## Persistent Pain in Premature Neonates in Neonatal Intensive Care Units: A Scoping Review

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## DESCRIPTION

Premature neonates, born before 37 weeks of gestational age, often require specialized care in Neonatal Intensive Care Units (NICUs), which is essential for their survival. However, this critical care can be painful, with research indicating that premature neonates undergo between 7.5 and 17.3 painful procedures daily. Common procedures include nasopharyngeal and endotracheal aspiration, heel for blood sampling and tape removal from delicate, immature skin. The repetitive nature of these painful experiences, especially in early life, warrants serious consideration as it can contribute to prolonged pain in premature neonates.

In recent decades, multidisciplinary efforts have advanced scientific understanding of neonatal pain. These efforts include refining definitions of the various types of pain premature neonates experience-procedural or acute, postoperative and prolonged pain. Progress has also been made in developing pain indicators, assessment methods and management strategies, along with research into the long-term effects of neonatal pain on neurodevelopment. However, despite these advancements, a standardized taxonomy for categorizing prolonged neonatal pain is still lacking. The terminology used to describe pain in neonates is often not clear, with terms like acute pain, procedural pain, continuous pain, prolonged pain, chronic pain and postoperative pain being used interchangeably. This confusion persists in the field of neonatology.

The neonatal pain-control experts' group highlighted the need for a clear distinction between acute and prolonged pain back in 2006, yet more than 15 years later, no consensus on a definition for prolonged pain has been established. According to the International Association for the Study of Pain (IASP), chronic pain is defined as pain lasting more than three months. However, this definition excludes neonates, who can experience pain from as early as 24 weeks of gestational age, even though their postnatal age may be less than three months. The three-month criterion set by the IASP minimizes the significance of pain experienced by premature neonates, whose average hospital stay is around 63.1 days (ranging from 54.0 to 70.1 days), as reported. This falls below the three-month threshold for chronic pain, making the term

"chronic pain" an inadequate description of the pain premature neonates endure during their NICU stay. For this reason, this scoping review will refer to the pain experienced by neonates in the NICU for the duration of their hospitalization as prolonged pain, acknowledging the unique context of their pain experience. Unfortunately, in the existing neonatal scientific literature, the terms "chronic pain" and "prolonged pain" are often used interchangeably, further contributing to the confusion and making it difficult to establish clear pain management strategies.

The lack of clarity surrounding the definition and nomenclature of prolonged pain hampers effective evaluation and management in the NICU. Prolonged pain in neonates can result in significant neurodevelopmental and gastrointestinal changes. These include primary hyperalgesia (increased sensitivity to pain), peripheral hypersensitivity, lowered pain thresholds and hyper reactivity to stimuli. In addition to these somatosensory changes, prolonged pain exposure can have lasting effects on brain maturation, extending beyond infancy. Premature neonates may experience altered development of white matter and sub-cortical grey matter, structural changes in the corticospinal tract and increased pain hypersensitivity. Longterm consequences may include cognitive and motor impairments, such as attention deficit disorders and cerebral palsy.

Given the negative effects of prolonged pain, it is essential to conduct a thorough analysis of the concept of prolonged pain in neonatology, which has yet to be fully explored. Understanding and addressing this issue is important for preventing the longterm neurodevelopmental and somatosensory consequences associated with early-life pain. Improving the definition, recognition and management of prolonged pain could mitigate these risks and significantly improve the quality of care for premature neonates.

## CONCLUSION

It identifies key contexts in the neonatal intensive care unit, such as mechanical ventilation, necrotizing enterocolitis and the postoperative period, that may contribute to prolonged pain.

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Various pain assessment tools are commonly used to measure prolonged pain. However, specific interventions to manage prolonged pain effectively still require further research to prevent the long-term neurodevelopmental consequences. Ultimately, more studies are needed to guide clinical practice and improve outcomes for premature neonates. Therefore, this scoping review aims to clarify the understanding of prolonged pain in neonates, address its potential long-term consequences and advocate for improved strategies in pain management in NICUs worldwide.