basic functions (short- and long-term memory, attention, orientation, knowledge of everyday events, and math ability). The scores were classified as normal (0-2 errors), mild cognitive impairment (3-4 errors), moderate cognitive impairment (5-7 errors), and severe cognitive impairment (8-10 errors) [9].

**Mini-mental state examination (MMSE):** The MMSE is a practical screening instrument for detecting cognitive alterations, usually administered by a neuropsychologist or psychologist. It is composed of a set of items that measure orientation (personal, spatial, and temporal), short- and long-term memory (fixation and delayed recall), attention, language praxis (verbal and written expression, verbal and written comprehension), and visuo-constructive skills. The scores were classified as follows: normal (greater than 28 points), mild cognitive impairment (between 25 and 27 points), and severe dementia (less than 24 points) [10].

#### *Anxiety*

The Hamilton scale was used to assess anxiety [11]. The test consists of a 14-item questionnaire that assesses the symptoms and behavior presented by the patient while taking the test. The 14 items are all scored from 0 to 4. A final score  $\geq 18$  indicated a state of anxiety.

#### *Depression*

Depression was assessed using the Beck Depression Inventory II (BDI-2). It is administered in person by professional psychologists or psychiatrists. It aims to identify and measure the severity of typical symptoms of depression in adults and adolescents aged  $\geq 13$  years. The items on the BDI-2 are consistent with the criteria outlined in the Diagnostic and Statistical Manual of Mental Disorders IV (DSM-IV) for the diagnosis of depressive disorders. The test consists of 21 items with a total score ranging from 0 to 63. The results are classified as mild depression (14-19 points), moderate depression (20-28 points), or severe depression (29-63 points) [12].

#### *Physical Disability*

Physical disability was measured using the Barthel scale [13,14], which assesses basic ADLs. The Barthel scale measures a person's ability to perform 10 basic ADLs. This method provides a quantitative estimate of the individual's degree of independence in ADLs. This scale is also known as the Maryland Disability Index.

The patients were classified into five categories: total dependence (0-20 points), severe dependence (21-60 points), moderate dependence (61-90 points), low dependence (91-99 points), and independence (100 points). The patient's condition was rated before admission to the ICU using the same scale. We scored the patients by administering this questionnaire to the patient or the patient's family and/or consulting the patient's medical records.

## Interviews

Two types of interviews were carried out: An initial telephone interview and a subsequent face-to-face interview. During the initial telephone interview, we explained the goals of the post-ICU syndrome evaluation to the patients. The patients were invited to participate, and informed consent was obtained. Once the patients completed the telephone interview, they were invited to a second in-person interview.

In the telephone interview, the Pfeiffer scale was administered. To assess cognitive status, the Hamilton scale was administered to assess anxiety, and the Barthel index was used to assess independence in ADLs. In the second face-to-face interview, the other questionnaires were administered. The MMSE was used to assess cognitive impairment, and the BDI-2 was used to assess depression.

## Relationships between delirium and the different components of PICS

After the interviews were conducted, the data obtained from the different scales for each patient were correlated with the presence or absence of delirium during the ICU stay.

## Ethical considerations

The Research Ethics Committee of Hospital Pasteur, State Administration of Health Services (ASSE), Montevideo, Uruguay, approved the study (Minutes 29/006/3/696/2017/0/0). All enrolled patients signed an informed consent form.

## Statistical analysis

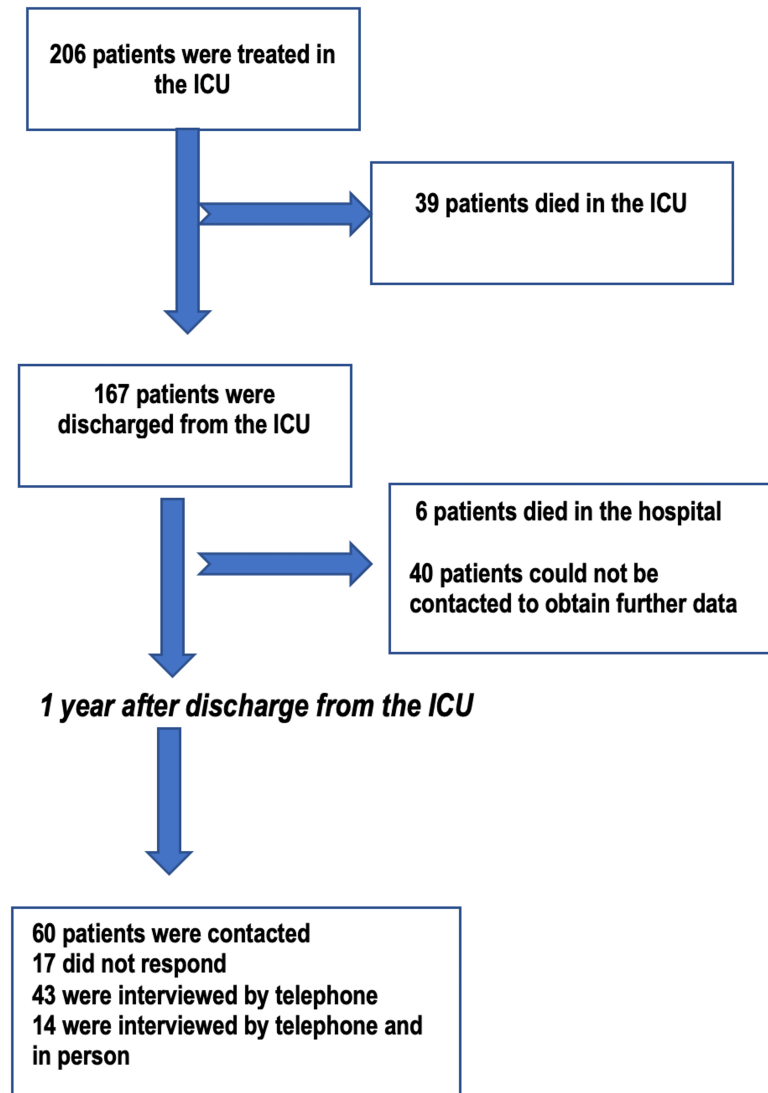
Demographic and clinical variables are summarized using descriptive statistics. Continuous variables are described as the mean and standard deviation (SD) (for normally distributed data) or the median and interquartile range (for nonnormally distributed data). The normality of the distribution for each variable was evaluated by the Kolmogorov–Smirnov test. Continuous variables were compared between the delirium and non-delirium groups by student's t-test for independent samples if the data were normally distributed and the Mann–Whitney U test otherwise. Qualitative variables were compared using the chi-squared test or Fisher's exact test.  $P < 0.05$  was considered to indicate statistical significance.

A power calculation was incorporated into the study to account for the sample size, as it was hypothesized that a small cohort could affect statistical significance. The statistical power of the analysis was determined to be 0.47, with a significance level (alpha) set at 0.05.

A non-probabilistic convenience sample was obtained. The sample size was determined by the number of patients admitted to the Pasteur ICU.

## Results

Between March 1 and May 31, 2017, 206 patients were treated in our ICU and were assessed with the CAM-ICU to diagnose delirium. Figure 1 shows the patient selection flowchart. During their stay in the ICU, 39/206 (18%) patients died, and the other 167 were discharged from the ICU, six of whom died in the hospital (Figure 1). Of the 161 patients discharged from the hospital, 43 were interviewed by phone one year after discharge from the ICU.



**FIGURE 1: Flowchart of the patient selection process**

ICU: Intensive care unit

Patients we could not contact were not interviewed by telephone or included. All 43 patients who completed the telephone interview were evaluated for PICS with the Pfeiffer, Hamilton, and Barthel scales. These same patients were invited to participate in a second, face-to-face interview in which two other scales were also used: the MMSE to assess cognitive impairment and the BDI-2 to assess depression. Fourteen patients participated in this face-to-face interview.

The 43 patients who completed the telephone interview were divided into two groups according to whether they experienced delirium in the ICU. Of these 43 patients, 15 (34%) presented with delirium in the ICU, and the other 28 (66%) did not. Table 1 shows the general characteristics of the 43 patients who completed the telephone interview and were separated into the delirium and non-delirium groups.

Variable	All Patients (n=43)	No Delirium (n=28)	Delirium (n=15)	p-value
Age, mean (SD)	55 (17)	53 (16)	58 (19)	0.30*
Male, n (%)	27 (61)	17 (61)	10 (67)	0.75***
Tobacco Use, n (%)	29 (65)	17 (61)	12 (80)	0.31***
Drug Abuse, n (%)	5 (12)	4 (14)	1 (7)	0.64***
Psychiatric Pathology, n (%)	10 (28)	5 (18)	5 (33)	0.28***
APACHE II Score, mean (SD)	15 (6)	15 (6)	24 (11)	0.003*
Mechanical Ventilation, n (%)	21 (49)	8 (29)	13 (87)	<0.001***
Pathology Medical, n (%)	28 (65)	18 (64)	10 (67)	1.00***
Pathology Surgical, n (%)	15 (35)	10 (36)	5 (33)	1.00***
In-ICU Length of Stay (days), mean (SD)	6 (5)	5 (6)	7 (4)	0.42*
In-Hospital Length of Stay (days), mean (SD)	17 (12)	16 (11)	20 (14)	0.33*
Mechanical Ventilation (days), mean (SD)	1 (2)	1 (2)	3 (3)	0.01**
Analgesia (days), mean (SD)	1 (1)	1 (1)	2 (1)	0.011**
Sedation (days), mean (SD)	1 (1)	0 (1)	1 (1)	0.003**

**TABLE 1: Baseline characteristics and clinical outcomes according to delirium status during ICU stay of the study population with PICS**

APACHE II: Acute Physiology and Chronic Health Evaluation; ICU: Intensive Care Unit; PICS: Post-intensive care unit syndrome.

Values are expressed as n (%), mean (SD: standard deviation), or median (IQR: interquartile range). \* Student's t-test for independent samples; \*\* Mann-Whitney U test for independent samples. \*\*\* Chi-squared test.

After administering these scales and correlating the results with the occurrence of delirium during the ICU stay, the Pfeiffer and MMSE scores were greater for patients who presented with delirium than for those who did not. When cognitive impairment was evaluated via the Pfeiffer scale, only the group of patients who presented with delirium during their stay in the ICU presented some degree of cognitive impairment.

While in the group of patients who did not present delirium during their ICU stay, none presented cognitive impairment (Table 2). The duration of delirium was five days for patients who developed cognitive impairment and one day for those who did not develop cognitive impairment ( $p < 0.001$ ).

Pfeiffer Classification	Total (N = 43)	No Delirium (n = 28)	Delirium (n=13)	p-value
Mild Cognitive Impairment, n (%)	3	0 (0)	3 (23)	<0.001***
Moderate Cognitive Impairment, n (%)	4	0 (0)	4 (30)	Not applicable
Normal, n (%)	35	28 (100)	6 (46)	Not applicable

**TABLE 2: Relationship between delirium during the ICU stay and cognitive impairment according to the Pfeiffer scale**

ICU: intensive care unit; CAM-ICU: Confusion assessment method for the intensive care unit

No Delirium: Patients who did not present with delirium during the ICU stay.

Delirium: Patients who presented with delirium during their stay in the ICU.

Delirium was defined as at least one positive result on the CAM-ICU during the ICU stay.

The Pfeiffer scale, which assesses cognitive impairment and consists of 10 questions, is scored as follows: normal (0-2 errors), mild cognitive impairment (3-4 errors), moderate cognitive impairment (5-7 errors), and severe cognitive impairment (8-10 errors).

\*\*\* The chi-squared test was performed on the data collected during the telephone interviews. Values are expressed as n (%). Note: One patient out of the total 43 could not be assessed. \*\*\* The chi-squared test was performed.

Among the 14 patients who completed the face-to-face interviews, six presented with delirium, and eight did not. According to the MMSE, 6/7 patients (86%) with delirium presented some degree of deterioration, compared with 1/7 patients (14%) without delirium ( $p = 0.007$ ).

We next evaluated cognitive impairment and dementia. Cognitive impairment was found in 3/6 patients (50%) who presented with delirium in the ICU, while 1/8 patients (13%) who did not present with delirium experienced cognitive impairment ( $p = 0.036$ ).

Dementia was found in 2/6 patients (33%) in the delirium group vs. 0/8 patients (0%) in the non-delirium group ( $p = 0.16$ ) (Table 3). Cognitive impairment was associated with the presence of delirium in the ICU according to both the Pfeiffer scale ( $p < 0.001$ ) and the MMSE ( $p = 0.007$ ) (see Table 4). The duration of delirium was four days in patients who developed cognitive impairment, compared to 1 day in those without cognitive impairment ( $p = 0.005$ ).

Mini Mental State Examination	All patients (n=14)	No Delirium (n=8)	Delirium (n=6)	p-value
Normal, n	8	7	1	Not applicable
Mild Cognitive Impairment, n	4	1	3	0.036***
Dementia, n	2	0	2	0.16***

**TABLE 3: Relationship between delirium during ICU stay and cognitive impairment according to the results of the MMSE performed in the face-to-face interview.**

ICU: intensive care unit; MMSE: Mini-Mental State Examination; CAM-ICU: Confusion assessment method for the intensive care unit

Notes: Values are expressed as n: number of patients. Only 14 patients could be assessed with the MMSE by face-to-face interview.

No Delirium: Patients who did not present with delirium during the ICU stay.

Delirium: Patients who presented with delirium during their stay in the ICU.

Delirium was defined as at least one positive result on the CAM-ICU during the ICU stay.

MMSE detects cognitive alterations with the following values: <24 indicates dementia; 25-27 indicates mild cognitive impairment; >28 indicates normal (no cognitive impairment). The MMSE was used only in face-to-face interviews.

\*\*\* The chi-squared test was performed on the data collected in the face-to-face interviews. Values are expressed as n: number of patients.

When depression was evaluated with the Beck Depression Inventory II (BDI-II), depression was found in 6/6 patients (100%) who experienced delirium and 8/8 patients (100%) without delirium ( $p = 0.57$ ). That is, 100% of the interviewees presented some degree of depression (Table 5).

Pfeiffer scale	All patients (n =43)	No Delirium (n =29)	Delirium (n =13)	p-value
Normal	35	29	6	Not applicable
Deterioration	7	0	7	< 0.001***
Mini-Mental State Examination	All patients (n=14)	No Delirium (n=8)	Delirium (n=6)	Not applicable
All patients	14	8	6	Not applicable
Normal	8	7	0	Not applicable
Deterioration	6	1	6	0.007***

**TABLE 4: Relationship between delirium and cognitive impairment according to the Pfeiffer scale and the MMSE.**

ICU: Intensive care unit; MMSE: Mini-Mental State Examination

Notes: Values are expressed as n: number of patients. No Delirium: Patients who did not present with delirium during the ICU stay.

Delirium: Patients who presented with delirium during their stay in the ICU were classified as having at least one positive result on the confusion assessment method for the intensive care unit (CAM-ICU) during the stay.

The Pfeiffer scale, which assesses cognitive impairment and consists of 10 questions, is scored as follows: normal (0-2 errors), mild cognitive impairment (3-4 errors), moderate cognitive impairment (5-7 errors), and severe cognitive impairment (8-10 errors). \*\*\* The chi-squared test was performed on the data collected during telephone interviews.

Values are expressed as n (%). Note: One patient out of the total 43 could not be assessed.

MMSE detects cognitive alterations with the following values: <24 indicates dementia; 25-27 indicates mild cognitive impairment; >28 indicates normal (no cognitive impairment). The MMSE was used only in face-to-face interviews. Only 14 patients could be assessed with the MMSE by face-to-face interview.

\*\*\* The chi-squared test was performed on the data collected by telephone and face-to-face interviews.

Beck Depression Inventory (BDI-2)	No Delirium (n=8)	Delirium (n=6)	p-value
Minimal depression, n (%)	3 (43)	5 (72)	0.57***
Mild depression, n (%)	2 (29)	1 (14)	Not applicable
Moderate depression, n (%)	0 (0)	0 (0)	Not applicable
Severe depression, n (%)	2 (29)	1 (14)	Not applicable

**TABLE 5: Relationships between delirium during ICU stay and results obtained with the BDI-II.**

BDI-II: Beck Depression Inventory II; ICU: Intensive care unit; CAM-ICU: Confusion assessment method for the intensive care unit

Notes: Values are expressed as n: number of patients and %. \*\*\* Chi-squared test.

No Delirium: Patients who did not present with delirium during the ICU stay.

Delirium: Patients who presented with delirium during their stay in the ICU.

Delirium was defined as at least one positive result on the CAM-ICU during the ICU stay.

The Beck Depression Inventory II (BDI-II) assesses depression. This scale was applied in a face-to-face interview. It consists of 21 items, with scores ranging from 0 to 63. The results are classified as mild depression (14 to 19 points), moderate depression (20 to 28 points) or severe depression (29-63 points). This instrument was used only in face-to-face interviews (14 patients).

The results obtained with the Barthel scale to assess ADLs showed the following: dependence in completing ADLs in 5/14 patients (33%) with delirium vs. 9/28 patients (32%) without delirium, but the differences were not statistically significant (p = 0.23) (Table 6).

Pre-ICU Barthel classification (n=43)	No Delirium (n=28)	Delirium (n=15)	p-value
Low dependence, n (%)	3 (11)	1 (7)	0.78 ***
Moderate dependence, n (%)	1 (4)	0 (0)	Not applicable
Severe dependence, n(%)	1 (4)	2 (13)	Not applicable
Total dependence, n (%)	0 (0)	0 (0)	Not applicable
Independence, n (%)	23 (82)	12 (80)	Not applicable
Post-ICU Barthel classification (n=43)			Not applicable
Low dependence, n (%)	5 (18)	1 (7)	0.23 ***
Moderate dependence, n (%) 2(7)	2 (7)	2 (13)	Not applicable
Severe dependence, n (%)	2 (7)	0 (0)	Not applicable
Total dependence, n (%)	0 (0)	2 (13)	Not applicable
Independence, n (%)	19 (68)	10 (67)	Not applicable

**TABLE 6: Relationships between delirium during ICU stay and the pre- and post-ICU results obtained with the Barthel scales.**

ICU: Intensive care unit; CAM-ICU: Confusion assessment method for the intensive care unit

Notes: Values are expressed as n: number of patients and %. \*\*\* Chi-squared test.

No Delirium: Patients who did not present with delirium during the ICU stay. ICU: intensive care unit

Delirium: Patients who presented with delirium during their stay in the ICU.

Delirium was defined as at least one positive result on the CAM-ICU during the ICU stay.

The Barthel scale assesses basic activities of daily living, and patients are classified into 5 categories: total dependence (0-20 points), severe dependence (21-60 points), moderate dependence (61-90 points), low dependence (91-99 points) and independence (100 points). Pre-ICU data were collected before admission to the ICU, and post-ICU data were collected 1 year after discharge from the ICU. This survey was carried out by telephone.

The results obtained with the Hamilton scale revealed anxiety in 9/28 patients (30%) who reported delirium vs. 19/28 patients (67%) without delirium, but the differences were not statistically significant ( $p = 1.0$ ) (Table 7). Table 7 also shows the relationships between delirium and all aspects of the post-ICU syndrome: cognitive impairment (MMSE and the Pfeiffer scale), depression (BDI-2), anxiety (Hamilton scale), and ADL dependence (Barthel scale).

Scale	Scale outcome	No Delirium	Delirium	p-value
Scale	Outcome	No	Yes	Not applicable
Pfeiffer scale	Normal	28 (100%)	10 (71%)	<0.001***
Pfeiffer scale	Deterioration	0 (0%)	4 (29%)	Not applicable
MMSE	Normal	7 (87%)	1 (17%)	0.007***
MMSE	Deterioration	1 (13%)	5 (83%)	Not applicable
BDI-2	Normal	0 (0%)	0 (0%)	1.0***
BDI-2	Deterioration	8 (100%)	6 (100%)	Not applicable
Hamilton scale	Normal	8 (30%)	3 (25%)	1.0***
Hamilton scale	Deterioration	19 (30%)	9 (75%)	Not applicable
Pre-ICU Barthel scale	Normal	23 (82%)	12 (80%)	1.0***
Pre-ICU Barthel scale	Deterioration	5 (18%)	3 (20%)	Not applicable
Post-ICU Barthel scale	Normal	19 (68%)	10 (67%)	1.0***
Post-ICU Barthel scale	Deterioration	9 (32%)	5 (33%)	Not applicable

**TABLE 7: Relationships between delirium and all aspects of post-ICU syndrome: cognitive impairment (MMSE and Pfeiffer scale), depression (BDI-2), anxiety (Hamilton scale) and dependence in activities of daily living (ADLs): (Barthel scale).**

MMSE: Mini-Mental State Examination; ICU: Intensive care unit; BDI-II: Beck Depression Inventory II; ADLs: Activities of daily living

Notes: Values are expressed as n: number of patients and %. \*\*\* Chi-squared test.

No Delirium: Patients who did not present with delirium during the ICU stay.

Delirium: Patients who presented with delirium during their stay in the ICU. Delirium was defined as at least one positive result on the CAM-ICU during the ICU stay.

The Barthel scale assesses basic activities of daily living, and patients are classified into 5 categories: total dependence (0-20 points), severe dependence (21-60 points), moderate dependence (61-90 points), low dependence (91-99 points) and independence (100 points).

Pre-ICU data were collected before admission to the ICU, and post-ICU data were collected one year after discharge from the ICU. This survey was carried out by telephone.

The Pfeiffer scale consists of 10 questions, which are classified according to the following errors: normal (0-2 errors), mild cognitive impairment (3-4 errors), moderate cognitive impairment (5-7 errors), and severe cognitive impairment (8-10 errors). This survey was carried out by telephone.

The BDI-II assesses depression. The test consists of 21 items, with scores ranging from 0 to 63. The results are classified as mild depression (14 to 19 points), moderate depression (20 to 28 points), or severe depression (29-63 points). This instrument was used only in face-to-face interviews.

MMSE detects cognitive alterations as follows: <24, dementia; 25-27, mild cognitive impairment; and > 28, normal cognition. This instrument was used only in face-to-face interviews. The Hamilton scale is used to evaluate anxiety, and it consists of a questionnaire with 14 items referring to the symptoms.

## Discussion

No published studies have examined the epidemiology of PICS in relation to delirium in the ICU in Uruguay [15]. In our study, all patients evaluated one year after discharge from the ICU presented at least some symptoms of PICS. Cognitive impairment (according to both the Pfeiffer scale and the MMSE) was associated with delirium when the scales were administered by telephone as well as in person.

Ely W. and Pandharipande (2013) [2,4] published a study of brain function in the ICU and showed that the deterioration of cognition after an ICU stay was associated with delirium for patients in all age ranges, and the severity of the deterioration was comparable to that of patients suffering a moderate traumatic injury and/or mild Alzheimer's disease [2].

One-third of the patients in our population who presented with delirium suffered cognitive impairment one

year after an ICU stay, in line with the above study, in which delirium and its duration were both risk factors for worse overall cognitive function at 3 and 12 months post-ICU admission [2].

Brummel and Jackson [16] also reported an association between the duration of delirium and cognitive alterations one year after discharge from the ICU in patients who required mechanical ventilation [1,2]. Our work observed an altered cognitive state in 50% of patients. The predisposing factors for cognitive decline after ICU discharge in ventilated patients include age, previous cognitive status, and delirium.

We found a relationship between delirium in the ICU and long-term cognitive impairment, as demonstrated by both the Pfeiffer scale and the MMSE. With the latter, cognitive impairment was detected in one-third of patients who had delirium.

Other authors, such as Girard, Ditus, and Ely, have also described the relationships between different cognitive aspects of PICS. They argue that the observed cognitive deterioration is due to brain injury, which can vary in severity and usually affects different domains of cognition, with delirium being one of the most important risk factors [17].

In a systematic review of potentially modifiable risk factors for cognitive impairment among critically ill individuals, Sakusic et al. [18] found that 6 out of 9 included studies reported associations of delirium and its duration with long-term cognitive impairment after an ICU stay. They found no relationship between mechanical ventilation, sedation, hypoxia, or other factors with cognitive impairment.

The strong association between delirium in the ICU and long-term cognitive impairment that has been demonstrated in multiple published studies is in line with the results of our work [19-21]. The cognitive impairment observed in this study can be contextualized within the findings of other multicenter trials, including the long-term cognitive impairment after critical illness (P.P. Pandharipande et al. [2]) study. In this study, 34% of patients with delirium exhibited cognitive impairment at 12 months following assessment, which is comparable to mild Alzheimer's disease.

The implementation of delirium prevention strategies may prove effective in reducing the incidence of delirium and associated adverse outcomes, such as cognitive decline. Consequently, delirium may be regarded as a modifiable risk factor for dementia, and interventions that prevent and minimize delirium may also reduce or prevent long-term cognitive impairment [21].

Regarding the psychological aspects of PICS, depression was found in all patients, regardless of whether they presented with delirium. Previous studies have shown that at least one-third of patients in the general ICU population experience mental health problems within one year after discharge [22]. In 2021, Andrews et al. [23] published a study on delirium, depression, and long-term cognition, with assessments performed using the BDI-2, and they reported that a history of depression before admission to the ICU was associated with greater severity of depressive symptoms one year after discharge from the ICU. One weakness of our work is that we did not have data on the history of depression in the patients included in this study [23]. However, Andrews et al. found no association between a personal history of depression and cognitive disorders at 12 months after discharge.

Nordnees et al. [24] reported a relationship between depression and long-term cognitive decline in ICU survivors. All our patients presented with some symptoms of depression upon discharge from the ICU, although there are other factors related to delirium that may influence the development of depression after an ICU stay [24].

Notably, we did not link depression with cognitive impairment since 100% of the patients presented with depression. Another weakness of our study was that a diagnosis of depression was made for only the 14 patients who completed the face-to-face interviews; therefore, the sample size was small. Additional studies on this topic that include more patients are needed.

In a study of 821 patients, Jackson et al. reported the occurrence of depression in 33% of the patients at 12 months post-discharge from the ICU [25]. They also observed that depression was 5 times more common than traumatic panic disorder after critical illness and was driven by somatic symptoms rather than cognitive-affective symptoms, which suggests that it may be related to PICS, among other causes [26].

Anxiety was found in 30% of the patients who presented with delirium and 67% of those who did not. Consistent with other studies, anxiety occurred in a high percentage of patients upon discharge from the ICU. No relationship was found between anxiety and delirium. Previous publications have shown that those who experience delirium in the ICU have a greater risk of developing cognitive impairment and psychiatric problems, such as depression and anxiety, after discharge.

Mikkelsen et al. reported that delirium was associated with cognitive impairment and anxiety in long-term ICU survivors [26]. We found a possible association between delirium in the ICU and long-term depression

and anxiety, given that most of the patients who presented with delirium in our study developed long-term cognitive impairment, as mentioned above. It is likely that the cognitive state of these patients prevented them from providing adequate responses to the questions about anxiety and depression.

Regarding physical disability, 33% of both delirium patients and non-delirious patients had some degree of disability related to ADLs 12 months after discharge from the ICU. These findings are consistent with the findings of a study by Jackson et al. [25], who also reported that disability related to physical ADLs was present in 32% of individuals at 12 months after an ICU stay.

Different tools have been proposed to improve PICS, such as the use of delirium prevention bundles through the application of non-pharmacological interventions, which are summarized in the ABCDEF bundle [27,28].

The ABCDEF bundle expresses a research-supported framework designed to guide healthcare providers in implementing organizational adjustments with the objective of enhancing the recovery and outcomes of ICU patients. It encompasses a range of components, including A: Assessment Prevention and Management Pain; B: Both Spontaneous Awakening trials and spontaneous breathing trials; C: Choice of Analgesia and Sedation; D: Delirium Assessment, Prevention, and Management; E: Early Mobility and Exercise; and F: Family Engagement and Empowerment [27,28]. Additionally, another prevention tool is the use of diaries by relatives of patients and/or patients who are able to describe their experience and day-to-day situations while they are in the ICU; the patient and the family can use such diaries to understand what happened to them and can serve as a tool to aid recovery [29]. On the other hand, the occurrence of ICU delirium has implications that extend beyond the patient's outcome; it also affects the family. This condition is associated with a series of psychological issues that fall under the phenomenon known as the family variant of PICS (PICS-F). The prospective study conducted by Kotfis et al. indicates that family members of patients with delirium in the ICU experience a notable increase in symptoms of anxiety, depression, and post-traumatic stress disorder (PTSD) compared to family members of patients who do not experience delirium [30].

### Limitations of the study

The present study is limited in the following ways: 1) Sample size: The study included a total of 43 patients, which represents a relatively small sample size. This may limit the generalizability of the findings to a larger or more diverse population. 2) Duration of follow-up: Although patients were followed for one year, this duration may prove insufficient to fully capture the long-term effects of PICS. Furthermore, changes occurring after this period were not evaluated. 3) Single-center study: Given that the study is being conducted at a single hospital center, the results may be influenced by clinical practices and demographic characteristics specific to that institution. This limits the extrapolation of results to other settings or populations where different treatment protocols may be used. 4) Logistic regression tests were performed in this study, and no significant values were obtained; this can be considered a study limitation. This may be due to several factors, such as sample size, variability in the data, or the choice of variables included in the model. It is important to mention that this result does not imply that there are no relationships between the variables but that further research may be necessary to obtain a clearer understanding. Future studies may be proposed to address these limitations.

### Conclusions

Cognitive impairment was associated with the occurrence and duration of delirium in the ICU. Although dependence in performing ADLs was more common in the delirium group, the difference was not significant, nor were the differences in the rates of anxiety and depression after the ICU stay. The most important risk factor that health professionals can influence to prevent cognitive dysfunction after an ICU stay is the occurrence of delirium during the ICU stay. Early identification, monitoring, and the application of multiple measures should be performed in a standardized way to reduce the incidence and shorten the duration of delirium, thereby preventing long-term cognitive impairment in survivors of critical illness.

### Appendices

**APPENDIX 1**  
**TELEPHONE QUESTIONNAIRE CARRIED OUT DURING TELEPHONE INTERVIEWS.**  
MONTEVIDEO  
PASTEUR HOSPITAL  
INTENSIVE CARE UNIT (ICU)  
TELEPHONE QUESTIONNAIRE

- 1- With whom do you live? Alone \_\_\_ Accompanied \_\_\_
- 2- Do you walk? Yes \_\_\_ No \_\_\_
- 3- Do you eat alone? Yes \_\_\_ No \_\_\_ with help \_\_\_
- 4- Have you resumed your daily activities? Yes \_\_\_ No \_\_\_ Which?  
Work \_\_\_ Leisure \_\_\_ Study \_\_\_ Sports \_\_\_
- 5- Have you had any consequences or after-effects from your stay in the ICU? Yes \_\_\_ No \_\_\_
- 6- How many hours of sleep do you get? \_\_\_
- 7- Do you need medication to help you sleep since your stay in the ICU? Yes \_\_\_ No \_\_\_ Which ones? \_\_\_\_\_
- 8- Do you have any pain? Yes \_\_\_ No \_\_\_
- 9- Have you had any follow-up examinations after your discharge from the Pasteur Hospital?

**APPENDIX 2**  
**DOCUMENT 2 INFORMED CONSENT: PATIENT INFORMATION.**

Patients were invited to a face-to-face interview and given an informed consent form explaining what the work involved and whether they agreed to take part.

**PROJECT: POST-INTENSIVE CARE UNIT SYNDROME.**

Thanks to scientific and technical advances, intensive care units (ICUs) are achieving higher and higher survival rates. However, attention to emotional health in the ICU and post-ICU care is becoming increasingly necessary.

A high percentage of patients may experience physical symptoms after ICU admission: such as pain, difficulty moving, weakness, sleep disturbance; symptoms of cognitive impairment: such as memory or concentration problems; and/or anxiety, depression or post-traumatic stress syndrome.

This is the post-ICU syndrome which, according to previous studies, can lead to a large percentage of patients being unable to reintegrate into society, return to work, study or their usual activities after discharge, and therefore needing help in many cases.

The aim of this study is to follow up all patients admitted to the Intensive Care Unit of the Pasteur Hospital between 1 March and 31 May 2015. To detect the presence of this syndrome.

They will be invited to an interview where they will be given a mini-test and a questionnaire to assess their general condition.

The interview will take between 20 and 30 minutes.

The information provided is confidential and will only be used by members of the research team for this or future studies.

**INFORMED CONSENT**

I have taken the time to read and understand the information given to me. The information is clear and all my questions have been answered to my satisfaction. I freely and voluntarily consent to the use of the data I have provided for this and future research studies.

I have received no payment for my participation in this study.

Patient's signature: \_\_\_\_\_  
 Clarification: \_\_\_\_\_  
 Date: \_\_\_\_\_

Signature of witness: \_\_\_\_\_  
 Clarification and relationship: \_\_\_\_\_  
 Date: \_\_\_\_\_

Investigator's signature: \_\_\_\_\_  
 Clarification: \_\_\_\_\_  
 Date: \_\_\_\_\_

**FIGURE 2: Telephone questionnaire and informed consent**

**PFEIFFER QUESTIONNAIRE (SPMSQ)**

1. What is today's date? (1)
2. What day of the week?
3. Where are we? (2)
4. What is your phone number? (If you don't have a telephone, what is your full address?)
5. How old are you?
6. Where were you born?
7. What is the president's name?
8. What is the name of the previous president?
9. What is your mother's maiden name?
10. Subtract by threes from 29 (3)

(1) Day, month and year  
 (2) Any correct description of the place is valid (3) Any error makes the answer wrong.

• It is one of the most used scales, especially in Primary Care, due to its brevity and ease of execution. Its administration is quick, since it only requires about five minutes. • Target population: It can be administered to anyone who requires an evaluation of their mental capacity. • Main limitation: It does not detect slight deteriorations or small changes in the evolution. A correction is introduced according to the level of schooling, allowing one more error if they have not received primary education and one less error if they have received higher education. • If the evaluations are extreme, no doubts arise. Intermediate scores are doubtful and require confirmation. • In the case of hospitalized patients, this evaluation must be carried out in the first 72 hours after the patient's admission and discharge. • It has a sensitivity close to 70% and a very high specificity (95%).


• For its interpretation, the following stratification is used. They score errors, 1 point per error. • 0-2 errors: normal • 3-4 errors: slight cognitive impairment • 5-7 errors: moderate cognitive impairment, pathological • 8-10 errors: significant cognitive deterioration 1 more error is allowed if you have not received primary education.

The Pfeiffer scale was extracted from the following reference:

De la Iglesia, J. M., Dueñas Herero, R.M., Onís Vilches, M. C. : *Adaptación y validación al castellano del cuestionario de Pfeiffer (SPMSQ) para detectar la existencia de deterioro cognitivo en personas mayores a 65 años. Medicina clínica, 117, Elsevier (ed): Medicina clínica, 2001. 10.1186/S0025-7753(01)72040-4* Se permite 1 error de menos si ha recibido estudios superiores

**FIGURE 3: Pfeiffer Questionnaire**

**MINI-MENTAL STATE EXAMINATION (MMSE)**

Maximum Score	Question	Orientation
5	1	What is the year (season) (date) (day) (month)?
5	1	Where are we (state) (county) (town) (hospital) (floor)?
<b>Registration</b>		
3	1	Name 3 objects: 1 second to say each. Then ask the patient if 3 after you have said them. Give 1 point for each correct answer. Then repeat them until he/she learns all 3. Count trials and record. Trials: _____
<b>Attention and Calculation</b>		
5	1	Serial 7's: 1 point for each correct answer. Stop after 5 answers. Alternatively spell "world" backward.
<b>Recall</b>		
3	1	Ask for the 3 objects repeated above. Give 1 point for each correct answer.
<b>Language</b>		
2	1	Name a pencil and watch.
1	1	Repeat the following "No ifs, ands, or buts!"
1	1	Follow a 3-stage command: "Take a paper in your hand, fold it in half, and put it on the floor."
1	1	Read and obey the following: <b>CLOSE YOUR EYES</b>
1	1	Write a sentence.
1	1	Copy the design shown.
		
<b>Total Score</b> ASSESS level of consciousness along a continuum _____ Alert                  Drowsy                  Stupor                  Coma		

The MMSE is a practical screening instrument for detecting cognitive alterations, and it is usually administered by a neuropsychologist or psychologist. It is composed of a set of items that measure orientation (personal, spatial and temporal), short- and long-term memory (fluent and delayed recall), attention, language (verbal and written expression, verbal and written comprehension), and visuo-constructive skills.

The scores were classified as follows: normal (greater than 28 points), mild cognitive impairment (between 25 and 27 points), and severe dementia (less than 24 points).

Age and educational level are two of the parameters that most influence the results of the mini-mental test. Thus, these are the scores that denote correct cognitive functions in the tests according to age and educational level:

Basic or primary education.	Intermediate education
- Age between 18 to 69: average score 22-25. - Age between 70 to 79: average score 21-22. - Age over 79: mean score 19-20.	- Age between 18 and 69: average score 26-27. - Age 70 to 79: mean score 25. - Age over 79: average score 23-25.
Higher education	University education
- Age between 18 and 69: average score 28-29. - Age 70-79: mean score 27. - Age over 79: mean score 25-26.	- Age between 18 and 69: average score 29. - Age 70-79: mean score 28. - Age over 79: mean score 27.

**FIGURE 4: Mini-Mental State Examination (MMSE)**

[10]

**Depression**

Depression was assessed using the Beck Depression Inventory II (BDI-II). It is administered in person by professional psychologists or psychiatrists. It aims to identify and measure the severity of typical symptoms of depression in adults and adolescents aged 13 years. The items on the BDI-2 are consistent with the criteria outlined in the Diagnostic and Statistical Manual of Mental Disorders IV (DSM-IV) for the diagnosis of depressive disorders. The test consists of 21 items with a total score ranging from 0 to 63. The results are classified as mild depression (14-19 points), moderate depression (20-28 points), or severe depression (29-63 points).

**BDI - II**

Instructions: This questionnaire consists of a group of statements. Please read each group of statements carefully, and then pick out the one statement in each group that best describes the way you have been feeling during the past two weeks, including today. Circle the number beside the statement you have picked. If several statements in the group seem to apply equally well, circle the number for the group. Be sure that you do not choose more than one statement in any group, including Item 8 (Changes in Sleeping Pattern) or Item 10 (Changes in Appetite).

- |  |  |   |   |
|--|--|---|---|
| <p><b>1. Sadness</b></p> <ol style="list-style-type: none"> <li>I do not feel sad.</li> <li>I feel sad much of the time.</li> <li>I am sad all the time.</li> <li>I am so sad or unhappy that I can't stand it.</li> </ol> <p><b>2. Frustration</b></p> <ol style="list-style-type: none"> <li>I am not discouraged about my future.</li> <li>I feel more discouraged about my future than I used to.</li> <li>I do not expect things to work out for me.</li> <li>I feel my future is hopeless and will only get worse.</li> </ol> <p><b>3. Fear failure</b></p> <ol style="list-style-type: none"> <li>I do not feel like a failure.</li> <li>All I look back on is a list of failures.</li> <li>I feel I am a total failure as a person.</li> </ol> <p><b>4. Loss of Pleasure</b></p> <ol style="list-style-type: none"> <li>I get a much pleasure as I ever did from the things I enjoy.</li> <li>I get very little pleasure from the things I used to enjoy.</li> <li>I can't get any pleasure from the things I used to enjoy.</li> </ol> <p><b>5. Guilty Feelings</b></p> <ol style="list-style-type: none"> <li>I don't feel particularly guilty.</li> <li>I feel guilty over many things I have done or should have done.</li> <li>I feel guilty guilty most of the time.</li> <li>I feel guilty all of the time.</li> </ol> <p><b>6. Punishment feelings</b></p> <ol style="list-style-type: none"> <li>I don't feel I am being punished.</li> <li>I feel I may be punished.</li> <li>I expect to be punished.</li> <li>I feel I am being punished.</li> </ol> <p><b>7. Self-blame</b></p> <ol style="list-style-type: none"> <li>I feel the same about myself as ever.</li> <li>I have lost confidence in myself.</li> <li>I am disappointed in myself.</li> <li>I dislike myself.</li> </ol> | <p><b>8. Self-Criticism</b></p> <ol style="list-style-type: none"> <li>I don't criticize or blame myself more than usual.</li> <li>I am more critical of myself than I used to be.</li> <li>I criticize myself for all of my faults.</li> <li>I blame myself for everything but that happens.</li> </ol> <p><b>9. Suicidal Thoughts or Wishes</b></p> <ol style="list-style-type: none"> <li>I don't have any thoughts of killing myself.</li> <li>I have thoughts of killing myself, but I would not carry them out.</li> <li>I would like to kill myself.</li> <li>I would kill myself if I had the chance.</li> </ol> <p><b>10. Crying</b></p> <ol style="list-style-type: none"> <li>I don't cry anyone than I used to.</li> <li>I cry more than I used to.</li> <li>I cry over every little thing.</li> <li>I feel like crying, but I can't.</li> </ol> <p><b>11. Agitation</b></p> <ol style="list-style-type: none"> <li>I am no more restless or wound up than usual.</li> <li>I feel more restless or wound up than usual.</li> <li>I am so restless or agitated, it's hard to stay still.</li> <li>I am so restless or agitated that I have to keep moving or doing something.</li> </ol> <p><b>12. Loss of interest</b></p> <ol style="list-style-type: none"> <li>I have not lost interest in other people or activities.</li> <li>I am less interested in other people or things than before.</li> <li>I have lost most of my interest in other people or things.</li> <li>It's hard to get interested in anything.</li> </ol> <p><b>13. Indecisiveness</b></p> <ol style="list-style-type: none"> <li>I make decisions about as well as ever.</li> <li>I find it more difficult to make decisions than usual.</li> <li>I have much greater difficulty in making decisions than I used to.</li> <li>I have trouble making any decisions.</li> </ol> | <p><b>14. Worthlessness</b></p> <ol style="list-style-type: none"> <li>I do not feel I am worthless.</li> <li>I don't consider myself as worthwhile and useful as I used to.</li> <li>I feel more worthless as compared to others.</li> <li>I feel utterly worthless.</li> </ol> <p><b>15. Less of energy</b></p> <ol style="list-style-type: none"> <li>I have as much energy as ever.</li> <li>I have less energy than I used to have.</li> <li>I don't have enough energy to do very much.</li> <li>I don't have enough energy to do anything.</li> </ol> <p><b>16. Changes in Sleeping Pattern</b></p> <ol style="list-style-type: none"> <li>I have not experienced any change in my sleeping.</li> <li>I sleep somewhat more than usual.</li> <li>I sleep somewhat less than usual.</li> <li>I sleep a lot more than usual.</li> <li>I sleep a lot less than usual.</li> <li>I sleep most of the day.</li> <li>I wake up 1/2 hours early and can't get back to sleep.</li> </ol> <p><b>17. Irritability</b></p> <ol style="list-style-type: none"> <li>I am not more irritable than usual.</li> <li>I am more irritable than usual.</li> <li>I am much more irritable than usual.</li> <li>I am irritable all the time.</li> </ol> <p><b>18. Changes in Appetite</b></p> <ol style="list-style-type: none"> <li>I have not experienced any change in my appetite.</li> <li>My appetite is somewhat less than usual.</li> <li>My appetite is somewhat greater than usual.</li> <li>My appetite is much less than before.</li> <li>My appetite is much greater than usual.</li> <li>I have no appetite at all.</li> <li>I crave food all the time.</li> </ol> | <p><b>19. Concentration Difficulty</b></p> <ol style="list-style-type: none"> <li>I can concentrate as well as ever.</li> <li>I can't concentrate as well as usual.</li> <li>It's hard to keep my mind on anything for very long.</li> <li>I find I can't concentrate on anything.</li> </ol> <p><b>20. Tiredness or Fatigue</b></p> <ol style="list-style-type: none"> <li>I am no more tired or fatigued than usual.</li> <li>I get more tired or fatigued more easily than usual.</li> <li>I am too tired or fatigued to do a lot of the things I used to do.</li> <li>I am too tired or fatigued to do most of the things I used to do.</li> </ol> <p><b>21. Loss of interest in sex</b></p> <ol style="list-style-type: none"> <li>I have not noticed any recent change in my interest in sex.</li> <li>I am less interested in sex than I used to be.</li> <li>I am much less interested in sex now.</li> <li>I have lost interest in sex completely.</li> </ol> <p style="text-align: right;">Total Score: _____</p> |
|--|--|---|---|

**FIGURE 5: Beck Depression Inventory (BDI-II)**

[12]

**HAMILTON SCALE THAT ASSESSES ANXIETY.**

The test consists of a questionnaire consisting of 14 items referring to the symptoms presented by the patient and the patient's behavior while performing the questionnaire. Each of the 14 items represents a group of symptoms rated from zero to four, with four being the highest score. The final score will define the severity of the patient's anxiety state.

Within the questionnaire we find questions about anxious signs and symptoms that help to assess the patient's condition. Each of the questions considers not only the intensity of the symptoms, but also the frequency with which they occur. The interview should be conducted in a maximum of 30 minutes and the last question, referring to the patient's behavior in the interview, is one of the most important keys that will define the state of tension of the interviewee. If the patient scores more than 18, he/she is suffering from an anxiety disorder.

**Hamilton Anxiety Scale**

Patient's name: \_\_\_\_\_  
Date of evaluation \_\_\_\_\_ Clinical record: \_\_\_\_\_

Hamilton Anxiety Rating Scale (HAM-A)				
Below is a list of phrases that describe certain feelings that people have. Rate the patient by finding the answer which best describes the answer to which he/she has these conditions. Select one of the five responses for each of the fourteen questions.				
0 = Not present, 1 = Mild, 2 = Moderate, 3 = Severe, 4 = Very severe.				
1 <b>Anxious mood</b> <input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4	8 <b>Somatic (sensory)</b> <input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4			
Worries, anticipation of the worst, fearful anticipation, irritability.	Tinnitus, blurring of vision, hot and cold flashes, feelings of weakness, grinding sensation.			
2 <b>Tension</b> <input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4	9 <b>Cardiovascular symptoms</b> <input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4			
Feelings of tension, palpability, cardiac reactions, speed of heart easy, trembling, feelings of restlessness, inability to relax.	Tachycardia, palpitation, pain in chest, throbbing of vessels, beating heart, missing beat.			
3 <b>Fears</b> <input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4	10 <b>Respiratory symptoms</b> <input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4			
Of dark, of strangers, of being left alone, of animals, of traffic, of crowds.	Pressure or constriction in chest, choking feelings, sighing, dyspnea.			
4 <b>Insomnia</b> <input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4	11 <b>Gastrointestinal symptoms</b> <input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4			
Difficulty in falling asleep, broken sleep, awakening sleep and fatigue on waking, dreams, nightmares, night terrors.	Difficulty in swallowing, acid indigestion, burning sensation, abdominal fullness, nausea, vomiting, hiccups, looseness of bowels, loss of weight, constipation.			
5 <b>Intellectual</b> <input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4	12 <b>Genitourinary symptoms</b> <input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4			
Difficulty in concentration, poor memory.	Frequency of micturition, urgency of micturition, incontinence, menorrhagia, development of leucopy, premature ejaculation, loss of libido, impotence.			
6 <b>Depressed mood</b> <input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4	13 <b>Autonomic symptoms</b> <input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4			
Loss of interest, lack of pleasure in hobbies, depression, early waking, diurnal swing.	Dry mouth, feeling of heat, tendency to sweat, coldness, tension headache, raising of hair.			
7 <b>Somatic (muscular)</b> <input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4	14 <b>Behavior as interview</b> <input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4			
Pains and aches, twitching, stiffness, myoclonic jerks, grinding of teeth, unsteady voice, increased muscular tone.	Fidgeting, restlessness or pacing, tremor of hands, frowning brows, strained face, sighing or rapid respiration, facial pallor, sweating, ...			

The Hamilton scale was extracted from the following reference:

Antonio Lobo, Lorenzo Chamorro, Antonio Luque, Rafael Del-Ré, Xavier Badia, Eva Baró, Validación de las versiones en español de la Montgomery-Asberg Depression Rating Scale y la Hamilton Anxiety Rating Scale para la evaluación de la depresión y de la ansiedad. *Medicina Clínica*, Volume 118, Issue 13, 2002, Pages 493-499, ISSN 0025-7753, [https://doi.org/10.1016/S0025-7753\(02\)72429-9](https://doi.org/10.1016/S0025-7753(02)72429-9) (<https://www.sciencedirect.com/science/article/pii/S0025775302724299>)

**FIGURE 6: Hamilton Scale**

[11]

#### BARTHEL SCALE

Physical disability was measured using the Barthel scale, which assesses basic activities of daily living (ADLs). The Barthel scale measures the ability of a person to perform 10 basic ADLs. In this way, a quantitative estimate of the individual's degree of independence in ADLs is obtained. This scale is also known as the Maryland Disability Index. The patients were classified into five categories: total dependence (0-20 points), severe dependence (21-60 points), moderate dependence (61-90 points), low dependence (91-99 points), and independence (100 points). The condition of the patients was ascertained before admission to the ICU using the same scale. We scored the patients by administering this questionnaire to the patient or the patient's family and/or consulting the patient's medical records.

<b>FEEDING</b>
0 = unable
5 = needs help cutting, spreading butter, etc., or requires modified diet
10 = independent
<b>BATHING</b>
0 = dependent
5 = independent (or in shower)
<b>GROOMING</b>
0 = needs to help with personal care
5 = independent face/hair/teeth/shaving (implements provided)
<b>DRESSING</b>
0 = dependent
5 = needs help but can do about half unaided
10 = independent (including buttons, zips, laces, etc.)
<b>BOWELS</b>
0 = incontinent (or needs to be given enemas)
5 = occasional accident
10 = continent
<b>BLADDER</b>
0 = incontinent, or catheterized and unable to manage alone
5 = occasional accident
10 = continent
<b>TOILET USE</b>
0 = dependent
5 = needs some help, but can do something alone
10 = independent (on and off, dressing, wiping)
<b>TRANSFERS (BED TO CHAIR AND BACK)</b>
0 = unable, no sitting balance
5 = major help (one or two people, physical), can sit
10 = minor help (verbal or physical)
15 = independent
<b>MOBILITY (ON LEVEL SURFACES)</b>
0 = immobile or < 50 yards
5 = wheelchair independent, including corners, > 50 yards
10 = walks with help of one person (verbal or physical) > 50 yards
15 = independent (but may use any aid; for example, stick) > 50 yards
<b>STAIRS</b>
0 = unable
5 = needs help (verbal, physical, carrying aid)

**FIGURE 7: Barthel Scale**

[14]

## Additional Information

### Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

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### Disclosures

**Human subjects:** Consent for treatment and open access publication was obtained or waived by all participants in this study. Pasteur Hospital issued approval Minutes 29/006/3/696/2017/0/0. The Research Ethics Committee of Hospital Pasteur, State Administration of Health Services (ASSE), Montevideo, Uruguay, approved the study (Minutes 29/006/3/696/2017/0/0). All enrolled patients signed an informed consent form. **Animal subjects:** All authors have confirmed that this study did not involve animal subjects

or tissue. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

## Acknowledgements

We thank the entire health team of the ICU of Hospital Pasteur for their support and dedication, without which this study could not have been carried out. We would like to express our sincere thanks to the following nurses: Claudia Peretti, Tina Cugliari, José da Luz, Lourdes Pereira, and Sonia Altez. The contribution and dedication they demonstrated in setting up and registering the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU), as well as in the daily execution of the cerebral pathway for all ICU patients at the Pasteur Hospital, was invaluable. We would also like to thank our heads of service, Dr Ana Soca and Dr Julio Pontet, for their continuous support and supervision of our work. Their leadership and guidance have been fundamental to the success of this project. Mariana Marra is also to be thanked for her participation and help with tables and design. We want to thank Engineer Rafael Alonso, Associate Professor of Quantitative Methods in the Faculty of Medicine of the University of the Oriental Republic of Uruguay, for his essential collaboration in carrying out the statistical analyses.

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