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What is the definition of acute episodic and chronic pain in critically ill neonates and infants? A global, four-stage consensus and validation study

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ABSTRACT

Objectives To define and validate types of pain in critically ill neonates and infants by researchers and clinicians working in the neonatal intensive care unit (NICU) and high dependency unit (HDU).

Design A qualitative descriptive mixed-methods design.

Procedure/s Each stage of the study was built on and confirmed the previous stages. Stage 1 was an expert panel to develop definitions; stage 2 was a different expert panel made up of neonatal clinicians to propose clinical characteristics associated with the definitions from stage 1; stage 3 was a focus group of neonatal clinicians to provide clinical case scenarios associated with each definition and clinical characteristics; and stage 4 was a survey administered to neonatal clinicians internationally to test the validity of the definitions using the clinical case scenarios.

Results In stage 1, the panel (n=10) developed consensus definitions for acute episodic pain and chronic pain in neonates and infants. In stage 2, a panel (n=8) established clinical characteristics that may be associated with each definition. In stage 3, a focus group (n=11) created clinical case scenarios of neonates and infants with acute episodic pain, chronic pain and no pain using the definitions and clinical characteristics. In stage 4, the survey (n=182) revealed that the definitions allowed an excellent level of discrimination between case scenarios that described neonates and infants with acute episodic pain and chronic pain (area under the receiver operating characteristic=0.87 and 0.89, respectively).

Conclusions This four-stage study enabled the development of consensus-based and clinically valid definitions of acute episodic pain and chronic pain. There is a need to define and validate other pain types to inform a taxonomy of pain experienced by neonates and infants in the NICU and HDU.

Strengths and limitations of this study

- Using a four-step process, engaging an international expert research and experienced clinician sample, this study provides a consensus definition on chronic pain and clarified definition of acute episodic pain.
- The Dutch Expert Panel (stage 2) and Focus Group in Brisbane (stage 3) were conducted in a single country.
- The definitions require validation in other clinical settings, countries and languages.
- This study did not define other types of pain such as prolonged pain in the neonatal intensive care unit and high-dependency unit.

INTRODUCTION

Following initial work[1] and advocacy, the updated definition of pain by the International Association for the Study of Pain[2] has acknowledged that neonates (younger than 28 days) and infants (younger than 1 year) in the neonatal intensive care unit (NICU) and high dependency unit (HDU) experience pain. However, assessing pain, especially ongoing pain, in the NICU and HDU is challenging. For example, the lack of an accepted definition of persistent pain hinders the assessment and identification of persistent pain by clinicians in the NICU.[3] Anand[4] has previously suggested and described the features of 5 types of neonatal and infant pain: acute episodic, acute recurrent, prolonged, persistent and chronic.

Such a taxonomy of pain in critically ill neonates and infants may assist researchers and clinicians to identify specific symptoms and signs, and optimise assessment, treatment, and prevention that are specific to a pain type. However, further work is required to confirm and empirically support these definitions.

Previous consensus efforts to classify neonatal and infant pain have focused on developing a definition for chronic pain.[4–6] Pillai Riddell *et al*[6] defined chronic pain as

pain that lasts longer than expected by the clinician, has no definite endpoint, and which often results from an ongoing painful condition. van Ganzewinkel *et al*[5] extended these findings by defining chronic pain as pain that was not proximate to an event and had no clear endpoint in sight. Following this progress, focused efforts are needed, not only to develop, but also to validate consensus-based definitions of different types of pain in this population.

Unlike previous consensus methods that have been used, the nominal group technique or expert panel enables real-time interactions between experts as they collectively work towards consensus by actively resolving uncertainties and disagreements at the time they appear.[7] Consensus definitions, however, also require triangulation to demonstrate their clinical applicability by testing their criterion validity among practising clinicians. Therefore, the overall aim of this study was to develop definitions of different types of pain in critically ill neonates and infants and to test the criterion validity of these definitions with clinicians in the NICU and HDU.

METHODS

Project design

This was a four-stage study that used a qualitative descriptive mixed methods design consisting of two independent expert panels, a focus group and a survey. Each stage of this study iteratively built on and confirmed the previous stages.

Stage 1: Basel expert panel for the development of consensus definitions

Participants

Individuals were invited by email or in person to take part in an expert panel at the International Symposium on Paediatric Pain (ISPP) in Basel, Switzerland, 2019. Individuals were approached if they (1) were attending the ISPP, and (2) had published extensively on neonatal and infant pain, or (3) were currently undertaking research on neonatal and infant pain, or (4) were involved in the advocacy or clinical care of neonatal and infant pain. The facilitator of the panel (EI) was a physiotherapist and neonatal and infant pain researcher.

Procedure

Prior to the Basel panel, potential panel members were encouraged to attend a workshop conducted by the authors (KJSA, C-jvG, RR and and EI) as part of the ISPP in Basel, 'Understanding non-acute pain in neonates and infants—where are we at?'.[8] During the meeting, panel members were provided with a background to the problem of developing definitions of different types of pain. The expert panel was then guided through four stages by the facilitator: (1) Silent generation of ideas, where panel members were given the following questions and asked to reflect on their ideas silently: 'What are the different types of pain in neonates and infants admitted to the NICU, and how would you define them?' Panel members were not allowed to discuss their ideas with others during this stage and were asked to submit their responses via an anonymous online survey; (2) Round robin, where non-identifiable responses from each panel member were made available to everyone, and the facilitator (EI) read out each definition, without providing or asking for explanations. Panel members were encouraged to reflect on these definitions silently and note any further ideas; (3) Idea clarification and discussion, where each definition was grouped, included, excluded and altered towards a single definition via discussion as a panel until no new changes were made, which indicated preliminary consensus and (4) Voting by panel members on whether they agreed with the final definitions using an anonymous online survey after the meeting. Consensus on the final definitions was defined a priori as agreement of 70% or more among panel members. Percent agreement is a commonly used criterion to define consensus in other expert consensus studies, which can range from 50% to 97%.[9]

Stage 2: Dutch expert panel for the development of consensus on clinical characteristics

Participants

Individuals who worked clinically in the Netherlands and were a member of the Dutch National Study-Group for Pain in NICUs (NSPN), were invited to participate. The NSPN was comprised of healthcare professionals who were active clinically with the management of critically ill neonates and infants and had an interest in neonatal and infant pain. Participants were ineligible if they were not available to attend on the day and were not able to read, write and understand English.

Procedure

The Dutch Expert Panel followed the same procedure as the Basel expert panel after they were provided with the definitions developed during the Basel expert panel. Panel members were asked: 'What are the key pieces of clinical characteristics that are needed to make decisions about (type of pain) in neonates and infants in the NICU?'. The Dutch Expert Panel was facilitated by EI.

Stage 3: development of clinical case scenarios using a focus group

Participants

Eligible participants in the focus group were (1) practising clinicians in the neonatal setting and (2) available to attend the focus group on the day. The focus group was convened at the Mater Mothers' Hospital's NICU in South Brisbane, Queensland, Australia and facilitated by EI.

Procedure

As in previous stages of this project, we provided the focus group with a brief introduction to the challenges of developing a taxonomy of neonatal and infant pain (online supplemental file 1). The Basel expert panel definitions

of acute episodic and chronic pain were discussed, followed by the clinical characteristics developed by the Dutch Expert Panel. The focus group was led and facilitated by the investigator (EI) who was involved in all stages of this project. The discussion in the focus group was audio-recorded. The purpose of the focus group was to develop the contextual elements (eg, the infant's medical condition) that were relevant for each pain type, as per the Basel expert panel (Stage 1), and clinical characteristic, as per the Dutch Expert Panel (stage 2). A 'no pain category' was also included. The contextual elements that the focus group created were presented on a PowerPoint slide as they were developed and discussed by the focus group. To synthesise the data arising from this focus group, three of the authors (LB, KS, and EI) combined, edited and reviewed these contextual elements to form authentic clinical case scenarios according to the Introduction, Situation, Background, Assessment and Recommendation format (ISBAR). ISBAR is a widely used clinical communication technique in Australia and New Zealand to ensure effective handover of patient information.[10] The ISBAR format was adopted because the aim was to ease the readability and clinical utility of the clinical characteristics and contextual elements for the survey. The detail and word count were also made to be relatively consistent across the scenarios to ensure these factors did not affect decisions in the survey. Once the scenarios were developed, each focus group participant was e-mailed the scenarios for member checking.

Stage 4: testing the criterion validity of the definitions using a survey

Participants

The purpose of this stage was to formally test the generalisability and applicability of the definitions to the clinical case scenarios. Survey respondents were eligible to participate if they were currently employed in an NICU or HDU in a clinical capacity. The anonymous online survey (online supplemental file 2) was administered to members of the Perinatal Society of Australia and New Zealand, clinicians in the Netherlands via a mail server, and clinicians globally via Twitter, Facebook and other networks: for example, using the authors' own social media accounts, the Paediatric Pain List Server, Physical and Occupational Therapy Paediatric Pain List Server, Pain Australia, Australian Pain Society, Australian College of Neonatal Nurses, Council of International Neonatal Nurses, NIDCAP Federation International distribution list, Swedish Paediatric Pain Association, the NEOPain Trial Network, NeoOpioid Consortium, Pain in Early Life network, and Canadian Association of Neonatal Nurses.

Procedure

A survey was designed using the clinical case scenarios developed during the focus group. A Dutch translation of the survey was completed by a medical secretary with experience in translation from English to Dutch. The survey consisted of questions about participants' demographics and confidence about whether neonates and infants can feel pain and are capable of experiencing chronic pain. Demographic questions included the participants' clinical roles and years of experience, gender, and their age bracket. Clinicians were then provided with the definitions of different types of pain and asked whether or not the neonates and infants that were described in the scenarios had acute episodic pain, chronic pain or no pain. The order of the clinical scenarios was randomised for each participant. In addition, to minimise the effect of infant sex on decision-making, the infant's sex was counter-balanced across the scenarios. The survey was available between December 2019 and July 2020.

Data analysis

The ability of participants to apply the definitions to clinical case scenarios was assessed by calculating the rate of correct responses for each pain type and no pain. Classification accuracy for each of the definitions was then determined by calculating sensitivity, specificity, positive likelihood ratio, and negative likelihood ratio. Finally, the area under the receiver operating characteristic curve (AUROC) was calculated to test the accuracy of the definitions in discriminating between pain types. Classification accuracy was calculated by comparing responses in the definition of interest (eg, chronic pain) to all other cases (eg, acute episodic pain and no pain). An AUROC of 0.5 indicates no discrimination between binary categories, 0.7 to 0.8 as acceptable, 0.8 to 0.9 as excellent, and 0.9 or more as outstanding.[11] Additional analyses included determining whether levels of confidence that neonates and infants (1) can feel pain and (2) are capable of experiencing chronic pain, correlated with years of clinical experience.

RESULTS

The overall flow of the project is described in figure 1.

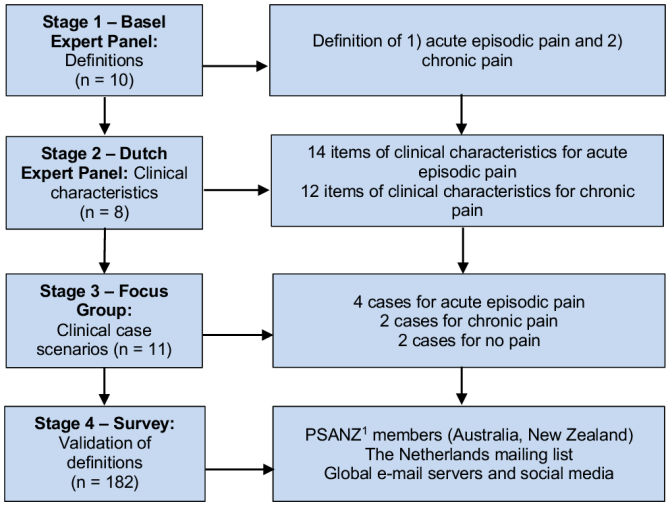

Figure 1 Process of consensus development and validation
[1]Perinatal Society of Australia and New Zealand (PSANZ) (https://www.psanz.com.au/).

Stage 1: Basel expert panel for the development of consensus definitions

Ten neonatal and infant pain experts were convened, consisting of an anaesthesiologist, a psychologist, a consumer representative, two neonatologists, two nurse practitioners, a clinical nurse specialist and two research nurses. All panel members were active neonatal and infant pain researchers and scientists or were involved in the advocacy of neonatal and infant critical care. Researchers had a median (SE) of 177 publications (21), where all authors' publications were cited a total median (SE) 2254 times (2,010). An analysis of the definitions of different types of pain that were finalised during the meeting and then achieved consensus with >70% agreement is described below.

Acute episodic pain

The expert panel described acute episodic pain as being a painful response to a procedure or an event (eg, injury or disease) which had an immediate onset. The procedure was described as being associated with tissue damage, such as a heel lance, but may not always be associated with tissue damage, such as intubation or eye examination. Panel members also considered that the painful response could arise from a medical condition (eg, osteogenesis imperfecta) or a disease state (eg, sepsis). When discussing the temporal features, panel members agreed that acute episodic pain was short lived, and the painful experience often resolved when the procedure ended, but this was not always the case. Panel members also agreed that although acute episodic pain referred to a single event, these episodes could recur over the course of a neonate's or infant's hospitalisation. Moreover, an episode was defined as being a single event or a sequence of events related to a procedure such as the process of inserting a peripherally inserted central catheter. A point of disagreement among panel members was in establishing a duration for acute episodic pain. Some panel members felt that providing a specific time-criterion may have the effect of excluding some neonates and infants, whereas others believed that a specified duration was beneficial for clinicians to aid in the identifying cases that were not acute episodic pain, such as pain that was prolonged or persistent. Despite this, consensus was reached for a specific time-criterion. Panellists also questioned which category post-surgical pain belonged to, which would most likely last for longer than the short timeframe endorsed by the group, but may not necessarily be chronic.

Chronic pain

Chronic pain was described as pain that was ongoing and which results in nervous system changes in response to a procedure, medical condition or disease process. Panel members agreed that a painful response in this category may last for days; however, a duration was difficult to establish. The panel emphasised the importance of symptoms and signs associated with nervous system changes in chronic pain in infants (eg, allodynia and hyperalgesia), rather than simply the duration of pain. Panel members agreed that those who were chronically pained, such as those who underwent mechanical ventilation or multiple surgeries, may be more susceptible to the nervous system changes observed in chronic pain.

Basel expert panel consensus definitions

Consensus definitions for acute episodic and chronic pain were established by the Basel expert panel, with 80% of the panel agreeing with the definition of acute episodic pain and 100% agreeing with the definition of chronic pain, as follows:

Acute episodic pain is a short-lasting (<30 min) painful experience in response to an event which may or may not be associated with tissue damage.

Chronic pain is pain that persists despite treatment, lasts longer than may be expected, is no longer proximate to an event, or a continuing painful disease state, and is associated with nervous system changes that may lead to primary and secondary hyperalgesia and allodynia.

Stage 2: Dutch expert panel for the development of consensus clinical characteristics

The Dutch expert panel included eight members of the NSPN, which was made up of registered nurses, nurse scientists and a nurse practitioner working in the NICU or HDU. Members had a total median (SE) of 23 (3.8) years of clinical experience. Each member of the NSPN was a representative of one of the NICUs or HDUs in the Netherlands.

The Dutch expert panel proposed clinical characteristics, which may be used by clinicians to make decisions[12] about whether an infant has acute episodic pain or chronic pain (table 1). Throughout the discussion about acute episodic pain, there was emphasis on being able to interpret the behaviour of the neonate or infant. There was also discussion about the context in which painful events occurred. For example, a stressful event such as diaper change for an infant who has a painful condition may be perceived as painful by the infant.

Although all the clinical characteristics proposed by the expert panel regarding chronic pain reached consensus, some items required considerable discussion to achieve this. Panel members questioned the relationship between pain and impaired growth (change in weight and length) because impaired growth could be caused by factors other than pain. Indeed, it was agreed that pain and stress were not distinguishable in neonates and infants; pain may be stressful, but stress may or may not be painful. In addition, the usefulness of assessing the neonate's and infant's sleep-wake cycle was discussed, as it was perceived as very difficult to evaluate. The panel affirmed that an infant who was always aroused was easy to recognise, which may have been a result of a non-acute pain state.

Stage 3: development of clinical case scenarios using a focus group

Eleven clinicians from Mater Mothers' Hospital NICU participated in the focus group. The group consisted of nurses (n=7), allied health (n=2) and neonatologists (n=2). The focus group developed eight clinical case scenarios based on the definitions of acute episodic pain and chronic pain using the clinical characteristics

Table 1 Clinical characteristics required to decide on the neonate's or infant's pain state

Type of pain	Clinical characteristics	Level of agreement n/total
Acute Episodic Pain	1. Has a painful or stressful procedure been performed within the last hour or more?	8/8
	2. What was the nature of the nociceptive/stressful event or situation? for example, surgery, birth trauma, suctioning skin trauma, respiratory support	8/8
	3. What is the infant's baseline behavioural state (within the last hour)?	8/8
	4. What is the infant's post-menstrual age?	7/8
	5. What is the infant's disease state or condition? for example, neurologically impaired, severity of critical illness, etc.	8/8
	6. What are external factors (environmental stimuli such as alarms) that may influence the infant's stress levels?	8/8
	7. Has sufficient pharmacological and non-pharmacological pain relief been provided either before, during, and/or after the nociceptive/stressful stimuli or event?	8/8
	8. What other pharmacological agents are being used? for example, muscle relaxants, sedatives, inotropes	8/8
	9. What is the infant's overall reactions (motor, behavioural, and physiological changes) to the painful/stressful event or situation?	8/8
	10. Does the infant use self-regulating/comforting behaviours? for example, flexed positioning, sucking, bringing hands together	7/8
	11. What tool has been used to assess the infant's pain and what is their score on the pain assessment tool?	7/8
	12. What are the parents'/guardians' impressions of the infant's pain?	8/8
	13. What are the clinician's and their colleague's impressions of the infant's pain?	7/8
	14. What are the internal (clinician's psychological state, experience, cultural biases) and external (environmental stimuli such as alarms) factors that may affect the assessment of pain?	8/8
Chronic Pain		
	1. What is the infant's medical history including any possible painful disease states and previous interventions and ventilation? for example, necrotising enterocolitis, epidermolysis bullosa, major surgery, mechanical ventilation	8/8
	2. Were there any recently performed painful/stressful events or procedures?	8/8
	3. How competent is the infant in coping with painful/stressful episodes (self-regulating behaviours), and daily care-taking procedures (life in general)?	8/8
	4. Does the infant show impaired growth (length, weight, head circumference), and is not meeting expectations?	7/8
	5. How is the infant's sleep-wake cycle, levels of restlessness, general motor behaviour and physiology? for example, heart rate, blood pressure, respiratory rate, ventilator asynchrony	8/8
	6. How arousable is the infant to smell, touch, and sound, and what is their reaction to non-nociceptive stimuli (eg, feeding, environmental stimuli) and nociceptive stimuli? Do they have negative reactions to positive stimuli such as skin-to-skin or feeding?	8/8
	7. Is the infant consolable by a parent or caregiver?	7/8
	8. How effective are pharmacological and non-pharmacological pain relief within typical dosing regimens (as per site-specific protocols), based on blood serum levels of concentration?	8/8
	9. What are the parents'/caregivers'/clinician's impression of the infant's pain?	7/8
	10. What tool is used to regularly assess the infant's non-acute pain and what is the score on the pain assessment tool?	8/8
	11. Are there markers of stress such as cortisol levels?	7/8
	12. Does the infant display age-appropriate developmental behaviours such as playing, following with eyes, vocalising?	7/8

to provide contextual elements. For example, if post-menstrual age at assessment was deemed important, the focus group decided on the infant's postmenstrual age (eg, table 2). The final list of scenarios was emailed to participants of the focus group for member checking; no further edits or changes were recommended.

Stage 4 survey: criterion validity of the definitions

One hundred and eighty-two participants provided responses to the clinical case scenarios (table 3). Participants were trained and practised clinically in The Netherlands, Australia, New Zealand, USA, Canada and throughout Europe, and were clinical nurses, including registered nurses and nurse specialists, research/academic nurses or medical doctors. Sixty-four per cent of participants had more than 10 years' experience in their clinical roles, were between 46 and 65 years of age (48%) and female (63%).

On average, participants were 98.4% (SD=6.8) confident that neonates and infants could feel pain and 91.8% (SD=14.2) that neonates and infants were capable of experiencing chronic pain. Confidence in neonatal and infant chronic pain was moderately and

Table 2 Examples of clinical case scenarios according to the ISBAR format

ISBAR format	Acute episodic pain	Chronic pain	No pain
Introduction	Baby E, female, is 1 week chronological age.	Baby A, male, is 6 weeks chronological age.	Baby C, male, is 1 week chronological age.
Situation	Baby E was born at 32 weeks postmenstrual age. She was admitted for respiratory distress syndrome. Baby E is currently being mechanically ventilated and is receiving 10 µgg/kg/hour of intravenous morphine. She tends to retain secretions in her lungs, so endotracheal suctioning is performed as required. An hour ago, when suctioning was performed, Baby E's heart rate climbed from 150 to 170 beats per minute. She also displayed a hyperextended posture and finger splaying. After the procedure, Baby E cried silently. After 3 min of containment, she settled and remained in a calm state.	Baby A was born at 37 weeks gestational age. He developed a wound breakdown following a laparotomy for malrotation of bowel; the wound has now healed. Before a heel lance this morning, Baby A was given sucrose. When undergoing the procedure, Baby A showed an exaggerated response, withdrawing both legs and displaying a hyperextended posture. Afterwards, he required swaddling and containment, but remained unsettled. He is charted for PRN paracetamol.	Baby C was born at 35 weeks gestational age. He was admitted to the special care nursery secondary to prematurity and for difficulties with regulating body temperature. This morning when his father was changing Baby C's nappy, Baby C cried. He then brought his hand to his mouth and sucked, settling immediately.
Background	During nappy changes, Baby E is rarely distressed. Baby E is receiving caffeine as part of her treatment.	Baby A has undergone regular dressing changes, routine blood tests, swabs, and handling. He was intubated and ventilated, and on morphine infusion which was ceased 3 days ago. He is unable to cope with daily clinical procedures and is rarely consolable. He also becomes startled with gentle touching when he is awake. He has a poor sleep-wake cycle and is generally restless. Baby A's parents state their baby often appears like he's in pain.	He is otherwise well and self-ventilating on room air. Baby C has also undergone routine clinical procedures including blood glucose monitoring. He receives sucrose when undergoing painful procedures. He is often seen bringing his hand to his mouth and sucking throughout the day.
Assessment	Baby E's score on the Premature Infant Pain Profile-Revised during the suctioning was seven which indicated pain. Baby E's grandmother was nearby watching and seemed distressed by the procedure.	Regular pain assessments indicate that he has pain, and his history does not indicate withdrawal. On assessment of his neurological status, Baby A shows some delays in tracking a bright red object horizontally.	Assessment of the open-plan nursery environment reveals that noise and light are kept low, but this is not always the case. Generally, Baby C has a well-defined sleep-wake cycle and his behavioural cues for hunger are age appropriate. Baby C's mother notes that he is a fairly settled baby.
Recommendation	Ongoing assessment of Baby E's behaviour.	Ongoing assessment of Baby A's behaviour.	Ongoing assessment of Baby C's behaviour.

ISBAR, Introduction, Situation, Background, Assessment and Recommendation.

positively correlated with confidence that neonates and infants can feel pain, participants' years of experience in the NICU or HDU, and participants' age (all, r=0.37, p<0.001). Clinicians with more than 10 years' experience (mean=99.38, SD=3.22) were no more confident that neonates and infants can feel pain than those with less experience (mean=96.79, SD=10.27), t(72.4)=−2.00, p=0.50; however, clinicians with more than 10 years' experience (mean=86.09, SD=17.72) were significantly more confident that neonates and infants are capable of experiencing chronic pain than those with less experience (mean=94.97, SD=10.54), t(91.7)=−3.71, p<0.001.

With 1397 responses to the case scenarios, representing 96% complete responses, assessed against the definitions, the mean (SD) correct responses for all the case scenarios presented was 85.3% (16.9). Scenarios (table 2) relating to acute episodic pain were correctly identified in 80.9% of cases, those relating to chronic pain in 83.0% of cases, and those relating to no pain in 81.0% of cases. This meant that the definitions allowed for the detection of acute episodic pain with 85.1% (95% CI 82.2% to 87.75%) sensitivity, 88.8% (95% CI 86.2% to 91.0%) specificity and a positive likelihood ratio of 7.6 and a negative likelihood ratio of 0.17. The ability of the definitions to discriminate between acute episodic pain cases from those that were not, was excellent (AUROC=0.87). In contrast, the definitions allowed for the detection of chronic pain with 84.0% (95% CI 79.7% to 87.5%) sensitivity, and 94.4% (95% CI 92.8% to 95.7%) specificity, and a positive likelihood ratio of 15.0 and a negative likelihood ratio of 0.17. The ability of the definitions to discriminate between chronic

Table 3 Demographic information and beliefs of survey respondents

Demographic information	N=182 (%)
Country/region of clinical practice	
Australia and NZ	37 (20)
The Netherlands	113 (62)
Europe	13 (7)
USA and Canada	12 (7)
Elsewhere	7 (4)
Current clinical role*	
Clinical nurse	36
Medical doctor	41
Nurse practitioner	6
Occupational therapist	1
Physiotherapist	9
Research/academic nurse	97
Years of clinical experience in the NICU/HDU	
<1 year	12 (7)
1–4 years	23 (12)
5–10 years	31 (17)
>10 years	116 (64)
Gender	
Female	114 (63)
Male	66 (36)
Prefer not to say	2 (1)
Respondent ages	
20–25 years	10 (6)
26–35 years	42 (23)
36–45 years	36 (20)
46–65 years	88 (48)
>65 years	6 (3)

*Categories are not mutually exclusive.
HDU, high-dependency unit; NICU, neonatal intensive care unit; NZ, New Zealand.

pain cases from those that were not, was also excellent (AUROC=0.89).

DISCUSSION

We developed and validated a consensus definition of chronic pain in critically ill neonates and infants, and clarified a definition of acute episodic pain. The definition of acute episodic pain included a specific timeframe and confirmed that non-tissue breaking procedures should be considered in episodes of acute pain.[13] This provides important guidance in the research of the impact of pain on neurodevelopmental outcomes, which have largely focused on the frequency of tissue-breaking procedures.[14] The definitions allow for an excellent level of classification accuracy when applied to clinical case scenarios. The consensus definitions of acute episodic and chronic pain align closely with the updated IASP definition of pain.[2] The definitions emphasise that contextual factors and the personal experiences of each neonate or infant may enable the detection of pain in non-verbal populations when triangulated with other assessment findings and expressions which 'resemble' pain.[15] These definitions support the social communications model of pain[16 17] by emphasising the importance of contextual factors, personal experiences and neurobiological factors in the expression of pain in infants. The clinical characteristics proposed by the Dutch Expert Panel also highlight the importance of contextual, personal and non-verbal expressions of pain, allowing researchers and clinicians to differentiate acute episodic from chronic pain. The consensus definitions and clinical characteristics support and expand on Anand's[4] proposed definitions by highlighting the need for contextual information to determine the presence of acute episodic and chronic pain.

These validated definitions may provide researchers and clinicians with useful anchor points on either side of a possible spectrum of pain that may be experienced by critically ill neonates and infants. Given the lack of pain assessment methods to detect chronic pain in this population,[18] future efforts may help identify these changes in terms of clinically useful signs and symptoms,[19 20] in the context of other clinical characteristics and assessment findings. Notably, however, the lack of a consensus about a time-criterion for chronic pain is consistent with other studies,[5 6] which suggests that further empirical data is needed to inform such a criterion.[21] More work is required to identify the transitional states between acute episodic and chronic pain. For example, postsurgical pain can be described as being acute episodic pain initially, will most likely be experienced for longer than 30 min, but may not always lead to a chronic pain state. The ability of these definitions to discriminate between pain states may diminish when they are compared with these transitional states as in the case of postsurgical pain. Given the definitions provided by the Basel expert panel, definitions for these transitional states are needed to better classify the spectrum of pain experienced by all critically ill neonates and infants. Nevertheless, these definitions are useful starting points towards developing an agreed taxonomy of neonatal and infant pain.

Strengths and limitations

The Basel expert panel consisted of an interdisciplinary and international group of researchers, clinicians and consumer representatives, and voting was anonymous which allowed panel members to vote in an honest and unbiased manner and without fear of reprisal. In addition, all stages of this project consisted of individuals who were at the forefront of research and clinical care of infants in the NICU and HDU. However, the following limitations are worth noting. The Basel expert panel lacked a developmental biologist who may have provided a more nuanced discussion of the definitions related to the mechanisms that may contribute to different types of pain. The Dutch expert panel and focus group were

limited by being conducted with participants who worked clinically in a single country. Additionally, participants in the survey were more experienced, more than 45 years of age, and were from nursing and medical professions. Therefore, it is important to explore how other health professionals, such as physiotherapists, from different settings and countries, apply the consensus definitions to clinical case scenarios. Another limitation of the survey was that it was written in English and Dutch, which meant that clinicians who did not speak these languages were excluded from the potential participant pool. Because the survey's widespread distribution was via social media, it was not possible to determine the response rate. Finally, although every effort was made to ensure the clinical case scenarios were authentic, participants were forced to make an artificial choice between three responses where greater choices exist in real-world clinical scenarios.

Implications for practice and future research

This work raises awareness that pathological pain states such as chronic pain is under-recognised and therefore undertreated (or potentially inappropriately treated) in neonates and infants.[22] The detection, treatment and long-term implications of chronic pain remain virtually unknown. Additionally, given that consensus on the constructs of chronic pain and acute episodic pain has been reached, researchers, clinicians and families are able to communicate about these more clearly. Because there is a lack of validated pain assessment scales for chronic pain,[23] we recommend that future studies should first aim to develop procedures and assessment techniques to accurately detect chronic pain in critically ill neonates and infants, then to focus on the development and evaluation of the efficacy and safety of pharmacological and non-pharmacological strategies to alleviate it. It should be emphasised, however, that due to the lack of safety studies for chronic pain medications in this population, we do not recommend their use in neonates and infants, particularly as animal studies[24] imply that infants may not develop chronic pain similarly to adults.

CONCLUSIONS

This study enabled definitions of the construct of chronic pain, and clarified the construct of acute episodic pain, in critically ill neonates and infants. Further follow-up studies using this stepwise procedure will be valuable to define transitional states of pain. A taxonomy of pain in neonates and infants in critical care is necessary to improve the study and clinical management of different types of pain. While most guidelines for pain management focus on certain clinical situations such as painful procedures and post-surgical pain management, management strategies that are specific to chronic pain are necessary.

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