

Elsevier required licence: © <2021>. This manuscript version is made available under the CC-BY-NC-ND 4.0 license <http://creativecommons.org/licenses/by-nc-nd/4.0/>. The definitive publisher version is available online at [insert DOI]

Journal of Neonatal Nursing

The effects of nurse-delivered caregiving in the neonatal setting: An integrative review --Manuscript Draft--

Manuscript Number:	JNEO-D-20-00153R1
Article Type:	Review article
Keywords:	nurse-delivered caregiving; neonatal intensive care; physiological responses; behavioural responses; temperament; infant development; behavioural outcomes
Corresponding Author:	Nadine Griffiths, BN, MN (Clin Ed) Children's Hospital at Westmead Westmead, NSW AUSTRALIA
First Author:	Nadine Griffiths, BN, MN (Clin Ed)
Order of Authors:	Nadine Griffiths, BN, MN (Clin Ed) Sharon Laing, Ba (Hons) Psych, PhD (Psych) Kaye Spence, BEd(N), MN(Research) Maralyn Foureur, RM, RN, BA, GradDip ClinEpi, PhD Lynn Sinclair, RN, RM, BSc (Hons) with Specialist Practitioner Qu
Abstract:	Infants hospitalised in neonatal intensive care units require interventions for lifesaving care and to meet basic human needs. Evidence that stress influences neurodevelopment suggests the effects of caregiving in the neonatal intensive care unit (NICU) warrant further investigation to assess links with infant developmental outcomes. This review explores the effects of nurse-delivered caregiving in the NICU on infant physiological and behavioural responses, and longer-term developmental outcomes (behaviour and temperament). CINHALL, MEDLINE and PsychINFO were systematically searched for studies in peer-reviewed journals related to nurse-delivered caregiving and developmental outcomes. Synthesis of the literature identified altered physiological and behavioural responses as immediate effects of caregiving in neonatal settings, and non-optimal developmental outcomes. Results indicate that caregiving is not innocuous. Yet, little is known about nurses' perceptions of the effects of caregiving. Identifying the care components that influence development is essential to minimise the potentially adverse impact of the NICU experience on infants and families.

The effects of nurse-delivered caregiving in the neonatal setting: An integrative review

ABSTRACT

Infants hospitalised in neonatal intensive care units require interventions for lifesaving care and to meet basic human needs. Evidence that stress influences neurodevelopment suggests the effects of caregiving in the neonatal intensive care unit (NICU) warrant further investigation to assess links with infant developmental outcomes. This review explores the effects of nurse-delivered caregiving in the NICU on infant physiological and behavioural responses, and longer-term developmental outcomes (behaviour and temperament). CINAHL, MEDLINE and PsychINFO were systematically searched for studies in peer-reviewed journals related to nurse-delivered caregiving and developmental outcomes. Synthesis of the literature identified altered physiological and behavioural responses as immediate effects of caregiving in neonatal settings, and non-optimal developmental outcomes. Results indicate that caregiving is not innocuous. Yet, little is known about nurses' perceptions of the effects of caregiving. Identifying the care components that influence development is essential to minimise the potentially adverse impact of the NICU experience on infants and families.

Key words: nurse-delivered caregiving; neonatal intensive care; physiological responses; behavioural responses; temperament; infant development; behavioural outcomes

INTRODUCTION

It has been well-established that stress and trauma in the first 1000 days of post-conceptual life can have adverse lifelong effects (D'Agata et al., 2017; Linnér and Almgren, 2020). Lifesaving and routine caregiving in the neonatal intensive care unit (NICU) occur during a period of sensitive, rapid and critical brain development. Despite the best intentions, the NICU environment cannot replicate the intrauterine experience, instead offering a 'sub-optimal' environment with infants subsequently vulnerable to brain injury and maldevelopment (Cheong et al., 2020). Increasingly, the influences of the early environment and biological and social factors are being explored as potential mediators for preterm infants' developmental outcomes (Burnett et al., 2018; Cheong et al., 2020). Exposure to the hospital environment, noise, pain, and disrupted parenting are suggested as affecting long-term neurodevelopment and areas that require a stronger research focus (Cheong et al., 2020). Because developmentally-supportive caregiving in the NICU addresses these factors, it may positively influence long-term health and developmental outcomes (Lean et al., 2018; McAnulty et al., 2010; O'Reilly et al., 2020; Robinson et al., 2020; Wolke et al., 2019) and therefore, warrants further investigation.

The concept of 'developmentally-supportive care', also referred to as 'developmental care', focuses on the infant and family; providing care aimed at optimising their developmental progression. Underpinned by Als' (1982) Synactive Theory of Development, developmental care operates within a developmental-maturation paradigm where infants' neurobehavioural organization skills develop over time. The development of these skills is influenced by prematurity, illness and congenital anomalies (Torowicz et al., 2012). In addition, developmental care-practices are informed by the Newborn Individualised Developmental Care Assessment Program (NIDCAP)(Als, 1982). This is a relationship-based model of care designed to modify the caregiving culture, interactions and the NICU environment (Lawhon and Hedlund, 2008). NIDCAP involves rigorous training with specialist education in infant-developmental observation, with application and assessment of caregiving and the NICU environment. **Each element focuses on facilitating relationships between infants, parents and staff members and the interplay of these relationships in the broader NICU** (Als, 1982). Based on infant cues, caregiving is modified to reduce the noxious effect of stressors on the developing brain (Als and McAnulty, 2011). Studies to date have mostly evaluated the impact of developmental care on short-term medical outcomes (e.g., days of mechanical ventilation/supplemental oxygen, weight gain, length of stay), with limited data about longer-term neurodevelopment (Byers, 2003; Rick,

2006; Soleimani et al., 2020; Symington and Pinelli, 2009). A lack of consensus regarding the evidence may not be surprising given that developmental care is a philosophy of care encompassing a broad category of interventions, with sporadic implementation (Carrier, 2002; Lubbe et al., 2012).

Caregiving can be provided by multiple individuals, most importantly the parents. Within a developmentally-supportive and family-centred framework, families are recognised as the primary caregivers (Als, 1982; De Bernardo et al., 2017; Lee and O'Brien, 2014). Models of care with parents as primary caregivers are being increasingly implemented in hospital settings (Lean et al., 2018; Lee and O'Brien, 2014), with research showing decreased parental stress and anxiety, and increased exclusive breastmilk feeding at discharge (O'Brien et al., 2018). Caregiving by nurses, however, continues to be one of the most frequent events experienced by an infant during their NICU admission (Godarzi et al., 2018; Murdoch and Darlow, 1984; Pereira et al., 2013). As the focus of this review was nurse-delivered caregiving of the infant, literature about parents as primary caregivers and the nurses' role in supporting parents in the hospital setting was not included. In this paper, the term 'caregiving' refers to 'nurse-delivered caregiving'.

Caregiving has been defined as a necessary single or clustered intervention ranging from vital sign monitoring, repositioning, feeding or nappy change through to suctioning and other invasive procedures (Peters, 1999). Caregiving can act as stimuli that elicits infant pain responses. There are numerous validated tools for assessing infant pain behaviours (Relland et al., 2019), yet differentiating between infant pain behaviours and stress responses remains difficult. Like other NICU interventions, caregiving is an event with the potential to alter physiological stability and behavioural state, and increase infant stress. The immediate effects of caregiving can be assessed by measuring an infant's physiological or behavioural stress responses. While pain per se was not the focus of this literature review, some studies included a broad classification of caregiving interventions ranging from vital sign assessment to painful interventions (e.g. heel stick).

In humans, stress responses occur via a complex system designed to counter internal and external stimulation, with an initial focus on achieving overall physiological stability (Zeiner et al., 2016). The autonomic nervous system (ANS), comprising the sympathetic and parasympathetic arms, plays a significant role in the overall regulation of physiological functions in response to stressful stimuli. Fluctuations in heart rate (HR), respiratory rate (RR), oxygen saturation (SaO₂), blood pressure (BP),

skin colour changes, the startle reflex, and tremors (Als, 1986), are recognised as physiological manifestations of stress in infants (DiPietro and Porges, 1991; Peters, 1999; Zahr and Balian, 1995). Repeated stressor exposure affects adaptive capability and self-regulation, with the occurrence and severity of stressors influencing cortical connectivity and potentially long-term development (McAnulty et al., 2009; McAnulty et al., 2010; Zeiner et al., 2016).

The ANS also regulates the complex interplay of physiological, biochemical and neurobehavioral systems that underlie behavioural state regulation (Als, 1986; Foreman et al., 2008; Prechtl, 1974). Infant behavioural states (e.g., deep sleep, quiet alertness, fussing, crying) are observable during interactions with caregivers and the environment. In stressful situations, infants change state as a self-regulation strategy (Foreman et al., 2008). In the NICU, behavioural responses to interventions vary across infants, based on gestational age, chronological age and level of illness (Als, 1982; Als, 1986; Prechtl, 1974). Infant behavioural responses can positively or negatively impact on a caregiver's perceptions of an infant and their subsequent interactions (Als et al., 2005). Within a developmentally-supportive framework, caregivers implement strategies to support an infant's self-regulation (Als and McAnulty, 2011; Lawhon and Hedlund, 2008).

Dysfunction of the ANS is identified as the mechanism by which exposure to early adversity affects emotional and behavioural outcomes, including temperament (McLaughlin et al., 2015).

Temperament has been defined as a moderately stable set of infant behavioural traits that affect both personality and behaviour (Gunnar et al., 1995). Infant measurements of temperament identify early regulatory problems predictive of subsequent behavioural difficulties (Abulizi et al., 2017; Gunnar et al., 1995; Sidor et al., 2017). Prematurity and hospitalisation in the neonatal period can adversely affect behavioural outcomes including temperament (Abulizi et al., 2017; Cassiano et al., 2020; Cassiano et al., 2019; Feldman, 2009).

Research exploring the effect of physiological and behavioural responses during caregiving has been published since the 1980's. Nurse-delivered caregiving is frequently categorised in studies by type, duration, patterns, nurse education, and infant responses to handling (Peters, 1999). Researchers have demonstrated that caregiving duration impacts adversely on sleep cycles in preterm infants (Godarzi et al., 2018; Maki et al., 2017; Murdoch and Darlow, 1984; Pereira et al., 2013). All aspects of the caregiving experience impose sensory input on the infant's nervous system. The use of developmentally-supportive interventions is considered a proactive approach with the potential to

mitigate infant stress in the NICU (Weber and Harrison, 2019). Given that recurrent stressful interventions may contribute to adverse developmental outcomes, it is imperative to assess the impact of developmental care as a buffering factor within the NICU and beyond hospital discharge.

AIM

The aim of this literature review was to explore what is known about the physiological and behavioural effects of nurse-delivered caregiving in the neonatal setting and potential links to infant developmental outcomes (behaviour and temperament) in the first 12 months of life. Synthesis of the literature provides insight into the cumulative effects of caregiving in the neonatal unit and potential associations with longer-term behavioural outcomes.

METHODS

A systematic electronic literature search was completed using CINHAL (EBSCO), MEDLINE (OVID) and PsychINFO (1 January 1982 to 1 May 2020). Search limitations were English-language, full-text, and peer-reviewed articles. Final screening of articles was undertaken by two of the authors. The literature screen focused on nurse-delivered caregiving and its effects on behavioural and physiological responses in the NICU and outcomes in the first 12 months following birth. Research after 1982 was included following the publication of seminal works by Dr Heidelise Als on the Synactive Theory of Development and the inception of developmentally-supportive care (Als, 1982).

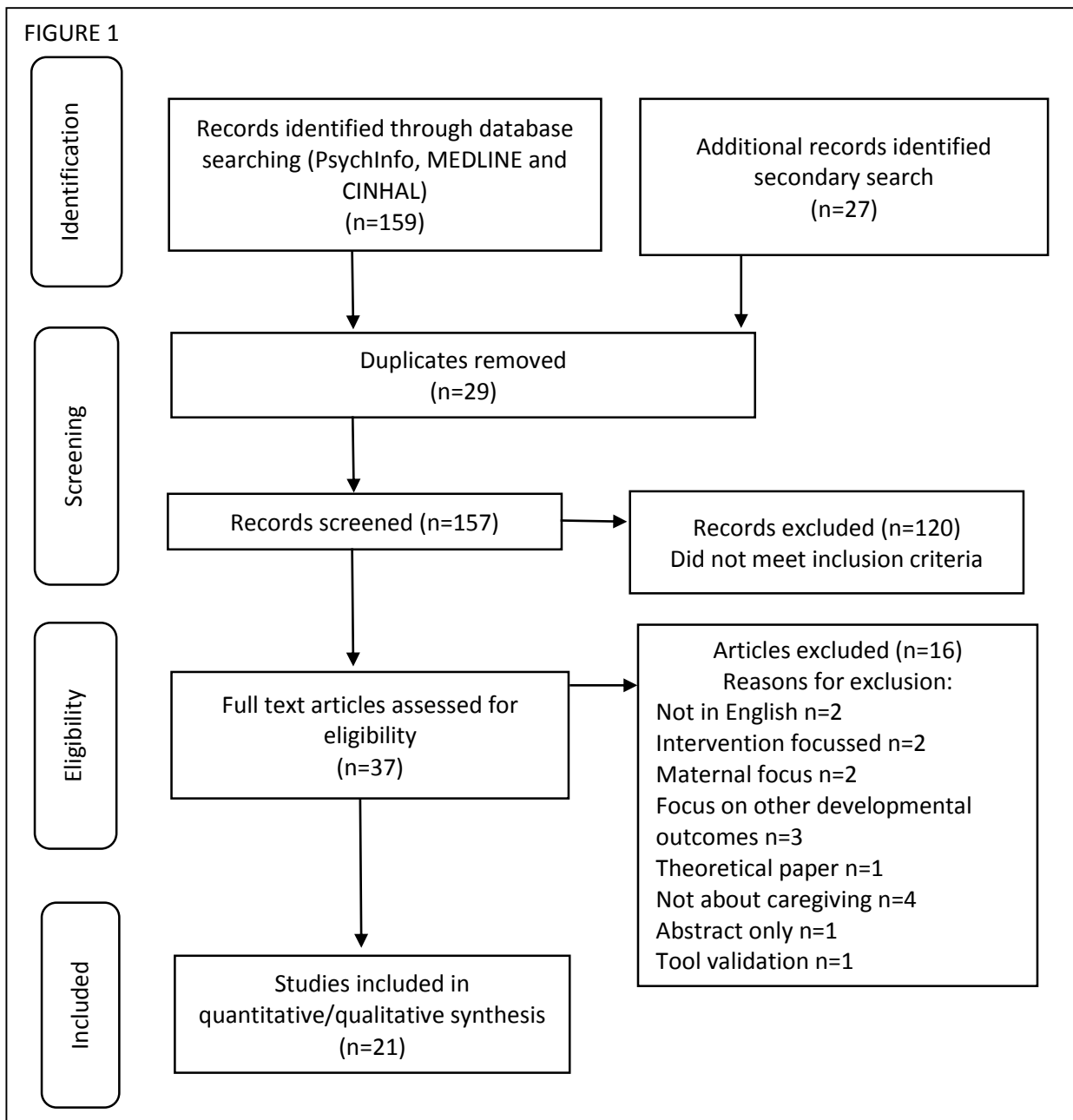
A combination of MeSH terms and subject terms were used in PsychINFO, CINHAL (EBSCO) and MEDLINE (OVID) to retrieve relevant citations. The MeSH search terms included 'intensive care unit, neonatal,' 'neonatal intensive care,' 'temperament,' 'NICU,' and 'nurse'. Subject terms used were 'neonatal unit,' 'NICU,' 'caregiving,' 'care,' 'behavioural response', 'physiological response', and 'behavioural outcome,' and 'outcome'. Truncation (*) to find any extension of the search term was used across all databases, proximity searching was used (Nx) for PsychINFO and CINHAL and (Adjx) for MEDLINE (Table 1).

The search engines identified 159 citations, 29 duplicates were found and removed, with an additional 27 articles sourced through a secondary citation search. After title and abstract review, 120 articles were discarded as they were not associated with caregiving in the NICU or subsequent outcomes. Of the 37 articles assessed as eligible for full-text review, 21 were included for analysis. The PRISMA flow diagram (Figure 1) presents the literature screening process.

Table 1. Summary of Database Search

Database	Filters	Search terms	Citations returned
CINHAL	1982-2020, English, Peer reviewed, full text	<p>Concept 1: 'Intensive care units, neonatal' [MeSH], OR 'neonatal unit*' OR 'NICU' [MeSH]</p> <p>Concept 2: 'Neonatal Intensive Care Nursing' OR 'caregiving' OR 'Nurse*' [MeSH] N3 'care*'</p> <p>Concept 3: '(behavi* OR physiolog*)' N3 '(response* OR outcome*)' OR 'temperament' [MeSH]</p> <p>Combined key concept search: 1 AND 2 AND 3</p>	47
PsychINFO		<p>Concept 1: 'Neonatal intensive care' [MeSH] OR 'neonatal unit*' OR 'NICU' [MeSH]</p> <p>Concept 2: 'Neonatal Intensive Care Nursing' OR 'caregiving' OR 'Nurse*' [MeSH] N3 'care*'</p> <p>Concept 3: '(behavi* OR physiolog*)' N3 '(response* OR outcome*)' OR 'temperament' [MeSH]</p> <p>Combined key concept search: 1 AND 2 AND 3</p>	71
MEDLINE		<p>Concept 1: 'Intensive care units, neonatal' [MeSH], OR 'neonatal unit*.mp' OR 'NICU.mp' [MeSH]</p> <p>Concept 2: 'Neonatal Intensive Care Nursing' OR 'caregiving.mp' OR 'Nurse*' [MeSH] adj3 'care*.mp'</p> <p>Concept 3: '(behavi* OR physiolog*)' adj3 '(response* OR outcome*).mp' OR 'temperament' [MeSH]</p> <p>Combined key concept search: 1 AND 2 AND 3</p>	41

Figure 1. PRISMA flow diagram screening of articles for review



RESULTS

Data from the 21 studies are organised under Matrix headings, including year/author/date, setting, sample/gestational age, research design, measures and main findings (Garrard, 2017) (see Table 4). Nineteen of the studies collected data in the NICU, one study collected data from both the NICU and postnatal unit in the maternity ward (Mörelus et al., 2006) and another from the postnatal unit only (Gunnar et al., 1995). Infant sample sizes ranged from 10 to 139 infants. The combined data explored the caregiving experience of 969 infants and 20 neonatal nurses. Research designs were mostly descriptive cross-sectional, but also included four randomised cross-over trials, three quasi-experimental cross-over studies, two longitudinal randomised controlled trials, two longitudinal cohort studies, three observational studies and one qualitative study. The studies predominately used quantitative methods, focusing on collection and analysis of physiological data (heart rate, respiratory rate, oxygenation, salivary cortisol, vagal tone, pain score, and blood pressure) and behavioural responses (pain score, stress, infant state, temperament, social and emotional assessments) in relation to caregiving. Three major themes were identified in the synthesis of the data associated with caregiving in the neonatal setting: the burden of caregiving on infants' physiological and behavioural responses; the effect of caregiving on longer-term outcomes; and factors contributing to the effects of caregiving, which comprised three categories – infant characteristics, nurse approaches to caregiving, and the effects of caregiving within a developmentally-supportive framework.

The burden of caregiving on infants' physiological and behavioural responses

Seventeen of the studies explored infants' physiological and behavioural responses to caregiving. Eleven studies reported both physiological and behavioural responses (Catelin et al., 2005; Comaru and Miura, 2009; de Freitas et al., 2018; Gunnar et al., 1995; Lee, 2002; Liaw et al., 2010; Liaw et al., 2012a; Mörelus et al., 2006; Peters, 1998; Sizun et al., 2002; Zeiner et al., 2016), four studies reported physiological responses (Danford et al., 1983; Evans, 1991; Peters, 1992; Yung-Weng and Ying-Ju, 2004), and two studies reported behavioural responses only (Becker et al., 1993; Liaw et al., 2012b).

Caregiving was classified as either an individual procedure; nappy change (Comaru and Miura, 2009; Mörelus et al., 2006; Sizun et al., 2002; Yung-Weng and Ying-Ju, 2004), infant weighing (Catelin et al., 2005), bathing (de Freitas et al., 2018; Lee, 2002; Liaw et al., 2010; Peters, 1998), performing a

heel stick (Gunnar et al., 1995), unit-based standard care (Zeiner et al., 2016), or listed as interventions defined by the study (Becker et al., 1993; Danford et al., 1983; Peters, 1992), and in two studies classified as social, routine or intrusive (Liaw et al., 2012a; Liaw et al., 2012b). One study did not articulate caregiving type beyond 'any nursing intervention that required tactile contact' (Evans, 1991).

Sixteen of the 17 studies found routine caregiving interventions were stressful for infants, showing adverse physiological or behavioural responses. The one study that found no significant changes in behavioural or physiological responses from baseline, reported a statistically non-significant increase in salivary cortisol related to caregiving (de Freitas et al., 2018).

Four studies hypothesised that routine caregiving was painful and included pain assessments in their data. All four studies found an increase in infant pain scores during routine caregiving involving nappy changing (Comaru and Miura, 2009; Mörelius et al., 2006; Sizun et al., 2002) or weighing (Catelin et al., 2005).

The effect of caregiving on longer-term outcomes

Four of the studies explored the effect of the NICU on outcomes beyond discharge, two within a developmentally-supportive framework. McNulty et al (2009) reported improved self-regulation and autonomic, motor and state system organisation at two weeks of age and significantly higher Bayley score at 9 months of age related to goal directedness, attention span and motor muscle coordination in the developmental care intervention group. Similarly, van der Paul et al (2008) reported that infants in the developmental care intervention group demonstrated better motivation and behavioural competence at 12 months.

Two studies compared infant distress responses in the neonatal setting to later behavioural and emotional outcomes. Greater heart rate variability was linked to non-optimal temperament outcomes at 6 months (Gunnar et al, 1995) and 9 months (Poehlmann et al,2012). In addition, Gunnar et al. (1995) linked behavioural responses to heel stick in full-term, healthy neonates to later maternal reports of temperament.

Factors contributing to the effects of caregiving

Factors contributing to the effects of caregiving were identified in study findings or noted by study authors (see Table 3). This theme comprised three components that at times over-lapped or were inter-related.

Infant stability, vulnerability, and immaturity

Several studies noted that infant stability, vulnerability and immaturity played a role in infant responses to caregiving, with some studies identifying severity of illness (Evans, 1991; Horns, 1998; Liaw et al., 2012a; Liaw et al., 2012b; Mörelius et al., 2006; Peters, 1998; Zeiner et al., 2016) and gestational age (Becker et al., 1993; Danford et al., 1983; Evans, 1991; Lee, 2002; Liaw et al., 2010; Liaw et al., 2012a; Liaw et al., 2012b; Mörelius et al., 2006; Peters, 1998; Yung-Weng and Ying-Ju, 2004; Zeiner et al., 2016) as variables that influenced caregiving effects. However, full-term healthy infants were also found to demonstrate pain responses during routine caregiving (Mörelius et al., 2006) and a heel stick (Gunnar et al., 1995).

Some studies found that gestational age and birth weight affected infant responses to caregiving. Gestational age effects to caregiving were identified in six studies (Becker et al., 1993; Catelin et al., 2005; Liaw et al., 2010; Liaw et al., 2012a; Liaw et al., 2012b; Mörelius et al., 2006). Lower gestational age negatively influenced behavioural state transition (Becker et al., 1993; Liaw et al., 2012b), the expression of grimace, fussing and crying responses (Liaw et al., 2010) and salivary cortisol responses (Mörelius et al., 2006). Increasing gestational age and post-menstrual age resulted in decreased startles, squirming and disorganised behaviour (Liaw et al., 2012a) and increased wake states (Liaw et al., 2012b). However, some studies found no similar infant pain and stress responses unrelated to gestational age (Catelin et al., 2005, Mörelius et al., 2006). Only a single study reported on the effect of birth weight, finding increased motor cues and attentional cues during stressful interventions in low-birth-weight infants (Zeiner et al., 2016).

Nurse perceptions of caregiving effects

Nurses' understanding of infant physiological and behavioural states was noted to inform their individual approach to caregiving. Studies by Liaw and colleagues (2010, 2012a) identified a link between nurse caregiver behaviours that included rough handling and intrusive caregiving and the effects on preterm infants. Only two studies evaluated nurses' perceptions of caregiving as a study measure. Catelin et al. (2005) found no significant correlation between occurrence of the intervention (weighing), the infant's pain score and nurses' level of satisfaction with caregiving

within a developmentally-supportive framework. In a qualitative analysis of 20 experienced neonatal nurses' perceptions of developmentally-supportive caregiving, Horns (1998) found infant physiological signs, perceived resilience during handling, infant behaviours, and complexity of the intervention, all contributed to nurses' perception of infant stability. 'Being-in-tune' with the infant, delivering care that was contingent, protective and individualised, was dependent on both the infant's stability and the nurse's approach to caregiving. The author postulated the approach taken was likely influenced by the availability of other nurses to assist with caregiving tasks, past experiences, infant handling practices and the nurses' understanding of infant behaviour.

Effect of caregiving in a developmentally-supportive framework

The effect of caregiving in a developmentally-supportive framework was explored in eight studies that compared routine caregiving to a developmentally-supportive caregiving model; three using NIDCAP (Catelin et al., 2005; McNulty et al., 2009; Sizun et al., 2002), and five using study-specific models or comparison of developmentally-supportive interventions (Becker et al., 1993; Comaru and Miura, 2009; de Freitas et al., 2018; Liaw et al., 2010; Liaw et al., 2012b; van der Pal et al., 2008). Seven of these studies found that supportive caregiving positively influenced infant physiological or behavioural responses. One study (de Freitas et al., 2018) compared supportive bathing (swaddled) and traditional tub-bathing, and found no difference between groups in infant physiological or behavioural responses pre- or post-intervention. However, the authors reported that both groups showed an increase in salivary cortisol compared to baseline physiological functioning.

Table 3. Factors identified as contributing to infant caregiving effects

Component	Identified in study findings	Suggested as a contributing factor by study authors
Infant stability, vulnerability, and immaturity (including illness severity)	Becker et al 1993 Danford et al 1983 Evans 1991 Horns 1998 Lee 2002 Liaw et al 2010 Liaw et al 2012a Liaw et al 2012b Morelius et al 2006 Peters 1992 Peters 1998 Zeiner et al 2016 Weng and Chang 2004	
Individual nurse approach to caregiving based on infant physiological and/or behavioural responses	Becker et al 1993 Horns 1998 Liaw et al 2010 Liaw et al 2012a Liaw et al 2012b Peters 1998 Weng and Chang 2004	Danford et al 1983 Peters 1992 Lee 2002 Evans 1991
Caregiving in a developmentally-supportive framework	Becker et al 1993 Catelin et al 2005 Comaru and Miura 2009 McAnulty et al 2009 Sizun et al 2002 van der Paul et al 2008 Liaw et al 2010 Liaw et al 2012b	Evans 1991 Lee 2002 Liaw et al 2012b Morelius et al 2006 Peters 1992 Peters 1998 Weng and Chang 2004

LIMITATIONS OF STUDIES

The studies included in this literature review have several limitations which potentially threaten the internal and external validity of the findings. There was a lack of consistency of measures used across studies to assess caregiving effects. The definition of developmental care and its components also varied, making comparisons difficult. Several studies did not assess the effect of caregiving during the intervention, only recording data pre- and post-event, limiting the conclusions that can be drawn from their findings (Comaru and Miura, 2009; de Freitas et al., 2018). Most studies consisted of small sample sizes (10- 50 infants).

The interpretation of stress associated with caregiving varied depending on the study focus and year of publication. For example, some researchers reported a nappy change as tolerable (Peters, 1992) compared with other routine caregiving, while others who examined nappy change in isolation described it as stressful and painful (Catelin et al., 2005; Mörelius et al., 2006). One of the studies had a recruitment period spanning 8 years which likely influenced the results as it may be assumed that caregiving practices changed during this period (McAnulty et al., 2009). Nineteen of the 22 studies were published more than 5 years ago (ranging between 8 to 37 years), suggesting there is a lack of current research exploring the issue. Given that approaches to caregiving and staff knowledge of developmental care have changed since these studies were conducted translation of their findings in the current clinical context is limited. The mediating effect of parent engagement and infant-support during nurse-delivered caregiving was not explored in the studies reviewed. This is an under-researched aspect of developmentally-supportive care.

DISCUSSION

The purpose of this integrative review was to explore what is known about nurse-delivered caregiving in the NICU with a focus on the physiological and behavioural effects and potential links to developmental outcomes. The evidence suggests that routine caregiving is not innocuous. Synthesis of the literature spanning 37 years shows there are immediate effects of caregiving, with research demonstrating altered physiological and behavioural responses, and links to longer-term outcomes.

Nineteen studies reported immediate effects of caregiving in the neonatal setting, with responses indicative of stress. Four studies utilised pain assessment tools when evaluating responses to caregiving. Interestingly, these studies focused on common caregiving interventions that are generally considered innocuous; weighing or nappy change. Catelin et al (2005) found significantly lower pain scores in preterm infants who received environmental and behavioural support during weighing. Changing an infant's nappy was among the caregiving interventions found to be both painful and stressful for preterm and term infants (Comaru and Miura, 2009; Mörelius et al., 2006; Sizun et al., 2002). This is a frequently experienced event for infants, particularly for infants with a prolonged NICU stay. It is well-documented that painful stimuli, such as heel stick and other similarly invasive interventions, precipitate stress responses (Relland et al., 2019) and strategies for minimising the effects of pain on neurodevelopmental outcomes have been widely-reported (American Academy of Pediatrics., 2016; McPherson et al., 2020). As the literature review here indicates stress responses can also be linked to caregiving activities not generally recognised as painful for sick and preterm infants as well as full term infants in the NICU. Consequently, measures are often not implemented to minimise this impact. Importantly, rather than the type of intervention, it appears that it is the manner in which the nurse delivers care that significantly affects the infant (Becker et al., 1993). Developmentally-supportive caregiving can result in immediate improvements in parasympathetic activity and self-regulation (De Rogalski Landrot et al., 2007; Pressler et al., 2001). Exploring the way in which caregiving is delivered and the factors influencing its application is warranted.

Initial research exploring the effects of caregiving likely coincided with the introduction of developmentally-supportive care. Yet only two studies conducted in the past five years examined the physiological and behavioural effects of this type of caregiving (de Freitas et al., 2018; Zeiner et al., 2016). The lack of recent studies in this area suggests the effects of caregiving may not be a

current research priority. Perhaps this also reflects the challenges associated with this type of research, including access to resources and funding. **Consequently**, the link to developmental outcomes is not yet fully explored. Of the twenty studies involving infants, only two looked at the longer-term effects of developmentally-supportive care beyond the NICU admission (McAnulty et al., 2009; van der Pal et al., 2008). The findings of this review suggest it is important that future research explores both the immediate and longer-term effects of nurse-delivered caregiving, including the mediating influence of parents.

The nature of the data used to evaluate the effects of caregiving is important, as infant's stress responses in the NICU manifest across multiple systems (Gunnar et al., 1995). The inclusion of physiological data (heart rate, respiratory rate, oxygen saturation) allows the identification of stress responses in vulnerable infants who may not be capable of outwardly displaying behavioural state changes in response to stress (Zeiner et al., 2016). Combining both physiological and behavioural observations is recommended to evaluate the complexity of an infant's stress response to a caregiving intervention (Zeiner et al., 2016). Yet, only half of the studies reported the combined physiological and behavioural effects of caregiving (Catelin et al., 2005; Comaru and Miura, 2009; de Freitas et al., 2018; Gunnar et al., 1995; Lee, 2002; Liaw et al., 2010; Liaw et al., 2012a; Mörelus et al., 2006; Peters, 1998; Sizun et al., 2002; Zeiner et al., 2016). Prematurity and prolonged exposure to stress in the NICU is thought to inhibit the parasympathetic arm of the ANS, accounting for greater variability in physiological responses to stimuli (De Rogalski Landrot et al., 2007). Promoting a set of standard behavioural and physiological variables to measure infant stress enables comparison of findings across studies. As physiological data is readily available at the bedside via continuous monitoring, nurse's responsiveness to monitoring alerts as indicators of infant stress during caregiving could be incorporated in future research.

This review incorporated literature exploring links between caregiving in the NICU and infant temperament and behavioural outcomes up to 12 months of age. Of the two studies that measured these parameters, both found a link between neonatal stress reactivity in the NICU and non-optimal outcomes for temperament and behaviour (Gunnar et al., 1995; Poehlmann et al., 2012). Despite the paucity of data, findings to-date suggest that temperament may be a useful measure for exploring relationships between infant responses during caregiving and longer-term developmental outcomes. An important component of infant behavioural state is self-regulation. An infant's self-regulatory abilities develop over time and in response to the environment, consisting of active efforts on the part of the infant to regulate their autonomic functions, motor control, level of arousal and

availability for socialisation (Als, 1982; Als, 1989); with caregiver support promoting these self-regulatory capacities (Feldman, 2009). The longer-term effects of poor self-regulation include sub-optimal social and cognitive development ranging from difficult temperament to regulatory disorders (Feldman, 2009; Sidor et al., 2017), predictive of subsequent behavioural difficulties. Further research investigating links between stress responses in the NICU and infant temperament is warranted.

Recommendations to modify caregiving based on study findings was highlighted in 18 of the studies (Becker et al., 1993; Catelin et al., 2005; Comaru and Miura, 2009; Danford et al., 1983; Evans, 1991; Horns, 1998; Lee, 2002; Liaw et al., 2010; Liaw et al., 2012a; Liaw et al., 2012b; McAnulty et al., 2009; Mörelius et al., 2006; Peters, 1992; Peters, 1998; Sizun et al., 2002; van der Pal et al., 2008; Yung-Weng and Ying-Ju, 2004; Zeiner et al., 2016). Suggestions to adapt caregiving could be broadly categorised into three taxonomies; the sensitive application of caregiving (Peters, 1998), identification of the infant's individualised needs (Mörelius et al., 2006), and an understanding of the relationship between caregiver and infant (Liaw et al., 2010). It is difficult to modify nurse-delivered caregiving practices if little is known of what motivates the caregiver and influences the application of caregiving.

While infant stability, vulnerability and immaturity, all of which can be related to gestational age, birth weight and severity of illness, were identified as factors contributing to caregiving effects, it appears that it is the nurses' perceptions and responsivity to infant physiological and behavioural responses that play the greater role (Liaw et al., 2010; Liaw et al., 2012a). Yet, only one study investigated nurses' perceptions of infant responses to caregiving (Horns, 1998). Individual nurse approaches to caregiving and valuing of developmentally-supportive care are influenced by access to education, personal experience, and management or organisational support for care practices (Austin et al., 2019; Park and Kim, 2019). NICU nurses appear interested in implementing developmentally-supportive care, yet there is possibly a difference between declared and actual nurse behaviour, with this difference not well explained in the literature. Research has found that despite developmental care education and nurses acknowledgment of the need to implement practice components, change was often sporadic with a focus on environmental rather than behavioural modifications (Milette et al., 2005). The translation of best available evidence into improved health outcomes is a complex and iterative process that requires cultural, behavioural and practice change (Curtis et al., 2017).

Consistency in the application of nurse-delivered caregiving in the NICU remains a challenge (Gonya et al., 2019) and, as highlighted in this literature review, practices may not align with best practice principles. Whilst neonatal nurses, like all nurses, have a moral-ethical-professional obligation to provide compassionate, quality patient care (Faber, 2013), there are several factors that may influence the interface between the caregiver and the caregiving. The ethical 'best interest principle', is a surrogate decision-making model, unique to infants as they are reliant on others to make decisions in their interests (Spence, 2000). Nurse-delivered caregiving where it is necessary to undertake certain tasks and interventions to achieve the best outcome for the infant can be placed within this model (Spence, 2000). Nurses initiate and undertake activities to meet basic human needs and the more complex medical needs of infants in the NICU. Nurses' personal and professional experience, how they view the infant and their perception of the infant's clinical condition and potential long-term outcomes may all influence their caregiving interactions (Spence, 2000).

Research is needed to ascertain whether there is a gap between nurses' perceptions of caregiving and the actual effects on the infant, and how this differentiates between caregiving performed to the infant and caregiving that is sensitively responsive to infant cues. Caregiving has been described as a dance; partners (nurse-baby, baby-nurse) who are 'in-tune' adjust to each other to move in synchrony (Liaw et al., 2010). Evaluating how often caregivers are dancing the same dance to the same rhythm as the infant may help to explain immediate effects of caregiving and consequent longer-term developmental outcomes.

RELEVANCE TO CLINICAL PRACTICE

Based on findings from this literature review caregiving interventions in the neonatal setting appear to have potentially adverse effects for infants, both immediate and long-term. It is essential that neonatal nurses understand the effects of caregiving, modify practices and are responsive to infants' needs. Modification of caregiving practices to benefit the infant will require the commitment of individual nurses, managers, and education providers. Identifying the components of care in the neonatal setting that are linked to developmental outcomes is essential to minimise the potential lifelong impact of the NICU environment on infants and their families.

LIMITATIONS OF THIS REVIEW

The main limitations of this review are that the search was limited to the English language and excluded publications before 1982. This has the potential to exclude relevant untranslated and older studies. However, given the changes in caregiving practices in neonatal settings since 1982 findings from studies prior to that date may no longer be relevant. The conceptualisation of this integrative review involving the linking of three concepts; nurse-delivered caregiving, the neonatal setting, and outcomes within the first 12 months of life, may also have excluded research. Some studies removed through early screening were relevant to the broader body of knowledge in this area, but were not specific to the purpose of this review. The findings of this review were intended to identify the current state of knowledge and potential gaps in the literature, not to inform best practice guidelines. As such, the review does not include an assessment of the quality of the evidence. While this may be a limitation of the review and a source of potential bias, the review does highlight the need for further research on nurse-delivered caregiving in the NICU and its effects on infants.

CONCLUSION

This literature review highlights the need for further research examining the physiological and behavioural effects of caregiving on infants in the NICU and the potential links to developmental outcomes. It is important to conduct research that looks beyond the immediate responses to caregiving. Capturing the cumulative effect within and beyond the NICU will ensure the overall impact of nurse-delivered caregiving is thoroughly evaluated. With this data, an individualised caregiving approach can be clearly articulated and the need for resources to buffer the effect of caregiving be effectively communicated to clinicians, families, administrators, and policymakers. Understanding the link between caregiving and developmental outcomes may strengthen the call for adequate staffing and education resources in the neonatal setting. To better understand neonatal nurse practices, future research must include nurses' perceptions of the effects of caregiving when exploring the relationship between cause (caregiving approach) and effect (infant behaviours and physiology). This information will be used to modify practices that may be linked to longer-term morbidity of infants following an NICU admission.

Authors Publication date (Country)	Setting	Sample Gestational age (range in weeks) *	Research design	Type of caregiving intervention	Measures	Main Findings
Becker et al 1997 (USA)	NICU	38 preterm infants; 25-32 (mean 28.3)	Quasi-experimental cross-over design; each infant served as its own control during four caregiving sessions	'Caregiving tasks' (not further detailed)	Behavioural state, caregiver intervention, video	Developmental caregiving supported behavioural state organisation by increasing sleep and drowsy periods with decreased fuss/cry time
Catelin et al 2005 (France)	NICU	45 infants; 15, <32 (mean 30.1) 15, >32 -36 (mean 34.2) 15, >37 (mean 39.1)	Randomised cross-over comparison of three groups of infants across different gestational ages (very preterm, late preterm, term) during a developmentally- supportive and not-supportive weight measurement. Infants were weighed twice in 24 hours and served as their own control	Weighing	HR, TCO ₂ , NIPS, EDIN, NIRS, salivary cortisol, number of procedures, nurse's satisfaction index, video	Developmentally-supportive environmental and behavioural interventions decreased heart rate, pain and discomfort scores in preterm and term infants during weighing
Comaru and Miura 2009 (Brazil)	NICU	47 preterm infants; <35	Randomised cross-over design, comparison of nest use during nappy change versus no nest, infants served as their own control	Nappy change	HR, SaO ₂ , NIDCAP stress behaviours, distress score, pain score	All infants displayed increased distress and pain scores during nappy changes despite postural support from a nest

Authors Publication date (Country)	Setting	Sample Gestational age (range in weeks) *	Research design	Type of caregiving intervention	Measures	Main Findings
Danford et al 1983 (USA)	NICU	36 infants; 24-38	Prospective observational design comparing term and preterm infants observed during invasive interventions or routine caregiving	11 different types ranging from vital sign measurements, nappy change to heel stick	TcPO ₂	Nearly all care-orientated stimuli resulted in a fall in oxygenation in 50-100% of preterm infants
de Freitas et al 2018 (Brazil)	NICU	43 preterm infants; 32-36 22, (mean 33) 21, (mean 34)	Randomised cross-over design comparing two groups allocated to either swaddled or non-swaddled bathing technique, measures taken pre- and post-intervention	Bathing	HR, SaO ₂ , axillary temperature, salivary cortisol, infant sleep wake state, video	No significant differences in vital signs, salivary cortisol, or sleep wake state between the two groups. Salivary cortisol increased from baseline in both groups during the interventions
Evans 1991 (USA)	NICU	13 preterm infants; 6, <30 7, 30-33	Prospective observational design, caregiving observed for one hour	6 different types from vital signs, nappy change to suctioning	TcPO ₂	Invasive and routine caregiving was associated with hypoxemia in the first 72 hours of life
Gunnar et al 1995 (USA)	Post- natal unit	50 full-term healthy infants; 37-41	Prospective longitudinal cohort, measures collected at mean 48 hours of age and temperament at 6 months	Heel stick	HR, vagal tone, behavioural state (Brazelton NBAS), salivary cortisol, IBQ	Greater physiological and behavioural activity responses to a heel stick were related to maternal report of subdued temperament at 6 months of age

Authors Publication date (Country)	Setting	Sample Gestational age (range in weeks) *	Research design	Type of caregiving intervention	Measures	Main Findings
Horns 1998 (USA)	NICU	20 NICU experienced nurses	Observational and focus group approach, observational technique used to develop questions for the focus group interviews	Not applicable	Focus group interviews	Infant physiological stability and the nurse's approach to caregiving impacted their perception of the infant's responses
Lee 2002 (South Korea)	NICU	40 preterm infants; 27-36 (mean 33.1)	Descriptive exploratory design examining the effects of sponge bathing (before, during and after)	Sponge bathing	HR, vagal tone, SaO ₂ , behavioural states	Sponge bathing of preterm infants was associated with a significantly increased HR and decreased vagal tone indicative of stress
Liaw et al 2010 (Taiwan)	NICU	24 preterm infants; 27-35 (mean 30.3)	Descriptive correlational design comparison of infants bathed by different nurses on different days	Bathing	Infant behaviour coding, nurse behaviour coding, video	Supportive caregiving behaviours from nurses reduced infant stress and increased infant self- regulation behaviours
Liaw et al 2012 (a) (Taiwan)	NICU	30 preterm infants; 27-36 (mean 31.5)	Prospective descriptive design with repeat measures and continuous video observation for three consecutive 24 hour periods	49 caregiving activities classified as no caregiving, social interaction, routine caregiving, intrusive caregiving	HR, RR, SaO ₂ , NTISS, infant behaviour coding, NIDCAP regulation behaviours	Occurrences of most infant stress- related behaviours increased during stress-inducing caregiving

Authors Publication date (Country)	Setting	Sample Gestational age (range in weeks) *	Research design	Type of caregiving intervention	Measures	Main Findings
Liaw et al 2012 (b) (Taiwan)	NICU	30 preterm infants; 27-36 (mean 31.5)	Prospective descriptive design with repeat measures and continuous video observation for three consecutive 24 hour periods	Classified as no caregiving, social interaction, routine caregiving, intrusive caregiving	NTISS, infant behaviour coding, NICU caregiving and support	Quiet sleep increased when infants received no caregiving, social interactions or NNS and were laterally positioned
McAnulty et al 2009 (USA)	NICU	107 preterm infants: 51 -control 56 – NIDCAP; <29	Longitudinal randomised control trial comparing standard care to NIDCAP care. Measures at 2 weeks corrected age and at 9 months corrected age	'Standard versus NIDCAP care' not further defined	2 weeks: APIB, Prechtl, EEG 9 months: Bayley Scales of Infant Development	NIDCAP care was associated with improved behavioural functioning at 2 weeks corrected and neurobehavioral functioning at 9 months
Mörelus et al 2006 (Sweden)	NICU & postnatal unit	39 NICU infants: 23, <30 16, >30 and 30 full- term healthy infants	Prospective descriptive design with repeat measures, comparing two NICU groups of different gestational age and a healthy full-term control group; pre-, during, and post- routine nappy change	Nappy change	HR, SaO ₂ , salivary cortisol, PIPP, NIPS	Preterm and full-term infants demonstrated pain responses during routine nappy changes
Peters 1992 (Canada)	NICU	10 preterm infants; 27-36 (mean 29.9)	Quasi-experimental repeat measure observation of caregiving over 3.5 days	28 different types of care from 'tender care', weighing,	HR, MABP, ICP, TcPO ₂ , TcCO ₂ , TcSaO ₂	Frequent periods of hypoxia, hyperoxia and increased ICP responses occurred either during or up to 5 minutes after routine care

Authors Publication date (Country)	Setting	Sample Gestational age (range in weeks) *	Research design	Type of caregiving intervention	Measures	Main Findings
Peters 1998 (Canada)	NICU	14 preterm infants; 7, 28-29 7, 30-31 (overall mean 29)	Prospective quasi- experimental repeat measure, comparing two gestational age groups responses to sponge bathing, each infant served as own control	nappy change, heel stick, suctioning Bathing	HR, SaO ₂ , NIDCAP behavioural state, video	Disruption in physiological and behavioural responses occurred in all neonates throughout the bathing intervention, with higher state and activity levels post-bath
Poehlmann et al ** 2012 (USA)	NICU	109 preterm infants; 23-36 (mean 31.7)	Prospective longitudinal cohort design, with baseline physiological measures in the NICU and repeat measures up to 36 months of age	Not applicable	9 months: Vagal tone, parenting interaction (PCERA), LAB-TAB	Temperamentally prone-to- distress preterm infants exhibited more externalising problems with a 'critical style' of parenting
Sizun et al 2002 (France)	NICU	19 preterm infants; 27-31 (mean 29.1)	Prospective cross-over, infants randomly assigned to receive developmental care or no developmental care during intervention, each infant served as own control	Nappy change	HR, SaO ₂ , PIPP, EDIN, video	Developmentally-supportive care during a nappy change significantly reduced pain and distress scores and hypoxic events
van der Pal et al 2008***	NICU	139 preterm infants 70, mean 29.5	Randomised control trial comparing groups of infants allocated to either environmental developmental	Basic developmental care (incubator cover and nest)	12 months: ITSEA, NOSI	A basic form of environmental developmental care had a positive influence on child competence

Authors Publication date (Country)	Setting	Sample Gestational age (range in weeks) *	Research design	Type of caregiving intervention	Measures	Main Findings
(The Netherlands)		69, mean 29.1	care or standard care; followed up to two years of age	versus standard care		behaviours at 12 months corrected age
Yung-Weng and Ying-Jui 2004 (Taiwan)	NICU	11 preterm infants 27-36 (mean 29.9)	Prospective descriptive design with repeat measures; each infant was observed during a nappy change at four different times on different days	Nappy change	HR, SaO ₂ , buttock lifting angle	90% of nappy changes resulted in increased or decreased HR and decreased SaO ₂ for premature infants, with a recovery time up to 10 minutes
Zeiner et al 2016 (USA)	NICU	30 preterm infants 28-35 (mean 32.7)	Prospective observational design, during standard morning caregiving	Temperature, nappy change and repositioning	HR, RR, skin conductance responses, NIDCAP stress behaviours	Stress responses significantly increased during care, with behavioural responses influenced by the infant's severity of illness

Table 4. Summary of articles included in literature review

Abbreviations: APIB: Assessment of Preterm Infant's Behaviour, BPSC: Baby Pediatric Symptom Checklist, Brazelton NBAS: Neonatal Behavioral Assessment Scale, EDIN: Échelle Douleur Inconfort Nouveau-Né, neonatal pain and discomfort scale, EEG: electroencephalogram, HR: heart rate, IBQ: Rothbart's Infant Behavioural Questionnaire, ICP: Intracranial pressure, ICQ: Infant Characteristics Questionnaire, ITQ: Carey's Infant Temperament Questionnaire, ITSEA: Infant-Toddler Social and Emotional Assessment, LAB-TAB: Laboratory assessment of Temperament, MABP: Mean arterial blood pressure, NICU: neonatal intensive care unit, NIPS: Neonatal Infant Pain Scale, NIRS: Near-Infrared Spectroscopy, NOSI: Nijmegen Parenting Stress Index, NNNS: NICU Network Neurobehavioral Scale, NIDCAP: Newborn Individualised Developmental Care Assessment Program, NNS: non-nutritive sucking, NTISS: National Therapeutic Intervention Scoring System, PCERA: Parent Child Early Relational Assessment, PIPP: Premature Infant Pain Profile, Prechtl: Prechtl Neurological Examination of the Full-term Newborn Infant, RR: respiratory rate, SaO₂: oxygen saturation levels, TCO₂: Transcutaneous carbon dioxide, TCPO₂: Transcutaneous oxygen, TCM: Transcutaneous Monitoring, TcSaO₂: Transcutaneous oxygen saturation.

* details of gestational age were not consistently available

** only results at 9 months are reported in this table

*** only results at 12 months are reported in this table

Reference List

- Abulizi, X., Pryor, L., Michel, G., Melchior, M., van der Waerden, J., Group, E.M.C.C.S., 2017. Temperament in infancy and behavioral and emotional problems at age 5.5: The EDEN mother-child cohort. *PLoS One* 12, e0171971-e0171971.
- Als, H., 1982. Toward a synactive theory of development: Promise for the assessment and support of infant individuality. *Infant Ment Health J*, 3, 229-243.
- Als, H., 1986. A synactive model of neonatal behavioral organization: Framework for the assessment of neurobehavioral development in the premature infant and for support of infants and parents in the neonatal intensive care environment. *Phys Occup Ther Pediatr*, 6, 3-53.
- Als, H., 1989. Self-regulation and motor development in preterm infants, Action in social context. Springer, pp. 65-97.
- Als, H., Butler, S., Kosta, S., McAnulty, G., 2005. The Assessment of Preterm Infants' Behavior (APIB): Furthering the understanding and measurement of neurodevelopmental competence in preterm and full-term infants. *Ment Retard Dev Disabil Res Rev*, 11, 94-102.
- Als, H., McAnulty, G., 2011. The newborn individualized developmental care and assessment program (NIDCAP) with kangaroo mother care (KMC): comprehensive care for preterm infants. *Curr Womens Health Rev*, 7, 288-301.
- Austin, B., Downing, C., Hastings-Tolsma, M., 2019. Experience of neonatal intensive care unit nurses in providing developmentally-supportive care: A qualitative study. *Nurs Health Sci*, 21, 336-344.
- Becker, P.T., Grunwald, P.C., Moorman, J., Stuhr, S., 1993. Effects of developmental care on behavioral organization in very-low-birth-weight infants. *Nurs Res* 42, 214-220.
- Burnett, A.C., Cheong, J.L.Y., Doyle, L.W., 2018. Biological and social influences on the neurodevelopmental outcomes of preterm infants. *Clin Perinatol* 45, 485-500.
- Byers, J.F., 2003. Components of developmental care and the evidence for their use in the NICU. *MCN Am J Matern Child Nurs*, 28, 174-180.
- Carrier, C.T., 2002. Individualized family-centered developmental care: Reflections on implementation. *Newborn Infant Nurs Rev*, 2, 27-34.
- Cassiano, R.G., Provenzi, L., Linhares, M.B.M., Gaspardo, C.M., Montiroso, R., 2020. Does preterm birth affect child temperament? A meta-analytic study. *Infant Behav Dev* 58, 101417.
- Cassiano, R.G.M., Gaspardo, C.M., Linhares, M.B.M., 2019. Temperament moderated by neonatal factors predicted behavioral problems in childhood: A prospective longitudinal study. *Early Hum Dev* 135, 37-43.
- Catelin, C., Tordjman, S., Morin, V., Oger, E., Sizun, J., 2005. Clinical, physiologic, and biologic impact of environmental and behavioral interventions in neonates during a routine nursing procedure. *J Pain*. 6, 791-797.
- Cheong, J.L.Y., Burnett, A.C., Treyvaud, K., Spittle, A.J., 2020. Early environment and long-term outcomes of preterm infants. *J Neural Transm (Vienna)* 127, 1-8.
- Comaru, T., Miura, E., 2009. Postural support improves distress and pain during diaper change in preterm infants. *J Perinatol*, 29, 504-507.
- American Academy of Pediatrics 'Committee on Fetus and Newborn & Section on Anesthesiology and Pain Medicine', 2016. Prevention and management of procedural pain in the neonate: An update. *Pediatrics*, 137(2), e20154271.
- Curtis, K., Fry, M., Shaban, R.Z., Considine, J., 2017. Translating research findings to clinical nursing practice. *J Clin Nurs* 26, 862-872.
- D'Agata, A.L., Sanders, M.R., Grasso, D.J., Young, E.E., Cong, X., McGrath, J.M., 2017. Unpacking the burden of care for infants in the NICU. *Infant Ment Health J*, 38, 306-317.
- Danford, D.A., Miske, S., Headley, J., Nelson, R.M., 1983. Effects of routine care procedures on transcutaneous oxygen in neonates: a quantitative approach. *Arch Dis Child*, 58, 20.
- De Bernardo, G., Svelto, M., Giordano, M., Sordino, D., Riccitelli, M., 2017. Supporting parents in taking care of their infants admitted to a neonatal intensive care unit: a prospective cohort pilot study. *Ital J Pediatr* 43, 36-36.

de Freitas, P., Bueno, M., Holditch-Davis, D., Santos, H.P., Kimura, A.F., 2018. Biobehavioral Responses of Preterm Infants to Conventional and Swaddled Tub Baths: A Randomized Crossover Trial. *J Perinat Neonatal Nurs*, 32.

De Rogalski Landrot, I., Roche, F., Pichot, V., Teyssier, G., Gaspoz, J.-M., Barthelemy, J.-C., Patural, H., 2007. Autonomic nervous system activity in premature and full-term infants from theoretical term to 7 years. *Auton Neurosci*, 136, 105-109.

DiPietro, J.A., Porges, S.W., 1991. Relations between neonatal states and 8-month developmental outcome in preterm infants. *Infant Behav Dev*, 14, 441-450.

Evans, J.C., 1991. Incidence of hypoxemia associated with caregiving in premature infants. *Neonatal Netw*, 10, 17.

Faber, K., 2013. Relationship-Based care in the neonatal intensive care unit. *Creat Nurs*, 19, 214-218.

Feldman, R., 2009. The Development of Regulatory Functions From Birth to 5 Years: Insights From Premature Infants. *Child Dev*, Mar-Apr 2009;80(2):544-61.

Foreman, S.W., Thomas, K.A., Blackburn, S.T., 2008. Individual and gender differences matter in preterm infant state development. *J Obstet Gynecol Neonatal Nurs*, 37, 657-665.

Garrard, J., 2017. Health sciences literature review made easy: The matrix method., 5th ed. Jones and Bartlett Learning, Burlington, MA.

Godarzi, z., Zarei, K., Shariat, M., Sadeghniat, k., Nikafs, N., Sepaseh, H., 2018. Correlations of handling procedures and sleep patterns of the infants admitted to the neonatal intensive care unit. *Iranian Journal of Neonatology*, 9, 35-41.

Gonya, J., Harrison, T., Feldman, K., Stein, M., Chawla, N., 2019. Nursing networks in the NICU and their association with maternal stress: A pilot study. *J Nurs Manag*, 27, 442-449.

Gunnar, M.R., Porter, F.L., Wolf, C.M., Rigatuso, J., Larson, M.C., 1995. Neonatal stress reactivity: predictions to later emotional temperament. *Child Dev*, 66, 1-13.

Horns, K.M., 1998. Being-in-tune caregiving. *J Perinat Neonatal Nurs*, 12, 38-49.

Lawhon, G., Hedlund, R.E., 2008. Newborn individualized developmental care and assessment program training and education. *J Perinat Neonatal Nurs* 22, 133-144; quiz 145-136.

Lean, R.E., Rogers, C.E., Paul, R.A., Gerstein, E.D., 2018. NICU Hospitalization: Long-Term implications on parenting and child behaviors. *Curr Treat Options Pediatr* 4, 49-69.

Lee, H.-K., 2002. Effects of sponge bathing on vagal tone and behavioural responses in premature infants. *J Clin Nurs*, 11, 510-519.

Lee, S.K., O'Brien, K., 2014. Parents as primary caregivers in the neonatal intensive care unit. *CMAJ* 186, 845-847.

Liaw, J.-J., Yang, L., Chou, H.-L., Yang, M.-H., Chao, S.-C., 2010. Relationships between nurse care-giving behaviours and preterm infant responses during bathing: a preliminary study. *J Clin Nurs*, 19, 89-99.

Liaw, J.-J., Yang, L., Hua, Y.-M., Chang, P.-W., Teng, C.C., Li, C.-C., 2012a. Preterm infants' biobehavioral responses to caregiving and positioning over 24 hours in a neonatal unit in Taiwan. *Res Nurs Health*, 35, 634-646.

Liaw, J.-J., Yang, L., Lo, C., Yuh, Y.-S., Fan, H.-C., Chang, Y.-C., Chao, S.-C., 2012b. Caregiving and positioning effects on preterm infant states over 24 hours in a neonatal unit in Taiwan. *Res Nurs Health*, 35, 132-145.

Linnér, A., Almgren, M., 2020. Epigenetic programming-The important first 1000 days. *Acta Paediatr*, 109, 443-452.

Lubbe, W., Van der Walt, C.S., Klopper, H.C., 2012. Integrative literature review defining evidence-based neurodevelopmental supportive care of the preterm infant. *J Perinat Neonatal Nurs* 26, 251-259.

Maki, M.T., Orsi, K.C.S.C., Tsunemi, M.H., Hallinan, M.P., Pinheiro, E.M., Avelar, A.F.M., 2017. The effects of handling on the sleep of preterm infants. *J Acta Paul Enferm*. 30, 489-496.

McAnulty, G., Duffy, F.H., Butler, S., Parad, R., Ringer, S., Zurakowski, D., Als, H., 2009. Individualized developmental care for a large sample of very preterm infants: health, neurobehaviour and neurophysiology. *Acta Paediatr*, 98, 1920-1926.

McAnulty, G.B., Duffy, F.H., Butler, S.C., Bernstein, J.H., Zurakowski, D., Als, H., 2010. Effects of the Newborn Individualized Developmental Care and Assessment Program (NIDCAP) at age 8 years: preliminary data. *Clin Pediatr*, 49, 258-270.

McLaughlin, K.A., Sheridan, M.A., Tibu, F., Fox, N.A., Zeanah, C.H., Nelson, C.A., 2015. Causal effects of the early caregiving environment on development of stress response systems in children. *Proc Natl Acad Sci USA*, 112, 5637.

McPherson, C., Miller, S.P., El-Dib, M., Massaro, A.N., Inder, T.E., 2020. The influence of pain, agitation, and their management on the immature brain. *Pediatr Res* 88, 168-175.

Milette, I.H., Richard, L., Martel, M.-J., 2005. Evaluation of a developmental care training programme for neonatal nurses. *J Child Health Care*, 9, 94-109.

Mörelus, E., Hellström-Westas, L., Carlén, C., Norman, E., Nelson, N., 2006. Is a nappy change stressful to neonates? *Early Hum Dev*, 82, 669-676.

Murdoch, D.R., Darlow, B.A., 1984. Handling during neonatal intensive care. *Arch Dis Child*, 59, 957-961.

O'Brien, K., Robson, K., Bracht, M., Cruz, M., Lui, K., Alvaro, R., da Silva, O., Monterrosa, L., Narvey, M., Ng, E., Soraisham, A., Ye, X.Y., Mirea, L., Tarnow-Mordi, W., Lee, S.K., 2018. Effectiveness of Family Integrated Care in neonatal intensive care units on infant and parent outcomes: a multicentre, multinational, cluster-randomised controlled trial. *Lancet Child Adolesc Health*, 2, 245-254.

O'Reilly, H., Johnson, S., Ni, Y., Wolke, D., Marlow, N., 2020. neuropsychological outcomes at 19 years of age following extremely preterm birth. *Pediatrics* 145.

Park, J., Kim, J.-S., 2019. Factors Influencing developmental care practice among neonatal intensive care unit nurses. *J Pediatr Nurs*, 47, e10-e15.

Pereira, F.L., Goes, F.d.S.N.d., Fonseca, L.M.M., Scochi, C.G.S., Castral, T.C., Leite, A.M., 2013. Handling of preterm infants in a neonatal intensive care unit. *Rev Esc Enferm USP*, 47, 1272-1278.

Peters, K., 1992. Does routine nursing care complicate the physiological status of the premature infant with respiratory distress. *J Perinat Neonatal Nurs*, 6, 74-91.

Peters, K.L., 1998. Bathing premature infants: Physiological and behavioral consequences. *Am J Crit Care*, 7, 90-100.

Peters, K.L., 1999. Infant handling in the NICU: does developmental care make a difference? An evaluative review of the literature. *J Perinat Neonatal Nurs* 13, 83-109.

Poehlmann, J., Hane, A., Burnson, C., Maleck, S., Hamburger, E., Shah, P.E., 2012. Preterm infants who are prone to distress: differential effects of parenting on 36-month behavioral and cognitive outcomes. *J Child Psychol Psychiatry*, 53, 1018-1025.

Prechtl, H.F., 1974. The behavioural states of the newborn infant (a review). *Brain research* 76, 185-212.

Pressler, J.L., Hepworth, J.T., Helm, J.M., Wells, N.L., 2001. Behaviors of very preterm neonates as documented using NIDCAP observations. *Neonatal Netw*, 20, 15-24.

Relland, L.M., Gehred, A., Maitre, N.L., 2019. Behavioral and physiological signs for pain assessment in preterm and term neonates during a nociception-specific response: A systematic review. *Pediatr Neurol* 90, 13-23.

Rick, S.L., 2006. Developmental care on newborn intensive care units: Nurses' experiences and neurodevelopmental, behavioural, and parenting outcomes. A critical review of the literature. *J Neonatal Nurs*, 12, 56-61.

Robinson, R., Lahti-Pulkkinen, M., Schnitzlein, D., Voit, F., Girchenko, P., Wolke, D., Lemola, S., Kajantie, E., Heinonen, K., Räikkönen, K., 2020. Mental health outcomes of adults born very preterm or with very low birth weight: A systematic review. *Semin Fetal Neonatal Med*, 25(3):101113.

Sidor, A., Fischer, C., Cierpka, M., 2017. The link between infant regulatory problems, temperament traits, maternal depressive symptoms and children's psychopathological symptoms at age three: a longitudinal study in a German at-risk sample. *Child Adolesc Psychiatry Ment Health* 11, 10-10.

Sizun, J., Ansquer, H., Browne, J., Tordjman, S., Morin, J.-F., 2002. Developmental care decreases physiologic and behavioral pain expression in preterm neonates. *J Pain*, 3, 446-450.

- Soleimani, F., Azari, N., Ghiasvand, H., Shahrokhi, A., Rahmani, N., Fatollahierad, S., 2020. Do NICU developmental care improve cognitive and motor outcomes for preterm infants? A systematic review and meta-analysis. *BMC Pediatrics*, 20, 67.
- Spence, K., 2000. The best interest principle as a standard for decision making in the care of neonates. *J Adv Nurs*, 31, 1286-1292.
- Symington, A., Pinelli, J.M., 2009. Developmental care for promoting development and preventing morbidity in preterm infants. *Cochrane Database Syst Rev*, Apr 19;(2):CD001814.
- Torowicz, D., Lisanti, A.J., Rim, J.S., Medoff-Cooper, B., 2012. A developmental care framework for a cardiac intensive care unit: a paradigm shift. *Adv Neonatal Care*, Oct;12 Suppl 5:S28-32.
- van der Pal, S.M., Maguire, C.M., Bruil, J., Cessie, S., van Zwieten, P., Veen, S., Wit, J.M., Walther, F.J., 2008. Very pre-term infants' behaviour at 1 and 2 years of age and parental stress following basic developmental care. *Br J Dev Psychol*, 26, 103-115.
- Weber, A., Harrison, T.M., 2019. Reducing toxic stress in the neonatal intensive care unit to improve infant outcomes. *Nurs Outlook*, 67, 169-189.
- Wolke, D., Johnson, S., Mendonça, M., 2019. The Life Course Consequences of Very Preterm Birth. *Annu Rev Dev Psychol*, 1, 69-92.
- Yung-Weng, W., Ying-Ju, C., 2004. A preliminary study of bottom care effects on premature infants' heart rate and oxygen saturation. *J Nurs Res* 12, 161-168.
- Zahr, L.K., Balian, S., 1995. Responses of premature infants to routine nursing interventions and noise in the NICU. *Nurs Res* 44, 179-185.
- Zeiner, V., Storm, H., Doheny, K.K., 2016. Preterm infants' behaviors and skin conductance responses to nurse handling in the NICU. *J Matern Fetal Neonatal Med*, 29, 2530-2535.

Response to reviewers

Reviewer one	Comments
<p>I have found your submission to be interesting and engaging. The clear heading and tables have clearly structured and illustrated clear process, which has made this easy to comprehend and enjoy.</p> <p>The conclusions you have made are unsurprising but your link of utilising these for evidence to ensure better staffing and resources are an interesting consequence.</p>	<p>Thank you for your encouraging feedback and recognition of the clinical value of this paper.</p>
Reviewer two	
<p>Keywords - the purpose of the keywords are to assist others to find the manuscript and should include words which are not in the title. Please remove the words, neonatal setting. In addition, I suggest that you search the MeSH terms which might help others to find your manuscript.</p>	<p>Thank you for this suggestion. I have removed 'neonatal setting' as suggested and utilised 'MeSH on demand' to identify relevant keywords and have included these in the paper.</p>
<p>Introduction - page 2, para 2: The sentence starting.... Each element - review the sentence, I suggest that you remove the words - the infant or remove them. Currently the sentence is clumsy.</p>	<p>The sentence has been revised as per your suggestion (as highlighted in text).</p>
<p>Caregiving by nurses was classified nappy change, infant weighing, bathing or heel pricks. In practice, there is a considerable difference between nappy changes and heel pricks. Despite the manuscripts reporting what appears to be similar measures about neonatal pain. Whereas, all babies and children require frequent nappy changes and only those at risk require heel pricks.</p> <p>I would encourage you to consider the large body of evidence about the pain caused by heel pricks, including methods to reduce the pain and neurodevelopmental outcome. Further, I encourage you to consider within your discussion the difference between hygiene cares and others forms of care and treatment such as heel pricks or suctioning, removing tapes from skin etc. By doing so, your findings will be placed into clinical practice.</p>	<p>Clarification of the focus and scope of this review, including the range of caregiving identified in the literature, have been added to the Introduction (page 3, paragraph 2) and to Table 4. Summary of articles (page 23), where an additional column now reports the caregiving focus for each study.</p> <p>Discussion of painful versus routine components of caregiving (which includes hygiene cares) has been further articulated in the Introduction (page 3, paragraph 2) and Discussion (page 16, paragraph 2). The information added to the manuscript also identifies the studies that used pain tools as part of their methodology and those that included skin breaking procedures. The potential for pain or stress to be experienced or expressed by infants during common NICU caregiving interactions (such as nappy change) is also discussed. The relevance of this to clinical practice is highlighted.</p>
<p>Also, both gestation or birthweight are known to have a considerable impact</p>	<p>Thank you for this suggestion. Content identifying study outcomes relating to gestation</p>

<p>neurodevelopmental outcomes. I appreciate that review is about the outcome of nursing care on hospitalised babies, yet without any discussion about gestation or birthweight there is considerable gap. My suggestion is that you include both in your findings and discussion.</p>	<p>and birth weight has now been added to the Results (page 12 , paragraph 3) and linked to the paragraph on infant stability, vulnerability and immaturity in the Discussion (page 18, paragraph 2).</p>
<p>The manner in which neonatal nurses deliver nursing care, is highlighted in the findings and it is suggested that some nurses are delivering care which is at odds with the newborn. This would also seem to be at odds with the fundamentals of nursing care. This point needs to be developed further in the discussion.</p>	<p>Based on your feedback, a paragraph has been added to the Discussion (page 18 to 19) framed within an ethical standard of care. Thank you for highlighting this important point.</p>
<p>Discussion Page 11 - para 3- Remove the word multiple, as Liaw has only 2 studies (there are three publications from 2 studies).</p>	<p>Thank you, this has been revised.</p>
<p>Discussion Page 15 - para 1 - remove the work overwhelming - the levels of evidence are not strong and therefore the evidence is not at all overwhelming!!!</p>	<p>Thank you, this has been revised.</p>
<p>Discussion Page 15 - para 3 - you have used the word subsequently and I wonder if you meant consequently.</p>	<p>Thank you, this has been revised.</p>
<p>Limitations. I suggest that you include within the limitations along with the lack of available published reports, the quality of evidence is a limitation to being able to determine the the aim of this review. This means that the review itself is at risk of bias.</p>	<p>Content has been added to the Limitations (page 21) highlighting the purpose and nature of the review and acknowledging potential limitations/bias.</p>
<p>Finally, I congratulate you on writing about an important aspect in the care of the newborn.</p>	<p>Thank you for your feedback, which has helped to further develop this submission.</p>

The effects of nurse-delivered caregiving in the neonatal setting: An integrative review

ABSTRACT

Infants hospitalised in neonatal intensive care units require interventions for lifesaving care and to meet basic human needs. Evidence that stress influences neurodevelopment suggests the effects of caregiving in the neonatal intensive care unit (NICU) warrant further investigation to assess links with infant developmental outcomes. This review explores the effects of nurse-delivered caregiving in the NICU on infant physiological and behavioural responses, and longer-term developmental outcomes (behaviour and temperament). CINAHL, MEDLINE and PsychINFO were systematically searched for studies in peer-reviewed journals related to nurse-delivered caregiving and developmental outcomes. Synthesis of the literature identified altered physiological and behavioural responses as immediate effects of caregiving in neonatal settings, and non-optimal developmental outcomes. Results indicate that caregiving is not innocuous. Yet, little is known about nurses' perceptions of the effects of caregiving. Identifying the care components that influence development is essential to minimise the potentially adverse impact of the NICU experience on infants and families.

Key words: nurse-delivered caregiving; neonatal intensive care; physiological responses; behavioural responses; temperament; infant development; behavioural outcomes

The effects of nurse-delivered caregiving in the neonatal setting: An integrative review

Author Details:

Griffiths, Nadine

1. Grace Centre for Newborn Intensive Care, The Children's Hospital at Westmead, Locked Bag 4001, Westmead 2145, NSW Australia
2. University of Technology Sydney, Centre of Midwifery, Child and Family Health, 15 Broadway, Ultimo NSW 2007

Nadine.griffiths@health.nsw.gov.au

Qualifications/postnominals: BN, MClInEd, GradCert Paeds

Laing, Sharon

1. Grace Centre for Newborn Intensive Care, The Children's Hospital at Westmead, Locked Bag 4001, Westmead 2145, NSW Australia

Qualifications/postnominals: Ba (Hons) Psych, PhD (Psych), MAPS

Spence, Kaye

1. Grace Centre for Newborn Intensive Care, The Children's Hospital at Westmead, Locked Bag 4001, Westmead 2145, NSW Australia
3. School of Nursing and Midwifery, Western Sydney University, Parramatta, NSW

Qualifications/postnominals: AM, BEd(N), MN(Research)

Foureur, Maralyn

4. Nursing and Midwifery Research Centre Hunter New England Local Health District, James Fletcher Hospital Campus, 77 Scott Street, Newcastle 2300 NSW, Australia
5. Faculty of Health and Medicine, University of Newcastle, Callaghan Campus, 2308 NSW, Australia
2. University of Technology Sydney, 15 Broadway, Ultimo NSW 2007

Qualifications/postnominals: RM, RN, BA, GradDip ClinEpi, PhD

Sinclair, Lynn

2. University of Technology Sydney, Faculty of Health, Ultimo, NSW 2007

Lynn.Sinclair@uts.edu.au

Quals: RN, RM, BSc (Hons) with Specialist Practitioner Qualification in Neonatal Nursing, PhD

Mailing address of Corresponding author:

Grace Centre for Newborn Intensive Care

Locked Bag 4001

Westmead 2145

New South Wales Australia

Nadine.griffiths@health.nsw.gov.au

Financial disclosure:

No funding was received by individual authors or the unit for the provision of this project.

Competing interests:

No competing interests are identified by the authors.

CRedit statement:

Nadine Griffiths: Conceptualization, Investigation, Methodology, Resources, Writing - Original Draft and revisions. **Kaye Spence:** Methodology, Formal analysis, Resources, Writing - Review & Editing, Supervision. **Sharon Laing:** Writing - Review & Editing, Supervision, Final draft review. **Maralyn Foureur:** Writing - Review & Editing, Supervision. **Lynn Sinclair:** Writing - Review & Editing, Supervision.

The effects of nurse-delivered caregiving in the neonatal setting: An integrative review

ABSTRACT

Infants hospitalised in neonatal intensive care units require interventions for lifesaving care and to meet basic human needs. Evidence that stress influences neurodevelopment suggests the effects of caregiving in the neonatal intensive care unit (NICU) warrant further investigation to assess links with infant developmental outcomes. This review explores the effects of nurse-delivered caregiving in the NICU on infant physiological and behavioural responses, and longer-term developmental outcomes (behaviour and temperament). CINAHL, MEDLINE and PsychINFO were systematically searched for studies in peer-reviewed journals related to nurse-delivered caregiving and developmental outcomes. Synthesis of the literature identified altered physiological and behavioural responses as immediate effects of caregiving in neonatal settings, and non-optimal developmental outcomes. Results indicate that caregiving is not innocuous. Yet, little is known about nurses' perceptions of the effects of caregiving. Identifying the care components that influence development is essential to minimise the potentially adverse impact of the NICU experience on infants and families.

Key words: nurse-delivered caregiving; neonatal intensive care; physiological responses; behavioural responses; temperament; infant development; behavioural outcomes

INTRODUCTION

It has been well-established that stress and trauma in the first 1000 days of post-conceptual life can have adverse lifelong effects (D'Agata et al., 2017; Linnér and Almgren, 2020). Lifesaving and routine caregiving in the neonatal intensive care unit (NICU) occur during a period of sensitive, rapid and critical brain development. Despite the best intentions, the NICU environment cannot replicate the intrauterine experience, instead offering a 'sub-optimal' environment with infants subsequently vulnerable to brain injury and maldevelopment (Cheong et al., 2020). Increasingly, the influences of the early environment and biological and social factors are being explored as potential mediators for preterm infants' developmental outcomes (Burnett et al., 2018; Cheong et al., 2020). Exposure to the hospital environment, noise, pain, and disrupted parenting are suggested as affecting long-term neurodevelopment and areas that require a stronger research focus (Cheong et al., 2020). Because developmentally-supportive caregiving in the NICU addresses these factors, it may positively influence long-term health and developmental outcomes (Lean et al., 2018; McAnulty et al., 2010; O'Reilly et al., 2020; Robinson et al., 2020; Wolke et al., 2019) and therefore, warrants further investigation.

The concept of 'developmentally-supportive care', also referred to as 'developmental care', focuses on the infant and family; providing care aimed at optimising their developmental progression. Underpinned by Als' (1982) Synactive Theory of Development, developmental care operates within a developmental-maturation paradigm where infants' neurobehavioural organization skills develop over time. The development of these skills is influenced by prematurity, illness and congenital anomalies (Torowicz et al., 2012). In addition, developmental care-practices are informed by the Newborn Individualised Developmental Care Assessment Program (NIDCAP)(Als, 1982). This is a relationship-based model of care designed to modify the caregiving culture, interactions and the NICU environment (Lawhon and Hedlund, 2008). NIDCAP involves rigorous training with specialist education in infant-developmental observation, with application and assessment of caregiving and the NICU environment. Each element focuses on facilitating relationships between infants, parents and staff members and the interplay of these relationships in the broader NICU (Als, 1982). Based on infant cues, caregiving is modified to reduce the noxious effect of stressors on the developing brain (Als and McAnulty, 2011). Studies to date have mostly evaluated the impact of developmental care on short-term medical outcomes (e.g., days of mechanical ventilation/supplemental oxygen, weight gain, length of stay), with limited data about longer-term neurodevelopment (Byers, 2003; Rick,

2006; Soleimani et al., 2020; Symington and Pinelli, 2009). A lack of consensus regarding the evidence may not be surprising given that developmental care is a philosophy of care encompassing a broad category of interventions, with sporadic implementation (Carrier, 2002; Lubbe et al., 2012).

Caregiving can be provided by multiple individuals, most importantly the parents. Within a developmentally-supportive and family-centred framework, families are recognised as the primary caregivers (Als, 1982; De Bernardo et al., 2017; Lee and O'Brien, 2014). Models of care with parents as primary caregivers are being increasingly implemented in hospital settings (Lean et al., 2018; Lee and O'Brien, 2014), with research showing decreased parental stress and anxiety, and increased exclusive breastmilk feeding at discharge (O'Brien et al., 2018). Caregiving by nurses, however, continues to be one of the most frequent events experienced by an infant during their NICU admission (Godarzi et al., 2018; Murdoch and Darlow, 1984; Pereira et al., 2013). As the focus of this review was nurse-delivered caregiving of the infant, literature about parents as primary caregivers and the nurses' role in supporting parents in the hospital setting was not included. In this paper, the term 'caregiving' refers to 'nurse-delivered caregiving'.

Caregiving has been defined as a necessary single or clustered intervention ranging from vital sign monitoring, repositioning, feeding or nappy change through to suctioning and other invasive procedures (Peters, 1999). Caregiving can act as stimuli that elicits infant pain responses. There are numerous validated tools for assessing infant pain behaviours (Relland et al., 2019), yet differentiating between infant pain behaviours and stress responses remains difficult. Like other NICU interventions, caregiving is an event with the potential to alter physiological stability and behavioural state, and increase infant stress. The immediate effects of caregiving can be assessed by measuring an infant's physiological or behavioural stress responses. While pain per se was not the focus of this literature review, some studies included a broad classification of caregiving interventions ranging from vital sign assessment to painful interventions (e.g. heel stick).

In humans, stress responses occur via a complex system designed to counter internal and external stimulation, with an initial focus on achieving overall physiological stability (Zeiner et al., 2016). The autonomic nervous system (ANS), comprising the sympathetic and parasympathetic arms, plays a significant role in the overall regulation of physiological functions in response to stressful stimuli. Fluctuations in heart rate (HR), respiratory rate (RR), oxygen saturation (SaO₂), blood pressure (BP),

skin colour changes, the startle reflex, and tremors (Als, 1986), are recognised as physiological manifestations of stress in infants (DiPietro and Porges, 1991; Peters, 1999; Zahr and Balian, 1995). Repeated stressor exposure affects adaptive capability and self-regulation, with the occurrence and severity of stressors influencing cortical connectivity and potentially long-term development (McAnulty et al., 2009; McAnulty et al., 2010; Zeiner et al., 2016).

The ANS also regulates the complex interplay of physiological, biochemical and neurobehavioral systems that underlie behavioural state regulation (Als, 1986; Foreman et al., 2008; Prechtl, 1974). Infant behavioural states (e.g., deep sleep, quiet alertness, fussing, crying) are observable during interactions with caregivers and the environment. In stressful situations, infants change state as a self-regulation strategy (Foreman et al., 2008). In the NICU, behavioural responses to interventions vary across infants, based on gestational age, chronological age and level of illness (Als, 1982; Als, 1986; Prechtl, 1974). Infant behavioural responses can positively or negatively impact on a caregiver's perceptions of an infant and their subsequent interactions (Als et al., 2005). Within a developmentally-supportive framework, caregivers implement strategies to support an infant's self-regulation (Als and McAnulty, 2011; Lawhon and Hedlund, 2008).

Dysfunction of the ANS is identified as the mechanism by which exposure to early adversity affects emotional and behavioural outcomes, including temperament (McLaughlin et al., 2015).

Temperament has been defined as a moderately stable set of infant behavioural traits that affect both personality and behaviour (Gunnar et al., 1995). Infant measurements of temperament identify early regulatory problems predictive of subsequent behavioural difficulties (Abulizi et al., 2017; Gunnar et al., 1995; Sidor et al., 2017). Prematurity and hospitalisation in the neonatal period can adversely affect behavioural outcomes including temperament (Abulizi et al., 2017; Cassiano et al., 2020; Cassiano et al., 2019; Feldman, 2009).

Research exploring the effect of physiological and behavioural responses during caregiving has been published since the 1980's. Nurse-delivered caregiving is frequently categorised in studies by type, duration, patterns, nurse education, and infant responses to handling (Peters, 1999). Researchers have demonstrated that caregiving duration impacts adversely on sleep cycles in preterm infants (Godarzi et al., 2018; Maki et al., 2017; Murdoch and Darlow, 1984; Pereira et al., 2013). All aspects of the caregiving experience impose sensory input on the infant's nervous system. The use of developmentally-supportive interventions is considered a proactive approach with the potential to

mitigate infant stress in the NICU (Weber and Harrison, 2019). Given that recurrent stressful interventions may contribute to adverse developmental outcomes, it is imperative to assess the impact of developmental care as a buffering factor within the NICU and beyond hospital discharge.

AIM

The aim of this literature review was to explore what is known about the physiological and behavioural effects of nurse-delivered caregiving in the neonatal setting and potential links to infant developmental outcomes (behaviour and temperament) in the first 12 months of life. Synthesis of the literature provides insight into the cumulative effects of caregiving in the neonatal unit and potential associations with longer-term behavioural outcomes.

METHODS

A systematic electronic literature search was completed using CINHAL (EBSCO), MEDLINE (OVID) and PsychINFO (1 January 1982 to 1 May 2020). Search limitations were English-language, full-text, and peer-reviewed articles. Final screening of articles was undertaken by two of the authors. The literature screen focused on nurse-delivered caregiving and its effects on behavioural and physiological responses in the NICU and outcomes in the first 12 months following birth. Research after 1982 was included following the publication of seminal works by Dr Heidelise Als on the Synactive Theory of Development and the inception of developmentally-supportive care (Als, 1982).

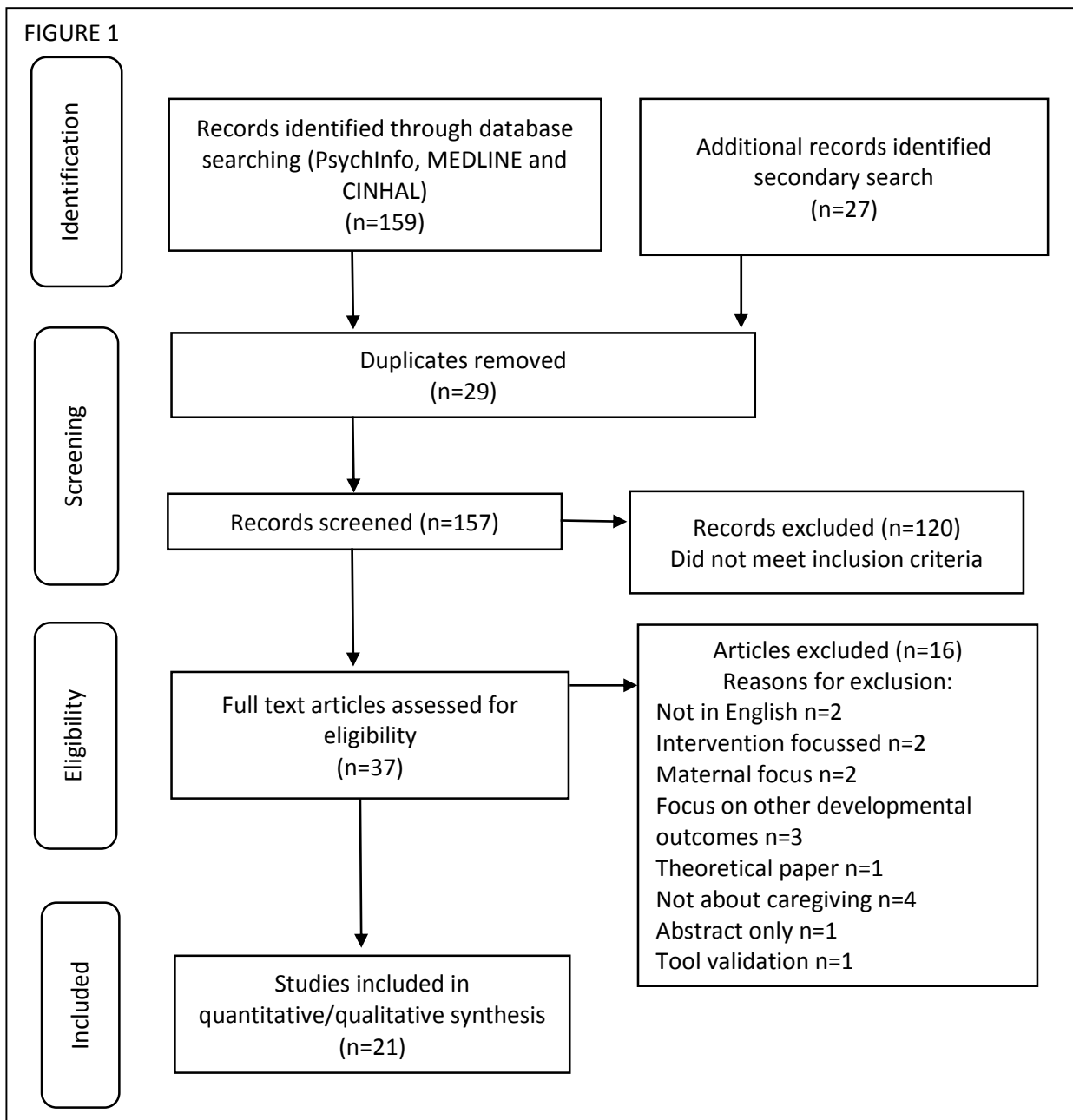
A combination of MeSH terms and subject terms were used in PsychINFO, CINHAL (EBSCO) and MEDLINE (OVID) to retrieve relevant citations. The MeSH search terms included 'intensive care unit, neonatal,' 'neonatal intensive care,' 'temperament,' 'NICU,' and 'nurse'. Subject terms used were 'neonatal unit,' 'NICU,' 'caregiving,' 'care,' 'behavioural response', 'physiological response', and 'behavioural outcome,' and 'outcome'. Truncation (*) to find any extension of the search term was used across all databases, proximity searching was used (Nx) for PsychINFO and CINHAL and (Adjx) for MEDLINE (Table 1).

The search engines identified 159 citations, 29 duplicates were found and removed, with an additional 27 articles sourced through a secondary citation search. After title and abstract review, 120 articles were discarded as they were not associated with caregiving in the NICU or subsequent outcomes. Of the 37 articles assessed as eligible for full-text review, 21 were included for analysis. The PRISMA flow diagram (Figure 1) presents the literature screening process.

Table 1. Summary of Database Search

Database	Filters	Search terms	Citations returned
CINHAL	1982-2020, English, Peer reviewed, full text	<p>Concept 1: 'Intensive care units, neonatal' [MeSH], OR 'neonatal unit*' OR 'NICU' [MeSH]</p> <p>Concept 2: 'Neonatal Intensive Care Nursing' OR 'caregiving' OR 'Nurse*' [MeSH] N3 'care*'</p> <p>Concept 3: '(behavi* OR physiolog*)' N3 '(response* OR outcome*)' OR 'temperament' [MeSH]</p> <p>Combined key concept search: 1 AND 2 AND 3</p>	47
PsychINFO		<p>Concept 1: 'Neonatal intensive care' [MeSH] OR 'neonatal unit*' OR 'NICU' [MeSH]</p> <p>Concept 2: 'Neonatal Intensive Care Nursing' OR 'caregiving' OR 'Nurse*' [MeSH] N3 'care*'</p> <p>Concept 3: '(behavi* OR physiolog*)' N3 '(response* OR outcome*)' OR 'temperament' [MeSH]</p> <p>Combined key concept search: 1 AND 2 AND 3</p>	71
MEDLINE		<p>Concept 1: 'Intensive care units, neonatal' [MeSH], OR 'neonatal unit*.mp' OR 'NICU.mp' [MeSH]</p> <p>Concept 2: 'Neonatal Intensive Care Nursing' OR 'caregiving.mp' OR 'Nurse*' [MeSH] adj3 'care*.mp'</p> <p>Concept 3: '(behavi* OR physiolog*)' adj3 '(response* OR outcome*).mp' OR 'temperament' [MeSH]</p> <p>Combined key concept search: 1 AND 2 AND 3</p>	41

Figure 1. PRISMA flow diagram screening of articles for review



RESULTS

Data from the 21 studies are organised under Matrix headings, including year/author/date, setting, sample/gestational age, research design, measures and main findings (Garrard, 2017) (see Table 4). Nineteen of the studies collected data in the NICU, one study collected data from both the NICU and postnatal unit in the maternity ward (Mörelus et al., 2006) and another from the postnatal unit only (Gunnar et al., 1995). Infant sample sizes ranged from 10 to 139 infants. The combined data explored the caregiving experience of 969 infants and 20 neonatal nurses. Research designs were mostly descriptive cross-sectional, but also included four randomised cross-over trials, three quasi-experimental cross-over studies, two longitudinal randomised controlled trials, two longitudinal cohort studies, three observational studies and one qualitative study. The studies predominately used quantitative methods, focusing on collection and analysis of physiological data (heart rate, respiratory rate, oxygenation, salivary cortisol, vagal tone, pain score, and blood pressure) and behavioural responses (pain score, stress, infant state, temperament, social and emotional assessments) in relation to caregiving. Three major themes were identified in the synthesis of the data associated with caregiving in the neonatal setting: the burden of caregiving on infants' physiological and behavioural responses; the effect of caregiving on longer-term outcomes; and factors contributing to the effects of caregiving, which comprised three categories – infant characteristics, nurse approaches to caregiving, and the effects of caregiving within a developmentally-supportive framework.

The burden of caregiving on infants' physiological and behavioural responses

Seventeen of the studies explored infants' physiological and behavioural responses to caregiving. Eleven studies reported both physiological and behavioural responses (Catelin et al., 2005; Comaru and Miura, 2009; de Freitas et al., 2018; Gunnar et al., 1995; Lee, 2002; Liaw et al., 2010; Liaw et al., 2012a; Mörelus et al., 2006; Peters, 1998; Sizun et al., 2002; Zeiner et al., 2016), four studies reported physiological responses (Danford et al., 1983; Evans, 1991; Peters, 1992; Yung-Weng and Ying-Ju, 2004), and two studies reported behavioural responses only (Becker et al., 1993; Liaw et al., 2012b).

Caregiving was classified as either an individual procedure; nappy change (Comaru and Miura, 2009; Mörelus et al., 2006; Sizun et al., 2002; Yung-Weng and Ying-Ju, 2004), infant weighing (Catelin et al., 2005), bathing (de Freitas et al., 2018; Lee, 2002; Liaw et al., 2010; Peters, 1998), performing a

heel stick (Gunnar et al., 1995), unit-based standard care (Zeiner et al., 2016), or listed as interventions defined by the study (Becker et al., 1993; Danford et al., 1983; Peters, 1992), and in two studies classified as social, routine or intrusive (Liaw et al., 2012a; Liaw et al., 2012b). One study did not articulate caregiving type beyond 'any nursing intervention that required tactile contact' (Evans, 1991).

Sixteen of the 17 studies found routine caregiving interventions were stressful for infants, showing adverse physiological or behavioural responses. The one study that found no significant changes in behavioural or physiological responses from baseline, reported a statistically non-significant increase in salivary cortisol related to caregiving (de Freitas et al., 2018).

Four studies hypothesised that routine caregiving was painful and included pain assessments in their data. All four studies found an increase in infant pain scores during routine caregiving involving nappy changing (Comaru and Miura, 2009; Mörelius et al., 2006; Sizun et al., 2002) or weighing (Catelin et al., 2005).

The effect of caregiving on longer-term outcomes

Four of the studies explored the effect of the NICU on outcomes beyond discharge, two within a developmentally-supportive framework. McNulty et al (2009) reported improved self-regulation and autonomic, motor and state system organisation at two weeks of age and significantly higher Bayley score at 9 months of age related to goal directedness, attention span and motor muscle coordination in the developmental care intervention group. Similarly, van der Paul et al (2008) reported that infants in the developmental care intervention group demonstrated better motivation and behavioural competence at 12 months.

Two studies compared infant distress responses in the neonatal setting to later behavioural and emotional outcomes. Greater heart rate variability was linked to non-optimal temperament outcomes at 6 months (Gunnar et al, 1995) and 9 months (Poehlmann et al,2012). In addition, Gunnar et al. (1995) linked behavioural responses to heel stick in full-term, healthy neonates to later maternal reports of temperament.

Factors contributing to the effects of caregiving

Factors contributing to the effects of caregiving were identified in study findings or noted by study authors (see Table 3). This theme comprised three components that at times over-lapped or were inter-related.

Infant stability, vulnerability, and immaturity

Several studies noted that infant stability, vulnerability and immaturity played a role in infant responses to caregiving, with some studies identifying severity of illness (Evans, 1991; Horns, 1998; Liaw et al., 2012a; Liaw et al., 2012b; Mörelius et al., 2006; Peters, 1998; Zeiner et al., 2016) and gestational age (Becker et al., 1993; Danford et al., 1983; Evans, 1991; Lee, 2002; Liaw et al., 2010; Liaw et al., 2012a; Liaw et al., 2012b; Mörelius et al., 2006; Peters, 1998; Yung-Weng and Ying-Ju, 2004; Zeiner et al., 2016) as variables that influenced caregiving effects. However, full-term healthy infants were also found to demonstrate pain responses during routine caregiving (Mörelius et al., 2006) and a heel stick (Gunnar et al., 1995).

Some studies found that gestational age and birth weight affected infant responses to caregiving. Gestational age effects to caregiving were identified in six studies (Becker et al., 1993; Catelin et al., 2005; Liaw et al., 2010; Liaw et al., 2012a; Liaw et al., 2012b; Mörelius et al., 2006). Lower gestational age negatively influenced behavioural state transition (Becker et al., 1993; Liaw et al., 2012b), the expression of grimace, fussing and crying responses (Liaw et al., 2010) and salivary cortisol responses (Mörelius et al., 2006). Increasing gestational age and post-menstrual age resulted in decreased startles, squirming and disorganised behaviour (Liaw et al., 2012a) and increased wake states (Liaw et al., 2012b). However, some studies found no similar infant pain and stress responses unrelated to gestational age (Catelin et al., 2005, Mörelius et al., 2006). Only a single study reported on the effect of birth weight, finding increased motor cues and attentional cues during stressful interventions in low-birth-weight infants (Zeiner et al., 2016).

Nurse perceptions of caregiving effects

Nurses' understanding of infant physiological and behavioural states was noted to inform their individual approach to caregiving. Studies by Liaw and colleagues (2010, 2012a) identified a link between nurse caregiver behaviours that included rough handling and intrusive caregiving and the effects on preterm infants. Only two studies evaluated nurses' perceptions of caregiving as a study measure. Catelin et al. (2005) found no significant correlation between occurrence of the intervention (weighing), the infant's pain score and nurses' level of satisfaction with caregiving

within a developmentally-supportive framework. In a qualitative analysis of 20 experienced neonatal nurses' perceptions of developmentally-supportive caregiving, Horns (1998) found infant physiological signs, perceived resilience during handling, infant behaviours, and complexity of the intervention, all contributed to nurses' perception of infant stability. 'Being-in-tune' with the infant, delivering care that was contingent, protective and individualised, was dependent on both the infant's stability and the nurse's approach to caregiving. The author postulated the approach taken was likely influenced by the availability of other nurses to assist with caregiving tasks, past experiences, infant handling practices and the nurses' understanding of infant behaviour.

Effect of caregiving in a developmentally-supportive framework

The effect of caregiving in a developmentally-supportive framework was explored in eight studies that compared routine caregiving to a developmentally-supportive caregiving model; three using NIDCAP (Catelin et al., 2005; McNulty et al., 2009; Sizun et al., 2002), and five using study-specific models or comparison of developmentally-supportive interventions (Becker et al., 1993; Comaru and Miura, 2009; de Freitas et al., 2018; Liaw et al., 2010; Liaw et al., 2012b; van der Pal et al., 2008). Seven of these studies found that supportive caregiving positively influenced infant physiological or behavioural responses. One study (de Freitas et al., 2018) compared supportive bathing (swaddled) and traditional tub-bathing, and found no difference between groups in infant physiological or behavioural responses pre- or post-intervention. However, the authors reported that both groups showed an increase in salivary cortisol compared to baseline physiological functioning.

Table 3. Factors identified as contributing to infant caregiving effects

Component	Identified in study findings	Suggested as a contributing factor by study authors
Infant stability, vulnerability, and immaturity (including illness severity)	Becker et al 1993 Danford et al 1983 Evans 1991 Horns 1998 Lee 2002 Liaw et al 2010 Liaw et al 2012a Liaw et al 2012b Morelius et al 2006 Peters 1992 Peters 1998 Zeiner et al 2016 Weng and Chang 2004	
Individual nurse approach to caregiving based on infant physiological and/or behavioural responses	Becker et al 1993 Horns 1998 Liaw et al 2010 Liaw et al 2012a Liaw et al 2012b Peters 1998 Weng and Chang 2004	Danford et al 1983 Peters 1992 Lee 2002 Evans 1991
Caregiving in a developmentally-supportive framework	Becker et al 1993 Catelin et al 2005 Comaru and Miura 2009 McAnulty et al 2009 Sizun et al 2002 van der Paul et al 2008 Liaw et al 2010 Liaw et al 2012b	Evans 1991 Lee 2002 Liaw et al 2012b Morelius et al 2006 Peters 1992 Peters 1998 Weng and Chang 2004

LIMITATIONS OF STUDIES

The studies included in this literature review have several limitations which potentially threaten the internal and external validity of the findings. There was a lack of consistency of measures used across studies to assess caregiving effects. The definition of developmental care and its components also varied, making comparisons difficult. Several studies did not assess the effect of caregiving during the intervention, only recording data pre- and post-event, limiting the conclusions that can be drawn from their findings (Comaru and Miura, 2009; de Freitas et al., 2018). Most studies consisted of small sample sizes (10- 50 infants).

The interpretation of stress associated with caregiving varied depending on the study focus and year of publication. For example, some researchers reported a nappy change as tolerable (Peters, 1992) compared with other routine caregiving, while others who examined nappy change in isolation described it as stressful and painful (Catelin et al., 2005; Mörelius et al., 2006). One of the studies had a recruitment period spanning 8 years which likely influenced the results as it may be assumed that caregiving practices changed during this period (McAnulty et al., 2009). Nineteen of the 22 studies were published more than 5 years ago (ranging between 8 to 37 years), suggesting there is a lack of current research exploring the issue. Given that approaches to caregiving and staff knowledge of developmental care have changed since these studies were conducted translation of their findings in the current clinical context is limited. The mediating effect of parent engagement and infant-support during nurse-delivered caregiving was not explored in the studies reviewed. This is an under-researched aspect of developmentally-supportive care.

DISCUSSION

The purpose of this integrative review was to explore what is known about nurse-delivered caregiving in the NICU with a focus on the physiological and behavioural effects and potential links to developmental outcomes. The evidence suggests that routine caregiving is not innocuous. Synthesis of the literature spanning 37 years shows there are immediate effects of caregiving, with research demonstrating altered physiological and behavioural responses, and links to longer-term outcomes.

Nineteen studies reported immediate effects of caregiving in the neonatal setting, with responses indicative of stress. Four studies utilised pain assessment tools when evaluating responses to caregiving. Interestingly, these studies focused on common caregiving interventions that are generally considered innocuous; weighing or nappy change. Catelin et al (2005) found significantly lower pain scores in preterm infants who received environmental and behavioural support during weighing. Changing an infant's nappy was among the caregiving interventions found to be both painful and stressful for preterm and term infants (Comaru and Miura, 2009; Mörelius et al., 2006; Sizun et al., 2002). This is a frequently experienced event for infants, particularly for infants with a prolonged NICU stay. It is well-documented that painful stimuli, such as heel stick and other similarly invasive interventions, precipitate stress responses (Relland et al., 2019) and strategies for minimising the effects of pain on neurodevelopmental outcomes have been widely-reported (American Academy of Pediatrics., 2016; McPherson et al., 2020). As the literature review here indicates stress responses can also be linked to caregiving activities not generally recognised as painful for sick and preterm infants as well as full term infants in the NICU. Consequently, measures are often not implemented to minimise this impact. Importantly, rather than the type of intervention, it appears that it is the manner in which the nurse delivers care that significantly affects the infant (Becker et al., 1993). Developmentally-supportive caregiving can result in immediate improvements in parasympathetic activity and self-regulation (De Rogalski Landrot et al., 2007; Pressler et al., 2001). Exploring the way in which caregiving is delivered and the factors influencing its application is warranted.

Initial research exploring the effects of caregiving likely coincided with the introduction of developmentally-supportive care. Yet only two studies conducted in the past five years examined the physiological and behavioural effects of this type of caregiving (de Freitas et al., 2018; Zeiner et al., 2016). The lack of recent studies in this area suggests the effects of caregiving may not be a

current research priority. Perhaps this also reflects the challenges associated with this type of research, including access to resources and funding. Consequently, the link to developmental outcomes is not yet fully explored. Of the twenty studies involving infants, only two looked at the longer-term effects of developmentally-supportive care beyond the NICU admission (McAnulty et al., 2009; van der Pal et al., 2008). The findings of this review suggest it is important that future research explores both the immediate and longer-term effects of nurse-delivered caregiving, including the mediating influence of parents.

The nature of the data used to evaluate the effects of caregiving is important, as infant's stress responses in the NICU manifest across multiple systems (Gunnar et al., 1995). The inclusion of physiological data (heart rate, respiratory rate, oxygen saturation) allows the identification of stress responses in vulnerable infants who may not be capable of outwardly displaying behavioural state changes in response to stress (Zeiner et al., 2016). Combining both physiological and behavioural observations is recommended to evaluate the complexity of an infant's stress response to a caregiving intervention (Zeiner et al., 2016). Yet, only half of the studies reported the combined physiological and behavioural effects of caregiving (Catelin et al., 2005; Comaru and Miura, 2009; de Freitas et al., 2018; Gunnar et al., 1995; Lee, 2002; Liaw et al., 2010; Liaw et al., 2012a; Mörelus et al., 2006; Peters, 1998; Sizun et al., 2002; Zeiner et al., 2016). Prematurity and prolonged exposure to stress in the NICU is thought to inhibit the parasympathetic arm of the ANS, accounting for greater variability in physiological responses to stimuli (De Rogalski Landrot et al., 2007). Promoting a set of standard behavioural and physiological variables to measure infant stress enables comparison of findings across studies. As physiological data is readily available at the bedside via continuous monitoring, nurse's responsiveness to monitoring alerts as indicators of infant stress during caregiving could be incorporated in future research.

This review incorporated literature exploring links between caregiving in the NICU and infant temperament and behavioural outcomes up to 12 months of age. Of the two studies that measured these parameters, both found a link between neonatal stress reactivity in the NICU and non-optimal outcomes for temperament and behaviour (Gunnar et al., 1995; Poehlmann et al., 2012). Despite the paucity of data, findings to-date suggest that temperament may be a useful measure for exploring relationships between infant responses during caregiving and longer-term developmental outcomes. An important component of infant behavioural state is self-regulation. An infant's self-regulatory abilities develop over time and in response to the environment, consisting of active efforts on the part of the infant to regulate their autonomic functions, motor control, level of arousal and

availability for socialisation (Als, 1982; Als, 1989); with caregiver support promoting these self-regulatory capacities (Feldman, 2009). The longer-term effects of poor self-regulation include sub-optimal social and cognitive development ranging from difficult temperament to regulatory disorders (Feldman, 2009; Sidor et al., 2017), predictive of subsequent behavioural difficulties. Further research investigating links between stress responses in the NICU and infant temperament is warranted.

Recommendations to modify caregiving based on study findings was highlighted in 18 of the studies (Becker et al., 1993; Catelin et al., 2005; Comaru and Miura, 2009; Danford et al., 1983; Evans, 1991; Horns, 1998; Lee, 2002; Liaw et al., 2010; Liaw et al., 2012a; Liaw et al., 2012b; McAnulty et al., 2009; Mörelius et al., 2006; Peters, 1992; Peters, 1998; Sizun et al., 2002; van der Pal et al., 2008; Yung-Weng and Ying-Ju, 2004; Zeiner et al., 2016). Suggestions to adapt caregiving could be broadly categorised into three taxonomies; the sensitive application of caregiving (Peters, 1998), identification of the infant's individualised needs (Mörelius et al., 2006), and an understanding of the relationship between caregiver and infant (Liaw et al., 2010). It is difficult to modify nurse-delivered caregiving practices if little is known of what motivates the caregiver and influences the application of caregiving.

While infant stability, vulnerability and immaturity, all of which can be related to gestational age, birth weight and severity of illness, were identified as factors contributing to caregiving effects, it appears that it is the nurses' perceptions and responsivity to infant physiological and behavioural responses that play the greater role (Liaw et al., 2010; Liaw et al., 2012a). Yet, only one study investigated nurses' perceptions of infant responses to caregiving (Horns, 1998). Individual nurse approaches to caregiving and valuing of developmentally-supportive care are influenced by access to education, personal experience, and management or organisational support for care practices (Austin et al., 2019; Park and Kim, 2019). NICU nurses appear interested in implementing developmentally-supportive care, yet there is possibly a difference between declared and actual nurse behaviour, with this difference not well explained in the literature. Research has found that despite developmental care education and nurses acknowledgment of the need to implement practice components, change was often sporadic with a focus on environmental rather than behavioural modifications (Milette et al., 2005). The translation of best available evidence into improved health outcomes is a complex and iterative process that requires cultural, behavioural and practice change (Curtis et al., 2017).

Consistency in the application of nurse-delivered caregiving in the NICU remains a challenge (Gonya et al., 2019) and, as highlighted in this literature review, practices may not align with best practice principles. Whilst neonatal nurses, like all nurses, have a moral-ethical-professional obligation to provide compassionate, quality patient care (Faber, 2013), there are several factors that may influence the interface between the caregiver and the caregiving. The ethical 'best interest principle', is a surrogate decision-making model, unique to infants as they are reliant on others to make decisions in their interests (Spence, 2000). Nurse-delivered caregiving where it is necessary to undertake certain tasks and interventions to achieve the best outcome for the infant can be placed within this model (Spence, 2000). Nurses initiate and undertake activities to meet basic human needs and the more complex medical needs of infants in the NICU. Nurses' personal and professional experience, how they view the infant and their perception of the infant's clinical condition and potential long-term outcomes may all influence their caregiving interactions (Spence, 2000).

Research is needed to ascertain whether there is a gap between nurses' perceptions of caregiving and the actual effects on the infant, and how this differentiates between caregiving performed *to* the infant and caregiving that is sensitively responsive to infant cues. Caregiving has been described as a dance; partners (nurse-baby, baby-nurse) who are 'in-tune' adjust to each other to move in synchrony (Liaw et al., 2010). Evaluating how often caregivers are dancing the same dance to the same rhythm as the infant may help to explain immediate effects of caregiving and consequent longer-term developmental outcomes.

RELEVANCE TO CLINICAL PRACTICE

Based on findings from this literature review caregiving interventions in the neonatal setting appear to have potentially adverse effects for infants, both immediate and long-term. It is essential that neonatal nurses understand the effects of caregiving, modify practices and are responsive to infants' needs. Modification of caregiving practices to benefit the infant will require the commitment of individual nurses, managers, and education providers. Identifying the components of care in the neonatal setting that are linked to developmental outcomes is essential to minimise the potential lifelong impact of the NICU environment on infants and their families.

LIMITATIONS OF THIS REVIEW

The main limitations of this review are that the search was limited to the English language and excluded publications before 1982. This has the potential to exclude relevant untranslated and older studies. However, given the changes in caregiving practices in neonatal settings since 1982 findings from studies prior to that date may no longer be relevant. The conceptualisation of this integrative review involving the linking of three concepts; nurse-delivered caregiving, the neonatal setting, and outcomes within the first 12 months of life, may also have excluded research. Some studies removed through early screening were relevant to the broader body of knowledge in this area, but were not specific to the purpose of this review. The findings of this review were intended to identify the current state of knowledge and potential gaps in the literature, not to inform best practice guidelines. As such, the review does not include an assessment of the quality of the evidence. While this may be a limitation of the review and a source of potential bias, the review does highlight the need for further research on nurse-delivered caregiving in the NICU and its effects on infants.

CONCLUSION

This literature review highlights the need for further research examining the physiological and behavioural effects of caregiving on infants in the NICU and the potential links to developmental outcomes. It is important to conduct research that looks beyond the immediate responses to caregiving. Capturing the cumulative effect within and beyond the NICU will ensure the overall impact of nurse-delivered caregiving is thoroughly evaluated. With this data, an individualised caregiving approach can be clearly articulated and the need for resources to buffer the effect of caregiving be effectively communicated to clinicians, families, administrators, and policymakers. Understanding the link between caregiving and developmental outcomes may strengthen the call for adequate staffing and education resources in the neonatal setting. To better understand neonatal nurse practices, future research must include nurses' perceptions of the effects of caregiving when exploring the relationship between cause (caregiving approach) and effect (infant behaviours and physiology). This information will be used to modify practices that may be linked to longer-term morbidity of infants following an NICU admission.

Authors Publication date (Country)	Setting	Sample Gestational age (range in weeks) *	Research design	Type of caregiving intervention	Measures	Main Findings
Becker et al 1997 (USA)	NICU	38 preterm infants; 25-32 (mean 28.3)	Quasi-experimental cross-over design; each infant served as its own control during four caregiving sessions	'Caregiving tasks' (not further detailed)	Behavioural state, caregiver intervention, video	Developmental caregiving supported behavioural state organisation by increasing sleep and drowsy periods with decreased fuss/cry time
Catelin et al 2005 (France)	NICU	45 infants; 15, <32 (mean 30.1) 15, >32 -36 (mean 34.2) 15, >37 (mean 39.1)	Randomised cross-over comparison of three groups of infants across different gestational ages (very preterm, late preterm, term) during a developmentally- supportive and not-supportive weight measurement. Infants were weighed twice in 24 hours and served as their own control	Weighing	HR, TCO ₂ , NIPS, EDIN, NIRS, salivary cortisol, number of procedures, nurse's satisfaction index, video	Developmentally-supportive environmental and behavioural interventions decreased heart rate, pain and discomfort scores in preterm and term infants during weighing
Comaru and Miura 2009 (Brazil)	NICU	47 preterm infants; <35	Randomised cross-over design, comparison of nest use during nappy change versus no nest, infants served as their own control	Nappy change	HR, SaO ₂ , NIDCAP stress behaviours, distress score, pain score	All infants displayed increased distress and pain scores during nappy changes despite postural support from a nest

Authors Publication date (Country)	Setting	Sample Gestational age (range in weeks) *	Research design	Type of caregiving intervention	Measures	Main Findings
Danford et al 1983 (USA)	NICU	36 infants; 24-38	Prospective observational design comparing term and preterm infants observed during invasive interventions or routine caregiving	11 different types ranging from vital sign measurements, nappy change to heel stick	TcPO ₂	Nearly all care-orientated stimuli resulted in a fall in oxygenation in 50-100% of preterm infants
de Freitas et al 2018 (Brazil)	NICU	43 preterm infants; 32-36 22, (mean 33) 21, (mean 34)	Randomised cross-over design comparing two groups allocated to either swaddled or non-swaddled bathing technique, measures taken pre- and post-intervention	Bathing	HR, SaO ₂ , axillary temperature, salivary cortisol, infant sleep wake state, video	No significant differences in vital signs, salivary cortisol, or sleep wake state between the two groups. Salivary cortisol increased from baseline in both groups during the interventions
Evans 1991 (USA)	NICU	13 preterm infants; 6, <30 7, 30-33	Prospective observational design, caregiving observed for one hour	6 different types from vital signs, nappy change to suctioning	TcPO ₂	Invasive and routine caregiving was associated with hypoxemia in the first 72 hours of life
Gunnar et al 1995 (USA)	Post-natal unit	50 full-term healthy infants; 37-41	Prospective longitudinal cohort, measures collected at mean 48 hours of age and temperament at 6 months	Heel stick	HR, vagal tone, behavioural state (Brazelton NBAS), salivary cortisol, IBQ	Greater physiological and behavioural activity responses to a heel stick were related to maternal report of subdued temperament at 6 months of age

Authors Publication date (Country)	Setting	Sample Gestational age (range in weeks) *	Research design	Type of caregiving intervention	Measures	Main Findings
Horns 1998 (USA)	NICU	20 NICU experienced nurses	Observational and focus group approach, observational technique used to develop questions for the focus group interviews	Not applicable	Focus group interviews	Infant physiological stability and the nurse's approach to caregiving impacted their perception of the infant's responses
Lee 2002 (South Korea)	NICU	40 preterm infants; 27-36 (mean 33.1)	Descriptive exploratory design examining the effects of sponge bathing (before, during and after)	Sponge bathing	HR, vagal tone, SaO ₂ , behavioural states	Sponge bathing of preterm infants was associated with a significantly increased HR and decreased vagal tone indicative of stress
Liaw et al 2010 (Taiwan)	NICU	24 preterm infants; 27-35 (mean 30.3)	Descriptive correlational design comparison of infants bathed by different nurses on different days	Bathing	Infant behaviour coding, nurse behaviour coding, video	Supportive caregiving behaviours from nurses reduced infant stress and increased infant self- regulation behaviours
Liaw et al 2012 (a) (Taiwan)	NICU	30 preterm infants; 27-36 (mean 31.5)	Prospective descriptive design with repeat measures and continuous video observation for three consecutive 24 hour periods	49 caregiving activities classified as no caregiving, social interaction, routine caregiving, intrusive caregiving	HR, RR, SaO ₂ , NTISS, infant behaviour coding, NIDCAP regulation behaviours	Occurrences of most infant stress- related behaviours increased during stress-inducing caregiving

Authors Publication date (Country)	Setting	Sample Gestational age (range in weeks) *	Research design	Type of caregiving intervention	Measures	Main Findings
Liaw et al 2012 (b) (Taiwan)	NICU	30 preterm infants; 27-36 (mean 31.5)	Prospective descriptive design with repeat measures and continuous video observation for three consecutive 24 hour periods	Classified as no caregiving, social interaction, routine caregiving, intrusive caregiving	NTISS, infant behaviour coding, NICU caregiving and support	Quiet sleep increased when infants received no caregiving, social interactions or NNS and were laterally positioned
McAnulty et al 2009 (USA)	NICU	107 preterm infants: 51 -control 56 – NIDCAP; <29	Longitudinal randomised control trial comparing standard care to NIDCAP care. Measures at 2 weeks corrected age and at 9 months corrected age	'Standard versus NIDCAP care' not further defined	2 weeks: APIB, Prechtl, EEG 9 months: Bayley Scales of Infant Development	NIDCAP care was associated with improved behavioural functioning at 2 weeks corrected and neurobehavioral functioning at 9 months
Mörelus et al 2006 (Sweden)	NICU & postnatal unit	39 NICU infants: 23, <30 16, >30 and 30 full- term healthy infants	Prospective descriptive design with repeat measures, comparing two NICU groups of different gestational age and a healthy full-term control group; pre-, during, and post- routine nappy change	Nappy change	HR, SaO ₂ , salivary cortisol, PIPP, NIPS	Preterm and full-term infants demonstrated pain responses during routine nappy changes
Peters 1992 (Canada)	NICU	10 preterm infants; 27-36 (mean 29.9)	Quasi-experimental repeat measure observation of caregiving over 3.5 days	28 different types of care from 'tender care', weighing,	HR, MABP, ICP, TcPO ₂ , TcCO ₂ , TcSaO ₂	Frequent periods of hypoxia, hyperoxia and increased ICP responses occurred either during or up to 5 minutes after routine care

Authors Publication date (Country)	Setting	Sample Gestational age (range in weeks) *	Research design	Type of caregiving intervention	Measures	Main Findings
Peters 1998 (Canada)	NICU	14 preterm infants; 7, 28-29 7, 30-31 (overall mean 29)	Prospective quasi- experimental repeat measure, comparing two gestational age groups responses to sponge bathing, each infant served as own control	Bathing	HR, SaO ₂ , NIDCAP behavioural state, video	Disruption in physiological and behavioural responses occurred in all neonates throughout the bathing intervention, with higher state and activity levels post-bath
Poehlmann et al ** 2012 (USA)	NICU	109 preterm infants; 23-36 (mean 31.7)	Prospective longitudinal cohort design, with baseline physiological measures in the NICU and repeat measures up to 36 months of age	Not applicable	9 months: Vagal tone, parenting interaction (PCERA), LAB-TAB	Temperamentally prone-to- distress preterm infants exhibited more externalising problems with a 'critical style' of parenting
Sizun et al 2002 (France)	NICU	19 preterm infants; 27-31 (mean 29.1)	Prospective cross-over, infants randomly assigned to receive developmental care or no developmental care during intervention, each infant served as own control	Nappy change	HR, SaO ₂ , PIPP, EDIN, video	Developmentally-supportive care during a nappy change significantly reduced pain and distress scores and hypoxic events
van der Pal et al 2008***	NICU	139 preterm infants 70, mean 29.5	Randomised control trial comparing groups of infants allocated to either environmental developmental	Basic developmental care (incubator cover and nest)	12 months: ITSEA, NOSI	A basic form of environmental developmental care had a positive influence on child competence

Authors Publication date (Country)	Setting	Sample Gestational age (range in weeks) *	Research design	Type of caregiving intervention	Measures	Main Findings
(The Netherlands)		69, mean 29.1	care or standard care; followed up to two years of age	versus standard care		behaviours at 12 months corrected age
Yung-Weng and Ying-Jui 2004 (Taiwan)	NICU	11 preterm infants 27-36 (mean 29.9)	Prospective descriptive design with repeat measures; each infant was observed during a nappy change at four different times on different days	Nappy change	HR, SaO ₂ , buttock lifting angle	90% of nappy changes resulted in increased or decreased HR and decreased SaO ₂ for premature infants, with a recovery time up to 10 minutes
Zeiner et al 2016 (USA)	NICU	30 preterm infants 28-35 (mean 32.7)	Prospective observational design, during standard morning caregiving	Temperature, nappy change and repositioning	HR, RR, skin conductance responses, NIDCAP stress behaviours	Stress responses significantly increased during care, with behavioural responses influenced by the infant's severity of illness

Table 4. Summary of articles included in literature review

Abbreviations: APIB: Assessment of Preterm Infant's Behaviour, BPSC: Baby Pediatric Symptom Checklist, Brazelton NBAS: Neonatal Behavioral Assessment Scale, EDIN: Échelle Douleur Inconfort Nouveau-Né, neonatal pain and discomfort scale, EEG: electroencephalogram, HR: heart rate, IBQ: Rothbart's Infant Behavioural Questionnaire, ICP: Intracranial pressure, ICQ: Infant Characteristics Questionnaire, ITQ: Carey's Infant Temperament Questionnaire, ITSEA: Infant-Toddler Social and Emotional Assessment, LAB-TAB: Laboratory assessment of Temperament, MABP: Mean arterial blood pressure, NICU: neonatal intensive care unit, NIPS: Neonatal Infant Pain Scale, NIRS: Near-Infrared Spectroscopy, NOSI: Nijmegen Parenting Stress Index, NNNS: NICU Network Neurobehavioral Scale, NIDCAP: Newborn Individualised Developmental Care Assessment Program, NNS: non-nutritive sucking, NTISS: National Therapeutic Intervention Scoring System, PCERA: Parent Child Early Relational Assessment, PIPP: Premature Infant Pain Profile, Prechtl: Prechtl Neurological Examination of the Full-term Newborn Infant, RR: respiratory rate, SaO₂: oxygen saturation levels, TCO₂: Transcutaneous carbon dioxide, TCPO₂: Transcutaneous oxygen, TCM: Transcutaneous Monitoring, TcSaO₂: Transcutaneous oxygen saturation.

* details of gestational age were not consistently available

** only results at 9 months are reported in this table

*** only results at 12 months are reported in this table

Reference List

- Abulizi, X., Pryor, L., Michel, G., Melchior, M., van der Waerden, J., Group, E.M.C.C.S., 2017. Temperament in infancy and behavioral and emotional problems at age 5.5: The EDEN mother-child cohort. *PLoS One* 12, e0171971-e0171971.
- Als, H., 1982. Toward a synactive theory of development: Promise for the assessment and support of infant individuality. *Infant Ment Health J*, 3, 229-243.
- Als, H., 1986. A synactive model of neonatal behavioral organization: Framework for the assessment of neurobehavioral development in the premature infant and for support of infants and parents in the neonatal intensive care environment. *Phys Occup Ther Pediatr*, 6, 3-53.
- Als, H., 1989. Self-regulation and motor development in preterm infants, Action in social context. Springer, pp. 65-97.
- Als, H., Butler, S., Kosta, S., McAnulty, G., 2005. The Assessment of Preterm Infants' Behavior (APIB): Furthering the understanding and measurement of neurodevelopmental competence in preterm and full-term infants. *Ment Retard Dev Disabil Res Rev*, 11, 94-102.
- Als, H., McAnulty, G., 2011. The newborn individualized developmental care and assessment program (NIDCAP) with kangaroo mother care (KMC): comprehensive care for preterm infants. *Curr Womens Health Rev*, 7, 288-301.
- American Academy of Pediatrics 'Committee on Fetus and Newborn & Section on Anesthesiology and Pain Medicine', 2016. Prevention and management of procedural pain in the neonate: An update. *Pediatrics*, 137(2), e20154271.
- Austin, B., Downing, C., Hastings-Tolsma, M., 2019. Experience of neonatal intensive care unit nurses in providing developmentally-supportive care: A qualitative study. *Nurs Health Sci*, 21, 336-344.
- Becker, P.T., Grunwald, P.C., Moorman, J., Stuhr, S., 1993. Effects of developmental care on behavioral organization in very-low-birth-weight infants. *Nurs Res* 42, 214-220.
- Burnett, A.C., Cheong, J.L.Y., Doyle, L.W., 2018. Biological and social influences on the neurodevelopmental outcomes of preterm infants. *Clin Perinatol* 45, 485-500.
- Byers, J.F., 2003. Components of developmental care and the evidence for their use in the NICU. *MCN Am J Matern Child Nurs*, 28, 174-180.
- Carrier, C.T., 2002. Individualized family-centered developmental care: Reflections on implementation. *Newborn Infant Nurs Rev*, 2, 27-34.
- Cassiano, R.G., Provenzi, L., Linhares, M.B.M., Gaspardo, C.M., Montiroso, R., 2020. Does preterm birth affect child temperament? A meta-analytic study. *Infant Behav Dev* 58, 101417.
- Cassiano, R.G.M., Gaspardo, C.M., Linhares, M.B.M., 2019. Temperament moderated by neonatal factors predicted behavioral problems in childhood: A prospective longitudinal study. *Early Hum Dev* 135, 37-43.
- Catelin, C., Tordjman, S., Morin, V., Oger, E., Sizun, J., 2005. Clinical, physiologic, and biologic impact of environmental and behavioral interventions in neonates during a routine nursing procedure. *J Pain*. 6, 791-797.
- Cheong, J.L.Y., Burnett, A.C., Treyvaud, K., Spittle, A.J., 2020. Early environment and long-term outcomes of preterm infants. *J Neural Transm (Vienna)* 127, 1-8.
- Comaru, T., Miura, E., 2009. Postural support improves distress and pain during diaper change in preterm infants. *J Perinatol*, 29, 504-507.
- Curtis, K., Fry, M., Shaban, R.Z., Considine, J., 2017. Translating research findings to clinical nursing practice. *J Clin Nurs* 26, 862-872.
- D'Agata, A.L., Sanders, M.R., Grasso, D.J., Young, E.E., Cong, X., McGrath, J.M., 2017. Unpacking the burden of care for infants in the NICU. *Infant Ment Health J*, 38, 306-317.
- Danford, D.A., Miske, S., Headley, J., Nelson, R.M., 1983. Effects of routine care procedures on transcutaneous oxygen in neonates: a quantitative approach. *Arch Dis Child*, 58, 20.
- De Bernardo, G., Svelto, M., Giordano, M., Sordino, D., Riccitelli, M., 2017. Supporting parents in taking care of their infants admitted to a neonatal intensive care unit: a prospective cohort pilot study. *Ital J Pediatr* 43, 36-36.

de Freitas, P., Bueno, M., Holditch-Davis, D., Santos, H.P., Kimura, A.F., 2018. Biobehavioral Responses of Preterm Infants to Conventional and Swaddled Tub Baths: A Randomized Crossover Trial. *J Perinat Neonatal Nurs*, 32.

De Rogalski Landrot, I., Roche, F., Pichot, V., Teyssier, G., Gaspoz, J.-M., Barthelemy, J.-C., Patural, H., 2007. Autonomic nervous system activity in premature and full-term infants from theoretical term to 7 years. *Auton Neurosci*, 136, 105-109.

DiPietro, J.A., Porges, S.W., 1991. Relations between neonatal states and 8-month developmental outcome in preterm infants. *Infant Behav Dev*, 14, 441-450.

Evans, J.C., 1991. Incidence of hypoxemia associated with caregiving in premature infants. *Neonatal Netw*, 10, 17.

Faber, K., 2013. Relationship-Based care in the neonatal intensive care unit. *Creat Nurs*, 19, 214-218.

Feldman, R., 2009. The Development of Regulatory Functions From Birth to 5 Years: Insights From Premature Infants. *Child Dev*, Mar-Apr 2009;80(2):544-61.

Foreman, S.W., Thomas, K.A., Blackburn, S.T., 2008. Individual and gender differences matter in preterm infant state development. *J Obstet Gynecol Neonatal Nurs*, 37, 657-665.

Garrard, J., 2017. Health sciences literature review made easy: The matrix method., 5th ed. Jones and Bartlett Learning, Burlington, MA.

Godarzi, z., Zarei, K., Shariat, M., Sadeghniat, k., Nikafs, N., Sepaseh, H., 2018. Correlations of handling procedures and sleep patterns of the infants admitted to the neonatal intensive care unit. *Iranian Journal of Neonatology*, 9, 35-41.

Gonya, J., Harrison, T., Feldman, K., Stein, M., Chawla, N., 2019. Nursing networks in the NICU and their association with maternal stress: A pilot study. *J Nurs Manag*, 27, 442-449.

Gunnar, M.R., Porter, F.L., Wolf, C.M., Rigatuso, J., Larson, M.C., 1995. Neonatal stress reactivity: predictions to later emotional temperament. *Child Dev*, 66, 1-13.

Horns, K.M., 1998. Being-in-tune caregiving. *J Perinat Neonatal Nurs*, 12, 38-49.

Lawhon, G., Hedlund, R.E., 2008. Newborn individualized developmental care and assessment program training and education. *J Perinat Neonatal Nurs* 22, 133-144; quiz 145-136.

Lean, R.E., Rogers, C.E., Paul, R.A., Gerstein, E.D., 2018. NICU Hospitalization: Long-Term implications on parenting and child behaviors. *Curr Treat Options Pediatr* 4, 49-69.

Lee, H.-K., 2002. Effects of sponge bathing on vagal tone and behavioural responses in premature infants. *J Clin Nurs*, 11, 510-519.

Lee, S.K., O'Brien, K., 2014. Parents as primary caregivers in the neonatal intensive care unit. *CMAJ* 186, 845-847.

Liaw, J.-J., Yang, L., Chou, H.-L., Yang, M.-H., Chao, S.-C., 2010. Relationships between nurse care-giving behaviours and preterm infant responses during bathing: a preliminary study. *J Clin Nurs*, 19, 89-99.

Liaw, J.-J., Yang, L., Hua, Y.-M., Chang, P.-W., Teng, C.C., Li, C.-C., 2012a. Preterm infants' biobehavioral responses to caregiving and positioning over 24 hours in a neonatal unit in Taiwan. *Res Nurs Health*, 35, 634-646.

Liaw, J.-J., Yang, L., Lo, C., Yuh, Y.-S., Fan, H.-C., Chang, Y.-C., Chao, S.-C., 2012b. Caregiving and positioning effects on preterm infant states over 24 hours in a neonatal unit in Taiwan. *Res Nurs Health*, 35, 132-145.

Linnér, A., Almgren, M., 2020. Epigenetic programming-The important first 1000 days. *Acta Paediatr*, 109, 443-452.

Lubbe, W., Van der Walt, C.S., Klopper, H.C., 2012. Integrative literature review defining evidence-based neurodevelopmental supportive care of the preterm infant. *J Perinat Neonatal Nurs* 26, 251-259.

Maki, M.T., Orsi, K.C.S.C., Tsunemi, M.H., Hallinan, M.P., Pinheiro, E.M., Avelar, A.F.M., 2017. The effects of handling on the sleep of preterm infants. *J Acta Paul Enferm*. 30, 489-496.

McAnulty, G., Duffy, F.H., Butler, S., Parad, R., Ringer, S., Zurakowski, D., Als, H., 2009. Individualized developmental care for a large sample of very preterm infants: health, neurobehaviour and neurophysiology. *Acta Paediatr*, 98, 1920-1926.

McAnulty, G.B., Duffy, F.H., Butler, S.C., Bernstein, J.H., Zurakowski, D., Als, H., 2010. Effects of the Newborn Individualized Developmental Care and Assessment Program (NIDCAP) at age 8 years: preliminary data. *Clin Pediatr*, 49, 258-270.

McLaughlin, K.A., Sheridan, M.A., Tibu, F., Fox, N.A., Zeanah, C.H., Nelson, C.A., 2015. Causal effects of the early caregiving environment on development of stress response systems in children. *Proc Natl Acad Sci USA*, 112, 5637.

McPherson, C., Miller, S.P., El-Dib, M., Massaro, A.N., Inder, T.E., 2020. The influence of pain, agitation, and their management on the immature brain. *Pediatr Res* 88, 168-175.

Milette, I.H., Richard, L., Martel, M.-J., 2005. Evaluation of a developmental care training programme for neonatal nurses. *J Child Health Care*, 9, 94-109.

Mörelus, E., Hellström-Westas, L., Carlén, C., Norman, E., Nelson, N., 2006. Is a nappy change stressful to neonates? *Early Hum Dev*, 82, 669-676.

Murdoch, D.R., Darlow, B.A., 1984. Handling during neonatal intensive care. *Arch Dis Child*, 59, 957-961.

O'Brien, K., Robson, K., Bracht, M., Cruz, M., Lui, K., Alvaro, R., da Silva, O., Monterrosa, L., Narvey, M., Ng, E., Soraisham, A., Ye, X.Y., Mirea, L., Tarnow-Mordi, W., Lee, S.K., 2018. Effectiveness of Family Integrated Care in neonatal intensive care units on infant and parent outcomes: a multicentre, multinational, cluster-randomised controlled trial. *Lancet Child Adolesc Health*, 2, 245-254.

O'Reilly, H., Johnson, S., Ni, Y., Wolke, D., Marlow, N., 2020. neuropsychological outcomes at 19 years of age following extremely preterm birth. *Pediatrics* 145.

Park, J., Kim, J.-S., 2019. Factors Influencing developmental care practice among neonatal intensive care unit nurses. *J Pediatr Nurs*, 47, e10-e15.

Pereira, F.L., Goes, F.d.S.N.d., Fonseca, L.M.M., Scochi, C.G.S., Castral, T.C., Leite, A.M., 2013. Handling of preterm infants in a neonatal intensive care unit. *Rev Esc Enferm USP*, 47, 1272-1278.

Peters, K., 1992. Does routine nursing care complicate the physiological status of the premature infant with respiratory distress. *J Perinat Neonatal Nurs*, 6, 74-91.

Peters, K.L., 1998. Bathing premature infants: Physiological and behavioral consequences. *Am J Crit Care*, 7, 90-100.

Peters, K.L., 1999. Infant handling in the NICU: does developmental care make a difference? An evaluative review of the literature. *J Perinat Neonatal Nurs* 13, 83-109.

Poehlmann, J., Hane, A., Burnson, C., Maleck, S., Hamburger, E., Shah, P.E., 2012. Preterm infants who are prone to distress: differential effects of parenting on 36-month behavioral and cognitive outcomes. *J Child Psychol Psychiatry*, 53, 1018-1025.

Prechtl, H.F., 1974. The behavioural states of the newborn infant (a review). *Brain research* 76, 185-212.

Pressler, J.L., Hepworth, J.T., Helm, J.M., Wells, N.L., 2001. Behaviors of very preterm neonates as documented using NIDCAP observations. *Neonatal Netw*, 20, 15-24.

Relland, L.M., Gehred, A., Maitre, N.L., 2019. Behavioral and physiological signs for pain assessment in preterm and term neonates during a nociception-specific response: A systematic review. *Pediatr Neurol* 90, 13-23.

Rick, S.L., 2006. Developmental care on newborn intensive care units: Nurses' experiences and neurodevelopmental, behavioural, and parenting outcomes. A critical review of the literature. *J Neonatal Nurs*, 12, 56-61.

Robinson, R., Lahti-Pulkkinen, M., Schnitzlein, D., Voit, F., Girchenko, P., Wolke, D., Lemola, S., Kajantie, E., Heinonen, K., Räikkönen, K., 2020. Mental health outcomes of adults born very preterm or with very low birth weight: A systematic review. *Semin Fetal Neonatal Med*, 25(3):101113.

Sidor, A., Fischer, C., Cierpka, M., 2017. The link between infant regulatory problems, temperament traits, maternal depressive symptoms and children's psychopathological symptoms at age three: a longitudinal study in a German at-risk sample. *Child Adolesc Psychiatry Ment Health* 11, 10-10.

Sizun, J., Ansquer, H., Browne, J., Tordjman, S., Morin, J.-F., 2002. Developmental care decreases physiologic and behavioral pain expression in preterm neonates. *J Pain*, 3, 446-450.

- Soleimani, F., Azari, N., Ghiasvand, H., Shahrokhi, A., Rahmani, N., Fatollahierad, S., 2020. Do NICU developmental care improve cognitive and motor outcomes for preterm infants? A systematic review and meta-analysis. *BMC Pediatrics*, 20, 67.
- Spence, K., 2000. The best interest principle as a standard for decision making in the care of neonates. *J Adv Nurs*, 31, 1286-1292.
- Symington, A., Pinelli, J.M., 2009. Developmental care for promoting development and preventing morbidity in preterm infants. *Cochrane Database Syst Rev*, Apr 19;(2):CD001814.
- Torowicz, D., Lisanti, A.J., Rim, J.S., Medoff-Cooper, B., 2012. A developmental care framework for a cardiac intensive care unit: a paradigm shift. *Adv Neonatal Care*, Oct;12 Suppl 5:S28-32.
- van der Pal, S.M., Maguire, C.M., Bruil, J., Cessie, S., van Zwieten, P., Veen, S., Wit, J.M., Walther, F.J., 2008. Very pre-term infants' behaviour at 1 and 2 years of age and parental stress following basic developmental care. *Br J Dev Psychol*, 26, 103-115.
- Weber, A., Harrison, T.M., 2019. Reducing toxic stress in the neonatal intensive care unit to improve infant outcomes. *Nurs Outlook*, 67, 169-189.
- Wolke, D., Johnson, S., Mendonça, M., 2019. The Life Course Consequences of Very Preterm Birth. *Annu Rev Dev Psychol*, 1, 69-92.
- Yung-Weng, W., Ying-Ju, C., 2004. A preliminary study of bottom care effects on premature infants' heart rate and oxygen saturation. *J Nurs Res* 12, 161-168.
- Zahr, L.K., Balian, S., 1995. Responses of premature infants to routine nursing interventions and noise in the NICU. *Nurs Res* 44, 179-185.
- Zeiner, V., Storm, H., Doheny, K.K., 2016. Preterm infants' behaviors and skin conductance responses to nurse handling in the NICU. *J Matern Fetal Neonatal Med*, 29, 2530-2535.