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REVIEW ARTICLE

Neonatal Pain, Agitation, and Sedation Scale's use, reliability, and validity: a systematic review

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Abstract

The Neonatal Pain, Agitation, and Sedation Scale (N-PASS) is recommended by the American Academy of Pediatrics to measure neonatal pain and sedation. However, little is known regarding its reliability and validity for diverse neonatal subpopulations. Twenty-nine studies were included in our review, demonstrating broad application of N-PASS and good or excellent reliability and validity for various neonatal subpopulations. Our systematic review found N-PASS to be valid and reliable for many but not all neonatal subpopulations. There is a lack of support for N-PASS reliability and validity for measuring prolonged pain and sedation in nonmechanically ventilated infants and for acute pain in postoperative infants in any gestational age category. Overall, N-PASS is a psychometrically sound and pragmatic instrument evaluating pain and sedation for most neonatal populations. Future research using N-PASS is encouraged to evaluate and report its validity and reliability, especially for neonatal subpopulations not included in this review.

Introduction

Infants admitted to neonatal intensive care units (NICUs) are vulnerable to pain related to procedures or disease etiology [1], may be more sensitive to pain than children or adults [2], and are often prescribed sedative and analgesic drugs for pain treatment [2–4]. Consequently, evaluation of infant pain and sedation is critical for guiding clinical treatment [5]. Heterogeneity of neonatal populations and potential variations among subpopulations (e.g., gestational age, respiratory status, congenital abnormalities, disease etiology) in clinical presentation and experience of pain and sedation must be considered [6]. Thus, pragmatic and psychometrically sound instruments assessing pain and sedation of heterogenous neonatal populations are critical for clinical and research applications.

Giordano et al. [7] identified 59 instruments for measuring infant pain or sedation. Of these, only two assessed both pain and sedation—the COMFORT scale [8] and the Neonatal Pain, Agitation, and Sedation Scale (N-PASS) [9]. N-PASS has demonstrated low risk for bias, multidimensionality, ease and quickness of use, clinician preferability, and is recommended by the American Academy of Pediatrics [5, 7, 10, 11]. N-PASS was developed by Hummel et al. as a multidimensional instrument rating pain and sedation in five domains: crying, behavior, facial expression, extremity tone, and vital signs [9]. For pain, each criterion is graded on a 0–2 scale. Scores on each criterion are summed for a total pain score of 0–10 with higher scores indicating greater pain. Sedation is scored using the same criterion as pain; however, each criterion is graded on a −2 to 0 scale. Scores on each criterion are summed for a total sedation score of −10 to 0, lower scores indicating a deeper level of sedation.

Although N-PASS is recommended and widely used clinically [5, 7], little is known about the extent and breadth of its research use, reliability, and validity. Reliability is the consistency of results and validity is the accuracy of measuring an intended element [12]. A more comprehensive understanding of N-PASS use, reliability, and validity for diverse neonatal subpopulations is needed to guide clinical practice and inform future research.

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Methods

Search strategy

Following the preferred reporting items for systematic reviews and meta-analyses guidelines [13], two investigators (MEM and CJS) performed an electronic database search in PubMed, CINAHL, Cochrane, and Embase for articles published up until February 2020. Search terms included "NPASS", "N-PASS", "Neonatal Pain, Agitation and Sedation Scale", "Neonatal Pain, Agitation, and Sedation Scale", and "Neonatal Pain Agitation and Sedation Scale". We hand-searched reference lists of included studies. Inclusion criteria were (1) sample age range of 0–12 months; (2) reports use of N-PASS to measure pain and/or sedation; and (3) full text available in the English language. We excluded dissertations, theses, letters to the editor, clinical guidelines, quality improvement reports, commentaries, conference proceedings, published abstracts, and articles not available in the English language.

Data extraction

Two investigators (MEM and CJS) extracted data from included studies using a standardized procedure. Investigators independently assessed each study for availability of data to extract and potential risk of bias. Disagreements were resolved until arriving at consensus. The quality of clinical data was graded from 1 to 5 according to the Oxford Centre for Evidence-Based Medicine [14], which considers study design. We extracted information pertaining to (1) measurement domain (pain (acute or prolonged) and/or sedation); (2) sample size; (3) sample age range; (4) sample ventilatory status if explicitly stated (e.g., mechanical ventilation and no respiratory support); (5) unique sample characteristics if explicitly stated (e.g., postoperative patients); and (6) reported results of reliability and/or validity. For sample age range, we used the categories for preterm birth, as described by the World Health Organization [15, 16]: extremely preterm (<28 weeks), very preterm (28 to <32 weeks), late preterm (32–37 weeks), term (>37 weeks).

Results

Study selection

Our initial database search yielded 169 articles, of which 83 were duplicates, resulting in 86 unique articles. Thirty-two studies were excluded following title and abstract screening. Full texts were retrieved and reviewed for the remaining 54 articles. No additional articles were identified through hand searching. After applying inclusion and exclusion criteria, 29 articles were included in this study (see Fig. 1). The quality of clinical data as graded using the Oxford Centre for Evidence-Based Medicine guidelines [14] is presented in Table 1.

N-PASS use

Of the 29 studies included in our review, 19 measured pain, 3 measured sedation, and 7 measured both pain and sedation (see Table 1). More specifically, 17 measured acute pain and 11 measured prolonged pain.

Acute pain

N-PASS was used to measure acute (e.g., procedural) pain in all neonatal gestational age categories as defined by WHO, including extremely preterm ($n = 5$) [17–21], very preterm ($n = 5$) [17, 18, 21–23], late preterm ($n = 5$) [10, 11, 17, 21, 24], and term infants ($n = 7$) [17, 21, 25–29]. N-PASS was also used to measure acute pain in infants age 1–36 months ($n = 1$) [30]. Although most studies were conducted in the NICU ($n = 13$) [10, 11, 17–25, 27, 28], N-PASS was used in other clinical settings, including postanesthesia care unit (PACU) ($n = 2$) [30, 31], procedure area ($n = 1$) [26], and the postpartum mother and baby unit ($n = 1$) [29].

In addition to variation observed by gestational age group and clinical setting, N-PASS was used to measure acute pain in neonatal subpopulations including mechanically ventilated infants ($n = 6$) [10, 11, 18–21], nonmechanically ventilated infants ($n = 8$) [18, 20, 21, 23, 27–29, 32], and postoperative infants ($n = 2$) [30, 32].

Prolonged pain

Similar to acute pain, prolonged pain was measured using N-PASS for all gestational age groups (extremely preterm ($n = 5$) [31, 33–36]; very preterm ($n = 6$) [22, 31, 33, 36–38]; late preterm ($n = 6$) [10, 31, 33, 36, 39, 40]; and term infants ($n = 4$) [31, 33, 36, 40]). All studies investigating prolonged pain were conducted in NICU settings only. Neonatal subpopulations assessed for prolonged pain using N-PASS included mechanically ventilated infants ($n = 8$) [10, 33–37, 39, 40], nonmechanically ventilated infants ($n = 2$) [34, 36], and postoperative infants ($n = 2$) [33, 39].

Sedation

Nine of the 29 studies reported use of the N-PASS sedation domain. Sedation was measured in extremely preterm ($n = 5$) [33–36, 41], very preterm ($n = 4$) [33, 36, 41, 42], late preterm ($n = 6$) [33, 36, 40–43], and term infants ($n = 5$) [33, 36, 40–42]. Sedation was measured in the NICU ($n = 8$) [33–36, 40–43] and PACU setting ($n = 1$) [30]. N-PASS

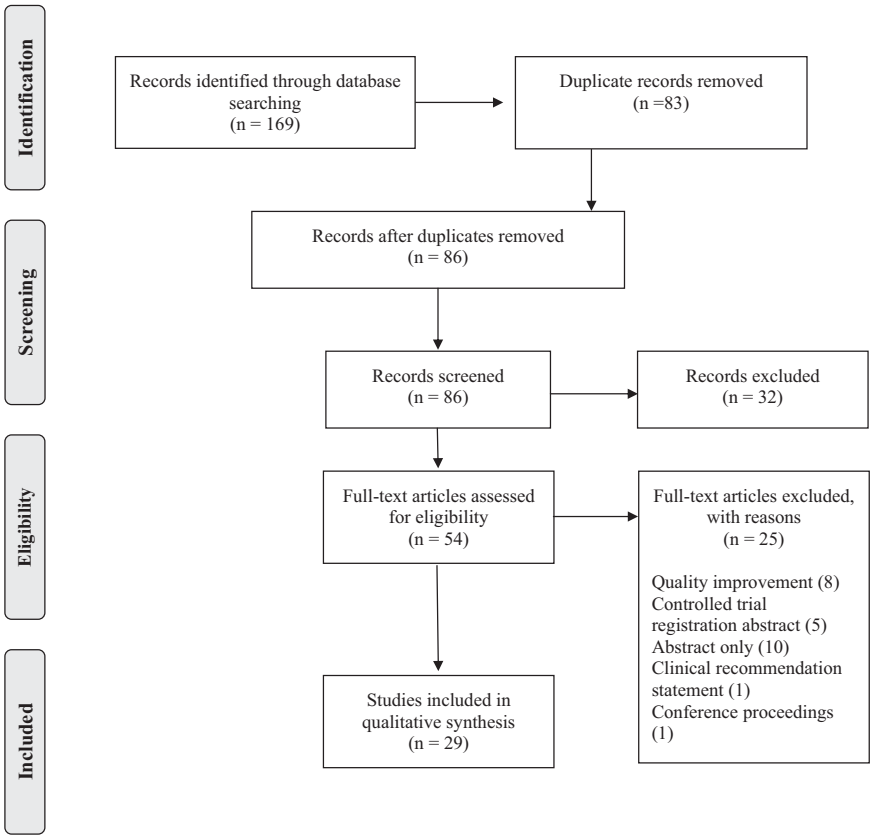

Fig. 1 PRISMA flow diagram. The PRISMA flow diagram demonstrates our study selection process.

sedation domain was measured for mechanically ventilated ($n = 8$) [33–36, 40–43], nonmechanically ventilated ($n = 2$) [34, 36], and postoperative ($n = 3$) infants [30, 33, 41].

N-PASS reliability

Six of the 29 studies reported reliability metrics of N-PASS for measuring acute pain ($n = 3$), sedation ($n = 1$), or pain and sedation ($n = 2$) (see Table 2 and Fig. 2). Specifically, one measured acute pain and sedation and one measured prolonged pain and sedation. All six studies reported N-PASS internal consistency reliability (Cronbach's alpha) for either acute pain, prolonged pain, and/or sedation. Five of the six studies additionally reported inter-rater reliability (Cohen's kappa or intraclass correlation coefficient (ICC)).

Acute pain

Four studies reported reliability of N-PASS for assessing acute pain with internal consistency reliability ranging from good to excellent [44] ($\alpha = 0.837$–0.971) [11, 21, 24, 30]. Inter-rater reliability was reported in three studies [11, 21, 24] and found to be excellent [45] (ICC = 0.93–0.99). Across the four studies, reliability estimates for using N-PASS to measure acute pain included representation from all gestational age groups (extremely preterm [21], very preterm [21], late preterm [11, 21, 24], and term infants [21]). Additionally, reliability estimates included mechanically ventilated [11, 21], nonmechanically ventilated [21], and postoperative neonates [30].

Prolonged pain

One study reported reliability of N-PASS for measuring prolonged pain of either mechanically ventilated or postoperative infants in all gestational age categories [33]. Between two raters, internal consistency reliability ranged from acceptable to excellent [44] ($\alpha = 0.72$–0.82) [33] and inter-rater reliability was excellent [45] ($r = 0.97$).

Sedation

Three studies reported reliability of the sedation domain of N-PASS [30, 33, 41]. Reliability was demonstrated for postoperative or mechanically ventilated infants in all gestational age categories. Of note, one study's sample included postoperative infants ranging from 1 to 36 months of age [30]. Internal consistency reliability ranged from good to excellent [44] ($\alpha = 0.854$–0.923). One of these studies demonstrated excellent [45] inter-rater reliability ($r = 0.92$) [33] and one demonstrated almost perfect agreement [46] ($k = 0.93$) [41].

Table 1 Articles included in review.

Authors [Ref. No.]	Quality rating[a]	Condition N-PASS assessed	Reliability or validity	Study design	Setting	Age	Special infant population	Sample size (*n*)	Study aim
Desai et al. [10]	2	Acute pain, prolonged pain	Validity	Prospective comparative cohort trial	NICU	Avg. 33.15 weeks	Mechanically ventilated	42	To compare N-PASS with PIPP when assessing mechanically ventilated infants for prolonged and acute pain
Huang et al. [11]	2	Acute pain	Reliability	Prospective comparative cohort trial	NICU	Avg. 32.9 weeks	Mechanically ventilated	1080	To compare the clinical reliability and nurse preference of PIPP, N-PASS, and the Neonatal Infant Acute Pain Assessment Scale in assessing procedural pain in mechanically ventilated neonates
Burnsed et al. [17]	3	Acute pain	–	Retrospective cohort study	NICU	23–40 weeks	–	16	To report a specific institution's experience with gabapentin therapy to manage agitation and pain in the NICU setting
Jiang et al. [18]	3	Acute pain	–	Retrospective cohort study	NICU	27–28 weeks	Mechanically ventilated, not mechanically ventilated	97	To consider the efficacy and complications of topical eye drops, general anesthesia, and fentanyl sedation with mechanical ventilation in neonates undergoing laser photocoagulation surgery for retinopathy of prematurity
Munsters et al. [19]	2	Acute pain	–	Prospective comparative cohort trial	NICU	22–27 weeks	Mechanically ventilated	10	To measure skin conductance of neonates during both heel lancing and during routine care
Novitskaya et al. [20]	3	Acute pain	–	Retrospective cohort study	NICU	Avg. 25 weeks	Not mechanically ventilated, mechanically ventilated	62	To examine the outcomes of laser treatment for retinopathy of prematurity when infants are under sub-tenon anesthetic with either oral or rectal sedation
Hummel et al. [21]	1	Acute pain	Reliability, validity	RCT	NICU	23–42 weeks	Mechanically ventilated, not mechanically ventilated	59	To establish validity and reliability of N-PASS when assessing infants for acute pain experienced by heel stick procedures
Kurdahi Badr et al. [22]	1	Acute pain, prolonged pain	–	RCT	NICU	Avg. 31.8 weeks	–	42	To assess whether listening to music that mother's listened to during pregnancy would impact pain during a heel stick procedure
O'Sullivan et al. [23]	1	Acute pain	–	RCT	NICU	Avg. 29.5–29.8 weeks	Not mechanically ventilated	40	To assess pain reduction with oral sucrose, swaddling, and nonnutritive sucking when screening for retinopathy of prematurity
Kappesser et al. [24]	2	Acute pain	Reliability	Prospective comparative trial	NICU	35.78 weeks	–	42	To compare N-PASS, PIPP, Neonatal Infant Pain Scale, Bernese Pain Scale Neonates, and Neonatal Facial Coding System-Revised in the assessment of procedural pain

Table 1 (continued)

Authors [Ref. No.]	Quality rating[a]	Condition N-PASS assessed	Reliability or validity	Study design	Setting	Age	Special infant population	Sample size (*n*)	Study aim
Patil et al. [25]	1	Acute pain	–	RCT	NICU	>37 0/7 weeks	–	22	To evaluate the difference in N-PASS scores between continuous arteriovenous exchange and pull–push techniques during partial exchange transfusion in neonates with polycythemia
Al Qahtani et al. [26]	1	Acute pain	–	RCT	Procedure area	>38 weeks	–	90	To compare the effectiveness of EMLA cream and oral sucrose in relieving infant circumcision pain
Vu-Ngoc et al. [27]	1	Acute pain	–	RCT	NICU	37–40 weeks	Not mechanically ventilated	42	To investigate the role of nonnutritive sucking in relieving heel stick pain in term neonates
McGinnis et al. [28]	1	Acute pain	–	RCT	NICU	>38 weeks	Not mechanically ventilated	56	To determine the safety and efficacy of mechanical vibration in relieving pain during heel stick procedures in neonates
Tekin et al. [29]	3	Acute pain	–	Case-control study	Postpartum mother–baby unit	Avg. 39 weeks	Not mechanically ventilated	60	To determine if there is a difference in pain perception during routine hepatitis B vaccination in infants who were born to mothers who smoked during pregnancy compared to infants born to mothers who did not smoke during pregnancy
Hummel [30]	2	Acute pain, sedation	Reliability, validity	Prospective comparative cohort trial	PACU	1–36 months	Postoperative	40	To assess N-PASS for reliability and validity in assessing sedation and acute pain in the postoperative recovery period
Veneziano et al. [32]	3	Acute pain	–	Retrospective cohort study	PACU	–	Not mechanically ventilated, postoperative	21	To determine the efficacy of continuous chloropropane epidural infusion as a primary postoperative analgesic modality compared to amide local anesthetics in neonates, infants, and children
Hummel et al. [33]	2	Prolonged pain, sedation (reliability only)	Reliability, validity	Prospective comparative cohort trial	NICU	23–40 weeks	Mechanically ventilated, postoperative	72	To explore reliability and validity of N-PASS in sedation and prolonged pain measurements for infants who are postoperative or mechanically ventilated
Drolet et al. [31]	2	Prolonged pain	–	Prospective comparative cohort trial	NICU	26–41 weeks	–	12	To determine feasibility in establishing a comfort care protocol using oral transmucosal medication for dying neonates
Giordano et al. [34]	2	Prolonged pain, sedation	–	Prospective comparative cohort trial	NICU	25 weeks	Mechanically ventilated, not mechanically ventilated	114	To analyze the 3-year effect of increased opiate exposure, as a result of the Vienna Protocol for the Management of Neonatal Pain and Sedation on motor, mental, and behavioral development

Table 1 (continued)

Authors [Ref. No.]	Quality rating[a]	Condition N-PASS assessed	Reliability or validity	Study design	Setting	Age	Special infant population	Sample size (*n*)	Study aim
Deindl et al. [35]	3	Prolonged pain, sedation	–	Retrospective cohort study	NICU	26.4–26.5 weeks	Mechanically ventilated	140	To examine short-term effect of implementing the Vienna Protocol for the Management of Neonatal Pain and Sedation on extremely preterm infants
Hillman et al. [36]	2	Prolonged pain, sedation	Validity	Prospective comparative cohort trial	NICU	23–41.7 weeks	Mechanically ventilated, not mechanically ventilated	218	To establish a relationship between N-PASS and the bedside nurse's assessment
Khan et al. [37]	1	Prolonged pain	–	RCT	NICU	Avg. 29.6–29.9 weeks	Mechanically ventilated	170	To explore nasal injury and comfort differences with various CPAP delivery systems that are used for the management of neonatal respiratory distress
Sacha et al. [38]	3	Prolonged pain	–	Retrospective cohort study	NICU	Avg. 28.3 weeks	–	22	To examine one institution's experience with using gabapentin to treat refractory pain and agitation in neonates
Garten et al. [39]	2	Prolonged pain	–	Prospective comparative cohort trial	NICU	Avg. 36 6/7 weeks	Mechanically ventilated, postoperative	528	To evaluate the association between Faces Pain Scale-Revised and N-PASS in assessing prolonged pain in infants
Abiramalatha et al. [40]	1	Prolonged pain, sedation	–	RCT	NICU	>32 weeks	Mechanically ventilated	100	To compare clinical outcomes between continuous infusion and intermittent bolus doses of fentanyl for analgesia and sedation in neonates
Giordano et al. [41]	2	Sedation	Reliability	Prospective comparative cohort trial	NICU	23 to >37 weeks	Mechanically ventilated, postoperative	503	To evaluate the reliability and validity of the sedation subsection of N-PASS via comparison of N-PASS scores to nurses' expert opinion
Chrysostomou et al. [42]	2	Sedation	–	Controlled trial without randomization	NICU	>28 to <36 weeks and >36 to <44 weeks	Mechanically ventilated	42	To investigate the safety, efficacy and pharmacokinetic profile of dexmedetomidine in sedation of neonates
Giordano et al. [43]	3	Sedation	–	Case-control study	NICU	34.6–36.6 weeks	Mechanically ventilated	27	To examine the ability of N-PASS, aEEG, and BIS in detecting different levels of sedation in neonates

– no data.

RCT randomized controlled trial, *Avg.* average.

[a]As outlined by the Oxford Center for Evidence-Based Medicine [14].

Table 2 Demonstrated validity and reliability for N-PASS.

Domain	Age	Mechanical ventilation	Nonmechanical ventilation	Postoperative
Acute pain	Extremely preterm	V, R	V, R	–
	Very preterm	V, R	V, R	–
	Late preterm	V, R	V, R	–
	Term	V, R	V, R	–
	Age 1–36 months	–	–	V, R
Prolonged pain	Extremely preterm	V, R	V	V, R
	Very preterm	V, R	V	V, R
	Late preterm	V, R	V	V, R
	Term	V, R	V	V, R
	Age 1–36 months	–	–	–
Sedation	Extremely preterm	V, R	V	V, R
	Very preterm	V, R	V	V, R
	Late preterm	V, R	V	V, R
	Term	V, R	V	V, R
	Age 1–36 months	–	–	V, R

– no data for reliability or validity.

V validity, *R* reliability.

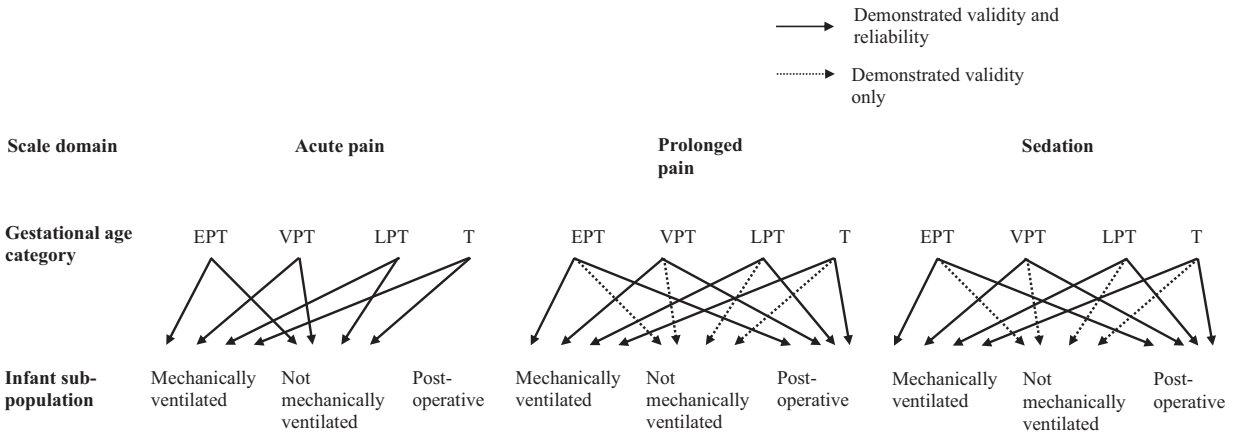

Fig. 2 N-PASS validity and reliability by gestational age and infant status. EPT extremely preterm, VPT very preterm, LPT late preterm, T term.

N-PASS validity

Five studies reported the validity (e.g., construct and content) of N-PASS for measuring acute pain ($n = 1$), prolonged pain ($n = 1$), both prolonged pain and sedation ($n = 1$), both acute and prolonged pain ($n = 1$), or both acute pain and sedation ($n = 1$) (see Table 2 and Fig. 2).

Acute pain

Three studies reported the validity of N-PASS for measuring acute pain [10, 21, 30]. Across the three studies all gestational ages were represented in the sample, including both ventilated and nonventilated infants. One study included a sample of postoperative infants and toddlers aged 1–36 months [30]. Two of the studies evaluated construct validity by comparing N-PASS to the premature infant pain profile (PIPP) [10, 21]. Spearman-rank coefficients ranged from moderate positive to high positive correlations [46] ($\rho = 0.62$–0.75) [10, 21], suggesting convergent validity. One study demonstrated construct validity by comparing N-PASS to the Face, Legs, Arms, Cry, Consolability Scale (FLACC) [30]. Correlations between N-PASS and FLACC were high ($r = 0.980$–0.996), indicating convergent validity.

Prolonged pain

Three studies reported the validity of N-PASS for assessing prolonged pain [10, 33, 36]. Construct validity for prolonged pain was evaluated by comparing N-PASS and PIPP in two studies [10, 33] with samples representing either mechanically ventilated or postoperative infants from all gestational age categories. Spearman-rank coefficients ranged from moderate to high positive correlations [47] ($\rho =$ 0.62–0.83) [10, 33], suggesting convergent validity. One study evaluated content validity in a sample of mechanically and nonmechanically ventilated infants' representative of all gestational age groups [36]. N-PASS pain domain was compared to a subjective questionnaire that captured expert neonatal nurse's assessments of prolonged pain and a low positive correlation [46] was found ($\rho = 0.37$) [36].

Sedation

Two studies evaluated the validity of the sedation subsection of N-PASS [30, 36, 41]. In one study, construct validity was evaluated by comparing the N-PASS sedation domain with the University of Michigan Sedation Scale for postoperative infants aged 1–36 months [30]. The correlation ranged from high positive to very high positive [47] ($r =$ 0.847–0.967), suggesting convergent validity. One study, with a sample inclusive of mechanically ventilated postoperative infants from all gestational age categories, evaluated content validity by comparing N-PASS to expert nurse's assessments [36]. Hillman et al. [36] correlated N-PASS to the bedside nurse's report, demonstrating a low positive correlation [47] ($\rho = -0.39$) [36].

Discussion

Many tools are available to clinicians and researchers for evaluating infant pain and/or sedation [7]; however, it is critically important to focus on reliable, valid, and pragmatic scales. Our systematic review is the first to comprehensively describe N-PASS use in published research, including its reported reliability and validity. We noted that N-PASS was used in a variety of settings (e.g., NICU, PACU, and postpartum unit), gestational age groups (e.g., extremely preterm, very preterm, late preterm, term, and 1–36 months), for mechanically and nonmechanically ventilated infants, and postoperative infants, and that it is valid and reliable for assessing acute pain, prolonged pain, and sedation for many of these patients and settings. Despite its breadth of use, however, very few studies reported the reliability and validity of N-PASS, and data are unavailable for its reliability and validity for prolonged pain and sedation of nonmechanically ventilated infants. Further research is warranted on N-PASS use, reliability, and validity in these clinical situations.

Neonatal populations are exceptionally heterogenous, especially infants cared for in the NICU. Broad implementation and use of pain and sedation instruments, like N-PASS, must consider reliability and validity for a variety of neonatal subpopulations. Although our study identified 29 studies using N-PASS, only 6 reported reliability and 5 reported validity of N-PASS. In the 21 studies not reporting any reliability or validity information, authors often referenced previous studies reporting N-PASS reliability and validity. However, in many cases, the sample in the study was arguably different from the one referenced. To expand our knowledge of its reliability and validity, future studies using N-PASS are encouraged to report its psychometric properties for their study and thoroughly describe their study sample.

A recent review by Giordano et al. [7] described existing pain and sedation instruments for neonatal and pediatric patients and included validity and reliability results. Similar to our study, the authors found N-PASS to be used, valid, and reliable for assessing acute pain, prolonged pain, and sedation in extremely preterm, very preterm, late preterm, and term infants. Giordano et al.'s review included four studies on N-PASS [21, 33, 39, 41]; our study builds on this existing evidence by identifying 29 articles and providing a more comprehensive analysis of validity and reliability for N-PASS, specifically. Our data extraction strategy considered the heterogeneity of NICU populations and classified samples into meaningful categories to more comprehensively describe the extent of N-PASS reliability and validity. This is critical because, for example, validation of N-PASS for measuring pain in a late preterm, mechanically ventilated neonate does not equate to validation of N-PASS for measuring pain in all late preterm neonates or all mechanically ventilated neonates. In addition, our review extends the contributions of Giordano et al.'s review by additionally identifying validity and reliability of N-PASS for assessing pain or sedation in postoperative and mechanically ventilated neonates.

Our study found that, when reported, N-PASS demonstrates good reliability and validity for many different neonatal subpopulations, adding further support for the American Academy of Pediatrics' recommendation to use N-PASS. Thus, clinicians can confidently use N-PASS to asses neonatal acute pain in mechanically ventilated or nonmechanically ventilated infants, prolonged pain in mechanically ventilated or postoperative infants, and sedation in mechanically ventilated or postoperative

infants. The reliability and validity of N-PASS for measuring sedation or prolonged pain in nonmechanically ventilated neonates are unknown; however, we recognize that nonmechanically ventilated neonates are rarely sedated and treatment of prolonged pain is rare (e.g., osteogenesis imperfecta and epidermolysis bullosa). Furthermore, Giordano et al. [41] compared N-PASS sedation subscale assessments with the opinion of expert neonatal nurses and concluded that N-PASS reliably identified over-sedation but did not reliably identify under-sedation. Overall, numerous studies have demonstrated good reliability and validity of N-PASS for many neonatal subpopulations. Future research can address subpopulations not identified in this review (e.g., infants with neurologic abnormalities such as hypoxic–ischemic encephalopathy), investigate reliability to detect over- and under-sedation, and test strategies to effectively implement N-PASS in clinical settings to improve measurement and treatment of neonatal pain and sedation.

It is important to consider the efficacy of behavioral assessment tools, such as N-PASS, when measuring pain and sedation in infants with neurologic abnormalities (e.g., encephalopathy, hemorrhage, and asphyxia). Not only do infants at risk for neurologic injury experience a greater number of painful procedures [48], but they also experience neurologic variances at baseline which present challenges when relying on behavioral assessments (e.g., facial expression) [49] to indicate pain and sedation level. Further research is needed to determine reliability and validity of N-PASS in this infant population. It is clinically critical to recognize the importance of accurate pain and sedation assessment with N-PASS (e.g., increased or decreased opiate prescriptions, pharmacologic intervention changes, and longer or shorter ICU admission) [50]. Following high-quality protocols developed for N-PASS, such as the Vienna Protocol for Neonatal Pain and Sedation [50], can be helpful for ensuring precise pain and sedation assessment and standardizing patient care.

While our review has several strengths, we do recognize potential limitations to our study. Most importantly, a meta-analysis was not feasible due to extreme variances in included studies (e.g., sample and study design). We did not include studies published in languages other than English, therefore cross-cultural validation is warranted for wider generalizability. Additionally, information extracted from included studies were limited by the demographic data reported in each study. Consequently, we were unable to describe N-PASS use, reliability, and validity by other important neonatal characteristics (e.g., primary medical diagnoses, gender, and comorbidities). Despite this, our methods are rigorous and the conclusions that we are able to draw remain strong.

Conclusion

Valid and reliable assessment of neonatal pain and sedation is vital for clinical care, treatment, and research. N-PASS is clinically relevant, pragmatic, recommended for use by the American Academy of Pediatrics, and valid and reliable for many neonatal subpopulations, including mechanically ventilated infants of all gestational age categories for both pain (acute and prolonged) and sedation, postoperative infants of all gestational age categories for prolonged pain and sedation, and nonmechanically ventilated infants of all gestational age categories for acute pain. Despite this, our review also identified important research gaps in N-PASS psychometric testing and reporting and encourages increased consideration of the heterogeneity of neonatal populations.

Author contributions MEM conceptualized, designed, and implemented the study, analyzed the results, and drafted the initial paper; SK provided clinical content expertise, revised the manuscript, reviewed analysis of data, and provided substantial comment and critical critique on the paper; MN helped conceptualize the study, provided clinical content expertise, revised the paper, reviewed analysis of data, and provided substantial comment and critical critique on the paper; CJS conceptualized, designed, and implemented the study, analyzed the results, and mentored the initial paper draft.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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