Development and evaluation of a systematic pain management algorithm for patients in intensive care units

Thesis for the degree of Philosophiae Doctor by

Brita Fosser Olsen

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Intensive and Postoperative Unit, Østfold Hospital Trust

Division of Emergencies and Critical Care, Oslo University Hospital

Institute of Clinical Medicine, Faculty of Medicine, University of Oslo

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Abbreviations

BPS	Behavioral Pain Scale
BPS-NI	Behavioral Pain Scale-Non Intubated
CPOT	Critical Care Pain Observation Tool
FLACC	Face, Legs, Activity, Cry, Consolability Scale
FPS	Face Pain Scale
IASP	The International Association for the Study of Pain
ICD	International Classification of Diseases
ICU	Intensive care unit
MAAS	Motor Activity Assessment Scale
NEMS	Nine Equivalents of Nursing Manpower Score
NRS	Numeric Rating Scale
NVPS	Nonverbal Pain Scale
PAIN	The Pain Assessment and Intervention Notation
RASS	Richmond Agitation–Sedation Scale
RCT	Randomized controlled trial
REK	The Regional Ethics Committee
SAPS	Simplified Acute Physiology Score
SD	Standard deviation
SPSS	Statistical Package for the Social Science
VAS	The Visual Analogue Scale
VRS	The Verbal Rating Scale

List of papers included in the thesis

This thesis is based on the following papers, which are referred to in the text by their numerals. Reprints were obtained with permission from the respective publishers.

- Paper 1** Olsen BF, Rustøen T, Sandvik L, Miaskowski C, Jacobsen M, Valeberg BT.
Development of a pain management algorithm for intensive care units.
Heart Lung. 2015;44:521–7.
- Paper 2** Olsen BF, Rustøen T, Sandvik L, Miaskowski C, Jacobsen M, Valeberg BT.
Implementation of a pain management algorithm in intensive care units and
evaluation of nurses' level of adherence with the algorithm.
Heart Lung. 2015;44:528–33.
- Paper 3** Olsen BF, Rustøen T, Sandvik L, Jacobsen M, Valeberg BT. Results of
implementing a pain management algorithm in intensive care unit patients: the
impact on pain assessment, length of stay and duration of ventilation.
J Crit Care. 2016;36:207-211.

1.0 Introduction

For many decades, intensive care unit (ICU) patients have identified pain as one of their greatest concern (1). In a survey from the early 1990s, 70% of patients recalled pain during treatment in medical and surgical ICUs, and 63% of them rated pain as moderate or severe (2). Findings from a more recent study were strikingly similar, 77% of patients from surgery ICUs recalled pain, and 64% of them rated the pain as moderate or severe (3). Despite extensive research on this issue during recent decades, pain is still reported to be one of the most distressing symptoms in ICU patients (4, 5), and one study from 2015 showed that 58% of patients perceived pain as a problem during their ICU stay (6). Unrelieved pain is a major source of stress (7, 8) and can result in chronic pain, post-traumatic stress disorder symptoms, and poorer health-related quality of life (9).

As an intensive care nurse, I was interested in getting more knowledge about pain in ICU patients. During my clinical work, I observed that nearly all patients received analgesia. However, pain was not documented systematically in the medical records. Further, many patients were unable to report pain. Consequently, it was difficult to assess pain trends, and pain management seemed to lack continuity. It was a challenge to discriminate between situations requiring sedation and those requiring analgesia, and in several cases, there was uncertainty about whether ICU patients received appropriate pain treatment.

During my work on a master's thesis, I carried out an extended literature search on pain in ICU patients. I found that simple pain assessment tools had been developed to assess pain intensity in this patient group. One of the most promising tools at that time for mechanically ventilated patients unable to self-report pain was translated into Norwegian and validated in ICU patients as a part of my master's thesis (10), but it was not implemented or used in clinical practice.

After working on my master's thesis, a question was raised: can pain management in ICU patients be improved if pain is assessed regularly and systematically with valid pain assessment tools? A survey including leaders and physicians in 54 Norwegian ICUs showed that only one pain assessment tool (i.e., visual analogue scale, VAS) was available (11). However, it could only be used in patients that were able to self-report pain, and only 32% of the respondents reported that it was used regularly. Recommendations and guidelines for pain in such patients have been developed from several organizations such as the American College of Critical Care Medicine (12), the American Pain Society (13), and the American Society for Pain Management Nursing (14). These organizations highlighted the need for regular pain assessment with validated tools for the documentation of pain intensity. Despite these recommendations and guidelines, studies found, as in the Norwegian study, that pain was not assessed regularly (15) and that valid pain assessment tools were not used in clinical practice (16).

In this PhD thesis, an algorithm that included pain assessment tools for different groups of adult ICU patients was developed. In addition, the algorithm offered a guide for both pain assessment and pain management, as in clinical practice, both aspects are important when treating pain. In the following, this algorithm is referred to as a “pain management algorithm”.

One pain assessment tool used in this algorithm (the Behavioral Pain Scale, BPS) had already been translated into Norwegian and been partly validated in ICU patients in my master's thesis (10). However, small changes in the wording of this pain assessment tool were presented in a newer study (17) compared with the original study (18). Gérald Chanques and Jean-Francois Payen were contacted, and the authors confirmed these changes, and explained that the changes had been done after comments from the users of the tool and should be considered as adjustments for a better understanding of the tool. Therefore, a new translation

of the tool was done including these changes as a part of my PhD thesis. In this translation process, the authors of the tool were consulted for clarification of some words. In addition, another pain assessment tool used in the algorithm (the Behavioral Pain Scale Non-Intubated, BPS-NI) was translated into Norwegian. Thus, in this thesis both the revised BPS and the BPS-NI were translated. Furthermore, the psychometric validation of these tools was more extensive in the PhD thesis compared to my master's thesis. The validation of the revised BPS was conducted on predetermined days with the PhD student as one of two nurses. In addition, we now chose to apply uniform statistical methods throughout the study that were more easily comparable to other validation studies.

Evaluating the level of adherence gives additional information about the usefulness of an algorithm in clinical practice. Since previous research had found barriers against, and resistance towards the use of pain assessment tools among clinicians (19-23), we identified characteristics associated with adherence. Initially we planned to document adherence to both pain assessment and management, but because of the varying quality on collected data on pain management, we were only able to evaluate adherence to pain assessment.

Finally, as the impact of implementing a pain management algorithm in adult ICU patients to our knowledge had not yet been evaluated, we felt a new study was warranted to shed light on these issues.

2.0 Background

The empirical foundation of this thesis was mainly built on research published between 1990 and 2012, as the literature review was performed in 2012 when the study was planned. All newer literature is presented in the discussion section of this thesis.

2.1. Intensive care unit patients

These patients are defined as those who have threatening or manifest acute failure in one or several vital functions, and the failure is assumed to be wholly or partially reversible (24). These patients form a complex group, including those with both medical and surgical treatments, different ages, different diagnoses, and receiving different treatments. Many of these patients are intubated and have altered levels of consciousness. Delirium affects between 50% and 80% of the patients (25-27) and causes an acute change or fluctuation in mental status, inattention, and either disorganized thinking or an altered level of consciousness. Additionally, many patients are not able to move properly because of attached equipment and high doses of sedative agents. As a result, many patients have difficulty communicating and expressing how they feel during the ICU stay. However, it is worth noting that during recent years, we have seen a trend toward more awake and cooperative ICU patients (28). Analgosedation, a strategy that manages patient pain and discomfort first, before providing sedative therapy, is associated with improved patient outcomes (i.e., shorter duration of mechanical ventilation, more rapid weaning from the ventilator, and shorter ICU stays) compared with standard sedative–hypnotic regimens (28). More awake and cooperative patients might mean that several are able to express how they feel during the ICU stay.

Many ICU patients experience pain. However, these critically ill patients report several other bothersome symptoms (29, 30). Dyspnea is frequent and is strongly associated with anxiety, especially in mechanically ventilated patients (31). Thirst is common and intense (4, 5), and is identified as a great stressor for the patients (32). Poor sleep quality

and/or insomnia are commonly encountered (33). One of the reasons might be that noise is a major problem in the ICU because monitors, infusion pumps, ventilators, dialysis machines, and health care provider conversations generate a wash of sound (34-36). In addition, many patients cannot sleep because of the lighting used at high levels at night and during treatments, examinations, and nursing activities (37). Noise and light can cause increased activation of the sympathetic nervous system, with increased adrenalin levels, and can make it harder for the patients to relax (35). Many ICU patients report anxiety, fear, tenseness, lack of control, nightmares, and loneliness (38). It seems highly unlikely that any ICU patient would present with only one or even just a few symptoms. It seems that such symptoms in ICU patients appear in clusters (39). However, in this thesis, the main focus is on pain. It is important that each of the symptoms in ICU patients such as pain should be treated and managed in the best possible way, so that the total burden of symptoms is reduced for this vulnerable and critically ill patient group.

2.2 Pain

2.2.1. Pain in general

Pain is a common and universal experience. The word *pain* comes from the Latin word *poena*, which means “punishment”. Pain has been considered to be a punishment from supreme spiritual beings for sin and evil activity. Over the years, people have discussed whether the heart or the brain was the center of sensation. The ancient Greeks demonstrated that the brain was the center of sensation (40). They also demonstrated that the brain and the peripheral nerves were intimately connected. Then, René Descartes proposed the Specificity Theory, or the “Hard wired system”. This theory transformed the perception of pain from a spiritual, mystical experience to a physical, mechanical sensation, where pain was transmitted directly from the periphery to the brain along an independent pathway. The Specificity

Theory became the dominant concept of most scientists during the middle to the latter portion of the 19th century (40). In 1965, Melzack and Wall presented the Gate Control Theory, suggesting that pain is a multidimensional experience with sensory, affective, and cognitive components, and that human thoughts, perceptions, and feelings affect the amount of pain felt from a given physical sensation (41).

The official definition of pain that has been widely accepted was formulated by a committee organized by the International Association for the Study of Pain (IASP). The definition was formulated in the 1980s and updated in 1994. IASP defines pain as “*an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage*”(42). Thus, pain is not only a direct result of tissue damage but is a more complex experience. The definition emphasizes that pain is a subjective, unpleasant experience and suggests that pain can be present only when reported by the person experiencing it. It is worth noting that IASP states that the inability to communicate verbally does not negate the possibility that an individual is experiencing pain and is in need of appropriate pain-relieving treatment (42).

2.2.2. Pain in intensive care unit patients

Several studies have evaluated pain in ICU patients. One study analyzing medical records from 230 such patients found that the incidence and intensity of pain was equal in medical patients and surgical-trauma patients (43). Pain is experienced both at rest (43) and during procedures (44, 45). Pain linked to procedures is ubiquitous, and inadequate treatment of procedural pain remains a significant problem for many ICU patients (45). The most painful and distressing procedure for adult ICU patients is being turned in bed (3, 45). Other painful experiences are the presence of chest tubes, endotracheal tube suctioning, and changing of dressings (46). Procedural pain is often described as sharp, stinging, stabbing, shooting, awful, tender, or heavy (45, 47). It is worth noting that one week after discharge

from an ICU, 82% of patients subjected to cardiac surgery reported pain as the most common traumatic memory from their ICU stay, and 6 months later, 38% still recalled pain as their most traumatic memory (48).

2.3 Pain assessment

2.3.1 Signs of pain

Many ICU patients have difficulty in communicating verbally and in expressing how they feel during their stay because of intubation, altered levels of consciousness, and delirium. Therefore, many of them are unable to self-report pain. To be able to give proper pain treatment, it is important that clinicians should know how ICU patients express pain. Evidence does not support the use of vital signs such as alterations in blood pressure (49), heart rate (49), respiratory rate (49), oxygen saturation (50), end-tidal carbon dioxide (49), or intracranial pressure (51) as single indicators of pain in such patients. Because changes in vital signs might occur along with fear, anxiety, and other psychological stressors, and many ICU patients receive medications such as vasopressors or beta-blockers that can affect these vital signs, they should be used with caution when assessing pain in this patient group (14). Skin conductance variability (52) and pupillary dilation response (53-55) have also been evaluated as indicators for pain. However, skin conductance variability needs to be evaluated in ICU patients in independent controlled studies, and pupil constriction needs to be considered when linked to fear and anxiety in the presence of severe pain. However, in ICU patients, there is a strong relationship between procedural pain and behavioral responses (18, 49, 56-58). In one study, pain-related behavior was evaluated during procedures such as being turned, central venous catheter insertion, wound drain removal, wound care, tracheal suction, and femoral sheath removal (56). Pain-related behavior was compared before and during a procedure, as well as in those procedures with and without procedural pain. Grimacing,

rigidity, wincing, shutting of eyes, verbalization, moaning, and clenching of fists were identified as specific procedural pain behaviors. Because of the strong relationship between procedural pain and behavioral responses in ICU patients, clinicians can use such responses to plan for, to implement, and to evaluate analgesic interventions in ICU patients unable to self-report pain (56).

2.3.2 Pain assessment tools

Pain assessment tools are recommended when assessing pain in ICU patients able to express pain (12-14). If they are able to self-report pain, self-report is the gold standard for assessment (14). Different unidimensional pain assessment tools exist. When using one of these tools, the patient rates his/her own pain intensity. The numeric rating scale (NRS) is a 0–10 numeric scale ranging from no pain (0) to worst possible pain (10). The visual analogue scale (VAS) is a continuous scale, usually 10 centimeters in length, ranging from no pain to worst possible pain. The verbal rating scale (VRS) is a list of adjectives describing different levels of pain intensity, and the face pain scale (FPS) is a set of photographs or drawings that illustrate facial expressions or persons experiencing different levels of pain severity (59, 60). The NRS was described as the easiest, the most accurate, the preferred, and the most discriminative tool in ICU patients able to self-report pain (61). Therefore, the NRS was included in the present study to measure pain in patients that could self-report pain.

For ICU patients unable to self-report pain, a number of behavioral tools have been developed, such as the Behavioral Pain Scale (BPS) (18), the Behavioral Pain Scale Non-Intubated (BPS-NI) (17), the Critical Care Pain Observation Tool (CPOT) (62), and the Nonverbal Pain Scale (NVPS) (63, 64). When using one of these behavioral tools, the clinicians observe the patients' behavior and use their observations to rate the patient's pain intensity.

The BPS was developed for this patient group in 2001 by Payen et al. and was one of the first behavioral pain assessment tools developed (18). It was based on a survey of ICU nurses (18), a literature review of pain scales for infants and children (65), and literature reviews of pain-related behavior (57, 66). The BPS contains three domains: facial expressions, movements of upper limbs, and compliance with ventilation. The facial expression domain was derived from a study by Prkachin (67). Movements of upper limbs and compliance with mechanical ventilation were adapted from the COMFORT scale (68) and the Harris Scale (69). Each domain in the BPS contains four descriptors rated on a 1–4 scale. The ratings for each domain are summed into a total score that can range from 3 (no pain) to 12 (worst possible pain).

The BPS-NI is an adaptation of the BPS. Chanques et al. developed it in 2009 because they lacked a tool for non-mechanically ventilated ICU patients who were unable to self-report their pain (17). The item “mechanical ventilation” in the BPS is replaced with the item “vocalization” in the BPS-NI (56). The BPS-NI contains three domains: facial expressions, movements of upper limbs, and vocalization. Each domain contains four descriptors rated on a 1–4 scale. The ratings for each domain are summed which results in a total score that can range from 3 to 12.

The CPOT was developed by Glinas et al. in 2006 (62). It contains four domains: facial expressions, body movements, muscle tension, and compliance with the ventilator for intubated patients, or vocalization for extubated patients. Each domain contains three descriptors rated on a 0–2 scale. The ratings for each domain are summed, resulting in a total score that can range from 0 to 8. The development of the CPOT was based on previously described instruments for pain assessment (18, 57, 68, 70), findings from a chart review of medical files of critically ill patients (71), and focus groups with critical care nurses and interviews with physicians (72).

Odhner et al. developed the NVPS in 2003 (63, 64). This contains five domains: face, activity (movement), guarding, physiological (vital signs), and respiratory. Each domain contains three descriptors rated on a 0–2 scale. The ratings for each domain are summed, resulting in a total score that can range from 0 to 8. The NVPS was patterned after the face, legs, activity, cry, consolability (FLACC) pain assessment tool (73) but was modified to reflect assessment components that are more appropriate to an adult population.

Compared with the other behavioral pain assessment tools, the BPS and CPOT are the tools that showed the best psychometric properties, with good evidence of validity and reliability (74-76). Because the BPS had been translated into Norwegian and validated in ICU patients as a part of my master's thesis, the BPS and BPS-NI were included in the present study.

2.4 A pain management algorithm

Several studies have implemented a single pain assessment tool (77-79) or a set of assessment tools to assess pain, agitation and delirium in ICU patients (80-82). When evaluating the impact of implementing these tools, decreases in pain and agitation (79, 81), ventilation time (77, 80, 81), length of ICU stay (77, 80), length of hospital stay (80), complications (77), nosocomial infections (81), and mortality (80) were found. In addition, more frequently charted pain assessments in the medical records (77-79, 81), and better and more dedicated analgesia (77, 78, 80-82) were found.

Even if these outcomes are positive, pain assessment tools do not include suggestions for pain management (77-82). A tool including both pain assessment and pain management was therefore warranted for use in clinical practice. A pain management algorithm is a more comprehensive approach than an assessment tool because it can guide clinicians to manage the patient's pain based on the findings from the assessment. Only one pain management algorithm for ICU patients was found that included both pain assessment tools and pain

management guidelines (83). The Pain Assessment and Intervention Notation (PAIN) algorithm was developed in the 1990s and was based on the best available evidence. The algorithm contains lists of behavioral and physiological indicators of pain that nurses could use to make inferences about a patient's pain intensity. Then, the nurses evaluated the patients for potential problems (e.g., hemodynamic and respiratory instability and/or oversedation) and made a decision about whether to administer an opioid analgesic. However, the PAIN algorithm was printed on several pages, and the nurses commented that it was too long and too complex to use in a busy ICU. In addition, this algorithm was evaluated only in patients who were able to self-report their pain. Because ICU patients are often unable to self-report pain, nurses need to infer pain through the use of valid and reliable tools that assess patients' behaviors. An algorithm that was relatively brief and simple, was easily accessible, and included valid pain assessment tools for patients who can and cannot self-report pain was needed.

Algorithms are sometimes referred to as "decision trees". A clinical algorithm can be presented as a flowchart that identifies what clinical process might follow from a patient's clinical status and response to prior treatments, thereby providing a more specific statement of priority, or what to do next if the initial treatment is not effective (84). Algorithms are rule-based deductive systems that operate with inputs, sequences, time frames, and outputs, and are intended to assist and not to limit clinical decision-making (84). The main goal of a clinical algorithm, according to Roche and Durieux, is to facilitate decisions by clinicians who cannot integrate all the published data concerning new technologies and knowledge into their daily practice (85). By providing the best treatment knowledge to clinicians, clinical algorithms intend to achieve a faster and more complete patient response to treatment than would occur with treatment uninformed by the algorithm; i.e., treatment as usual (86). Algorithms can reduce unnecessary variations in clinical practice caused by clinician

uncertainties. In addition, algorithms used successfully in the treatment of patients have been shown to improve safety and efficacy, and to save money (87-93). Therefore, using algorithms for managing acute pain might offer a safe and effective way to manage acute pain, thereby decreasing variations in practice and improving safety and satisfaction (94). Consequently, for this study, an evidence-based pain management algorithm was developed. The algorithm was relatively brief and simple, and included both pain assessment and pain management of ICU patients. The algorithm is intended to guide nurses to assess patients' pain systematically and regularly using valid pain assessment tools for patients who can and cannot self-report their pain. In addition, the algorithm provides guidance on pain treatment based on the findings from the pain assessment.

2.5 Adherence to a pain management algorithm

In medical research, adherence to treatment is the degree to which those in an intervention group adhere to protocols or continue getting the treatment (95). Evaluating the level of adherence could give information about the implementation and usefulness of the algorithm in clinical practice. Adherence in the present study is defined as the degree to which the nurses perform pain assessment as instructed by the algorithm in clinical practice. Previous research had found barriers against, and resistance towards the use of pain assessment tools among clinicians (19-23). A high degree of adherence to the algorithm would thus strengthen the study and indicate that the instrument was applicable in clinical practice. Unfortunately, it was not possible to evaluate nurses' adherence to the pain management part of the algorithm. The nurses were instructed to register pain treatment actions (i.e., increasing, decreasing or continuing already prescribed pain treatment, or the use of non-pharmacological interventions such as positioning) on pain assessment sheets developed for the present study. However, the nurses did not document pain treatment actions regularly, and therefore we lack satisfactory data to evaluate adherence to pain management

in this thesis. Furthermore, detailed data on pain treatment actions after pain assessments were not available in the medical records.

A wide range of factors can influence pain assessment and pain management in ICU patients. In the present study, these factors are divided into nurse, patient, and unit characteristics. Nurse characteristics could be barriers to effective pain management, as nurses' level of knowledge, misconceptions about pain assessment, and attitudes and resistance to using valid tools might influence their use of pain assessment tools (19-21, 23). Patient characteristics in critically ill patients could be barriers to effective pain management, as nurses reported that hemodynamic instability and patient inability to communicate were barriers considered to interfere with pain assessment and management in such patients (22). In addition, unit characteristics could be barriers, as the learning culture in the units (23) and nursing workload (22) are reported to interfere with pain assessment and management in ICU patients. Because there are barriers against using pain assessment tools in ICU patients, an evaluation of nurses' level of adherence to a pain management algorithm following its implementation was warranted.

Adherence to pain management protocols has been evaluated in several studies showing different levels of adherence (96-98). In a systematic review including 23 studies that evaluated pain assessment protocols in hospitals, the level of adherence varied from 24% to 100% (98). Educational and feedback strategies were often used in these studies and seemed to be largely effective. However, because of heterogeneity in the implementation strategies, it was not possible to recommend a preferred one (98). In another study, the use of sedative, analgesic, and neuromuscular blocking agent guidelines in mechanically ventilated ICU patients was evaluated, and the level of adherence was 58% (96). In a third study, the level of adherence to a guideline of pain assessment and intervention in internal medicine wards was 66% (97).

When implementing a pain management algorithm in clinical practice, it could be difficult to change clinicians' behavior because of barriers (19-23). Often, an active implementation is required, and in this study, a multifaceted approach, inspired by the Agency for Healthcare Research and Quality report from 2001 was used (99). This report highlights several principal education techniques for changing clinicians' behavior in clinical practice. One technique is academic detailing or "one-on-one education", including enlisting agents of change interacting with clinicians to promote particularly desirable aspects of practice that may lead to improved outcomes (100). Another technique is audit and feedback. This strategy entail the collection and review of usage data. Then, a clinician's practice and outcomes are compared with local or national benchmarks and/or evidence-based standards, and presented as feedback (101). A third technique is reminder systems, such as computerized reminders in patient records or other such forms, to prompt clinicians to provide care according to certain guidelines (102). Other techniques previously shown to be effective for changing clinicians' behavior in clinical practice include appointing local leaders or clinicians who assume a leadership role in championing regional best practices (103), as well as passive dissemination of information through lectures, conference proceedings, and printed materials (104).

2.6 Impact of implementing a pain management algorithm

It is worth noting that in the studies implementing assessment tools in ICU patients showing positive outcomes (77-82), there was a limitation that in some of these studies not all the ICU patients able to express pain (e.g., patients with delirium or cognitive impairment) were included (77-79). Other studies included tools for assessing agitation and delirium, together with the implementation of different pain assessment tools (80-82). When introducing several tools targeting different variables at the same time, it is difficult to evaluate the impact of implementing the individual pain assessment tools. No controlled study has previously measured the impact of a specific pain algorithm for pain assessment and

management in adult ICU patients throughout their stay, including not only patients able to self-report pain and to express pain behavior but also intubated and non-intubated patients. Therefore, an evaluation of implementing a pain management algorithm in ICU patients was warranted.

2.7 Theoretical framework – the Symptom Management Model

In this thesis, the Symptom Management Model was used as a theoretical framework. This model was developed at the University of California, San Francisco School of Nursing Centre for System Management, published in 1994 (105), revised in 2001 (106), and later presented in the book “Middle Range Theory for Nursing” (107) . The model (Figure 1) has three dimensions: symptom experience, symptom management strategies, and symptom outcomes. The symptom experience is described as an individual’s perception of a symptom, evaluation of the meaning of a symptom, and response to a symptom. Symptom management begins with assessment of the symptom experience from the individual’s perspective. Identifying the focus for intervention strategies follows the assessment. The goal of symptom management is to avert or delay a negative outcome. Outcomes emerge from symptom management strategies as well as from the symptom experience. Bidirectional arrows within the model indicate a simultaneous interaction among all three dimensions. In addition, the domains of person, health/illness and environment are contextual variables that influence, affect, and modify symptom experience, symptom management, and outcomes. In this way, the Symptom Management Model describes the complexity of a symptom. The model gives an overview of what a symptom is, what influence it, how a symptom can be managed, and how a symptom affects other parts of the patients’ life. The goal of the model is to advance knowledge in the field of symptom management and thereby to improve clinicians’ practice and individual’s symptom outcomes.

Figure 1 The Symptom Management Model

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The symptom focused on in this study was pain. The purpose of using the Symptom Management Model as a theoretical framework in this study was to improve the understanding of pain in ICU patients and in turn to develop and evaluate systematic pain management. The literature on pain experience reports that most ICU patients experience pain during their stay, both at rest and during different procedures. The literature on pain management strategies shows that self-reporting of pain is the gold standard for pain assessment, observation of behavior is recommended for patients unable to self-report pain, and regular and systematic pain assessment using valid pain assessment tools is recommended. However, a pain management algorithm with these properties could not be found. Therefore, for the present study, a pain management algorithm was developed and included as a symptom management strategy. The literature on pain outcomes shows that implementing tools for pain assessment was associated with positive outcomes. However, the

impact of implementing an algorithm for pain assessment and pain management has not been evaluated. Therefore, for the present study, the impact on selected outcomes after implementing the algorithm was evaluated. The literature shows that the personal domain (e.g., gender), the health/illness domain (e.g., diagnosis), and the environmental domain (e.g., nursing workload) influence, affect, and modify pain experience, pain management strategies, and pain outcomes. Therefore, available variables from these three domains were collected in this study.

3.0 Aims of the study

The overall study aim was to develop, implement, and evaluate an algorithm for systematic pain management of ICU patients; specifically:

- to develop a pain management algorithm for ICU patients and to evaluate the psychometric properties of the translated pain assessment tools used in the algorithm (Paper 1),
- to implement a pain management algorithm in ICUs and to evaluate nurses' levels of adherence to the algorithm (Paper 2), and
- to measure the impact of implementing a pain management algorithm in adult ICU patients able to express pain (Paper 3).

4.0 Methods

4.1 Design

This thesis can be defined as intervention research, which involves the development, implementation, and testing of an intervention (95). Here, a pain management algorithm for adult ICU patients is developed, implemented, and tested.

4.1.1 Development of the pain management algorithm

Earlier research was used as a basis for the development of the algorithm to ensure validity. The literature was searched in PubMed, Excerpta Medica Database (EMBASE), Cumulative Index to Nursing and Allied Health Literature (CINAHL), and Cochrane databases using different combinations of the following terms: “critical care”, “intensive”, “intensive care”, “acute care”, “critical care nursing”, “intensive care units”, “critical illness”, “critically ill patients”, “respiration artificial”, “artificial ventilation”, “sedation”, “deep sedation”, and “conscious sedation”, combined with different combinations of the terms “pain”, “pain assessment”, “pain measurement”, “pain management”, “pain experience” and “pain control”. The search was limited to papers that were published between 1990 and 2012, included participants aged ≥ 18 years, and were written in English. This search generated 1,340 articles. Abstracts from all these articles were reviewed. The complete paper was reviewed if it addressed acute pain in the ICU. Studies that included a specific pain treatment (e.g., propofol versus midazolam), specific diagnoses (e.g., chest pain), or therapies (e.g., music therapy) were excluded. In total, 128 articles were used as a background to develop a draft of the pain management algorithm.

An expert panel that reaches consensus through open discussion was used to evaluate the content validity of the algorithm. This method is called *informal consensus development* (108). Here, an expert panel consisting of ICU nurses and physicians evaluated the draft of the

algorithm. While small changes (e.g., more precise text, more succinct layout) were made to the algorithm, no changes to the content were made after the expert panel discussions.

The algorithm was pilot tested in one medical/surgical ICU. Thirty-four bedside nurses were asked to use the algorithm in the pain management of all their ICU patients. The PhD student (author of this thesis) assessed the same patient simultaneously. For each patient evaluated, all of the nurses, except one, chose the same pain assessment tool as the PhD student. After this assessment, the one nurse reevaluated the algorithm and chose the same tool as the PhD student. All the nurses chose the same pain treatment option as the PhD student. Small changes in the layout of the algorithm (e.g., larger fonts) were made after the pilot testing. During the pilot testing, it was found that the ICU nurses needed more information about pain assessment (e.g., information on different nuances in facial expressions and information about which ICU patients could not be assessed using the tools in the algorithm). Finally, the physicians who were in charge of the medical management of the patients in the three units (one medical/surgical ICU, one surgical ICU, and one postanesthesia care unit) at the two hospitals approved the algorithm.

The BPS and the BPS-NI were translated into Norwegian using a recommended back-translation procedure (95). The PhD student and two bilingual ICU nurses translated the tools into Norwegian independently. Then, they met and compared the translated tools and agreed on one Norwegian version of each of the tools. Furthermore, a third bilingual ICU nurse blinded to the original wording, back-translated the tools into English, before a comparison between the wording of the original tool and the back-translated tool were done. Thereafter, a consensus on one translated version of the BPS and one translated version of the BPS-NI was achieved among the participants. During the translation process, the authors of the two tools (i.e., Payen and Chanques) were consulted several times per mail for clarification of some of the words before they approved the back-translated version of each tool.

To test the psychometric properties of the two translated tools, interrater reliability and discriminant validity were evaluated. Interrater reliability is the degree to which two raters or observers—operating independently—assign the same ratings or values for an attribute being measured or observed (95). Pain intensity scores using the BPS and the BPS-NI assessed by two nurses were collected on predetermined days in one medical/surgical ICU at the start of the implementation period. Paired pain intensity scores were collected until 30 paired pain intensity scores with the BPS and 30 paired pain intensity scores with the BPS-NI were obtained. The nurses did not communicate with each other during these assessments. The bedside nurse and the PhD student observed each patient at rest for 1 minute before they separately scored the patient's pain intensity. Then, they turned the patient and scored his/her pain intensity during turning. Turning was chosen because it was described as the most painful and distressing procedure for adult ICU patients (3, 45). Only patients who were unable to self-report pain were assessed using the BPS (i.e., mechanically ventilated patients) or the BPS-NI (i.e., not mechanically ventilated patients). As each patient's sedation level, pain intensity, and bedside nurse could vary, data used to evaluate interrater reliability could be collected several times from the same patient.

Discriminant validity was evaluated by comparing the different pain scores during turning (a painful procedure) and at rest (low pain). Based on earlier research, we assumed that pain scores when being turned (3, 45) would be higher than pain scores at rest. Discriminant validity is an approach that involves assessing the degree to which a single method of measuring two distinct constructs yields different results (95). Pain scores from the day shift on the second day of each patient's ICU stay were used for evaluating the discriminant validity of the tools. This shift was chosen because it was the shift that involved most of the patients in the ICU.

4.1.2 Implementation of the pain management algorithm

Nurses employed at one medical/surgical ICU, one surgical ICU, and one postanesthesia care unit received 1.5 h of education in pain assessment and pain management by the PhD student. The lecture focused on the occurrence of pain in ICU patients, the importance of assessing pain, and how to assess their pain. Information was provided on the psychometric properties of the three pain assessment tools, as well as on their use. The nurses were educated about clinically meaningful cutoff points and how to make decisions about changing each patient's pain treatment. Finally, the entire algorithm and a description of the entire project were presented. All temporary staff members were given a written summary of this education. The physicians were informed about the algorithm in a meeting prior to its implementation, and they received an email giving written information about the project.

After the educational program, nurses practiced using the algorithm over a 3-week period. The PhD student and a resource person, an ICU nurse especially educated by the PhD student, were available in the units to answer questions and to provide support. During this period, it was verified that the nurses did the pain assessments and used the algorithm correctly. At the end of this practice period, initial levels of adherence to the algorithm were evaluated on a single day. Twenty patients who were enrolled on this day were included in the pilot study of adherence. These patients had an ICU stay that ranged from 1 to 11 days, for a total of 360 shifts. Pain was assessed during 281 of these shifts (i.e., an adherence rate of 78%).

After the 3-week period of practice, patients enrolled at the three units during a 22-week period were pain assessed using the different pain assessment tools in the algorithm. Each patient's pain was assessed for his/her whole ICU stay. The pain management algorithm was placed at the bedside of every patient. Written reminders on how to use the algorithm were placed at a number of sites in the three units. Written information (i.e., emails, the units'

websites) about the progression of the study was provided to the nurses. The PhD student and the resource person continued to remind the nurses to use the algorithm during the whole period. They were available to answer questions and to provide support every day and had telephone, email, and/or personal contact during the whole implementation period. All these strategies were used to reinforce the use of the algorithm.

The nurses' level of adherence to the algorithm and associations between the levels of adherence and patient and unit characteristics were evaluated, as there are several barriers against using pain assessment tools in ICU patients. Levels of adherence were evaluated the first 6 days of each patient's ICU stay, as the median length of stay was approximately 3 days. Therefore, we believe that the study result regarding nurses' level of adherence would be representative.

4.1.3 Evaluation of the impact of using the pain management algorithm

The impact of implementing the algorithm in adult ICU patients was evaluated. No study has previously measured the impact of using a specific pain algorithm for pain assessment and management in adult ICU patients throughout their ICU stay, including not only patients able to self-report pain, but also intubated and non-intubated patients able to express pain behavior. A pre/postintervention design was used to evaluate the impact of the intervention. In such a design—also called a before–after design—data are collected from research subjects both before and after introducing an intervention (95). In this study, outcomes in a period after implementing the algorithm (intervention group) was compared with outcomes in a period the previous year (control group). Pain assessments, ventilation time, length of ICU stay, length of hospital stay, use of analgesic and sedative medications, and the incidence of agitation events were chosen as outcome variables, as these variables were available in medical records and were found to be associated with implementing assessment tools in similar previous studies (77-82).

4.2 Patient recruitment

Patients were recruited from one medical/surgical ICU at Østfold Hospital Trust, and one surgical ICU and one postanesthesia care unit at Oslo University Hospital. The following inclusion criteria were used: patients needed to be ≥ 18 years of age and able to self-report pain or to express pain behavior. Patients were excluded if they could not self-report pain or express pain behavior (e.g., if they were quadriplegic, receiving neuromuscular blockade or paralyzing drugs, or being investigated for brain death). Patients were recruited in a period in 2011 (control group) and in the same period in 2012 (intervention group), to cover the same part of the year.

A sample size calculation was performed using the variable “ventilation time”. This variable was chosen because it has been shown to be associated with implementing pain assessment tools or protocols for the evaluation and management of pain, sedation, and delirium (77, 80, 81). In a study by Chanques et al. (81), the median ventilation time was 120 and 65 h in the control group and the intervention group, respectively, and the interquartile ranges (IQR) were 264 and 168 h, respectively. In normally distributed data, the standard deviation (SD) is $0.694 \times \text{IQR}$. The SDs of ventilation time in Chanques’ study were 183 and 117, respectively. On this background, we assumed that in the present study, the mean difference in mean ventilation time between the groups would at least be 55 h, and the SD would be ± 150 h in each group. To have 80% test power, at least 117 mechanically ventilated patients needed to be included in each period. Because we included both mechanically ventilated and non-mechanically ventilated patients in the study, data from all ICU patients enrolled were collected until at least 117 of the included patients in each group had been mechanically ventilated.

4.3 Data collection

Data about ventilation status, ventilator time, length of ICU stay, hospital length of stay, age, gender, disease severity, and diagnosis of the ICU patient, in addition to nursing workload were collected from the hospital information database. Data about analgesics, sedative medications, and sedation levels were collected from the daily ICU schemas. All these data were collected from both the intervention and the control groups. Pain assessment scores were collected from pain assessment sheets developed for the project from patients in the intervention group. In addition, the daily ICU schemas were searched for pain assessment scores in both the intervention and the control groups.

4.4 Instruments

Three different pain assessment tools were used in the algorithm, to cover different groups of ICU patients.

The numeric rating scale (NRS) was used to measure pain intensity when patients were able to self-report pain. When using the NRS, patients rated their pain intensity on a scale from 0 (no pain) to 10 (worst possible pain). The negative predictive value for the NRS, calculated from true or false negatives and defined by the real or false absence of pain, is reported at 90% (61) . The success rate for the NRS (defined by obtaining a response, such as the ability to point at any number on the NRS) was 91% when ratings of pain intensity at enrollment versus pain intensity after analgesic administration, or pain intensity after a nociceptive procedure were compared (61).

The Behavioral Pain Scale (BPS) was used to measure pain intensity when patients were mechanically ventilated and unable to self-report their pain. The BPS contains three domains (i.e., facial expressions, movements of upper limbs, compliance with ventilation). Each domain contains four descriptors rated on a 1–4 scale. The ratings for each domain are summed into a total score that can range from 3 (no pain) to 12 (worst possible pain). The

BPS has been evaluated in more than 500 medical, surgical, trauma, neurological, and emergency department patients (18, 58, 81, 109-112) and in ICU patients with different levels of sedation (113). In addition, compared with other behavioral assessment tools, the BPS was shown to have among the best psychometric properties (74-76). Cronbach's α coefficients for the BPS ranged from 0.63 to 0.72 in different samples of ICU patients (58, 109, 111, 113). Interrater reliability (kappa coefficient) for the BPS was satisfactory (i.e., a range of 0.67–0.83 (18, 110, 113)) with intraclass correlation coefficients that ranged from 0.46 to 0.95 (58, 111). Criterion validity was demonstrated by a Spearman correlation coefficient of 0.67 ($p < .001$) between BPS scores and the patient's self-report of pain intensity during a painful procedure (113). Discriminant validity was supported by significant increases in BPS scores following nociceptive procedures, compared with BPS scores at rest or following non-nociceptive procedures (18, 58, 109, 111-113). In addition, in a survey, most clinicians (86% of 28 participants) were satisfied with the tool's ease of use, and all agreed that it took a minimal amount of time to complete (18).

The Behavioral Pain Scale-Non Intubated (BPS-NI) was used to measure pain intensity when patients were not mechanically ventilated but were unable to self-report their pain. The BPS-NI contains three domains (facial expressions, movements of upper limbs, and vocalization). Each domain contains four descriptors rated on a 1–4 scale. The ratings for each domain are summed, which results in a total score that can range from 3 (no pain) to 12 (worst possible pain). The BPS-NI has been validated in one study including 30 adult ICU patients with a medical or surgical diagnosis (17). The Cronbach's α coefficient was 0.79, and the kappa coefficients ranged from 0.82 to 0.89. The discriminant validity of the BPS-NI was supported by increases in median BPS-NI scores measured at rest (i.e., 3) and during nociceptive procedures (i.e., 6, $p < .001$). Of note, median BPS-NI values did not increase significantly following non-nociceptive procedures (i.e., 3 versus 3, $p = .11$).

The Motor Activity Assessment Scale (MAAS) (114) or Richmond Agitation–Sedation Scale (RASS) (115) was used to measure patients’ sedation level, depending on what sedation scale the units in the study used. The MAAS has been found to be valid and reliable for use with mechanically ventilated ICU patients (114). MAAS scores can range from 0 (unresponsive) to 6 (dangerous agitation), and 3 denotes a calm and cooperative patient. The RASS demonstrated excellent interrater reliability, and criteria, construct, and face validity (115). RASS scores can range from –5 (unarousable) to +4 (combative), and 0 denotes an alert and calm patient.

The Simplified Acute Physiology Score (SAPS II) (116) was used to measure the patients’ disease severity. Goodness-of-fit tests have indicated that SAPS II provides an accurate estimate of the risk of death without having to specify a primary diagnosis (116). SAPS is a widely used severity score and mortality estimation tool and is calculated during the first 24 h of the ICU stay. The SAPS includes 17 variables: age, type of admission, 12 physiological variables (e.g., vital signs, and oxygenation status), and three underlying disease variables (metastatic cancer, acquired immune deficiency syndrome (AIDS), and hematologic malignancy). The scoring range is 0–163, with higher scores indicating higher disease severity and a higher risk of in-hospital mortality.

The Nine Equivalent of Nursing Manpower Score (NEMS) (117) was used to measure nurses’ workload. The intraclass correlation coefficient for the NEMS is reported at 0.92 (117). NEMS includes nine variables: basic monitoring, intravenous medication, mechanical ventilator support, supplementary ventilator care, single vasoactive medication, multiple vasoactive medications, dialysis techniques, specific interventions in the ICU, and specific interventions outside the ICU. The scoring range is from 0 (a low workload) to 66 (a very high workload).

The International Classification of Diseases (ICD-10 codes) was used to measure the diagnosis of the patients. ICD-10 codes are the standard diagnostic tool for epidemiology, health management, and clinical purposes. The codes are divided into 22 main groups of diagnosis, with several subgroups.

4.5 Statistical analysis

In this study, all patient and unit characteristics are listed using descriptive statistics. Diagnostic categories representing fewer than 5% of the patients were merged into the category “other diagnoses”. The mean daily nursing workload (NEMS) score was calculated for each ICU patient. Ventilator time was calculated for patients receiving mechanical ventilation or noninvasive ventilation. Sedation levels were divided into no-agitation events (i.e., RASS $\leq$ 1 or MAAS $\leq$ 4), and agitation events (i.e., RASS $>$ 1 or MAAS $>$ 4) (81, 114, 115).

Throughout the study, a p -value of $< .05$ was considered to be statistically significant. All statistical analyses were performed using IBM SPSS Statistics for Windows, version 21.0 (IBM Corp., Armonk, NY, USA), with the exception of the weighted kappa analysis, which was performed using Stata version 11.1 (StataCorp LP, College Station, TX, USA). Different methodological approaches were used to evaluate the study aims.

4.5.1 Paper 1

When evaluating the interrater reliability of the two tools translated into Norwegian, data from patients in the intervention group (from predetermined days in one medical/surgical ICU at the start of the implementation period) were analyzed. Weighted kappa, percentage agreements, and agreements within 1 scale point were used to compare pain intensity scores between bedside nurses and the PhD student. A weighted kappa value of < 0.20 was defined as poor, 0.21–0.40 as fair, 0.41–0.60 as moderate, 0.61–0.80 as good, and 0.81–1.00 as very

good (118). When evaluating discriminant validity, data from patients in the intervention group (from the day shift on the second day of each patient's ICU stay) were analyzed. Descriptive statistics and Wilcoxon signed-rank tests were used to compare pain intensity scores at rest and pain intensity scores when being turned in bed.

4.5.2 Paper 2

We studied level of nurses' adherence to the algorithm by analyzing data from the first six days of each patients stay in the ICU. When evaluating the level of adherence to the algorithm regarding if the patients were pain assessed according to the algorithm, data from the first 6 days of each patient's ICU stay in the intervention group were analyzed. Before the analysis, three patient and unit characteristics were divided into categorical variables. SAPS and NEMS were categorized into quartiles to examine differences among risk groups and to enable a comparison of our findings with those from a similar study (81). Patient age was divided into four age groups: 18–39, 40–59, 60–79, and 80–99 years.

The level of adherence to the algorithm was defined as the total number of pain scores recorded during the first 6 days of the patients' ICU stay, divided by the total number of pain scores that should have been recorded based on the number of shifts that they were cared for in the ICU, multiplied by 100. The level of adherence was calculated for each patient and could range from 0% to 100%.

To determine whether nurses' level of adherence was associated with patient or unit characteristics, the levels of adherence were correlated with patients' age, gender, diagnosis, ventilation status, severity of disease, nursing workload, and shift. Paired sample *t* tests, independent sample *t* tests, and analyses of variance with Bonferroni correction were used to evaluate associations between level of adherence and demographic and clinical characteristics of the patients, as well as unit characteristics.

Variables with p values of $< .05$ in bivariate analyses were included simultaneously as independent variables in a multivariate regression model to predict adherence. Shift was not included in the multivariate analysis because the same patients were pain assessed every shift. A p value of $< .05$ was considered statistically significant. Categorical pairwise contrasts were evaluated using Bonferroni correction. Therefore, a p -value of $< .017$ for characteristics with three dummy coded variables and a p value of $< .01$ for characteristics with five dummy coded variables were considered statistically significant.

4.5.3 Paper 3

When evaluating the impact of the intervention, data from patients in both the control group and the intervention group were analyzed. Data from the first 6 days of each patient's ICU stay (medications, sedation level, and pain assessments) or the whole ICU stay (ventilation time, length of ICU stay, and length of hospital stay) were analyzed. An intention to treat analysis (95) was used to avoid selection biases and faulty inferences about treatment effects. This analysis assumes that each person received the intervention to which he/she was assigned. Patients in the intervention group and patients in the control group were compared, using chi-squared tests for categorical variables and t tests or Mann–Whitney nonparametric U tests for continuous variables. Outcome variables that differed significantly between the two groups were included in a regression analyses to control for confounding variables. Linear regression analysis was performed with the outcome variables as dependent variables (ventilation time and length of ICU stay), and with “group” and confounders (i.e., baseline variables that differed significantly between the control group and the intervention group) as independent variables. The distribution of the outcome variables length of ICU stay and ventilation time was quite skewed and was log-transformed before regression analysis.

Only data regarding analgesic and sedative medications used in more than 5% of patients was analyzed when evaluating the impact of the intervention (119). Median daily

dosages of each medication were calculated for each ICU patient. Doses of ketobemidone (120), morphine (120), oxycodone (120), fentanyl (121), remifentanyl (121), and alfentanil (121) were converted into intravenous morphine equianalgesic dosages.

4.6 Ethical considerations

According to our Regional Ethics Committee (REK), informed consent from the ICU patients was not required, because the data used in this study are anonymous (2011/2582D). According to section § 13 in the Norwegian Act on Medical and Health Research (122), consent must be obtained from participants in medical and health research. The consent must be informed, voluntary, expressed, and documented, and should be based on specific information about a concrete research project. Because ICU patients are critically ill and often unconscious when they are enrolled in the unit, most of them are not able to give consent at enrollment. Collecting consent retrospectively from ICU patients is also difficult, as many ICU patients develop mental handicaps, are on prolonged convalescence, are still critically ill, or even die shortly after ICU discharge. Collecting consent in the present study could have produced a big dropout, induced selection bias, and threatened the internal validity of the study (123).

According to section § 20 in the Norwegian Act on Medical and Health Research (122), consent is not required for research on anonymous data. Therefore, resource persons employed at the respective units collected and anonymized the data. Patients' names and personal identity numbers were removed and replaced with "Patient 1", "Patient 2", and so on. Data were stored according to the hospitals' procedures. Finally, the leadership at the hospitals participating in the study approved this study, and it was registered at <https://clinicaltrials.gov> (NCT01599663).

Table 1. Overview of study aim, study design, methods, and data collection

Paper	Aims	Study design and methods	Data collection
Paper 1	To develop a pain management algorithm for ICU patients and to evaluate the psychometric properties of the translated pain assessment tools used in the algorithm.	Literature review, expert panel, and pilot testing. Back-translation procedure. Interrater reliability between two nurses. Discriminant validity between turning and rest.	Gender, age, ICD-10 codes, SAPS, ventilation status, NEMS. Paired BPS and BPS-NI scores. BPS and BPS-NI scores at rest and during turning. Data were collected from the intervention group.
Paper 2	To implement a pain management algorithm in ICUs and to evaluate nurses' levels of adherence to the algorithm.	Education and a practice period over 3 weeks. Multivariate regression analysis.	Gender, age ICD-10 codes, SAPS, ventilation status, NEMS. NRS, BPS, BPS-NI scores. Data were collected from the intervention group.
Paper 3	To measure the impact of implementing a pain management algorithm in adult ICU patients able to express pain.	Pre- and postintervention design. A period after implementing the algorithm (intervention group) was compared with a similar period the previous year (control group).	Gender, age ICD-10 codes, SAPS, ventilation status, NEMS. Ventilation time, ICU length of stay, Hospital length of stay, analgesic and sedative medications, MAAS/RASS NRS, BPS, BPS-NI scores. Data were collected from the control and intervention groups.

5.0 Results

5.1 Participants

5.1.1 Nurses' participation

Overall, 217 nurses (94%) participated in the educational program prior to the implementation of the pain management algorithm. Nurses who did not participate in the educational program ($n = 15$) were given a written summary of the lecture.

5.1.2 Patients

Participants in this study were recruited from two hospitals during two periods: 2011 (control group, $n = 252$) and 2012 (intervention group, $n = 398$). To evaluate the different study aims, data from different samples were used in the three papers.

To evaluate interrater reliability for the BPS, 30 paired pain assessments were used from 11 ICU patients in the intervention group. The mean age of these patients was 61 years ($SD = 15$), 73% were male, and 64% were medical patients. Overall, 87% received analgesics, and 70% received sedatives. To evaluate interrater reliability for the BPS-NI, 30 paired pain assessments from 17 ICU patients from the intervention group were used. The mean age on these patients was 64 years ($SD = 14$), 59% were male, and 71% were medical patients. Overall, 60% received analgesics, and 20% received sedatives.

When evaluating the discriminant validity of the BPS and the BPS-NI, patients from the intervention group who were assessed and treated according to the algorithm were included ($n = 285$). The mean age of these patients was 59 years ($SD = 19$), 67% were male, and the most common diagnosis was “injury, poisoning, or certain other consequences of external causes” (33%) (ICD SS00-T98). More than half of the patients (52%) received mechanical ventilation. However, on the shift when data were collected, 93 of these patients

had no pain scores both at rest and during turning, and 81 patients had only documented NRS scores. Therefore, the analysis of discriminant validity was based on 111 patients: 82 patients with BPS scores, and 29 patients with BPS-NI scores.

When evaluating the level of adherence to the algorithm, patients from the intervention group who were assessed and treated according to the algorithm were included ($n = 285$). It is worth noting that a total of 461 patients were hospitalized during the intervention period. Of these eligible patients, 63 did not fulfill the inclusion criteria, because their ICU stay was < 24 h ($n = 56$) or they were not able to express pain ($n = 4$) or were aged < 18 years ($n = 3$). For the remaining 113 patients, documentation of pain assessments was not available. Compared with the 285 patients who had documentation that the algorithm was initiated, these patients had a significantly shorter length of stay (mean 2.4 vs. 6.1 days, $p < .001$), and a higher percentage had spontaneous ventilation (80.0% vs. 48.1%, $p < .001$) and a lower NEMS score per day (27.8 vs. 32.0, $p = .001$).

To evaluate the impact of the algorithm, patients from the control group ($n = 252$) and from the intervention group ($n = 398$) were included. In this part of the study, the intervention group included patients who had available documentation on pain assessment ($n = 285$) and patients for whom documentation of pain assessment was not available ($n = 113$). The intervention group and the control group were similar regarding gender, age, diagnoses, and use of ventilation. Patients in the intervention group had significantly lower disease severity (mean SAPS 36 versus 40, $p = .02$) and lower nursing workload (mean NEMS 31 versus 36, $p < .001$) compared with the control group.

5.2 Summary of papers – main results

The following pages summarize the main findings from each study in the thesis. Each published paper describes the results in greater detail.

5.2.1 Paper 1

In Paper 1, a pain management algorithm (Figure 2) for adult ICU patients was developed to assist nurses to assess and manage pain systematically.

Figure 2 The Pain Management Algorithm

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The pain management algorithm guided nurses to assess patients' pain at least once per shift, both at rest and during turning, throughout their ICU stay. Pain assessment tools were used for patients able to self-report pain and patients able to express pain behavior, both intubated and non-intubated patients. NRS was used when patients could self-report pain (61). The BPS was used when patients received mechanical ventilation and were unable to self-report pain (18). The BPS-NI was used in non-intubated patients who were unable to self-report pain (17). An NRS score of > 3 , (81, 125), a BPS-score of > 5 (18, 81), and a BPS-NI score of > 5 (17) were defined as indicating pain events. If the pain intensity score was higher than the specified cutoff point (i.e., a pain event), the nurses were directed to consider increasing pain treatment. If the pain intensity score was less than the cutoff point (i.e., not a pain event), the nurses were encouraged to consider either decreasing or continuing pain treatment. Pain treatments included analgesics specified by each patient's prescription or non-pharmacologic interventions such as changing the patient's position.

In the psychometric evaluation of the translated tools, the weighted kappa values for the BPS indicated very good interrater reliability at rest (i.e., 1.00). Because all of the individual pain intensity scores were the same, a weighted kappa could not be calculated for the item "compliance with ventilation" at rest. During turning, the weighted kappa values indicated moderate to good interrater reliability (range 0.46–0.79). The weighted kappa values for the BPS-NI indicated fair to good interrater reliability at rest (range 0.21–0.63). The item "facial expression at rest" had the lowest interrater reliability (0.21). During turning, the weighted kappa values indicated moderate to good interrater reliability (range 0.38–0.63). Regarding the discriminant validity of the two tools, both the BPS and the BPS-NI showed statistically significantly higher subscale and total pain scores during turning compared with being at rest.

5.2.2 Paper 2

The 285 patients who were pain assessed with the algorithm were in the ICU for a total of 2832 shifts, equated with 5664 pain assessments (i.e., each patient had pain assessed at rest and during turning in every shift). A total of 4223 pain assessments was recorded, which equates to an overall mean adherence rate of 74.6%.

Level of adherence were significantly lower in evening shifts (71.2%, $t = 3.44$, $p = .001$) and night shifts (71.4%, $t = 3.21$, $p = .002$) compared with day shifts (77.7%). Patients in the 1st and 4th NEMS quartiles were assessed significantly less frequently than patients in the 3rd NEMS quartile ($p = .003$). The analysis showed that male patients were assessed for pain significantly less frequently than female patients. Patients with “injury, poisoning, or certain other consequences of external causes”, “other diagnosis”, and “diseases of the digestive system” were pain assessed significantly less frequently than patients with “diseases of the respiratory system”. Patients with a lower severity of disease (i.e., lower SAPS) were pain assessed significantly less frequently than patients with a higher severity of disease. No significant differences in the levels of adherence were found between ventilated and non-ventilated patients or among different age groups.

In the multivariate regression analysis, only gender and diagnosis were significantly associated with the level of adherence. Adherence rates were lower for male patients compared to female patients. In addition, compared with patients with diseases of the respiratory system, patients with “injury, poisoning and certain other consequences of external causes” had a significantly lower level of adherence. The overall model explained 16.2% of the variance in the level of adherence, and the diagnosis of the patients made the largest unique contribution to the explained variance (4.4%).

5.2.3 Paper 3

In the intervention group, a total of 4223 pain assessments using NRS, BPS, or BPS-NI were recorded for a total of 2832 shifts, which should have equated to 5664 assessments if each patient had been pain assessed at rest and during turning in every shift (i.e., 74.6% adherence). In the control group, a total of 370 pain assessments using NRS were recorded for 2542 shifts, which should have equated to 5084 pain assessments (i.e., 7.3% adherence).

Compared with the control group (i.e., patients whose pain was not assessed with the algorithm), patients in the intervention group (i.e., whose pain was assessed with the algorithm) had shorter ventilation times (median 46 h versus 79 h, $p = .01$), shorter ICU length of stay (median 2.6 days versus 3.0 days, $p = .04$), and fewer agitation events (3% versus 6%, $p = .02$). When adjusting for confounding variables, the SAPS outcome was included as an independent variable in the regression analysis. Because the NEMS might be considered as an effect outcome in this study, it was not included as an independent variable in the regression analyses. When adjusting for SAPS using linear regression analyses, the differences between the two groups remained significant for ventilation time ($p = .01$) and ICU length of stay ($p = .03$). The use of analgesics and sedatives was similar in the two groups. In all, 96% in the intervention group and 97% in the control group received analgesics, and 78% in the intervention group and 81% in the control group received sedatives. As regards dosages of the medications, the use of epidural Fentanyl increased significantly (median 310 μg versus 223 μg , $p = .01$), and the use of intravenous Midazolam decreased significantly (77 mg versus 105 mg, $p = .03$) in the intervention group compared with the control group.

6.0 Discussion

This section will be organized into two main parts: a methodological discussion and a general discussion about the main findings. In addition, at the end of the discussion, the use of the theoretical framework will be discussed.

6.1 Methodological discussion

6.1.1 Development of the pain management algorithm

The development of a pain management algorithm was considered to be appropriate for several reasons. First, this algorithm included suggestions about both pain assessment and pain management in ICU patients, and in clinical practice, both aspects are important when treating pain. Second, an effective algorithm organizes information and knowledge from diverse sources into an easily accessible format (126). In this way, pain assessment and management can be based on the best evidence. Third, the algorithm standardized interventions, so unnecessary variations in clinical practice could decrease, as every ICU nurse used the same tools to assess pain and the same cutoff points to treat pain. In addition, the algorithm might have contributed to the clinicians' achieving a similar understanding of pain and pain management. Having a shared acknowledgment of when ICU patients have pain could enhance the communication of patients' pain within the various ICUs. Additionally, using an algorithm makes it easier to replicate the intervention in other studies, and in this way, the study results can be more generalized.

To ensure the validity of the algorithm, earlier research papers were searched thoroughly and used as a basis for the development. It was a strength of this project that the search generated a huge amount of research about pain and ICU patients, and could be used as a basis for the development of the algorithm.

Thereafter, a draft of the algorithm was made. This draft was presented to a group of experts, and they reached consensus through open discussion. This method has some limitations. First, because a group of individuals think that a practice is beneficial does not ensure that it actually is. Second, the lack of explicit methods raises questions about how the consensus was reached. Third, the absence of documented methods makes it difficult for readers to judge whether the development of the algorithm was influenced by scientific evidence or whether the evidence was overlooked because of expert panel biases. However, the method is relatively cheap, easy, fast, and free of complex analytic procedures. To ensure that the individuals of the expert group had different clinical experience, both ICU nurses and physicians from two different hospitals were included. Therefore, we consider the method to have been appropriate.

In the pilot testing of the algorithm, nurses were asked to use it in their care of the ICU patients, and the PhD student assessed the same patients simultaneously. All the nurses, except one, chose the same pain assessment tool as the PhD student, and all nurses chose the same pain treatment option as the PhD student. Even though the pilot test was not extensive, its findings suggested that the algorithm would be useful in clinical practice.

There are several methods for language translation (127). Here, a recommended back-translation procedure was used (95), in which an instrument is translated from the original source language into a target language and then translated back into the source language by translators who are unfamiliar with the original wording. As many words and concepts used in the ICU are specialized, nurses who were familiar with the ICU context were used as translators to avoid misinterpretations. We assume that the close collaboration with the authors of the tools during the translation process, the choice of translators and the back-translation procedure were successful, as only subtle nuances in some of the words were

discussed before the translators agreed on a common Norwegian version of each tool, and the two authors of the BPS and the BPS-NI approved the back-translated versions of each tool.

The translated tools were tested for reliability and validity, as recommended after translation of the tools (95, 128). It might be a limitation that the interrater reliability by paired pain assessment scores was evaluated at the start of the implementation period when the nurses were far from experts in using the tools. In similar studies, specially trained researchers or specialists evaluated pain (58, 112). Pain scores at rest and during turning were compared by evaluating the discriminant validity of the tools. We assume that using turning as a painful procedure was appropriate, as turning is described as the most painful procedure for adult ICU patients (3, 45, 129).

6.1.2 Implementation of the pain management algorithm

The present study used a multifaceted approach inspired by the Agency for Healthcare Research and Quality Report from 2001 (99) to implement the algorithm in the three participating units. During the 1.5 h education prior to the study, the nurses had the opportunity to ask questions and to discuss relevant topics. This education and having the algorithm at the bedside of every ICU patient enabled passive dissemination of information to the nurses (104). The use of resource persons interacting with nurses in clinical practice during the 3-week practice period gave opportunity to guide the nurses in a one-to-one situation (100), in addition to championing best practice (103). Written information (i.e., e-mails to clinicians and each unit's website) and written reminders at several sites in the units were used as a reminder system to prompt nurses to manage pain according to the algorithm (102). The multifaceted implementation strategy used in this study was feasible in an active practice setting as it was not expensive or time-consuming. However, audit and feedback—where usage data are collected and reviewed, each clinician's practice is compared with evidence-based standards, and the findings are presented as feedback to the clinicians—were

not used extensively. One exception was that the level of adherence to the algorithm was evaluated and presented to the nurses once at the end of the implementation process. As audit and feedback generally leads to potentially important improvements in professional practice (101), the somewhat limited use of these factors might have been a weakness in the study. One may speculate if evaluating data about the documentation of pain treatment actions and presenting these findings to the nurses during the intervention period could have made the evaluation of level of adherence regarding pain management possible in the present study.

The level of adherence to the algorithm during the intervention period was evaluated to see whether the clinical practice changed as intended after the implementation. It would have been interesting to evaluate the level of adherence after some months, as this seems to decrease over time (130). However, this was not done in the present study. It could be a shortcoming that the level of adherence was only evaluated during the first 6 days of the ICU stay and not for the entire stay. However, as the median length of stay was 3.2 days, and most of the patients (205/285 patients) were enrolled for < 6 days, we assume that the analysis regarding nurses' level of adherence is representative. Another shortcoming is the lack of evaluating the level of adherence regarding pain management, and not simply regarding pain assessment. Interestingly, pain management and the level of adherence to a sedative, analgesic, and neuromuscular blocking agent guideline was evaluated in a similar study (96). One explanation for this could be that in this study, specific doses of medications was used as treatment actions in the guideline, and level of adherence was measured to which degree physicians chose a given drug from the guideline, and nurses administered the prescribed medications. This type of evaluation was not possible in the present study, as no specific pain treatment actions was given in the algorithm, only to increase, decrease or continue already prescribed pain treatment. Moreover, because detailed data on pain treatment actions after pain assessment were missing due to lack of compliance, an evaluation of whether nurses

used the algorithm to increase, to decrease, or to continue each patient's prescribed medications after pain assessment was not possible in the present study. The present data do not allow any conclusion as to why the nurses omitted the registration of changes in medications. However, reluctance to register the same data twice might be one explanation for the missing data in the present study as medications are already documented in other files than the pain assessment sheets developed for the study.

6.1.3 Evaluation of the impact of using the pain management algorithm

To evaluate the impact of the algorithm, a pre/postintervention design was used. Outcomes from patients from a period after implementing the algorithm (the intervention group) were compared with patients from the same period the prior year (the control group). We chose the same period of the year when comparing the intervention and the control groups, as we assumed that some conditions—for example, pneumonia—could occur more frequently in some periods of the year. The fact that the diagnoses in the control and intervention groups did not differ from each other showed that the choice to cover the same period of the year was appropriate. There might have been a limitation in that there was 1 year between the two study periods, as practices and procedures in a unit can change during this time. However, the patient mix and the staff were the same in the two study periods, and the included units did not implement new medications or new procedures between these two study periods.

Several studies have used a pre/postintervention design (77-82, 131). However, this design has weaknesses. When individuals are not assigned randomly to groups, there is always a possibility that the groups are nonequivalent. This could be a threat to internal validity, as confounding variables could influence the outcome. Therefore, when possible, a randomized controlled trial (RCT) design is considered to be most appropriate for evaluating the effects of interventions. However, in the present study, it was not possible to randomize

admitted patients regarding pain assessment, as pain assessment is already highly recommended, and it would be unethical not to do so. To randomize patients in the same unit to be assessed for pain with or without the algorithm could be difficult because of treatment diffusion (123), as clinicians who assessed the pain of patients without using the algorithm could be affected by clinicians who did use it. To randomize units, many ICUs would have needed to be included in the study, and this would be nearly impossible in a PhD project with limited resources. Another method for ensuring that two groups are similar is pair matching subjects on key confounding variables. However, this method requires knowledge of which variables to use for matching, and we were not able to determine which could be confounding variables. In addition, this method could result in many patients being dismissed from the study. Therefore, to strengthen the validity of inference when using the pre/postintervention design, differences in outcome variables between the intervention group and the control group were controlled for in the statistical analysis by analysis of covariance. In conclusion, we believe that our design was appropriate for answering the research questions, despite its limitations.

6.1.4 Patient recruitment and representativeness

All adult ICU patients who fulfilled the inclusion criteria were included in this study. Children were excluded, as pain assessment of children requires different tools (132). The algorithm was implemented in three units to include enough patients over a relatively short period while maintaining manageable organization of the study. Because informed consent was not needed, the study did not have any dropout of patients who were unable to give informed consent. In addition, as the algorithm included pain assessment tools for all ICU patients able to express pain and not only those who could self-report pain, the study appears to have recruited a representative sample of ICU patients. Therefore, the study results could

be generalizable to a larger population of ICU patients, enhancing the external validity of the study (123).

Unfortunately, not all available patients in the intervention group were included in our analysis of adherence. As documentation of pain assessment was not available for 113 patients, we do not know how or whether these patients were assessed for pain. Therefore, the analysis of adherence was based on data from the 285 patients in the intervention group who had documentation of pain assessment. The 113 patients without pain assessment documentation had a significantly shorter length of stay, and more had spontaneous ventilation and a lower NEMS per day compared with the 285 patients who had documentation of pain assessment. Including only those data from the 285 patients might have caused selection biases and could be a threat to internal validity in our analysis of the level of adherence (123).

When evaluating the interrater reliability of the two tools, 30 paired pain assessments with the BPS and 30 paired pain assessments with the BPS-NI at rest and during turning were included in the analysis. The choice of the number of paired pain assessments was based on sample sizes in similar studies (18, 58). However, those studies collected paired pain assessments from several procedures per patient, resulting in higher numbers of paired assessments compared with the present study. If we had included higher numbers of paired assessments in the present study, the statistical power would have been stronger (123).

When evaluating discriminant validity, 82 patients were included in the analysis of the BPS, and 29 patients were included in the analysis of the BPS-NI. The numbers of patients included depended on how many patients were subjected to the different pain assessment tools in the day shift when the data were collected. Thus, the statistical power was lower when evaluating BPS-NI than for BPS, and this might have threatened the validity of our statistical conclusions (123). In the evaluation of level of adherence, 285 patients were included. This

appears to be an appropriate sample size compared with similar studies, which evaluated levels of adherence in 100 (96) and 59 patients (97). When evaluating the impact of the intervention, a sample size calculation was performed to confirm the test's power.

It is worth noting that more patients were included in the intervention group ($n = 398$) than in the control group ($n = 252$). According to the target sample size calculation, at least 117 mechanically ventilated patients should be included in each group. As not all patients were treated in this way, we aimed to include all patients until at least 117 of the patients in each group were mechanically ventilated. However, as 113 of the patients included in the intervention group had no documentation of pain assessment, we included patients until at least 117 patients with documented pain assessment were mechanically ventilated ($n = 398$). Therefore, the sample size in the intervention group was larger than in the control group.

6.1.5 Choice of pain assessment tools

It was a strength of this study that the algorithm used pain assessment tools for different groups of ICU patients including tools for patients unable to self-report pain, as translated tools for such patients were not available prior to the study (11). In the pain management algorithm, only unidimensional pain assessment tools able to identify pain intensity were chosen. These tools allow clinicians to evaluate pain intensity and pain treatment. The use of more complex pain assessment tools such as the Brief Pain Inventory (133) could give more information about pain (e.g., localization, type of pain, and information about how pain affects daily life). However, these tools are not appropriate for the majority of ICU patients because many are intubated, have altered levels of consciousness, and receive high doses of sedative agents.

Research suggests that the NRS is appropriate for ICU patients able to self-report pain (61). Since the algorithm was developed, the NRS has been recommended in a recent

guideline for ICU patients (128) and is commonly used in other studies (129, 134). Therefore, we consider that the NRS is an appropriate tool for ICU patients able to self-report.

When the algorithm was developed, the BPS had been evaluated in several studies (18, 58, 81, 109-113). Since the algorithm was developed, the BPS has been studied in countries worldwide such as the Netherlands (135), China (136), the United States (137), France (138), Finland (139), and Sweden (140). These studies reported good psychometric properties for the BPS, including satisfactory interrater reliability (135-138, 140), discriminant validity (135-138, 140), internal consistency (136-138), and test–retest reliability (136). In addition, the feasibility of the BPS has been evaluated. In one study, most of the evaluators were satisfied or very satisfied by the ease of use of the BPS, although some of them expressed concerns regarding its relative complexity (18). In another study, the BPS was rated as the easiest tool to remember compared with the CPOT and the NVPS, but there was no significant difference with regard to users' preference (137). However, in 2013, a review of studies published between January 1997 and June 2012 was published, evaluating psychometric properties of several behavioral pain assessment tools (141). Of the eight behavioral pain tools developed for use in adult ICU patients, two tools were considered to be the most valid and reliable for this patient group. The BPS was one of the tools, and the CPOT was the other. This finding was supported by a published clinical practice guideline for adult ICU patients (128). Therefore, in recent years, several studies have compared the CPOT with the BPS to decide which tool is the best. Liu et al. (136) and Chanques et al. (137) found that both the CPOT and the BPS demonstrate similar psychometric properties and are reliable and valid tools for assessing pain in ICU patients. Rijkenberg et al. (135) found that both tools are reliable and valid for use in ICU patients, but the CPOT appears to be preferable, especially with regard to its discriminant ability. In contrast, Al Darwish et al. (138) found that the BPS was the most reliable, valid, and sensitive tool. Based on psychometric testing of the two tools, we consider

that both the BPS and the CPOT are suitable for assessing pain in ICU patients unable to self-report pain. Thus, both tools could have been used in the algorithm. However, the evidence available at the time when the algorithm was developed was that the BPS had been studied in more than 500 medical, surgical, trauma, neurological, and emergency patients, and in ICU patients with different levels of sedation. Moreover, the BPS had been translated and validated in Norwegian ICU patients as a part of my master's thesis. Therefore, we have assumed that the choice of the BPS as the tool for mechanical ventilated patients unable to self-report pain was appropriate in the present study.

The BPS-NI had only been evaluated in one study when the algorithm was developed, showing promising validity (17). In addition, clinical practice guidelines for adult ICU patients suggested that the BPS-NI should be further tested in other studies (128). To our knowledge, no studies have further evaluated the BPS-NI since our algorithm was developed, except for a few studies evaluating the BPS and the BPS-NI together. Those studies had drawbacks in that the results from the BPS and the BPS-NI were presented together. Thus, it was difficult to evaluate only one of the tools. However, one of these studies evaluated the tools in 151 neuro ICU patients showing excellent interrater reliability (intraclass correlation coefficient, 0.83) between nurses and physicians (142). Two other studies demonstrated that the tools were valid and reliable for assessing pain in ICU patients (136, 137), with Cronbach's α coefficients ranging from 0.79 to 0.80, weighted kappa values ranging from 0.81 to 0.96, and a test-retest reliability of 0.94. However, further validation of the BPS-NI is needed.

6.1.6 Data collection

To ensure confidentiality, resource persons employed at the different units collected and anonymized the data. Data were collected from the hospital information database, from daily ICU schemas, and from the pain assessment sheets developed for the project.

In our analysis of the level of adherence, multivariate regression analysis showed that the overall model explained 16.2% of the variance. Because this explained variance was relatively small, other factors that were not assessed in this study warrant consideration. Prior research found that nurse characteristics (e.g., knowledge deficits or misconceptions about pain assessment, and resistance to use valid tools) (19-21) as well as patient characteristics (e.g., hemodynamic instability in critically ill patients) (22) and systemic factors (e.g., learning culture in the units) (23) could be barriers to effective pain management. Unfortunately, these variables were not available in the current study.

In our analysis of the impact of the algorithm, several other outcomes such as nosocomial infections (81) and complications (77) could have been evaluated, as the implementation of pain assessment tools are known to be associated with these variables. However, because such data were not documented or available in the hospital information database or in the daily ICU schemas, they could not be collected. It would also have been interesting clinically to evaluate whether pain intensity changed after implementing the algorithm. Such an analysis was not possible, as pain intensity was documented in only 7.3% of the nurses' shifts in the control group. However, Chanques et al. (81) used independent observers to assess patients in their control group when they evaluated the impact of implementing pain and sedation tools on the level of pain intensity and agitation events. In this way, they could compare pain intensity between the control and intervention groups. Unfortunately, we did not use this method in our study.

6.1.7 Statistical analyses

The study presents results from analyses on both cross-sectional and longitudinal data. All data analyses have been conducted in close collaboration with a statistician. Regarding patients and unit characteristics, missing values were found in the NEMS and SAPS outcomes. In the intervention group, frequencies of missing data were low (1.4% for NEMS

and 6.7% for SAPS). In the control group, there were more missing data for NEMS (20.6%), while there were no missing data for SAPS. We have no logical explanation for these differences in missing data between the two groups. However, because of these missing values, the description of NEMS and SAPS was based on fewer patients than the other characteristics.

When evaluating interrater reliability of the tools, Weighted Kappa values were used because these take into account the degree of disagreement (143). To evaluate the discriminant validity of the tools, the Wilcoxon signed-rank test was used, as the same patients were measured on two occasions, and the data were far from being normally distributed (95). Associations between patient and unit characteristics and the level of adherence to the algorithm (the dependent variable) were evaluated using bivariate and multivariate regression analyses. Using a multiple regression analysis, the dependence of one outcome variable on two or more other variables can be examined simultaneously (143). Linear regression analysis was used when evaluating the impact of the algorithm on various outcomes. It is a shortcoming of the study that no written documentation on pain, medications, or sedation levels was available for 113 patients. However, as nurses in the three units were educated and trained in using the algorithm, we included data from all patients enrolled in our evaluation of the impact of the algorithm. An intention-to-treat analysis (95) was used to avoid selection biases and faulty inferences about treatment effects. This analysis assumes that each person received the intervention to which he/she was assigned. An per-protocol analysis (95), which includes patients in an intervention group only if they actually received the intervention, could be problematic, as the 113 patients who had no documented pain assessment had significantly shorter lengths of stay, a higher percentage had spontaneous ventilation, and their NEMS were lower than those of the 285 patients who had documentation on pain assessment. If we had only included the 285 patients in the

intervention group who had documented pain assessments, the study would no longer be representative of ICU patients.

6.1.8 Ethical considerations

This study includes a vulnerable patient group, so it is worth noting that the interventions did not cause any additional risk, discomfort, or stress for the patients. The interventions included pain assessment with the patient at rest and when being turned in bed, and this is one of the most common procedures in an ICU. New treatment was not implemented, as all patients should be assessed for pain. New medications were not implemented, as the algorithm required that each patient's already prescribed pain treatment should be increased, decreased or continued according to defined cutoff points. Physicians who were responsible for the medical management of the patients approved the algorithm before it was implemented. In addition, the welfare and the integrity of the patients were taken care of throughout the collection, storage, and management of data, and in the publications. Therefore, ethical principles were respected in the present study.

6.2 Main results

6.2.1 Development of the pain management algorithm

This pain management algorithm was developed in 2012. In 2013, revised clinical practice guidelines were published by the American College of Critical Care Medicine for the management of pain, agitation, and delirium in adult ICU patients (128). These guidelines were developed by a 20-person, multidisciplinary, multi-institutional task force with expertise in guideline formulation, development, pain, agitation and sedation, delirium management, and associated outcomes in critically ill adult patients. The pain management algorithm developed in this study is consistent with these guidelines. First, pain should be routinely monitored. Second, self-reporting of pain is the gold standard in pain assessment, and if this is

not possible, observation of patients' behavior is recommended. Third, the use of pain assessment tools is recommended. As the pain assessment tools and the process in the algorithm were consistent with the recommendations in the updated clinical practice guidelines (128), we consider that this algorithm can be used effectively as a tool for assessing ICU patients who can and cannot self-report pain.

It is a strength of our study that the algorithm includes specific tools for detecting pain, as this can help clinicians in discriminating between situations requiring sedation and those requiring analgesia. This discrimination is still a challenge for clinicians (144). In addition, correlations found between pain and anxiety (145), or pain, fear, and anxiety (146) and indications of their coexistence in ICU patients emphasize the importance of using pain assessment tools that are sensitive and specific for such patients. Furthermore, including pain assessment tools based on self-reporting of pain and observation of pain behavior could make the pain assessment of ICU patients more evidence based, as patients' physiological stability is still used as a principal indicator for making decisions in pain management (144).

It is a strength of the study that both of the translated tools used in the algorithm discriminated between pain scores at rest and when the patients were being turned in bed. This finding is consistent with previous reports for the BPS (18, 58, 109, 111-113, 135-138) and the BPS-NI (17). The mean differences between pain scores during turning and at rest were at least 1 point higher for both tools. In similar studies, the difference between pain at rest and pain during turning were 2–3 points (18, 58, 111, 135, 138). However, we consider the difference at 1 point in the present study to be of clinical importance, as the difference in total pain score was 24% higher for the BPS and 29% higher for the BPS-NI during turning compared with the pain scores at rest. In addition, in the present study all of the subscale scores for both tools were significantly higher during turning than at rest. These findings suggest that the translated tools were sensitive to changes in pain intensity and that all of the

subscale scores contributed unique information about pain. Therefore, we believe that the Norwegian versions of the BPS and the BPS-NI are valid tools to use when assessing pain in ICU patients. However, it is worth noting that relatively few patients were included in the evaluation of the BPS-NI, and so these results should be interpreted with some caution.

It is a little worrying that the interrater reliabilities of the BPS and the BPS-NI were somewhat higher in similar studies compared with the present study. Interrater reliability for the BPS scores varied from moderate to very good (i.e., weighted kappa values of 0.46–1.00) in the present study, while interrater reliability varied from good with a weighted kappa value of 0.67 (110) to very good with a value of 0.83 (113) in previous similar studies. For the BPS-NI, interrater reliability varied from fair to good (weighted kappa values of 0.21–0.63), while interrater reliability in the study of Chanques et al. (17) showed good interrater reliability (weighted kappa values of 0.82–0.89). One explanation for the lower interrater reliabilities for both the BPS and the BPS-NI in the current study might be that different nurses evaluated pain. The most effective way to enhance reliability in observational studies is through training of observers (95), and in other studies, specially trained researchers or specialists evaluated the patients' pain (58, 112). Compared with those studies, the results in our study might be more representative of actual nursing practice. Another explanation for the difference could be that paired pain assessment scores were collected at the start of the implementation period. Collecting data so early in the project might have meant that some of the nurses were still far from expert in using the tools. A third explanation for the difference could be that in the present study, only one observation (i.e., being turned in bed) from each subject was used for the calculation of coefficients, while repeated observations within subjects (e.g., endotracheal suction, or peripheral venous cannulation) were used in other studies (18, 58), which tend to lead to higher results (147). It is worth noting that in the current study, all paired assessment BPS scores were within 1 scale point. For the BPS-NI, the agreements within 1 scale point

ranged from 83% to 100%. These data suggest that little discrepancy occurred between the nurses. Therefore, although the interrater reliability of the BPS and the BPS-NI was somewhat higher in similar studies compared with the present one, it appears that the Norwegian version of the BPS and the BPS-NI can be used for assessing pain in ICU patients. However, the BPS-NI had lower weighted kappa values than the BPS in this study. One explanation for these differences is that it might be more difficult to agree on a pain level in non-intubated ICU patients who are unable to self-report pain as some patients might suffer from delirium (17). However, additional research on how to improve the interrater reliability of the BPS-NI is needed.

Even if the best available evidence shows a strong relationship between behavioral responses and pain in ICU patients, we cannot be sure that patient's behavior reflects exactly each pain experience. For example, in some cases, a patient's behavior might be associated with anxiety and fear, and not pain. In other cases, a patient's pain intensity might be higher or lower than a patient's behavior reflects. Because these patients are unable to self-report pain, it is not possible to validate these tools against the "gold standard" of pain (i.e., self-reporting). Therefore, when using these tools, it is important for clinicians to be aware of several things. First, we cannot be sure that patient's behavior reflects exactly each pain experience. Second, it is a weakness that the pain assessment is not done by the patient him/her self. Third, the tools are based on indirectly measures on pain. Therefore, when using these tools, clinicians also need to use their knowledge and clinical experience.

It is also worth noting that in some groups of ICU patients, the adaptation and validation of behavioral pain assessment tools is still required. Traumatic brain injury ICU patients with altered levels of consciousness show atypical behavioral responses to nociceptive procedures, such as relaxed face, relaxed muscles, sudden eye opening, eye weeping, and limb flexion (49, 148). In addition, typical pain behaviors such as grimacing and

muscle rigidity (56) were less frequent (49, 148). In these patients, lower pain intensity scores have been reported, questioning the validity of the behavioral pain assessment tools in these patients (18, 149, 150). The opposite finding occurred in conscious elective brain surgery ICU patients where higher pain intensity scores were obtained (151). Therefore, existing pain tools might require content adaption and further validation in brain injury ICU patients.

The algorithm included pain management in addition to pain assessment, as the algorithm provided guidance on pain treatment based on the findings from the pain assessment. If a pain intensity score was higher than the prescribed cutoff point, the algorithm guided the nurses to consider increasing pain treatment. If a pain intensity score was below the cutoff point, the algorithm guided the nurses to consider whether to decrease or continue pain treatment. However, decisions about pain management in ICU patients are often complex, as these patients are not a homogeneous patient group. The pain management algorithm could be too simple in some situations and too restricted to guide pain management for all ICU patients and in all types of situations. For example, if a patient able to self-report pain does not want more analgesics, the clinicians should consider and take into account the patient's wishes and maybe not increase the pain medication even if the pain intensity scores are higher than the cutoff point. Alternatively, if a patient is going through major surgery in the near future, pain treatment should maybe not be decreased even if pain intensity scores are lower than the cutoff point, because one would expect that pain would increase after surgery. Therefore, it is important that clinicians use their experience and knowledge when using the algorithm.

It could be a limitation that our approach in guiding the nurses in pain treatment could be somewhat diffuse regarding pain treatment, compared with other studies that include a special pain treatment action (e.g., 2.5 mg or 5 mg bolus doses of morphine) (152). The algorithm does not prescribe specific pain treatments. The focus of the algorithm was on the

provision of guidance on whether to increase, to decrease, or to continue each patient's pain management plan. However, ICU patients are a complex group, including both medical and surgical treatments, with different ages, diagnoses, and treatments. An algorithm with a standardized pain treatment might not be appropriate for this patient group, as the need for analgesic and sedative medications and dosage of medications would differ from one patient to another. Therefore, despite limitations and challenges with the algorithm, we believe that the algorithm can be a useful tool for improving pain assessment and management in adult ICU patients.

6.2.2 Implementation of the pain management algorithm

In this study, the average level of adherence to the algorithm regarding pain assessment of ICU patients was 74.6%. The 285 patients who were assessed with the algorithm were in the ICU for a total of 2832 shifts entailing 5664 pain assessments (i.e., each patient had pain assessed in every shift at rest and when being turned in bed), and a total of 4223 pain assessments were recorded, giving an overall level of adherence of 74.6%. Even if a direct comparison of levels of adherence across studies is difficult because of different ways of calculating it, the level of adherence in the current study was higher than the 58% associated with the use of sedative, analgesic, and neuromuscular blocking agent guidelines in mechanically ventilated ICU patients (96), and the 66% found in a study of patients on general medical wards (97). Of note, in a systematic review of 23 studies (98), the overall level of adherence to pain assessment protocols in hospitals ranged from 24% to 100%. Our nurses had a relatively high level of adherence to the algorithm, suggesting that they could use the algorithm consistently.

One explanation for the relatively high level of adherence to the algorithm in the present study might be the choice of implementation techniques, as the use of one-on-one education, audit and feedback, a reminder system, local leaders, and printed material have

been identified as changing behavior in clinical practice (153). A review of the evidence for implementation strategies aiming to improve nurses' adherence to pain assessment recommendations found that most of these studies used multifaceted approaches (98), as in the current study. Because of the heterogeneity of implementation strategies in the studies included in the literature review, it was not possible to recommend one preferred strategy, but educational and feedback strategies seem to be largely effective (98). In the present study, education of the nurses was one of the techniques that were used, and most (94%) of the nurses employed at the three units participated in the education program prior to the implementation of the algorithm. Audit and feedback were not used extensively, but using them more extensively might have increased the level of adherence.

Using an expanded training program where these implementation techniques (99) were presented over several cycles might increase the level of adherence (154). One study used these implementation techniques to implement assessment tools regarding sedation, pain, and delirium in ICU patients using both an expanded training program (over three cycles) and a traditional training program (one cycle) (154). They found that sustained documentation rates for sedation, pain, and delirium scores increased significantly when using the expanded training program compared with the traditional training program. Therefore, our level of adherence could have been higher if we had used an expanded training program. However, the cost would have increased substantially. As we assume that many ICUs have limited resources and are not able to use expanded training programs, the results in the present study might be more representative of actual clinical practice.

The multivariate regression analysis showed that gender and diagnosis were significantly associated with the level of adherence. Male patients were assessed significantly less frequently than female patients. As women report higher intensity scores for experimental (155) and clinical (156) pain and more fear of pain than men (155), one explanation for the

finding might be that female expression of pain encouraged nurses to assess their pain more frequently. Interestingly, in another Norwegian study (134), the opposite finding occurred: women had a higher probability of not being asked about pain compared with men. It is worth noting that this study included a different study population compared with ours, being based in an Emergency Department, where all patients were conscious and assessed with the NRS. Therefore, it is difficult to compare the findings in the two studies. However, it is interesting that a patient's gender might be associated with how often pain is assessed in hospitalized patients, so additional research in this area is warranted.

Patients with “injury, poisoning and certain other consequences of external causes” were assessed less often than patients with “diseases of the respiratory system”. This finding is somewhat surprising as one would expect that patients with injury would experience more pain and therefore would lead nurses to assess their pain more frequently. On the other hand, one study found that the prevalence and intensity of pain in medical ICU patients was not lower than in surgical trauma patients (43). It is worth noting that patients with an injury had a lower mean SAPS (mean score 29.6; SD = 16.5) than patients with respiratory diseases (mean score 41.6; SD = 14.5; $p = .001$), suggesting that other factors influenced nurses' pain assessments in these patients. Therefore, additional research is warranted to determine which specific patient characteristics influence nurses' adherence to pain assessment guidelines. In addition, pain assessments were documented significantly less often during evening and night shifts compared with day shifts. One possible explanation is that the resource persons were available primarily during the day, and one of their main tasks was to remind and support the nurses to use the algorithm, to use one-to-one education, and to show a leadership role in championing best practices. Another explanation might be that the nurses wanted to reduce the frequencies of examinations and nursing activities on these shifts to avoid interrupting the patients who needed relaxation and sleep.

It is interesting that some patient and unit characteristics were associated with how often the patient was pain assessed, but it is worth noting that these characteristics cannot be changed to improve the level of adherence to the algorithm. However, it is important that clinicians who assess and document ICU patients' pain should be aware that some patient characteristics are associated with how often these patients are pain assessed. Therefore, advancing the knowledge in this field might improve pain assessment for these patients.

Other factors that were not measured in this study might have affected the level of adherence. In the multivariate regression analysis, gender, SAPS, diagnosis, and NEMS explained 16.2% of the variance in the level of adherence. Given that the explained variance was relatively small, other factors such as nurses' characteristics (e.g., knowledge deficits or misconceptions about pain assessment, resistance to using valid tools) (19-21), patient characteristics (e.g., hemodynamic instability in critically ill patients) (22), and systemic factors (e.g., learning culture in the units) (23) might affect level of adherence. Therefore, further consideration is wanted.

6.2.3 Evaluation of the impact of using the pain management algorithm

Findings from this study suggest that implementing a pain management algorithm can improve some outcomes for ICU patients. These results are consistent with findings from a review of the literature from 1995 to 2013 regarding the impact of pain assessment on critically ill patients' outcomes (157). The review identified 10 eligible studies (77-79, 81, 82, 131, 154, 158-160) and showed that implementation of systematic approaches to pain assessment appears to be associated with more frequently documented reports of pain and more efficient decisions for pain management (77-79, 81). There was evidence of favorable effects on pain intensity (79, 81, 160), duration of mechanical ventilation (77, 81, 158), length of ICU stay (77, 131, 158, 159), mortality (154), and adverse events and complications (77, 81, 158).

In the present study, there were more documented pain assessments in the intervention group compared to the control group. This result is consistent with other studies (77-79, 81), showing that pain assessments and identification of pain episodes are more frequently documented after the implementation of pain assessment tools. Interestingly, data from an international postoperative acute pain registry found that patients reported high levels of pain despite the implementation of evidence-based recommended practices (161). The authors suggested that there is no assurance that excellent pain documentation translates into excellent pain care in postoperative patients. The present study was not able to evaluate the impact of implementing the algorithm on pain intensity. However, it is worth noting that several other studies suggest that systematic assessment and documentation of pain in ICU patients is associated with decreased pain intensity (79, 81, 160). Therefore, further studies on the impact of implementing an algorithm on pain intensity are warranted.

Of the patient outcomes measured in this study, two improved. The median decrease in ventilation time was 33 h. This decrease is consistent with previous research (77, 81, 158). As an increased ventilation time is associated with a higher incidence of ventilator-associated pneumonia (162), ventilation-induced lung damage (163), and higher treatment costs (164), we consider our finding to be of clinical importance. In addition, the length of ICU stay decreased significantly in the intervention group compared with the control group and is consistent with prior research (77, 131, 158, 159). As treatment of ICU patients is expensive (165, 166), a reduced ICU stay could have beneficial socioeconomic consequences. It is worth noting that despite the decreased length of ICU stay, no impact on the overall length of hospital stay was found. This could indicate that application of the algorithm had an impact during the ICU stay but lacked a long-term impact on hospitalization.

We hypothesized originally that implementing a pain management algorithm might help to identify pain intensity and contribute to adoption of an appropriate pain treatment, and

have an impact on patient outcomes, such as a patient's ventilator time and length of ICU stay. Therefore, it is a little puzzling that despite the decreased ventilator time and length of ICU stay, the daily dosages of analgesic and sedative medications did not change after implementing the algorithm. However, there are several aspects regarding the data quality that might affect these analyses. The analysis included daily dosages of analgesic and sedative medications but not detailed pain treatment actions. Therefore, nuances in the pain treatment actions disappeared. In addition, calculating morphine equivalents in ICU patients might cause some uncertainties because of the properties and the bioavailability of these medications (167), as some of the opioids have extremely short half-lives. In addition, 97% of patients in the control group received analgesia, and this high incidence could explain why the use of analgesia did not increase after implementing the algorithm. Therefore, our results from evaluating analgesic and sedative medications in ICU patients should be interpreted with some caution. However, for two of the medications, the daily dosages changed after implementing the algorithm. The median daily dosage of epidural fentanyl increased, and the median daily dosage of midazolam decreased. A decrease in the dosages of midazolam was also found in a study by Payen et al. (158). During recent years, we have seen a trend toward more alert and cooperative ICU patients (168), and analgosedation has been recommended (28). The units included in this study did not implement any such new treatment procedure between the two study periods, and we did not find a change in sedation level enabling more alert and cooperative patients, as measured by the MAAS or RASS tools. However, we cannot exclude the possibility that the trend identified above has influenced the use of midazolam.

6.3 The Symptom Management Model

In this thesis, the Symptom Management Model was used as a theoretical framework. The model has been useful in identifying the different dimensions and domains of pain and in

understanding the interactions among them. In this way, the model contributed to a broader picture of the complexity of pain in ICU patients.

Furthermore, the model has been useful in structuring available literature about pain in ICU patients. Structuring the literature in the different dimensions and domains of pain made it easier to get an overview of the huge amount of research in this area. The overview was useful in the development of the algorithm, and in planning the evaluation of the algorithm, especially regarding decisions about statistical analysis, translation method, sample size, data collection, implementation strategies, and choice of outcome measures.

Figure 3. The present study included in the Symptom Management Model

In the present study, a pain management algorithm was included as a symptom management strategy (Figure 3). The symptom management strategy included the development of the algorithm, the testing of pain assessment tools used in the algorithm, and the implementation of the algorithm in clinical practice.

The model showed that pain management strategy interacts with pain outcomes, and that adherence was situated between these two dimensions. In the present study, nurses' level of adherence with the algorithm was evaluated. The study found that the overall mean level of adherence with the algorithm was 74.6%, indicating that the algorithm was a useful tool to increase ICU nurses adherence with pain assessment.

Further, outcomes such as pain assessments, duration of ventilation, length of ICU stay, length of hospital stay, use of analgesic and sedative medications, and the incidence of agitation events were evaluated after implementing the algorithm in clinical practice. The present study found that implementing the pain management algorithm was associated with increased documentation of pain assessment, which might improve health care providers' practice. The implementation of the algorithm was also associated with decreased ventilator time and length of ICU stay, which improved individual's symptom outcomes. An outcome measure that could have been evaluated in the present study is cost, as cost is presented as an outcome in the original model (Figure 1), and because literature describes that treatment cost is associated with ventilator time and length of ICU stay. Another outcome measure that could have been evaluated in the present study is pain intensity. Unfortunately, we were not able to evaluate the effect on pain intensity after implementing the pain management algorithm, due to a lack of documentation of pain intensity scores in the control group.

Symptom experience is one of the three dimensions in the model. Symptom experience should be based on the individual's own experience of symptoms. Therefore, in the present study, the patients' pain experiences were measured by using self-report of pain or observation of pain behavior. When using tools for self-reporting pain, the patient rates his/her own pain intensity. In this way, the response is based on the patient's own experience. When using tools based on pain-related behavior, we cannot be sure that patient's behavior reflects exactly each pain experience. However, as evidence shows a strong relationship

between behavioral responses and pain in ICU patients, we consider behavioral pain assessment tools to be the best available tools to measure the individual's own experience of pain, such as the Symptom Management Model emphasizes.

The model demonstrated that in symptom research, it is important to include data from person, health/illness, and environment domains in the data collection. Therefore, in the present study, data such as gender (person domain), diagnosis (health/illness domain), and nursing workload (environmental domain) were collected and used in the analysis. However, only limited data from these three domains were included. Collecting additional data, for example data about analgesic medications used before ICU admission (person domain), occurrence of anxiety in the patients (health/illness domain), and use of equipment such as chest tubes (environment domain) would have given a more nuanced and broader picture of ICU patients and pain.

The Symptom Management Model was originally designed for one symptom, or for clusters of symptoms (107). In the present study, pain was the main focus. Even if we were not able to evaluate the impact on pain intensity after implementing the pain management algorithm, studies published after the development of the algorithm show that many patients still have memories of pain during their ICU stay (169). In one study, 58% of ICU patients perceived pain as a problem (6). In another study, 71% of ICU patients reported that they constantly experienced pain during hospitalization (170). In addition, former ICU patients reported pain as one of the key symptoms that they experienced 4 months after ICU discharge (171), and 33% of surgical and "mixed ICU" patients (172) and 44% of medical-surgical ICU patients (173) experienced chronic pain 6 months after ICU discharge. Therefore, providing sufficient pain management to ICU patients is essential for promoting comfort and rehabilitation while avoiding any transition from acute to chronic pain (174).

Even though pain was the main focus here, research still shows that ICU patients experience several distressing symptoms during their stay, and these symptoms might have an impact on each other. New research highlights that pain, dyspnea, and thirst are the most prevalent, intense, and distressing symptoms for ICU patients (175) in addition to anxiety, and poor sleep quality and/or insomnia (176). Therefore, using the Symptom Management Model on clusters of symptoms in ICU patients could demonstrate a broader picture of the ICU patients than we have studied in this thesis.

7.0 Main conclusions

In this thesis, pain management in ICU patients has been investigated. The main findings can be summarized as follows.

- Findings from Paper 1 suggest that the pain management algorithm is based on current clinical practice guideline recommendations and incorporates valid and reliable pain assessment tools for ICU patients. Therefore, this algorithm could be used on a routine basis in critical care units to assess ICU patients who can and cannot self-report pain.
- Findings from Paper 2 demonstrated that the nurses involved had a relatively high level of adherence to the algorithm, suggesting that they could use the algorithm consistently and that it was a useful tool to increase ICU nurses' adherence with pain assessment.
- Findings from Paper 3 demonstrated that several outcome variables were significantly improved after implementation of the algorithm compared with the control period. This indicates that implementing a pain management algorithm can improve outcomes for ICU patients.

7.1 Implications for clinical practice

Findings from this thesis might have important implications for clinical practice. First, the findings suggest that valid pain assessment tools for different groups of ICU patients should be a part of pain management. Norwegian ICUs should implement pain assessment tools in clinical practice, nurses should use them, pain scores should be documented, and pain scores should be a part of daily discussions in ICUs about pain management.

Second, our findings suggest that pain should be assessed regularly and systematically, so that pain and pain treatment could be evaluated. The choice of a proper implementation

strategy is important. In addition, it is important to evaluate adherence when implementing new routines and procedures in clinical practice and to act to improve such adherence.

7.2. Future research

This thesis has focused on the development, implementation, and evaluation of a systematic pain management algorithm for ICU patients. Future research should focus on how to improve the interrater reliability for the Norwegian version of the BPS-NI. An exploration of what might influence nurses' level of adherence to a pain management algorithm is also warranted. An evaluation of other outcomes after implementing a systematic pain assessment and management algorithm, including the occurrence of pain and pain intensity, is needed.

In this thesis, the symptom pain has been discussed. Because published studies have reported that ICU patients experience several symptoms during and after their stay, intervention studies that involve several of these symptoms are warranted.

8.0 References

1. Jones J, Hoggart B, Withey J, Donaghue K, Ellis BW. What the patients say: a study of reactions to an intensive care unit. *Intensive Care Med.* 1979;5(2):89-92.
2. Puntillo KA. Pain experiences of intensive care unit patients. *Heart Lung.* 1990;19(5 Pt 1):526-33.
3. Gélinas C. Management of pain in cardiac surgery ICU patients: have we improved over time? *Intensive Crit Care Nurs.* 2007;23(5):298-303.
4. Puntillo KA, Arai S, Cohen NH, Gropper MA, Neuhaus J, Paul SM, et al. Symptoms experienced by intensive care unit patients at high risk of dying. *Crit Care Med.* 2010;38(11):2155-60.
5. Kalfon P, Mimos O, Auquier P, Loundou A, Gauzit R, Lepape A, et al. Development and validation of a questionnaire for quantitative assessment of perceived discomforts in critically ill patients. *Intensive Care Med.* 2010;36(10):1751-8.
6. Alasad JA, Abu Tabar N, Ahmad MM. Patients' experience of being in intensive care units. *J Crit Care.* 2015;30(4):859 e7-11.
7. So HM, Chan DS. Perception of stressors by patients and nurses of critical care units in Hong Kong. *Int J Nurs Stud.* 2004;41(1):77-84.
8. Hweidi IM. Jordanian patients' perception of stressors in critical care units: a questionnaire survey. *Int J Nurs Stud.* 2007;44(2):227-35.
9. Schelling G, Stoll C, Haller M, Briegel J, Manert W, Hummel T, et al. Health-related quality of life and posttraumatic stress disorder in survivors of the acute respiratory distress syndrome. *Crit Care Med.* 1998;26(4):651-9.
10. Olsen BF. Er den norske versjonen av "Behavioral Pain Scale" pålitelig og anvendbar for å vurdere smerter hos sederte respiratorpasienter [masteroppgave]: Avdeling for sykepleierutdanning, Høgskolen i Oslo; 2010.
11. Woien H, Stubhaug A, Bjork IT. Analgesia and sedation of mechanically ventilated patients - a national survey of clinical practice. *Acta Anaesthesiol Scand.* 2011;56(1):23-9.
12. Jacobi J, Fraser GL, Coursin DB, Riker RR, Fontaine D, Wittbrodt ET, et al. Clinical practice guidelines for the sustained use of sedatives and analgesics in the critically ill adult. *Crit Care Med.* 2002;30(1):119-41.
13. Gordon DB, Dahl JL, Miaskowski C, McCarberg B, Todd KH, Paice JA, et al. American pain society recommendations for improving the quality of acute and cancer pain management: American Pain Society Quality of Care Task Force. *Arch Intern Med.* 2005;165(14):1574-80.

14. Herr K, Coyne PJ, McCaffery M, Manworren R, Merkel S. Pain assessment in the patient unable to self-report: position statement with clinical practice recommendations. *Pain Manag Nurs*. 2011;12(4):230-50.
15. 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(4):687-95.
16. Rose L, Smith O, Gélinas C, Haslam L, Dale C, Luk E, et al. Critical care nurses' pain assessment and management practices: a survey in Canada. *Am J Crit Care*. 2012;21(4):251-9.
17. Chanques G, Payen JF, Mercier G, de Lattre S, Viel E, Jung B, et al. Assessing pain in non-intubated critically ill patients unable to self report: an adaptation of the Behavioral Pain Scale. *Intensive Care Med*. 2009;35(12):2060-7.
18. 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(12):2258-63.
19. Berben SA, Meijis TH, van Grunsven PM, Schoonhoven L, van Achterberg T. Facilitators and barriers in pain management for trauma patients in the chain of emergency care. *Injury*. 2012;43(9):1397-402.
20. Horbury C, Henderson A, Bromley B. Influences of patient behavior on clinical nurses' pain assessment: implications for continuing education. *J Contin Educ Nurs*. 2005;36(1):18-24; quiz 46-7.
21. Yildirim YK, Cicek F, Uyar M. Knowledge and attitudes of Turkish oncology nurses about cancer pain management. *Pain Manag Nurs*. 2008;9(1):17-25.
22. Rose L, Haslam L, Dale C, Knechtel L, Fraser M, Pinto R, et al. Survey of assessment and management of pain for critically ill adults. *Intensive Crit Care Nurs*. 2011;27(3):121-8.
23. Bennetts S, Campbell-Brophy E, Huckson S, Doherty S, National H. Pain management in Australian emergency departments: current practice, enablers, barriers and future directions. *Emerg Med Australas*. 2012;24(2):136-43.
24. Norsk Sykepleierforbund (Norwegian nurses organization) (2006) Definisjoner [Internet]. Oslo: Norsk Sykepleierforbund. Available from: <https://www.nsf.no/vis-artikkel/125357/270500/Definisjoner>.
25. Thomason JW, Shintani A, Peterson JF, Pun BT, Jackson JC, Ely EW. Intensive care unit delirium is an independent predictor of longer hospital stay: a prospective analysis of 261 non-ventilated patients. *Crit Care*. 2005;9(4):R375-81.
26. Ely EW, Gautam S, Margolin R, Francis J, May L, Speroff T, et al. The impact of delirium in the intensive care unit on hospital length of stay. *Intensive Care Med*. 2001;27(12):1892-1900.

27. 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(14):1753-62.
28. Devabhakthuni S, Armahizer MJ, Dasta JF, Kane-Gill SL. Analgosedation: a paradigm shift in intensive care unit sedation practice. *Ann Pharmacother*. 2012;46(4):530-40.
29. Nelson JE, Meier DE, Oei EJ, Nierman DM, Senzel RS, Manfredi PL, et al. Self-reported symptom experience of critically ill cancer patients receiving intensive care. *Crit Care Med*. 2001;29(2):277-82.
30. Puntillo KA, Smith D, Arai S, Stotts N. Critical care nurses provide their perspectives of patients' symptoms in intensive care units. *Heart Lung*. 2008;37(6):466-75.
31. Schmidt M, Demoule A, Polito A, Porchet R, Aboab J, Siami S, et al. Dyspnea in mechanically ventilated critically ill patients. *Crit Care Med*. 2011;39(9):2059-65.
32. Wilson VS. Identification of stressors related to patients' psychologic responses to the surgical intensive care unit. *Heart Lung*. 1987;16(3):267-73.
33. Figueroa-Ramos MI, Arroyo-Novoa CM, Lee KA, Padilla G, èKA. Sleep and delirium in ICU patients: a review of mechanisms and manifestations. *Intensive Care Med*. 2009;35(5):781-95.
34. Johansson L, Bergbom I, Lindahl B. Meanings of being critically ill in a sound-intensive ICU patient room - a phenomenological hermeneutical study. *Open Nurs J*. 2012;6:108-16.
35. Kamdar BB, Needham DM, Collop NA. Sleep deprivation in critical illness: its role in physical and psychological recovery. *J Intensive Care Med*. 2012;27(2):97-111.
36. Tembo AC, Parker V. Factors that impact on sleep in intensive care patients. *Intensive Crit Care Nurs*. 2009;25(6):314-22.
37. Matthews EE. Sleep disturbances and fatigue in critically ill patients. *AACN Adv Crit Care*. 2011;22(3):204-24.
38. Rotondi AJ, Chelluri L, Sirio C, Mendelsohn A, Schulz R, Belle S, et al. Patients' recollections of stressful experiences while receiving prolonged mechanical ventilation in an intensive care unit. *Crit Care Med*. 2002;30(4):746-52.
39. Sousa KH, McDermott CM, Weiss J. The importance of assessing symptoms and symptom clusters in critical care units. *AACN Adv Crit Care*. 2011;22(3):275-82.
40. Weiner RS. Pain management: a practical guide for clinicians. 6th ed. Boca Raton: CRC Press; 2002.
41. Melzack R, Wall PD. Pain mechanisms: a new theory. *Science*. 1965;150(3699):971-9.

42. International Association for the study of Pain (1994) IASP Taxonomy [Internet]. Washington: International Association for the study of Pain. Available from: <http://www.iasp-pain.org/Taxonomy>.
43. Chanques G, Sebbane M, Barbotte E, Viel E, Eledjam JJ, Jaber S. A prospective study of pain at rest: incidence and characteristics of an unrecognized symptom in surgical and trauma versus medical intensive care unit patients. *Anesthesiology*. 2007;107(5):858-60.
44. Stanik-Hutt JA, Soeken KL, Belcher AE, Fontaine DK, Gift AG. Pain experiences of traumatically injured patients in a critical care setting. *Am J Crit Care*. 2001;10(4):252-9.
45. Puntillo KA, White C, Morris AB, Perdue ST, Stanik-Hutt J, Thompson CL, et al. Patients' perceptions and responses to procedural pain: results from Thunder Project II. *Am J Crit Care*. 2001;10(4):238-51.
46. Aslan FE, Badir A, Arli SK, Cakmakci H. Patients' experience of pain after cardiac surgery. *Contemp Nurse*. 2009;34(1):48-54.
47. Puntillo KA. Dimensions of procedural pain and its analgesic management in critically ill surgical patients. *Am J Crit Care*. 1994;3(2):116-22.
48. Schelling G, Richter M, Roozendaal B, Rothenhausler HB, Krauseneck T, Stoll C, et al. Exposure to high stress in the intensive care unit may have negative effects on health-related quality-of-life outcomes after cardiac surgery. *Crit Care Med*. 2003;31(7):1971-80.
49. Gélinas C, Arbour C. Behavioral and physiologic indicators during a nociceptive procedure in conscious and unconscious mechanically ventilated adults: similar or different? *J Crit Care*. 2009;24(4):628.e7-.17.
50. Vazquez M, Pardavila M, Lucia M, Aguado Y, Margall M, Asiain MC. Pain assessment in turning procedures for patients with invasive mechanical ventilation. *Nurs Crit Care*. 2011;16(4):178-85.
51. Gélinas C, Johnston C. Pain assessment in the critically ill ventilated adult: validation of the Critical-Care Pain Observation Tool and physiologic indicators. *Clin J Pain*. 2007;23(6):497-505.
52. Storm H. Changes in skin conductance as a tool to monitor nociceptive stimulation and pain. *Curr Opin Anaesthesiol*. 2008;21(6):796-804.
53. Larson MD, Sessler DI. Pupillometry to guide postoperative analgesia. *Anesthesiology*. 2012;116(5):980-2.
54. Aissou M, Snauwaert A, Dupuis C, Atchabahian A, Aubrun F, Beaussier M. Objective assessment of the immediate postoperative analgesia using pupillary reflex

- measurement: a prospective and observational study. *Anesthesiology*. 2012;116(5):1006-12.
55. Li D, Miaskowski C, Burkhardt D, Puntillo K. Evaluations of physiologic reactivity and reflexive behaviors during noxious procedures in sedated critically ill patients. *J Crit Care*. 2009;24(3):472.e9-13.
 56. Puntillo KA, Morris AB, Thompson CL, Stanik-Hutt J, White CA, Wild LR. Pain behaviors observed during six common procedures: results from Thunder Project II. *Crit Care Med*. 2004;32(2):421-7.
 57. Puntillo KA, Miaskowski C, Kehrl K, Stannard D, Gleeson S, Nye P. Relationship between behavioral and physiological indicators of pain, critical care patients' self-reports of pain, and opioid administration. *Crit Care Med*. 1997;25(7):1159-66.
 58. 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(5):1470-6.
 59. Hjermstad MJ, Fayers PM, Haugen DF, Caraceni A, Hanks GW, Loge JH, et al. Studies comparing Numerical Rating Scales, Verbal Rating Scales, and Visual Analogue Scales for assessment of pain intensity in adults: a systematic literature review. *J Pain Symptom Manage*. 2011;41(6):1073-93.
 60. Ferreira-Valente MA, Pais-Ribeiro JL, Jensen MP. Validity of four pain intensity rating scales. *Pain*. 2011;152(10):2399-404.
 61. Chanques G, Viel E, Constantin JM, Jung B, de Lattre S, Carr J, et al. The measurement of pain in intensive care unit: comparison of 5 self-report intensity scales. *Pain*. 2010;151(3):711-21.
 62. Gélinas C, Fillion L, Puntillo KA, Viens C, Fortier M. Validation of the critical-care pain observation tool in adult patients. *Am J Crit Care*. 2006;15(4):420-7.
 63. Odhner M, Wegman D, Freeland N, Steinmetz A, Ingersoll GL. Assessing pain control in nonverbal critically ill adults. *Dimens Crit Care Nurs*. 2003;22(6):260-7.
 64. Kabes AM, Graves JK, Norris J. Further validation of the nonverbal pain scale in intensive care patients. *Crit Care Nurse*. 2009;29(1):59-66.
 65. Franck LS, Greenberg CS, Stevens B. Pain assessment in infants and children. *Pediatr Clin North Am*. 2000;47(3):487-512.
 66. Hamill-Ruth RJ, Marohn ML. Evaluation of pain in the critically ill patient. *Crit Care Clin*. 1999;15(1):35-54.
 67. Prkachin KM. The consistency of facial expressions of pain: a comparison across modalities. *Pain*. 1992;51(3):297-306.

68. Ambuel B, Hamlett KW, Marx CM, Blumer JL. Assessing distress in pediatric intensive care environments: the COMFORT scale. *J Pediatr Psychol.* 1992;17(1):95-109.
69. Riker RR, Picard JT, Fraser GL. Prospective evaluation of the Sedation-Agitation Scale for adult critically ill patients. *Crit Care Med.* 1999;27(7):1325-9.
70. Mateo OM, Krenzischek DA. A pilot study to assess the relationship between behavioral manifestations and self-report of pain in postanesthesia care unit patients. *J Post Anesth Nurs.* 1992;7(1):15-21.
71. Gélinas C, Fortier M, Viens C, Fillion L, Puntillo K. Pain assessment and management in critically ill intubated patients: a retrospective study. *Am J Crit Care.* 2004;13(2):126-35.
72. Gélinas C, Viens C, Fortier M, Fillion L. [Pain indicators in critical care]. *Perspect Infirm.* 2005;2(4):12-4, 6-20, 22.
73. Merkel SI, Voepel-Lewis T, Shayevitz JR, Malviya S. The FLACC: a behavioral scale for scoring postoperative pain in young children. *Pediatr Nurs.* 1997;23(3):293-7.
74. Li D, Puntillo K, Miaskowski C. A review of objective pain measures for use with critical care adult patients unable to self-report. *J Pain.* 2008;9(1):2-10.
75. Cade CH. Clinical tools for the assessment of pain in sedated critically ill adults. *Nurs Crit Care.* 2008;13(6):288-97.
76. Pudas-Tahka SM, Axelin A, Aantaa R, Lund V, Salanterä S. Pain assessment tools for unconscious or sedated intensive care patients: a systematic review. *J Adv Nurs.* 2009;65(5):946-56.
77. Arbour C, Gélinas C, Michaud C. Impact of the implementation of the critical-care pain observation tool (CPOT) on pain management and clinical outcomes in mechanically ventilated trauma intensive care unit patients: a pilot study. *J Trauma Nurs.* 2011;18(1):52-60.
78. Gélinas C, Arbour C, Michaud C, Vaillant F, Desjardins S. Implementation of the critical-care pain observation tool on pain assessment/management nursing practices in an intensive care unit with nonverbal critically ill adults: a before and after study. *Int J Nurs Stud.* 2011;48(12):1495-504.
79. Topolovec-Vranic J, Canzian S, Innis J, Pollmann-Mudryj MA, McFarlan AW, Baker AJ. Patient satisfaction and documentation of pain assessments and management after implementing the adult nonverbal pain scale. *Am J Crit Care.* 2010;19(4):345-54; quiz 55.
80. Skrobik Y, Ahern S, Leblanc M, Marquis F, Awissi DK, Kavanagh BP. Protocolized intensive care unit management of analgesia, sedation, and delirium improves analgesia and subsyndromal delirium rates. *Anesth Analg.* 2010;111(2):451-63.

81. Chanques G, Jaber S, Barbotte E, Violet S, Sebbane M, Perrigault PF, et al. Impact of systematic evaluation of pain and agitation in an intensive care unit. *Crit Care Med*. 2006;34(6):1691-9.
82. Williams TA, Martin S, Leslie G, Thomas L, Leen T, Tamaliunas S, et al. Duration of mechanical ventilation in an adult intensive care unit after introduction of sedation and pain scales. *Am J Crit Care*. 2008;17(4):349-56.
83. Puntillo KA, Stannard D, Miaskowski C, Kehrle K, Gleeson S. Use of a pain assessment and intervention notation (P.A.I.N.) tool in critical care nursing practice: nurses' evaluations. *Heart Lung*. 2002;31(4):303-14.
84. Gilbert DA, Altshuler KZ, Rago WV, Shon SP, Crismon ML, Toprac MG, et al. Texas Medication Algorithm Project: definitions, rationale, and methods to develop medication algorithms. *J Clin Psychiatry*. 1998;59(7):345-51.
85. Roche N, Durieux P. Clinical practice guidelines: from methodological to practical issues. *Intensive Care Med*. 1994;20(8):593-601.
86. Jobson KO, Potter WZ. International Psychopharmacology Algorithm Project Report. *Psychopharmacol Bull*. 1995;31(3):457-9, 91-500.
87. Carey K, Stefos T. Measuring the cost of hospital adverse patient safety events. *Health Econ*. 2011;20(12):1417-30.
88. Fitzgerald M, Farrow N, Scicluna P, Murray A, Xiao Y, Mackenzie CF. Challenges to real-time decision support in health care. In: Henriksen K, Battles JB, Keyes MA, Grady ML, editors. *Advances in patient safety: new directions and alternative approaches (Vol 2: Culture and Redesign)*. Rockville: Agency for Healthcare Research and Quality; 2008.
89. Newton CA, Smiley D, Bode BW, Kitabchi AE, Davidson PC, Jacobs S, et al. A comparison study of continuous insulin infusion protocols in the medical intensive care unit: computer-guided vs. standard column-based algorithms. *J Hosp Med*. 2010;5(8):432-7.
90. Schmeltz LR. Safe insulin use in the hospital setting. *Hosp Pract* (1995). 2009;37(1):51-9.
91. Tsai CL, Clark S, Camargo CA, Jr. Risk stratification for hospitalization in acute asthma: the CHOP classification tree. *Am J Emerg Med*. 2010;28(7):803-8.
92. Undeland DK, Kowalski TJ, Berth WL, Gundrum JD. Appropriately prescribing antibiotics for patients with pharyngitis: a physician-based approach vs a nurse-only triage and treatment algorithm. *Mayo Clin Proc*. 2010;85(11):1011-5.
93. Zaratkiewicz S, Whitney JD, Lowe JR, Taylor S, O'Donnell F, Minton-Foltz P. Development and implementation of a hospital-acquired pressure ulcer incidence tracking system and algorithm. *J Healthc Qual*. 2010;32(6):44-51.

94. Coyne P, Lyckholm L, Bobb B, Blaney-Brouse D, Harrington S, Yanni L. Managing pain with algorithms: an opportunity for improvement? Or: the development and utilization of algorithms to manage acute pain. *Pain Manag Nurs*. 2013;14(4):e185-8.
95. Polit DF, Beck CT. *Nursing research : generating and assessing evidence for nursing practice*. 9th ed. Philadelphia, PA: Wolters Kluwer Health; 2012.
96. Bair N, Bobek MB, Hoffman-Hogg L, Mion LC, Slomka J, Arroliga AC. Introduction of sedative, analgesic, and neuromuscular blocking agent guidelines in a medical intensive care unit: physician and nurse adherence. *Crit Care Med*. 2000;28(3):707-13.
97. Kerner Y, Plakht Y, Shiyovich A, Schlaeffer P. Adherence to guidelines of pain assessment and intervention in internal medicine wards. *Pain Manag Nurs*. 2013;14(4):302-9.
98. Ista E, van Dijk M, van Achterberg T. Do implementation strategies increase adherence to pain assessment in hospitals? A systematic review. *Int J Nurs Stud*. 2013;50(4):552-68.
99. Agency for healthcare research and quality: making health care safer: A critical analysis of patient safety practices. Evidence report/technology assessment number 43. Chapter 54. Educational Techniques used in changing provider behavior. Rockville, MD, Agency for healthcare research and quality, U.S.Department of health and human services, 2001.
100. O'Brien MA, Rogers S, Jamtvedt G, Oxman AD, Odgaard-Jensen J, Kristoffersen DT, et al. Educational outreach visits: effects on professional practice and health care outcomes. *Cochrane Database Syst Rev*. 2007(4):CD000409.
101. Ivers N, Jamtvedt G, Flottorp S, Young JM, Odgaard-Jensen J, French SD, et al. Audit and feedback: effects on professional practice and healthcare outcomes. *Cochrane Database Syst Rev*. 2012(6):CD000259.
102. Shojania KG, Jennings A, Mayhew A, Ramsay CR, Eccles MP, Grimshaw J. The effects of on-screen, point of care computer reminders on processes and outcomes of care. *Cochrane Database Syst Rev*. 2009(3):CD001096.
103. Flodgren G, Parmelli E, Doumit G, Gattellari M, O'Brien MA, Grimshaw J, et al. Local opinion leaders: effects on professional practice and health care outcomes. *Cochrane Database Syst Rev*. 2011(8):CD000125.
104. Giguère A, Legare F, Grimshaw J, Turcotte S, Fiander M, Grudniewicz A, et al. Printed educational materials: effects on professional practice and healthcare outcomes. *Cochrane Database Syst Rev*. 2012;10:CD004398.
105. The University of California, San Francisco School of Nursing Symptom Management Faculty Group. A model for symptom management. *Image J Nurs Sch*. 1994;26(4):272-6.

106. Dodd M, Janson S, Facione N, Faucett J, Froelicher ES, Humphreys J, et al. Advancing the science of symptom management. *J Adv Nurs*. 2001;33(5):668-76.
107. Smith MJ, Liehr PR. *Middle range theory for nursing*. 3rd. ed. New York: Springer Publishing Company; 2014.
108. Woolf SH. Practice guidelines, a new reality in medicine. II. Methods of developing guidelines. *Arch Intern Med*. 1992;152(5):946-52.
109. Young J, Siffleet J, Nikoletti S, Shaw T. Use of a Behavioural Pain Scale to assess pain in ventilated, unconscious and/or sedated patients. *Intensive Crit Care Nurs*. 2006;22(1):32-9.
110. Ahlers SJ, van Gulik L, van der Veen AM, van Dongen HP, Bruins P, Belitser SV, et al. Comparison of different pain scoring systems in critically ill patients in a general ICU. *Crit Care*. 2008;12(1):R15.
111. Juarez P, Bach A, Baker M, Duey D, Durkin S, Gulczynski B, et al. Comparison of two pain scales for the assessment of pain in the ventilated adult patient. *Dimens Crit Care Nurs*. 2010;29(6):307-15.
112. Chen YY, Lai YH, Shun SC, Chi NH, Tsai PS, Liao YM. The Chinese Behavior Pain Scale for critically ill patients: translation and psychometric testing. *Int J Nurs Stud*. 2011;48(4):438-48.
113. 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(1):127-33.
114. Devlin JW, Boleski G, Mlynarek M, Nerenz DR, Peterson E, Jankowski M, et al. Motor Activity Assessment Scale: a valid and reliable sedation scale for use with mechanically ventilated patients in an adult surgical intensive care unit. *Crit Care Med*. 1999;27(7):1271-5.
115. 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(22):2983-91.
116. Le Gall JR, Lemeshow S, Saulnier F. A new Simplified Acute Physiology Score (SAPS II) based on a European/North American multicenter study. *JAMA*. 1993;270(24):2957-63.
117. Reis Miranda D, Moreno R, Iapichino G. Nine equivalents of nursing manpower use score (NEMS). *Intensive Care Med*. 1997;23(7):760-5.
118. Landis JR, Koch GG. The measurement of observer agreement for categorical data. *Biometrics*. 1977;33(1):159-74.

119. Bucknall TK, Manias E, Presneill JJ. A randomized trial of protocol-directed sedation management for mechanical ventilation in an Australian intensive care unit. *Crit Care Med.* 2008;36(5):1444-50.
120. Svendsen K, Borchgrevink PC, Fredheim O, Hamunen K, Mellbye A, Dale O. Choosing the unit of measurement counts: the use of oral morphine equivalents in studies of opioid consumption is a useful addition to defined daily doses. *Palliat Med.* 2011;25(7):725-32.
121. Goodman LS, Brunton LL, Chabner B, Knollmann BC, editors. *Goodman & Gilman's pharmacological basis of therapeutics.* 12th ed. New York: McGraw-Hill; 2011.
122. Helse og omsorgsdepartementet (Health and Care Department) (2008) ACT 2008-06-20 no. 44: Act on Medical and Health Research (the Health Research Act) [Internet]. Oslo: Helse og omsorgsdepartementet. Available from: <http://app.uio.no/ub/ujur/oversatte-lover/data/lov-20080620-044-eng.pdf>.
123. Shadish WR, Cook TD, Campbell DT. *Experimental and quasi-experimental designs for generalized causal inference.* Boston: Houghton Mifflin; 2002.
124. Olsen BF, Rustoen T, Sandvik L, Miaskowski C, Jacobsen M, Valeberg BT. Development of a pain management algorithm for intensive care units. *Heart Lung.* 2015;44(6):521-7.
125. Gerbershagen HJ, Rothaug J, Kalkman CJ, Meissner W. Determination of moderate-to-severe postoperative pain on the numeric rating scale: a cut-off point analysis applying four different methods. *Br J Anaesth.* 2011;107(4):619-26.
126. Suppes T, Swann AC, Dennehy EB, Habermacher ED, Mason M, Crismon ML, et al. Texas Medication Algorithm Project: development and feasibility testing of a treatment algorithm for patients with bipolar disorder. *J Clin Psychiatry.* 2001;62(6):439-47.
127. Maneesriwongul W, Dixon JK. Instrument translation process: a methods review. *J Adv Nurs.* 2004;48(2):175-86.
128. Barr J, Fraser GL, Puntillo K, Ely EW, Gélinas 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(1):263-306.
129. Puntillo KA, Max A, Timsit JF, Vignoud L, Chanques G, Robleda G, et al. Determinants of procedural pain intensity in the intensive care unit. The Europain(r) study. *Am J Respir Crit Care Med.* 2014;189(1):39-47.
130. Dell'Oglio P, Abou-Haidar H, Leyh-Bannurah SR, Tian Z, Larcher A, Gandaglia G, et al. Assessment of the rate of adherence to international guidelines for androgen deprivation therapy with external-beam radiation therapy: a population-based study. *Eur Urol.* 2016;70(3):429-35.

131. Rose L, Haslam L, Dale C, Knechtel L, McGillion M. Behavioral pain assessment tool for critically ill adults unable to self-report pain. *Am J Crit Care*. 2013;22(3):246-55.
132. Johnson PN, Miller JL, Hagemann TM. Sedation and analgesia in critically ill children. *AACN Adv Crit Care*. 2012;23(4):415-34; quiz 35-6.
133. Cleeland CS, Ryan KM. Pain assessment: global use of the Brief Pain Inventory. *Ann Acad Med Singapore*. 1994;23(2):129-38.
134. Dale J, Bjornsen LP. Assessment of pain in a Norwegian emergency department. *Scand J Trauma Resusc Emerg Med*. 2015;23:86.
135. Rijkenberg S, Stilma W, Endeman H, Bosman RJ, Oudemans-van Straaten HM. Pain measurement in mechanically ventilated critically ill patients: Behavioral Pain Scale versus Critical-Care Pain Observation Tool. *J Crit Care*. 2015;30(1):167-72.
136. Liu Y, Li L, Herr K. Evaluation of two observational pain assessment tools in Chinese critically ill patients. *Pain Med*. 2015;16(8):1622-8.
137. Chanques G, Pohlman A, Kress JP, Molinari N, de Jong A, Jaber S, et al. Psychometric comparison of three behavioural scales for the assessment of pain in critically ill patients unable to self-report. *Crit Care*. 2014;18(4):R160.
138. Al Darwish ZQ, Hamdi R, Fallatah S. Evaluation of pain assessment tools in patients receiving mechanical ventilation. *AACN Adv Crit Care*. 2016;27(2):162-72.
139. Pudas-Tahka SM, Axelin A, Aantaa R, Lund V, Salanterä S. Translation and cultural adaptation of an objective pain assessment tool for Finnish ICU patients. *Scand J Caring Sci*. 2014;28(4):885-94.
140. Hylen M, Akerman E, Alm-Roijer C, Idvall E. Behavioral Pain Scale - translation, reliability, and validity in a Swedish context. *Acta Anaesthesiol Scand*. 2016;60(6):821-8.
141. Gélinas C, Puntillo KA, Joffe AM, Barr J. A validated approach to evaluating psychometric properties of pain assessment tools for use in nonverbal critically ill adults. *Semin Respir Crit Care Med*. 2013;34(2):153-68.
142. Yu A, Teitelbaum J, Scott J, Gesin G, Russell B, Huynh T, et al. Evaluating pain, sedation, and delirium in the neurologically critically ill-feasibility and reliability of standardized tools: a multi-institutional study. *Crit Care Med*. 2013;41(8):2002-7.
143. Altman DG. *Practical statistics for medical research*. London: Chapman and Hall; 1999.
144. Gerber A, Thevoz AL, Ramelet AS. Expert clinical reasoning and pain assessment in mechanically ventilated patients: a descriptive study. *Aust Crit Care*. 2015;28(1):2-8; quiz 9.

145. Oh J, Sohn JH, Shin CS, Na SH, Yoon HJ, Kim JJ, et al. Mutual relationship between anxiety and pain in the intensive care unit and its effect on medications. *J Crit Care*. 2015;30(5):1043-8.
146. Gélinas C, Chanques G, Puntillo K. In pursuit of pain: recent advances and future directions in pain assessment in the ICU. *Intensive Care Med*. 2014;40(7):1009-14.
147. Streiner DL, Norman GR. Health measurement scales: a practical guide to their development and use. 4th ed. Oxford: Oxford University Press; 2008.
148. Arbour C, Choiniere M, Topolovec-Vranic J, Loiselle CG, Puntillo K, Gélinas C. Detecting pain in traumatic brain-injured patients with different levels of consciousness during common procedures in the ICU: typical or atypical behaviors? *Clin J Pain*. 2014;30(11):960-9.
149. Lee K, Oh H, Suh Y, Seo W. Patterns and clinical correlates of pain among brain injury patients in critical care assessed with the critical care pain observation tool. *Pain Manag Nurs*. 2013;14(4):259-67.
150. Dehghani H, Tavangar H, Ghandehari A. Validity and reliability of behavioral pain scale in patients with low level of consciousness due to head trauma hospitalized in intensive care unit. *Arch Trauma Res*. 2014;3(1):e18608.
151. Echegaray-Benites C, Kapoustina O, Gélinas C. Validation of the use of the Critical-Care Pain Observation Tool (CPOT) with brain surgery patients in the neurosurgical intensive care unit. *Intensive Crit Care Nurs*. 2014;30(5):257-65.
152. Strom T, Martinussen T, Toft P. A protocol of no sedation for critically ill patients receiving mechanical ventilation: a randomised trial. *Lancet*. 2010;375(9713):475-80.
153. Landry MD, Sibbald WJ. Changing physician behavior: a review of patient safety in critical care medicine. *J Crit Care*. 2002;17(2):138-45.
154. Radtke FM, Heymann A, Franck M, Maechler F, Drews T, Luetz A, et al. How to implement monitoring tools for sedation, pain and delirium in the intensive care unit: an experimental cohort study. *Intensive Care Med*. 2012;38(12):1974-81.
155. Meulders A, Vansteenwegen D, Vlaeyen JW. Women, but not men, report increasingly more pain during repeated (un)predictable painful electrocutaneous stimulation: Evidence for mediation by fear of pain. *Pain*. 2012;153(5):1030-41.
156. Rosseland LA, Stubhaug A. Gender is a confounding factor in pain trials: women report more pain than men after arthroscopic surgery. *Pain*. 2004;112(3):248-53.
157. Georgiou E, Hadjibalassi M, Lambrinou E, Andreou P, Papathanassoglou ED. The impact of pain assessment on critically ill patients' outcomes: a systematic review. *Biomed Res Int*. 2015; 503830.
158. Payen JF, Bosson JL, Chanques G, Mantz J, Labarere J, Investigators D. Pain assessment is associated with decreased duration of mechanical ventilation in the

- intensive care unit: a post Hoc analysis of the DOLOREA study. *Anesthesiology*. 2009;111(6):1308-16.
159. Meehan DA, McRae ME, Rourke DA, Eisenring C, Imperial FA. Analgesic administration, pain intensity, and patient satisfaction in cardiac surgical patients. *Am J Crit Care*. 1995;4(6):435-42.
 160. Voigt L, Paice JA, Pouliot J. Standardized pain flowsheet: impact on patient-reported pain experiences after cardiovascular surgery. *Am J Crit Care*. 1995;4(4):308-13.
 161. Zaslansky R, Rothaug J, Chapman CR, Backstrom R, Brill S, Fletcher D, et al. PAIN OUT: the making of an international acute pain registry. *Eur J Pain*. 2015;19(4):490-502.
 162. Craven DE, Lei Y, Ruthazer R, Sarwar A, Hudcova J. Incidence and outcomes of ventilator-associated tracheobronchitis and pneumonia. *Am J Med*. 2013;126(6):542-9.
 163. Slutsky AS, Ranieri VM. Ventilator-induced lung injury. *N Engl J Med*. 2013;369(22):2126-36.
 164. Wunsch H, Linde-Zwirble WT, Angus DC, Hartman ME, Milbrandt EB, Kahn JM. The epidemiology of mechanical ventilation use in the United States. *Crit Care Med*. 2010;38(10):1947-53.
 165. Mullins PM, Goyal M, Pines JM. National growth in intensive care unit admissions from emergency departments in the United States from 2002 to 2009. *Acad Emerg Med*. 2013;20(5):479-86.
 166. Lefrant JY, Garrigues B, Pribil C, Bardoulat I, Courtial F, Maurel F, et al. The daily cost of ICU patients: a micro-costing study in 23 French Intensive Care Units. *Anaesth Crit Care Pain Med*. 2015;34(3):151-7.
 167. Patanwala AE, Duby J, Waters D, Erstad BL. Opioid conversions in acute care. *Ann Pharmacother*. 2007;41(2):255-66.
 168. DeBiasi EM, Akgun KM, Pisani M. Awake or Sedated: trends in the evaluation and management of agitation in the intensive care unit. *Semin Respir Crit Care Med*. 2015;36(6):899-913.
 169. Fink RM, Makic MB, Poteet AW, Oman KS. The Ventilated Patient's Experience. *Dimens Crit Care Nurs*. 2015;34(5):301-8.
 170. Demir Y, Korhan EA, Eser I, Khorshid L. Factors affecting experiences of intensive care patients in Turkey: patient outcomes in critical care setting. *J Pak Med Assoc*. 2013;63(7):821-5.
 171. Choi J, Hoffman LA, Schulz R, Tate JA, Donahoe MP, Ren D, et al. Self-reported physical symptoms in intensive care unit (ICU) survivors: pilot exploration over four months post-ICU discharge. *J Pain Symptom Manage*. 2014;47(2):257-70.

172. Baumbach P, Gotz T, Gunther A, Weiss T, Meissner W. Prevalence and characteristics of chronic intensive care-related pain: the role of severe sepsis and septic shock. *Crit Care Med*. 2016;44(6):1129-37.
173. Battle CE, Lovett S, Hutchings H. Chronic pain in survivors of critical illness: a retrospective analysis of incidence and risk factors. *Crit Care*. 2013;17(3):R101.
174. Puntillo KA, Naidu R. Chronic pain disorders after critical illness and ICU-acquired opioid dependence: two clinical conundra. *Curr Opin Crit Care*. 2016;22(5):506-12.
175. Puntillo K, Nelson JE, Weissman D, Curtis R, Weiss S, Frontera J, et al. Palliative care in the ICU: relief of pain, dyspnea, and thirst-a report from the IPAL-ICU Advisory Board. *Intensive Care Med*. 2014;40(2):235-48.
176. Chanques G, Nelson J, Puntillo K. Five patient symptoms that you should evaluate every day. *Intensive Care Med*. 2015;41(7):1347-50.