

This provisional PDF corresponds to the article as it appeared upon acceptance.

A copyedited and fully formatted version will be made available soon.

The final version may contain major or minor changes.

---

## **Neurological assessment with validated tools in general ICU: multicenter, randomized, before and after, pragmatic study to evaluate the effectiveness of an e-learning platform for continuous medical education.**

Giovanni MISTRALETTI, Michele UMBRELLO, Stefania ANANIA, Elisa ANDRIGHI, Alessandra DI CARLO, Federica MARTINETTI, Serena BARELLO, Giovanni SABBATINI, Paolo FORMENTI, Tommaso MARAFFI, Francesco MARRAZZO, Alessandra PALO, Giacomo BELLANI, Riccarda RUSSO, Silvia FRANCESCONI, Federico VALDAMBRINI, Marco CIGADA, Francesca RICCARDI, Egidio Aldo MOJA, Gaetano IAPICHINO for the SedalCU investigators.

Minerva Anesthesiol 2016 Sep 20 [Epub ahead of print]

### ***MINERVA ANESTESIOLOGICA***

Rivista di Anestesia, Rianimazione, Terapia Antalgica e Terapia Intensiva

pISSN 0375-9393 - eISSN 1827-1596

Article type: Original Paper

The online version of this article is located at <http://www.minervamedica.it>

---

Subscription: Information about subscribing to Minerva Medica journals is online at:

<http://www.minervamedica.it/en/how-to-order-journals.php>

Reprints and permissions: For information about reprints and permissions send an email to:

[journals.dept@minervamedica.it](mailto:journals.dept@minervamedica.it) - [journals2.dept@minervamedica.it](mailto:journals2.dept@minervamedica.it) - [journals6.dept@minervamedica.it](mailto:journals6.dept@minervamedica.it)

---

# Neurological assessment with validated tools in general ICU: multicenter, randomized, before and after, pragmatic study to evaluate the effectiveness of an e-learning platform for continuous medical education.

Giovanni Mistraletti<sup>\*,1,2</sup>, Michele Umbrello<sup>2</sup>, Stefania Anania<sup>2</sup>, Elisa Andrichi<sup>2</sup>, Alessandra Di Carlo<sup>2</sup>, Federica Martinetti<sup>2</sup>, Serena Barello<sup>2</sup>, Giovanni Sabbatini<sup>2</sup>, Paolo Formenti<sup>2</sup>, Tommaso Maraffi<sup>1</sup>, Francesco Marrasso<sup>1</sup>, Alessandra Palo<sup>3</sup>, Giacomo Bellani<sup>4</sup>, Riccarda Russo<sup>5</sup>, Silvia Francesconi<sup>6</sup>, Federico Valdambri<sup>7</sup>, Marco Cigada<sup>8</sup>, Francesca Riccardi<sup>9</sup>, Egidio A. Moja<sup>10</sup>, Gaetano Iapichino<sup>1,2</sup> for the SedalICU investigators.

<sup>1</sup> Dipartimento di Fisiopatologia Medico-Chirurgica e dei Trapianti, Università degli Studi di Milano; <sup>2</sup> U.O. Anestesia e Rianimazione, Dipartimento Emergenza-Urgenza, A.O. San Paolo – Polo Universitario, Milano; <sup>3</sup> U.O. Anestesia e Rianimazione 1, I.R.C.C.S. San Matteo, Pavia; <sup>4</sup> Dipartimento di Scienze della Salute, Università degli Studi Milano Bicocca, A.O. San Gerardo, Monza (MI); <sup>5</sup> U.O.C. Rianimazione e Terapia Intensiva, Fondazione I.R.C.C.S. Ca' Granda, Ospedale Maggiore Policlinico, Milano; <sup>6</sup> U.O.C. Anestesia e Rianimazione, A. O. Ospedale Civile di Desio (MI); <sup>7</sup> U.O. Anestesia e Rianimazione, A.O. Ospedale Civile di Legnano (MI); <sup>8</sup> U.O. Anestesia e Rianimazione, A.O. Fatebenefratelli e Oftalmico, Milano; <sup>9</sup> U.O. Anestesia e Rianimazione 2, I.R.C.C.S. San Matteo, Pavia; <sup>10</sup> Dipartimento di Scienze della Salute, Università degli Studi di Milano.

**Running title:** e-learning program for neurological assessment in ICU.

## Corresponding author:

Giovanni Mistraletti, MD

Università degli Studi di Milano, Dipartimento di Fisiopatologia Medico-chirurgica e dei Trapianti

A.O. San Paolo - Polo Universitario, Via A. Di Rudini, 8 - 20142 Milano - Italy

Phone +39.02.50323134

Fax +39.02.50323137

Mobile +39.339.8245014

Email [giovanni.mistraletti@unimi.it](mailto:giovanni.mistraletti@unimi.it)

**Key words:** Distance Learning – Continuing Medical Education – Neurophysiological Monitoring – Pain – Delirium.

<b>Word count:</b>	<b>abstract</b>	<b>233</b>	<b>Character count:</b>	<b>title</b>	<b>209</b>
	<b>paper</b>	<b>2707</b>		<b>running title</b>	<b>53</b>
	<b>references</b>	<b>33</b>			
	<b>tables</b>	<b>1 + 9S</b>			
	<b>figures</b>	<b>4 + 2S</b>			

Giovanni Mistraletti	<a href="mailto:giovanni.mistraletti@unimi.it">giovanni.mistraletti@unimi.it</a>
Michele Umbrello	<a href="mailto:michele.umbrello@ao-sanpaolo.it">michele.umbrello@ao-sanpaolo.it</a>
Stefania Anania	<a href="mailto:stefania.anania@gmail.com">stefania.anania@gmail.com</a>
Elisa Andrichi	<a href="mailto:elisa_andrichi@hotmail.com">elisa_andrichi@hotmail.com</a>
Alessandra Di Carlo	<a href="mailto:alessandradicarlo@libero.it">alessandradicarlo@libero.it</a>
Federica Martinetti	<a href="mailto:federica.martinetti@libero.it">federica.martinetti@libero.it</a>
Serena Barello	<a href="mailto:serena.barello@gmail.com">serena.barello@gmail.com</a>
Giovanni Sabbatini	<a href="mailto:giovanni.sabbatini1@gmail.com">giovanni.sabbatini1@gmail.com</a>
Paolo Formenti	<a href="mailto:formenti.paolo@fastwebnet.it">formenti.paolo@fastwebnet.it</a>
Tommaso Maraffi	<a href="mailto:tommaso.maraffi@gmail.com">tommaso.maraffi@gmail.com</a>
Francesco Marrasso	<a href="mailto:fram88@gmail.com">fram88@gmail.com</a>
Alessandra Palo	<a href="mailto:a.palo@smatteo.pv.it">a.palo@smatteo.pv.it</a>
Giacomo Bellani	<a href="mailto:giacomo.bellani1@unimib.it">giacomo.bellani1@unimib.it</a>
Riccarda Russo	<a href="mailto:riccarda.russo@gmail.com">riccarda.russo@gmail.com</a>
Silvia Francesconi	<a href="mailto:francesconi.silvia@alice.it">francesconi.silvia@alice.it</a>
Federico Valdambri	<a href="mailto:federico.valdambri@ao-legnano.it">federico.valdambri@ao-legnano.it</a>
Marco Cigada	<a href="mailto:marcocigada@yahoo.it">marcocigada@yahoo.it</a>
Francesca Riccardi	<a href="mailto:f.riccardi@smatteo.pv.it">f.riccardi@smatteo.pv.it</a>
Egidio A. Moja	<a href="mailto:egidio.moja@unimi.it">egidio.moja@unimi.it</a>
Gaetano Iapichino	<a href="mailto:g.iapichino@unimi.it">g.iapichino@unimi.it</a>

## Abstract

**BACKGROUND:** International guidelines recommend systematic assessment of pain, agitation/sedation and delirium with validated scales for all ICU patients. However, these evaluations are often not done. We have created an e-learning training platform for the continuous medical education, and assessed its efficacy in increasing the use of validated tools by all medical and nursing staff of the participating ICUs during their daily practice.

**METHODS:** Multicenter, randomized, before and after study. The eight participating centers were randomized in two groups, and received training at different times. The use of validated tools (Verbal Numeric Rating or Behavioral Pain Scale for pain; Richmond Agitation-Sedation Scale for agitation; Confusion Assessment Method for the ICU for delirium) was evaluated from clinical data recorded in medical charts during a week, with follow-up up to six months after the training. All the operators were invited to complete a questionnaire, at baseline and after the training.

**RESULTS:** Among the 374 nurses and physicians involved, 140 (37.4%) completed at least one of the three courses. The assessment of pain (38.1 vs. 92.9%,  $p<0.01$ ) and delirium (0 vs. 78.6%,  $p<0.01$ ) using validated tools significantly increased after training. Observation in the follow-up showed further improvement in delirium monitoring, with no signs of extinction for pain and sedation/agitation measurements.

**CONCLUSIONS:** This e-learning program shows encouraging effectiveness, and the increase in the use of validated tools for neurological monitoring in critically ill patients lasts over time.

## Introduction

International guidelines recommend systematic assessment of pain, agitation/sedation and delirium in all ICU patients, through the use of validated tools.<sup>1, 2</sup> These tools provide repeatable and comparable measurements, to titrate the therapy and to keep patients awake, cooperative, and well adapted to the harsh ICU environment.<sup>3</sup> In fact, excessive use of analgesics and sedatives<sup>4</sup> correlates with longer ICU stay and a greater risk of short- and long-term neurological sequelae.<sup>5, 6</sup>

There is increasing scientific evidence that the side effects of sedative drugs compromise clinical stability. Deep sedation may prolong the need for mechanical ventilation,<sup>7</sup> increase sepsis severity,<sup>8</sup> and result in new neurological failures both in hospital (delirium) and after discharge.<sup>5</sup> For these reasons, any unnecessary sedative should be avoided:<sup>9</sup> therapy should be titrated with the use of validated scales. Since proper identification of pain symptoms in critically ill patients poses a challenge, specific behavioral scales have been designed and validated for unconscious/sedated<sup>10</sup> and conscious/awake patients.<sup>11</sup>

The literature offers encouraging results regarding pain and agitation assessments,<sup>12</sup> but recognition of delirium is more challenging, with regard to effective and lasting staff training.<sup>14</sup> Delirium has a very high prevalence in critically ill patients<sup>15</sup> and there is a direct relationship between increased morbidity and mortality and its duration.<sup>16, 17</sup> It correlates with a significant deterioration in quality of life after ICU discharge.<sup>18</sup> As a result, a significant body of literature recommends the use of validated tools for delirium.<sup>19</sup>

Among these, the scales with the highest psychometric properties<sup>20</sup> are the Verbal Numeric Rating (VNR) and the Behavioral Pain Scale (BPS)<sup>21</sup> for pain; the Richmond Agitation-Sedation Scale (RASS)<sup>22, 23</sup> and the Sedation Agitation Scale (SAS)<sup>24</sup> for agitation/sedation; the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU)<sup>25</sup> and the Intensive Care Delirium Screening Checklist (ICDSC)<sup>26</sup> for delirium.

Although international guidelines prescribe monitoring pain/agitation/delirium with three tools, it is often difficult to implement their use in ICU.<sup>27</sup> Even if they do not usually take much time, the need for a specifically planned learning process remains a significant barrier.<sup>12</sup> In addition, the learning process has to be sustained with refresher courses to avoid extinction.<sup>28</sup>

The literature supports the need for training on the use of these tools, because proper detection of neurological status may enable the medical staff to titrate drug administration, possibly reducing mortality and morbidity.<sup>29</sup> A specific challenge right now is how to calibrate the use of teaching resources in relation to their effectiveness, maintaining neurological monitoring performance over time. E-learning methods may offer the best generalizability without disproportionate human resources use.<sup>30</sup>

## Outcomes

The aim of the present study was to evaluate the effectiveness of an e-learning program for medical and nursing ICU staff<sup>31, 32</sup>. The main hypothesis tested was that e-learning could significantly increase the number of pain/agitation/delirium assessments done using validated instruments in ICUs where staff were trained early (intervention arm) in comparison to the ICUs where staff were trained later (control arm), i.e. still not trained at the time when data was collected.

Educational objectives were pursued only through a website ([www.sedaicu.it](http://www.sedaicu.it)) where users could follow educational courses or consult the scales. Flowchart/pocket cards/posters for the management of pain, sedation and delirium in ICU, in Italian and English, were always available. Three Continuous Medical Education (CME) courses were offered: 1) Monitoring analgesia and sedation in ICU; 2) Evaluating delirium in critically ill patients; 3) Management of the “awake critically ill patient”. Each course comprised several lessons, each made up of a two-page text summarizing a specific topic, together with full text references from the international literature. The website provided 14 lessons, 105 papers, 22 ready-to-use instruments, and 11 videos, for a total of 158 webpages.

Secondary outcomes were: 1) use of validated tools after training compared to pre-training; 2) maintenance of neurological monitoring performances over time, in this case up to six months; 3) investigation of the perceived difficulties and workload, as reported by the staff members; 4) the length of ICU stay (ICU-LOS).

## Materials and methods

### *Participating centers*

This study involved staff nurses and physicians from eight ICUs in the area of Milan, Italy: San Paolo (HSP); Ospedale Civile di Desio (DES); Fatebenefratelli e Oftalmico (FBF); two different ICUs at San Matteo, Pavia (PVU and PVD); San Gerardo, Monza (MON); Ospedale Maggiore Policlinico (POL); Ospedale Civile di Legnano (LEG).

The centers were selected on the basis of their availability, regardless of whether they had hospital guidelines for neurological assessment, experience with the use of validated tools, or university/non-university hospital status, or the case-mix of patients treated. The heterogeneity of the study group was explicitly planned to achieve the best generalizability of the results.

Each ICU organized the training in a specific period. Two groups were randomly created: in the intervention arm “ICU-A” (HSP, LEG, DES, and FBF), nurses and physicians were invited to do the training at an early stage, while in the control arm “ICU-B” (PVU, MON, PVD and POL) nurses and physicians had access to the program later.

### *Data collection in participating centers*

A specially designed sheet (Fig.1S) was used to detect the frequency of use of each validated tool (VNR and BPS for pain, RASS for agitation/sedation, and CAM-ICU for delirium), or other neurological observations in the clinical chart. Data was collected by the same four psychologists on five separate occasions for each of the eight participating centers, gathering data from one-week retrospective chart examination.

Surveys were scheduled as shown in Fig.1. After the Baseline survey, a pre-training survey (Pre-period) was done in the four intervention arm centers (ICU-A). Then training was opened and all the ICU-A staff were

invited to participate, with three subsequent personal e-mails that suggested the opportunity to earn CME credits. After that, a new survey was carried out simultaneously in ICU-A (Post-period) and ICU-B (Pre-period). The four centers in the control arm (ICU-B) started the training a month later, with their subsequent Post-period observation. Both groups were again observed at three (3mFollowUp) and six months (6mFollowUp).

### ***Questionnaire for operators***

To detect the technical abilities, the knowledge, habits, and any trouble regarding the use of the validated tools, and the perceived workload for their use, a specifically-designed questionnaire was proposed to all staff members of the participating ICUs during the Baseline and Post-period surveys. The questionnaire also investigated their motivation to improve their professional knowledge on these topics.

### ***Statistical analysis***

Data from clinical observations were analyzed in three steps. First, we calculated the prevalence of neurological assessments carried out with validated tools (adequately gathered detections as a percentage of the total number of patients in the ICU); then, the average prevalence of each center for each studied period was calculated using the median of the surveys relating to each patients' bed. Last, these findings were compared using an appropriate non-parametric test: Wilcoxon rank-sum test or Friedman's multiple comparison test. Predefined sub-analyses were planned to compare university and non-university hospitals; patient/nurse ratio  $\geq 0.5$  or  $< 0.5$ ; hospital with or without existing guidelines on neurologic monitoring. Questionnaire replies were analyzed using non-parametric tests for paired data (Wilcoxon rank sum test). In both cases, normally-distributed continuous variables were investigated with Student's t test. All analyses were done with the statistical package STATA 12 (Stata Corporation, College Station, Texas, USA).

## **Results**

### ***Surveys***

The use of validated tools was surveyed according to schedule in all cases but one: for organizational reasons, it was not possible to accomplish the "Post-period", "3mFollowUp" and "6mFollowUp" surveys in the LEG center. This center had therefore to be excluded from the statistical analysis on the use of validated tools. Baseline characteristics of the two ICU groups are described in Table 1S.

### ***E-learning courses***

During the nine-month study (12 Dec.11-15 Sept. 12), out of the 374 staff doctors and nurses involved, 140 (37.4%) completed the first CME course; 135 (36.1%) completed the second; 119 (31.8%) completed the third. Staff were not obliged to follow the courses in any preset order, but 117 (98.0%) who completed the third course had also taken the first two.

### ***Main Outcome***

The main outcome is presented in Fig.2 and Tab.2S. The percentage of pain assessments using validated tools was significantly higher in ICU-A during the Post-period than in ICU-B during the Pre-period (92.9% vs. 38.1%,  $P<0.01$ ). The same held for delirium assessments (78.6% vs. 0%,  $P<0.01$ ), while agitation/sedation assessments were not different. At the same time, there was a significant decrease in the “missing assessments” for delirium (6.3 vs. 69.2%,  $P<0.01$ ). A significant increase in the use of validated tools was also observed considering the differences within each center between the Pre and Post periods (Tab.3S).

We compared the use of validated tools use by two ICU groups on the Pre-period (ICU-A: 34.6 [29.5-66.7]% vs. ICU-B: 34.9 [27.4-66.7]%,  $p=0.72$ ) to exclude differences before the study intervention. We also compared the Baseline and Pre periods within each ICU group to exclude differences due to staff awareness that a study on these topics was ongoing (ICU-A: 33.3 [22.2-44.4]% vs. 34.6 [29.5-66.7]%,  $p=0.22$ ; ICU-B: 58.2 [35.2-66.7]% vs. 34.9 [27.4-66.7]%,  $p=0.18$ ).

### ***Secondary outcomes***

The results for the five periods are shown in Fig.2S. The proportion of surveys with validated tools for pain and delirium rose steadily up to the 6mFollowUp, whereas for sedation, even though it remained higher than 90%, it tended to drop slightly and non-significantly in the two follow-up periods (Fig.3).

Statistical sub-analysis showed that the percentage of assessments with validated tools was higher in centers with more nurses available, and missing or non-validated assessments were lower. Unlike pain and sedation, not all eight ICU had hospital guidelines for delirium management before the study; ICU staff from centers with such guidelines were more used to monitoring delirium correctly. Lastly, there were more overall correct assessments in university hospitals.

The mean ICU-LOS was  $6.3 \pm 1.2$  days in the Pre-period and  $6.2 \pm 1.0$  days in the Post-period, without statistical significance ( $p=0.94$ ). No differences were found even when correcting for the number of staff members involved in each center.

### ***Questionnaire for operators***

Among the 374 doctors and nurses of the 8 ICUs, 222 (59.4%) questionnaires were collected at Baseline, and 210 (56.1%) in the Post-period. The main details of the staff members who answered are listed in Tab.4S.

The questionnaire analysis illustrates, albeit indirectly, the use of validated tools. There was an increase in the use of BPS after the training program (8.7% vs. 56.7%,  $p<0.01$ ) with a consequent decrease in the use of non-validated methods (28.8% vs. 17.8%,  $p<0.01$ ). BPS became better known (39.8 vs. 81.1%,  $p<0.01$ ) and considered more effective (35.2% vs. 74.8%,  $p<0.01$ ). Delirium monitoring changed significantly, too, with a halving of the number of ICU staff members who said they had done no validated delirium surveys after the intervention (50.5% vs. 25.7%,  $p<0.01$ ), together with a substantial increase in the use of CAM-ICU (40.2% vs. 70.8%,  $p<0.01$ ).

The number of ICU staff members declaring they did not routinely assess consciousness with validated scales, already very low at Baseline, dropped further (19.5% vs. 11.1%,  $p=0.02$ ). The questionnaire also indicated an increase in the time spent on neurological assessment after training, together with a better understanding of its importance during ICU rounds (Table 5S). Interestingly, training led to a reduction in the number of patients considered to need a sedative (75% vs. 70%,  $p<0.01$ , Tab.7S).

Training increased the knowledge of the correct definition of delirium (Tab.8S) (64.9% vs. 82.7%,  $p<0.01$ ). The estimates of the prevalence of delirium increased (10% vs 20%,  $p<0.01$ ), together with the perceived number of patients adequately treated, according to their needs. CAM-ICU was more widely known (52.5 vs. 85.0%,  $p<0.01$ ), and was more frequently judged effective (43.1% vs. 70.4%,  $p<0.01$ ) after the training.

Finally, more than half the operators considered it useful to pursue their education on pain, sedation, and delirium management through methods including meetings, websites for e-learning and brochures or pocket cards. This indicates the importance of different pedagogical strategies (Tab.9S). Fig.4 highlights some of the findings from the questionnaires.

## **Discussion**

This randomized, multicenter, before and after study was designed to detect the pragmatic effectiveness of an e-learning training program ([www.sedaicu.it](http://www.sedaicu.it)). ICU staff (nurses and physicians) from eight different centers were involved and we observed their daily clinical use of validated tools for neurological monitoring in critically ill patients. Overall, though only a third of the staff members involved completed all three online CME courses, there was still a significant effect on properly performed neurological assessments, particularly as regards pain and delirium monitoring. Considering the small amount of human resources used for this educational program, the cost/effectiveness ratio seems promising.

## ***Questionnaires***

During the baseline period, the questionnaires generally showed a lack of knowledge about validated tools for pain and delirium.<sup>27</sup> At the same time, however, the respondents showed lively interest in learning about them. For example, pain was mainly assessed through the VNR, but operators were willing to learn and use behavioral scales like BPS, a tool judged very useful to directly investigate ventilated or sedated critically ill patients. Monitoring sedation/agitation instead was shown not to require specific educational interventions because it was already done properly in very high percentages in the pre-training period. For delirium, not only was a very high proportion of operators not using any validated tool, but they did not even know their existence, as reported elsewhere.<sup>33</sup> Overall, the perceived workload did not change with the introduction of validated tools.

## ***Clinical observations***

The number of missing pain assessments was low in the pre-training period and it decreased thereafter with further improvement in the follow-up periods, probably thanks to a better knowledge of the BPS, which was well accepted by staff members. Sedation was assessed with validated tools in high proportions even before the training so this might explain the lack of significant results after it.

The validated scale for delirium monitoring had later diffusion. In the pre-training period, there were more missing detections than at baseline, together with a decrease in assessments made with non-validated tools. Then, after the training period there was a stable increase in the use of CAM-ICU, reaching up to 60% at six months follow-up. As the literature also shows,<sup>14, 28</sup> delirium monitoring was harder to introduce in clinical practice.



Considering all the observation periods, the use of validated tools was lower in non-university hospitals, in ICUs with lower nurse/patient ratios, and in centers without guidelines for the management of delirium. In these situations, a medical education training program could very likely be even more effective.

During follow-up, properly performed neurological assessments remained high. The use of validated tools for the assessment of pain and delirium showed steady increases. There was also a significant drop in missing assessments between Baseline and 6mFollowUp. This means we can consider extinction virtually negligible.

This intervention did not change the ICU-LOS, which was similar in the Pre- and Post-periods, probably because it depends on too many other factors. The results were not significant even comparing the ICU-LOS for centers with high (>65%) or low (<30%) participation of staff members in the online CME. These observations may suggest a scatter of competences even with non-official instruments.

### ***Study limitations***

First, only a very small number of ICUs was involved. Their differences in 'cultural background' on neurological monitoring permits some kind of generalizability, but it could explain at least part of the results. However, the main outcome is supported by intra-ICU comparisons. Second, a significant share of the ICUs introduced at least one of the validated tools during the study; a "surprise effect" might be assumed. Third, only 30% of staff members followed the online education; even if at least some of the others could have been reached by word of mouth, the investigated effect could be higher with stronger motivation. Fourth, data acquisition was based on a single visit to each center for each period, without gathering information on individual pre-post performances. The data were obtained retrospectively by reviewing medical records. This caused some unexpected and unjustifiable intra-ICU differences in the prevalence of observed data. Fifth, no inferences can be drawn on the correctness of the neurological assessments, since no clinical evaluations by certified evaluators were done. Last, clinical decisions were not measured, so we cannot know whether e-learning changed drug prescriptions.

### **Conclusions**

This e-learning program showed encouraging effectiveness, leading to an increase in the use of validated tools for neurological monitoring in critically ill patients.

### **Key messages**

- Neurological monitoring with validated tools for systematic assessment of pain, agitation, and delirium is mandatory for good clinical practice in general ICUs, but these evaluations are still not done in a large proportion of cases.
- Many training programs produced not-fully-encouraging results, especially for delirium monitoring, which appears to need repeated lessons.
- An online platform was created in Italian and English languages, together with CME courses about pain and sedation, delirium monitoring, and awake critical patient management.
- The present multicenter, before and after, randomized trial found an increase in the use of validated tools for neurological monitoring in critically ill patients after the e-learning intervention, which was sustained over time.

## Disclosure

This study was funded by a grant for independent research provided by Regione Lombardia (DRL 13465 of December 22, 2010), which covers all costs. The funders have no way of controlling the publication of study results, this being the full responsibility of the authors. All the authors declare they have no conflict of interest. The results of the present study were presented at the SIAARTI Congress 2015, in Bologna (October 16<sup>th</sup>, 2015).

## Acknowledgement

The authors especially thank all the staff members of the participating ICUs. This paper endorses the HEROIC bundle project ([www.heroicbundle.org](http://www.heroicbundle.org)). The educational project [www.sedaicu.it](http://www.sedaicu.it) has now been adopted by the *Gruppo di Studio per la Bioetica* of *Società Italiana di Anestesia, Analgesia, Rianimazione e Terapia Intensiva (SIAARTI)*.

## Authors' contributions

GM is the principal investigator of the study and is responsible for the conception, protocol design, study coordination, and organization of financial support. GM, SA, EA, ADC, FM, and SB contributed to building the website [www.sedaicu.it](http://www.sedaicu.it) and gathered the data from each ICU. FM and MU did the statistical analysis. PF, TM, and GS contributed to building the ECM courses. PF, AP, GB, RR, SF, FV, MC, FR were contact people for each participating ICU. EAM contributed significantly to the study design. GI submitted and received financial support for this clinical trial from Regione Lombardia. GM, EA, and ADC wrote the first manuscript draft; MU, EAM, GI, revised the draft for important intellectual content. The English was professionally edited by an author's editor in Milan, J.D. Baggott. All authors have read and approved the final version of the present manuscript and its submission to *Minerva Anestesiologica*.

Complete list of participating centers and SedaICU investigators:

**A.O. San Paolo - Polo Universitario, Milano:** Paolo Spanu, Gianfranco Cappello, Luca Baglio, Bruno Sabatelli, Giovanni Brenna, Morena Astori, Cristina Villa, and Pietro Placido.

**I.R.C.C.S Ospedale Maggiore Policlinico, Milano:** Luciano Gattinoni, Alessandro Protti, Francesca Pagan, Virna Berto, Cristina Carin Sparacino, and Paola Roselli.

**A.O. Fatebenefratelli e Oftalmico, Milano:** Erica Noè, Ilaria Mauri, and Floriana Poti.

**A. O. Ospedale Civile di Desio (MI):** Giulio Ronzoni, Eduardo Beck, and Maurizio Gaiotto.

**A.O. Ospedale Civile di Legnano (MI):** Danilo Radrizzani, Luca Ferla, Riccardo Giudici, and Laura Merlini.

**A.O. San Gerardo, Monza (MB):** Antonio Pesenti, Emanuele Rezoagli, Alessia La Bruna, and Alberto Lucchini.

**I.R.C.C.S. San Matteo, Università degli Studi di Pavia:** AR1 Antonio Braschi, Alessandra Palo, Thekla Niebel, Marina Selvini, Sergio Cortesi and Attilio Quaini; AR2 Giorgio Iotti, Enrico Contri, and Antonella Sacchi.

**Internet providers of on-line ECM courses ([www.webperformance.it](http://www.webperformance.it)):** Alessandro Scartezzini, Gessica Malagò, Francesco Furletti, and Michele Morandini.

## Bibliografia

1. Barr J, Fraser GL, Puntillo K, Ely EW, Gelinas C, Dasta JF, et al. Clinical practice guidelines for the management of pain, agitation, and delirium in adult patients in the intensive care unit. *Crit Care Med*. 2013;41:263-306.
2. Baron R, Binder A, Biniek R, Braune S, Buerkle H, Dall P, et al. Evidence and consensus based guideline for the management of delirium, analgesia, and sedation in intensive care medicine. Revision 2015 (DAS-Guideline 2015) - short version. *Ger Med Sci*. 2015;13:Doc19.
3. Mistraretti G, Mantovani ES, Cadringer P, Cerri B, Corbella D, Umbrello M, et al. Enteral vs. intravenous ICU sedation management: study protocol for a randomized controlled trial. *Trials*. 2013;14:92.
4. Payen JF, Chanques G, Mantz J, Hercule C, Auriant I, Leguillou JL, et al. Current practices in sedation and analgesia for mechanically ventilated critically ill patients: a prospective multicenter patient-based study. *Anesthesiology*. 2007;106:687-95; quiz 891-2.
5. Pandharipande PP, Girard TD, Jackson JC, Morandi A, Thompson JL, Pun BT, et al. Long-term cognitive impairment after critical illness. *N Engl J Med*. 2013;369:1306-16.
6. Jackson DL, Proudfoot CW, Cann KF, Walsh T. A systematic review of the impact of sedation practice in the ICU on resource use, costs and patient safety. *Crit Care*. 2010;14:R59.
7. Strom T, Martinussen T, Toft P. A protocol of no sedation for critically ill patients receiving mechanical ventilation: a randomised trial. *Lancet*. 2010;375:475-80.
8. Nseir S, Makris D, Mathieu D, Durocher A, Marquette CH. Intensive Care Unit-acquired infection as a side effect of sedation. *Crit Care*. 2010;14:R30.
9. Cigada M, Corbella D, Mistraretti G, Forster CR, Tommasino C, Morabito A, et al. Conscious sedation in the critically ill ventilated patient. *J Crit Care*. 2008;23:349-53.
10. Aissaoui Y, Zeggwagh AA, Zekraoui A, Abidi K, Abouqal R. Validation of a behavioral pain scale in critically ill, sedated, and mechanically ventilated patients. *Anesth Analg*. 2005;101:1470-6.
11. Ahlers SJ, van der Veen AM, van Dijk M, Tibboel D, Knibbe CA. The use of the Behavioral Pain Scale to assess pain in conscious sedated patients. *Anesth Analg*. 2010;110:127-33.
12. Pun BT, Gordon SM, Peterson JF, Shintani AK, Jackson JC, Foss J, et al. Large-scale implementation of sedation and delirium monitoring in the intensive care unit: a report from two medical centers. *Crit Care Med*. 2005;33:1199-205.
13. Morandi A, Pandharipande P, Trabucchi M, Rozzini R, Mistraretti G, Trompeo AC, et al. Understanding international differences in terminology for delirium and other types of acute brain dysfunction in critically ill patients. *Intensive Care Med*. 2008;34:1907-15.
14. Spronk PE, Riekerk B, Hofhuis J, Rommes JH. Occurrence of delirium is severely underestimated in the ICU during daily care. *Intensive Care Med*. 2009;35:1276-80.
15. Vasilevskis EE, Han JH, Hughes CG, Ely EW. Epidemiology and risk factors for delirium across hospital settings. *Best Pract Res Clin Anaesthesiol*. 2012;26:277-87.
16. Pisani MA, Kong SY, Kasl SV, Murphy TE, Araujo KL, Van Ness PH. Days of delirium are associated with 1-year mortality in an older intensive care unit population. *Am J Respir Crit Care Med*. 2009;180:1092-7.
17. Ely EW, Shintani A, Truman B, Speroff T, Gordon SM, Harrell FE, Jr., et al. Delirium as a predictor of mortality in mechanically ventilated patients in the intensive care unit. *JAMA*. 2004;291:1753-62.
18. Mistraretti G, Pelosi P, Mantovani ES, Berardino M, Gregoret C. Delirium: clinical approach and prevention. *Best Pract Res Clin Anaesthesiol*. 2012;26:311-26.
19. Devlin JW, Fong JJ, Schumaker G, O'Connor H, Ruthazer R, Garpestad E. Use of a validated delirium assessment tool improves the ability of physicians to identify delirium in medical intensive care unit patients. *Crit Care Med*. 2007;35:2721-4; quiz 5.
20. Robinson BR, Berube M, Barr J, Riker R, Gelinas C. Psychometric analysis of subjective sedation scales in critically ill adults. *Crit Care Med*. 2013;41:S16-29.
21. Payen JF, Bru O, Bosson JL, Lagrasta A, Novel E, Deschaux I, et al. Assessing pain in critically ill sedated patients by using a behavioral pain scale. *Crit Care Med*. 2001;29:2258-63.
22. Sessler CN, Gosnell MS, Grap MJ, Brophy GM, O'Neal PV, Keane KA, et al. The Richmond Agitation-Sedation Scale: validity and reliability in adult intensive care unit patients. *Am J Respir Crit Care Med*. 2002;166:1338-44.
23. Ely EW, Truman B, Shintani A, Thomason JW, Wheeler AP, Gordon S, et al. Monitoring sedation status over time in ICU patients: reliability and validity of the Richmond Agitation-Sedation Scale (RASS). *JAMA*. 2003;289:2983-91.
24. Riker RR, Picard JT, Fraser GL. Prospective evaluation of the Sedation-Agitation Scale for adult critically ill patients. *Crit Care Med*. 1999;27:1275-9.

25. Ely EW, Margolin R, Francis J, May L, Truman B, Dittus R, et al. Evaluation of delirium in critically ill patients: validation of the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU). *Crit Care Med*. 2001;29:1370-9.
26. Bergeron N, Dubois MJ, Dumont M, Dial S, Skrobik Y. Intensive Care Delirium Screening Checklist: evaluation of a new screening tool. *Intensive Care Med*. 2001;27:859-64.
27. Trogrlic Z, van der Jagt M, Bakker J, Balas MC, Ely EW, van der Voort PH, et al. A systematic review of implementation strategies for assessment, prevention, and management of ICU delirium and their effect on clinical outcomes. *Crit Care*. 2015;19:157.
28. Riekerk B, Pen EJ, Hofhuis JG, Rommes JH, Schultz MJ, Spronk PE. Limitations and practicalities of CAM-ICU implementation, a delirium scoring system, in a Dutch intensive care unit. *Intensive Crit Care Nurs*. 2009;25:242-9.
29. Vasilevskis EE, Morandi A, Boehm L, Pandharipande PP, Girard TD, Jackson JC, et al. Delirium and sedation recognition using validated instruments: reliability of bedside intensive care unit nursing assessments from 2007 to 2010. *J Am Geriatr Soc*. 2011;59 Suppl 2:S249-55.
30. Soja SL, Pandharipande PP, Fleming SB, Cotton BA, Miller LR, Weaver SG, et al. Implementation, reliability testing, and compliance monitoring of the Confusion Assessment Method for the Intensive Care Unit in trauma patients. *Intensive Care Med*. 2008;34:1263-8.
31. Cook DA, Levinson AJ, Garside S, Dupras DM, Erwin PJ, Montori VM. Internet-based learning in the health professions: a meta-analysis. *JAMA*. 2008;300:1181-96.
32. Du S, Liu Z, Liu S, Yin H, Xu G, Zhang H, et al. Web-based distance learning for nurse education: a systematic review. *Int Nurs Rev*. 2013;60:167-77.
33. Glynn L, Corry M. Intensive care nurses' opinions and current practice in relation to delirium in the intensive care setting. *Intensive Crit Care Nurs*. 2015;31:269-75.

**Tab. 1 - Comparison of ICUs**

	<b>ICU with nurses/pt ratio <math>\geq 0.5</math></b>	<b>ICU with nurses/pt ratio <math>&lt; 0.5</math></b>	<b><i>p</i></b>
Surveys of pain/sedation/delirium with validated instruments	77.8 [65; 92.1]	62.5 [33.3; 68.6]	<0.01
Surveys of pain/sedation/delirium not done	10.3 [4.8; 26.7]	19 [7.4; 39.7]	<0.01
Surveys of pain/sedation/delirium with not validated instruments	3.2 [0; 19]	14.8 [0; 31.7]	<0.01
	<b>ICU with guidelines</b>	<b>ICU without guidelines</b>	<b><i>p</i></b>
Surveys of delirium with validated instruments	73.3 [30.8; 92.9]	0 [0; 42.9]	< 0.01
Surveys of delirium not done	7.7 [0; 19]	33.3 [9.5; 61.5]	< 0.01
Surveys of delirium with not validated instruments	6.7 [0; 53.3]	42.9 [0; 71.4]	< 0.01
	<b>University ICUs</b>	<b>Non-University ICUs</b>	<b><i>p</i></b>
Surveys of pain/sedation/delirium with validated instruments	71.4 [61.4; 89.6]	44.4 [27.8; 66.7]	<0.01
Surveys of pain/sedation/delirium not done	11.1 [3.3; 25.9]	31.7 [16.7; 66.7]	<0.01
Surveys of pain/sedation/delirium with not validated instruments	7.9 [0; 23.8]	12.5 [0; 27.4]	0.35

**Table 1 – Comparison of ICUs.** This table was built considering together all the surveys done in the five study periods, and comparing ICUs according to specific characteristics (nurses/pt ratio, delirium management guidelines, university or non- university). Values are median [interquartile range]. Variables were compared using the Wilcoxon rank sum test.

# Neurological assessment with validated tools in general ICU: multicenter, randomized, before and after, pragmatic study to evaluate the effectiveness of an e-learning platform for continuous medical education.

Giovanni Mistraletti<sup>\*1,2</sup>, Michele Umbrello<sup>2</sup>, Stefania Anania<sup>2</sup>, Elisa Andrichi<sup>2</sup>, Alessandra Di Carlo<sup>2</sup>, Federica Martinetti<sup>2</sup>, Serena Barello<sup>2</sup>, Giovanni Sabbatini<sup>2</sup>, Paolo Formenti<sup>2</sup>, Tommaso Maraffi<sup>1</sup>, Francesco Marrazzo<sup>1</sup>, Alessandra Palo<sup>3</sup>, Giacomo Bellani<sup>4</sup>, Riccarda Russo<sup>5</sup>, Silvia Francesconi<sup>6</sup>, Federico Valdambri<sup>7</sup>, Marco Cigada<sup>8</sup>, Francesca Riccardi<sup>9</sup>, Egidio A. Moja<sup>10</sup>, Gaetano Iapichino<sup>1,2</sup> for the SedalICU investigators.

<sup>1</sup> Dipartimento di Fisiopatologia Medico-Chirurgica e dei Trapianti, Università degli Studi di Milano; <sup>2</sup> U.O. Anestesia e Rianimazione, Dipartimento Emergenza-Urgenza, A.O. San Paolo – Polo Universitario, Milano; <sup>3</sup> U.O. Anestesia e Rianimazione 1, I.R.C.C.S. San Matteo, Pavia; <sup>4</sup> Dipartimento di Scienze della Salute, Università degli Studi Milano Bicocca, A.O. San Gerardo, Monza (MI); <sup>5</sup> U.O.C. Rianimazione e Terapia Intensiva, Fondazione I.R.C.C.S. Ca' Granda, Ospedale Maggiore Policlinico, Milano; <sup>6</sup> U.O.C. Anestesia e Rianimazione, A. O. Ospedale Civile di Desio (MI); <sup>7</sup> U.O. Anestesia e Rianimazione, A.O. Ospedale Civile di Legnano (MI); <sup>8</sup> U.O. Anestesia e Rianimazione, A.O. Fatebenefratelli e Oftalmico, Milano; <sup>9</sup> U.O. Anestesia e Rianimazione 2, I.R.C.C.S. San Matteo, Pavia; <sup>10</sup> Dipartimento di Scienze della Salute, Università degli Studi di Milano.

## ELECTRONIC SUPPLEMENTARY MATERIAL

**Tab.1S - General characteristics of the two ICU groups.**

Variables	ICU A (3)	ICU B (4)	P
Nurses per shift - n			
Morning	3 [3; 4]	5 [3; 8]	0.25
Afternoon	3 [3; 3]	5 [3; 6]	0.12
Night	3 [2; 3]	4 [3; 5]	0.10
Doctors per shift - n			
Morning	2 [2; 3]	3 [2; 4]	0.34
Afternoon	2 [1; 2]	2 [2; 2]	0.32
Night	1 [1; 1]	1 [1; 1]	> 0.99
Hours per shift	8 [8; 8]	8 [8; 8]	> 0.99
ICU using guidelines for the assessment of... - n (%)			
Pain	3 (100)	3 (75)	> 0.99
Sedation/agitation	2 (67)	3 (75)	0.27
Delirium	1 (33)	1 (25)	> 0.99
Mixed ICUs - n (%)	3 (100)	3 (75)	> 0.99
ICUs with neurological patients - n (%)	1 (33)	0 (0)	0.27
Hospitalization per year - n	300 [236; 1000]	500 [300; 518]	0.66
Type of admission - (%)			
Medical	60.5 [60; 61]	41.8 [35; 70]	0.35
Surgical scheduled	15.5 [14; 17]	34.7 [20; 44]	0.06
Surgical unscheduled	24 [23; 25]	21 [10; 25.5]	0.81
University hospitals - n (%)	1 (33)	3 (75)	0.08
Hospital beds - n	320 [280; 1400]	900 [800; 1000]	0.56
ICU beds - n	6 [5; 10]	8 [6; 10]	0.50
ICUs without electronic charts – n (%)	3 (100)	1 (25)	0.08

**Table 1S - General characteristics of the two ICU groups.** The seven ICUs where the surveys were conducted are presented in the two ICU :

This document is protected by international copyright laws. No additional reproduction is authorized. It is permitted for personal use to download and save only one file and print only one copy of this Article. It is not permitted to make additional copies (either sporadically or systematically, either printed or electronic) of the Article for any purpose. It is not permitted to distribute the electronic copy of the article through online internet and/or intranet file sharing systems, electronic mailing or any other means which may allow access to the Article. The use of all or part of the Article for any Commercial Use is not permitted. The creation of derivative works from the Article is not permitted. The production of reprints for personal or commercial use is not permitted.

**Tab. 2S – Main outcome**

		<b>ICU A</b>	<b>ICU B</b>	<b>P</b>
		<b>Post period</b>	<b>Pre period</b>	
Surveys with validated tools - (%)	Pain	92.9 [83.3; 97.6]	38.1 [0; 95.2]	<0.01
	Sedation/agitation	91.7 [83.8; 97.6]	89.5 [75; 100]	0.94
	Delirium	78.6 [16; 97.1]	0 [0; 0]	<0.01
Missing surveys - (%)	Pain	6.5 [0; 16.7]	18.7 [0; 50]	0.19
	Sedation/agitation	7.7 [0; 15.8]	0 [0; 11.8]	0.40
	Delirium	6.3 [0; 21.4]	69.2 [19; 100]	<0.01
Surveys without validated tools - (%)	Pain	0 [0; 0]	0 [0; 54.5]	0.03
	Sedation/agitation	0 [0; 0]	0 [0; 9.5]	0.04
	Delirium	3.3 [0; 57.6]	25 [0; 66.7]	0.43

**Table 2S – Main outcome.** The percentages of pain, sedation/agitation and delirium evaluations with validated tools. The comparison was between ICU A in the post period and ICU B in the pre period. Values are median [interquartile range]. The variables were compared using the Wilcoxon rank sum test. ICU A, intervention arm centers ; ICU B, control arm centers.

**Tab 3S – Comparison of Pre period and Post period in all ICUs.**

		<b>Pre period</b>	<b>Post period</b>	<b><i>p</i></b>
Surveys with validated tools				
	Pain	66.6 [0; 100]	83.8 [54.8; 100]	0.03
	Sedation/agitation	85.7 [45.4; 100]	93.7 [78.2; 100]	0.05
	Delirium	0 [0; 0]	29.3 [7.9; 83.8]	0.01
Missing surveys				
	Pain	16.7 [0; 45.4]	14.3 [0; 40.5]	0.98
	Sedation/agitation	9.5 [0; 25]	2.4 [0; 21.8]	0.28
	Delirium	62.5 [14.3; 100]	19.5 [4.8; 42.9]	<0.01
Surveys without validated tools				
	Pain	0 [0; 42.9]	0 [0;0]	> 0.99
	Sedation/agitation	0 [0; 6.7]	0 [0; 0]	> 0.99
	Delirium	5.3 [0; 62.5]	33.3 [0; 53.3]	> 0.99

**Table 3S – Comparison of Pre period and Post periods in all ICUs.** Percentages of surveys with validated tools, missing, or without validated tools: comparison of the pre-training and post-training periods in all the ICUs considered together. Values are median [interquartile range] or absolute number (percentage). The variables were compared using the Wilcoxon rank sum test.



**Tab 4S – Main socio-demographic characteristics of nurses and physicians answering the questionnaire.**

		<b>Pre (222)</b>	<b>Post (210)</b>	<b><i>P</i></b>
Age - years		37 [32; 43]	38 [32; 44]	0.86
Females - n (%)		116 (52.2)	118 (56.2)	0.41
Italian nationality - n (%)		217 (97.8)	206 (98.6)	0.53
Employment - n (%)	Physicians	85 (38.3)	68 (32.7)	0.23
	Nurses	137 (61.7)	140 (67.3)	
Years of experience		9 [4; 16]	10 [4; 16]	0.78
Working position - n (%)	Coordinators	10 (4.5)	5 (2.4)	0.23
	Staff members	212 (95.5)	205 (97.6)	

**Table 4S – Main socio-demographic characteristics of nurses and physicians answering the questionnaire.** Values are median [interquartile range] or absolute number (percentage). The variables were compared using the Wilcoxon rank sum test or Fisher's exact test (exact), as appropriate.

**Tab 5S – Questionnaire: general habits.**

Variables	Pre (222)	Post (210)	<i>P</i>
Enteral sedation - (%)	30 [15; 70]	40 [20; 70]	0.15
Conscious sedation during mechanical ventilation - (%)	60 [30; 80]	60 [40; 80]	0.69
Reasons for the current approach - n (%)			
Habit	59 (28.9)	67 (33.3)	0.34
International guidelines	96 (47.1)	83 (41.3)	0.24
Convenience	20 (9.8)	13 (6.5)	0.22
Cost-benefit ratio	59 (28.9)	65 (32.3)	0.46
Methods used to assess pain - n (%)			
None	11 (5)	6 (2.9)	0.26
VNR	154 (70.3)	145 (69.7)	0.89
BPS	19 (8.7)	118 (56.7)	<0.01
Other	63 (28.8)	37 (17.8)	<0.01
Methods used to assess sedation - n (%)			
None	43 (19.5)	23 (11.1)	0.02
RASS	171 (77.4)	175 (84.1)	0.08
RAMSAY	5 (2.3)	3 (1.4)	0.53
Other	8 (3.6)	7 (3.4)	0.89
Methods used to assess delirium - n (%)			
None	108 (50.5)	53 (25.7)	<0.01
CAM-ICU	86 (40.2)	148 (71.8)	<0.01
Other	11 (5.1)	5 (2.4)	0.15
Daily neurological assessment - n	3 [3; 4]	3 [3; 3]	<0.01
Time (in minutes) for the measurements of pain, sedation/agitation and delirium in a single work shift - n (%)			
< 5	57 (27)	30 (14.8)	0.02
5 - 15	127 (60.2)	139 (68.5)	
15 - 30	21 (10)	28 (13.8)	
> 30	6 (2.8)	6 (2.9)	
Neurological monitoring judged adequately clear during shift handover - n (%)			
Never	0	0	0.02
Rarely	14 (6.6)	23 (11.3)	
Often	103 (48.8)	115 (56.7)	
Always	94 (44.6)	65 (32)	
Definition of "validated instrument" - n (%)			
Considered valid in a conference of experts	54 (25)	34 (17.6)	0.05
Used at least in ten reference centers	8 (3.7)	4 (2.1)	
Gives the same results when used by different operators	101 (46.8)	116 (60.1)	
Based on values measured instrumentally	53 (24.5)	39 (20.2)	

**Table 5S – Questionnaire: general habits.** First part of the questionnaire regarding the management of pain, sedation/agitation and delirium. Values are as median [interquartile range] or absolute number (percentage). The variables were compared using the Wilcoxon rank sum test or Fisher's exact test, as appropriate. VNR: Verbal Numerical Rating; BPS: Behavioral Pain Scale; RASS: Richmond Agitation Sedation Scale; CAM-ICU: Confusion Assessment Method for Intensive Care Unit.

**Tab 6S – Questionnaire: pain.**

Variables	Pre (222)	Post (210)	<i>p</i>
When do you think it is necessary to investigate pain? - n (%)			
When the analgesic therapy changes	148 (67.9)	150 (72.5)	0.30
At least every 6 hours	148 (67.9)	135 (65.2)	0.56
When sedation is reduced	120 (55)	120 (58)	0.54
After returning from the operating room	115 (52.8)	108 (52.2)	0.90
Patients with pain detection using a validated tool - (%)	90 [60; 100]	100 [70; 100]	<0.01
Patients with pain - (%)	30 [20; 50]	40 [20; 50]	0.14
Patients with pain who received analgesia - (%)			
Insufficient	10 [0; 20]	10 [0; 20]	0.73
Adequate	80 [70; 90]	80 [70; 90]	0.43
Excessive	0 [0; 10]	0 [0; 10]	0.30
What you believe to be the correlation between pain and clinical outcome? - n (%)			
Close	161 (74.9)	175 (84.5)	
Partial	53 (24.6)	31 (15)	0.04
None	1 (0.5)	1 (0.5)	
Limitations of the application of VNR - n (%)			
Excessive workload	14 (6.4)	11 (5.4)	0.66
Cooperation of the patient	109 (49.6)	94 (45.8)	0.45
Neurological status of the patient	171 (77.7)	176 (85.8)	0.03
I don't know the VNR	26 (11.8)	7 (3.4)	<0.01
Do you think the BPS is... - n (%)			
Effective	76 (35.2)	154 (74.8)	
Effective but steals time from more important tasks	8 (3.7)	7 (3.4)	<0.01
Ineffective	2 (0.9)	6 (2.9)	
I don't know the BPS	130 (60.2)	39 (18.9)	
Limitations of the application of BPS - n (%)			
Excessive workload	18 (22.8)	18 (11.9)	0.03
Cooperation of the patient	29 (36.7)	38 (25.2)	0.07
Neurological status of the patient	44 (55.7)	99 (65.6)	0.14
Previous participation in training events on pain assessment - n (%)	79 (36.4)	105 (52.2)	<0.01

**Table 6S – Questionnaire: pain.** Values are median [interquartile range] or absolute number (percentage). The variables were compared using the Wilcoxon rank sum test or Fisher's exact test (exact), as appropriate. VNR, Verbal Numerical Rating; BPS, Behavioral Pain Scale.

**Tab 7S – Questionnaire: sedation/ agitation.**

Variables	Pre (222)	Post (210)	<i>p</i>
Have you ever had an excessive workload due to a light sedative target in ICU patients? - n (%)			
Never	10 (4.8)	14 (6.8)	0.45
Rarely	105 (50.5)	89 (43.4)	
Often	89 (42.8)	99 (48.3)	
Always	4 (1.9)	3 (1.5)	
Were alternative treatments in your opinion? - n (%)			
Never	15 (6.9)	14 (6.9)	0.45
Rarely	120 (55.3)	107 (53)	
Often	80 (36.9)	75 (37.1)	
Always	2 (0.9)	6 (3)	
Patients undergoing sedation detection with a validated tool - (%)	90 [50; 100]	100 [60; 100]	0.25
Patients needing sedation - (%)	75 [50; 80]	70 [50; 80]	0.92
Patients who received sedation... - (%)			
Insufficient	10 [5; 30]	10 [5; 30]	0.36
Adequate	80 [60; 80]	80 [60; 90]	0.91
Excessive	10 [0; 15]	5 [0; 10]	0.68
Do you think the RASS is... - n (%)			
Effective	171 (79.2)	181 (88.3)	0.07
Effective but steals time from more important tasks	12 (5.5)	4 (1.9)	
Ineffective	3 (1.4)	2 (1)	
I don't know the RASS	30 (13.9)	18 (8.8)	
Limitations of the application of RASS - n (%)			
Excessive workload	24 (14.5)	15 (9.5)	0.17
Cooperation of the patient	41 (24.7)	34 (21.5)	0.50
Neurological status of the patient	113 (68.1)	113 (71.5)	0.50
Previous participation in training events on assessment of sedation/agitation - n (%)	72 (32.9)	102 (49.8)	<0.01

**Table 7S – Questionnaire: sedation/agitation.** Values are median [interquartile range] or absolute number (percentage). The variables were compared using the Wilcoxon rank sum test or Fisher's exact test (exact), as appropriate. RASS: Richmond Agitation Sedation Scale.

**Tab 8S – Questionnaire: delirium.**

Variables	Pre (222)	Post (210)	<i>p</i>
How do you define delirium? - no. (%)			
Abstinence from neuroactive substances	1 (0.5)	3 (1.5)	<0.01
Hallucinatory symptoms	48 (23.1)	13 (6.4)	
State of agitation	24 (11.5)	19 (9.4)	
Fluctuating state of consciousness with inattention and disorganized thinking	135 (64.9)	167 (82.7)	
When do you think one should investigate the presence of delirium? - n (%)			
When analgesic therapy is changed	66 (32.0)	80 (39.8)	0.10
At least every 6 hours	131 (63.6)	135 (67.2)	0.45
When sedation is reduced	111 (53.9)	118 (58.7)	0.33
After returning from the operating room	45 (21.8)	35 (17.4)	0.26
Patients undergoing delirium detection with a validated tool - (%)	0 [0; 50]	60 [10; 100]	<0.01
Patients with delirium - (%)	10 [2.5; 20]	20 [10; 30]	<0.01
Patients with delirium who received therapy - (%)			
Insufficient	20 [0; 50]	10 [0; 30]	0.03
Adequate	70 [40; 90]	80 [60; 100]	<0.01
Ecessive	0 [0; 10]	0 [0; 10]	0.79
Do you think the CAM-ICU is... - n (%)			
Effective	87 (43.1)	145 (70.4)	<0.01
Effective but steal time to more important tasks	16 (7.9)	23 (11.2)	
Ineffective	3 (1.5)	7 (3.4)	
I don't know the CAM-ICU	96 (47.5)	31 (15.0)	
Limitations of the application of CAM-ICU - n (%)			
Excessive workload	39 (35.1)	64 (38.3)	0.59
Cooperation of the patient	53 (47.8)	73 (43.7)	0.51
Neurological status of the patient	50 (44.6)	79 (47.3)	0.66
Previous participation in training events on assessment of delirium - n (%)	38 (18.2)	87 (42.0)	<0.01

**Table 8S – Questionnaire: delirium.** Values are median [interquartile range] or absolute number (percentage). The variables were compared using the Wilcoxon rank sum test or Fisher's exact test (exact), as appropriate. CAM-ICU, Confusion Assessment Method for Intensive Care Unit.

**Tab 9S – Questionnaire: daily practice.**

Variables	Pre (222)	Post (210)	P
Do you think there is room to improve pain management? - n (%)			
None at all	8 (3.8)	8 (3.9)	0.87
Little	93 (43.9)	97 (46.8)	
Enough	87 (41)	83 (40.1)	
Plenty	24 (11.3)	19 (9.2)	
Do you think there is room to improve sedation management? - n (%)			
None at all	6 (2.8)	7 (3.4)	0.21
Little	66 (31.3)	85 (40.9)	
Enough	109 (51.7)	91 (43.7)	
Plenty	30 (14.2)	25 (12)	
Do you think there is room to improve delirium management? - n (%)			
None at all	4 (1.9)	10 (4.9)	<0.01
Little	33 (15.7)	45 (21.9)	
Enough	79 (37.4)	93 (45.4)	
Plenty	95 (45.0)	57 (27.8)	
To improve the monitoring of pain, sedation/agitation and delirium, would you consider useful to plan... - n (%)			
Regular team meetings	182 (92.4)	186 (92.5)	0.95
Residential courses	156 (84.3)	149 (80.1)	0.29
Brochures or pocket cards	123 (68.7)	122 (64.9)	0.44
Individual meetings with staff	109 (59.2)	113 (63.5)	0.41
Online training	100 (55.6)	100 (58.6)	0.89
Do you think the use of analgesics, sedatives and antipsychotics in the ward where you work corresponds to good clinical practice? - n (%)			
Not at all	0 (0)	2 (1)	0.48
Little	23 (11)	19 (9.1)	
Enough	146 (69.9)	149 (71.6)	
Closely	40 (19.1)	38 (18.3)	
From 0 to 100 how much are you motivated for training on these topics? - (%)	85 [72; 94]	77 [55; 90]	<0.01

**Table 9S - Questionnaire on daily practice and future training programs.** Values are absolute number (percentage) or median [interquartile range]. The variables were compared using the Wilcoxon rank sum test or Fisher's exact test (exact), as appropriate.

**Fig. 1S - Detection board used for data collection in the ICUs.**

**DETECTION BOARD for WP3 - CENTER ..... BED n° ..... PSYCH .....**

<b>SCALES</b>	DAY 1		DAY 2		DAY 3		DAY 4		DAY 5		DAY 6		DAY 7		
	date .....		date .....		date .....		date .....		date .....		date .....		date .....		
SHIFTS	M	A	N	M	A	N	M	A	N	M	A	N	M	A	N
<i><b>PAIN</b></i>															
VNR or BPS															
OTHER															
.....															
<i><b>SEDATION</b></i>															
RASS															
OTHER															
.....															
<i><b>DELIRIUM</b></i>															
CAM-ICU															
OTHER															
.....															

Survey period: **baseline / pre / post / fu3m / fu6m**  
 N° nurses on duty: **M** ..... - **A** ..... - **N** .....  
 N° intensivists on duty: **M** ..... - **A** ..... - **N** .....  
 Times of shift: **M** ..... - **A** ..... - **N** .....

Presence of hospital or ward guidelines with validated instruments  
 for detection of: pain **y / n** - sedation **y / n** - delirium **y / n**  
 Type of ICU: **Medical / Surgical / Mixed**. Neuro pts: **y / n**  
 N° hospitalizations / year in ICU: ..... - **M** ..... **SS** ..... **SU** ..... %  
 Type of hospital: **Uni / nonUni** - Beds H: .....

Parameters: **paper form / electronic form** - Daily: **paper / electronic**

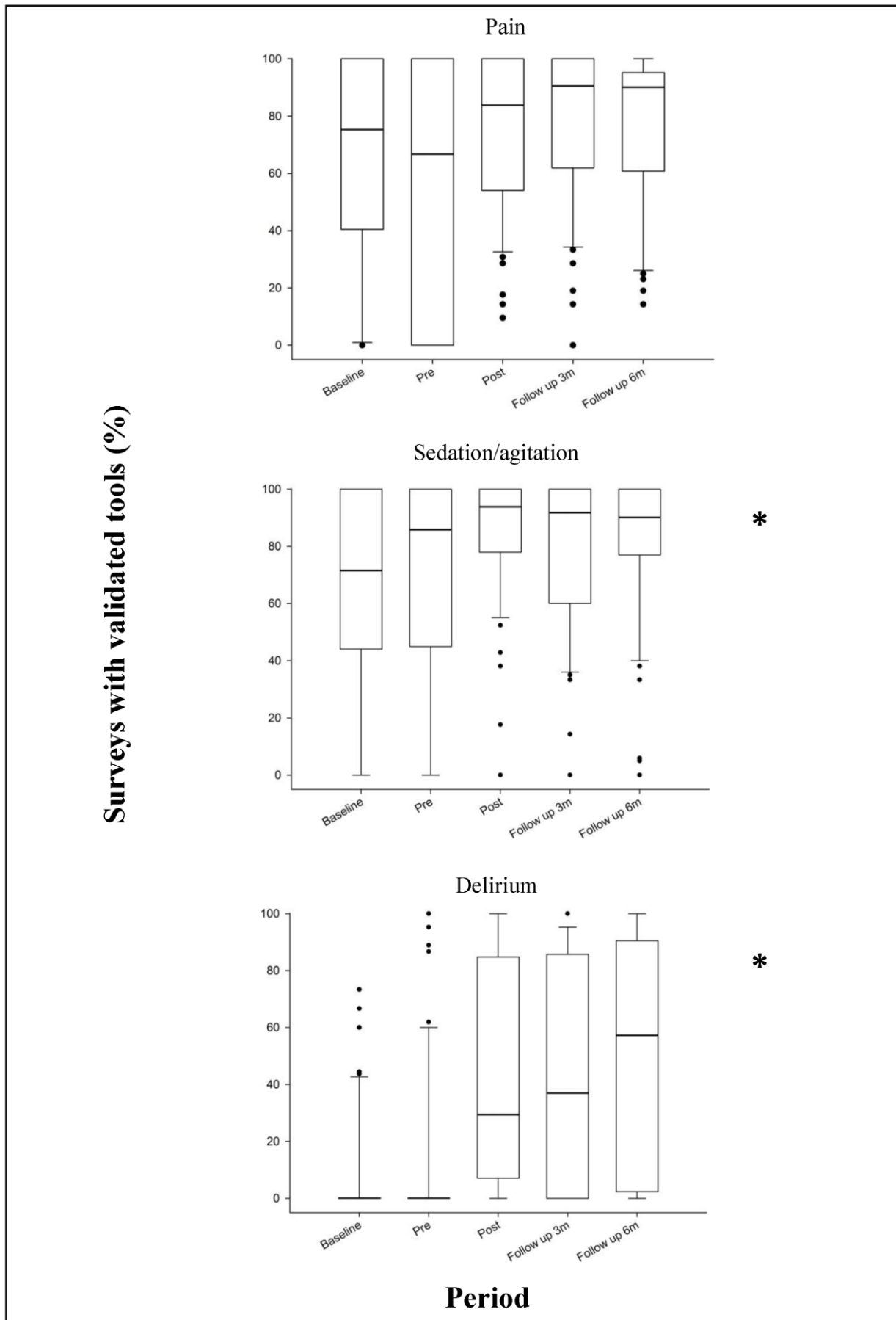
Legend: data unknown **S** (sconosciuto)  
 survey not done **NE** (non eff)  
 survey done **E** (effettuata)  
 empty bed **V** (vuoto)

Rules:  
 1 - check entry / discharge times for each patient: if present for more than 1 hour from the beginning or end of a shift, mark as present.  
 2 - check both nurses sheet parameters and medical report: it is sufficient that survey is reported once.  
 3 - if is written NV (non-assessable) in the medical record, the survey is to be scored as done.

**Fig. 1S - Detection board used for the data collection in the ICUs. At each ICU visit, the psychologist in charge had to complete this by retrospective analysis of medical charts.**

This document is protected by international copyright laws. No additional reproduction is authorized. It is permitted for personal use to download and save only one file and print only one page of this Article. It is not permitted to modify or translate any part of the Article for any purpose, to reproduce or translate any part of the Article for advertising or promotional purposes, to create new collective works, to disseminate in any form or by any means electronic or mechanical, including photocopying, recording, or by any information storage or retrieval system, without the written permission of the publisher, Acta Psychiatrica Scandinavica. For more information, contact the publisher: Taylor & Francis Ltd, 4 Park Square, Milton Park, Abingdon, Oxon, OX14 4RN, UK. Email: taylorandfrancis.com. The production of derivative works from the Article is not permitted. The production of derivative works from the Article is not permitted for personal or commercial use is not permitted.

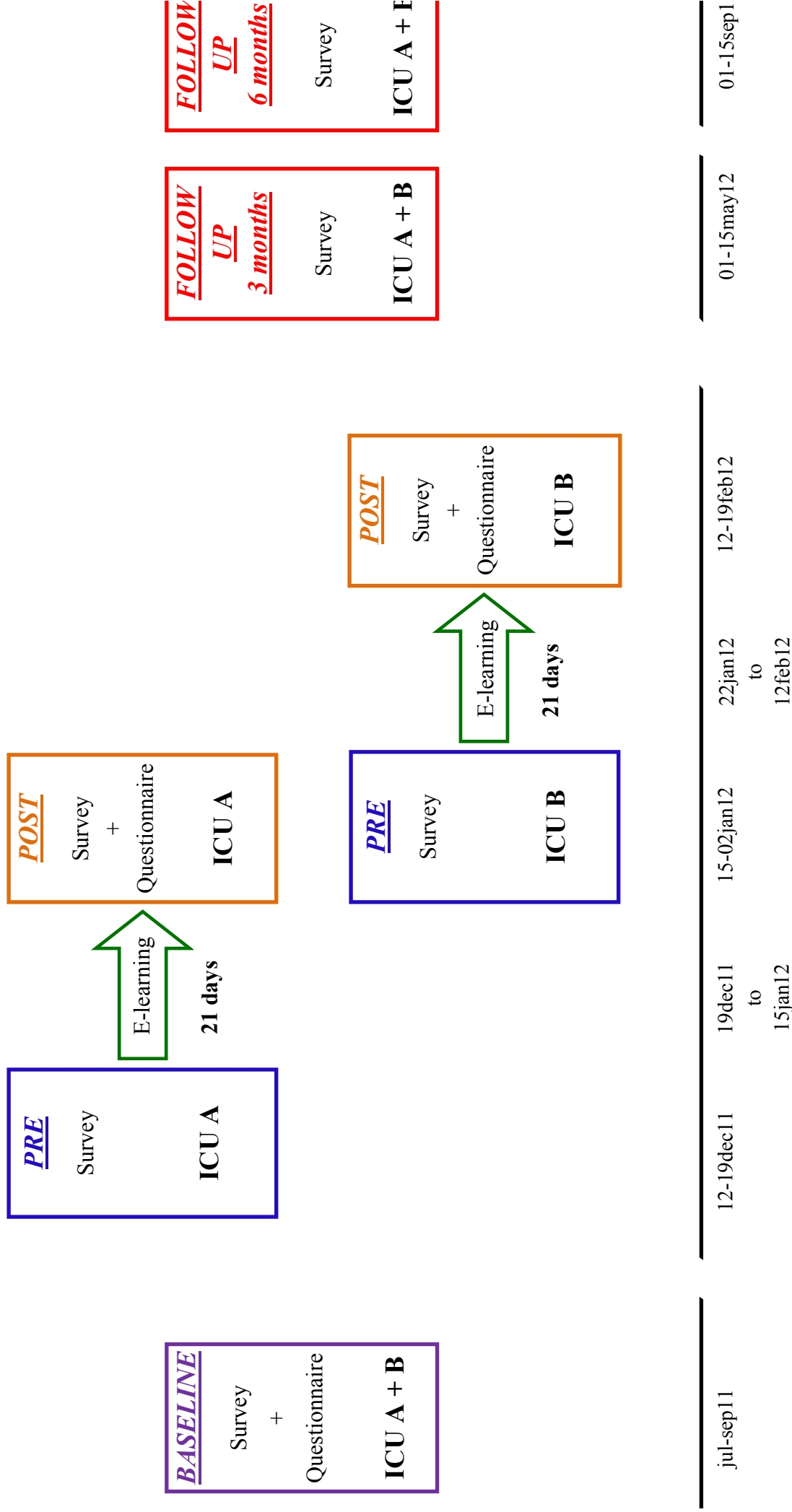
**Fig. 2S - Surveys with validated tools.**



**Figure 2S - Surveys with validated tools.** The box plot presents the median and interquartile range of neurological observations with validated tools in the five study periods. The lines outside rectangles indicate the 95% confidence interval.



**Fig. 1 - Schedule**



**Figure 1 – Schedule.** The diagram shows the validated-tools-use observation periods, with the training time and the questionnaire administration. Hospitals were randomly allocated to the intervention arm (ICU A) or the control arm (ICU B).

This document is protected by international copyright laws. No additional reproduction is authorized. It is permitted for personal use to download and save only one file and print only one page of this article. It is prohibited to make copies, to disseminate, to publish or use in any form, to be translated or to be stored in any retrieval system or to be transmitted in any form or by any means, electronic, mechanical, photocopying, recording, or otherwise, without the prior written permission of the publisher. The use of all or part of this document for any commercial purpose is not permitted. The production of derivative works from the Article is not permitted. The production of reprints for personal or commercial use is not permitted.

Fig. 2 - Main outcome

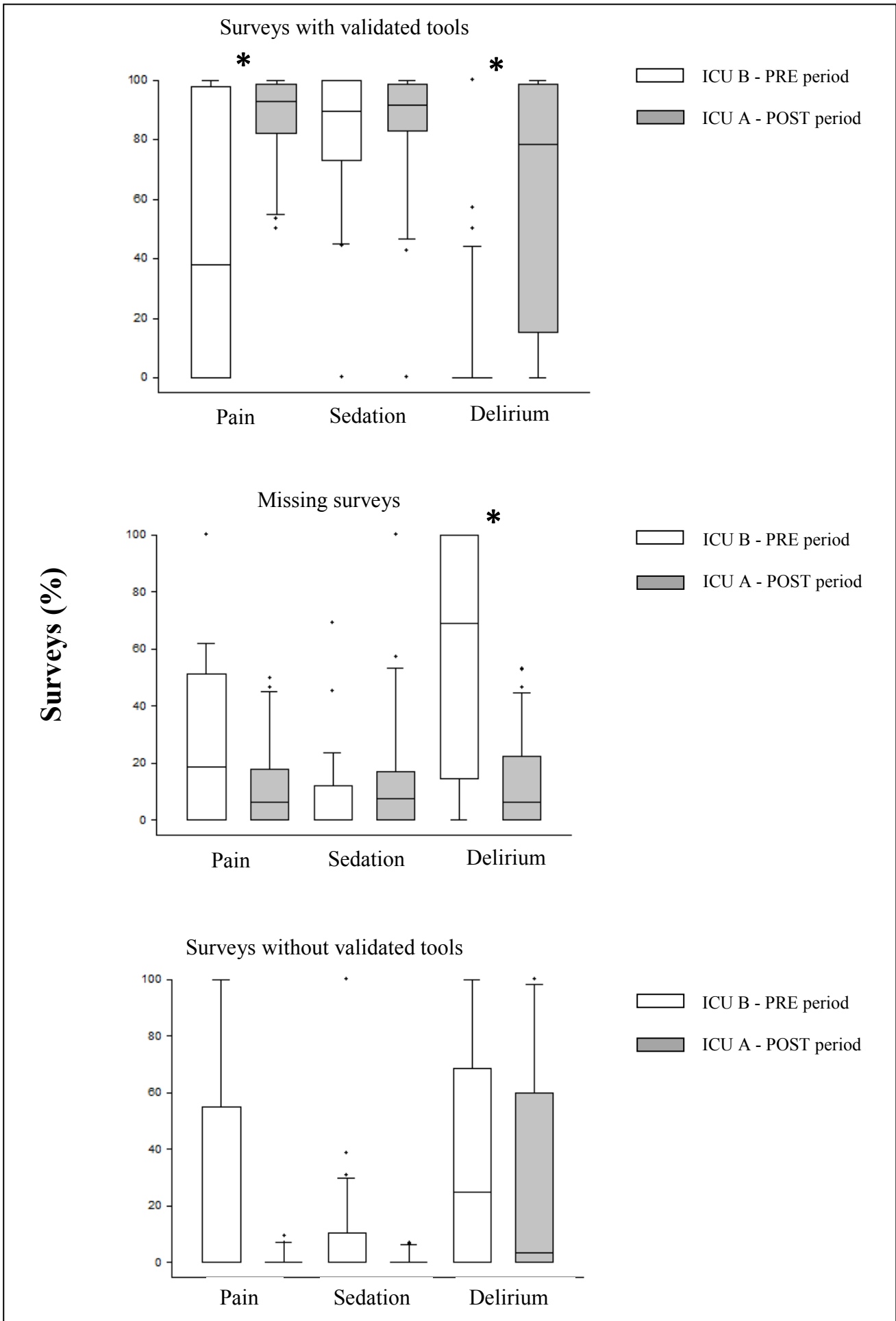
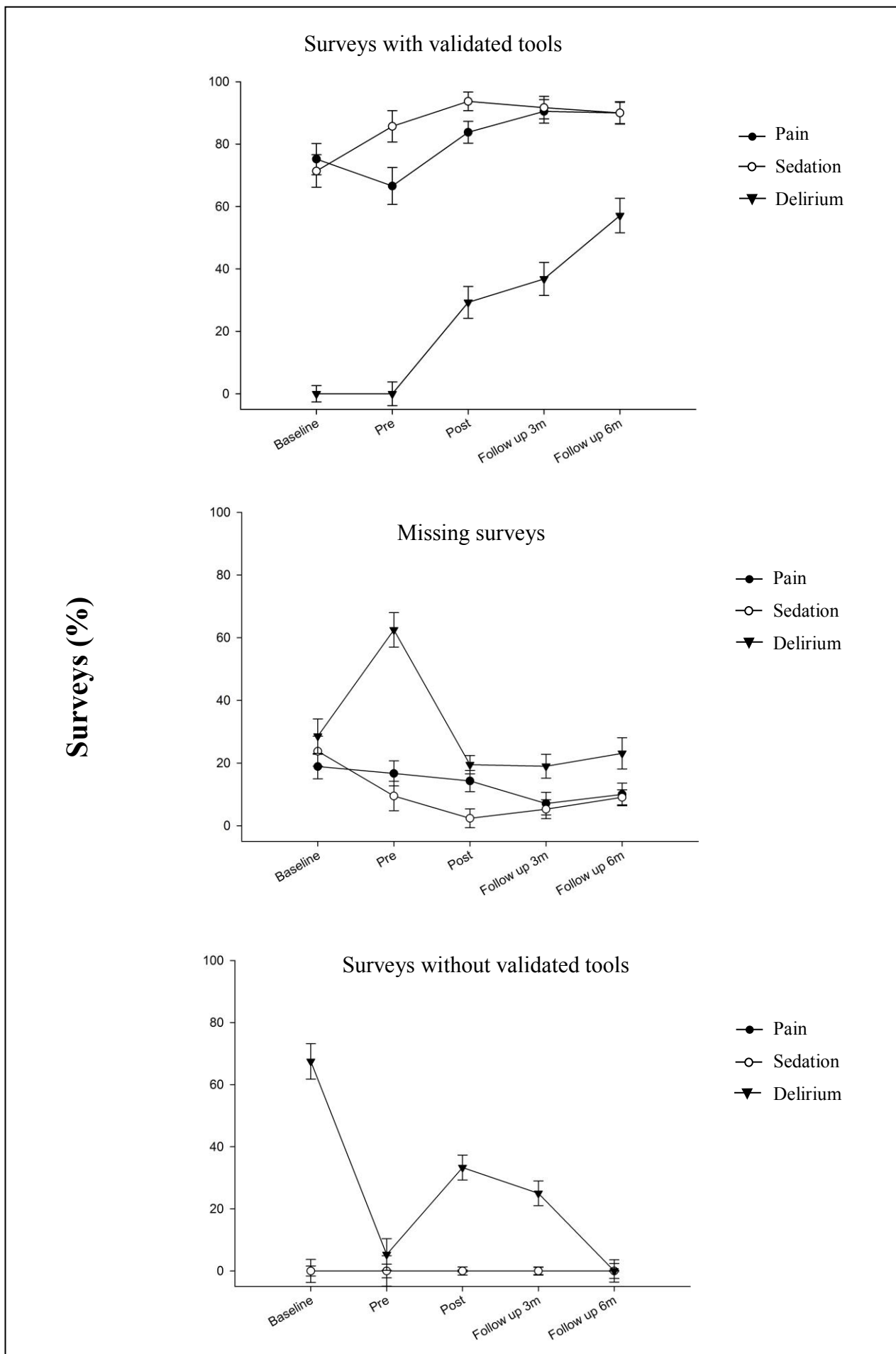


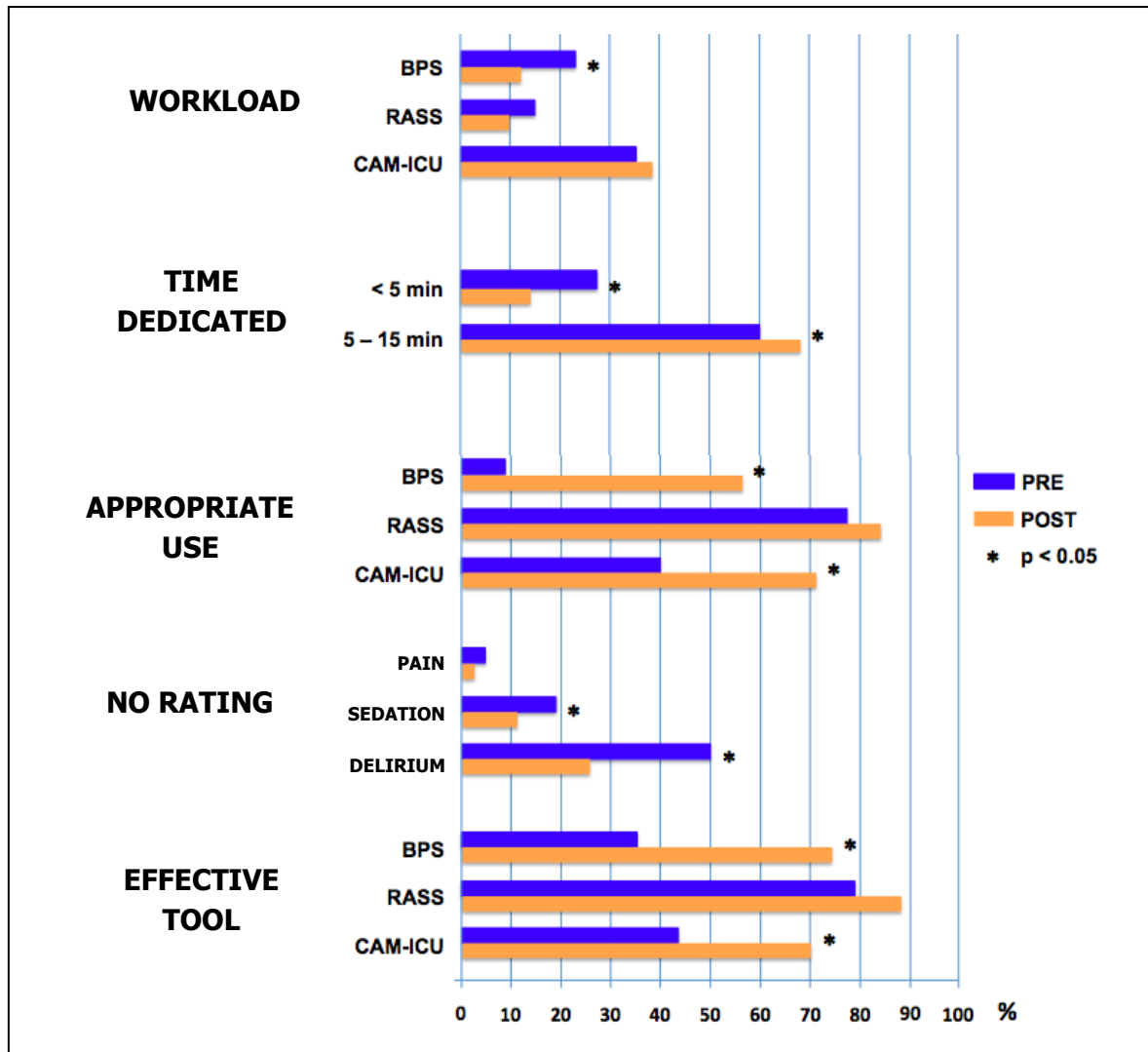
Figure 2 - Main outcome. The box plots represent the median and interquartile ranges of surveys of pain,

sedation, delirium and delirium control in the PRE period of ICU B and in the POST period of ICU A (intervention). The lines outside rectangles indicate the 95% confidence interval, and the black circles outliers. The



**Figure 3 – Summary of all survey findings.** Median and standard errors of neurological observations during the five study

**Fig. 4 – Answers to the questionnaire.**



**Figure 4 - Answers to the questionnaire.** Presentation of some of the answers given by staff nurses and physicians on the questionnaires pre and post-training. BPS, Behavioral Pain Scale; RASS, Richmond Agitation Sedation Scale; CAM-ICU, Confusion Assessment Method for Intensive Care Unit.