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Review article

Pain management interventions in the Paediatric Intensive Care Unit: A scoping review

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ABSTRACT

Objective: To map research based pain management interventions used in the paediatric intensive care unit.
Methodology: A scoping review of research literature has been conducted. Five databases were searched from their inception to end 2015 (CINAHL, EMBASE, MEDLINE, PsychINFO, and ProQuest Dissertations & Theses Global). Reference lists from the screened full text articles were reviewed.
Results: 7046 articles were identified, 100 underwent full text screening and 27 were included in the scoping review. Seventeen (63%) were non-experimental, and 10 (37%) were experimental, of which 8 (30%) were randomised controlled trials. The majority of the articles focused on pharmacological interventions (n = 21, 78%), one on physical, and one on psychological interventions. Four studies included more than one category of interventions. The majority of the studies focused on post-operative pain management (n = 18, 67%), three (11%) on analgesia and sedation management and six (22%) on other pain management for different conditions.
Discussion: Most studies included in this scoping review focused on medications and post-operative pain management and most were non clinical trials. More research, including clinical trials, is warranted to determine the effectiveness of pharmacological and non-pharmacological interventions for pain management in the paediatric intensive care unit.

Implications for clinical practice

- The use of analgesic agents (other than morphine and fentanyl) in the paediatric intensive care unit requires caution due to the paucity of research that studied their use, effectiveness, and safety.
- Nurses are encouraged to increase of the use of validated pain scales for children, for example, COMFORT-B and FLACC scales.
- More research is needed on non-pharmacological interventions in the paediatric intensive care unit.
- Encourage multidisciplinary (physicians, nurses, and pharmacists) collaboration for pain management in the paediatric intensive care unit.

Introduction

Access to appropriate pain management is considered one of the human rights (International Association for Study of Pain (IASP), 2015). Pain management in the Paediatric Intensive Care Unit (PICU) however is challenging (Ismail, 2016) and has been reported to be sub-optimal (Agarwal et al., 2010; Grant et al., 2012; LaFond et al., 2014). Poorly managed pain in the PICU can lead to harmful physical and psychological consequences (Ismail, 2016). Recurrent pain as a result of hospitalised children's exposure to invasive procedures in the PICU, reported as an average of 13 procedures/day (Stevens et al., 2011), is an important factor

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for the development of negative psychological outcomes post discharge from the PICU including medical fears and posttraumatic stress (Rennick et al., 2004; Rennick et al., 2002).

Two most commonly used definitions for pain are defined by the IASP and by McCaffery (1977). Forty years ago, McCaffery defined pain as "*what the patient says it is, and exists whenever the patient says it does*" (McCaffery, 1977, p. 11). The IASP defines pain as "*an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage*" (IASP, 2015, p. 1). Recently, Williams and Craig (2016) suggested including cognitive and social components of pain. These definitions indicate that pain is mainly a subjective experience.

Assessment of pain in children is complex, and involves physiological, psychological, behavioural, social and developmental factors. In the PICU, one has to take into consideration the critical nature of the children's illness and their ability to participate in the assessment of pain (Ismail, 2016; Oakes, 2011; Ramelet et al., 2004; Srouji et al., 2010). Verbal self-report of pain can be considered the most important way to communicate the subjective emotional and sensory experience about pain to others. For sick infants and young children in the PICU, not only are their cognitive and expressive language capabilities not well developed, but they are critically ill and may be unconscious and intubated (Gelinas et al., 2004; Ismail, 2016; Oakes, 2011; Srouji et al., 2010; Turner, 2005). In addition, self-report of pain can be compromised by many factors common in the PICU such as the complex condition of the child, administration of pharmacological agents, such as the use of sedative and neuromuscular blocking agents which affecting the ability to react with stimulus, and the use of mechanical ventilation and other supportive devices necessary to maintain vital functions (American Association of Critical-Care Nurses, 2014; Gelinas et al., 2004; Ismail, 2016; Oakes, 2011; Turner, 2005). Caring for unconscious and intubated infants, children and adults, who cannot self-report, mandate healthcare providers (HCPs) to use physiological and behavioral indicators of pain.

Physiological measures such as vital signs of heart rate, respiratory rate, blood pressure, can be compromised by different factors including administration of vasoactive medications, which are commonly used in the critical care settings. Behavioural indicators could be masked or altered by commonly used medications in the PICU such as sedatives and paralytic agents (Ismail, 2016). A number of composite pain assessment tools exist which are suitable for use in the PICU. The two most common validated pain assessment scales used in the PICU are the COMFORT and the FLACC (Face, Legs, Activity, Cry, and Consolability) scales (Ambuel et al., 1992; Ismail, 2016; Johansson and Kokinsky, 2009; Oakes, 2011; Voepel-Lewis et al., 2010).

Healthcare staff can use research findings to guide and help them manage pain (Registered Nurses Association of Ontario, 2013; Rycroft-Malone, 2004; Samuels and Fetzer, 2009). In critical care settings, however, there is a wide gap between clinical practice and the findings of research (Samuels and Fetzer, 2009). In addition, there are concerns regarding the quality of research findings used to create recommendations for pain management in the PICU. Playfor et al. (2006) stated "*the quality of evidence available in the literature to support these recommendations is poor*" (p. 1133). Identifying, summarising and synthesising the available research on pain management interventions used in the PICU is needed to inform future directions for practice and research. Therefore, the aim of this study is to identify research based pain management interventions used in the PICU, by conducting a scoping review on pain management interventions evaluated and used in the PICU.

Method

Arksey and O'Malley's framework for scoping reviews guided this study (Arksey and O'Malley, 2005). The five steps of this framework include: (1) identifying the research question, (2) identifying relevant studies, (3) study selection, (4) charting the data and (5) collating, summarising, and reporting the results.

Literature search

The specific question for this review was: "Which pain management interventions are evaluated and used for patients in the Pediatric Intensive Care Unit (PICU)?" The search strategy included five databases (CINAHL, EMBASE, MEDLINE, PsychINFO, and ProQuest Dissertations and Theses Global), reference lists of included studies, and consultations with pain experts. The search was conducted by a medical librarian using the following search terms: Pain, pain treatment, pain intervention, Pediatric Intensive Care Unit, children, child, critically ill, critical care, critical illness and terminal illness (Appendix A) as well as database specific subject headings. Since no similar review was conducted in the past, no date limit in terms of publication time was set.

Article selection

The citations from the electronic data search were uploaded into the Covidence software (Covidence, 2017). Duplicates were identified by Covidence and then removed. Two independent reviewers (AI and WD) screened the titles and abstracts to identify articles that met the inclusion criteria. The inclusion criteria were: (1) studies with a primary focus on pain management interventions studied or used in the PICU; (2) published in English; (3) quantitative designs; (4) primary research and (5) patients from 0 to 18 years of age in the PICU. The exclusion criteria were: (1) books, book chapters, conference papers or abstracts, editorials and commentaries; (2) studies primarily focused on sedation; and (3) studies primarily focused on sedatives or opioid withdrawal. A third independent reviewer (DH) resolved disagreements at this stage of screening. All articles screened for inclusion were read in full by the two reviewers (AI and WD) to ensure that they met the inclusion criteria and disagreements at the full text stage were resolved by the third reviewer (DH).

Reference list of articles retained after full text review were read to determine other potential studies not found in the database searches, and subjected to the same screening method as described above. Furthermore, a panel of eight experts from the fields of research, pain and child health were consulted to identify additional articles not captured by the search.

Data charting

In keeping with the process for data extraction described by Arksey and O'Malley, two independent reviewers were involved in data extraction. Using a customised data extraction form, the first reviewer extracted the following data: Authors' names, year of publication, country where the study was conducted, aim of the study, study design, sample characteristics, data collection methods and outcome measures, pain management intervention (s), and the major findings. The second reviewer read each article and reviewed the data extraction forms to ensure accuracy of the data extraction.

The literature was organised according to four intervention types. That helped to organize the findings to best understand the state of the science based on intervention type. These four main categories of interventions were: Pharmacological;

psychological; physical; and others e.g., music. Some studies contained data related to more than one category.

Results

As shown in Fig. 1, after duplicates were removed, 5969 records were screened, 100 full-text records were assessed for eligibility, and 27 studies were included in this study.

Twenty-seven studies relating to pain management interventions evaluated or used in the PICU were identified; 25 from the database search and two from reference lists. Seventeen studies (63%) were non-experimental, and 10 (37%) were experimental, of which 8 (30%) were randomised controlled trials (RCTs) (Table 1).

The majority of the studies focused on pharmacological interventions (n = 21, 78%), one on physical, one on psychological interventions and four studies included more than one category of interventions. The most commonly studied pharmacological agents to manage pain used or evaluated in the PICU were morphine and fentanyl. Non-pharmacological strategies were reported in six studies (Table 2). The most common reported pain assessment tool was the FLACC scale (11 studies). Studies included

Table 1
Design, Condition, and Intervention Category for Included Studies.

	N (%)
Design	
Observational	17 (63%)
Randomised controlled trial	8 (30%)
Nonrandomised controlled trial	2 (7%)
Condition studied	
Post-operative	18 (67%)
Mechanically ventilated children	6 (22%)
Trauma	2 (7%)
Invasive procedures	1 (4%)
Category of intervention	
Pharmacological	21 (78%)
Physical	1 (4%)
Psychological	1 (4%)
More than one category	4 (15%)

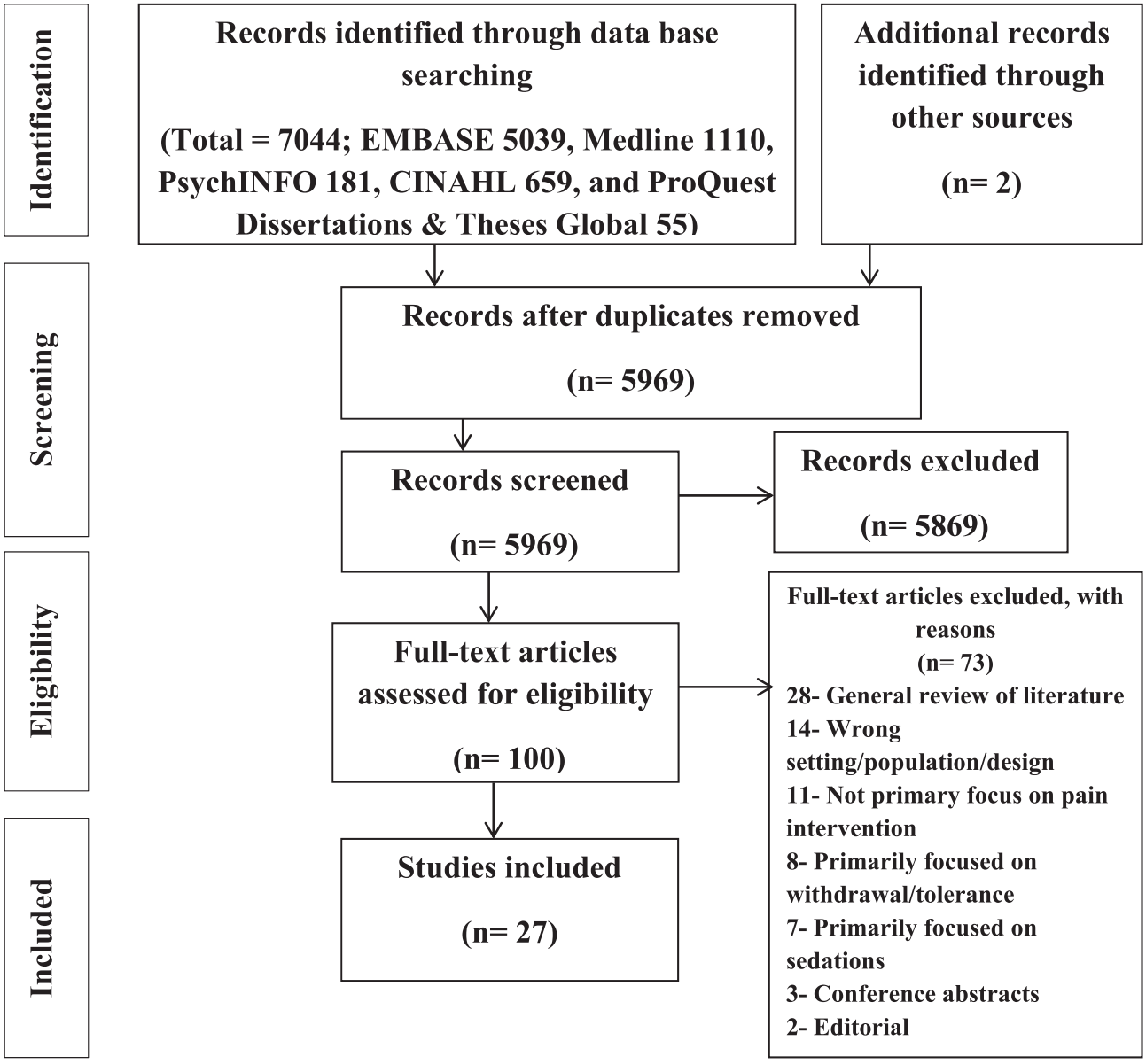

Fig. 1. Selection process for studies of pain management interventions in the Pediatric Intensive Care Units.

Table 2
Pain Management Intervention (Used or Tested) in the 27 Studies *Some studies included more than one intervention.

Intervention	N (%)
Medication	
Fentanyl	14 (52%)
Morphine	10 (37%)
Dexmedetomidine	4 (15%)
Acetaminophen	3 (11%)
Bupivacaine (Regional)	2 (7%)
Remifentanil	2 (7%)
Tramadol	2 (7%)
Hydromorphone	1 (4%)
Lidocaine (Local)	1 (4%)
Meperidine	1 (4%)
Psychological	
Mental imagery	3 (11%)
Hypnosis	2 (7%)
Detailed inquiry	1 (4%)
Distraction	1 (4%)
Parent's presence	1 (4%)
Physical	
Acupuncture	2 (7%)
Positioning	2 (7%)
Holding	1 (4%)
Rocking	1 (4%)
Soothing	1 (4%)
Stroking	1 (4%)
Swaddling	1 (4%)
Touch	1 (4%)
Others	
Music	2 (7%)
Environmental modification	2 (7%)

in this review were published between 1992 and 2015. Six studies were published between 1992 and 1999, thirteen (48%) between 2000 and 2009, and eight between 2010 and 2015. Appendix B lists and summarises the 27 studies included in this review.

Pharmacological interventions

The most commonly studied pharmacological agents for pain control were opioids, including morphine and fentanyl. They were used for a wide range of patients and different conditions such as post-operative pain, invasive procedures, and mechanically ventilated patients. Other agents less frequently used for pain management included remifentanil, tramadol, dexmedetomidine, acetaminophen, hydromorphone and ketorolac. Regional (bupivacaine) and local anesthetic agents (lidocaine) were reported in three studies (Table 2).

As shown in Table 3, 10 studies conducted in five different countries demonstrated the use of morphine in critically ill children (Bauchner et al., 1992; Chu et al., 2006; Coffman et al., 1997; Van Dijk et al., 2002; Larson et al., 2013; Lieh-Lai et al., 1999; Reiter et al., 2012; Shayevitz et al., 1996; Sheridan et al., 2001; Weldon et al., 1993). The majority of studies of morphine were conducted in the United States of America (USA) (70%), and published between 1992 and 2013. Five experimental studies (50%) demonstrated the effectiveness morphine for post-operative pain control in the PICU. The other five (non-experimental) reported the use of morphine in the PICU in mechanically ventilated children, and during invasive procedures. Morphine was administered by different methods (intravenous, epidural, continuous infusion, intermittent infusion, patient-controlled analgesia (PCA) and nurse-controlled analgesia (Table 3).

As summarised in Table 4, 14 studies conducted in six different countries included fentanyl for pain management in the PICU for a wide range of patients undergoing surgery or for management during mechanical ventilation (Akinci et al., 2005; Amigoni et al., 2012; Bauchner et al., 1992; Benini et al., 2010; Butkovic et al., 2007; Chrysostomou et al., 2009; Coffman et al., 1997; DeBerry

Table 3
Studies reporting on the use or evaluation of morphine in the PICU (n = 10).

Author(s)	Country	Year	Study Design	Main findings
Bauchner et al.	USA and Canada	1992	Cross sectional, multisite survey on the use of analgesic agents during invasive procedures	Morphine one of the most commonly used analgesics
Weldon et al.	USA	1993	RCT on the use of PCA and PCA plus continuous infusion of morphine post elective scoliosis surgery in older alert children	PCA and PCA plus continuous infusion of morphine achieved the same pain control
Shayevitz et al.	USA	1996	Retrospective patients' records review, case control Lumbar epidural morphine infusion vs. other IV opioid post cardiac surgery	Pain scores in lumber epidural morphine patients were significantly less than in the IV opioid on day one post-operation ($p = 0.03$)
Coffman et al.	USA	1997	Descriptive of the nurses' assessment and management of pain	Morphine was used in 59 out of 112 pain observations (53%)
Lieh-Lai et al.	USA	1999	RCT, children who received IV morphine vs. IV ketorolac postoperative	Sixty eight percent of patients who received ketorolac reported pain relief during the first 2 hrs after dosing, compared to 58% of those who received morphine ($p = 0.2$)
Sheridan et al.	USA	2001	Retrospective review, burned children requiring prolonged mechanical ventilation	Doses of morphine were high than in other conditions, averaged 0.40 mg/kg/hr ± 0.24 mg/kg/hour
Van Dijk et al.	Netherlands	2002	RCT, continuous vs. equivalent bolus dose of morphine post major thoracic or abdominal surgery	No differences in pain scores between continuous morphine infusion and bolus ($p = 0.84$)
Chu et al.	Taiwan	2006	RCT, children who received morphine vs. tramadol post cardiac surgery	No difference in pain scores during the 48 hrs post operation, except at first hour after surgery (higher in morphine group, $p = 0.03$)
Reiter et al.	USA	2012	Retrospective charts review of pain management agents for mechanically ventilated children	Morphine or fentanyl were used in 90% of the patients as a first line opioid
Larson et al.	Australia	2013	A pre and post chart audit pre and post analgesia sedation guideline introduction	The dosage and administration of morphine were according to the guidelines. As per the guidelines, oral clonidine use increased and ketamine use decreased

Hr = Hour.
IV = Intravenous.
Kg = Kilogram.
NCA = Nurse Controlled Analgesia.
PCA = Patient Controlled Analgesia.
RCT = Randomised Clinical Trial.
USA = United States of America.
Mg = Milligram.

Table 4
Studies reporting the use or evaluation of fentanyl in the PICU (n = 14).

Author(s)	Country	Year	Study Design	Main findings
Bauchner et al.	USA and Canada	1992	Cross sectional on the use of analgesic agents during invasive procedures	Fentanyl was one of the most commonly used analgesics
Shayevitz et al.	USA	1996	Retrospective compared between lumber infusion of morphine and IV infusion of fentanyl post cardiac surgury	Pain scores for IV fentanyl group were higher than for lumber epidural morphine patients on day one post cardiac surgery ($p = 0.03$)
Coffman et al.	USA	1997	Descriptive of the nurses' assessment and management of pain	Fentanyl was used in 12 out of 112 pain observations (11%).
Akinci et al.	Turkey	2005	RCT compared between remifentanil and fentanyl infusion postoperative	No differences in pain scores between children who received fentanyl or remifentanil
DeBerry et al.	USA	2005	Survey on pain and sedation management in children during ECMO	Fentanyl was the most commonly used pain medication (62% of the ECMO centres).
Chrysostomou et al.	USA	2009	Retrospective case series on dexmedetomidine use post cardiac surgery	No difference in pain scores between patients who received dexmedetomidine plus fentanyl infusion and those who received dexmedetomidine only
Renfrow	USA	2009	Retrospective chart review of pain management of extubated postoperative children	Fentanyl was administered in 28% of patients
Benini et al.	Italy	2010	Multisite survey on analgesia and sedation	Fentanyl was the analgesic of choice for patients requiring combination of sedatives and analgesics e.g. for mechanical ventilation
Amigoni et al.	Italy	2012	Descriptive multisite survey on analgesia and sedation	In 16 (66.6%) of PICUs, the most commonly used opioid was fentanyl.
Naguib et al.	USA	2012	Retrospective review on pain management post cardiac surgery	NCA with fentanyl was used in 64% of patients. Continuous infusion of fentanyl was used in 36% of patients
Reiter et al.	USA	2012	Retrospective charts review of pain management agents for mechanically ventilated children	Fentanyl or morphine were used in 90% of the patients as a first line opioid.
Larson et al.	Australia	2013	A pre and post chart audit pre and post analgesia sedation guideline introduction	The dosage of fentanyl was consistent with sedoanalgesia guidelines
Horvath et al.	USA	2015	Retrospective cohort on the use of dexmedetomidine post cardiac surgery	86% of the patients received fentanyl in combination with dexmedetomidine

ECMO = Extracorporeal Membrane Oxygenation.
IV = Intravenous.
NCA = Nurse Controlled Analgesia.
PCA = Patient Controlled Analgesia.
RCT = Randomised Clinical Trial.
USA = United States of America.

et al., 2005; Horvath et al., 2015; Larson et al., 2013; Naguib et al., 2012; Reiter et al., 2012; Renfrow, 2009; Shayevitz et al., 1996). Nine studies were conducted in USA, and published between 1992 and 2015. Three of the studies were experimental. Seven studies reported that fentanyl was used to manage children's post-operative pain after different kinds of surgery including cardiac, spinal and thoracic surgery. The use of continuous intravenous infusion of fentanyl was reported as a key analgesic agent for patients requiring mechanical ventilation in five studies. One study of pain management practices in the PICU reported that fentanyl was one of the most commonly studied pharmacological analgesics during invasive procedures such as central line insertion

The use of other analgesics were less examined compared to morphine and fentanyl and are summarized in Table 5. These include remifentanil, dexmedetomidine, tramadol, acetaminophen, ketorolac, regional and local anesthetics.

The use of remifentanil was reported in only two studies for short term analgesia post orthopedic spinal surgery in children requiring mechanical ventilation and as a second choice for analgesia after fentanyl (Akinci et al., 2005; Benini et al., 2010). The use of tramadol was reported in two clinical trials (Chu et al., 2006; Maldini et al., 1997). The older study by Maldini, a non-randomised-clinical trial, found that continuous administration of tramadol achieved improved pain control compared to intermittent tramadol in 42 children aged one month to 16 years after major surgery (Maldini et al., 1997). Chu reported that tramadol provided an equivalent analgesic efficacy to morphine post cardiac surgery as well as equivalent adverse effect of nausea and vomiting (Chu et al., 2006).

Four studies conducted in the USA demonstrated the effectiveness of using dexmedetomidine for pain management after cardiac surgery, either as a primary or adjunct analgesic (Chrysostomou et al., 2006, 2009; Horvath et al., 2015; Naguib et al., 2012). The total number of patients who received dexmedetomidine in these four studies was 250 and included spontaneously breathing and mechanically ventilated patients. The age of the children ranged from newborn to 17.5 years (Table 5).

Three studies reported the use of acetaminophen in the PICU for non-ventilated children (Van Der Marel et al., 2001; Prins et al., 2008; Renfrow, 2009). Two RCTs examined the effectiveness of acetaminophen after craniofacial surgery in infants and children (6 months to two years). The two trials used a 10-cm Visual Analog Scale (VAS) (McGrath et al., 1985) scale to measure pain. Van Der Marel et al. (2001) found that rectally administered acetaminophen provided superior analgesia than when orally administered (Van Der Marel et al., 2001) and Prins et al. (2008) found that rectally administered acetaminophen provided less effective analgesia than when administered intravenously (Prins et al., 2008). A descriptive study reported that acetaminophen was one of the most commonly agents studied in infants and children (6 months to 17 years) who had undergone 32 different surgical procedures (Renfrow, 2009). One study found that intravenous ketorolac as effective as intravenous morphine to manage moderate to severe pain post-operative (Lieh-Lai et al., 1999) (Table 5).

The use of bupivacaine was reported in two studies. One study found no difference in pain scores between children, aged 10–18 years post spinal surgery, who received bupivacaine compared to those who did not, however, children who received bupivacaine were less likely to require morphine infusions (32.6% versus 85.2%, $p < 0.001$) (Ross et al., 2011). No significant differences in pain scores between epidural infusion (with bupivacaine plus fentanyl) and PCA (with fentanyl) in patients aged between 8 and 19 years

Table 5
Studies reporting the use or evaluation of dexmedetomidine, remifentanil, tramadol, acetaminophen, ketorolac, bupivacaine, and lidocaine (n = 15).

Name	Author(s)	Country	Year	Study Design	Main findings
Remifentanil (n = 2)	Akinci et al.	Turkey	2005	RCT, children received remifentanil vs.fentanyl infusion postoperative	No differences in pain scores between children who received fentanyl and remifentanil
	Benini et al.	Italy	2010	Multisite survey on analgesia and sedation	Remifentanil was the second analgesic of choice (after fentanyl)
Tramadol (n = 2)	Maldini et al.	Croatia	1997	Cohort study on tramadol post major surgeries	Continuous infusion of tramadol was more effective than intermittent administration
	Chu et al.	Taiwan	2006	RCT, children received morphine vs. tramadol post cardiac surgery	Pain scores were significantly higher in morphine group in the first hour post-operatively
Dexmedetomidine (n = 4)	Chrysostomou et al.	USA	2006	Retrospective, case series post cardiac surgery	Dexmedetomidine was the primary used sedative and analgesic agent.
	Chrysostomou et al.	USA	2009	Retrospective case series post cardiac surgery	No difference in pain scores between using dexmedetomidine alone and in combination with sedatives/analgesics
	Naguib et al.	USA	2012	Retrospective review on pain management post cardiac surgery	Dexmedetomidine was used as an adjunct in 5 out of 33 patients and led to decrease in fentanyl use.
	Horvath et al.	USA	2015	Retrospective cohort post cardiac surgery	Pain scores indicated adequate analgesia
Acetaminophen (n = 3)	Van Der Marel et al.	Netherlands	2001	RCT, compared between rectal and oral acetaminophen	Rectal administration of acetaminophen resulted in lower pain scores compared to oral acetaminophen post craniofacial surgery
	Prins et al.	Netherlands	2008	RCT, compared between rectal and IV acetaminophen post craniofacial surgery	No difference in pain scores between IV and rectal acetaminophen. Children who received rectal acetaminophen experienced more discomfort.
	Renfrow	USA	2009	Retrospective chart review of extubated postoperative	Acetaminophen was administered in 52% in post-operative children
Bupivacaine (n = 2)	Butkovic et al.	Croatia	2007	RCT, epidural bupivacaine with fentanyl vs. IV fentanyl using PCA	No difference in pain scores between epidural bupivacaine with fentanyl and IV fentanyl by PCA
	Ross et al.	USA	2011	Retrospective post spinal surgery	Children who received bupivacaine required fewer infusion of opioid than who did not
Lidocaine (n = 1)	Bauchner et al.	USA and Canada	1992	Cross sectional on the use of analgesic agents during invasive procedures	Lidocaine was one of the most commonly used analgesics to control pain during invasive procedures
Ketorolac (n = 1)	Lieh-Lai et al.	USA	1999	RCT, compared between children who received IV morphine vs. IV ketorolac postoperative	Children who received ketorolac reported pain relief in the first 2 hrs after dosing as the ones to who received morphine ($p = 0.2$). Vomiting was more common in children received ketorolac

IV = Intravenous.
PCA = Patient Controlled Analgesia.
RCT = Randomised Clinical Trial.

post thoracoscopic surgery were reported (Butkovic et al., 2007). Therefore, the evidence supporting regional anesthetics in the PICU remains mixed. The use of local anaesthetic (lidocaine) during invasive procedures such as central line insertion was reported in only one descriptive study as one of the most used pharmacological analgesics during invasive procedures (Bauchner et al., 1992) (Table 5). No evidence of analgesic efficacy in the PICU has however been reported.

Psychological interventions

The use of psychological interventions in the PICU for pain management was reported in only four studies, all conducted in North America (Bauchner et al., 1992; Coffman et al., 1997; Kline et al., 2010; Sharek et al., 2006). All three were observational studies. Guided imagery was reported in three studies. Other psychological interventions reported were hypnosis, detailed inquiry, parent's presence and distraction (Bauchner et al., 1992; Coffman et al., 1997; Kline et al., 2010). One descriptive cohort study determined the impact of implementing a combination of psychological, physical, and pharmacological interventions (such as positioning, guided imagery, hypnosis, and parental education) on pain control post liver transplantation (Sharek et al., 2006). Comparisons were made between two groups; the group of children who received the combination of interventions (n = 14, mean age = 5.3 years) and a control group who underwent liver transplantation before introduction of the intervention when only pharmacological pain interventions were provided (n = 13, mean age = 4.4 years). Mean pain scores were statistically significantly lower in the children who received the combination of interventions (2.12 versus 2.84) ($p \leq 0.05$), however results need to be interpreted with caution given the small sample sizes and the descriptive pre-post study design.

Physical interventions

Physical interventions to reduce pain in the PICU were reported in only four studies (Bauchner et al., 1992; Coffman et al., 1997; Sharek et al., 2006; Wu et al., 2009), three of which also included psychological interventions as previously discussed (Bauchner et al., 1992; Coffman et al., 1997; Sharek et al., 2006). Three were observational studies (Bauchner et al., 1992; Coffman et al., 1997; Sharek et al., 2006) and the fourth was a nonrandomized clinical trial (Wu et al., 2009). The four studies were conducted in North America. Two studies reported on acupuncture (Sharek et al., 2006; Wu et al., 2009), two studies reported the use of positioning (Coffman et al., 1997; Sharek et al., 2006), one study reported on stroking and soothing (Bauchner et al., 1992), and

one study reported on touch, holding, and rocking (Coffman et al., 1997). Acupuncture was shown to be effective in reducing post-operative pain in children from 7 months to 18 years ($p \leq 0.05$) (Wu et al., 2009). Two studies just reported the use of physical interventions and not the effectiveness (Bauchner et al., 1992; Coffman et al., 1997) while Sharek et al reported that the combination of pharmacological as well as physical (e.g., positioning and acupuncture) and psychological (e.g. guided imagery) interventions resulted in reduced pain scores in children post liver transplantation ($p \leq 0.05$) (Sharek et al., 2006).

Others (Environmental modification and music Therapy)

Music therapy and environmental modifications were reported in only two observational studies (Coffman et al., 1997; Renfrow, 2009). A study from the USA reviewed 100 charts of extubated infants and children (6 months to 17 years) following surgery (Renfrow, 2009). Methods reported were environmental, such as a quiet environment (27%), dim lights (12%), limiting visitors (9%) and music (9%) (Renfrow, 2009). These studies reported the use of these interventions and not the effectiveness.

Pain assessment tools

The most commonly reported pain assessment tools across the studies were the FLACC and the VAS scales. The FLACC scale was reported as used in 11 studies, to assess pain in children from zero to 18 years and for a wide range of conditions including mechanical ventilation and post-operative pain (Amigoni et al., 2012; Chrysostomou et al., 2006, 2009; Horvath et al., 2015; Larson et al., 2013; Naguib et al., 2012; Reiter et al., 2012; Renfrow, 2009; Ross et al., 2011; Sharek et al., 2006; Wu et al., 2009). The VAS scale was reported in six studies and was used for post-operative pain assessment for children from zero to 18 years (Butkovic et al., 2007; Prins et al., 2008; Ross et al., 2011; Van Der Marel et al., 2001; Van Dijk et al., 2002; Weldon et al., 1993). The self-reported VAS scale was used in three studies for children aged eight years and older (Butkovic et al., 2007; Ross et al., 2011; Weldon et al., 1993). Three studies reported the use of observational VAS scale for small children from six months to three years old (Prins et al., 2008; Van Der Marel et al., 2001; Van Dijk et al., 2002). The COMFORT-B scale was reported in three studies in children needing pain and sedation management e.g., mechanically ventilated children and for post-operative pain assessment (Table 6).

Discussion

This scoping review included 27 studies published over a period of three decades, most of which focused on pharmacological interventions and for post-operative pain management. This review demonstrated that there is a paucity of research regarding pain management interventions in the PICU. Pharmacological strategies were studied more than non-pharmacological interventions with opioids being the most commonly studied pharmacological agents.

Pharmacological interventions

For opioids, the existing guidelines recommend opioids to manage moderate to severe pain in children. The majority of children in the PICU experience moderate to severe pain as a result of different pain sources including underlying illness, surgery, trauma, supportive and monitoring systems, and invasive procedures (Ismail, 2016; Stevens et al., 2011). Morphine and fentanyl are the most

Table 6
Pain assessment tools used across the studies.

Scale	Age of the patient	Condition	Authors
FLACC (n = 11 studies)	0–18	Post-operative, pain and sedation management, mechanically ventilation management	Amigoni et al., 2012; Chrysostomou et al., 2006; Chrysostomou et al., 2009; Horvath et al., 2015; Larson et al., 2013; Naguib et al., 2012; Renfrow, 2009; Reiter et al., 2012; Ross et al., 2011; Sharek et al., 2006; Wu et al., 2009
VAS (n = 6 studies)	0–18 years	Post-operative	Butkovic et al., 2007; Prins et al., 2008; Ross et al., 2011; Van Der Marel et al., 2001; Van Dijk et al., 2002; Weldon et al., 1993
Wong-Baker Faces Scale (n = 4 studies)	3–18 years or verbal children	Post-operative, trauma	Kline et al., 2010; Renfrow, 2009; Ross et al., 2011; Sharek et al., 2006
COMFORT-B (n = 3 studies)	0–12	Post-operative, pain and sedation management	Larson et al., 2013; Prins et al., 2008; Van Dijk et al., 2002
COMFORT (n = 3 studies)	0–18	Pain and sedation management	Amigoni et al., 2012; Benini et al., 2010; Van Der Marel et al., 2001
CHEOPS (n = 2 studies)	2 months to 18 years	Post-operative	Chu et al., 2006; Lieh-Lai et al., 1999
N-PASS (n = 2 studies)	0–3 months	Pain and sedation management, post-operative	Amigoni et al., 2012; Naguib et al., 2012
CRIES (n = 2 studies)	0–6 months	Pain and sedation management, post-operative	Amigoni et al., 2012; Chrysostomou et al., 2009
Numeric pain scale (0–10) (n = 2 studies)	7 months to 18 years)	Post-operative	Sharek et al., 2006; Wu et al., 2009
Pain intensity score from 0 to 10 (Ross & Ross, 1988) (n = 1 study)	3–18 years	Post-operative	Shayevitz et al., 1996
Behavioural pain scale (Payen, Bru, & Bosson, 2001) (n = 1 study)	3–16 years	Post-operative	Akinci et al., 2005
Numeric Visual Analog Scale (Wong et al. 1999) (n = 1 study)	7–9 years	Post-operative	Chrysostomou et al., 2006

CHEOPS = Children's Hospital of Eastern Ontario Pain Scale.
CRIES = Crying, requires oxygen, increased vital signs, expression and sleeplessness scale.
FLACC = Face Legs Activity Cry Consolability.
N-PASS = Neonatal pain, agitation and sedation scale.
VAS = Visual Analogue Scale.

studied and reported as used opioids in terms of efficacy, dose, methods of administration, and adverse effects. The wide-spread use of these opioids is consistent with the recommendations of the World Health Organization (WHO), which recommends administration of opioid analgesics for moderate to severe pain in children (WHO, 2012). Previous to the WHO recommendations, Playfor et al. (2006) recommend either morphine or fentanyl by continuous intravenous infusion for severe pain in the PICU. Other opioids have been studied less frequently than morphine and fentanyl. For example, remifentanil and tramadol were studied in four studies only. It is not surprising that tramadol and remifentanil were less frequently used and studied as the existing guidelines do not support their use in the PICU due to the safety and pacuity of research that supporting their use (Playfor et al., 2006, WHO, 2012).

Non-opioid analgesics were studied to manage moderate to severe pain. Dexmedetomidine has been used as a primary or adjunct agent post cardiac surgery. However, dexmedetomidine administration can lead to increase the risk of bradycardia, hypotension, and withdrawal symptoms that can occur after a short period of administration, highlighting safety concerns for use of this medication. Ketorolac was effective to manage moderate to severe pain, however some children who received ketorolac developed nausea and vomiting. Acetaminophen was shown to reduce pain in the PICU after craniofacial surgery in non-ventilated infants and children. Intravenous administration was more effective than oral or rectal. The existed recommendations do not support the use of acetaminophen alone for moderate or severe pain. Acetaminophen is recommended for children with mild pain and to use it concurrently, if possible with opioids (Playfor et al., 2006; WHO, 2012). These agents are less studied in the PICU. Further research on the comparable and additive analgesic benefits of non-opioid analgesics, especially when compared to systemic opioids alone is warranted.

Non-pharmacological interventions

Implementing non-pharmacological (physical, psychological and others) strategies as appropriate to reduce pain and discomfort for children in the PICU, such as noise reduction, guided imagery, music, positioning, hypnosis and normalisation of sleep pattern, are recommended (Keogh et al., 2015; Kline et al., 2010; Playfor et al., 2006; Sharek et al., 2006; Thomas et al., 2010). The majority of non-pharmacological interventions can be applied by nurses and leverage readily modifiable variables that contribute to increased pain (Ismail, 2016; Thomas et al., 2010). However, this scoping review showed that there was very few efficacy, effectiveness or observational studies of non-pharmacological interventions, highlighting the need for more research on the effectiveness and challenges of use of non-pharmacological interventions in the PICU. Potential challenges that may face nurses are shortage of staff and time, less awareness and education on the use of these interventions, and low priority given to use these interventions compared to pharmacological interventions.

This review included studies regarding pain management interventions in the PICU published up to 2015. Couple of studies have been published after 2015 (Ayulo et al., 2018; Ismail et al., 2018; Reiter and Clevenger, 2019; Zeilmaker-Roest et al., 2017). Consistent with the results of this review, these studies show that pharmacological interventions, mainly opioids, are the main methods used to manage children's pain in the PICU.

Pain assessment

The most commonly reported pain assessment tool was the FLACC scale (Merkel et al., 1997) which was used in 11 studies. This is not surprising, as the majority of patients in the PICU cannot verbally communicate their pain and pain assessment using behavioural signs is therefore suitable for this population (Ismail, 2016). Moreover, the FLACC scale has been used and validated for assessment of children's pain in a wide range of settings and during various procedures (Bai et al., 2012; Crellin et al., 2015; Merkel et al., 1997; Voepel-Lewis et al., 2010). The use of the COMFORT scale was reported in only three studies. Of note, the modified COMFORT-B version has been validated for use in the PICU since its publication more than 15 years ago, in 2002. This modified version does not include physiological indicators for the presence of pain, as physiological indicators can be altered by severity of illness, hydration status and medications commonly used in PICUs such as inotropes (Carnavale and Razack, 2002). The observational VAS scale was reported in three studies for small children and infants who cannot self-report their pain. However, previous studies have shown that the validity and reliability of the VAS for pain assessment in children is not well-established (Van Dijk et al., 2002), especially in young children less than five years old (De Jong et al., 2005, 2010). Using different pain assessment tools for children could potentially alter findings regarding the effectiveness of the interventions applied. The COMFORT-B and the FLACC scales are the most recommended and validated scales to be used for young children and children unable to self-report their pain (Carnavale and Razack, 2002; Harris et al., 2016; Playfor et al., 2006; Thomas et al., 2010). Future research on pain management interventions in PICU should consider using these two recommended and valid pain assessment tools to evaluate the effectiveness of the interventions.

Limitations

This scoping review transparently mapped the primary quantitative research regarding the pain management interventions used or examined in the PICU. However, there are a number of limitations, including the fact that all the articles identified from the literature search are published in English. It is not known if a broader search may have identified studies published in other languages. Secondly, this study focused only on quantitative designs. Although qualitative studies are not designed to evaluate or compare the effectiveness of interventions, they can provide further insights into the preferences of treatments from the child's and family's point of view as well as the caregivers', and barriers and facilitators to using the different interventions. Nevertheless, this scoping review may be used to support health care professionals in the PICU in terms of using the research findings for pain management. Future research on pharmacological and non-pharmacological pain interventions is warranted.

Conclusion

In conclusion, pharmacological pain management interventions are the most commonly studied and used in the PICU. Safety and paucity of literature are the main limitations to using other pharmacological agents than fentanyl and morphine. Non-pharmacological interventions are not widely studied in the PICU, and they were mainly studied in North America. Further high quality rigorous research is warranted to understand the challenges and effectiveness of using pharmacological and non-pharmacological pain management interventions in the PICU.

Declaration of Competing Interest

The authors declare that they have no conflict or competing interests

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Appendix A. Supplementary data

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