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A systematic review of the evidence to support perinatal palliative care for the fetus and neonate

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Perinatal palliative care is the planning and provision of supportive care during life and end-of-life care for a fetus, newborn infant or infant and their family in the management of an appropriate candidate condition (British Association of Perinatal Medicine, 2010, p.1)

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Glossary

TERM	DEFINITION
ANTICIPATORY GRIEF	Describes the normal grief response that occurs prior to death that includes sadness, sorrow, anger, crying and emotional preparation for death.
BARRIERS	Factors that impede the translation of evidence into clinical practice
EARLY NEONATAL DEATH	refers to a death of a live-born baby within the first seven days of life
END OF LIFE CARE	Describes the perinatal palliative care of a baby when life expectancy is limited and death is imminent. It encompasses care of the baby from the time of diagnosis through to his or her death and care of the baby and parents following death.
EXTREME PRETERM	**Preterm** is defined as babies born alive before 37 weeks of pregnancy are completed. There are sub-categories of **preterm** birth, based on gestational age: **extremely preterm** (<28 weeks) very **preterm** (28 to <32 weeks)
FACILITATORS	Factors that expedite the translation of evidence into clinical practice
FETUS	The developing baby after 8 weeks of pregnancy.
GRIEF	The reaction to loss and bereavement.
HOSPICE	A philosophy of care with a focus on the physical, emotional and spiritual support of a person at end of life.
INTRA-UTERINE FETAL DEATH	Describes the death of a baby in the womb.
LIFE LIMITING CONDITIONS	Conditions that are expected to result in an early death.
NEONATAL	Refers to the period after birth up until the fourth completed week of life
NICU	Neonatal Intensive Care Unit
PALLIATIVE CARE	Care of the terminally ill and their families- a philosophy of care.
PERINATAL PERIOD	The period from 20 weeks gestation to 28 days following birth
POSTNATAL PERIOD	The postnatal period refers to the six weeks following birth
RETROSPECTIVE CHART REVIEW	Chart review studies facilitate the rapid collection of clinical, safety, and healthcare resource utilization (HRU) data.

Executive Summary

Perinatal palliative care is a developing model of care aimed at providing care to the fetus, neonate, mother and family. Historically, the early focus of palliative care was in cancer diagnosis in adults (Hain and Singh Jassal 2010). During the 1960's advocates of holistic and patient centred care emerged, namely, Dr Cicely Saunders and Dr Elisabeth Kubler Ross. While adult and paediatric palliative care are distinct disciplines, the concept of palliative care principles in the field of neonatology have not been embraced as rapidly, as in other areas of medicine (Gilmour et al. 2016). The British Association of Perinatal Medicine (2010) (BAPM) has suggested categories were neonatal palliative care is indicated. These five categories include:

1. An antenatal or postnatal diagnosis of a condition which is not compatible with long term survival, or
2. An antenatal or postnatal diagnosis which carries a high risk of significant morbidity or death,
3. Babies born at the margins of viability, where intensive care has been deemed inappropriate,
4. Postnatal conditions with a high risk of severe impairment of quality of life or when the baby needs or may need life support and,
5. Postnatal conditions where the baby may experience "unbearable suffering" in the course of their illness or treatment

The broad aim of this systematic review was to explore the available evidence to support perinatal palliative care for the fetus and neonate. Key databases were searched and a total of 30 papers were included in this systematic review. The findings identified that there was a lack of high quality evidence and heterogeneity of methodologies. This scoping review of the literature is therefore based on evidence which is considered to be of low quality. An exploration of grey literature identified National and International Neonatal Palliative Care Guidelines and Position Statements. Recommendations for clinical practice within these guidelines are as a result of expert opinion, text and opinion papers and a small number of qualitative studies.

From the analysis of papers there is evidence to support perinatal palliative care for the fetus and neonate. The first gap is that further research is required in relation to the provision of perinatal palliative care and the experiences of parents and health care providers with perinatal palliative care programmes. Research which explores the relationship between the existing palliative care programme available within the NICU and the actual palliative care provided to individual infants (American Academy of Paediatrics 2013., Samsel & Lechner 2015). Additionally the experiences of staff and parents with individual palliative care plans are important to inform National Policy.

The second gap relates to education and training in perinatal palliative care to support staff provide evidence based care to mothers and babies. The development of a National Perinatal Palliative Care Policy will support and inform clinical decision making to ensure safe and effective palliative care of the fetus and neonate. The implementation of guidance in clinical practice will benefit from the inclusion of protocols, algorithms and checklists (Hegarty et al. 2015) to include end of life neonatal medication tables with dose, infant age/weight and route of administration suggested. Research should also assess and evaluate pain and symptom management in infants, at end of life (Stenekes et al. 2014).

The findings of this systematic review will direct and inform further research during the antenatal, perinatal and post-natal period which will support perinatal palliative care for the fetus and neonate. A National Perinatal Palliative Care Policy is recommended.

Chapter 1

Background

The concept of palliative care and specialised care of the dying is not a new phenomenon. It is reputed that as early as the 12th century monastic societies created hospitals within their walls to care for the sick and dying. Historically, the early focus of palliative care was in cancer diagnosis in adults (Hain and Singh Jassal 2010). During the 1960's advocates of holistic and patient centred care emerged, namely, Dr Cicely Saunders and Dr Elisabeth Kubler Ross. In the United Kingdom, the pioneering work of Dr Saunders was instrumental in the recognition of the importance of end-of-life care needs of patients with advanced malignancies, notably cancer (Clarke 2007). Palliative care became synonymous with the physical, social, psychological and spiritual care of patients, provided by a multidisciplinary team (Clarke 2007). In 1967 Dr Saunders opened the first hospice in London, providing care to cancer patients. Meanwhile, in Chicago the Swiss- born psychiatrist Dr Elizabeth Kubler Ross was working with end –of-life patients and subsequently published her first book "On Death and Dying" during this period.

Dr Jonathan Whitfield introduced the concept of the adult hospice to the care of the dying infant and their family in 1982 (Leuthner & Pierucci 2015). Dr Whitfield's interest in neonatal palliative care brought about the transfer in decision making from the attending neonatologist to the entire NICU healthcare team. A family room was created with the goal of achieving a home-like environment, privacy and comfort; as opposed to the medical atmosphere of the NICU. In 1990 Dr Henry Mangurten described his experience with terminally ill infants who were supported to die at home (Mangurten 1990). The terms "palliative care" and "hospice care" are used interchangeably within the literature because of their core values and philosophical approaches to care provision at end of life (Ferrell, 2016: 2).

Palliative care

The term “palliative” is derived from the Latin word *pallium,* meaning a ‘cloak’ or ‘cover’ (Abu-Saad, 2001) while symbolically, Rallison & Moules (2004) describe palliative care as a cloak of warmth and protective care offered to terminally ill patients, by their care providers.

Palliative care

- is holistic
- provides relief from pain and symptom management
- integrates physical, psychological and spiritual aspects of care
- enhances dignity and the quality of life
- offers a support system to families
- incorporates bereavement care
- can be provided with cure orientated care and then intensified when that level of care is not helpful or appropriate

(Gale & Brooks 2006, Price & McNeilly, 2009, Mancini et al. 2014)

Palliative care is provided at three different levels a) palliative care approach, b) general palliative care and c) specialist palliative care (Palliative Care Competence Framework Steering Group, 2014).

The definition of perinatal and paediatric palliative care

The World Health Organisation (WHO) created one of the earliest definitions of paediatric palliative care, describing it as “ the active total care of the child’s body, mind and spirit, involving an evaluation of a child’s psychological, physical and social distress” (WHO 1998). The British Association of Perinatal Medicine (2010, p.2) describe perinatal palliative care as the planning and provision of supportive care during life and end-of-life care for a fetus, newborn infant or infant and their family in the management of an appropriate candidate condition. Perinatal Palliative Care as described by The National Institute for Health and Care

Excellence (NICE) (2016) provides a definition that has evolved to support palliative care during the antenatal, perinatal and post-natal period and reflects the philosophy of palliative care.

> *Perinatal palliative care involves providing integrated ongoing support from the diagnosis of a life limiting condition in a fetus, and during pregnancy, delivery, post-natal care and (if needed) bereavement care. NICE (2016)*

Historical development of the Hospice

The term "hospice care" refers to a specific model to deliver palliative care (Price & McNeilly 2009, p. 3). The philosophy of hospice care is centred on dignity at end of life and supports the physical, emotional and spiritual care of dying patients and their families (Clarke 2007). The period from the 1970's onwards saw an expansion of palliative care programmes within the UK, Europe and North America with an increasing number of hospices emerging. Palliative care for children had its roots in the hospice movement, with the provision of a flexible approach to care in a variety of settings to include the home, hospital or hospice (Price & McFarlane 2009, p. 1). While adult and paediatric palliative care are distinct disciplines, the concept of palliative care principles in the field of neonatology have not been embraced as rapidly, as in other areas of medicine (Gilmour et al. 2016).

Introduction

The World Health Organisation (2011) reports that greater than one third of all child deaths occur during the first month of life. In the United States, the National Centre for Health Statistics (NCHS) report the perinatal mortality rate as 6.24 per 1,000 live births (Mac Dorman & Gregory 2015). In the United Kingdom, MBRRACE-UK report the perinatal mortality rate as 5.92 per 1,000 births (Manktelow et al. (2016); while in Ireland, the National Perinatal Reporting System (NPRS) (2016) reports a perinatal mortality rate of 6.2 per 1000 livebirths. The leading cause of early neonatal death in Ireland is reported as congenital malformations (37.4%) with immaturity contributing to 17.6% of total early neonatal deaths. Internationally, The NCHS (2015) report congenital malformations, chromosomal abnormalities and low birth weight as the leading causes of perinatal death. The majority of neonatal deaths from these causes will occur in neonatal intensive care units (Gale & Brooks 2006). The responsibility of staff within the neonatal intensive care units is to provide end-of-life care for infants and their families (Wright et al. 2011). The need for palliative care principles in the NICU is therefore imperative. Similarly parents, who are informed as a result of antenatal investigations that their baby has a life limiting condition that will result in death, require a palliative care programme (Leong Marc-Aurele & Nelesen, 2013). The reasons for implementing palliative care practices to the care of a fetus and neonate are many and varied. The British Association of Perinatal Medicine (BAPM) has suggested categories were neonatal palliative care is indicated (BAPM 2010). These five categories include:

1. An antenatal or postnatal diagnosis of a condition which is not compatible with long term survival, or
2. An antenatal or postnatal diagnosis which carries a high risk of significant morbidity or death,
3. Babies born at the margins of viability, where intensive care has been deemed inappropriate,
4. Postnatal conditions with a high risk of severe impairment of quality of life or when the baby needs or may need life support and,
5. Postnatal conditions where the baby may experience “unbearable suffering” in the course of their illness or treatment

Perinatal palliative care is a developing model of care aimed at providing care to the fetus, newborn, mother and family. Antenatally, advanced diagnostic ultrasound, coupled with molecular genetic testing and maternal serum screening has facilitated the early detection of life threatening conditions, life limiting or lethal problems early in pregnancy (American Association of Pro-Life Obstetricians & Gynecologists (AAPLOG) 2015; Kenner et al. 2015). Liben et al. (2008) refer to the terms "life limiting" (no realistic hope of a cure) and "life threatening" (where a cure is possible) in the context of appropriateness when outlining conditions were perinatal palliative care may be indicated. In the context of this review life limiting conditions are those that are expected to result in an early death, where there is no reasonable hope of cure (NICE 2016, ACT 2009).

Following confirmation of a life limiting condition parents are faced with decisions in relation to the remainder of the pregnancy; giving birth and seeing and holding their new born baby (Wool 2013). It is reported in the literature that infants with a life limiting condition may live for hours, days or months (Mancini et al. 2014, Wool 2013). Perinatal palliative care provides a multidimensional approach to care for families where a life- limiting fetal diagnosis has been made, throughout the infant's life, death and beyond (Association for Children's Palliative Care (ACT) 2009).

Additionally, technology has supported the birth, life and death of the very fragile infant on the cusp of viability. Following birth some infants will receive resuscitative measures in the delivery unit and subsequent transfer to the neonatal intensive care unit for further care and management. Neonatal intensive units play an important role in end of life care, and create the setting that the majority of new born babies born with a life limiting condition or extreme prematurity will die. Perinatal palliative care has at its core the prevention of pain and distress of the infant, with emphasis on the psychological, social and spiritual support of the family (Leong Marc-Aurele, 2013., Mancini et al. 2014., Stenekes et al. 2014., Ferrell, 2016). The physical, psychological and social needs of babies and their families are central to quality neonatal care (NICE 2010). Perinatal palliative care programmes provide early and integrative care (Wool 2013). Caitlin & Carter (2002*)* developed a neonatal end-of-life palliative care protocol in the USA following a Delphi consensus with national and international experts in the field of neonatal palliative care. This programme highlighted the importance of a structured plan for delivering neonatal palliative care (Kenner et al. 2015) and informed the development of similar protocols nationally and internationally.

In summary, Perinatal Palliative care is a developing model of care. It has been described as:

> "*the provision of ongoing support from the diagnosis of a life limiting condition in a fetus, and during pregnancy, delivery, post-natal care and (if needed) bereavement care*" (NICE, 2016)
>
> AND
>
> "*It embraces physical, emotional, social and spiritual elements and focuses on the enhancement of quality of life. It includes the management of distressing symptoms, provision of short breaks and care through death and bereavement*" (ACT, 2009, p. 13).

The focus of care is on pain and symptom management while at the same time maintaining respect for the cultural, spiritual beliefs and practices of the respective family (Gale & Brooks 2006).

Perinatal palliative care continues to evolve and there are a number of identified antenatal and post-natal conditions where perinatal palliative care is indicated in the best interest of the fetus, neonate and family (BAPM 2010). Nationally, there is a Palliative Care Competence Framework (2014) which directs palliative care provision by health care professionals, from basic care to specialist level. There is little evidence to support perinatal palliative care. This systematic review will explore the available evidence to support the developing model of perinatal palliative care for the fetus and neonate. The findings will direct and inform further research during the antenatal, perinatal and post-natal period in order to inform the care and management of the fetus, neonate, mother and family with a life limiting condition.

Structure of the review

This systematic review of the evidence for perinatal palliative care is presented over seven chapters. In Chapter 2 the methods of the review are presented. Chapter 3 introduces the evidence for perinatal palliative care; Chapter 4 introduces the evidence for pain and symptom management, while Chapter 5 introduces the evidence identifying barriers and facilitators to perinatal palliative care. Chapter 6 identifies national and international policy statements and guidelines to support perinatal palliative care and finally chapter 7 concludes the review with a discussion, conclusion and recommendations for future research.

Chapter 2

Methodology

Review Methods

The purpose of this systematic review is to explore the available evidence to support perinatal palliative care for the fetus and neonate.

This review will identify

1. The key features of perinatal palliative care
2. The evidence to support antenatal perinatal palliative care plans
3. The barriers and facilitators to perinatal palliative care for nurses and midwives

Primary outcome

To identify and synthesise the available evidence and establish the robustness for perinatal palliative care.

Secondary outcomes

To establish the barriers and facilitators experienced by health care professionals in the provision of palliative care to the neonate with a life limiting condition.

Selection criteria for studies

A scoping review of the literature was undertaken utilising the Joanna Briggs Institute (JBI) Population, Concept and Context elements (www.joannabriggs.org). While a systematic review addresses relatively specific questions, a scoping review in this instance was utilised to map key concepts underpinning the evidence for perinatal palliative care, clarify working definitions and the conceptual boundaries of the topic (Arksey & O' Malley, 2005). Because of a lack of empirical research the scoping review provided an opportunity to report on the types of evidence that are available to address and inform practice within the field of perinatal palliative care. The broad nature of the scoping review further proved useful in bringing together evidence from disparate and heterogeneous sources (The Joanna Briggs Institute 2015).

Population

Fetus and Neonate

Concept:

Perinatal Palliative care

Context:

Perinatal Palliative care in the health care setting or home *and*

Facilitators or Barriers to Perinatal Palliative care

Papers were included if they reported on:

The five categories identified by The British Association of Perinatal Medicine (2010) where neonatal palliative care is indicated:

1. An antenatal or postnatal diagnosis of a condition which is not compatible with long term survival, or
2. An antenatal or post-natal diagnosis which carries a high risk of significant morbidity or death,
3. Babies born at the margins of viability, where intensive care has been deemed inappropriate,
4. Postnatal conditions with a high risk of severe impairment of quality of life or when the baby needs or may need life support and,
5. Postnatal conditions where the baby may experience “unbearable suffering” in the course of their illness or treatment.

Papers were excluded if they reported on:

1. Medical, legal and ethical implications of withdrawal of mechanical ventilation/ life support.
2. Withdrawal of artificial nutrition, mechanical ventilation.
3. Educational training programmes, training interventions.
4. Moral distress of neonatal intensive care unit staff.

Search Strategy

This scoping review of the evidence for perinatal palliative care is the result of rigorous and comprehensive search of the literature. This extensive search was carried out on June 28th 2016. No limits were placed on the search. The bibliographic databases searched and results retrieved are as follows:

PubMed	**4360**
The Cumulative Index to Nursing and Allied Health Literature (CINAHL)	**921**
Maternity and Infant Care (MIDIRS)	**358**
Psych INFO	**254**
Scopus	**3291**
PDAT A and I	**57**
PDAT UK and IE	**86**

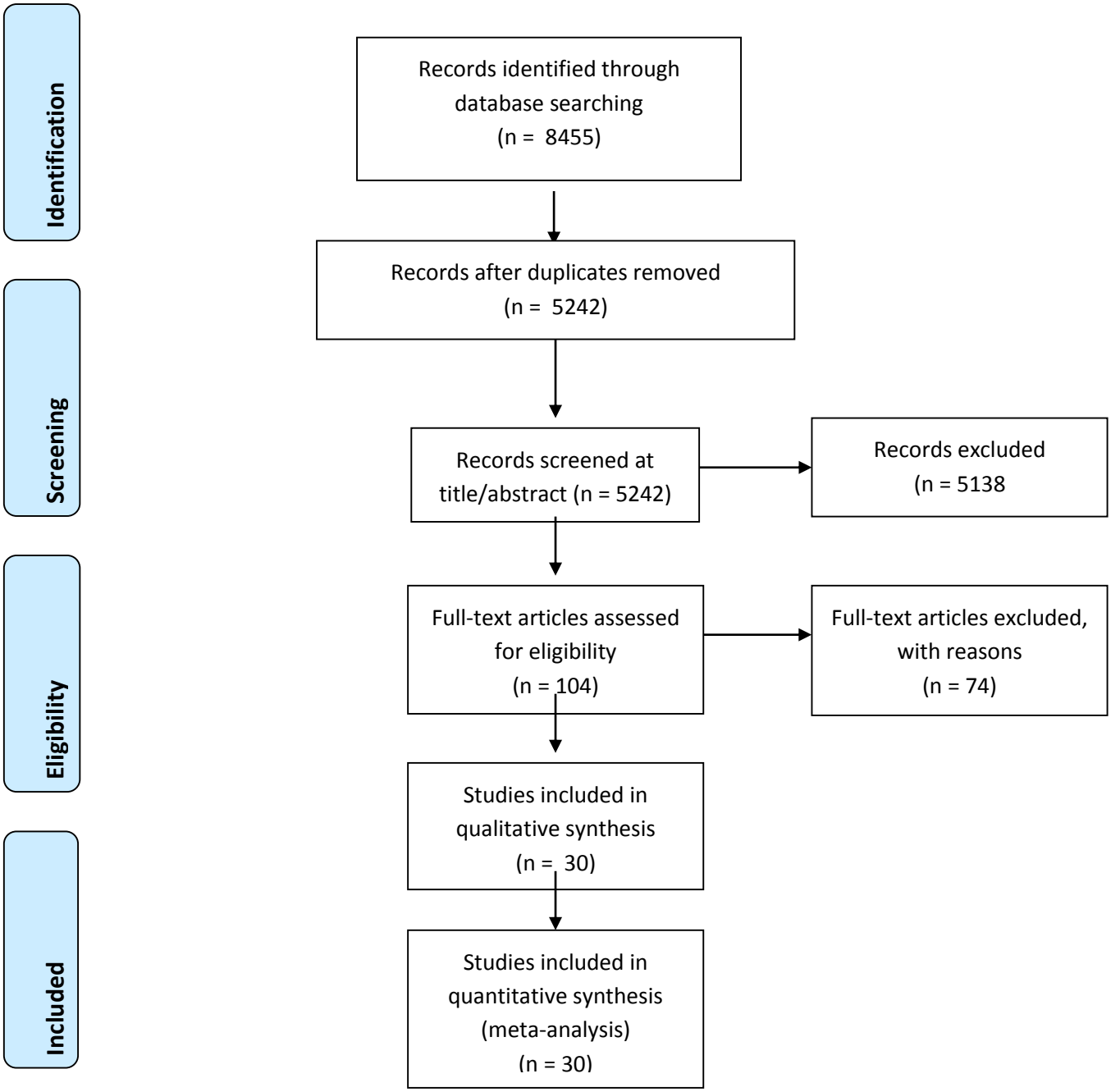
The search strategy (Appendix 1) was developed with the support of the librarian, Mr Greg Sheaf, Trinity College Dublin. The extensive search comprised of searches both for keywords and medical subject headings (Mesh) within the structure of existing databases. Language restrictions were not applied to the search strategy but the selection of relevant papers for full inclusion in this review was restricted to English only. The reference lists of all identified guidelines and papers were searched for additional studies.

"Palliative care" OR "Hospice care" OR "Terminal care" OR "Life limiting" OR "End of life" OR "Lethal anomaly" OR "lethal anomalies" OR "incompatible with life" OR "life shortening"

AND

Newborn OR newborns OR baby OR babies OR neonate OR neonates OR fetus OR fetuses OR Foetus OR foetuses OR Neonatal OR Perinatal OR "Previable birth" OR "Low gestational age" OR premature OR prematurity OR "Very preterm".

Table 1 Steps undertaken for the review, using the PRISMA flow diagram for systematic reviews



Document management

All identified papers for title and abstract review where imported in to *Covidence*, a web based systematic review tool to facilitate screening, quality appraisal, data extraction and analysis (www.covidence.org). All references were managed and categorised using Endnote. Endnote also was utilised to remove any duplicates and to ensure an accurate reference list.

Screening citations

The initial search was undertaken by the author, Denise McGuinness (DMcG) and the librarian, Mr Greg Sheaf (GS). At this stage the title and abstracts in *Covidence* were reviewed for inclusion/exclusion independently by DMcG. As the abstract identified themes that were not consistent with the aims of the review, studies were excluded.

Full Text Screening

Full text screening followed where DMcG and Professor Joan Lalor (JL) reviewed each full text paper for inclusion/exclusion independently. *Covidence* was utilised to record the reasons for exclusion.

Quality Assessment

While *Covidence* provided a facility to undertake quality assessment and data extraction the customised forms were found to be applicable to clinical trials and not the quality appraisal and extraction of text applicable to non-clinical trials. This review identified papers that were of a qualitative approach, in addition to text and opinion papers. It was therefore deemed necessary to utilise the Joanna Briggs Critical Appraisal Tools to undertake quality assessment (www.joannabriggs.org). The data extraction forms were developed with reference to the population, concept and context of this review and outcomes were documented in a tabulated format. The initial search identified 5241 Papers (following duplicate removal).

A full text review was subsequently undertaken by DMcG and JGL which identified 30 papers that addressed the aims of the review. Any conflict that arose was addressed by discussion between DMcG and JL. The final papers represented a broad review of international material. The findings of the review are based on evidence which is considered to be of low quality (level 4 studies) (Appendix 2, 3).

An exploration of the grey literature identified key National and International Neonatal Palliative Care Guidelines and Position Statements. Additionally, reviewing the reference

lists of relevant subject papers and direct contact with professional organisations supported the retrieval papers.

Summary of the evidence

The findings of the review are based on evidence which is considered to be of low and very low quality. Most studies (n=15) in this review were retrospective and prospective chart reviews which are reliant on adequate documentation in individual charts. The remaining papers were qualitative (n=8), cross sectional studies (n=4) and survey (3).Therefore, from a quality assessment perspective the majority of the studies were graded as low or very low using the GRADE levels of evidence (Schunemann et al. 2011) (Appendix 2) The majority of guidelines and position papers were also based on evidence which is considered to be of low quality. A systematic review by Mancini et al. (2014) and the recently published NICE guideline NG61 (2016) support the standardisation of guidance provision and the development of clinical guidelines on perinatal palliative care. The Agree 11 instrument was applied to each guideline and position statement. The guidelines and position statements are presented in chapter 6. The following chapters 3, 4 and 5 present the evidence identified to support perinatal palliative care for the fetus and neonate: A) perinatal palliative care, B) pain and symptom management and C) barriers and facilitators to perinatal palliative care.

Chapter 3

Perinatal Palliative care

This chapter provides evidence to support the view that perinatal palliative care is an emerging speciality and model of care dedicated to the needs of the fetus and neonate with a life limiting condition (Wool 2011). Empirical research was lacking in relation to perinatal palliative care and the impact a perinatal palliative care programme can have on end of life care; suggesting palliative care to the neonate is somewhat ad hoc. The findings of the review are based on evidence which is considered to be of low and very low quality. Most studies (n=21) in this chapter were of a retrospective or/and prospective chart review (n=14). The remaining papers were qualitative (n= 4), cross sectional studies (n=1) and survey style (2). The country of origin was as follows: USA (n=13), UK (n=3), Australia (n=1), Canada (n=2), Portugal (n=1), The Netherlands (n=1).

Catlin and Carter (2002) describe a perinatal palliative care protocol that was developed following a Delphi consensus which included 93 locations in the USA and 4 outside of the USA. This study provides a description of palliative care, categories of candidates for neonatal palliative care, planning and education required to implement the protocol, family centred care considerations, ventilator removal, pain and symptom management of the neonate, family follow up care and staff support.

Perinatal palliative care programmes do not increase the incidence of withdrawal of life support or overall death in the NICU (Younge et al. 2015). They do however lead to fewer resuscitation efforts and life sustaining treatments for sick and dying neonates (Cortezzo et al. 2014). This is in contrast to NICU's where perinatal palliative care programmes are not in place and infants may die while on ventilator support (Moura et al. 2011). Do Not Resuscitate orders were more frequent among a cohort of infants where the clinician providing palliative care for an infant at end of life had activated an electronic palliative order set (Younge et al. 2015)

Table A

Summary of evidence for perinatal palliative care

Author Year Country	Aim of paper	Population	Methodology	Results	Limitations	Classification of evidence level	Key points
Australia Ahern K. (2013) What Neonatal Intensive Care Nurses Need to Know About Neonatal Palliative care	To identify topics that HCP's who work in the field of neonatology consider to be priorities for a professional development programme in neonatal Palliative care	276 Nurses and Midwives (NICU) And 26 international HCP's NICU and Palliative care	Delphi Technique	97% of participant felt that the programme should be based on a palliative care framework. Include general clinical practice guidelines, medication list for neonatal pain and symptom relief	Delphi study and three rounds of data collection- low response rate of the NICU nurses was (19%)	3C	23 High priority topics were identified to include: Care of the dying infant- physical needs. Assessing and managing pain in the dying infant. How to provide emotional support to grieving parents.
Canada Drolet, C Roy, H. Laflamme J., Marcotte ME. (2015) Feasibility of a comfort care protocol using oral transmucosal medication delivery in a palliative neonatal population.	To determine the feasibility of implementing a standardized comfort care protocol using Oral Transmucosal Medication (OTM) in dying neonates	12 Neonates/ Nurses satisfaction was assessed with a questionnaire	Prospective Observational Study	Each neonate was assessed for pain and discomfort using the N-PASS scale (Neonatal Pain, Agitation and Sedation scale). The protocol was judged as feasible and safe. No adverse events were reported. Apnoea was reported in 7 patients- no intervention was recorded.	Adherence was limited because of too frequent evaluations and misunderstanding the protocol Missing data is reported. Authors suggest a second training session at midpoint in the study would have improved protocol understanding.	3C	The oral transmucosal route (OTM) is feasible and safe. 17/18 nurses said they would recommend this protocol to other institutions

Canada Harlos M.S., Stenekes S Lambert D Hohl C Chochinov H M (2012) Canada Intranasal Fentanyl in the palliative care of newborns and infants	To describe the experience using intranasal fentanyl in the management of distress in a case series of 11 dying neonates	Retrospective Chart review	58 consecutive referrals of neonates	Intranasal fentanyl was used in 11 patients, was tolerated well. In most cases laboured breathing and restlessness settled after fentanyl was administered.	Retrospective study- potential for bias. Small study number.	3C	Symptom management in a non- invasive manner Can be utilised in a variety of settings.
Portugal Moura, H Costa V Rodrigues M Almeida F Maia T Guimaraes H. (2011) End of life in the neonatal intensive care unit.	To examine end of life care given to neonates and their families in the NICU and the changes that had occurred one decade later.	256 charts	Retrospective Chart review	Two cohorts 1992-1995 and 2002-2005 Key points in the 2nd cohort Use of the neonatal pain scale More effective pain and distress relief No clear written orders to discontinue life support or withhold resuscitation.	Dependent on documentation - Infant charts.	4C	At end of life some neonates still receive curative and aggressive treatment. 1.Therapeutic activities 2.Pain and distress relief 3.Family support 4.Decision making 5.Parental presence during infant death

The Netherlands Bijma, H., Schoonde-rwaldt, E.M Van der Heide, A., Wildschut H.I.J., Van der Maas, PJ., Wladimir-off, J.W. (2004) The Netherlands Ultrasound diagnosis of fetal anomalies: an analysis of perinatal management of 318 consecutive pregnancies in a multidisciplinary setting	To analyse the perinatal management decisions made following the prenatal diagnosis of fetal anomaly	318 pregnancies	Retrospective collection of data from obstetric and paediatric records.	In the majority of cases the perinatal team did not plan neonatal management before birth, not linking obstetric and neonatal management to each other.	Generalisation – one centre in The Netherlands Outcome of the multidisciplinary meetings, not the process to reach a conclusion in individual cases	4D	Generalisation – one centre in The Netherlands Outcome of the multidisciplinary meetings, not the process to reach a conclusion in individual cases
UK Branchett, K Stretton, J. (2012) Neonatal Palliative and end of life care: What parents want from professionals	To determine parents experiences in relation to end of life and palliative care and utilise this information to inform practice	57 respondents; 54 mothers 3 Fathers	Online bereavement support community- emails, comments and feed- back at study days	Eight themes: 1. Creating memories 2. Empathy 3. Time and space 4. Practical help and understanding 5. Sensitivity 6. Communication with parents 7. Accurate record keeping 8. communication	No ethics. Scoping exercise Responses are from questions asked on a support group forum that bereaved parent's replied to.	4D	Narratives from bereaved parents. Experiences both positive and negative are remembered by parents.

UK Breeze, A. C. Lees, C. C. Kumar, A. Missfelder-Lobos, H. H. Murdoch E.M. (2007) Palliative care for prenatally diagnosed lethal fetal abnormality	To offer palliative care to parents following an antenatal diagnosis of a lethal fetal abnormality	20 antenatal women with a pregnancy complicated by lethal fetal abnormality	Prospective study with 20 pregnant women with a pregnancy complicated by lethal fetal abnormality	8 parents chose palliative care. Clearly documented plans were developed. Consultant neonatologist attended at the birth.	Small study NICU UK	3C	Proposed framework with 8 Actions and benefits outlined.
UK Chaudhary R., Silwal, A., Gupta, A., Kelsall, W. (2012) Drugs used for comfort care after withdrawal of intensive treatment in tertiary neonatal units in the UK	To identify drugs used for comfort care after withdrawal of intensive treatment in tertiary neonatal units in the UK.	Nursing/ Medical staff in neonatal units in the UK	Structured questionnaire Telephone Survey Neonatal units in the UK	Information received from 94% of tertiary referral NICU's in the UK. 44 (98%) units used sedatives and analgesia to alleviate pain and discomfort. Morphine was used- there were wide variations in dose. The second most commonly used drug was midazolam n=11 (24%)	Structured questionnaire may have prohibited some information in relation to drugs used for PPC	3D	Wide variation in therapeutic management of the neonate during palliative care. Drugs used and their dosages should be clearly defined to provide effective analgesia and sedation.

USA Calhoun, CC Napolitano P., Terry, M., Bussey, C., Hoeldtke, N. (2003) Comprehensive care for the family of the fetus with a lethal condition	To describe the experience of providing a programme of structured interdisciplinary care for the families of foetuses prenatally diagnosed with a lethal fetal abnormality	33 women with a clearly diagnosed lethal fetal abnormality during pregnancy	Qualitative prospective study where a Perinatal hospice programme was offered to 33 antenatal women with a pregnancy complicated with lethal fetal abnormality	28 (85%) women participated in the perinatal hospice programme. 11/28 (39%) had an intrauterine fetal death and 17/28 (61%) delivered a live born infant. Babies born alive lived for 20 minutes to 2 months.	Small sample size	3C	Antepartum consultation and planning with the neonatal team. Importance of Comprehensive, multidisciplinary, individualised care informed choice.
USA Catlin, A Carter, B. (2002) Creation of a Neonatal End of Care Palliative care Protocol	To create a neonatal end - of -life palliative care protocol	101 participants Health care professional with expert knowledge 93 locations in the USA and 4 outside USA	Delphi Methodology 4 rounds of analysis	Detailed description of palliative care to include education, planning, categories of neonates for PCC, community/ tertiary centre, cultural spiritual and practical needs, ventilator withdrawal, pain and symptom management. Family follow up Staff support	Delphi method utilised- 95 % retention rate over 4 rounds. Email and internet limitations	3B	Dedicated PPC programme allows consistency of approach in caring for new born infants with a life limiting condition. Teaching tool

USA Clarke, F.N. Smith, S.L (2004) Palliative/End of Life care in the newborn intensive care unit	To determine the presence of a palliative care /end of life care programmes at 2 selected NICU's	139 Registered nurses and Neonatal nurses	Retrospective survey	97% reported that a palliative care programme would be beneficial in the NICU. 66% had no education in relation to palliative care while 72% cared for infants at end of life	Two NICU's in the USA	3D	Provision of palliative care is less challenging for experienced nurses. Mentorship of less experienced nurses
USA Cortezzo, D.M., Sanders, M.R., Brownwell, E.A., Moss, K. (2014) End –of-life care in the Neonatal Intensive Care unit: Experiences of Staff and Parents.	"To determine the perception of end of life care practices and experience with infants who have died in the NICU among neonatologists, advance practice nurses and parents"	Nurses n=184; Advance practice nurses n=40; Neonatologists n= 14 Parents n= 28 (no palliative care team)	Descriptive exploratory cross-sectional study-survey utilised	Most practitioners reported that they felt comfortable delivering end of life care. Conflict between parents and team members perceptions of pain and comfort during end of life care	Small sample size Accuracy of self-reporting Survey was pilot tested but not validated Poor response rate 50% for practitioners and 40.8% for NICU nurses. Response rate for parents was 30.4%.	3C	Areas identified for improvement Education in palliative care, Consistency among healthcare professionals, early communication with families, Bereavement support for families and staff, reflection for staff.

USA Currie, E.R Christian, B.J. Hinds, P.S. Perna, S.J. Robinson, C. Day, S. Meneses, K. (2016) Parents perspectives of neonatal intensive care at end of life.	To explore parent experiences of end of life care, NICU hospitalization and Palliative care in relation to their infants NICU experience	10 parents to include 7 mothers 3 Fathers	Descriptive qualitative study	Primary theme- Life and death in the NICU. Sub themes were 1. Ups and downs of parenting in the NICU 2.Decision making challenges in the NICU 3. Parent support	Recall of events that occurred in the past may contain some inaccuracy. Fathers experiences limited due to inclusion of three fathers only. Small sample size n=10	3C	Being a parent in the NICU was very important. NICU nurses facilitate parenting by teaching parents how to interact with their critically ill infant and act as a source of support. Barriers to parenting such as communication conflicts between health care providers, financial burden. Palliative care was valued.
USA Falck A.J. Moorthy S. Hussey-Gardner, B. (2016) Perceptions of Palliative Care in the NICU	To examine the provision of palliative care as experienced by mothers and health care professionals of NICU infants with life threatening illnesses	6 mothers and 5 nurses identified by mothers in the study and 1 physician, also identified by mothers in the study	Qualitative descriptive study Semi structured interviews	Five themes emerged: 1. Communication 2. Privacy 3. Continuity of care and relationship building 4. Maternal knowledge seeking 5. Emotional turmoil	Exclusion of fathers, Generalizability, While mothers interviewed were coping with a baby with a life limiting illness all babies were well at the time of interview.	3C	Conflicting opinion among mothers and staff re privacy and infant monitoring.

USA Leong Marc Aurele, K Nelesen, R. (2013) A five year review of referrals for perinatal palliative care	A Five-Year review of Referrals for perinatal Palliative care (referred to a home perinatal palliative programme)	66 women	Exploratory retrospective chart review	Hospice care Average gestation at referral was 27/40. Most women had a birth plan and chose palliative care. 41 infants were live-born. 12 live-born infants lived past 72 hours and were admitted to the hospice.		4D	1/3 of women had a meeting with the palliative care team 1-2 occasions prior to delivery; earlier referral is indicated to support women and provide a comprehensive service.
USA Matthews AL O'Connor Van (2007) Administration of comfort medication at end of life in neonates: Effects on weight.	To identify if a relationship exists between a neonates weight and receipt of comfort medication between four hours prior to planned withdrawal of ventilation and death.	171 neonates	Retrospective chart review.	Neonates who weighed < 800g were less likely to receive comfort medication than heavier babies	Convenience sample One geographic location	4D	End of life care for smaller neonates in relation to comfort medication requires further research

USA Parravicini E Lorenz JM (2014) Neonatal outcomes of foetuses diagnosed with life limiting conditions when individualised comfort measures are proposed	To describe the neonatal outcomes of a case series of infants diagnosed prenatally with a life limiting condition when individualized comfort measures were offered when appropriate	49 infants	Retrospective descriptive consecutive case series	Prenatal diagnosis was confirmed in 45 neonates. Discrepancies between prenatal and postnatal diagnosis were identified in three cases. The case studies also identified the difficulty in estimating time of death in relation to birth.	Small number of cases.	4C	Antenatal diagnostic accuracy is the principle determinant of outcomes
USA Partridge JC Wall SN (1997) Analgesia for dying infants whose life support is withdrawn or withheld.	To determine the frequency of opiate administration at the time of life support discontinuation in neonates	121 infants	Retrospective chart review	Opioid analgesia was provided to 84% of infants as their life support was withheld or withdrawn. Extremely low birth weight infants were less likely to receive opiate analgesia.	Retrospective chart – reliance on chart documentation Bias	4C	The development of clinical guidelines for opiate administration in the dying neonate is required to improve standards of care based on a trilogy of physiologic data, physician beliefs and physician/parental attitudes in relation to neonatal pain

USA Samsel C Lechner BE (2015) End of life care in a regional level IV neonatal intensive care unit after implementation of a palliative care initiative	The implementation of a palliative care initiative and end of life care	106 infants	Retrospective and prospective chart review	The introduction of a palliative care programme is correlated with an increase in palliative medicine during the final 48 hours of the infant's life.	Bias in relation to the prospective and retrospective nature comparing two epochs.	4C	No separate PPC team. Interventions developed within the NICU.
USA Younge, N Smith B Goldberg R Brandon DH Simmons C Cotton M Bidegain M (2015) Impact of a palliative care program on end of life care in a neonatal intensive care unit.	To evaluate changes in end of life care following the initiation of a palliative care programme in a neonatal intensive care unit	(Era 1)82 infants RIP (Era 2)68 infants RIP	Retrospective study	The study compared infant deaths prior to and following implementation of a Palliative Care programme. Morphine use was similar 88%vs 81% P=0.17; Benzodiazepine use increase following implementation of the programme (Era 2) 26%vs 43% p=0.03 Do-not-resuscitate orders and Family meeting were increased among Era 2 infants with activate palliative care orders.	Exclusion of infants who died within 24 hours following birth (study design) Did not include an evaluation of the clinical response to benzodiazepines at end of life which is in the medication guideline.	4C	Palliative care programme resulted in Increased end- of -life family meetings and Increased use of benzodiazepines Adherence to guidelines Improved communication

USA Zimmerman K Hornik CP Ku L., Watt K Laughon MM Bidegain M Clarke R H Smith B.P (2015) Sedatives and analgesics given to infants in neonatal intensive care units at end of life	To describe the administration of sedatives and analgesics at end of life in a large cohort of infants in neonatal care units	19, 726 infants who died from 1997 to 2012 in 348 neonatal intensive care units	Retrospective study	Increasing gestational age, increasing post-natal age, mechanical ventilation, inotropic support were associated with administration of analgesia or sedatives	Collection of data is limited by written information in the infants chart on the day of death.	4C	Infants with lower birth weight (<800 g) are less likely to receive comfort drugs at end of life

There were a number of components identified by Samsel & Lechner (2015) that have a role to play in the provision of quality end of life care. These include written clinical guidelines, the presence of an electronic palliative order set, appropriate pain management and the opportunity for parental bonding. Post implantation of a palliative care intervention in the NICU there was a re direction of care and increased palliative medication usage, with statistically significant findings (P= 0.01 and P= 0.02, respectively). Moura et al. (2011) reports on the management of end of life care over a 10 year period. The authors were interested in five aspects of care which included decision making and pain relief. This retrospective chart review identified that while the NICU had initiated more withdrawal of therapeutic activities and more pain and distress medication, a significant number of infants had received invasive ventilator support, antibiotic therapy and inotropic agents at end of life.

A number of studies report that if Perinatal Palliative care is to be practised effectively it requires an interdisciplinary team of professionals from the fields of nursing, midwifery, obstetricians, paediatricians, fetal medicine, social work, pharmacy, physiotherapy, chaplaincy (Calhoun 2003; Wool 2013., Williams Reade 2015., Falck et al. 2016).

Perinatal Palliative care- antenatal period

The literature addressed perinatal palliative care following an ante natal diagnosis (Calhoun et al. 2003., Bijma et al. 2004., Breeze et al. 2006., Marc- Aurele & Nelesen, 2013). Advances in ultrasound technology have facilitated early prenatal diagnosis of infants with a life limiting condition. Many infants with life limiting conditions can be identified during the routine 18-20 week anomaly scan (Breeze et al. 2007). Pregnancy complicated by fetal anomaly presents challenges for parents and clinicians. Parents rely on clinicians to provide information in relation to ongoing support and care during the pregnancy, birth and immediate post-natal period. Leong Marc-Aurele & Nelesen (2013) suggests that women agreed on average to perinatal palliative care services about 14 days following referral from their obstetrician. A birth plan which is completed during the antenatal period by women in consultation with their obstetrician and midwife is supportive of the philosophy of perinatal palliative care (Calhoun et al. 2003., Leong Marc-Aurele & Nelesen , 2013). Breeze et al. (2006) describe a proposed framework for perinatal palliative care which provides an individualised plan of care for

parents with a prenatal diagnosis of an infant with a life limiting condition. Again the birth plan was clearly documented with the multi-disciplinary team involved and parents had an opportunity to revise their birth plan at any stage.

The importance of an accurate antenatal diagnosis of an infant with a life limiting condition and subsequent confirmation of diagnosis following birth was described in the literature. To ensure consistent clinical care and management, a consultant neonatologist was present during delivery. Parravicini & Lorenz (2014) also refer to the neonatology team present at the birth, whether there has been a confirmed diagnosis of a life limiting condition or not. The final management plan is dependent on the post-natal confirmation of the prenatal diagnosis. This is in contrast to Bijma et al. (2004) who found that while obstetric management was satisfactory, the perinatal team did not attune obstetric and neonatal management to each other, with a resultant inconsistency of perinatal palliative care provision. Calhoun et al. (2003) further emphasises the importance of antepartum consultation and planning meetings with the neonatology team. This prenatal consultation ensures that the neonatology staff and parents are thoroughly informed of the diagnostic findings and a plan of care for birth is documented antenatally. *Perinatal hospice care* is described by Calhoun et al. (2003) whereby comprehensive, multidisciplinary, individualised support is offered to parents from the time of pregnancy diagnosis with a life limiting condition, through birth and the postpartum period (Table 2). Both Calhoun et al (2003) and Breeze et al. (2007) (Table 3) provide information on comprehensive frameworks that support perinatal palliative care from the point of diagnosis during the antenatal period. Perinatal palliative care frameworks clearly documented in the maternal obstetric notes ensure consistent management in clinical practice by all healthcare professionals. Plans can be individualised, revised and agreed by parents, obstetrics, fetal medicine, midwives and neonatology, aiming to optimise outcomes, both physical and psychological in the provision of family -centred care (Breeze et al. 2007).

Parravicini and Lorenz (2014) suggest diagnostic accuracy prenatally as the main determinant of outcomes, in relation to infant survival and length of life. The authors caution that in cases where the prenatal diagnosis or prognosis is not certain, the birth plan reflects the confirmation of a life limiting condition following birth. The authors also identify the difficulty in estimating time to death following birth. While early demise was anticipated for some infants in the study, longer survival is possible, therefore, it is important to discuss with

parents comfort care management for their infant. This is further supported by Leong Marc-Aurele & Nelesen (2013) who following a five year review of referrals for perinatal palliative care (n=66) found that while 62% (n=41) of deliveries resulted in a live born infant, 18% (n=12) of infants survived more than 72 hours.

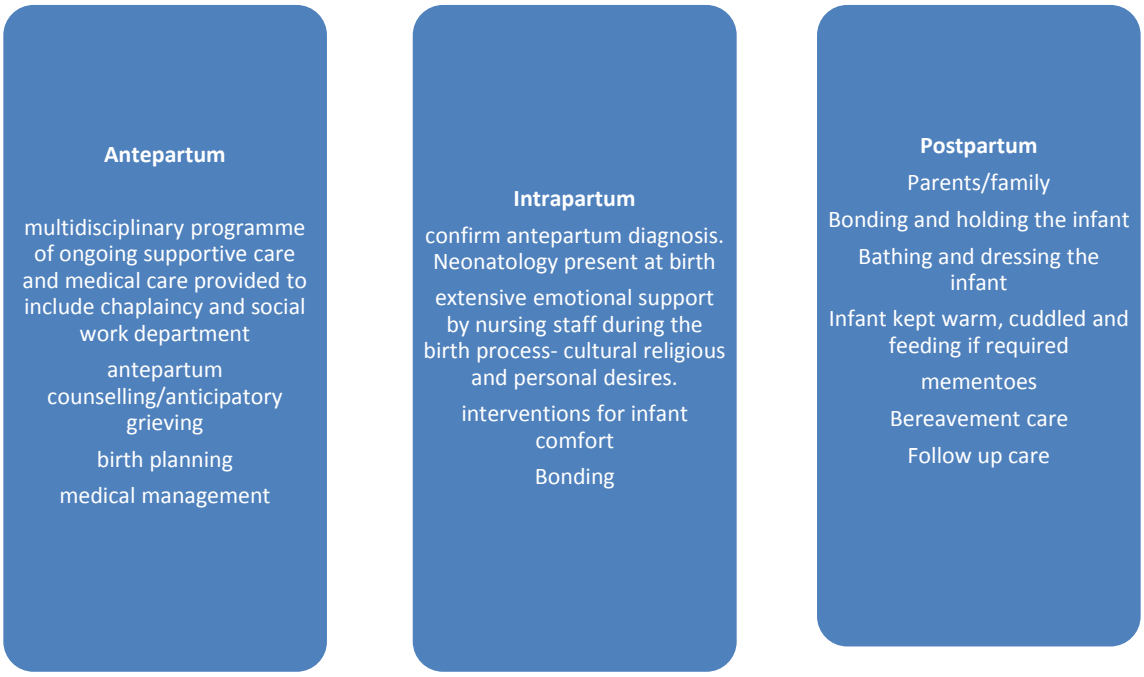


Table 2 Calhoun et al. (2003) "Perinatal Hospice "programme.

Action	Benefit
Multidisciplinary joint counselling- fetal medicine specialist, neonatologist, midwife counsellor	Agree diagnosis and prognosis
Clearly documented plan for delivery and perinatal period- mothers obstetric chart, copy for parents and referring centre	Key information available for all staff- avoids repeated discussions with parents
Liaison with community partners supporting palliative care- GP, hospice	Supports communication and planning
Liaison with chaplaincy, other faiths, religions	Parents' wishes at time of baby's death can be discussed and organised.
Discussion of case at multidisciplinary meetings, ongoing discussion and liaison to referring centres	Provides a forum for ongoing discussion
Offer parents support group information. Provide parents with a specialist second opinion, if requested.	Parents have full available information, independent of the hospital health care team
Senior neonatologist attends the birth	Avoids inappropriate resuscitation and intervention by junior staff. The attendance of the senior doctor to confirm diagnosis and outlook acts as a reassurance for parents and staff
Postnatal follow with key obstetric, neonatal and midwifery staff.	Debriefing for parents at a suitable time frame following the birth of their baby. Post mortem result, further investigations if required.

Table 3 Breeze et al. (2007) Proposed framework for perinatal palliative care service pp. f57

Newborn infants eligible for perinatal palliative care

Several papers identified infants with a life limiting condition where palliative care is described as the most appropriate form of care. Congenital malformations, Genetic syndromes and complications of prematurity, Trisomy (13 and 18), renal tract abnormality and major skeletal dysplasia; central system abnormalities to include anencephaly, heart problems i.e. hypoplastic left heart syndrome, new-born's not responding to intensive care treatment and where an infant's condition is deteriorating despite all interventions made available (Catlin & Carter, 2002., Calhoun et al. 2002., Breeze et al. 2007., Leong Marc- Aurele, 2013., Paravicini & Lorenz 2014., Samsel & Lechner, 2015., Young et al. 2015),

Parenting a neonate receiving end of life care

A cross sectional study by Cortezzo et al. (2014) describes end of life care in the neonatal intensive care unit where a palliative care team is not in place. Interestingly all neonatologists and advanced practitioners, and most of the nursing staff (88%, n = 66) described that they felt the baby in their care was comfortable during end of life care. However, only half of the parents described their baby as comfortable (57.1%, n =4). A definite palliative care team would provide consistency of care and ensure accurate pain and symptom management. Family meetings to discuss end-of –life palliative care were more frequent when an activated palliative care protocol was in place. (Young et al. 2015)

The views of mothers and fathers who parented a neonate who received palliative care are important. The themes of communication, privacy, and continuity of care, maternal knowledge seeking and emotional turmoil are described by Falck et al. (2016) following interviews with mothers of neonates with life threatening illnesses. Branchett & Stretton (2012) sought to determine the experiences of parents of palliative and end of life neonatal care. Questions were posted on a parents support website and following an overwhelming response further research was planned. While there are limitations to this paper and the quality is of a low level, rich narratives emerged that are worthy of inclusion in this review. The key themes that emerged from the survey which included 57 parents (54 mothers and 3 Fathers) are:

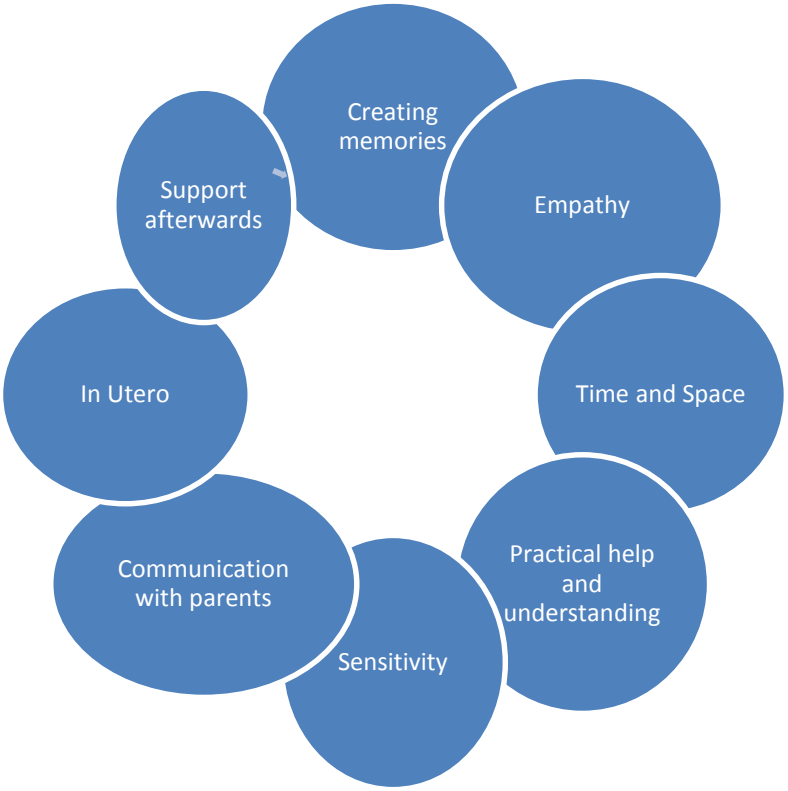


Table 4 Branchett, K. and Stretton, J. (2012) Neonatal, Palliative and End-of –life-care: what parents want from professionals?

Communication with families and increased frequency of meetings at end of life in the NICU was identified by Younge et al. (2015) as a positive outcome following the impact of a perinatal palliative care programme. Communication was an overarching theme that emerged from a study by Stenekes et al. (2014). Good communication was crucial to the effective and efficient perinatal palliative care process. It facilitated the involvement of all team members and the development of a cohesive plan with the family. This ensured that upon arrival of a woman in labour to the hospital, the plan of care was clear to all staff. Speaking to parents about the introduction of palliative care is recognised as a challenging conversation. It is beneficial to hold conversations in a quiet, seated, private area allowing sufficient time for the conversation to take place to include questions (Caitlin & Carter 2002). Health professionals should be mindful of the language skills utilised in relation to end of life care i.e. "withdrawal of care" conjures negative components as opposed to "we will offer the best medical care for your baby" (Catlin & Carter, 2002). The re direction of care from active curative measures which may involve painful interventions and aggressive treatments, when appropriate, is

important (Samsel & Lechner, 2015) and improves the quality of life of the dying neonate. Comfort care involved the establishment of an individualized plan of care with a focus on family-infant bonding, warmth provided by kangaroo care or swaddling, nutrition and hydration and management of respiratory distress or pain and discomfort (Parravicini & Lorenz, 2014).

The importance of informed collaboration among the multidisciplinary team as the best approach to perinatal palliative care (Ahern 2013., Young et al. 2015., Falck et al. 2016) was identified. Interestingly, while Samsel & Lecher (2015) introduced a palliative care initiative for neonates, the hospital did not have a separate perinatal palliative care team. The authors allude to the embeddedness of this initiative within existing service provision to impart better quality end of life care. This avoided the associated challenges of integrating a new palliative care team into the NICU.

Privacy in the NICU

Physical space and privacy in the NICU was addressed in the literature (Caitlin & Carter 2002). The NICU is a high technology environment with many units embracing the "nightingale style" layout. This facilitates an open view of all babies by health care professionals. While some mothers appreciate this NICU layout, others mothers feel it is a barrier to privacy during end of life care. Falck et al. (2016) found that while mothers desired a degree of privacy, they also appreciated the open room NICU layout, as this provided safety, security and comfort because multiple care providers were nearby at all times. In situations where it may be necessary to move an infant from the NICU to a quieter room it is important that staff provide continuity of care (Caitlin & Carter 2002). Similarly, health care professionals valued the open plan environment as it provided an open view of all infants simultaneously, in addition to proximity of staff in the event of an emergency.

Spirituality and end of life care to the neonate

The importance of religion and prayer was described by Currie et al. (2016) as a major source of support at end of life in the NICU. Parents relied on their spirituality to guide them during the emotionally stressful period while caring for their infant (Moura et al. 2011). The

development of dedicated Perinatal Palliative Care would facilitate the transition from end of life care and provide necessary resources during the bereavement period (Cortezzo et al. 2014). Calhoun et al. (2002) describes that following the demise of an infant at the hospital, care of parents did not end. Parents were provided with bereavement support for the year following the death of an infant. A sympathy card, signed by staff was sent to parents and a dedicated person from the perinatal bereavement team contacted parents after discharge and again at 3, 6 and 12 months following the loss of their baby. Additionally, parents were invited to participate in a parent support group, facilitated by the nursing and social work department.

Conclusion

Perinatal palliative care is an evolving strand of palliative care. Despite a lack of empirical research, available evidence to date suggests that perinatal palliative care programmes directed at improved care to the fetus and neonate with a life limiting condition is valued among parents and health care professionals. Palliative care is holistic, interdisciplinary and family centred with a focus on enhancing the quality of life of the fetus and neonate (Falck et al. 2016) from the point of diagnosis to end of life.

This chapter highlighted the importance of prenatal palliative care following an antenatal diagnosis (Calhoun et al. 2003., Bijma et al. 2004., Breeze et al. 2006., Marc Aurele & Nelesen 2013). The literature identified infants presenting with life limiting conditions and these conditions were listed. The NICU and the provision of perinatal palliative care programmes were discussed. The literature also identified the importance of communication, both with parents and within the multidisciplinary team. The following chapter will explore the evidence in relation to pain and symptom management of the neonate at end of life.

Chapter 4

Pain and Symptom management

This chapter seeks to provide a summary of evidence in relation to medication utilised in the therapeutic management of the neonate during perinatal palliative care. Again empirical research was lacking with papers available of low or very low quality. There was one prospective observational study, n=1; the majority of papers presenting the results of a retrospective chart review n= 6; retrospective and prospective chart review n=1; and one survey, n=1. In total 9 papers were identified that discussed analgesics and sedatives at end of life. The country of origin for most paper was the USA n=5; with Canada n=2 and one paper from the United Kingdom and Portugal, respectfully.

The goal of perinatal palliative care is to prevent and relieve suffering for the neonate at end of life (Ferrell 2016). A paper by Catlin & Carter (2002) presents a comprehensive plan for delivering perinatal palliative care. The paper discusses pharmacological and non-pharmacological pain relief. Relevant medication referred to in the protocol includes pain relief, relief for laboured respirations or seizures. It is suggested that medication doses are sufficient to provide comfort and prevent air hunger. Antibiotics and vasopressor drugs are discontinued. Medication doses are not included; however, the authors refer the reader to standard reference resources. Non pharmacological pain relief is referred to in the form of a calm environment with noise reduction, infant massage, kangaroo mother care. A Delphi consensus informed the palliative care protocol.

Table B

Summary of evidence in relation to pain and symptom management

Author/year Country Title	Aim of paper	Population	Methodology	Results	Limitations	Classificat-ion of evidence level	Key points
UK Chaudhary R., Silwal, A., Gupta, A., Kelsall, W. (2012) Drugs used for comfort care after withdrawal of intensive treatment in tertiary neonatal units in the UK.	To identify drugs used for comfort care after withdrawal of intensive treatment in tertiary neonatal units in the UK	Nursing/ Medical staff in neonatal units in the UK	Structured questionnaire Telephone Survey Neonatal units in the UK	Information received from 45 (94%) of tertiary referral NICU's in the UK. 44 (98%) units used sedatives and analgesia to alleviate pain and discomfort. Morphine was used- there were wide variations in dose. The second most commonly used drug was midazolam n=11 (24%)	Structured questionnaire may have prohibited some information in relation to drugs used for PPC	3D	Wide variation in therapeutic management of the neonate during palliative care. Drugs used and their dosages should be clearly defined to provide effective analgesia and sedation.

Canada Drolet, C Roy, H. Laflamme J Marcotte ME. (2015) Canada Feasibility of a comfort care protocol using oral transmucosal medication delivery in a palliative neonatal population.	To determine the feasibility of implementing a standardized comfort care protocol using Oral Transmucosal Medication (OTM) in dying neonates	12 Neonates/ Nurses satisfaction was assessed with a questionnaire	Prospective Observational Study	Each neonate was assessed for pain and discomfort using the N-PASS scale (Neonatal Pain, Agitation and Sedation scale). The protocol was judged as feasible and safe. No adverse events were reported. Apnoea was reported in 7 patients- no intervention was recorded.	Adherence was limited because of too frequent evaluations and misunderstanding the protocol Missing data is reported. Authors suggest a second training session at midpoint in the study would have improved protocol understanding.	**3C**	The oral transmucosal route (OTM) is feasible and safe. 17/18 nurses said they would recommend this protocol to other institutions
Canada Harlos M.S., Stenekes S Lambert D Hohl C Chochinov H M (2012) Intranasal Fentanyl in the palliative care of new-born's and infants	To describe the experience using intranasal fentanyl in the management of distress in a case series of 11 dying neonates	Retrospective Chart review	58 consecutive referrals of neonates	Intranasal fentanyl was used in 11 patients, was tolerated well. In most cases laboured breathing and restlessness settled after fentanyl was administered.	Retrospective study- potential for bias. Small study number.	4D	Symptom management in a non-invasive manner Can be utilised in a variety of settings.

USA Matthews AL O'Connor Van (2007) Administration of comfort medication at end of life in neonates: Effects on weight.	To identify if a relationship exists between a neonate's weight and receipt of comfort medication between four hours prior to planned withdrawal of ventilation and death.	171 neonates	Retrospective chart review.	Neonates who weighed < 800g were less likely to receive comfort medication than heavier babies	Convenience sample One geographic location	4D	End of life care for smaller neonates in relation to comfort medication requires further research
USA Partridge JC Wall SN (1997) USA Analgesia for dying infants whose life support is withdrawn or withheld.	*To determine the frequency of opiate administration at the time of life support discontinuation in neonates*	*121 infants*	*Retrospective chart review*	Opioid analgesia was provided to 84% of infants as their life support was withheld or withdrawn. Extremely low birth weight infants were less likely to receive opiate analgesia.	*Retrospective chart – reliance on chart documentation Bias*	4D	*The development of clinical guidelines for opiate administration in the dying neonate is required to improve standards of care based on a trilogy of physiologic data, physician beliefs and physician/parental attitudes in relation to neonatal pain*

USA Zimmerman K Hornik CP Ku L., Watt K Laughon MM Bidegain M Clarke R H Smith B.P (2015) Sedatives and analgesics given to infants in neonatal intensive care units at end of life	To describe the administration of sedatives and analgesics at end of life in a large cohort of infants in neonatal care units	19, 726 infants who died from 1997 to 2012 in 348 neonatal intensive care units	Retrospective study	Increasing gestational age, increasing post-natal age, mechanical ventilation, inotropic support were associated with administration of analgesia or sedatives	Collection of data is limited by written information in the infants chart on the day of death.	4D	Infants with lower birth weight (<800 g) are less likely to receive comfort drugs at end of life
USA Catlin, A Carter, B. (2002) USA Creation of a Neonatal End of Care Palliative care Protocol	To create a neonatal end - of -life palliative care protocol	101 participants Health care professional with expert knowledge 93 locations in the USA and 4 outside USA	Delphi Methodology 4 rounds of analysis	Pain and symptom management- IV access for symptom relief Pharmacy support- prepare drugs – buccal, IV/suppository Narcotic/non- narcotic analgesia. Standard references are available	Delphi method utilised- 95 % retention rate over 4 rounds. Email and internet limitations Medication dose not suggested in the protocol	2B	Dedicated PPC programme allows consistency of approach in caring for new born infants with a life limiting condition. Standard references are available- medication

USA Samsel C Lechner B E (2015) End of life care in a regional level IV neonatal Intensive care unit after implementation of a palliative care initiative	The implementation of a palliative care initiative and end of life care	106 infants	Retrospective and Prospective chart review	The introduction of a palliative care programme is correlated with an increase in palliative medicine during the final 48 hours of the infant's life. Palliative medicine increased from 36% pre-implementation to 64% post implementation (p=0.02)	Retrospective and Prospective chart review Authors were involved in patient care	3C	No separate perinatal palliative care team

Portugal Moura, H Costa V Rodrigues M Almeida F Maia T Guimaraes H. (2011) End of life in the neonatal intensive care unit.	To examine end of life care given to neonates and their families in the NICU and the changes that had occurred one decade later	256 charts	Retrospective chart review	Two cohorts 1992-1995 and 2002-2005 Key points in the 2nd cohort- Use of the neonatal pain scale- 71 (76.3%) and 54(58.1%) infants received opioids and sedatives respectively	Dependent on information in the charts	3C	Neurobiology and pain relief Infants vulnerable to many procedures.

Medication and the neonate at end of life

Medications referred to in several papers include the following: Opioids (Partridge & Wall 1997; Chaudhary et al. 2012; Drolet et al. 2016); benzodiazepines (Chaudhary et al. 2012; Drolet et al. 2016); paracetamol, sucrose, hyoscine patch (Chaudhary et al. 2012); Scopolamine, Robinul (Drolet et al. 2016) Fentanyl IN (Harlos et al. 2013)., central alpha-2 agonists (Zimmerman et al. 2015) and neuromuscular agents, anticonvulsants (Zimmerman et al. 2015), anticholinergics and diuretics (Catlin & Carter 2002) and morphine (Catlin & Carter 2002) who suggest that it may be more appropriate to administer morphine where an infant exhibits shortness of breath, nasal flaring or grunting noises. There is a variation in morphine administered to achieve infant comfort (Chaudhary et al. 2012; Samsel & Lecher 2015., Zimmerman et al. 2015). Midazolam was reported as the 2nd most commonly used drug (Partridge & Wall 1997; Chaudhary et al. 2012; Drolet et al. 2016).

Analgesia and Infant comfort

Infants with lower birth weight (<800 g) are less likely to receive comfort drugs at end of life (Zimmermann et al. 2015 Matthews & O' Connor-Von, 2008. Neonates in the 800g -1500g group were more likely to receive comfort medication than neonates in the > 1500g group (Matthews & O Connor –Von, 2008). Partridge & Wall (1997) report that opioid analgesia was administered to 101 (84%) infants in the NICU, during the time life support was withheld or withdrawn. The diagnosis of infants at the time life support was withdrawn or withheld in relation to opiate administration was as follows:

Diagnosis	**Opiate administered n (%)**
Extremely low birth weight	**19 (66)**
Intracranial haemorrhage	20 (87)
Necrotizing enterocolitis	12 (81)
Respiratory failure	54 (81)
Hypoxic ischaemic encephalopathy	14 (78)
Congenital anomalies	54(93)

Table 5 Opioid analgesia to infants at the time life support was withheld or withdrawn (Partridge & Wall, 1997)

This retrospective chart review identified that infants with necrotising enterocolitis (NEC) and major congenital anomalies were more likely to receive opioid analgesia at time of life support discontinuation, than were other infants. Importantly the authors describe that infants with low birth weight were less likely than heavier babies to receive opioid analgesia (66% vs 90%). Samsel & Lechner (2015) support the view that infants of lower birth weight receive less comfort medication at end of life, when compared to older neonates.

Moura et al. (2011) analysed 256 charts in a retrospective chart review between two periods, (1992- 1995 and 2002-2005) and found a difference in the care of infants between the two periods. While the latter cohort received more effective pain and distress management; on the last day of life the authors found that 25.8% of neonates did not receive sedatives or opioids. Matthews & O' Connor-Von (2008) similarly reported that 27.5% (n=47) of neonates were not administered comfort medication prior to death. The implementation of a palliative care programme at a regional level 1V neonatal intensive care unit in the USA saw the administration of palliative medication increase from 36% prior to the intervention to 64% following the intervention, with statistically significant findings (P=0.02) (Samsel & Lechner 2015). In the context of their paper palliative medication was described as medication documented to support the comfort of a neonate at end of life.

Young et al. (2015) reports on comfort medication use prior to and following the implementation of a palliative care programme. While morphine use was similar in both cohort of infants (88 % vs 81%); benzodiazepine use increased following the active palliative care programme (26% vs 43%). A minority of infants received neuromuscular blockade in both era's during the last 24 hours of life (17% vs 18%, P=0.95). Neuromuscular blockade is not indicated at the time of withdrawal from life support as it will interfere with respiratory function, in addition to masking signs of pain and distress. In situations where a new born infant has received neuromuscular blockade, the drug should be discontinued and weaned between hours to days prior to a ventilator being withdrawn (Catlin & Carter 2002).

Zimmermann et al. (2015) in a retrospective analysis of computerized data identified all infants who died between 1997 and 2012 (n= 19, 726) in 348 neonatal intensive care units in the USA. The analysis identified that the use of sedatives or analgesics was widely variable across the 348 neonatal intensive care units in this North American study. The authors offer

the opinion that the number of infants exposed to sedatives or analgesics at end of life is limited but has increased over time, from 16/283 infants (6%) in 1997 to 523/1465 infants (36%) in 2012 (p <.001). The overall administration of benzodiazepines on the day of neonatal demise also increased from 16/283 (6%) in 1997 to 295/1465 (20%) in 2012 (p < .001). Following multi variable analysis the authors identified that administration of analgesia or sedatives on the day of neonatal demise was associated with increasing gestational age, increasing post-natal age, invasive procedure within two days of death, inotropic support and antibiotics on the day of death.

Medication and route of administration

Route of medication administration is an important consideration for the neonate affected by a life limiting condition. The seminal paper by Catlin & Carter (2002) identified the buccal, intravenous and suppository format. While the Intravenous route (IV) provides ease of access into the circulation and is effective within a short duration following administration, it is invasive and painful. Medication administration via less invasive means supports the palliative management of the dying neonate. The exploration of new routes of drug administration is therefore indicated. Harlos et al. (2013) described the experience using intranasal fentanyl in the management of respiratory distress in a series of neonates at end of life. Although a small study with 11 neonates, fentanyl via the intranasal route was tolerated well, with laboured breathing and restlessness in the neonate improving following administration. The mean initial dose described was 1.3 mcg/kg and the median dose was 1mcg/kg. A distinct advantage of this medication and route is that it can be utilised to support symptom relief in the neonate at end of life in a variety of care settings and is not dependent on equipment or clinical skills.

Drolet et al. (2015) determined the feasibility of introducing a comfort care protocol using oral transmucosal medication delivery, for end of life neonates. The authors describe the distinct advantage of the oral transmucosal route for this cohort of neonates as ease of use and avoidance of painful injections. A Comfort Care Protocol using the oral transmucosal medication route is attached as Appendix 5. Drugs included are morphine, midazolam, scopolamine and lorazepam. The Neonatal Pain, Agitation and Sedation Scale (N-PASS) was utilised. Appropriate tools to assess pain and symptom management will support healthcare professionals provide appropriate pain relief and treat related symptoms. Withholding

medication and poor understanding of medication for fear of hastening death or other reasons is unethical.

Conclusion

One of the goals of perinatal palliative care is to provide optimum pain and symptom management of the neonate at end of life. Again there was a lack of evidence based research in the area of medication management. Although a variety of pain scales are available for use with the paediatric and neonatal cohort of patients, the literature did not identify a standardized assessment pertinent for use with the infant at end of life. Zimmermann et al. (2015) found that the number of infants exposed to sedatives and analgesics at end of life have increased over time and this was evident among others studies (Matthews & O' Conner-Von 2008; Samsel & Lechner 2015; Young et al. 2015) however, infants of lower birth weight are less likely to receive comfort medication at end of life (Matthews & O Conner-Von 2008; Samsel & Lechner 2015). A perinatal palliative care medication protocol specifically for the neonate at end of life will educate and support clinicians in the provision of optimum pain and symptom management.

Chapter 5

Barriers and facilitators to perinatal palliative care

Perinatal palliative care is a developing speciality which faces challenges along the pathway as it emerges as a distinct discipline (Wool 2015). Health care professionals are in a central position to identify the barriers and facilitators to perinatal palliative care during the antenatal, perinatal and neonatal period, which will inform clinical practice and improve care. The findings from this review of the evidence to the barriers and facilitators to perinatal palliative care are presented in this chapter. There was, however, little empirical evidence identified. Nine papers which supported the evidence are as follows: Delphi Study (1); Cross sectional study (3); focus group (1); Descriptive (2) focused ethnography (1). The country of origin for most of the studies was the USA (n=6) with Australia (1), Canada (1) and China (1). Two papers are included by Wool (2013 and 2015) which report from a cross sectional study which addressed clinician barriers to perinatal palliative care.

Table C

Summary of evidence -Barriers and facilitators to the delivery of perinatal palliative care in the NICU

Author Year Country	Aim of paper	Population	Methodology	Results	Limitations	Classification of evidence level	Key points
Australia Kain, V. (2011) Exploring the barriers to palliative care practice in neonatal nursing: A focus group.	To explore previously identified barriers to palliative care in neonatal nursing practice	24 NICU Nurses 3 tertiary hospitals	Qualitative, focus groups (6-8 per group) NVIVO data management programme	Utilised themes from previous research by author to inform the focus group discussion. Inadequate staffing Unconducive environment Neonatal nurses have concerns about technological imperatives to prolong life and parental demands to maintain life – challenging the nurse's values and moral position.	Focus groups – three states in Australia, moderated by the author	3C	Policy development to clearly outline correct use of medical technology. Media as a challenge to care provision as it portrays the image that babies "do not die"

Canada Stenekes, S.J., Ens, C.D.L., Harlos, M., Chochinov, H.M., Mytopher, K. (2014) A Descriptive study evaluating perinatal healthcare provider's perspectives of palliative programming in 3 Canadian institutions.	To examine the views of health care providers involved in perinatal palliative care in 3 tertiary care hospitals in Canada	29 health care providers 4 focus groups 5 individual interviews	Qualitative descriptive design 4 Focus groups and 5 individual interviews	Communication was identified as the most crucial element in providing Perinatal Palliative care. Palliative care education remains inadequate, which can lead to misconceptions in relation to the goals and philosophy of palliative care. Incorporate families into the care planning process.	Cross section of health care professionals involved in the delivery of perinatal palliative care in 2 provinces in Canada. Small sample size- 29 health care professionals. Telephone interviews- 5 participants.	3C	The study supports palliative care programmes. Palliative care education of health care teams is necessary.

China Chen, Chao-Huei., Huang, Li-Chi., Liu, Hsin-Li., Lee, Ho-Yu., Wu, Shu-Ya., Chang, Yue-Cune., Peng, Niang-Huei (2013) To explore the neonatal nurse's beliefs and attitudes towards caring for dying neonates in Taiwan	To explore attitudes and beliefs of neonatal nurses toward nursing care for dying neonates	80 neonatal nurses Four level 111 NICUs Taiwan	Cross sectional design questionnaire	The research findings identified eight barriers that hindered neonatal palliative care practices in the NICU's in Taiwan: 1. Communication was insufficient 2. A lack of counselling availability for clinicians 3. There was an inability to express personal opinions, values and beliefs in relation to neonatal palliative care 4. Poor staffing levels 5. Lack of policies and guidelines to support palliative care 6. The technological imperative 7. Parental demands 8. Personal beliefs about death and Nursing experience in the care of the dying infant	Small sample size with 80 neonatal nurses in Taiwan Research setting Questionnaire- self report	3D	Personal attitudes about death affected the nurse's willingness to deliver palliative care, which may be cultural.

USA Cortezzo, D.E., Sanders, M.R., Brownell, E., Moss, K. (2013) Neonatologists perspectives of palliative and end of life care in NICU's	To determine palliative care/end of life practices among neonatologists	Survey sent to 1885 neonatolo-gists. 653 completed the survey.	cross sectional survey	58% (n=379) have PC teams and 72% (n=470) have staff support groups. Barriers include emotional challenges, staff disagreements and the formation of palliative care teams. Palliative care definition provided for consistency with the term.	Small response rate	3D	Neonatologists support palliative care. Few received formal training. Education and palliative care teams support quality care.

USA Falck A.J., Moorty S., Hussey Gardner B. (2016) Perceptions of Palliative care in the NICU	To examine the provision of palliative care as experienced by mothers and health care providers	6 mothers 5 nurses 1 physician	Qualitative descriptive	Five themes identified include: 1.Communication 2.Privacy 3.Continuity of care and relationship building 4..Maternal knowledge seeking 5.Emotional turmoil Conflicting opinion in relation to privacy in the NICU	At the time of interview all infants were stable.	3C	Communication-individualised-information needs of mothers. Shared decision making
USA Williams-Reade, J., Lamson, A.L., Knight, S.M., White, M.B., Ballard, S.M., Desai, P.P. (2015) The clinical, operational and financial worlds of neonatal palliative care: A focused ethnography.	To explore the perspective of health administrators, finance officers and clinicians in relation to the implementation of a formal neonatal palliative care programme at a major regional medical centre.	39 study participants	Focused ethnography Semi structured interviews-individual and focus groups	The study identified health care professional's experiences that influenced their views in relation to neonatal palliative care. Themes identified included 1.The uniqueness of perinatal palliative care 2. Communication and conflict between providers 3. Policy and protocol discrepancies and 4. Lack of administrative support.	Single centre study in a regional medical centre.	3C	The study identified gaps in communication and understanding among clinical, operational and financial professionals that impacted on the implementation of a formal palliative care programme.

USA Wool, C. (2015) Clinician Perspectives of Barriers in Perinatal Palliative care	To measure the perception of physicians and advance practice nurses and to explore their comfort in providing and referring patients for perinatal palliative care	Physicians, advance practice nurses and other clinicians	A cross sectional survey design. The perinatal Palliative Care and Perceptions Barriers Scale was used to collect data (PPCPBS)	The study found physicians were more comfortable with perinatal palliative care than nurses and physicians were also more comfortable referring patients to perinatal palliative care than their nursing colleagues. Physicians were more confident in facilitating and managing perinatal palliative care.	The study focus was Advanced nurse practitioners and physicians and is therefore generalised to this group.	3C	PPC team and co-ordinator required Educate clinicians, administrators about PPC. Staff to become familiar with current research on PPC
USA Wool C. (2013) Clinician confidence and comfort in providing perinatal palliative care	To provide a report of the differences between advance nurse practitioners and physicians in relation to perinatal palliative care provision	n=66 physicians n= 146 advance nurse practitioners other clinicians n=90	Cross sectional survey	Physicians and nurses report differences in their comfort with providing and referral of neonates for perinatal palliative care. Physicians and nurses usually do not receive training in end of life issues therefore wide variation in skills, knowledge and beliefs.	The author cites difficulty with practitioners reluctant to talk about PCC as it has moral, religious and political implications.	3C	Ethics and PC Education initiatives to increase comfort and confidence with palliative care delivery

USA Wright, V Prasun, MA Hilgenberg C. (2011) Why is End- of-life Care Delivery Sporadic? A quantitative look at the barriers to and the facilitators of providing end of life care in the neonatal intensive care unit.	To examine the barriers to and facilitators of providing quality end of life care in one large Mid-western tertiary NICU	50 NICU Nurses – level 111 unit	Quantitative prospective cross sectional	5 Barriers and 8 Facilitators to end of life care practice in NICU identified. Barriers= Nurses inability to express opinions, values and beliefs regarding palliative care; physical environment; technological imperatives; parental demands; lack of education. Facilitators= supportive medical staff; parental involvement of decisions; parents informed of options; support from medical team when palliative care is implemented; staffing; time spent with dying baby; policies/guidelines supporting palliative care; available counselling.	One unit- Level 111; 25 beds, Tertiary NICU, USA. Views of physicians and views of parents not identified. N= 52 (26%) staff worked in NICU for 5 years or less. Education for NICU nurses to provide end of life care. Improved anticipation of symptom management for the infant required. Understanding of the needs of families with a dying infant.	3C	It is important for NICU nurses to recognise the barriers to and facilitators of palliative care in individual units.

A parsimonious synthesis of the data identified the main barriers and facilitators of perinatal palliative care as:

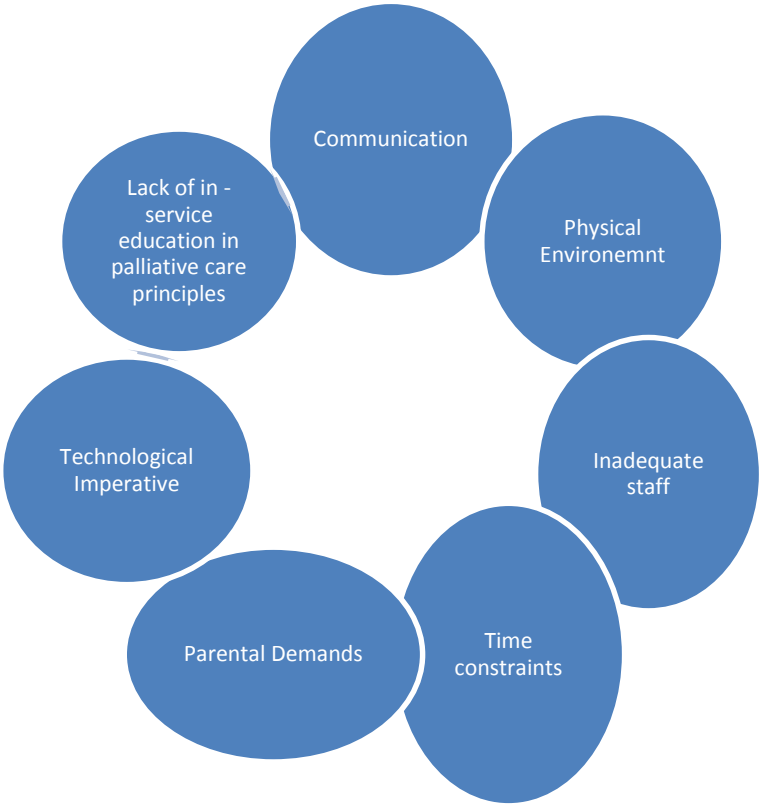


Table 6 Barriers to the provision of Perinatal Palliative Care

(Ahern 2011, Kain 2011., Wright 2011, Chen 2012, Cortezzo et al. 2013., Stenekes et al. 2014., Wool 2015., Samsel & Lechner 2015., Williams- Reade 2015., Falck 2016)

Table 7 Facilitators of Perinatal Palliative Care

(Ahern 2011, Kain 2011, Wright 2011., Chen 2012., Cortezzo et al. 2013., Stenekes et al., 2014., Wool 2015., Samsel & Lechner 2015, Williams- Reade 2015, Falck 2016)

Barriers to Perinatal Palliative Care

Kain (2011, p.10) utilised *"a priori"* knowledge to examine previously identified barriers to palliative care in the NICU i.e. inadequate staffing, unconducive environment; in addition to technological imperatives and parental expectations. The rich qualitative data describe the challenges NICU nurses face to provide a palliative care model. Inadequate staffing challenged the provision of highly specialised nursing care in addition to continuity of care. The environment of the NICU also was an additional stress for staff. The traditional NICU environment was open and busy while the transfer of a baby requiring palliative care to a single room brought with it additional stress. Participants offered the opinion that parents

may feel abandoned vacating the environment that they had become accustomed to for a single room.

Wright et al. (2011) identified five barriers to the provision of palliative care in the NICU and the results concur with themes that arise within the literature- technological imperatives, lack of in-service training, inability to express opinions, parental demands and the NICU environment. While 100% of the nursing participants agreed that palliative care education was important for neonatal nurses only 46% (M=2.86, SD =1.44) had received education that enabled them support and communicate with parents of dying babies. More than half of the study respondents reported that there was an inability to express opinions, values and beliefs in relation to palliative care; which would concur with findings described by Chen (2012) and Wool (2013, 2015). The study respondents also refer to the physical environment of the NICU as a barrier in the provision of palliative care with 38% (n=19) of nurses somewhat or strongly agreeing with this principle. Kain (2011, p.11) also describes the *"unconducive environment of the NICU"* and suggests that offering a choice to parents is preferable when end of life approaches in the traditional NICU environment. The physical environment was not an issue that affected care in a study described by Cortezzo et al. (2013) however, 42% of the neonatologists had private room units, and may not have encountered the traditional NICU environment. Similarly, Stenekes et al. (2014) found health care professionals could engage in better care when parents had a private room for births of infants not expected to survive. This enabled staff to provide all care in relation to the birth, to include post- natal care in one designated area of the hospital.

The focus of a study by Wool (2015) was to measure barriers that advance nurse practitioners and physicians experienced in the provision and referral of patients for perinatal palliative care. The main barrier identified by both nurses and physicians related to a lack of societal understanding and support for perinatal palliative care. Barriers for nurses arose in relation to administrative support and access to interdisciplinary personnel for meetings and direct pressure from administrators, when offering perinatal palliative care. Nurses expressed the opinion that they felt uncomfortable talking to expectant parents about the prognosis of an infant diagnosed with a life limiting condition. On the other hand physicians had more confidence counselling parents on the subject.

Emotionally, caring for the dying neonate is very challenging for nurses and clinicians; requiring time, empathy, sensitivity and staff who will listen (Stenekes et al. 2014., Wool 2015). Barriers in relation to time (Wool 2015) are described particularly in relation to counselling patients. While Wright (2011) found that the majority of nurses (66%) had time to spend with a family following a neonatal death, there was however a degree of variability within the results.

Falck et al. (2016) offer the opinion that study mothers were interested in the NICU equipment and technology and sought information, possibly, as a coping mechanism to understand the NICU environment. Study mothers also utilised external resources to further explain their infant's condition. The literature describes the difficulty neonatal nurses and clinicians experience in relation to technological imperatives and parental demands to continue life sustaining efforts to dying babies (Wright 2011, Wool 2015, Kain 2011.) Wool (2015) states that this main barrier, identified by both physicians and nursing staff is as a result of a lack of societal understanding and support for perinatal palliative care. Chen et al. (2012) described that only 21.2% (n=26.2) of participants agreed that there was support for neonatal palliative care within society. Interestingly, Kain (2011) suggests that the expectations parents hold, in relation to long term outcomes of critically ill new-borns may be idealistically high. The possible impact of the media, who often report positive outcomes in relation to neonatal challenges places additional stress on clinicians. Wright (2011) identified that 62% nurses would provide care beyond their comfort level in using technological life support (mean 3.22; SD 1.11); notwithstanding the fact that 86% of nurses reported the fact that they were asked by parents to continue life –extending treatment beyond their comfort level (mean 3.46; SD= 1.07). The technological imperative, in addition to parental demands, may result in the overtreatment and management of the dying neonate, increasing ethical and moral dilemmas for clinicians (Chen et al. 2012).

Williams-Reade et al. (2015) highlight that both nurses and physicians in their study held deep concerns in relation to the suffering of patients and families and shared a desire to minimise the suffering experienced. Physicians struggled with the responsibility in relation to the actual end –of –life care decisions while nurses experienced challenges as treatment decisions were beyond their control. Chen et al. (2012) identified that the personal beliefs and attitudes of nurses in relation to death, affected their willingness to deliver palliative care. While the

majority of neonatologists disagreed that their beliefs could interfere with their ability to provide palliative care, some however did allude to the challenges when clinicians mix personal feelings with medical care and appropriate choices for families are not discussed (Cortezzo et al. 2013). Physicians and nurses in perinatal services may not receive formal training in end of life issues. This in turn may account for a wide variation in skills, knowledge and belief as clinicians discuss end of life care with parents (Wool 2013).

Facilitators of Perinatal Palliative Care

Good communication is central to the philosophy of nursing and midwifery practice (NMBI, 2016). Communication as a dominant theme arose in a descriptive study by Stenekes et al. (2014) with participants describing that communication skills were important to facilitate best practice. Participants identified timely and effective communication with parents as central to the perinatal palliative care process, communication that was transparent and individualized (Wool 2015, Falck et al. 2016). A lack of team communication affected care plans and subsequently resulted in unclear goals. The geography of the unit also increased or decreased communication among perinatal staff, with a closer proximity facilitating a connectedness between staff. The findings of Williams- Reade et al. (2015) support this communication discussion with emphasis on nurse- physician communication and physicians and family members. Nurses reported that on occasion's communication between physicians and family members could be poorly timed or inadequate and this resulted in conflict or stress for the nursing staff. Falck et al. (2016) address the theme of information seeking within the environment of the NICU. Mothers in the study sought to "understand the system" in relation to nurses and physicians specialist roles and level of training.

Not surprisingly a lack of a formal palliative care education module to support perinatal palliative care is described in the literature; for both nursing and medical staff (Cortezzo et al. 2013, Wool 2013). Education and supportive staff services (Wool 2015) supports perinatal palliative care. Knowledge of the palliative care philosophy is a facilitator to the successful implementation of new programmes. Inadequate knowledge leads to a lack of understanding and misconceptions regarding the goals of palliative care (Stenekes et al. 2014). Palliative care educational interventions may directly support nursing staff comfort levels in the provision of care to the dying neonate. Clear perinatal palliative care policies that state the judicious use of medical technology when caring for the critically ill new-born at end of life (Kain 2011). This

in turn may support an increase in palliative care and palliative medication use (Samsel & Lechner 2015).

Conclusion

In summary, perinatal palliative care is an emerging model of care which will provide an enhanced quality of life to the fetus, neonate and family at end of life. Health care professionals involved in perinatal palliative care are in a central position to identify and report the facilitators and barriers to strengthen this model of care and improve outcomes (Wool, 2015). Identified barriers include communication (Chen et al. 2013, Stenekes et al. 2014., Williams Reade et al. 2015., Falck et al. 2016) emotional challenges (Cortezzo et al. 2013., Falck et al. 2016), a lack of counselling for clinicians (Chen et al. 2013); while facilitators include education and supportive staff services (Wright et al. 2011., Stenekes et al. 2014., Wool 2015) communication, policies and guidelines (Kain 2011., Cortezzo et al. 2013., Samsel & Lechner 2015., Williams Reade et al. 2015). There is evidence to suggest that neonatal nurses and clinicians experience challenges in relation to technological imperatives and parental demands to continue life sustaining efforts to dying babies (Wright 2011, Wool 2015, Kain, 2011). A lack of societal knowledge and support additionally presents barriers to the perinatal palliative care model (Wool 2015).

While barriers exist, there is growing recognition developing for a perinatal palliative care model that has emerged in this review. The further development of national policy and guidelines will assist healthcare professionals provide quality perinatal palliative care. The following chapter will provide evidence in relation to available policies and guidelines.

Chapter 6

National and International Neonatal Palliative Care Guidelines and Position Statements

A limited number of quality national and international guidelines and position statements exist specifically on perinatal palliative care indicating the development of this new and emerging field. All the guidelines and position statements provide a supportive and caring approach to the infant and family during the perinatal period. The majority of guidelines were written following expert opinion and consensus statements with a small number of guidelines only demonstrating the full criteria as outlined by the Appraisal of Guidelines for Research and Evaluation 11 Instrument (2013). The majority of guidelines did not meet the criteria outlined in Domain 3 which relates to the process utilised to gather and synthesise the available evidence. The methods utilised to formulate the recommendations were unclear on occasions and were not evidence based.

The WHO Global Atlas of Palliative Care (2014) provided a more general approach to palliative care of the adult and child and not perinatal palliative care. The Department of Health National Policy, Palliative Care for Children with a Life Limiting Condition (2009) would also benefit from specific perinatal palliative care information with a clear set of principles to underpin care within this specialised division of palliative care. As the majority of children's deaths occur in children under age 1 year, specific guidance in relation to the neonate is indicated.

Systematic methods to explore the literature were utilised by Mancini et al. (2014) to develop a "Practical guidance for the management of palliative care on neonatal units". The National Institute for Health and Care Excellence (NICE) in the UK (www.nice.org.uk/guidance/ng61) recently developed a guideline "End of life Care for infants, children and young people with life-limiting conditions" NG61 (2016). This UK guideline will support the development and articulation of national clinical guidelines (Hegarty et al. 2015). There is however, a lack of empirical research to provide an explicit link between the recommendations suggested and

the supporting evidence. Clinical and health service research is indicated (American Academy of Pediatrics 2013) to increase the body of knowledge in relation to perinatal palliative care.

The Appraisal of Guidelines for Research and Evaluation (AGREE) Instrument (2013) was utilised to assess the quality of the perinatal palliative care guidelines identified at national and international level. The Agree 11 instrument consists of 23 key items organised in to 6 domains.

Each domain identifies a specific dimension of the quality of the guideline:

1. Domain 1. Scope and Purpose.
2. Domain 2. Stakeholder Involvement
3. Domain 3. Rigour of Development
4. Domain 4. Clarity of Presentation
5. Domain 5. Applicability
6. Domain 6. Editorial Independence

Table 8 Rating Scale

All AGREE 11 items are rated on a 7 point scale (AGREE 11, 2013)

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Table D Summary of evidence for National and International Neonatal Palliative Care Guidelines and Position Statements

Developer	Title	Neonatal Palliative care guideline	Agree 11	Limitations	Includes recommendations related to perinatal palliative care
World Health Organisation (WHO) 2014 Worldwide Palliative Care Alliance	Global Atlas of Palliative Care at end of life	No	7	Not specific to perinatal palliative care	General recommendations include 1.Review and improve evidence base in relation to palliative care (PC) 2. Review and develop guidance on PC within health and community systems 3. Leadership and accountability within health care systems.
USA American Academy of Pediatrics 2013	Pediatric Palliative care and Hospice care commitments, Guidelines and Recommendations	Yes	4	Not specifically neonate. Recommendations are applicable to perinatal palliative care	12 guidelines and recommendations 1.Dedicated PPC teams 2. Relationship between hospital and hospice 3. Collaboration by team 4. Communication and decision support 5. Patient care safety and quality 6. Family support 7. Sibling support 8. Health care staff support 9. Education and Training 10. Research and quality improvement 11. Ethical considerations 12. Financial and regulatory issues.
National Association of Neonatal Nurses Position Statement 2015 Caitlin et al. (2015)	Palliative and End of Life care for Newborns and Infants	Yes	2-4		15 Recommendations include: Memory making activities Pain and symptom management- basic level Artificial nutrition and hydration Bereavement care
National Perinatal Association 2009 Caitlin, A (2009)	Palliative Care Position paper	no	2-4	No perinatal palliative care protocol	Leadership, creating a supportive educated staff, anticipate and alleviate infant suffering.

<u>Canada</u> Gunderson Medical Foundation Limbo et al. 2016	Perinatal Palliative care- A Position Statement. When parents choose to continue a pregnancy after their baby is diagnosed with a life limiting condition.	No	2-4		Key Points 1.A continuum of care 2. Importance of perinatal Palliative care 3. Elements of successful perinatal Palliative care services 4. Principles of care
<u>UK</u> British Association of Perinatal Medicine 2010	Palliative Care (supportive and end of life care) A framework for clinical practice in Perinatal Medicine	Yes	4		**Stages of palliative care planning** A. Establish eligibility of fetus/baby for palliative care B. Family care C. Communication and documentation D. Flexible parallel care planning E. Pre-birth care F. Transition from active post- natal care to supportive care G. End of life care H. Post end of life care
National Institute for Health and Care Excellence (NICE) **NICE Guideline NG61** 2016	End of life Care for infants children and young people with life-limiting conditions- planning and management.	Yes	6-7		Yes… perinatal palliative care Advance Care Planning Emotional and Psychological support Managing distressing symptoms i.e. pain, agitation, seizures, respiratory distress Care and support for parents, carers and health care professionals after the death of a child Care at home
Royal College of Paediatrics and Child Health/NHS 2014 Mancini et al. (2014)	Practical guidance for the management of palliative care on neonatal units.	Yes	6		1.Discussion with parents 2.Pain relief and comfort care 3. Symptom control 4.physiological monitoring 5. fluids and nutrition 6. ventilation and oxygen 7. location of care 8. conflicts between parents and staff 9. conflicts among members of staff 10. religious, pastoral and spiritual support 11. psychological and emotional support 12. organ donation 13. staff support

Association for Children's Palliative Care (ACT) 2009 McNamara-Goodger K. (2009)	A neonatal pathway for babies with palliative care needs.	Yes	4		Neonatal pathway for babies with palliative care needs: Stage 1: Entry to the pathway 2: Living with a life limiting condition 3: End of life and bereavement
Belgium Belgium Paediatric Palliative Care (BPPC) 2016 (in progress)	Development *in progress.* Five Domains identified				Development *in progress.* Five Domains identified
Australia Australian College of Neonatal Nurses 2010 Reid et al. (2010)	Palliative Care in the Neonatal Nursery: guidelines for neonatal nurses in Australia.	Yes	2	low evidence	Palliative care: The family Environment Implementation Care after death The unexpected outcome Making the decision The parent's perspective Culture and religion Continued care of the family
Department of Health, Government of Western Australia 2015	Perinatal Palliative Care Model of Care.	Yes	4		Principles of the model: Right care Right time Right team Right place 3 Stages: 1.Entry to perinatal loss service 2. living with the condition 3.End of life and bereavement care
New Zealand Neonatal Nurses College Aotearoa/New Zealand Nurses Organisation **2015** Gifford et al. (2015)	Neonatal Palliative Care for New Zealand Neonatal Units. Comfort as a model of care	Developed in association with PSANZ (Perinatal Society of Australia and New Zealand)	4-5	Include care plan for ante natal period, care plan for in-hospital diagnosis, no pain and symptom management	Guideline recommendations- 1.Communication 2.Nurse to work with the family 3. Care plan in advance of resuscitation developed with parents 4. Template to note family wishes and avoid repetitive questions Staff training in palliative principles De briefing for staff.

Ireland					
Department of Health (DOH) 2009 Children's Palliative Care Working Group (2009)	Palliative Care for Children with Life Limiting Conditions: A National Policy	No	5	Not specific to perinatal palliative care	Focus on Children, not the neonate Key principles underpinning care include: 1.Inclusiveness 2.Partnership 3.Comprehensiveness 4.Flexibility
Health Service Executive (HSE) 2014 Palliative Care Competence framework Steering Group (2014)	Palliative Care Competence framework- discipline specific	No	5	Not specific to perinatal Palliative care	Domains of Competence: 1Principles of palliative care 2.Communication 3. Optimising comfort and quality 4. care planning and collaborative practice 5. loss, grief and bereavement 6. Professional and ethical practice in the context of Palliative care. Levels of palliative care specialisation: 1.Level 1 Palliative care approach 2. General Palliative care 3. Specialist palliative Care

Chapter 7

Discussion

Perinatal Palliative care is a newly emerging field of palliative medicine. A review of the evidence to date identified that there is a lack of research in the field of perinatal palliative care with available evidence identified to be of a low quality. There is a poor evidence base available on the experiences of families who received perinatal palliative care for an infant with a life limiting condition (NICE 2016).

The provision of a perinatal palliative care programme, Williams Reade et al. (2015, p. 179) assert, requires the inclusion of multidisciplinary stakeholders from within the clinical, operational and financial worlds of health care. While there is evidence to support the implementation of perinatal palliative care policies and guidelines within each maternity hospital, operational processes and financial aspects must be addressed (Liben et al. 2008) in order to provide consistent and coordinated care (Williams Reade et al. 2015).

The importance of a comprehensive plan for parents following a diagnosis during pregnancy of a baby with a life limiting condition was identified (Calhoun et al. 2003., Breeze et al. 2007., Leong Marc Aurele & Nielsen 2013). Advance Directive Planning (NICE, 2016) and the implementation of a perinatal palliative care protocol during the antenatal, perinatal and postnatal period was identified (Calhoun et al. 2003., Breeze et al. 2007., Leong Marc Aurele & Nielsen 2013). There is a variable and unpredictable post-natal course for babies with a life limiting condition ranging from immediate neonatal death to survival for several days or weeks (Breeze et al. 2007., Moura 2011). Where prenatal discussion and decisions are made in advance by the multidisciplinary team and parents, resuscitation may not take place following birth, and the infant will receive palliative care with family support (Catlin & Carter 2002). The importance of a birth plan with key obstetric and neonatal involvement to ensure that all clinicians are comfortable with the plan of care is paramount (Catlin & Carter 2002., Calhoun et al. 2003., Leong Marc- Aurele & Nelesen 2013).

Some infants will live following birth and death may be imminent or not. The majority of new born deaths will occur in the neonatal intensive care unit (Gale & Brooks 2006., Kain 2011., Falck et al. 2016). Perinatal Palliative care for parents and professionals within the highly

technical neonatal intensive care unit is challenging, however, neonatal hospice and palliative care is not widely available nationally and internationally (Toce et al. 2011). A palliative care pathway and a more collaborative approach to pain and symptom management would ensure that infants' symptoms at end of life are well managed (Cortezzo et al. 2014), that the place of death will occur in a non- intensive care setting (Pierucci et al. 2001) and that infants are not submitted to aggressive treatment in the face of death.

A palliative care programme implemented at a regional NICU in the USA was associated with increased palliative interventions for neonates in the final 48 hours of life. There was an increase in re direction of care to a palliative approach and increased use of palliative medication (Samsel & Lecher 2015). A retrospective chart review by Moura (2011) analysed 256 infant charts between two periods (1992-1995 and 2002-2005). The authors report that there was a strong tendency not to speed up the dying process by withholding or withdrawing medical intervention. It was also observed that in 92.6% of the charts identified there were no clear instructions to discontinue life support or withhold resuscitation.

Pain and symptom management is an integral component of perinatal palliative care. Pharmacological and non- pharmacological pain relief strategies are indicated to ensure adequate pain relief. Non pharmacological methods that modify mild pain include swaddling, holding the infant in skin to skin contact, non -nutritive suckling and sucrose (NICE, 2016). Lights can be dimmed; noise reduced to a minimum and the infant may be dressed in an effort to promote comfort (Gale & Brooks 2006). Infant bonding is promoted (Paravicini and Lorenz 2014). When pain is not adequately managed with these interventions, pharmacologic pain relief is important and necessary (Toce et al. 2011., NICE 2016). A poor understanding of pain in new borns, in addition to fear of hastening death, at end of life present barriers to effective pain management (Moura et al. 2011.,Toce et al. 2011., Ahern, 2013), in this vulnerable population. While recent advances in the field of neurobiology suggest that both the fetus and neonate experience degrees of pain and express abnormal biochemistry (Simons et al. 2003) a perinatal palliative medication protocol was not evident across papers identified. More recently, Toce et al. (2011), Mancini et al. (2014) and Ferrell (2016) provide a list of suggested medications for neonatal palliative care which include dose and route of administration.

A difference in the perception of health care professionals and parents in relation to infant comfort at end of life was addressed by Cortezzo et al. 2014. Interestingly, Ahern (2013) identified that less experienced practitioners included medication for pain and symptom relief as a priority topic in palliative education programmes, suggesting a lack of knowledge or that a more consistent level of pain assessment and management was indicated. Other interventions to support the comfort of the neonate include managing secretions, minimising sleep disturbances, treating agitation and optimising family- centred time (Thaxton et al. 2011). Appropriate tools to assess pain and other symptoms may aid health care professionals in the assessment and management of pain relief at end of life (Toce et al. 2011). Drolet et al. (2016) utilised the Neonatal Pain, Agitation and Sedation Scale (N-PASS) that assesses crying and irritability, behaviour state, facial expression, extremities tone and vital signs. Moura et al. (2011) observed the use of a neonatal pain scale assessment tool; however, despite its use, 25.8% of infants with life limiting conditions did not receive any pain relief during the dying process. While care givers may be concerned in relation to hastening death, it is not an appropriate reason to withhold pain relief (Gale & Brooks, 2006). Gale & Brooks (2006) offer the opinion that neonatal pain scales may not be an effective measurement of pain in the dying neonate who may be too ill to exhibit behavioural signs of pain.

Perinatal palliative care is associated with fewer blood tests, feeding tubes, endotracheal tubes and x-rays (Pierucci et al. 2001). Infants will require pain relief, relief for laboured breathing or seizures, whereby narcotic and non- narcotic analgesia should be available to provide comfort (Carter & Catlin, 2002). Moura et al (2011) describe that 95.7% of infants remained connected to a ventilator until death, 76.3% received antibiotics and 58.1% received inotropes. Zimmermann et al. (2015) offers the opinion that administration of analgesia and sedatives at end of life may be limited due to a fear of hastening death, limited data in relation to analgesia and sedatives with the infant population and a lack of validated tools to assess pain in this cohort of infants. Neonatal pain tools as a method of assessing neonatal pain at end of life would benefit from further research.

The use of a neonatal pain assessment tool and palliative care plan promotes consistent and effective care provision to the neonate at end of life. Continuity of care provider is recognised as important in the therapeutic relationship of health care professionals and clients. Where NICU nursing staff are a constant presence in the neonatal unit this supported trust

relationships and confidence in the nurse's ability to care for infant at end of life. On the other hand, the medical team rotation policy presented difficulties with communication styles and management strategies (Falck et al. 2016). A number of NICU's are located within a traditional open room setting. Notwithstanding the fact that some parents appreciate an open room design, describing a level of security from the close proximity of healthcare professionals (Falck et al. 2016); physical space was a challenge to other parents as they felt uncomfortable expressing emotions which challenged family bonding (Falck et al. 2016). It is important to recognise that barriers can be overcome and palliative care principles can be applied within different settings, with some creativity and resourcefulness (Liben et al. 2008). A supportive environment for parents can be created by staff within the NICU which may be more important than the actual physical location of care (Catlin & Carter, 2002; Thaxton et al. 2011). Infants may be transferred to a quiet room adjacent to the NICU (Toce et al. 2011) or private screens may be utilised, to partition a private family space within the NICU (Falck et al. 2016). Confidential meetings should take place in a private room or office.

Crucial aspects of optimal care as end of life approaches include privacy, open and honest communication (Branchett & Stretton 2012., Stenekes et al. 2014) and shared decision making (Falck et al. 2016). The importance of parents as partners in the care of each infant is a fundamental tenet of perinatal palliative care (Toce et al. 2011). Private time with the baby is important (Calhoun et al. 2002., Branchett & Stretton 2012., Wool 2015) memory making (Branchett & Stretton 2012., Cortezzo et al. 2014) in addition to spiritual and emotional support (Calhoun et al. 2002.,Moura 2011., Falck et al. 2016.,. Some parents may not appreciate mementoes of a new born infant due to cultural preferences (Thaxton et al. 2011). Following the death of an infant the family will require immediate and long term psychosocial support (Moura 2011).

There is increasing evidence that formal, integrated educational programmes are vital to impart the perinatal palliative care philosophy (Ahern 2013; Stenekes 2013; Falck 2016). Where perinatal protocols are not in place nurses are informally self-taught by observing their co-workers (Wright et al. 2011). It is acknowledged that both Catlin & Carter (2002) and Gale & Brooks (2006) have implemented palliative care protocols with international success, however, both fail to address specifically medication doses for pain and symptom management. Specific protocols inclusive of suggested medication, usual dose and special

considerations (Toce et al. 2011., Ferrell 2016) will provide clear guidance to ensure pain and suffering is alleviated at end of life (Appendix 3). The formation of palliative care teams, consistency during end of life care provision, end of life symptom management, bereavement support and de briefing all support perinatal palliative care (Moura et al. 2011., Wool 2012., Cortezzo et al. 2014., Williams Reade et al. 2015). The Health Service Executive (HSE) Palliative Care Competence Framework (2014) *facilitates* health care professionals to assess, plan and implement high quality perinatal palliative care and addresses the following Domains of Competence:

- Domain of Competence 1- Principles of Palliative care
- Domain of Competence 2- Communication
- Domain of Competence 3- Optimising comfort and quality of life
- Domain of Competence 4- Care Planning and Collaborative Practice
- Domain of Competence 5- Loss, grief and bereavement
- Domain of Competence 6- Professional and ethical practice in the context of palliative care.

This framework will inform national academic and professional development programmes and in turn enhance the care provided to infants at end of life (Palliative Care Competence Framework Steering Group, 2014). The aforementioned, in conjunction with The National Maternity Strategy (2016) and a National Perinatal Palliative Care Policy and Protocol will ensure a successful national perinatal palliative care programme. The ability of health care professionals to confidently and compassionately provide information, care and support and coordinate services to parents throughout the trajectory of a life limiting condition will have a lasting impression on parents (Wool 2013). There is however, a lack of empirical research to provide an explicit link between the recommendations suggested in many guidelines and position statements. Clinical and health service research is indicated (American Academy of Pediatrics 2013) to increase the body of knowledge in relation to perinatal palliative care. In summary, this systematic review has provided a review of evidence to date, albeit a low quality evidence to support perinatal palliative care for the fetus and neonate.

Conclusion

Palliative care as a holistic, family centred approach has much to offer the field of perinatal care. There is an increasing knowledge base emerging that is supporting the implementation of perinatal palliative care at clinical, educational, institutional and research level that can support infants with life limiting conditions and their families (Gale & Brooks 2006., Liben et. al. 2008). The HSE National Maternity Strategy (2016) acknowledges that there is presently a developing programme of work which will assist hospitals in the formation of comprehensive palliative, end of life care plans (HSE 2016). Further research will ensure that national and international perinatal palliative care documents and guidelines are informed by rigorous research methods.

A pregnancy diagnosis and subsequent birth of a baby with a life limiting condition or anticipated early demise is in stark contrast to the expected outcomes of pregnancy and birth (Toce et al. 2011). Parents anticipating a perinatal loss would benefit from a multidisciplinary approach to their care. Perinatal palliative care offers parents and their infant the best quality end of life care, embroiling the domains of physical, psychological, social and spiritual wellbeing (American Academy of Pediatrics, 2013., Liben et al. 2008). A multidisciplinary perinatal palliative care team typically consists of obstetricians, neonatologists, fetal medicine specialists, nurses, midwives, pharmacist, social worker and chaplaincy. The palliative care team connect families to much needed resources and support mechanisms during the perinatal, intra partum and postnatal period (Leong Marc- Aurele et al. 2013). Engaging with parents to develop a birth plan which outlines preferences for labour and birth, a plan in relation to resuscitation of the baby following birth and a palliative care plan to include symptom management, infant discomfort and nutrition is practical and supportive to parents (Kenner et al. 2015). Bereavement support provides direction and emotional support as the family make final arrangements for the baby's funeral or church service (Calhoun et al. 2002, Kenner et al. 2015).

The studies identified in this systematic review lay the foundations for further research and have provided an insight in to perinatal palliative care where a lack of empirical research and heterogeneity of methodologies is evident.

The first gap is that further research is required in relation to the provision of perinatal palliative care and the experiences of parents and health care providers with perinatal palliative care programmes. Research which explores the relationship between the existing palliative care programme available within the NICU and the actual palliative care provided to individual infants (American Academy of Pediatrics 2013., Samsel & Lechner 2015). Additionally the experiences of staff and parents with individual palliative care plans are important to inform National Policy.

The second gap relates to education and training in perinatal palliative care to support staff provide evidence based care to mothers and babies. The development of a National Perinatal Palliative Care Policy will support and inform clinical decision making to ensure safe and effective palliative care of the fetus and neonate. The implementation of guidance in clinical practice will benefit from the inclusion of protocols, algorithms and checklists (Hegarty et al. 2015) to include end of life neonatal medication tables with dose, infant age/weight and route of administration suggested. Research should also assess and evaluate pain and symptom management in infants, at end of life (Stenekes et al. 2014).

The third gap relates to culture and how palliative care principles may be applied to different communities and ethnic minorities. Health care professionals may misunderstand the needs of parents from ethnic minority groups where knowledge and education is lacking. This in turn may influence parents experience with decision making and with loss and bereavement following the death of an infant.

And finally the fourth gap relates to the experiences of mothers and fathers choosing to continue a pregnancy to term, following an antenatal diagnosis of a life limiting condition (Stenekes et al. 2014).

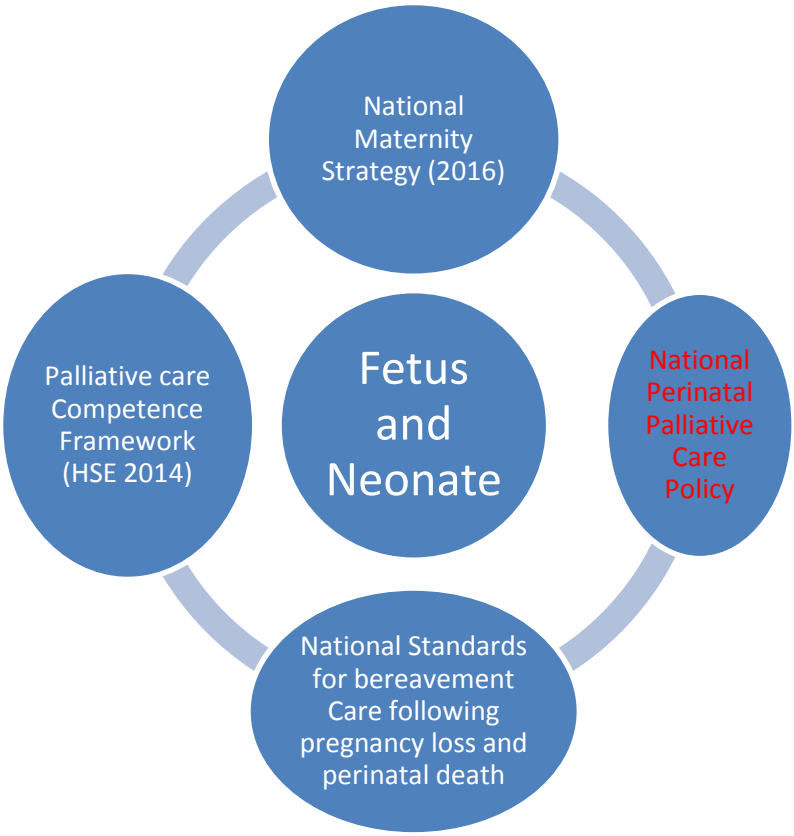


Table 9 The Proposed National Perinatal Palliative Care Model in relation to other National quality programmes

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Appendix 1
Search Strategy

GENERAL APPROACH

“Palliative care” OR “Hospice care” OR “Terminal care” OR “Life limiting” OR “End of life” OR “Lethal anomaly” OR “lethal anomalies” OR “incompatible with life” OR "life shortening"

AND

Newborn OR newborns OR baby OR babies OR neonate OR neonates OR fetus OR fetuses OR Foetus OR foetuses OR Neonatal OR Perinatal OR “Previable birth” OR “Low gestational age” OR premature OR prematurity OR “Very preterm”

PubMed 4360

("Terminal Care"[Mesh] OR "Hospice and Palliative Care Nursing"[Mesh] OR "Palliative Care"[Mesh] OR “Palliative care”[Title/Abstract] OR “Hospice care”[Title/Abstract] OR “Terminal care”[Title/Abstract] OR “Life limiting”[Title/Abstract] OR “End of life”[Title/Abstract] OR “Lethal anomaly”[Title/Abstract] OR “lethal anomalies”[Title/Abstract] OR “incompatible with life”[Title/Abstract] OR "life shortening"[Title/Abstract]) AND ("Infant, Newborn"[Mesh] OR "Infant, Newborn, Diseases"[Mesh] OR Newborn[Title/Abstract] OR newborns[Title/Abstract] OR baby[Title/Abstract] OR babies[Title/Abstract] OR neonate[Title/Abstract] OR neonates[Title/Abstract] OR fetus[Title/Abstract] OR fetuses[Title/Abstract] OR Foetus[Title/Abstract] OR foetuses[Title/Abstract] OR Neonatal[Title/Abstract] OR Perinatal[Title/Abstract] OR “Previable birth”[Title/Abstract] OR “Low gestational age”[Title/Abstract] OR premature[Title/Abstract] OR prematurity[Title/Abstract] OR “Very preterm”[Title/Abstract])

CINAHL 921

((MH "Terminal Care") OR (MH "Hospice Care") OR (MH "Palliative Care") OR (MH "Resuscitation Orders") OR TI (“Palliative care” OR “Hospice care” OR “Terminal care” OR “Life limiting” OR “End of life” OR “Lethal anomaly” OR “lethal anomalies” OR “incompatible with life” OR "life shortening") OR AB (“Palliative care” OR “Hospice care” OR “Terminal care” OR “Life limiting” OR “End of life” OR “Lethal anomaly” OR “lethal anomalies” OR “incompatible with life” OR "life shortening")) AND ((MH "Infant, Newborn, Diseases+") OR (MH "Infant, Newborn") OR (MH "Infant, Premature") OR (MH "Infant, Low Birth Weight") OR (MH "Infant, Small for Gestational Age") OR (MH "Infant, Very Low Birth Weight") OR TI (Newborn OR newborns OR baby OR babies OR neonate OR neonates OR fetus OR fetuses OR Foetus OR foetuses OR Neonatal OR Perinatal OR “Previable birth” OR “Low gestational age” OR premature OR prematurity OR “Very preterm”) OR AB (Newborn OR newborns OR baby OR babies OR neonate OR neonates OR fetus OR fetuses OR Foetus OR foetuses OR Neonatal OR Perinatal OR “Previable birth” OR “Low gestational age” OR premature OR prematurity OR “Very preterm”))

MWIC 358

(Palliative care OR Hospice care OR Terminal care OR Life limiting OR End of life OR Lethal anomaly OR lethal anomalies OR incompatible with life OR life shortening) AND (Newborn OR newborns OR baby OR babies OR neonate OR neonates OR fetus OR fetuses OR Foetus OR foetuses OR Neonatal OR Perinatal OR Previable birth OR Low gestational age OR premature OR prematurity OR Very preterm)

PsycINFO 254

("Palliative care" OR "Hospice care" OR "Terminal care" OR "Life limiting" OR "End of life" OR "Lethal anomaly" OR "lethal anomalies" OR "incompatible with life" OR "life shortening") AND (Newborn OR newborns OR baby OR babies OR neonate OR neonates OR fetus OR fetuses OR Foetus OR foetuses OR Neonatal OR Perinatal OR "Previable birth" OR "Low gestational age" OR premature OR prematurity OR "Very preterm")

PDAT UK & IE 86

("Palliative care" OR "Hospice care" OR "Terminal care" OR "Life limiting" OR "End of life" OR "Lethal anomaly" OR "lethal anomalies" OR "incompatible with life" OR "life shortening") AND (Newborn OR newborns OR baby OR babies OR neonate OR neonates OR fetus OR fetuses OR Foetus OR foetuses OR Neonatal OR Perinatal OR "Previable birth" OR "Low gestational age" OR premature OR prematurity OR "Very preterm")

PDAT A&I 57

LIMIT TO "Anywhere but full text"

("Palliative care" OR "Hospice care" OR "Terminal care" OR "Life limiting" OR "End of life" OR "Lethal anomaly" OR "lethal anomalies" OR "incompatible with life" OR "life shortening") AND (Newborn OR newborns OR baby OR babies OR neonate OR neonates OR fetus OR fetuses OR Foetus OR foetuses OR Neonatal OR Perinatal OR "Previable birth" OR "Low gestational age" OR premature OR prematurity OR "Very preterm")

SCOPUS 3291

"Palliative care" OR "Hospice care" OR "Terminal care" OR "Life limiting" OR "End of life" OR "Lethal anomaly" OR "lethal anomalies" OR "incompatible with life" OR "life shortening"

AND

Newborn OR newborns OR baby OR babies OR neonate OR neonates OR fetus OR fetuses OR Foetus OR foetuses OR Neonatal OR Perinatal OR "Previable birth" OR "Low gestational age" OR premature OR prematurity OR "Very preterm"

Appendix 2
Classification of Evidence Levels

Classification of Evidence Levels
1++ High quality meta-analyses, systematic reviews of RCT's or RCT's with a very low risk of bias
1+ Well conducted meta-analyses, systematic reviews or RCT's with a low risk of bias
1- Meta- analyses, systematic reviews or RCT's with a high risk of bias
2++ High quality systematic reviews of case control or cohort studies, High quality case control or cohort studies with very low risk of confounding or bias and a moderate probability that the relationship is causal
2+ Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
2- Case control cohort or cross sectional studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
3 Non-analytic studies i.e. case reports/case series
4 Expert Opinion

Appendix 3

Studies included in this review were graded using the GRADE levels of evidence (Schunemann et al. 2011):

Code	Quality of Evidence	Definition
A	High	Further research is very unlikely to change our confidence in the estimate of effect • Several high quality studies with consistent results • In special cases: one large, high quality multicentre trial.
B	Moderate	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. • One high quality study • Several studies with some limitations
C	Low	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. • One or more studies with severe limitations
D	Very Low	Any estimate of effect is very uncertain • Expert opinion • No direct research evidence • One or more studies with very severe limitations

Source: GRADE (Grading of Recommendations Assessment Development and Evaluation) Working Group 2007 1 (modified by EBM Guidelines Editorial Team)

Appendix 4

Medication	Usual Dose	Special Considerations
For Pain		
Morphine	0.02-0.1mg/kg IV 2-4 hourly PRN	Opioid : medication of choice for pain management in palliative and end of life care May use in combination with benzodiazepine
Acetaminophen	10-15mgs /kg PO 4-6 hourly PRN	Analgesic ; Antipyretic
For Sedation		
Midazolam	0.05-0.1mg/kg IV 1 hour PRN	Very short acting benzodiazepine

Palliative Care Medication for Neonatal Patients. Adapted from Ferrell, B. (2016:85) Pediatric Palliative Care

Appendix 5

APPENDIX A. COMFORT CARE PROTOCOL USING ORAL TRANSMUCOSAL MEDICATION ROUTE DELIVERY

presence of **PAIN** (N-PASS score ≥4) and/or **DYSPNEA** (Respiratory rate ≥70 AND spiratory effort 2 or +) :

MORPHINE[1] 0.05 mg/kg whether _____ mg (_____ mL) TM q4h PRN
[1]Use the intravenous solution 2 mg/mL

If ≥2 doses per 8 h or ≥4 doses per 24 h necessary :
MORPHINE[1] 0.05 mg/kg whether _____ mg (_____ mL) TM q4h **REGULAR**
PLUS Breakthrough (BTD) dose MORPHINE[1] 0,025 mg/kg _____ mg (_____ mL) TM q30 min PRN (by N-PASS score ≥4)

Advise if ≥3 BTD / 8 h or ≥4 BTD / 24 h (for adjustment of regular doses)

presence of **ANXIETY OR AGITATION** (Criteria N-PASS/Behavior = 2 OR ırsing assessment score - Anxiety ≥4) :

MIDAZOLAM[2] 0.05 mg/kg whether _____ mg (_____ mL) TM q 30 min PRN
[2]Use the intravenous solution 5 mg/mL

If ≥3 doses/8 h or ≥4 doses/24 h necessary :
Stop MIDAZOLAM
Begin LORAZEPAM[3] 0.025 mg/kg_____mg (_____ mL) TM q 6h PRN
[3]Use the intravenous solution 4 mg/mL

RESPIRATORY DISTRESS (Secretions ≥1 AND respiratory effort 2 or + OR Respiratory ate ≥70) :

☐ SCOPOLAMINE[4] 6 µg/kg either _____ mg (_____ mL) TM q 2h PRN
OR
☐ ROBINUL[4] 6 µg/kg _____ mg (_____ mL) SC q 2h PRN
[4]Use the intravenous solution 200 µg/mL

STRESS PROTOCOL
f a sudden event (suffocation, panic, very acute dyspnea, massive bleeding) in a conscious atient requires an emergency intervention

MIDAZOLAM[2] 0.05 mg/kg _____ mg (_____ mL) TM
*Use the intravenous solution 5 mg/mL
AND
MORPHINE[1] 0.05 mg/kg _____ mg (_____ mL) TM
*Use the intravenous solution 2 mg/mL.
AND (If respiratory distress)
☐ SCOPOLAMINE[4] 6 µg/kg either _____ mg (_____ mL) TM
OR
☐ ROBINUL[4] 6 µg/kg _____ mg (_____ mL) SC

Drolet et al. (2016) Oral Transmucosal Route in Neonatal Palliative Care.