**Supplementary Table 1.** Characteristics of reviewed guidelines and consensus statements

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Authors** | **Year** | **Country** | **Society** | **Funding** | **Targeting audience** | **Methods** |
| Hawryluck et al (20) | 2002 | Canada | Not reported | Not mentioned | ICU health care professionals administering analgesics and sedatives to dying ICU patients | Delphi technique |
| Carlet et al (21) | 2003 | Belgium | 5th International Consensus Conference in Critical Care: Brussels, Belgium, April 2003 | ATS, ERS, ESICM, SCCM, SRLF | End-of-life care health care professionals in the ICU | Two-day conference; 10 jurors, including 1 anthropologist and 9 intensivists; presentations by 30 experts and subsequent discussions to answer 5 predetermined questions |
| Clarke et al (5) | 2003 | USA | Robert Wood Johnson Foundation Critical Care End-of-Life Peer Workgroup | The Robert Wood Johnson Foundation | Clinicians and researchers working in the ICU | In-depth literature review; consensus regarding key EOLC domains in the ICU and quality performance indicators within each domain; iterative process |
| SIAARTI (17) | 2006 | Italy | SIAARTI Bioethical Board | Not mentioned | Critical care specialists | Individuation of the objectives of the final article; literature review by team of experts, including 4 intensivists, 1 bioethical theorist, and 1 clinical psychologist; review of article draft by 39 reviewers; collecting and debating on reviewers comments; document subdivision; reviewer approval and publication (iterative group process) |
| Mularski et al. (14) | 2006 | USA | Robert Wood Johnson Foundation Critical Care End-of-Life Peer Workgroup | The Robert Wood Johnson Foundation | Health care professionals involved in palliative care of the critically ill | Informal iterative consensus process |
| Monzón Marín et al (19) | 2008 | Spain | SEMICYUC | Not mentioned | Health care professionals involved in palliative care of the critically ill | Not mentioned |
| Lanken et al (15) | 2008 | USA | ATS | Not mentioned | Members of the ATS: physicians, researchers, advanced practice nurses, respiratory therapists, and other health care professionals | Principle- and values-based approach; iterative modified group process |
| Truog et al (16) | 2008 | USA | American College of Critical Care Medicine | Not mentioned | Health care professionals involved in end-of-life care in the ICU | Not mentioned |
| Myatra et al (22) | 2014 | India | Indian Society of Critical Care Medicnie and Indian Association of Palliative Care | Not reported | Health care professionals involved in end-of-life care in the ICU | Expert committee of members of the ISCCM and IAPC was formed  to make a joint EOLC policy for the dying patients. Recommendations were formulated through a consensus  process |
| Orsi and Gristina (18) | 2017 | Italy | SIAARTI Bioethical Board | Not mentioned | Health professionals caring for dying patients in palliative and intensive care settings | Experts’ opinion |

ATS: American Thoracic Society; EOLC: end-of-life care; ERS: European Respiratory Society; ESICM: European Society of Intensive Care Medicine; ICU: intensive care unit; SEMICYUC: Spanish Society of Intensive, Critical Medicine and Coronary Units; SCCM: Society of Critical Care Medicine; SIAARTI: Società Italiana di Anestesia Analgesia Rianimazione e Terapia Intensiva; SRLF: Société de Réanimation de Langue Française; USA: United States of America.

Supplementary Table 2. Recommended quality indicators and measures for pain management at the end-of-life in the ICU

|  |  |
| --- | --- |
| **Suggested quality indicators** (5) | **Suggested quality measures** (14) |
| * Emphasizing comprehensive comfort care that is provided to the patient rather than removal of life-sustaining treatments * Instituting the use of uniform quantitative symptom assessment scales that are appropriate for communicative and non-communicative patients on a routine basis * Standardizing and following best clinical practices for symptom management; using pharmacologic and non-pharmacologic measures to maximize comfort according to patient and family preferences * Knowing and following best clinical practices for withdrawal of life support * Eliminating unnecessary tests and procedures, maintaining only intravenous catheters for symptom management when life support is being withdrawn * Minimizing noxious stimuli, such as monitors or strong lights | *Indicator definition:* Documentation of pain assessment every 4 hrs  *Numerator:* Total number of 4-hr periods during the portion of the 4-hr day that a patient is in the ICU for which pain is assessed and recorded using a quantitative rating scale  *Denominator:* Total number of 4-hr periods that a patient is in the ICU during the portion of the 24-hr day that the patient is in the ICU or under the care of the ICU nurse (unit of analysis: ICU patient days)  Intended sample: All patients admitted to the ICU for >4 hrs |
| *Indicator definition*: Treatment of pain that is assessed as >3 on a 0–10 scale or greater than mild on other scales, with reassessment after treatment  *Numerator:* Total number of 4-hr periods during the portion of the 24-hr day that a patient is in the ICU for which pain is assessed as >3 (or greater than mild) and there is a documented treatment provided and documented reassessment within 2 hrs after treatment  *Denominator:* Total number of 4-hr periods during the portion of the 24-hr day that a patient in the ICU or under the care of the ICU nurse for which pain is assessed as >3 (or greater than mild)  *Unit of analysis:* ICU patient days  *Intended sample*: All patients admitted to the ICU for >4 hrs |

ICU: intensive care unit.

Supplementary Table 3. AGREE-II domain scores for reviewed guidelines and consensus statements

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Authors** | **Year** | **Scope and purpose** | **Stakeholder involvement** | **Rigour of development** | **Clarity of presentation** | **Applicability** | **Editorial independence** | **Overall assessment** | | |
| **%** | **Recommended** | |
| Hawryluck et al (20) | 2002 | 61.1% | 48.6% | 39.6% | 79.2% | 36.5% | 79.2% | 70.8% | Yes | |
| Carlet et al (21) | 2003 | 63.9% | 47.2% | 31.3% | 50.0% | 30.2% | 41.7% | 54.2% | YWM | |
| Clarke et al (5) | 2003 | 80.6% | 47.2% | 39.1% | 59.7% | 20.8% | 72.9% | 75.0% | Yes | |
| SIAARTI (17) | 2006 | 63.9% | 62.5% | 36.5% | 69.4% | 24.0% | 22.9% | 58.3% | YWM | |
| Mularski et al (14) | 2006 | 59.7% | 40.3% | 20.8% | 50.0% | 16.7% | 66.7% | 54.2% | YWM | |
| Monzón Marín et al (19) | 2008 | 73.6% | 59.7% | 36.5% | 63.9% | 34.4% | 43.8% | 58.3% | YWM | |
| Lanken et al (15) | 2008 | 65.3% | 59.7% | 41.7% | 73.6% | 44.8% | 41.7% | 62.5% | YWM | |
| Truog et al (16) | 2008 | 47.2% | 50.0% | 27.6% | 77.8% | 27.1% | 45.8% | 62.5% | YWM | |
| Myatra SN et al (22) | 2014 | 61.9% | 57.1% | 35.7% | 57.1% | 61.9% | 100% | 62.5% | YMW | |
| Orsi and Gristina GR (18) | 2017 | 73.6% | 34.7% | 9.9% | 68.1% | 8.3% | 100.0% | 58.3% | YWM | |
| **Assessment scores for each domain in the AGREE-II quality assessment tool** | | | | | | | | | | | |
| Median (min, max) |  | 63.9%  (47.2%-80.6% | 49.3%  (34.7%-62.5%) | 36.1%  (9.9%-41.7%) | 66%  (50.0%-79.2%) | 28.6%  (8.3%-61.9%) | 56.2%  (22.9%-100.0%) | 58.3%  (54.2%-75.0%) | | - |

AGREE: Appraisal of Guidelines Research and Evaluation; SIAARTI: Società Italiana di Anestesia Analgesia Rianimazione e Terapia Intensiva; YWM: yes with modifications.

Supplementary Table 4. Summary of recommendations for end-of-life pain management in the ICU

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Recommendation** | **Hawryluck et al 2002** (20) | **Carlet et al 2003** (21) | **Clarke et al 2003** (5) | **SIAARTI 2006** (17) | **Mularski et al 2006** (14) | **Lanken et al 2008** (15) | **Truog et al 2008** (16) | **Monzón Marín et al 2008** (19) | **Myatra SN et al 2014**(22) | **Orsi and Gristina GR 2017** (18) |
| **Pain assessment** | | | | | | | | | | |
| Use of functional quantitative rating scales for pain assessment |  |  |  |  |  |  |  |  |  |  |
| Teaching the values through which individual pain is perceived in the ICU as a strategy to improve pain assessment |  |  |  |  |  |  |  |  |  |  |
| **Pain management** | | | | | | | | | | |
| Use of narcotics and BZD for management of pain and anxiety or agitation, respectively |  |  |  |  |  |  |  |  | ✓ |  |
| Ensuring the presence of family members, friends, or spiritual support; creating a peaceful ICU environment; accommodating the care plan to the patient’s spiritual and cultural beliefs |  |  |  |  |  |  |  |  | ✓ |  |
| ***Dosing, titration, and route of administration*** | | | | | | | | | | |
| The initial dosing of opioids should be adjusted depending on the previous amounts of opioids received. |  |  |  |  |  |  |  |  | ✓ |  |
| The initial dosing of opioids should be based on the patient’s age, previous alcohol or drug addiction, present clinical condition, present levels of consciousness and pain, and wishes concerning pain and sedation. |  |  |  |  |  |  |  |  |  |  |
| Sedatives and analgesics should be adjusted in response to the patient’s request or physiological or behavioral signs of pain and according to reassessment of the drug’s effect on the patient. |  |  |  |  |  |  |  |  |  |  |
| When administering opioids and sedatives, no maximum dose exists. The adequate dose is that which alleviates the patient’s pain and suffering. |  |  |  |  |  |  |  |  | ✓ |  |
| The pre-emptive administration (before pain ensues) of analgesics and sedatives is recommended. |  |  |  |  |  |  |  |  |  |  |
| A routine use of bolus over a background infusion is recommended for opioids, with boluses used for rapid effect when increasing the rate of infusion because of the re-emergence of signs or symptoms of suffering. |  |  |  |  |  |  |  |  |  |  |
| Oral opioids and sedatives, or combined oral and IV or subcutaneous administration, may be used in patients who are able to swallow. |  |  |  |  |  |  |  |  |  |  |
| In patients who do not have intravenous access, subcutaneous administration may be used, except for propofol, which can only be given IV. |  |  |  |  |  |  |  |  |  |  |
| ***Management of side effects*** | | | | | | | | | | |
| Initiation of a bowel stimulant and stool softener is recommended concomitantly with opioids, with its dose being increased as the opioid dose is escalated. |  |  |  |  |  |  |  |  |  |  |
| Nausea can be relieved by antiemetics (e.g., prochlorperazine or metoclopramide) or in persistent cases, by switching opioids. |  |  |  |  |  |  |  |  |  |  |
| Morphine is associated with a greater risk of histamine release, causing urticaria, pruritus, and flushing, which may be relieved by antihistamine therapy. |  |  |  |  |  |  |  |  |  |  |
| ***Palliative sedation and double effect principle*** | | | | | | | | | | |
| Palliative sedation is an ethical practice and should be used when there is unbearable and persistent suffering at the end of life that is refractory to analgesic medication, assuming that it has been extensively discussed with the patient (if possible) and his or her family and clearly documenting the intention of doing so. |  |  |  |  |  |  |  |  |  |  |
| The principle of double effect supports the use of narcotics or sedatives to alleviate terminal pain and suffering, even if they hasten death. |  |  |  |  |  |  |  |  | ✓ |  |
| Palliative sedation has not been shown to hasten death and thus does not need to be justified by the principle of double effect. |  |  |  |  |  |  |  |  | ✓ |  |
| ***Neuromuscular blockade*** | | | | | | | | | | |
| When withdrawing life support interventions such as mechanical ventilation, the effect of the neuromuscular blockade must wear off to allow intensivists to accurately assess patients’ pain and suffering. |  |  |  |  |  |  |  |  |  |  |
| If the neuromuscular blocks takes too long to wear off, withdrawing life support can be initiated while ensuring that the patient comfortably proceeds through the dying process. |  |  |  |  |  |  |  |  |  |  |
| ***Palliative care consultation*** | | | | | | | | | | |
| A palliative care consultation should be requested when the limits of the intensivist’s knowledge and skills have been reached. |  |  |  |  |  |  |  |  |  |  |