CLINICAL PRACTICE GUIDELINES FOR THE MANAGEMENT OF NEONATAL ABSTINENCE SYNDROME: A SYSTEMATIC REVIEW AND EVALUATION

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"You can't go back and change the beginning, but you can start where you are and change the ending" (C.S. Lewis).

Preface

Statement of Contributions and Co-Authorship

There were multiple authors who have contributed to the development of this thesis. A summary of the authors' contribution to this thesis can be found below.

1. Christine Figeys, RN, BScN

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I (CF) am the primary author of my master's thesis. I conducted a systematic review, participated in the quality assessments of guidelines, and analyzed and interpreted the findings. I also developed and piloted a new family-centred appraisal tool. I wrote and revised the chapters throughout this thesis while incorporating feedback from my co-authors.

2. Wendy Peterson, RN, PhD

   Full Professor, School of Nursing, Faculty of Health Sciences, University of Ottawa

Dr. Wendy Peterson (WP) is my thesis supervisor. Dr. Peterson provided guidance throughout all stages of this research. She participated in the quality appraisal and assisted in the design and piloting of the family-centred care tool. Dr. Peterson reviewed and provided feedback on each draft of the chapters in this thesis. This version of the thesis was reviewed and approved by Dr. Peterson.

3. Ian Graham, PhD

   Distinguished Professor, School of Epidemiology and Public Health, Faculty of Medicine, University of Ottawa

Dr. Ian Graham (IG) is a member of my thesis committee and was integral to the development of the proposal, design, methodology and data analysis for this systematic review.

In particular, Dr. Graham assisted in the development and refinement of the research questions. Dr. Graham provided valuable feedback throughout the systematic review process, development and refinement of the family-centred care tool and on each chapter of this thesis.

4. Denise Harrison, RN, PhD

   Professor, Department of Nursing, School of Health Sciences, Faculty of Medicine, Dentistry and Health Sciences, University of Melbourne and Adjuvant Professor, School of Nursing, Faculty of Health Sciences, University of Ottawa

Dr. Denise Harrison (DH) is a member of my thesis committee and provided valuable feedback on the proposal, design, methodology, and data analysis of this systematic review. Dr. Harrison reviewed the family-centred care tool and provided expert advice which was incorporated during refinement of the tool. Dr. Harrison reviewed and provided valuable feedback on each chapter of this thesis.

5. Christina Cantin, RN, PhD Candidate

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Ms. Christina Cantin (CC) participated in the screening and selection of eligible guidelines in this systematic review. Ms. Cantin participated in the quality assessment of the guidelines. Ms. Cantin also reviewed and provided valuable feedback on the family-centred care tool.

6. Megan Bulmer, RN, MScN

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Ms. Megan Bulmer (MB) participated in the quality appraisal of the guidelines in this systematic review.

Abstract

Neonatal abstinence syndrome (NAS) refers to the withdrawal symptoms experienced when an infant has been exposed to certain substances (e.g., opioids) in-utero, resulting in health challenges for infants. Previous studies have reported substantial variations in the clinical management of NAS, suggesting that some infants may not be receiving optimal care. High-quality clinical practice guidelines are crucial to support optimal patient outcomes and standardize care. In response, I conducted a systematic review and quality appraisal of available NAS guidelines and recommendations using the AGREE-II and AGREE-REX tools. I also developed and piloted a tool to measure family-centred care in guidelines. Most guidelines received low-quality appraisal scores on the AGREE-II and the AGREE-REX appraisals (16/20 and 10/20, respectively) and have conflicting pharmacological recommendations. Findings will improve clinicians' awareness of the variation in the quality of guidelines and assist them to make care decisions that are from the best available evidence and family-centred.

Acknowledgement

I would like to express my deepest gratitude to my thesis supervisor, Dr. Wendy Peterson. Dr. Peterson, you have provided me with unwavering support, guidance and encouragement, which has been instrumental throughout my journey working on this thesis. I am truly grateful to have had the opportunity to be mentored by someone so committed to my success and growth. I have learnt so much from you over the past few years, and your expertise and passion for maternal-newborn care have been a source of inspiration for me. I am incredibly honoured and humbled to have been your student. Thank you for supporting me every step of this journey.

Next, I would like to thank my thesis advisory committee members, Dr. Ian Graham and Dr. Denise Harrison, for their invaluable support and feedback. Together, your expertise and guidance have greatly contributed to the quality of this research and to my development as a researcher. Thank you for taking the time to support me throughout this journey.

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Mat, and partner Jared, thank you for always being my rock, believing in me, and for instilling a passion in me to help others just as you all do every day.

Table of Contents

Chapter One: Introduction

As healthcare providers, we have the potential to facilitate the transformation of individuals' lives. We often have the privilege and opportunity to support a positive outcome even when our patients are in the midst of what may be the most challenging time of their lives. As a neonatal intensive care nurse, I have the honour of taking care of the smallest of patients, and to be with them for their very first breath. Some of the extraordinary newborns I take care of are those experiencing withdrawal symptoms after being exposed to opioids and/or other substances in-utero (neonatal abstinence syndrome [NAS]). These newborns enter the world experiencing pain and discomfort shortly after birth. At the same time, many of their families continue to undergo their own physical and psychological pain. The experience of witnessing their baby in pain triggers an immense sense of guilt for many parents, some of them not knowing their baby would suffer from withdrawal symptoms soon after birth. A few of the most memorable moments in my career are helping these families care for and bond with their newborn and watching them become confident and resilient. In particular, I remember one incredible mother who held her baby tightly in her arms one early morning, looked at me and said: "I want to change my life for him." It is moments like these that inspires me as a neonatal nurse and drives my passion for improving the care of infants with NAS and their families. My passion for providing care to these brave infants and their families has motivated me to conduct this research.

This is an article-based thesis and is organized into four chapters. This first chapter will describe NAS, present the research problem and objectives, provide a literature review, and explain a unique integrated theoretical framework used to guide the systematic review. Chapter two is a manuscript written for submission to *The Journal of Perinatal and Neonatal Nursing,*

which describes the methods and findings of the systematic review. Chapter three of this thesis describes the development and pilot of the Family-Centred Maternal-Newborn Care Tool (FCMNC-T) for clinical practice guidelines (CPG). Finally, chapter four concludes this thesis with a meaningful discussion of how findings from this systematic review can contribute to nursing knowledge, health policies, research, and clinical practice using a social-ecological framework.

I use “pregnant persons/individuals” throughout this thesis to refer to all pregnant individuals. However, when citing or referring to other authors’ work, I will use the authors' terminology (e.g., pregnant women). Family-centred care (FCC) is used throughout this thesis and includes patients/persons and their families as active care team members. The definition of a family can encompass various forms and meanings for individuals (Shajan & Snell, 2019). A family does not mean that individuals must be related or live together. A family is described throughout this thesis as the unit of individuals who support the patient and whom the patient states to be their family. The words “family” and “caregivers” will be used interchangeably.

Neonatal Abstinence Syndrome

Opioid use during pregnancy poses harm not only to pregnant persons but also to their newborns, who are at risk of developing NAS. NAS is described as the withdrawal symptoms experienced when an infant has been exposed to opioids or other substances in-utero and their exposure has been abruptly discontinued after birth (Edwards & Brown, 2016). NAS is also known as neonatal withdrawal syndrome, neonatal opioid withdrawal syndrome (NOWS), neonatal drug withdrawal syndrome, and neonatal withdrawal. Neonatal withdrawal symptoms can result from other classes of agents, including alcohol, sedative-hypnotics, stimulants, and selective serotonin reuptake inhibitors; however, withdrawal symptoms are more common and

are often more clinically significant for newborns who have been exposed to opioids in-utero (Hoffman & Sharma, 2007; Hudak et al., 2012; Minnes et al., 2011). NAS symptoms are multi-systemic with varying severity, including central nervous system hyperactivity, irritability, seizures, tremors, rigid muscle tone, vomiting, loose stool, and weight loss (Finnegan, 2013). Infants with NAS are at an increased risk for birth complications, need for pharmacological treatments, and prolonged hospital admissions to the Neonatal Intensive Care Unit (NICU) or Special Care Nursery (SCN; McQueen & Murphy-Oikonen, 2016).

Corsi et al. (2020) conducted a Canadian population-based retrospective cohort study investigating the trends of prenatal opioid use and the association between adverse perinatal outcomes of all births from women 15 years and older from April 1st to March 31st 2018 in Ontario, Canada (analytic sample = 710,911). In this study, Corsi et al. (2020) reported that the crude rate of having a preterm birth (defined as less than 37 weeks gestational age) was 14% (*n* = 1127) for those who reported using opioids during pregnancy compared to 6.0% (*n* = 42,226) among women in an unmatched cohort who did not use opioids during pregnancy (unadjusted risk difference [RD] = 7.97%; 95% Confidence Interval [CI]: 7.21%-8.73%). Corsi et al. (2020) found that newborns exposed to opioids in-utero have a higher rate of being born small for gestational age ([SGA], defined as weight less than the 10th percentile; 14.6% [*n* = 1173] for opioid-exposed newborns compared to 9.4% [*n* = 65,760] in non-opioid exposed newborns [unadjusted RD = 5.21; 95% CI: 4.43-5.98]). Corsi et al. (2020) also found that newborns exposed to opioids in-utero are at an increased rate of having a five-minute Apgar score of less than four (1.2% [*n* = 93]) in comparison to unexposed newborns (0.6% [*n* = 4183] in non-opioid exposed newborn; unadjusted RR = 0.55; 95% CI: 0.32-0.78). According to Corsi et al. (2020), the risk for transfer to the NICU was 40.5% (*n* = 2635) for newborns with perinatal opioid

exposure compared to 13.9% (*n* = 61,977) for newborns with no perinatal opioid exposure (Relative Risk [RR] = 2.91; 95% CI: 2.80-3.03). Furthermore, NAS can result in harmful long-term effects, including growth delays and impairments in cognitive and behavioral development (Behnke & Smith, 2013; Maguire et al., 2016).

Research Problem

There is wide variation in the care of newborns with NAS (Marcellus et al., 2015; Murphy et al., 2017; Wood et al., 2019; Young et al., 2021). A Canadian survey of 65 NICU healthcare workers/health administrators conducted in 2014 found that although many NICUs do have a practice guideline on the management of NAS (92.3%; 58/62), differences remain in how NAS is managed across institutions (Murphy et al., 2017). On the other hand, a cross-sectional survey of 878 physicians conducted by the Canadian Pediatric Surveillance Program in 2018 revealed that 35.8% of Canadian institutions do not have established guidelines for NAS (Puvitharan et al., 2019). Of the 64.2% of physician respondents who reported that their institution has a NAS guideline, only 28.9% referred to the Canadian Pediatric Society practice point for management (Puvitharan et al., 2019). Puvitharan et al. (2019) and Murphy et al. (2017) studies both reported considerable variation across institutions of care and management of NAS, including the recommendations for breastfeeding, rooming-in, adjuvant medications, and the location for observation and care. Furthermore, Dr. Bernard Laubscher, a physician from Switzerland, commented on a report from the American Academy of Pediatrics ([AAP]; Kocherlakota, 2014) in 2018 indicating improper usage of abbreviations for dose and day. Infants in this Switzerland hospital received up to five times the AAP (2014) recommended morphine dose (AAP recommends a maximum of 1.3mg/kg/day). The hospital based their actions on the interpretation of other studies' recommendations as 1.3mg/kg/d (Kraft & Van den

Anker, 2012; O'Grady et al., 2009). These infants, however, had no adverse effects when receiving morphine doses at this range. Dr. Laubscher suggested that the AAP (Kocherlakota, 2014) morphine recommendations may have been based on misread abbreviations of "d" from the initial research studies on morphine treatment for NAS. The extensive variation in the care of infants with NAS likely reflects that many newborns are not receiving optimal or effective care (Young et al., 2021).

High-quality CPGs that are evidence-driven can improve patient outcomes and improve the standardization of patient care (Sciarra, 2012). CPGs are defined as "statements that include recommendations, intended to optimize patient care, that are informed by a systematic review of evidence and as assessment of the benefits and harms of alternative care options" (Institute of Medicine [IOM], 2011, p. 4). The purpose of CPGs are "to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances" (IOM, 1990, p. 8). For the translation of guidelines into practice, they must be both high-quality and evidence-based (Wood et al., 2019). Practice guidelines incorporating the best available evidence can support the consistent use of high-quality recommendations for managing infants with NAS (Marcellus, 2015). Many healthcare organizations and medical societies have increasingly issued their own guidance in the form of CPGs that are of variable methodological quality, often containing differing or contradicting recommendations which may be caused by bias in the guideline process (Boltin et al., 2020). CPGs are considered most effective and valuable when they are produced using appropriate methods, meet specific development criteria to ensure rigor, and include recommendations of high-quality clinical content (Grol et al., 2003; Semlitsch et al., 2015). When quality is at the forefront of guideline development, CPGs can promote best practices, reduce variations in care, and improve resource utilization (Rosenfeld & Shiffman,

2009). However, clinicians may not be aware of the CPGs that are available for them to use, nor the quality of the CPGs and the recommendations that clinicians are using to assist their clinical decisions. Therefore, an evaluation of the quality of CPGs for the management of NAS and their recommendations is warranted to provide clinicians with the knowledge of CPGs and recommendations that are reliable, high-quality, and available for them to access.

Research Objective

The purpose of this research is to evaluate the quality of CPGs for the management of NAS caused by in-utero opioid exposure available to clinicians, to synthesize the non-pharmacological and pharmacological recommendations, and to evaluate the quality and applicability of the recommendations.

Research Questions

This systematic review addresses the following research questions:

1) What CPGs for the management of NAS are available for use by clinicians?
2) What is the quality of currently available CPGs for the management of NAS?
3) What are the recommendations for the non-pharmacological and pharmacological management of NAS?
4) What is the quality and applicability of the non-pharmacological and pharmacological recommendations for the management of NAS?

Literature Review

This literature review provides an overview of the current opioid crisis, prenatal opioid use, the incidence of NAS and its associated healthcare system costs. Various management strategies identified in current NAS literature and the importance of FCC when caring for infants will be explored in this literature review.

The Current State of the Opioid Crisis in Canada

The opioid crisis refers to the alarmingly widespread misuse of prescribed and non-prescribed opioids (United States [U.S.] Department of Health and Human Services, 2021). The opioid crisis is a complex public health issue affecting the health and safety of many individuals worldwide (Canadian Centre on Substance Use and Addiction [CCSA], 2019). Opioids are a class of psychoactive drug that exists in both natural and synthetic forms, often used for pain management (CCSA, 2020a). Canada's most commonly used (and misused) opioids are codeine, hydromorphone, morphine, oxycodone, and fentanyl (CCSA, 2020a). In Canada, opioids are legal when a licensed practitioner prescribes them and when used by the person for whom they were prescribed (CCSA, 2020a). Opioids are illegal when they are made, shared, sold or consumed in an illicit context (Government of Canada, 2021b). Illegal opioids include street drugs, opioids given to an individual by someone who is not their healthcare provider, and opioids consumed but not prescribed to that individual (Government of Canada, 2021b).

Prescription opioids are most commonly used to treat acute and chronic pain; however, they can also be used to control persistent cough or diarrhea, as well as for the management of opioid use disorder (CCSA, 2020a). In 2018, an estimated 13% of Canadians over the age of 15 years had used an opiate within the past year (n = 3.7 million; Statistics Canada, 2019). Approximately 10% of Canadians who used an opioid pain medication within the same year reported some form of misuse (n = 351,000), such as taking a larger dose or using the opioid more frequently than prescribed (7%), using it to get high (3%), using for another purpose than pain relief (4%), or altering the medication form prior to consumption (2%; Statistics Canada, 2019). The current number of Canadians who illicitly use opiates remains largely unknown (Belzak & Halverson, 2018). However, in 2017, 3% of the Canadian population (987,000

individuals) reported using any illicit drug (excluding cannabis) within the past year (Government of Canada, 2019).

Opioids can be obtained not only through prescription, but also illegally by "double doctoring" (visiting multiple doctors in an attempt for prescriptions), sharing between family members, prescription fraud, and through street markets (Belzak & Halverson, 2018). Fentanyl, an extremely potent synthetic opioid derivative, has become more prevalent on the streets (Belzak & Halverson, 2018). Fentanyl is often combined with other substances, resulting in an increase in toxicity and subsequent related harm to users (Belzak & Halverson, 2018). Sproule et al. (2009) found that of individuals who were admitted to the Centre for Addiction and Mental Health from 2000 to 2004 in Toronto, Canada with opioid dependence ($N = 428$), 37% of individuals reported obtaining opioids prescribed by their physicians, 26% reported receiving opioids from both prescription and from the street, and 21% reported obtaining opioids solely from the street. The opioid crisis, driven by prescription and illegal opioid use, is considered a national public health crisis affecting all communities of various ages and socioeconomic groups across Canada (Belzak & Halverson, 2018). Regardless of the method by which opioids are obtained, opioid misuse has hazardous effects, including addiction, overdose, and death (CCSA, 2020a).

Multiple, complex factors have contributed to the opioid crisis, including inadequate housing, poorly managed pain, untreated psychiatric disorders, family history of substance misuse, and adverse early life experiences (Leyton & Stewart, 2014; Webster, 2017). Mental illness and/or pain comorbidities are highly co-prevalent in individuals who use drugs illicitly (Amari et al., 2011). The *Diagnostic and Statistical Manual of Mental Disorders* [DSM-5] defines opioid use disorder as "a problematic pattern of opioid use leading to clinically

significant impairment or distress, occurring within a 12-month period" (DSM-5; American Psychiatric Association, 2013). Treatment for opioid dependence and addictions can limit adverse effects and improve an individual's daily living (Kosten & George, 2002). Access to treatment, nonetheless, can be challenging. For example, those with an opioid use disorder who rely heavily on the healthcare system for medication-assisted treatment and mental health support have been significantly affected by disruptions in the healthcare system from the global COVID-19 pandemic (CCSA, 2020b, 2020c).

During the COVID-19 pandemic, greater opioid use, opioid toxicity, and deaths were reported across Canada and the United States (Centers for Disease Control [CDC], 2020; Government of Canada, 2021a). In Canada, there were 15,134 opioid toxicity-related deaths from April 2020 to March 2022, a 91% increase in deaths compared to April 2018 to March 2020 time frame (Government of Canada, 2021a). The COVID-19 pandemic posed additional barriers to treatment for individuals misusing opioids, such as restrictions to in-person treatment, transportation issues, and technology limitations in accessing psychotherapy (Alexander et al., 2021). In April 2020, the CCSA conducted qualitative interviews with 17 participants with lived experience of substance use, friends or family members of someone who uses substances, or those with professional knowledge of substance abuse and addiction, to better understand the impact of the COVID-19 pandemic on individuals who misuse substances (CCSA, 2020b). Substance use, in this report, refers to those who have used psychoactive substances resulting in experienced harms (CCSA, 2020b). All participants in this study voiced that the pandemic measures disrupted their treatment and harm reduction services (CCSA, 2020b). Similarly, another Canadian qualitative study consisting of 19 interviews with participants recruited between June and September 2020 with lived experiences of substance use also reported having

decreased access to medical care services, harm reduction services, and housing during the pandemic (Galarneau et al., 2021). Galarneau et al. (2021) further found that respondents were consuming drugs alone more often, consuming different drugs due to supply shortages, and using drugs less safely compared to their drug use behaviors prior to the COVID-19 pandemic.

Prenatal Opioid Use

A particularly marginalized population of those who misuse opioids or have substance use disorders are pregnant persons. The number of women in the United States with an opioid use disorder during pregnancy quadrupled in the five-year period from 1999 to 2014, from 1.5 per 1,000 hospital births to 6.5 per 1,000 hospital births (Haight et al., 2018). Ko et al. (2020) conducted a survey of women across 34 U.S. jurisdictions in 2019 and found that of 20,643 respondents who provided information about opioid use during pregnancy, 6.6% of women self-reported using a prescribed opioid during pregnancy, of which 21.2% reported misusing opioids. However, the rate of opioid use during pregnancy determined by self-report may be underestimated due to the stigma and legal implications associated with opioid use (Ko et al., 2020).

The findings from Canadian studies regarding opioid use during pregnancy show variations among provinces. Grywacheski et al. (2021) surveyed 7,111 Canadian postpartum women on topics including their postpartum mental health, substance use during their pregnancy, and breastfeeding. Grywacheski et al. (2021) found that 1.4% of the participants reported using opioids at some point during their pregnancy (95% CI: 1.1%-1.8%). Women who reported symptoms of postpartum depression and/or anxiety disorders were almost three times more likely to have reported using opioids during pregnancy compared to those who did not report these symptoms (95% CI: 1.10-8.03; Grywacheski et al., 2021). A limitation of this study was that the

relatively small sample size may have resulted in an underestimation of the true extent of maternal opioid use (Grywacheski et al., 2021).

Falk et al. (2017) examined pregnancy administrative health claim data and pharmacy drug dispensing claims for all pregnant women in Manitoba, Canada, from 2001-2013 for a total of 175,174 completed pregnancies. Falk et al. (2017) found that 6.7% of the sample were dispensed a prescribed opioid from their pharmacy three months prior to pregnancy (n = 11,692), and 7.7% of women were dispensed an opioid at any time during their pregnancy (n = 13,408). Opioid use during pregnancy declined from 4.2% in the first trimester of pregnancy to 3.0% in the second trimester, and further reduced to 2.9% by the third trimester (Falk et al., 2017). Although many women using opioids prior to pregnancy discontinued their opioid use during pregnancy, for those who continued using opioids, the volume of opioids used (defined as oral morphine equivalents) remained constant to their pre-pregnancy volume ($p > .09$ for all comparisons before and during pregnancy; Falk et al., 2017). The mean oral morphine equivalent dose for women who filled a prescription during their pregnancy increased by more than four-fold throughout the study period, from 284 mg in 2001 to 1,218 mg in 2013 ($p < .001$; Falk et al., 2017). Falk et al. (2017) suggest that women who use opioids during pregnancy may be switching towards more potent opioids, reflecting the greater increase in the oral morphine equivalent from 2001-2013. Furthermore, Falk et al. (2017) found that the proportion of women who filled a prescription for opioids during pregnancy increased from 7.3% in 2001 to 7.7% in 2013 ($p = .03$), which shows an increase in maternal opioid use over time. The several limitations of this study may not allow for the true extent of opioid use during pregnancy to be identified. For example, determining opioid use based on pharmacy dispensing claims may have overestimated the percentage of women who actually consumed their prescribed opioids during

pregnancy (Falk et al., 2017). On the other hand, pharmacy dispensing claims could not capture hospital inpatient opioid use or illicit opioid use (Falk et al., 2017).

Two recent studies from Ontario, Canada have also examined opioid use during pregnancy with larger sample sizes compared to the research performed by Falk et al. (2017) and Grywacheski et al. (2021). Corsi et al. (2020) conducted a population-based retrospective cohort study using the health information from the Better Outcomes Registry & Network (BORN) to look at maternal opioid use during pregnancy from April 1st, 2012 to March 31st, 2018 in Ontario, Canada. From their eligible sample for analysis (n = 710,911), 1.1% of women were found to have used an opioid during pregnancy (Corsi et al., 2020). Unlike Falk et al. (2017) study, Corsi et al. (2020) found a decrease in the rate of opioid use during pregnancy over time, from 1.31% in the fiscal year of 2012-2013 to 1.05% in the fiscal year of 2017-2018 ($p < .001$). Another recent study by Camden et al. (2021) linked health administrative data provided by the Institute for Clinical Evaluative Sciences (IC/ES) across births in Ontario, Canada, from January 1st, 2014 to December 31st, 2019 (n = 701,896). In this study, prenatal opioid exposure (including prescribed and illicit use) during this time frame was reported as 5.3% (Camden et al., 2021). However, similar to Corsi et al.'s study (2020), prenatal opioid use decreased over Camden et al.'s (2021) study period, from 6.1% in 2014 to 4.5% in 2019 ($p < .001$). The difference in findings of prenatal opioid exposure between Corsi et al.'s (2020) and Camden et al.'s (2021) population-based studies may be due to an underreporting of prenatal opioid exposure, particularly seen when using clinical registries as used in Corsi et al.'s (2020) study.

Research on maternal opioid use during pregnancy poses various methodological challenges and limitations. Prenatal opioid use is often under-reported due to concerns of possible associated legal implications. Although trends in the United States have demonstrated

an increasing proportion of individuals consuming opioids during pregnancy (Haight et al., 2018), the trends reported in Canada are conflicting. Research on Canadian prenatal opioid use has demonstrated that prenatal opioid use may range between 1.1% to 7.7%, although the true extent remains unknown (Camden et al., 2021; Corsi et al., 2020; Falk et al., 2017; Grywacheski et al., 2021).

Incidence of Neonatal Abstinence Syndrome in Canada

Filteau et al. (2018) used data from the Canadian Institute of Health Information (CIHI), Statistics Canada and the Ontario Provincial Council for Maternal and Newborn Health to examine the national incidence of NAS. In Canada, despite the conflicting findings regarding the rate of prenatal opioid use, the incidence of NAS tripled between the years of 2003 and 2014, from 0.18% to 0.54% (1.8 to 5.4 per 1,000 live births; Filteau et al., 2018). A limitation of this study, however, is that the incidence for Newfoundland and Labrador, Prince Edward Island, the three Territories, and Quebec could not be examined (Filteau et al., 2018). In 2014, the Territories had the fourth highest rate of opioid-poisoning-related hospitalizations, which may suggest a correspondingly higher incidence of NAS (CIHI, 2016; Filteau et al., 2018). The exclusion of Quebec, the second most populous province in Canada, may have also skewed the results of this study (Filteau et al., 2018). Based on retrospective hospital admission data in 36 local public health agencies across Ontario, Canada, the incidence of NAS was found to have increased from 0.099% in 2003 to 0.594% in 2016 (0.99 per 1,000 live births in 2003 to 5.94 per 1,000 live births; Dawson et al., 2019). A Canadian national retrospective, population-based cross-sectional study including all singleton live births in all provinces and territories excluding Quebec (N = 2,881,789) found an increase in the incidence of NAS from 0.20% in 2005-2006 to

0.51% in 2015-2016, following similar tends as the United States, England, and Australia (Lisonkova et al., 2019).

Infant Hospitalizations and Healthcare Expenditures

As the number of infants with NAS increases, the hospitalization rates and the associated costs have also increased. Between 2013 and 2017, hospitalizations for NAS in Canada increased by 21%, from 1,592 hospitalizations in 2013 to 1,908 hospitalizations in 2017 (CIHI, 2018). The increase in the incidence of NAS has placed a burden on the healthcare system, with the total costs of care rising from CAN$ 15.7 million in 2010 to CAN$ 26.9 million in 2014 (Filteau et al., 2018). Parallel to Canada, the United States has also seen an alarming increase in the incidence of NAS, hospitalizations for NAS, and associated healthcare costs. The incidence of NAS in the United States increased approximately six-fold, from 1.2 to 6.7/1,000 hospital births per year from 2000 to 2016 (Patrick et al., 2012; Strahan et al., 2020). Neonatal hospitalizations in the United States for NAS have increased over the past decade, with the percentage of total days of hospitalization for NAS increasing from 0.6% in 2004 to 4.0% in 2013 (Tolia et al., 2015). Hospital costs for the care of infants with NAS from 2009 to 2012 in the United States have increased from US$ 732 million to US$ 1.5 billion, respectively (Patrick et al., 2015). Among births in the United States covered by Medicaid, hospital costs for infants with NAS increased from 1.6% in 2004 to 6.7% in 2014 (Winkelman et al., 2018). Evidently, the incidence of NAS and, consequently, the costs associated with the management of NAS are on the rise (Dawson et al., 2019; Patrick et al., 2015; Winkelman et al., 2018). Effective and standardized management strategies can improve patient care and may ultimately lessen the financial burden on our healthcare system.

Management of Neonatal Abstinence Syndrome

NAS treatment goals include preventing complications and restoring normal newborn activities such as sleep, nutritional intake, adequate weight gain, and social environment adaptation (Siu & Robinson, 2014). Current management strategies for NAS comprise of pharmacological and non-pharmacological interventions. A review article by Kocherlakota (2014) summarizing the management options for NAS concluded that the initial management of infants presenting with NAS symptoms should comprise of non-pharmacological interventions. Kocherlakota (2014) suggested that non-pharmacological therapies should be attempted before initiating pharmacological therapy, as they may be sufficient for managing infants presenting with mild withdrawal symptoms (Kocherlakota, 2014). Pharmacologic therapy can be used as an adjuvant to non-pharmacological interventions to treat infants demonstrating more severe withdrawal symptoms of NAS (Kocherlakota, 2014). Scoring tools are available to help clinicians determine when to begin management for NAS.

Scoring Tools for Neonatal Abstinence Syndrome. Jansson & Patrick (2019) stated that an infant with NAS should be assessed for severity of withdrawal with a scoring tool which informs the effectiveness of management, when the initiation of pharmacological treatment should begin, dosing parameters, and weaning eligibility. There is currently a wide variation in the scoring tools used in clinical practice, and psychometric testing for many of these assessment tools is lacking (Bagley et al., 2014; Jansson & Patrick, 2019).

The most commonly used scoring tool for assessing the severity of withdrawal is the Finnegan scoring tool in its modified and original version (Finnegan et al., 1975; Jansson & Patrick., 2019; Mehta et al., 2013). The *Finnegan Neonatal Abstinence Scoring Tool* (FNAST), first published in 1975, consists of 21 items with subcategories representing the central nervous

system, metabolic, vasomotor, respiratory, and gastrointestinal withdrawal symptoms (Finnegan et al., 1975). Symptoms with less pathological significance are scored out of 1 (with 0 being no evidence of symptoms), while symptoms with more moderate significance are given a range of point values to score from (Finnegan et al., 1975). Symptoms with the greatest potential for adverse effects (i.e., seizures) are scored 5 (Finnegan et al., 1975). Several modified versions of the Finnegan tool exist; however, they may not have been validated and may have poor inter-rater reliability due to the subjectiveness of the assessment (Singh & Davis, 2021).

The *Eat Sleep Console Tool* (ESC; Grossman et al., 2017), a newer scoring tool, assesses the infant's disturbances in functions such as feeding, sleeping, and their ability to be consoled (Grossman et al., 2018). According to Grossman et al. (2018), pharmacologic treatment should only begin if there are disturbances in these functions which non-pharmacological interventions cannot alleviate. Several studies have reported an association between the use of the ESC as part of an infant's care with a reduced hospital length of stay for the infant, along with a decrease in the need for and duration of pharmacological treatment (Hein et al., 2021; Miller & Willier, 2021; Ryan et al., 2021). Other assessment tools for NAS include the *Narcotic Withdrawal Score* (Lipsitz, 1975), the *Neonatal Narcotic Withdrawal Index* (Green & Suffet,1981), and the *Neonatal Withdrawal Inventory* (Zahorodny et al., 1998).

Non-pharmacological Interventions. Non-pharmacological interventions are considered safe, cost-effective, and often easy to implement (Kocherlakota, 2014; Mangat et al., 2019). The goal of non-pharmacologic therapy is to alleviate withdrawal symptoms and to reduce the need for pharmacologic treatment. Jansson & Patrick (2019) state that non-pharmacological management is independent of the initiation of medications and should begin at birth and continue throughout hospitalization. Systematic reviews have demonstrated the effectiveness of

non-pharmacological interventions for the management of NAS, including rooming in and reducing the separation between infant and family (Bagley et al., 2014, Edwards & Brown, 2016; MacMillan et al., 2018; MacVicar & Kelly, 2019; Wachman et al., 2018), breastfeeding (Bagley et al., 2014; McQueen et al., 2019; Wachman et al., 2018), environmental modifications (i.e., decrease in light and nose, and temperature regulation; Oostlander et al., 2019), bed type such as rocking beds or non-oscillating waterbed (Edwards & Brown, 2016; Oostlander et al., 2019; Ryan et al., 2019), positioning and firm holding (Bagley et al., 2014, Edwards & Brown, 2016, MacMullen et al., 2014; Oostlander et al., 2019), swaddling (Oostlander et al., 2019; Ryan et al., 2019), and acupuncture (Bagley et al., 2014; Edward & Brown, 2016; MacVicar & Kelly, 2019; Wachman et al., 2018). Although systematic reviews have identified that many non-pharmacological interventions are based on low-quality evidence, non-pharmacological interventions can still be incorporated into clinical practice due to their potential benefits, at no harm to the infant. Furthermore, Patrick et al. (2020) stated that non-pharmacological interventions that engage the participation of the family caregiver are foundational for the care of an infant with NAS.

Unfortunately, the use of non-pharmacological interventions may not be effectively implemented into practice. For example, a Canadian study by Murphy et al. (2017) found that 69% of NICUs (44/64) in 2014 implemented non-pharmacological interventions as soon as the infant had been identified as being at risk for developing NAS, whereas 31.2% (20/64) indicated that they would only begin to implement non-pharmacological interventions when the infant reaches a certain threshold on a scoring tool. The differences in the initiation of non-pharmacological interventions may cause some infants to have more severe withdrawal symptoms than others.

Pharmacological Interventions. Pharmacological interventions can begin when an infant is not responding to non-pharmacological management strategies or if an infant is presenting with moderate to severe withdrawal symptoms (Kocherlakota, 2014). The goal of pharmacological therapy is to provide short-term relief of withdrawal symptoms (Shukla et al., 2021). There has been an increase in the use of pharmacological therapy for infants with NAS within the past decade. Tolia et al. (2015) found that the proportion of U.S. infants with NAS who were given pharmacological therapy had increased from 74% in 2004-2005 to 87% in 2012-2013 ($N = 10{,}327$; $p < .001$). As a result, the mean duration of the therapy increased, along with the days of treatment in the NICU (Tolia et al., 2015).

There is variability in the pharmacological interventions being used for the management of NAS and how it is being delivered across institutions in Canada and the United States (Byerley et al., 2021; Murphy et al., 2017; Young et al., 2021). Although medications are available to help ameliorate withdrawal symptoms, Kocherlakota (2014) indicated that there are no uniformly accepted or standardized pharmacological treatments. The lack of standardization and variability in the medications that are being used as first-line, second-line, and adjuvant therapies may be due to the conflicting and limited research on the pharmacological management of NAS (Murphy et al., 2017; Patrick et al., 2014). The most commonly used first-line medications include morphine, methadone, and buprenorphine (Bogen et al., 2017; Wachman et al., 2018). However, the optimal medication for NAS treatment has not been defined (Hudak et al., 2012).

The lack of standardization of pharmacological treatment has resulted in variations in NAS management. Byerley et al. (2021) assessed the pharmacological treatments used for the management of NAS across 56 organizations in the United States in 2019. Byerley et al. (2021)

identified that morphine was the most commonly used first-line agent used in institutions (80%), followed by methadone (9%), clonidine (4%), and buprenorphine (4%). Mian et al.'s (2019) systematic review of morphine regimens to treat NAS included 43 articles. Although morphine is the most common first-line agent for the treatment of NAS, Mian et al. (2019) identified variations in the use of morphine for NAS, including variations on the threshold to initiate treatment, dosing, dosing intervals, dosing regimen strategies (by weight or by symptom), and morphine weaning.

Similarly, in Canada, Murphy et al. (2017) identified morphine to be the most common first-line agent used in 2014 (62/64 institutions; 97%), demonstrating that Canada and the United States are relatively consistent in using morphine as first-line therapy. However, there is variation among Canadian NICUs regarding which adjunct medication is used (Murphy et al., 2017). Furthermore, Canadian hospitals have conflicting practices regarding discharging infants home with first-line medications. For example, 36.9% of sites discharge infants home on first-line medications, and 38.9% will discharge infants home on adjuvant medications (Murphy et al., 2017).

Although morphine is frequently used as a first-line medication for NAS management in United States and Canada, morphine may not be the most effective pharmacological treatment. Research has shown that the opioid buprenorphine may also be beneficial as a first-line medication (Jansson & Patrick, 2019). A systematic review and meta-analysis by Lee et al. (2019) analyzed eight studies and found that morphine has a 1.5-fold overall increase in the rate of adjunct drug use compared to methadone (RR = 1.51, 95% CI: 1.35-1.69). Findings from Lee et al.'s (2019) systematic review suggest that methadone may be effective in reducing withdrawal from polydrug exposure. In Slowiczek et al.'s (2018) systematic review of morphine

and methadone for the management of NAS, Slowiczek et al. (2018) identified that there is little clinical evidence in the comparison of the effectiveness of morphine to methadone and a recommendation of which to use could not be made. A recent Cochrane systematic review identified that although buprenorphine can reduce the duration of hospitalization and treatment compared to morphine, there is insufficient evidence to determine its safety (Zankl et al., 2021). Furthermore, Zankl et al. (2021) identified that the type of opioid used may have little to no effect on treatment failure.

On the other hand, Lee et al. (2019) review suggests that methadone and buprenorphine may have better short-term treatment outcomes than morphine and should therefore be considered for broader implementation. Zankl et al. (2021) found that the use of an opioid for the management of NAS may reduce treatment failure compared to phenobarbital, diazepam, or chlorpromazine, but opioids may have little to no effect on the duration of hospitalization. A recent retrospective review by Badar et al. (2021) found that when clonidine was added to morphine as the initial therapy for NAS, the cumulative days of exposure to morphine was reduced, and the hospital length of stay decreased compared to morphine alone (20 days vs. 30 days, $p = .001$; 15 days vs. 26 days, $p = .02$ respectively).

There is emerging research evaluating the effectiveness of various pharmacological treatments for NAS, but the evidence is often conflicting or unclear. Evaluating the quality of recommendations for the management of NAS in CPGs is necessary as it provides clinicians with information about the level of quality of the treatment recommendations in CPGs. When the most optimal medications are used for managing NAS symptoms, medications can help to ameliorate withdrawal symptoms and reduce hospital length of stay, which may lessen emotional and financial burdens on families.

Newborn Attachment and Family Experiences in the Neonatal Intensive Care Unit

Newborn Attachment. A newborn's family is an essential part of the management of NAS and are integral members to include in their care team. According to Whalen et al.'s (2019) review of care models for NAS, models that center on the mother (or infant's primary caregiver) as the primary means of treatment for newborns with NAS may be more effective in reducing the length of treatment and hospital stay compared to other models. A retrospective, single-cohort study of 86 mother-newborn dyads in Boston, United States with infants born between March 2015 and April 2016 with in-utero opioid exposure found that greater parental presence was associated with a decrease in NAS severity, decreased length of stay, and decreased length of pharmacotherapy (Howard et al., 2017). Howard et al. (2017) highlighted that CPGs should encourage parental presence.

The early postnatal period is important for newborns to develop a secure attachment and bond (Shannon et al., 2021). The separation caused by hospitalization may impair maternal-newborn bonding and have lasting developmental consequences for the newborn (Boucher, 2017). When a caregiver consistently responds to an infant's cry, the infant develops basic trust and confidence, the first stage in Erikson's Stages of Psychosocial Development (Erikson, 1994). Attachment is a pivotal event in an infant's emotional development, as it is the foundation for the child's sense of security, self-esteem, emotional regulation, and development of skills for self-control (Malik & Marwaha, 2021).

The quality of the infant-parent attachment is a powerful predictor of the infant's social and emotional outcomes later in life (Benoit, 2004). On the contrary, failure to meet the infant's needs can result in insecure attachment styles as the infant does not develop a sense of trust and security which can predispose the infant to later mental health issues (Ainsworth et al., 1978).

Although research has been conducted on various strategies to promote secure attachments between at-risk mothers and their infants, few studies investigate the impact of attachment-based interventions for infants with NAS (Kondili & Duryea, 2019).

Newborn Attachment in the NICU/SCN. A recent Australian study conducted by Shannon et al. (2021) interviewed nine participants who were nurses or midwives to explore their experiences in caring for infants with NAS and their efforts in facilitating attachment relationships within families. Shannon et al. (2021) acknowledged that the NICU/SCN environment for infants with NAS likely contributes to the development of an insecure attachment (Shannon et al., 2021). Shannon et al. (2021) highlighted that this is likely due to the absence of the infants' caregivers at their bedside, competing priorities in nursing/midwifery care, and the prioritization of the infants' physiological well-being rather than psychological well-being. For example, some of the participants in this study voiced many instances whereby infants who did not have parents present were often left to cry, as nurses had to prioritize their high workload volume (Shannon et al., 2021). The participants discussed the benefits of parental presence and attachment on the short-term physical outcomes, including newborns being less irritable, feeding better, gaining weight, reducing the need for pharmacological therapy, and reducing hospital length of stay. This research raises awareness of the potential need for strategies to promote secure attachment relationships between infants with NAS in the NICU/SCN and their caregivers (Shannon et al., 2021). Healthcare providers in the NICU/SCN can support newborn attachment with their families by encouraging mothers/caregivers to be involved with their newborns' care at every opportunity (Shannon et al., 2021).

Family Experiences of Caring for their Infant in the NICU/SCN. In a qualitative study, Atwood et al. (2016) interviewed 20 families in the United States regarding their

experience of their hospitalized infant with NAS. Atwood et al. (2016) highlighted five domains that influenced families' experiences during hospitalization:

1) Education and preparation.
2) Parents as partners in care (e.g., involvement with care and scoring).
3) Interpersonal interactions and communication (e.g., support from staff).
4) Hospital environment and transitions (e.g., different unit routines).
5) External factors (e.g., economic limitations that affected their ability to visit their infant).

Addressing the needs of families as defined by the five domains may allow for improved FCC to be received by NICU families (Atwood et al., 2016).

Parental presence is crucial for developing a secure attachment and can significantly influence short-term and long-term health outcomes for infants with NAS (Kondili & Duryea, 2019). Therefore, it is essential that the management strategies for infants with NAS in clinical settings fully support families in their infants' care. Efforts should be made to enhance families' involvement in their infants' care, such as providing emotional support for families in the NICU/SCN, educating families on NAS, and reducing barriers that may impede families from caring for their infants. Including FCC recommendations in CPGs for the management of NAS may improve the short-term and long-term health outcomes for infants with NAS.

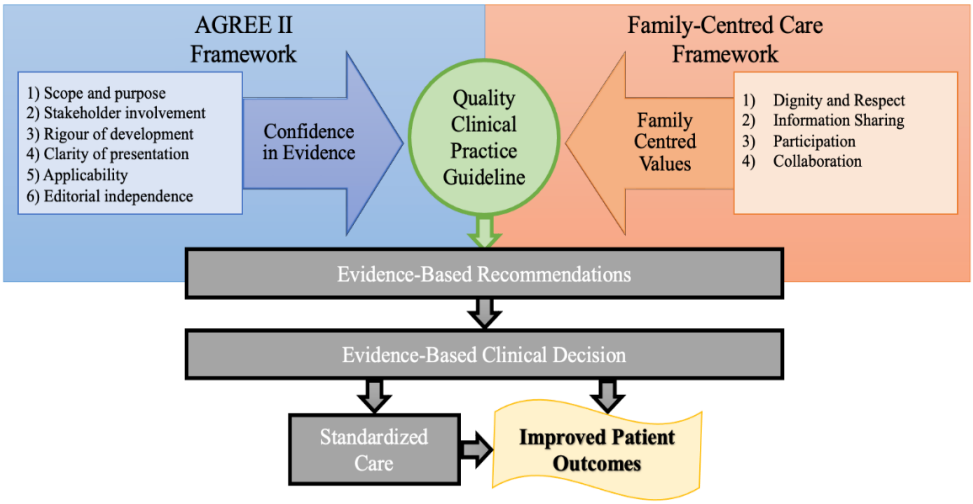
Integrated Framework

This thesis takes a unique approach to how guideline quality is defined and used by integrating two frameworks to conceptualize quality: The Appraisal of Guidelines for Research & Evaluation framework ([AGREE-II]; AGREE Next Steps Consortium, 2017) and a Family-Centered Care framework (Johnson et al., 2008). The AGREE-II framework guided the

pragmatic and normative component in this systematic review by examining the quality of CPGs. The Family-Centered Care framework guided the assessment of the values underlying the clinical recommendations. *Quality* in this thesis research incorporates two distinct but interrelated concepts to define "quality" clinical practice guidelines: confidence in the evidence and development process and FCC values. I created an integrated framework using the AGREE-II Framework and the Family-Centred Care Framework to explain how "quality" in this research is conceptualized (see Figure 1).

Figure 1

Conceptualization of the Integrated Framework



Relevance of This Research

Supportive care based on best practices in the early neonatal period is critical to support the recovery and development of infants with NAS (Marcellus, 2002). In 2012, the AAP released a policy statement indicating the need for standardizing care delivered to infants with NAS (Hudak et al., 2012). Patrick et al. (2016) identified that standardization of policies and care in their multi-center quality-improvement initiative was associated with improved outcomes for infants with NAS and a decrease in healthcare utilization. The standardization of care in this

quality-improvement initiative also resulted in a reduced length of treatment and length of hospital stay for infants with NAS (Patrick et al., 2016). Furthermore, using high-quality CPGs in practice can have several potential benefits, including improving the quality and consistency of care given to patients and the quality of clinical decisions (Woolf et al., 1999). In order to assist clinicians in making the best decisions regarding the care for infants with NAS resulting from in-utero opioid exposure and to achieve optimal patient outcomes, existing guidelines and recommendations for management must be evaluated. Additionally, there is emerging research that demonstrates improved patient health outcomes and enhanced patient and family satisfaction when FCC practices are prioritized by healthcare professionals, predominantly within perinatal and pediatric settings (Cooper et al., 2007; Dien et al., 2022; Kuo et al., 2012; Ortenstrand et al., 2010). CPGs that do not reflect family-centred values or do not consider individual family contexts can create conflict and tension between healthcare workers and families (Jones et al., 2015). CPGs must therefore also contain high-quality recommendations that reflect FCC to support optimal patient and family outcomes.

The systematic review that I have conducted expands on the limited knowledge of the quality and content of the CPGs for NAS and assesses the quality of their recommendations, a direction that has not been explored in NAS research. I also present the first quality appraisal tool to evaluate FCC values in CPGs. Findings from this research will contribute to the generation of knowledge about high-quality CPGs and recommendations for managing NAS. The outcomes of this research have the potential to inform clinicians' decisions for NAS management, assist in standardizing care, reduce variations in practice, and, most importantly, improve outcomes for infants with NAS and their families. In the next chapter (Chapter two), I assess the quality of CPGs within the framework of the AGREE-II (left of the integrated

framework). In Chapter three, I describe the development and piloting of the quality appraisal tool to evaluate the quality of CPGs under the context of FCC (right of the integrated framework).

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Chapter Two: Manuscript

Clinical Practice Guidelines for the Management of Neonatal Abstinence Syndrome: A Systematic Review and Evaluation

This chapter is an unpublished manuscript written for submission to the Journal of Perinatal and Neonatal Nursing.

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Abstract

Neonatal abstinence syndrome (NAS) is described as the withdrawal symptoms experienced when an infant has been exposed to certain substances (e.g., opioids) in-utero. The incidence of NAS is on the rise in North America and poses significant health challenges on infants. To support optimal patient outcomes and to standardize care, the knowledge of the quality guideline development is crucial. We conducted a systematic review of NAS management guidelines retrieved from EMBASE, CINAHL, PubMed and a grey literature review. Twenty guidelines met our inclusion criteria. We conducted a quality appraisal of these guidelines using the AGREE-II and AGREE-REX instruments. Overall, guidelines scored poorly on the AGREE-II (16/20) and AGREE-REX (10/20) quality appraisals. We identified one guideline from the AGREE-II appraisal and three guidelines from the AGREE-REX appraisal that were high-quality in terms of their guideline development (AGREE-II) and recommendations (AGREE-REX) based on our cut-off scores to define low, moderate, and high-quality. Most non-nonpharmacological recommendations were consistent across guidelines however pharmacological recommendations varied considerably amongst guidelines. Findings will improve clinicians' awareness of the variation in quality of the available guidelines and recommendations and assist them to make care decisions that are from the best available evidence.

Keywords: Neonatal abstinence syndrome, systematic review, quality appraisal, clinical practice guidelines

Introduction

Neonatal abstinence syndrome (NAS) is described as the withdrawal symptoms experienced when a newborn has been exposed to opioids or other substances (e.g., selective serotonin reuptake inhibitors and selective hypnotics[1]) in-utero and their exposure is abruptly discontinued upon their birth.[2] NAS is also known as neonatal withdrawal syndrome, neonatal opioid withdrawal syndrome (NOWS), neonatal drug withdrawal syndrome, and neonatal withdrawal. NAS symptoms are multi-systemic with a wide range of severity.[3] Symptoms include central nervous system hyperactivity, irritability, seizures, tremors, rigid muscle tone, respiratory distress, vomiting, loose stool, and weight loss.[3,4] Infants with NAS may require pharmacological treatments for symptom management and extended hospital stays in a Neonatal Intensive Care Unit (NICU) or Special Care Nursery (SCN).[5-7] NAS can result in negative long-term effects, including growth delays and impairments in cognitive and behavioral development.[5,8] Hospitalizations, particularly in the NICU/SCN, can cause the development of insecure attachment due to the separation of infants from their caregivers.[9] An impairment in maternal-newborn bonding can have lasting developmental consequences for the infant.[10]

The United States (U.S.) has seen an alarming increase in the incidence of NAS resulting in prolonged hospitalizations and associated healthcare costs. The rate of NAS in the United States has increased from 4.0/1,000 hospital births (95% Confidence Interval [CI]: 3.3-4.7) in 2010 to 7.3/1,000 in 2017 (95% CI: 6.8-7.7), a relative increase of 82%.[11] Other studies with retrospective samples of infants during the time frame of 2009-2016 have also shown increasing incidence of NAS in hospitals.[12-14] From 2004-2005 to 2012-2013, infants who required pharmacological therapy increased from 74% to 87% ($p < .001$).[13] Strahan et al[12] found infants with NAS had a length of stay (LOS) averaging 15.9 days (Standard Deviation [SD] = 20.4

days). The total hospital costs were US$ 316 million in 2012 and increased to US$ 572.7 million by 2016.[12,15]

Likewise, the incidence of NAS in Canada has increased over the past decade. The Canadian Institute of Health Information[16] (CIHI) found that hospitalizations for NAS in Canada increased by 21% between 2013 and 2019, from 1,592 hospitalizations in 2013 to 1,908 hospitalizations in 2017. A recent analysis of Canadian hospitalization data (excluding Quebec) demonstrates an increased rate of hospitalization related to NAS by 80% between 2010 and 2020, from 3.5 per 1,000 live births in 2010 to 6.3 per 1,000 live births in 2020.[17] Other published Canadian literature similarly demonstrates an increase in the incidence of NAS.[6,18-19] There is limited Canadian research evaluating the effects of the COVID-19 pandemic on the incidence and hospitalization rates for NAS. The rate of hospitalizations, however, increased by 5% from 2019 (n = 1,665) to 2020 (n = 1,755), with 2020 having the highest recorded rate of NAS hospitalizations.[17] The average Canadian hospital LOS for infants with NAS from April 2020 to March 2021 was 20 days for pre-term infants and 14.7 days for term infants ($t[1] = 5.97$, $p < .0001$[17]), which remains consistent with the LOS in 2003 (mean hospital LOS = 14.4 days[6]). Subsequently, the total per-patient cost of NAS care in Canada increased from CAN$ 15.7 million in 2010 to CAN$ 26.9 million in 2014.[6]

Over the past two decades, the incidence of NAS has increased in North America and other countries, such as England.[20-21] The incidence of NAS in Western Australia, however, has remained steady from 2003 to 2018.[22] This overall increasing trend of NAS worldwide reflects a significant global clinical health concern of maternal use of opioids and other drugs during pregnancy and the resulting later consequence of newborn withdrawal.

The use of high-quality clinical practice guidelines (CPGs) can have several benefits, including the improvement of the quality and consistency of care that is given to patients and the quality of clinical decisions.[23] CPGs are defined as "statements that include recommendations, intended to optimize patient care, that are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options."[24(p.4)] The purpose of CPGs is "to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances."[25(p8)] Many healthcare organizations and medical societies have issued their own guidance in the form of CPGs that vary in quality and may contain differing or even contradicting recommendations compared to other guidelines on the same topic.[26] CPGs are most effective when they are produced using appropriate methods, meet specific development criteria to ensure rigor, include recommendations of high-quality clinical content and expertise, and address issues of feasibility and implementability.[27,28] When quality is at the forefront of guideline development, CPGs can promote best practices, reduce variations in care, and improve resource utilization.[29] Alternatively, when guidelines are adopted without considering the quality of evidence, patients may be subjected to ineffective or even potentially harmful interventions.[23]

Although there are numerous CPGs addressing NAS care, there is a wide variation of care and management for these infants in the United States and Canada.[30-33] The variability in care seen for infants with NAS indicates that many infants may not be receiving effective care.[33] In order to optimize the health outcomes of this population of infants and to standardize the management of care, an evaluation of the content and quality of existing guidelines for NAS is warranted. There has not yet been an assessment of both the quality of NAS guidelines along with their recommendations. This article describes a systematic review conducted to critically appraise the quality of CPGs for the management of NAS resulting from in-utero opioid

exposure using the Appraisal of Guidelines for Research and Evaluation II[34] (AGREE-II) and the Appraisal of Guidelines Research & Evaluation-Recommendation Excellence[35] (AGREE-REX) instruments. This systematic review will address the following research questions:

1. What CPGs for the management of NAS are available for use by clinicians?
2. What is the quality of currently available CPGs for the management of NAS?
3. What are the recommendations for the non-pharmacological and pharmacological management of NAS?
4. What is the quality and applicability of the non-pharmacological and pharmacological recommendations for the management of NAS?

Methods

Design

We conducted a systematic review of CPGs for NAS management resulting from in-utero exposure to opioids. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses[36] guided the reporting of the CPGs (PRISMA; see Appendix A for PRISMA Checklist). The protocol for this systematic review is registered with *The International Prospective Register of Systematic Reviews* (PROSPERO; Registration number: CRD42022323307).

Eligibility Criteria

We used the PICAR (P= Population, I = Intervention, C= Comparison, A= Attributes, R= Recommendations) framework to guide the identification of eligible guidelines (see Appendix B). We identified the eligible CPGs for appraisal according to the following eligibility criteria.

Inclusion Criteria

The following were the inclusion criteria: guidelines regarding hospitalized newborns with NAS as a result of in-utero opioid exposure and provided at least one pharmacological

and/or non-pharmacological recommendation for NAS; available in English or French; published in the time frame of January 1st 2011-April 22nd 2022; published in peer-reviewed national/international journals published by professional organizations or associations, or from hospitals, healthcare, and research institutes; have indicated or demonstrated that they were evidence and/or consensus-based; met the IOM[24] definition of a guideline; available to the public and free on the internet; contains the word "guideline" within the text; and was the most up-to-date version of the guideline.

Exclusion Criteria

The following were the exclusion criteria: guidelines that pertained to the outpatient management of NAS or addressed non-opioid related NAS management; publications with recommendations from systematic reviews, clinical reports, clinical trials, case series, conference posters, presentations, abstracts, or dissertations; and incomplete publications (e.g., draft guideline, lacking full text).

Search Strategy and Data Sources

We developed the search strategy in consultation with a health science librarian at the University of Ottawa and the search was peer-reviewed according to the *Peer Review of Electronic Search Strategies Statement*[37] (PRESS; See Appendix C for MEDLINE search strategy). We then conducted the search on MEDLINE, EMBASE, and CINAHL databases and a grey literature search on clinical guideline registries/databases and health organization/association websites (see Appendix D). Finally, we conducted a Google review with the first 100 results of each search using the following keywords: *neonatal abstinence syndrome*, *neonatal opioid withdrawal*, *neonatal passive addiction,* or *neonatal opioid withdrawal syndrome,* and *guideline, or clinical practice guideline,* or *practice guideline*.

Screening and Data Selection

We uploaded the CPGs identified from the databases and registries into Distiller Systematic Review[38] (DSR) and recorded findings from the grey literature in an Excel file. Two reviewers (CF and CC) independently screened each record on the Excel file, and records that demonstrated evidence of eligibility were uploaded into DSR for screening.

We conducted the screening and selection of CPGs for inclusion in two steps: 1) title/abstract screening and 2) full-text screening. In the first step, two reviewers (CF and CC) independently screened the title/abstract on DSR for eligibility based on the inclusion and exclusion criteria. In the second step, the two reviewers did a full-text screening of those records selected from step 1. The two reviewers used the hierarchy for exclusion as follows: 1) not a CPG, 2) no relevant recommendations, 3) not for hospital care, and 4) other (does not meet other eligibility criteria). The two reviewers met to address any discrepancies identified after each screening step.

Guideline Appraisal

Quality Assessment Tools

AGREE-II. We used the AGREE-II instrument to assess the quality of CPGs in this review. The AGREE-II instrument is a widely used tool for the assessment of the process of guideline development and reporting.[39]

AGREE-REX. We used the AGREE-REX, a complement to the AGREE-II, to evaluate the recommendations from CPGs.[40] The AGREE-REX addresses the clinical credibility and implementability of the recommendations.[40]

Appraisal of CPGs

The appraisal team consisted of a total of four appraisers (CF, CC, MB, and WP). The appraisers read the AGREE-II and AGREE-REX user manuals, supporting documents, and completed the tutorials on the AGREE enterprise website. To establish agreement, each appraiser independently appraised three guidelines with the AGREE-II and AGREE-REX instruments. We used a minimum cut-off score of 0.6 on the intraclass correlation (ICC) between the four appraisers to ensure adequate inter-rater reliability on the three training guidelines prior to appraising the selected NAS guidelines. The average measures of the ICC between the four appraisers ranged from 0.789- 0.955 ($p = .000-<0.001$) on the AGREE-II and 0.729-0.877 ($p = <$ .001-.003) on the AGREE-REX appraisals (see Appendix E).

The developers of the AGREE-II instrument recommend having at least two appraisers to assess each guideline.[34] In our review, two appraisers assessed the guidelines. CF, the primary evaluator, independently appraised all guidelines with the AGREE-II and the AGREE-REX tools. Next, we divided the guidelines amongst the other members of the appraisal team (CC, MB, and WP) to be the second appraiser. CF and the second appraiser met to discuss the findings from each guideline and reach a consensus score for each item of the AGREE-II and AGREE-REX. We used the following two rules to help facilitate a final score when we were unable to achieve a consensus agreement: 1) If the scores differed by one point, the higher score would be selected, and 2) If the scores differed by two points, the middle number between the score would be selected.

Data Extraction and Analysis

In response to research question 1 *(What CPGs for the management of NAS are available for use by clinicians?),* we extracted the following characteristics of each CPG and displayed the

findings in a table: year of publication, country, journal/association, methodology, funding, and target audience.

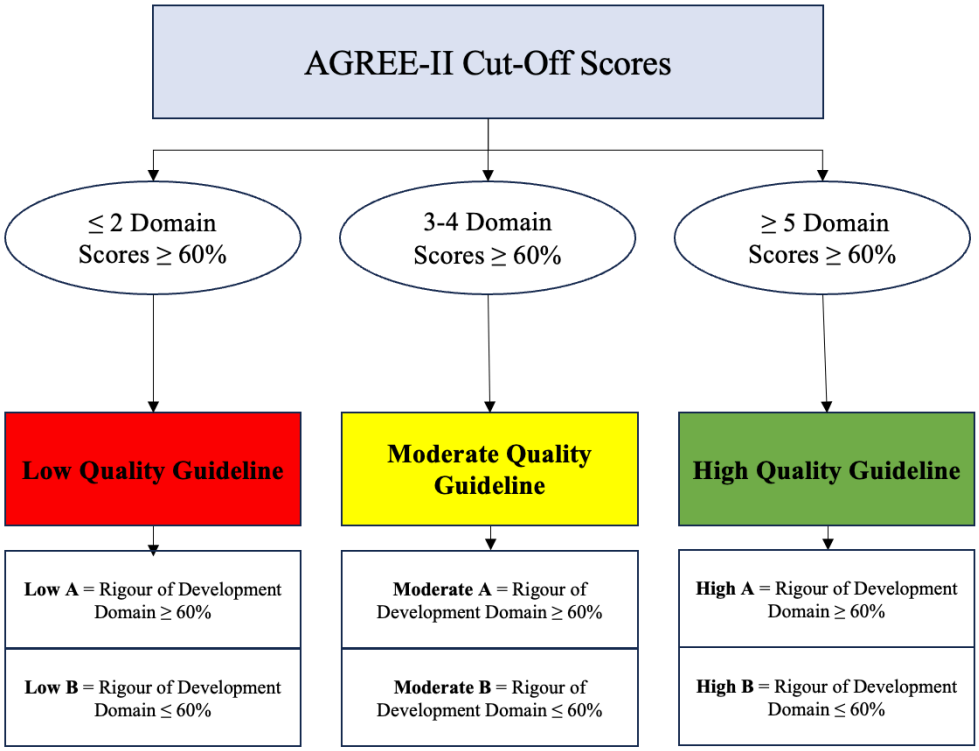
To address research question 2 *(What is the quality of currently available clinical practice guidelines for the management of NAS)* and research question 4 (*What is the quality and applicability of the non-pharmacological and pharmacological recommendations for the management of NAS?),* we calculated the domain scores from the AGREE-II and AGREE-REX appraisals of each guideline, and an overall score for the AGREE-REX. We calculated the domain scores from the AGREE-II and AGREE-REX as follows:

$$\text{Scaled Domain Score} = \frac{\text{Obtained score-Minimum possible score}}{\text{Maximum possible score-Minimum possible score}} \text{ x } 100$$

The AGREE-II and AGREE-REX do not have a fixed cut-off to differentiate between low-level and high-level quality guidelines and recommendations based on their domain scores.[34-35] This allows for the flexibility to consider the contextual factors and overall quality of knowledge pertaining to the topic of interest. [34-35] There are numerous systematic reviews using the AGREE-II appraisal with various definitions for cut-off scores for quality.[41] Many research studies use a cut-off 60% to define "high-quality domain" but how the scores are interpreted to define a "high-quality guideline" may vary.[41-45] Our research team agreed to define domain quality as follows: "high-quality domain" as a score of $\geq$ 60%; "moderate quality domain" as between 30-60%; and a "low-quality domain" as a score < 30%. We defined "high-quality guideline" based on previous studies and created a slightly modified definition.[42-45] First, we defined a "high-quality guideline" based on the AGREE-II appraisal as a guideline that had five or more domain scores above 60%; "moderate quality guideline" if three to four domain scores were scored above 60%; and "low-quality guideline" if less than two domains were scored above 60% (refer to Figure 1). Some studies have exclusively used the *rigour of development* domain

on the AGREE-II tool to define high-quality guidelines, as this domain is a stronger indicator of guideline quality compared to other domains.[41] Therefore, to provide this information, guidelines that had a domain score of ≥ 60% on the *rigour of development* were subclassified as "a", and guidelines that did not have a *rigour of development* score ≥ 60% were subclassified as "b". We defined a "high-quality" score on the AGREE-REX as a total overall score ≥ 60%.

Figure 1: *AGREE-II Tool Quality Score*



In the following section, the results of the AGREE-II and AGREE-REX domains and the overall AGREE-REX scores are presented in a heat map format and domains are colour-coded based on their quality scores as follows: high-quality = green; moderate-quality = yellow; and low-quality = red. This visualization allows for a clear distinction between the areas where the guideline and their recommendations score in quality on the given AGREE-II and AGREE-REX

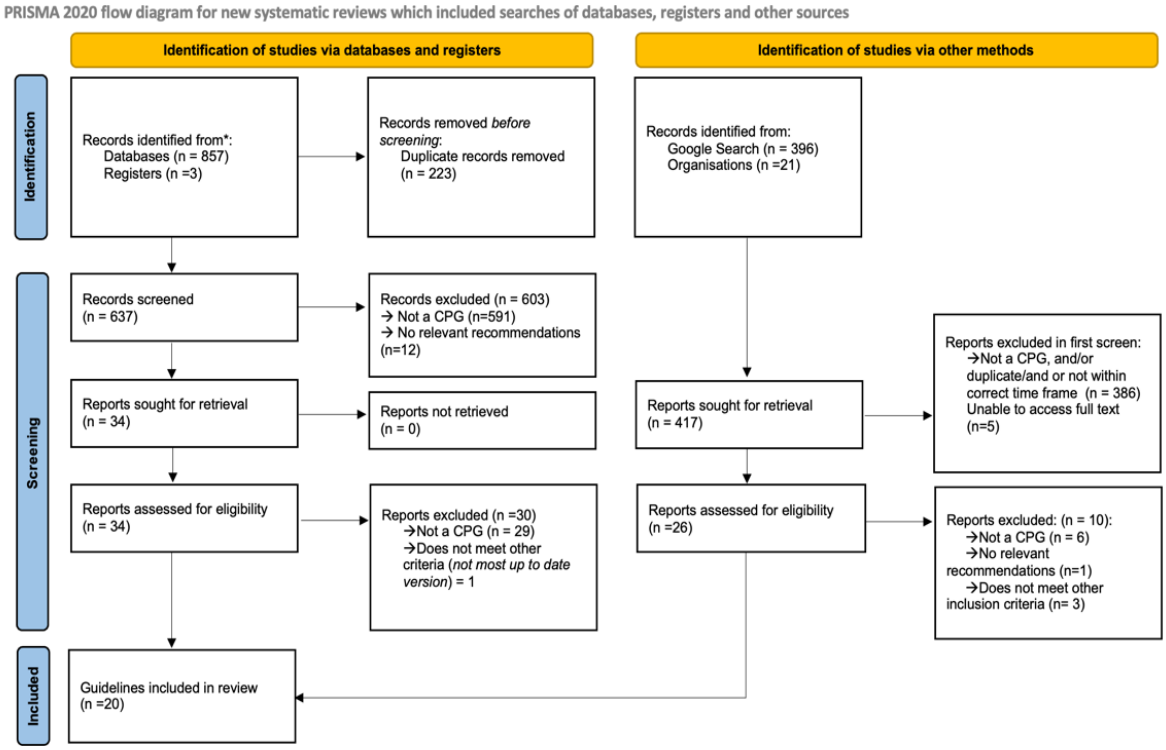
domains. We present the mean domain scores from the AGREE-II and AGREE-REX in a bar graph. We discuss key findings from the AGREE-II and AGREE-REX appraisals in a descriptive synthesis.

In response to research question 3 *(What are the recommendations for the non-pharmacological and pharmacological management of NAS),* the non-pharmacological and pharmacological recommendations for each CPG were extracted, presented in a recommendation matrix, and findings were synthesized in a narrative format.

Results

857 articles were found using MEDLINE (219), CINHAL (124) and EMBASE (514) databases, and 3 articles were found from clinical practice database registries. We found 417 articles/weblinks using the grey literature search (396 from Google search and 21 from health associations/organization websites) of which 26 were uploaded onto DSR to review eligibility. A total of 20 guidelines were included in this review (4 from database/guideline registries and 16 from the grey literature search; see Figure 2).

Figure 2: *PRISMA Flow Chart*



Features of Clinical Practice Guidelines

The characteristics of the CPGs are illustrated in Table 1 (p. 58). All of the guidelines were published in English, with no evidence of available versions in other languages. The countries with the highest number of published guidelines were the United States[51,54,57,59,61,62] and Australia[47,49,50,53,55,64] (six each), followed by three from England[46,48,58] and Canada[52,60,63] and one from Switzerland[65] and Scotland.[56] Authors of six guidelines indicated that the CPGs were developed using evidence-informed consensus-based recommendations.[47,50,61,63-65] While we did not identify clear statements in guidelines indicating the development process for the remaining 14 guidelines, we found indications that they were evidence-based and/or consensus-based (e.g., the inclusion of a reference list/citations and information about the group membership of those involved in the guideline development). The authors for three of the guidelines followed a version of the Grading of Recommendations Assessment, Development and Evaluation

(GRADE) framework for their quality assessment of the evidence.[50,63,65] The author for one guideline used an adapted level of evidence from the National Health and Medical Research Council Australia for their quality appraisal.[64] A quality appraisal of the level of evidence was not indicated in the remaining 16 guidelines. We identified a total of 11 guidelines from distinct hospitals/medical centres[46,48,49,51,54-60] of which four guidelines are from the National Health Services (NHS) of the United Kingdom (UK). These four guidelines serve as guidelines for providers of the hospitals/centres within their region of the NHS.[46,48,56,58] We found five guidelines from government organizations,[47,50,53,61,64] two from professional associations/organizations,[62,65] one from the provincial health authority[52] and one guideline from a provincial council.[63] Some guidelines are intended for healthcare providers working within a particular hospital unit[49,51,54,55,57,59,60] while others are intended for a range of healthcare providers, educators, researchers, and others in the wider healthcare domain that provide direct or indirect care to infants with NAS and their families.

Table 1: *Features of Clinical Practice Guidelines*

Guideline Number (g#), Reference, and Guideline Information		Guideline Development			Funding
		Evidence Used to Generate Recommendations	**Quality Appraisal of Evidence**	**Method used to Formulate/Select Recommendations**	
g1[46]	***Author (Year):*** Royal Cornwall Hospitals, V3.1 Dr. C. Bell, Consultant Neonatologist (2022) ***Title:*** Neonatal Abstinence Syndrome (NAS) Clinical Guideline (Hospitals) ***Issuing Society:*** Royal Cornwall Hospitals England, National Health Service (Hospital(s); Government) ***Country:*** England ***Type of Guideline***: Evidence-Informed Consensus Guideline *	Reference list available (unclear how literature was obtained)	Not completed	Consulted with workforce (neonatal audit and guidelines group) for guideline development	Not stated in document
g2[47]	***Author (Year):*** South Australia Maternal, Neonatal & Gynecology Community of Practice (2022) ***Title:*** South Australian Perinatal Practice Guideline Neonatal Abstinence Syndrome (NAS) ***Issuing Society***: Department for Health and Wellbeing, Government of South Australia (Government) ***Country:*** Australia ***Type of Guideline***: Evidence-Informed Consensus Guideline	Reference list available (unclear how literature was obtained)	Not completed	"This guideline is based on a review of published evidence and expert opinion" (SA Government, 2022, p. 1)	Not stated in document
g3[48]	***Author (Year):*** Dr. M. P. Dyke Consultant Pediatrician (2021) ***Title:*** Joint Trust Guideline for the Management of Neonatal Abstinence Syndrome ***Issuing Society:*** Norfolk and Norwich University Hospitals, National Health Service (Hospital(s); Government) ***Country:*** England ***Type of Guideline***: Evidence-Informed Consensus Guideline *	Reference list available (unclear how literature was obtained)	Not completed	Not stated/unclear	Not stated in document
g4[49]	***Author (Year):*** Grace Centre for Newborn Care, The Children's Hospital at Westmead (2021) ***Title:*** Neonatal Abstinence Syndrome Assessment and management – GCNIC- CHW Practice Guideline ***Issuing Society:*** The Children's Hospital at Westmead (Hospital); The Sydney Children's Hospitals Network ***Country:*** Australia ***Type of Guideline***: Evidence-Informed Consensus Guideline *	Reference list available (unclear how literature was obtained)	Not completed	Not stated/unclear	Not stated in document
g5[50]	***Author (Year):*** Queensland Clinical Guidelines (2021) Working party clinical lead: Dr. Christopher Edwards (Pediatrician), Ms Anndrea Flint (Neonatal Nurse Practitioner), Dr. Karen Whitfield, Senior Pharmacist ***Title:*** Perinatal Substance Use: Neonatal ***Issuing Society:*** Queensland Health (Government) ***Country:*** Australia ***Type of Guideline***: Evidence-Informed Consensus Guideline	A search of the literature was performed (PubMed, CINAHL, Medline, Cochrane, EBSCO, Embase) along with available national/international clinical practice guideline	GRADE[66]	Working party and Statewide consulted for expert opinion	Healthcare Improvement Unit, Queensland Health
g6[51]	***Author (Year):*** Alaska Native Medical Center (ANMC, 2020). ***Title:*** ANMC Maternal Child Health Neonatal Abstinence Syndrome Guide with Eat, Sleep Console Tools (ESC)	Reference list available (unclear how literature was obtained)	Not completed	Not stated/unclear	Not stated in document

	Issuing Society: Alaska Native Medical Center (Hospital) ***Country:*** US ***Type of Guideline***: Evidence-Informed Consensus Guideline *				
g7[52]	***Author (Year):*** Alberta Health Services (2020) ***Title:*** Neonatal Abstinence Syndrome: Non-Pharmacological and Pharmacological Management, Assessment and Discharge ***Issuing Society:*** Alberta Health Services Canada (Provincial Health Authority) ***Country:*** Canada ***Type of Guideline***: Evidence-Informed Consensus Guideline *	Reference list available (unclear how literature was obtained)	Not completed	Not stated/unclear	Not stated in document
g8[53]	***Author (Year):*** Child and Adolescent Health Service - Neonatology (2020) ***Title:*** Clinical Guideline – Neonatal Abstinence Syndrome (NAS) ***Issuing Society:*** Government of Western Australia Child and Adolescent Health Service Australia (Government) ***Country:*** Australia ***Type of Guideline***: Evidence-Informed Consensus Guideline *	Reference list available (unclear how literature was obtained)	Not completed	Not stated/unclear	Unable to open disclaimer links
g9[54]	***Author (Year):*** Newborn Critical Care Center (NCCC) Clinical Guidelines (2020) ***Title:*** Guidelines for Management of Neonatal Abstinence Syndrome ***Issuing Society:*** University of North Carolina Health (Hospital) ***Country:*** US ***Type of Guideline***: Evidence-Informed Consensus Guideline *	Reference list available (unclear how literature was obtained)	Not completed	Not stated/unclear	Not stated in document
g10[55]	***Author (Year):*** The Royal Women's Hospital (2020) ***Title:*** Drug and Alcohol – Neonatal Abstinence Syndrome ***Issuing Society:*** The Royal Women's Hospital (Hospital) ***Country:*** Australia ***Type of Guideline***: Evidence-Informed Consensus Guideline *	Reference list available (unclear how literature was obtained)	Not completed	Not stated/unclear	Not stated in document
g11[56]	***Author (Year):*** Dr. H Mactier – Neonatal Consultant PRM; Co Authors Dr. L Ellis, D. L McGrory, & J. Grant (2019) ***Title:*** Neonatal Abstinence Syndrome ***Issuing Society:*** Greater Glasgow and Clyde – National Health Service (Hospital(s); Government) ***Country:*** Scotland ***Type of Guideline***: Evidence-Informed Consensus Guideline *	Reference list available (unclear how literature was obtained)	Not completed	Not stated/unclear	Not stated in document
g12[57]	***Author (Year):*** K. Ponder & G Dudell (2019) ***Title:*** EBNS Neonatal Abstinence Syndrome Guideline ***Issuing Society:*** East Bay Newborn Specialists (Hospital/Medical Centre) ***Country***: US ***Type of Guideline***: Evidence-Informed Consensus Guideline *	Reference list available (unclear how literature was obtained)	Not completed	Not stated/unclear	Not stated in document
g13[58]	***Author (Year):*** Northern Devon Healthcare (2019) ***Title:*** Neonatal Abstinence Syndrome – Guidelines for Management ***Issuing Society:*** Northern Devon Healthcare – National Health Service (Hospital(s); Government) ***Country:*** England ***Type of Guideline***: Evidence-Informed Consensus Guideline *	Reference list available (unclear how literature was obtained)	Not completed	Not stated/unclear	Not stated in document

g14[59]	***Author (Year):*** Department of Pediatric Newborn Medicine, Brigham and Women's Hospital (2018) ***Title:*** Care of the Neonate with Neonatal Abstinence Syndrome ***Issuing Society:*** Brigham and Women's Hospital (Hospital) ***Country:*** US ***Type of Guideline:*** Evidence-Informed Consensus Guideline*	A literature review was conducted (reference list available) however it is unclear how this literature was obtained	Not completed	Not stated/unclear	Not stated in document
g15[60]	***Author (Year):*** Fabiana Postolow, Lisa Merrill, Jarrid McKitrick, Cathy Sabiston (2018) ***Title:*** Neonatal Substance Exposure: Assessment and Clinical Management ***Issuing Society:*** Winnipeg Regional Health Authority (Hospital) ***Country:*** Canada ***Type of Guideline:*** Evidence-Informed Consensus Guideline*	A reference list is available (It is unclear how literature was obtained)	Not completed	Not stated/unclear	Not stated in document
g16[61]	***Author (Year):*** Substance Abuse and Mental Health Services Administration (SAMSHA, 2018) ***Title:*** Clinical Guidance for Treating Pregnant and Parenting Women with Opioid Use Disorder and their Infants ***Issuing Society:*** Substance Abuse and Mental Health Services Administration (Government) ***Country:*** US ***Type of Guideline:*** Evidence-Informed Consensus Guideline	A literature review was conducted (It is unclear how literature was obtained)	Not completed	RAND/UCLA Appropriateness Method (RAM) modified Delphi was used to establish the best recommendations	Not stated in document
g17[62]	***Author (Year):*** American Academy of Pediatrics Committee on Fetus and Newborn and the American College of Obstetricians and Gynecologist Committee on Obstetric Practice (2017) ***Title:*** Guidelines for Perinatal Care, 8th Edition ***Issuing Society:*** American Academy of Pediatrics (Professional Association) ***Country:*** US ***Type of Guideline:*** Evidence-Informed Consensus Guideline*	Although not stated, this appears to be an evidence-informed consensus guideline based on the best available evidence. The "most scientific information, professional opinions, and clinical practices have been used to create this document" (AAP, 2017, p. xii)	Not completed	Not stated/unclear	Not stated in document
g18[63]	***Author (Year):*** Provincial Council for Maternal and Child Health (PCMCH) work group and expert panel (2016) ***Title:*** Neonatal Abstinence Syndrome (NAS) Clinical Practice Guidelines ***Issuing Society***: PCMCH (Provincial Organization) ***Country:*** Canada ***Type of Guideline:*** Evidence-Informed Consensus Guideline	Literature Review (unspecified how this was conducted).	GRADE Canadian Task Force on Preventative Health Care[67]	Recommendations selected based on the level of evidence, and rational for recommendation provided.	Not stated in document
g19[64]	***Author (Year):*** New South Wales Ministry of Health (2014) Title: Clinical Guidelines for the Management of Substance Use During Pregnancy, Birth, and the Postnatal Period ***Issuing Society***: New South Wales Ministry of Health (Government) ***Country:*** Australia ***Type of Guideline***: Evidence-Informed Consensus Guideline	International and Australian literature reviewed by experts.	An adapted level of evidence was used based on the National Health and Medical Research Council Australia[68]	Evidence and expert opinion	Australian Federal, State and Territory Governments and New Zealand Government under the Ministerial Council on Drug Strategy Cost
g20[65]	***Author (Year):*** World Health Organization (WHO, 2014) ***Title:*** Guidelines for the Identification and Management of Substance Use and Substance Use Disorders in Pregnancy	A systematic review of evidence using Cochrane methods and meta-analysis. A survey of values and preferences was conducted	GRADE[66]	Recommendations formulated with a guideline group consisting of members with content expertise	USA Government: United Nations Office on Drugs

Issuing Society: World Health Organization (Intergovernmental Organization) ***Country:*** Switzerland ***Type of Guideline***: Evidence-Informed Consensus Guideline	and Crime and the Government of the Kingdom of Norway

Type of guideline with a * indicates that it was not indicated by authors but can be implied.

AGREE-II and AGREE-REX Results

The domain scores of each CPG from both the AGREE-II and AGREE-REX appraisals are illustrated together in a heat map (Table 2, p. 63). A detailed narrative description of the findings from the AGREE-II and AGREE-REX appraisals are presented individually. The mean domain scores from the AGREE-II and AGREE-REX scores are displayed in Figure 3 and Figure 4 (p. 65 and 66, respectively).

Table 2: *AGREE-II and AGREE-REX Heat Map*

	Guideline 1[46]	Guideline 2[47]	Guideline 3[48]	Guideline 4[49]	Guideline 5[50]	Guideline 6[51]	Guideline 7[52]	Guideline 8[53]	Guideline 9[54]	Guideline 10[55]
AGREE-II Domains										
1. Scope and Purpose	50%	66.67%	27.78%	50%	100%	55.56%	50%	11.11%	22.22%	38.89%
2. Stakeholder Involvement	55.56%	50%	38.89%	44.44%	83.33%	38.89%	33.33%	16.67%	5.56%	33.33%
3. Rigour of Development	18.75%	29.17%	18.75%	22.92%	43.75%	6.25%	4.17%	14.58%	4.17%	6.25%
4. Clarity of Presentation	61.11%	88.89%	44.44%	77.78%	94.44%	72.22%	55.56%	88.89%	55.56%	72.22%
5. Applicability	29.17%	29.17%	20.83%	16.67%	58.33%	12.50%	25%	20.83%	16.67%	20.83%
6. Editorial Independence	0%	25%	0%	0%	75%	0%	8.33%	16.67%	0%	0%
AGREE-REX Domains										
1. Clinical Applicability	44.44%	50%	33.33%	50%	72.22%	44.44%	33.33%	38.89%	27.78%	44.44%
2. Values and Preferences	25%	4.17%	0%	0%	70.83%	12.5%	25%	29.17%	8.33%	8.33%
3. Implementability	41.67%	75%	16.67%	58.33%	75%	66.67%	33.33%	33.33%	16.67%	33.33%
AGREE-REX Total Score	35.19%	35.19%	14.81%	29.63%	72.22%	35.19%	29.63%	33.33%	16.67%	25.93%

	Guideline 11[56]	Guideline 12[57]	Guideline 13[58]	Guideline 14[59]	Guideline 15[60]	Guideline 16[61]	Guideline 17[62]	Guideline 18[63]	Guideline 19[64]	Guideline 20[65]
AGREE-II Domains										
1. Scope and Purpose	11.11%	44.44%	66.67%	55.56%	61.11%	77.78%	44.44%	94.44%	94.44%	94.44%
2. Stakeholder Involvement	27.78%	16.67%	33.33%	11.11%	27.78%	88.89%	61.11%	55.56%	72.22%	100%
3. Rigour of Development	2.08%	8.33%	12.50%	14.58%	2.08%	62.50%	33.33%	35.42%	39.58%	93.75%
4. Clarity of Presentation	33.33%	77.78%	38.89%	72.22%	44.44%	100%	61.11%	100%	94.44%	100%
5. Applicability	4.17%	20.83%	8.33%	16.67%	16.67%	58.33%	25%	41.67%	50%	45.83%
6. Editorial Independence	0%	0%	8.33%	0%	0%	50%	0%	0%	33.33%	83.33%
AGREE-REX Domains										
1. Clinical Applicability	16.67%	44.44%	22.22%	50%	27.78%	88.89%	44.44%	44.44%	38.89%	100%
2. Values and Preferences	0%	4.17%	8.33%	0%	12.50%	75%	37.50%	45.83%	25%	50%
3. Implementability	16.67%	0%	25%	33.33%	0%	75%	33.33%	58.33%	58.33%	83.33%
AGREE-REX Total Score	9.26%	16.67%	16.67%	24.07%	14.81%	79.63%	38.89%	48.15%	37.04%	74.07%

AGREE-II Results (Table 2; Figure 3)

Scope and Purpose. The scope and purpose refer to the overall aim of the guideline, the health questions, and the target population.[34] The majority of the guidelines achieved moderate-high quality scores in this domain (8/20 = moderate quality, 8/20 = high quality); however, the scores across all guidelines ranged between 11.11%[53,55] and 100%.[50]

Stakeholder Involvement. The stakeholder involvement domain refers to the extent of the appropriate group membership of stakeholders and the views of the target users.[34] Most of the guidelines scored within the moderate quality range for this domain (9/20), while 6/20 scored low and 5/20 scored high. In this domain, scores ranged from 11.11%[59] to 100%.[65]

Rigour of Development. The domain of rigour of development pertains to the process of gathering, synthesizing and formulating recommendations, as well as the process of updating the recommendations.[34] The majority of the guidelines scored low in this domain (14/20). Scores in this domain ranged from 2.08%[60] to 93.75%.[65]

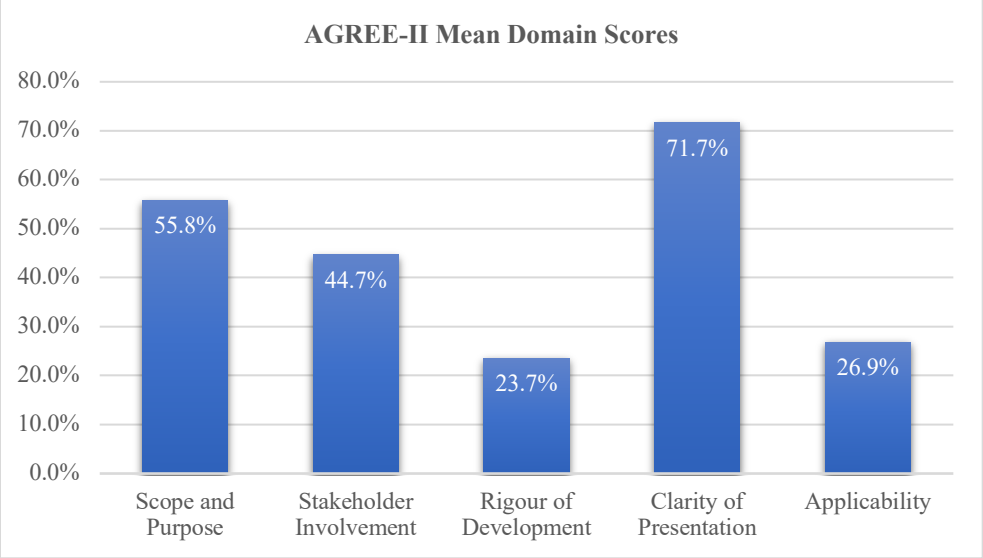
Clarity of Presentation. The clarity of the presentation domain refers to the formatting of the guideline, including the structure and language.[34] Overall, most guidelines scored high in this domain (13/20). Domains scores ranged between 33.33%[56] to 100%.[61,63,65]

Applicability. The applicability domain refers to the barriers and facilitators to implementations, strategies for implementation, and resource implications.[34] In this domain, the majority of the guidelines (15/20) scored low. Scores ranged from 4.17%[56] to 58.33%.[50,61]

Editorial Independence. The editorial independence domain refers to the formulation of recommendations that is not biased with competing interests.[34] In this domain, most of the guidelines scored low (16/20). The scores ranged from 0%[46-49,51-60,62,63] to 83.33%.[65]

Overall Score. The World Health Organization (WHO) received the highest guideline score on the AGREE-II.[65] The next highest-scored guidelines were achieved from the Substance Abuse and Mental Health Services Administration[61] (SAMSHA; Moderate A), followed by Queensland Health[50] (Moderate B). The majority of guidelines achieved low quality score on the AGREE-II (16/20; low B). Guidelines prominently scored lower in the following AGREE-II domains: *editorial independence* (mean = 15.0%), followed *by rigour of development* (mean = 23.7%), and *applicability* (mean = 26.9%; see figure 2). The AGREE-II domains that guidelines scored the highest on was *clarity of presentation* (mean = 71.7%), followed by *scope and purpose* (mean = 55.8%) and *stakeholder involvement* (mean = 44.7%).

Figure 3: *AGREE-II Mean Domain Scores of CPGs*



AGREE-REX Results (Table 2; Figure 4)

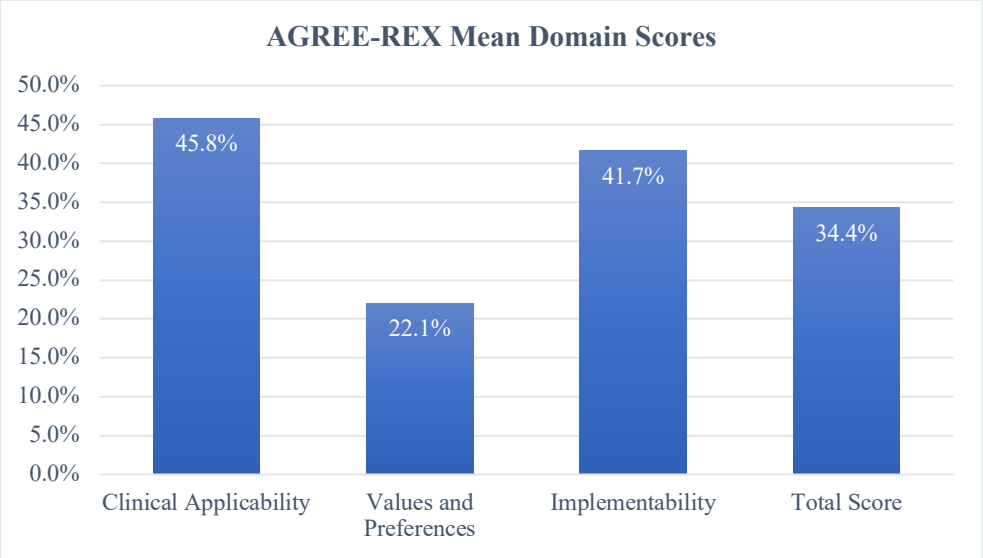
Clinical Applicability. Clinical applicability refers to the quality of the evidence and how evidence was obtained to formulate recommendations, applicability to the target users, and applicability to the patients.[35] Scores in this domain ranged from 16.67%[56] to 100%,[65] with the majority of guidelines demonstrating moderate quality (13/20).

Values and Preferences. This domain refers to the values and preferences of target users, patients, policy/decision-makers, and guideline developers.[35] Most of the guidelines scored poorly in this domain (15/20), and only two guidelines scored high.[50,61] Scores ranged from 0%[48,49,56,59] to 75%.[61]

Implementability. The implementability domain refers to the purpose of the recommendations, how recommendations align implementation goals, local application and adoption, and the required change in current practice.[35] Scores in this domain ranged from 0%[57,60] to 83.33%.[65]

Overall Score. Similar to the AGREE-II results, most of the guidelines had an overall low score on the AGREE-REX (10/20[48,49,52,54-60]). The three guidelines that scored the highest are SAMSHA[61] (79.63%), followed by WHO[65] (74.07%), and Queensland Health[50] (72.22%). The AGREE-REX domains that guidelines scored the highest to lowest on are *clinical applicability* (mean = 45.8%), followed by implementability (41.7%), and *values and preferences* (mean = 22.1%).

Figure 4: *AGREE-REX Mean Domain Scores*



Recommendations

Table 3 (p. 70) presents a recommendation matrix of the top ten guidelines from the AGREE-REX overall score. A recommendation matrix for the remaining ten guidelines and can be found in Appendix F. Table 4 (p. 73) presents the pharmacological recommendations, including the type of medication and their dosages, extracted from the guidelines that contain these recommendations.

Screening and Assessment

A number of guidelines recommended that the decision to conduct an infant drug screen should be at the discretion of the clinical team, as there may be legal implications and a duty to report positive screen results.[46,47,53,61,62,64] One U.S. guideline recommended that clinicians should obtain an infant drug screening when withdrawal is suspected and obtaining parental consent is not required to do so.[61] The most commonly recommended NAS scoring tools are the Finnegan or a modified version of the Finnegan,[47,50,53,62,64] followed by a general recommendation of a standardized scoring system[61,63,65] and the Eat, Sleep, Console[50,51] (ESC). One guideline recommended using a tool that scores on the severity of central nervous system, metabolic/vasomotor/respiratory and gastrointestinal symptoms.[46] However, the name of this tool was not specified, and we could not access the links to the supplement documents provided in the guideline. We found slight variations regarding the recommendations on when to start scoring for withdrawal and the recommended observation period for infants with NAS. For infants exposed to short-acting opioids, the recommendations for the observation period varied between two to three days,[51,63] whereas the observation period for longer-acting opioids (methadone/buprenorphine) ranged between four and seven days.[51,63] Some guidelines recommended a prolonged observation period regardless of the type of opioid used (stay of

greater than five days[47,64]). We found that most guidelines recommended to start withdrawal scoring when the infant is two hours of age[50,63-65] while one guideline recommended to begin scoring only if withdrawal is suspected.[47]

Non-pharmacological Interventions

We found a considerable degree of agreement for the non-pharmacological interventions recommended across guidelines from the top ten guidelines. All guidelines had recommendations encouraging breastfeeding, with 8/10 specifically indicating that it is safe for infants to breastfeed when the mother is taking methadone/buprenorphine.[46,47,50,54,61,63-65] Most guidelines (6/10;[46,47,50,53,62,63]) recommended giving infants small, frequent feedings, and 4/10 guidelines recommended adding hypercaloric feeds.[50,51,62,63] Decreasing noise/light/stimulation and swaddling were recommendations found in all guidelines (10/10). Other recommendations we identified across guidelines were kangaroo care/skin-to-skin (8/10[47,50,51,53,61,63-65]), rooming-in (7/10[46,47,50,51,61,63,65]), use of pacifier/hand-to-mouth (6/10[46,47,50,51,53,61]), gentle handlings or firm pressure (6/10[46,47,51,53,61,63]), vertical rocking (5/10[47,50,51,53,63]), use of positional supports and/or water bed (4/10[46,50,61,63]), infant massage (3/10[47,50,51]), music therapy (1/10[47]), and bathing (1/10[47]). Acupuncture was noted to be a current practice in two guidelines although not explicitly recommended.[50,61] Caution was indicated if using an electric swing/rocking bed as evidence as shown that it may be overstimulating.[50,61,63] Furthermore, non-oscillating waterbeds have been recommended over standard beds.[50,61]

Pharmacological therapy

We found slight variation in the interpretation of when to commence pharmacological treatment with the Finnegan scoring. For example, three guidelines[50,53,64] indicated to start treatment when there are 3 consecutive FNAS scores that average 8 or more, or 2 consecutive

FNAS scores of 12 or more, whereas one guideline[63] recommended starting if 3 consecutive scores >8 or the average of two scores or score for two consecutive intervals is >12 on a standardized NAS scoring. Meanwhile, another guideline recommended to start treatment when ≥ 8 for 3 consecutive scores or one score ≥ 12.[47] Variability is also seen in the interpretation of when to start pharmacological therapy in the ten lower-rated guidelines (see Appendix F).

From the top ten overall scored guidelines from the AGREE-REX, the most commonly recommended medication as a primary treatment for NAS is morphine (8/10[46,47,50,53,61-64]). Methadone is recommended as a primary treatment in one guideline.[51] One guideline recommended an opioid (unspecified) as the primary treatment for NAS.[65] Interestingly, one lower-rated guideline on the AGREE-REX appraisal recommended using morphine and clonidine together as a first line of treatment (see Table 4).[59]

While morphine is the most frequently recommended first-line treatment for NAS, there is some variability in the guidelines regarding the timing of medication initiation, how to increase the medication, maximum dose, and weaning schedule seen throughout all the appraised guidelines (see Table 4). For example, out of the nine guidelines that discuss adjuvant therapies, 2/9 recommended clonidine as the primary adjuvant therapy,[53,63] and 2/9 recommended phenobarbital as the primary adjuvant.[47,65] Five of the nine guidelines recommended using either clonidine or phenobarbital under certain circumstances.[50,51,61,62,64] We additionally identified conflicting recommendations regarding the preferred primary adjuvant medication in the lower ten guidelines from the AGREE-II appraisal (see Appendix F) and dosing (see Table 4).

Table 3: *Recommendation Matrix (Top Ten Guidelines according to the AGREE-REX Appraisal)*

CATEGORY ⇓	Guideline ⇒ *(Presented in order of the highest AGREE-REX scores)* / SUBCATEGORY ⇓	**Guideline 16[61]**	**Guideline 20[65]**	**Guideline 5[50]**	**Guideline 18[63]**	**Guideline 17[62]**	**Guideline 19[64]**	**Guideline 2[47]**	**Guideline 6[51]**	**Guideline 1[46]**	**Guideline 8[53]**
SCREENING/SCORING	**Toxicology Screening** *(Urine/Meconium/Hair)*	Y[1]		N!		!	!	Y!		Y!	!
	Scoring Tool:										
	Recommends a standardized scoring system	Y	Strong/Low		II-1						
	Finnegan Neonatal Abstinence Scoring (FNAS)			Y			Y				
	Modified Finnegan Neonatal Abstinence Syndrome Tool					Y	Y	Y			Y
	Eat, Sleep, Console (ESC)			Y					Y		
	Other (system disturbance)									Y	
	Initiation Of Screening:										
	2 hr after birth		Y	Y	Y		Y				Y
	4-6 hr after birth								Y		
	When NAS is suspected							Y			
	Observation Period:										
	2 days								Y (short acting)		
	3 days				Y (short acting) II-1					Y (minimum)	
	4-7 days	Y	Y								
	5+ days				Y (long acting) II-1		Y	Y	Y (long acting)		
FEEDING	**Breastfeeding:**										
	Breastfeeding			Y				Y!	Y	Y!	Y!
	Breastfeeding on drugs/alcohol		Conditional/ Low		N II-2 B						
	Breastfeeding on Methadone/Buprenorphine	Y	Strong/Low	Y	II-2 B	Y	Consensus	Y		Y	Y
	Hypercaloric Feeds			Y	III B	Y			Y		
	Sensitive Formula										
	Frequent, Small Volume Feeds			Y	III B	Y		Y		Y	Y

CATEGORY ⇓	Guideline ⇒ *(Presented in order of the highest AGREE-REX scores)* / SUBCATEGORY ⇓	Guideline 16[61]	Guideline 20[65]	Guideline 5[50]	Guideline 18[63]	Guideline 17[62]	Guideline 19[64]	Guideline 2[47]	Guideline 6[51]	Guideline 1[46]	Guideline 8[53]
NON-PHARMACOLOGICAL RECOMMENDATIONS	**Rooming In**	Y	Y	Y	II-2B			Y	Y	Y	
	Kangaroo Care/Skin to Skin	Y	Strong/Low	Y	III B		Consensus	Y	Y		Y
	Swaddling	Y	Y	Y	III B	Y	Y	Y	Y	Y	Y
	Pacifier/Hand to Mouth	Y		Y				Y	Y	Y	Y
	Vertical Rocking			Y	III B			Y	Y		Y
	Gentle Handlings, Firm Pressure	Y			III B			Y	Y	Y	Y
	Electric Swing				!						
	Decrease Light/Noise	Y	Y	Y	III B	Y	Y	Y	Y	Y	Y
	Positional Support **Water Beds**	Y Y		Y	Y					Y	
	Skin Protection Skin Barriers Padding				III	Y Y				Y	Y
	Infant Massage			Y				Y	Y		
	Laser Acupuncture/Acupuncture (adjuvant to pharmacological therapy)	Y		Y							
	Bathing							Y			
	Music Therapy							Y			
PHARMACOLOGICAL RECOMMENDATIONS	**Initiation of Medication:**										
	3 consecutive scores >8 or the average of two scores or score for two consecutive intervals is >12				Y						
	3 consecutive scores average ≥ than 8, or two consecutive scores ≥ 12 on FNAS			Y			Y				Y
	3 consecutive scores ≥ 8, or 1 score ≥ 12							Y			

CATEGORY ⇓	Guideline ⇒ *(Presented in order of the highest AGREE-REX scores)* / SUBCATEGORY ⇓	Guideline 16[61]	Guideline 20[65]	Guideline 5[50]	Guideline 18[63]	Guideline 17[62]	Guideline 19[64]	Guideline 2[47]	Guideline 6[51]	Guideline 1[46]	Guideline 8[53]
PHARMACOLOGICAL RECOMMENDATIONS (Cont.)	*Eat Sleep Console:* Any question answered "YES" or consoling score of "3" required.			Y					Y		
	Other									Y	
	First Line Treatment:										
	An Opioid (unspecified)		Strong/Very Low								
	Morphine	Y		Y	III B	Y	Y	Y		Y	Y
	Phenobarphital										
	Methadone	OR Y				Y			Y		
	Buprenorphine										
	Second Line Treatment:										
	Clonidine	Y		Y	III B (1st) Level I RCT to support	Y	Y		Y		Y(1st)
	Phenobarbital	OR Y	Y	Y	III B	Y	Y	Y(1st)	Y		Y (2nd)
EDUCATION	*Antenatal Education*	Y	Y		Y	Y	Y	Y	Y	Y	
	Admission Education	Y	Y	Y	Y		Y	Y	Y		Y
	Family Discharge Preparation	Y		Y	Y		Y?	Y		Y	
	Community Follow-Up	Y		Y	Y	Y		Y	Y	Y	Y

! = with caution/with certain indications; ? = unclear.

Table 4: *Pharmacological Dosing Recommendations From Guidelines (ordered by most recent dates)*

MORPHINE				
GUIDELINE	**INITIATION TO BEGIN MEDICATION**	**DOSE**	**MEDICATION INCREASE**	**MEDICATION WEAN**
Guideline 1[46]	• If demonstrating moderate system disturbances for 2 consecutive sets of post-feed observations(100mcg/ml).	• Initial Dose: at 40mcg/kg/dose q4h.	• Increase dose by 20-40mcg/kg/dose q8h until symptoms controlled. • Maximum dose: 100mcg/kg/dose.	• After 24-48 hours of symptom control, can wean by 10-20% each 24-48 hours until dose of 20mcg/kg has been reached. • Next, reduce frequently until 40mcg/kg/DAY and stable to discontinue.
Guideline 2[47]	• If equal to or greater than 8 for 3 consecutive scores, or one score equal to or above 12.	• Start with stat doses of morphine 0.1mg/kg/dose up to 3 doses.	• If symptoms persists after 3 doses, start morphine 0.1mg/kg/dose q6h. • If symptoms persists, increase to 0.125 mg/kg/dose q6h. • If symptoms persists, increase to 0.175mg/kg/dose q6h. • If symptoms persists, increase to 0.225mg/kg/dose q6h. Consider adding phenobarbital at this time. • Where control is difficult, give total daily dose in 6 divided doses.	• Initiate weaning by decreasing dose 0.05mg every 24-48 hours. 4 hour doses may be reduced to 6 hourly. • Can discontinue morphine when on 0.1mg/dose.
Guideline 3[48]		• Initial Dose: 50mcg/kg • Maximum first dose = 125mcg • Dose intervals q4h.	• Increase by 50mcg/dose.	• Once symptoms have been controlled for 48-72 hours, can begin the wean treatment. Wean by 10-15% of the maximum dose that the infant has received every 48-72 hours.
Guideline 4[49]	• If scores are equal or greater than 8 for 3 scores start morphine.	• Initial dose 0.5mg/kg/day in 4-6 doses.	• If scores persists, can increase to 0.7mg/kg/day divided in 6 doses.	• Decrease dose by 10-25% every 2-4 days.

			• If scores persists, can increase to 0.9mg/kg/day divided into 6 doses. • If infants are on morphine at 0.9mg/kg/day, consider adding phenobarbital.	
Guideline 5[50]	• Start pharmacological therapy if: →On FNAS: 3 consecutive FNAS average 8 or more, or 2 consecutive FNAS scores of 12 or more. →On ESC: Any question answered "YES" or consoling score of 3 needed.	• Start at 0.5mg/kg/day in 4 doses (0.125mg/kg q6h).	• If not controlled, increase to 0.7mg/kg/day (0.175mg/kg q6h). • If not controlled, increase to 0.9mg/kg/day (0.225mg/kg q6h). • If not controlled, increase to 1mg/kg/day (0.25mg/kg q4h) and consider adding phenobarbital.	• If on a 6 hour dosing schedule, reduce dose by 0.1-0.2mg/kg/day and no more than every 48 hours.
Guideline 7[52]	• Consider pharmacologic therapy if: -8 or greater FNAST score for 3 consecutive readings -12 or eater for 2 consecutive readings -The average of 3 consecutive readings is 8 or greater, the average of 2 consecutive readings is 12 or greater	• Start with a dose of 0.05/kg/dose q3h (lower starting dose of 0.03mg/kg/dose can be considered).	• After 6 hours, morphine can be titrated up at 6 hour intervals in 0.015mg/kg/dose increments to a maximum dose of 0.125mg/kg/dose (or 1mg/kg/day divided into 8 doses.	
Guideline 8[53]	• If scores 3 consecutive scores >8 or 2 consecutive scores >12, pharmacologic treatment is usually indicated.	• Start with 125mcg/kg/dose q6h, with a maximum of 500mcg/kg in 24 hr.	• If scores >8 despite morphine at 500mcg/kg/day, increase morphine to 175mcg/kg/dose q6h or 110mcg/kg/dose q4h (Maximum of 700mcg/kg in 24 hr) • If scores >8 despite being on 700mcg/kg/day, can go up to 225mcg/kg dose q6h Or 150mcg/kg/dose q4h • (Maximum of 900mcg/kg in 24 hours).	• Weaning can begin when the average scores fall below treatment line (</=8) for 48 hours. A suggested rate of weaning is 0.05mL (0.05mg) per dose every 2-3 days.

Guideline 9[54]	• Start at 0.05mg/kg/dose every 3 hours if scores are equal to or greater than 8 for 3 consecutive scores, or 2 scores equal to or greater than 12 within a 24 hour period.	• Increase by 0.02mg/kg/dose for 2 scores in a row of 8-11. • Increase by 0.04mg/kg/dose for 2 scores equal to or greater than 12	• If morphine dose is equal to or greater than 0.3mg/kg/dose, consider adding phenobarbital.	• Wean if stable for 48 hours (or 73 hours if dose is >0.4mg/kg/dose of morphine or if phenobarbital is used). Wean by 10% of original dose every 24 hours. May discontinue once dose is at 0.02mg/kg/dose.
Guideline 10[55]		• Morphine Hydrochloride (1000mcg/mL) • If 3 scores average 8 or more: 125mcg/kg/dose q6h or 85mcg/kg/dose q4h • 2 scores average 11 or more: 125-175mcg/kg//dose q6h or 85-120mcg/kg/dose q4h	• Increase morphine by 30mcg/kg/dose until scores controlled. • Maximum dose: 1200mcg/kg/day	• Once symptoms have been controlled (less than 8) can decrease morphine by 10% of initial dose every 48 hours.
Guideline 11[56]		• Start at 60mcg/kg four hourly.	• If symptoms are not controlled within 24 hours, increase by 10mcg/kg per dose to a maximum of 80mcg/kg/dose. • If symptoms are not controlled after maximum dose of morphine, then add phenobarbital.	• Each day, wean morphine by 10mcg/kg/dose.
Guideline 12[57]	• Finnegan scores equal or greater than 9 for 3x in a row or equal to and greater than 12 2x in an row with a functional impairment (poor feeding, poor sleeping, etc.).	• Start morphine at 0.04mg/kg/dose PO q3h.	• Can consider a bolus of 0.02mg/kg once PO. • Can increase baseline by 0.02mg/kg/dose PO to a maximum of 0.12mg/kg/dose PO q3h. • Consider clonidine if morphine fails.	• If the stabilization dose is equal to or less than 0.1mg/kg/dose, can wean by 0.01mg/kg/dose PO q24h. • If the stabilization dose is greater than 0.1mg/kg/dose PO, wean by 10%.
Guideline 13[58]		• Morphine Sulphate 40mcg/kg/dose q4h.	• Increase dose 20-40mcg/kg/dose q8h until symptoms controlled. • Suggested maximum: 100mcg/kg/dose.	• After 24-48 hours of symptom control, reduce dose by 10-20% of original dose each 24-48 hours until dose of 20mcg/kg has been reached.

				Next, reduce frequency until 40mcg/kg/day, and stable to discontinue.
Guideline 14[49]	• *MORPHINE + CLONDINE used together.	• <u>NAS score 8-10</u>**:** • 0.05mg/kg/dose of morphine AND 1.5mcg/kg of clonidine q6h. • <u>11-13:</u> 0.1mg/kg/dose q6h of morphine AND 2mcg/kg/dose of clonidine q6h. • <u>14-16:</u> 0.15mg/kg/dose q6h of morphine AND 2.5mcg/kg/dose of clonidine q6h. • <u>>17:</u> 0.2mg/kg/dose q6h of morphine AND clonidine 3mcg/kg/dose q6h.	• NAS score >12 • Increase morphine by 10% or decrease interval to q3h or q4h. Increase clonidine by 1mcg/kg/dose to a maximum of 6mcg/kg/dose. • <u>8-12:</u> No change in morphine unless clonidine is maximized. Clonidine can be increased by 1mcg/kg/dose to a maximum of 6mcg/kg/dose.	• If scores <8 for 24 hours, can wean by 10% of dose. Once morphine is 10% of maximum dose, can discontinue. • Once morphine is off for 24 hours, can discontinue clonidine by 1mcg/kg/dose every 24 hours until off.
Guideline 15[60]		• <u>Loading dose: 0.</u>1-0.2mg/kg/dose q2h and prn until symptoms control. Maximum of 2 initial loading dose with max dose of 1mg/kg/24h. • <u>Maintenance (escalate to next step only if needed):</u> Step 1: 0.05mg/kg q4h Step 2: 0.1mg/kg/dose q4h Step 3: 0.15mg/kg/dose q4h Step 4: 0.2mg//kg/dose q4h <u>Loading doses = 2mg/kg/day.</u>	** If symptoms are controlled following 1 loading dose, then start maintenance at Step 1. If symptoms are not controlled after 1 loading dose, then start Step 2. ** Do not increase past Step 2 in the first 24 hours.	<u>First Step:</u> 0.15mg/kg/dose q4h <u>Second Step:</u> 0.12mg/dose q4h <u>Third Step:</u> 0.1mg/kg/dose q4h <u>Fourth Step:</u> 0.08mg/kg/dose q4h <u>Fifth Step:</u> 0.05mg/kg/dose q4h-> q6h→ q8h → q12h for 48 hours then stop. • Only one change in 48 hours until morphine reaches 0.05mg/kg/dose q4h.
Guideline 17[62]	• Indicates that the optimal criteria for initiation of pharmacological therapy is unknown. • Most institutions use the modified Finnegan Neonatal Abstinence	• With moderate signs of NAS, start at 0.24mg/kg/d (0.03mg/kg q3h or 0.04mg/kg q4h). • Maintenance dose is most commonly between 0.2-0.3mg/kg/day q3-4h.	• Increase by 0.08-0.16mg/kg/day. • <u>Maximum dose:</u> 1.2mg/kg/day.	• Opioid can be weaned 10-20% every 1-2 days based on the average scores.

	Scoring Tool to decide when to start pharmacologic therapy.			
Guideline 18[63]	• If 3 consecutive scores >8, or average of two scores or score for two consecutive intervals is >12 on standardized NAS scoring.	• Score 8-10: 0.32mg/kg/day q4-6h • Score 11-13: 0.48mg/kg/day q4-6h • Score 14-16: 0.64mg/kg/day divided q4—6h • Score 17+ : 0.80mg/kg/day divided q4-6h	• If the score remain >8 for 3 consecutive sores, or >12 on 2 occasions, increase to the next range. • Maximum dose: 0.96-1.0mg/kg/day. • Consider starting clonidine at this point.	• Start wean when scores are less than 8 for 24-48 hours. Decrease by 10% of total daily dose. Wean occurs no more than every 48-72 hours. When dose is at <0.2mg/kg/day, may wean every 24 hours at the discretion of team. OR • Alterative approach by 0.05mg/kg/day every 48-96 hours.

PHENOBARBITAL

GUIDELINE	INITIATION TO BEGIN MEDICATION	DOSE	MEDICATION INCREASE	MEDICATION WEAN
Guideline 1[46]	• Used as an adjuvant to morphine	• Start with a loading dose of 20mg/kg orally. After 24 hours from loading dose, start maintenance dose of 4-5mg/kg daily in 2 doses.	• No increase mentioned in guideline.	• After 24-48 hours of stability, can reduce dose by 2mg/kg/dose every 48 hours as tolerated.
Guideline 2[47]	• When morphine fails (primary adjuvant).	• Start with loading dose of 15mg/kg, then start maintenance 12 hours later of 2.5mg/kg dose q12 h.	• If scores are equal to or greater than 8 after first dose of 2.5mg/kg, can increase to 4mg/kg/dose q12h. • If scores remain equal to or greater than 8, can increase to 5mg/kg/dose q12h.	• After scores decrease below treatment line for 24-48 hours, dose should be reduced by 10%-20% from previous dose.
Guideline 4[49]	• When morphine fails.	• If already on morphine of 0.9mg/kg/day, do not give loading dose.	• If equal to or greater than 8 for 3 consecutive scores, can increase to 8mg/kg/day in 2 doses.	

		→ start 5mg/kg/day in 1-2 doses. • If not on morphine, then load with 8mg/kg orally. After 12-24 hours, start maintenance of 5mg/kg/day in 1-2 doses.		
Guideline 5[50]	• Wean morphine fails to control symptoms.	• Start with a loading dose of 10-15mg/kg once. • Maintenance: After 12 hours from loading dose, start maintenance at 2.5mg/kg/dose q12h.	• If not controlled, increase to 4mg/kg q12 h. • If not controlled, increase to 5mg/kg q12h.	• Do not reduce dose by more than 10-20% within 72 hours.
Guideline 7[52]		• Loading dose of 16mg/kg is recommended due to long half-life.	• After loading dose, maintenance dose is 2.5mg/kg/dose q12h.	
Guideline 8[53]	• When morphine fails (scores >8 for 3 consecutive scores despite being on 900mcg/kg/day of morphine). Clonidine, however, is the first line of treatment as an adjuvant.	• Loading dose is 10mg/kg day. • Maintenance dose: 1.5 - 2.5mg/kg/dose q12h.	• No increase mentioned in guideline.	No weaning plan mentioned.
Guideline 9[54]	• When morphine fails.	Give loading dose of 20mg/kg/dose for 2 dose. • Can consider given 10mg/kg/dose q12h x2 doses.	• Maintenance dose is 5mg/kg/dose PO.	• Discontinue when morphine wean is completed.
Guideline 10[55]	• When morphine fails.	• Loading dose 10-15mg/kg/dose.	• Maintenance dose: Average score of 8 or more for 3 scores: 3mg/kg/dose q12h. Average score of 11 for 2 scores: 3-4mg/kg/dose q12h.	• Wean morphine first. Dose should be reduced by 2mg/dose q4 days.
Guideline 17[62]	• Used as an adjuvant to morphine.	• Loading dose of 10-20mg/kg. • Maintenance:5mg/kg/day every 12 hours.	• No increase mentioned in guideline.	• No weaning plan mentioned.

Guideline 18[63]	• When morphine fails. May be used in combination with morphine when infant had polysubstance abuse exposure.	• Give 3 doses of 10mg/kg every 12 hours, then begin 5mg/kg/day as maintenance.	• Doses of morphine in combination with phenobarbital are lower. • Morphine dose with phenobarbital. • No increase mentioned in guideline.	• No weaning plan mentioned.

CLONIDINE

GUIDELINE	INITIATION TO BEGIN MEDICATION	DOSE	MEDICATION INCREASE	MEDICATION WEAN
Guideline 7[52]		• Start with 0.5mcg/kg/dose every 4-6hr for 24 hours	• After 24 hours, can be titrated up at 12-24 hour intervals to a maximum of 1mcg/kg/dose q4h	
Guideline 8[53]	• As an adjuvant to morphine.	• If scores >8 x3, despite morphine being >800mcg/kg/day, start clonidine at 0.5-1mcg/kg/dose q6h	• If scores remain >8, increase dose by 25-50% increments to a maximum of 12mcg/kg in 24 hr.	• Wean every 1-2 days by 25% if score is equal to or less than 8.
Guideline 11[56]	• When morphine fails.	• Start a loading dose of 15mg/kg, followed by a maintenance of 8mg/kg once daily.		• Wean morphine first by 10mcg/kg/dose. • Then phenobarbital can be weaned by 2mg/kg every 2 days.
Guideline 12[57]	• If morphine fails at max dose.	• 1mcg/kg/dose PO q4h.		• When off opiates for 48 hours, wean the dose to 0.5mcg/kg dose PO q4h for 28 hours, then can discontinue.
Guideline 15[60]	• If morphine fails at maintenance dose of 0.15mg/kg/dose q4h and there has been 3 scores greater than 8 or two greater than 9, add clonidine	• Start at 1mcg/kg/dose q6h.	• After 24 hours, increase to 1.5mcg/kg/dose q6h if needed. • After an additional 24 hours, increase to 2mcg/kg/dose q6h if needed. • Maximum dose 8mcg/kg/24 hour.	• Once morphine reaches 0.05mg/dose q4h, then decrease clonidine by 0.5mg/kg/dose q48 hours until dose reaches 1mcg/kg/dose q6h for 48 hours. Then lengthen the interval to 1mcg/kg/dose q8h for 24 hours.

				• If weaning well, then consider alternating weaning doses between morphine and clonidine (one change every 24 hours).
Guideline 17[62]	• Used as an adjuvant to morphine when morphine fails to control symptoms.	• 0.5 -1mcg every 6 hrs.	• Maximum dose: 1mcg every 4 hrs.	• If NAS signs are controlled, wean adjuvant opioid first, when wean clonidine.
Guideline 18[63]	• When morphine fails.	• 0.5-1mcg/kg q4-6hr • Notes that clinical trials are still required to establish a safe and effective dose.	• Some studies increase doses over 1-2 days.	• Some studies taper doses by 0.25mcg every 6 hours (or by 25% of the total daily dose every second day).

METHADONE

GUIDELINE	INITIATION TO BEGIN MEDICATION	DOSE	MEDICATION INCREASE	MEDICATION WEAN
Guideline 6[51]	• *Methadone as primary treatment.	• Step 1: Start methadone at 0.05mg/kg/dose q12h.	• Step 2: 0.05mg/kg q8h • Step 3: 0.05mg/kg q6h • Step 4: 0.075mg/kg q6h • Step 5: Consider adding secondary agent.	• Taper daily or every other day by 2-5% of initial dose.
Guideline 7[52]		• Start at 0.05mg/kg q6h	• After a minimum of 24 hours on starting dose, can increase dose by 0.05mg/kg every 24 hours to a maximum of 1mg/kg/day.	
Guideline 17[62]	• *As a primary medication for management (although not as commonly used as morphine).	• Maintenance dose: 0.2-0.3mg/kg/day divided by every 6-12 hours.	• 0.1-0.2mg/kg/day. • Maximum dose: 0.5-0.6mg/kg/day.	• No weaning plan mentioned.

Discussion

This systematic review is among the first to evaluate the quality of NAS guidelines and their recommendations. The majority of the guidelines scored low on the AGREE-II and AGREE-REX appraisals (16/20 and 10/20, respectively). The top three guidelines from the AGREE-II appraisal (one high-quality A[65], one moderate quality-A[61], and one moderate-quality B[50]) were also the only three guidelines that demonstrated a high overall score on the AGREE-REX appraisal. Guidelines were fairly consistent in their quality ranking when comparing their AGREE-II and AGREE-REX scores (low-quality, moderate-quality, and high-quality ranks). Out of the appraised guidelines, 12/20 guidelines achieved the same quality range in their AGREE-II and AGREE-REX appraisals, while 8/20 guidelines ranked lower in the AGREE-II compared to their corresponding AGREE-REX appraisal.

Many guidelines demonstrated a clear presentation and were well-formatted, which may lead guideline users to perceive them as reliable resources to use in their practice (*clarity of presentation* = 13/20; ≥ 60%). However, the majority of guidelines demonstrated a poor *rigour of development* (14/20 scored < 30%), which indicates insufficiencies in the developers' process used to gather and synthesize the evidence, the methods used to formulate the recommendations and the process for updating.[34] Furthermore, a significant proportion of recommendations were based on consensus and lacked high quality evidence to support the recommendations. The reliance on consensus-based recommendations is most likely to be attributed to the limited availability of robust research on NAS management. The majority of the guidelines received low scores for editorial independence (16/20), raising concerns about the potential bias in the formulation of recommendations.

No guideline received a score of ≥ 60% for the *applicability* domain of the AGREE-II. Recommendations may not be effectively implemented into practice when barriers and facilitators have not been adequately addressed within the guideline. The lack of implementation considerations is also reflected in the AGREE-REX domains. For example, 17/20 of the guidelines scored < 60% in *clinical applicability*, and 15/20 scored < 60 % in *implementability.* This reflects that the recommendations throughout the appraised guidelines may not be practical or can be implemented effectively. While developing guidelines for NAS, policymakers must consider the barriers and facilitators for the recommendations so they may be effectively implemented into practice, with family-centred care serving as a fundamental goal. Further research is required to better understand the specific barriers and facilitators to this unique population of infants in the SCN/NICU environment, along with the preferences and values of families of infants with NAS.

Despite the varying quality of scores from the AGREE-REX, most guidelines addressed similar non-pharmacological recommendations to implement in practice. The lack of research to support recommendations may have impacted the quality assessment of the recommendations. The recommendations that appeared the most consistently across the guidelines (breastfeeding, decreasing light/noise, skin-to-skin, and rooming in) have the most evidence from the literature to support the use in practice. Less frequently seen recommendations (e.g., infant massage, bathing, and acupuncture) may need further research evaluating the effectiveness of these interventions to support their integration into clinical practice.

Young et al[33] found inconsistencies in pharmacological therapy used for the management of NAS across the United States. Similarly, our systematic review has identified inconsistencies in pharmacological therapy, including primary therapy, adjuvant therapies, and dosing between

the guidelines originating from the United States, England, Canada, Australia, Switzerland, and Scotland. The discrepancies in pharmacological regimes may cause less effective symptom management and prolonged hospitalization for some infants. To optimize the management of NAS, further research is required to evaluate the effectiveness and safety of pharmacological treatments. Research is needed to identify the optimal medication combinations and dosage regimes to ensure that infants are receiving a safe and effective dose that allows symptoms to be best controlled while reducing hospital length of stay. The knowledge about the potential benefits and risks of pharmacological treatment can help clinicians in creating well-informed treatment plans for infants with NAS.

The Canadian Pediatric Society (CPS) Practice Point[69] and the American Academy of Pediatrics Neonatal Withdrawal Report[4] are commonly referred-to documents used by clinicians that were not eligible in our review. The CPS[69] and AAP[4] documents demonstrate similar non-pharmacological recommendations as we identified in this review (see Appendix G). There are a few variations in the pharmacological recommendations. For example, the CPS[69] recommends starting pharmacological treatment when Finnegan scores are ≥ 8 on 3 (or ≥ 12 on 2) consecutive evaluations, unlike many guidelines seen in this review that average scores. Additionally, the CPS[66] indicates that buprenorphine may be used as a primary opioid for therapy, and it may in fact be superior to morphine. We did not find buprenorphine discussed within the guidelines included in this review. This reiterates our findings of the wide variations of pharmacological recommendations in guidelines, and other documents.

Practice Implications

The heat map illustrating the AGREE-II and AGREE-REX domain scores offers valuable insights for guideline developers, highlighting areas that require improvement in NAS

guidelines. This systematic review provides clinicians and policymakers with an overview of recommendations across global guidelines. With this knowledge, clinicians and policymakers may compare and contrast different recommendations and can consider the quality of the guidelines and overall recommendations. The recommendation matrix can serve as a valuable tool for clinicians to facilitate the adoption of a specific approach in NAS management or even question their current practices based on what is currently being recommended elsewhere based on higher quality guidelines and recommendations.

Strengths & Limitations

A strength of this systematic review is that it has followed a rigorous methodology. For example, our protocol was developed following PRISMA,[36] which created a strong foundation for the identification and selection of guidelines. Next, our search strategy was peer-reviewed to capture the most appropriate guidelines, and a comprehensive grey literature search was conducted in a systematic manner allowing additional guidelines to have been identified. The grey literature search enabled us to include numerous additional guidelines in this review that otherwise would not have been identified. The guidelines identified in the grey literature are easily accessible for clinicians to refer to, as they do not involve membership nor entail associated fees. The four appraisers demonstrated good inter-rater reliability in training scores prior to beginning the appraisal of the selected guidelines. Finally, the use of the AGREE-REX in conjunction with the AGREE-II appraisal provides notable information regarding the clinical credibility of recommendations that cannot be obtained through the AGREE-II appraisal alone.

A limitation of this review is that some guidelines and commonly referred-to documents for NAS management were not included in this review. For example, due to the restriction of having the word “guideline” in the text, some documents were not eligible.[4,66] Additionally,

some of the guidelines included in this review had properties that indicated they may be a policy document. However, because some of these documents were referred to as a "guideline" by authors and satisfied our inclusion criteria, we considered them to be eligible. There were two appraisers involved in our quality assessment. Although two appraisers is sufficient for the AGREE-II quality appraisal, four appraisers is recommended to improve the reliability of the findings.[34] The first appraiser conducted the quality assessments on the 20 guidelines, however the second appraiser was not consistent given that the guidelines were distributed across three appraisers to score. This division of guidelines across the three secondary appraisers may potentially decrease the reliability of our findings, as it could have led to minor scoring variations compared to if there had been only one second appraiser. Finally, although one of our inclusion criterion was guidelines available in French or English, we only conducted the grey literature search in English.

Conclusion

This systematic review is likely the first to evaluate the quality of NAS management guidelines and their recommendations using the AGREE-II and AGREE-REX instruments. We identified one high-quality guideline[65] and two moderate-quality guidelines[5,16] that clinicians may use with high confidence. Most guidelines included in this review, however, have a low quality of guideline reporting and recommendations. A lack of robust research on NAS management and unclear synthesis for recommendations may have contributed to some of these lower scores. Regardless of the quality scores between guidelines, the majority of the guidelines support similar non-pharmacological recommendations. We identified a wide variation in the pharmacological recommendations which has also been highlighted in other reviews of pharmacological practices. Further clinical trials are recommended to ascertain the effectiveness

of therapies that are currently in practice in order to optimize infant and family outcomes and reduce the risk of harm. Finally, further research is required to gain a greater understanding of effective implementation strategies, including the values of family members of infants with NAS.

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Chapter Three: Development and Piloting of a Tool to Measure Family-Centred Care Values in Perinatal Clinical Practice Guidelines

Introduction

An integrated framework is used throughout this thesis to evaluate the quality of clinical practice guidelines (CPGs). Two key concepts are foundational to this definition of quality; confidence in evidence and in family-centred care (FCC) values (see p. 24). In Chapter two, I reported on the evaluation of quality in terms of confidence of the evidence in CPGs for neonatal abstinence syndrome (NAS) using the Appraisal of Guidelines for Research & Evaluation II (AGREE-II) and AGREE-Recommendation Excellence (AGREE-REX) quality appraisal tools. In this chapter, I will describe the development and pilot testing of the Family-Centred Maternal-Newborn Care Tool (FCMNC-T); the first tool to appraise the integration of FCC values within perinatal CPGs. I will begin by describing FCC and close this chapter by exploring future directions for FCC in perinatal health.

Patient and family-centred care is defined by the Institute of Patient-and Family-Centered Care as "an approach to the planning, delivery, and evaluation of health care that is grounded in mutually beneficial partnerships among patients, families, and health care professions" (Johnson et al., 2008, p. vi). FCC has been identified as a priority and a standard of care in many pediatric health settings and institutions (Kuo et al., 2012). There is emerging research that demonstrates improved patient health outcomes and enhanced patient and family satisfaction when FCC practices are prioritized by healthcare professionals, predominantly within perinatal and pediatric settings (Cooper et al., 2007; Dien et al., 2022; Kuo et al., 2012; Ortenstrand et al., 2010). Despite substantial knowledge of the benefits of FCC, it is often insufficiently implemented within healthcare organizations (Kuo et al., 2012; Larocque et al., 2021). Kiwanuka et al. (2019)

identified several barriers to FCC, including the lack of understanding of what patient and FCC is, organizational barriers (including lack of guidelines and inappropriate workplace environments), individual barriers (lack of motivation or time), and interdisciplinary barriers. Coyne et al. (2011) identified barriers to FCC from a nursing perspective, which include inadequate staffing, lack of recognition of the impact of families on nurses' workload, inadequate facilities and psychosocial support for families, and lack of practical educational workshops/training. There is an apparent need to improve family engagement within healthcare settings.

The shift towards creating a family-centred institution may be supported when clinicians use high-quality CPGs that support the provision of FCC. CPGs serve as a valuable tool for healthcare providers, providing clinicians with statements to base clinical decisions on and inform their practice (Institute of Medicine [IOM], 2011). Optimal patient outcomes are achieved when CPGs are based on high-quality research and contain evidence-based recommendations (Sciarra, 2012). Support from leadership teams is necessary for any critical shifts to occur within organizations (Larocque et al., 2021). Organizations should regularly evaluate their CPGs and policies for the degree to which they support FCC and question practices that may not align with FCC values. CPGs and policies that are not consistently implemented, do not reflect family-centred values, or do not consider individual family contexts can create conflict and tension between healthcare workers and families (Jones et al., 2015). Therefore, CPGs should contain high-quality recommendations and reflect FCC to support optimal patient and family outcomes.

Several tools are available for guideline developers and users to appraise the quality of guidelines. For example, the AGREE-II tool can be used by guideline developers to ensure that their CPGs follow a structured and rigorous methodology (AGREE Next Steps Consortium,

2017; Brouwers et al., 2010). The AGREE-REX can be used to determine if recommendations in CPGs are appropriate to inform practice strategies (AGREE-REX Research Team, 2019; Brouwers et al., 2020). Patient/client-centred care, a model of care that is often used in adult settings, is often used interchangeably with "patient and family-centred care" or FCC as it shares the same principle of family involvement (Kuo et al., 2012; Nurses and Nurse Practitioners of British Columbia, 2020). Considering that patient-centred care is a defined attribute of "quality" in Ontario's healthcare system (Health Quality Ontario's System Quality Advisory Committee [HQOSQAC], 2017) and by the IOM (2001), tools must be available to measure the quality of FCC, particularly within CPGs. Currently, there are no tools available for guideline developers and users to appraise the quality of FCC values within CPGs. HQOSQAC (2017) recognizes the need for greater development and standardization in measurement tools that focus on patient-centric care (which includes attributes of FCC) so that performance measures and accountability reporting may be conducted. In response, I led the development and piloting of a FCC tool to appraise the integration of FCC values in perinatal CPGs.

Before detailing the development and pilot testing of this novel tool, I provide a description of FCC, the benefits of FCC models, the current use of FCC models, and an exploration of the future directions of FCC in perinatal healthcare. The description of other healthcare models used in clinical practice along with the history and evolution of FCC can be found in Appendix H.

Background

Definition and Principles of Family-Centred Care

FCC is a philosophical approach used to guide healthcare delivery (Franck & O'Brien., 2019) and is the preferred philosophy of care for children (Coyne et al., 2018). Various organizations define FCC differently, and a consensus definition for FCC has not been achieved (Kokorelias et al., 2019; Kuo et al., 2012). Over a decade ago, Kuo et al. (2012) described family-centred care as "a partnership approach to health care decision-making" (p. 297). In the pediatric setting, FCC is defined by Shields et al. (2007) as "a way of caring for children and their families within health services which ensures that care is planned around the whole family, not just the individual child/person, and in which all the family members are recognized as care recipients" (p. 9). Although a universally accepted definition does not exist for FCC, many definitions reflect the same principles in their definition (Kuo et al., 2012). FCC applies to those of all ages receiving healthcare and acknowledges that families (however they may be defined) are important for patients' well-being and are allies for achieving quality within healthcare (Johnson et al., 2008, p. vii).

In 2017, the Public Health Agency of Canada [PHAC] published the *Principles of Family-Centred Maternity and Newborn Care* (FCMNC) with the goal of increasing the participation of families in the decision-making of their care during pregnancy and their early postpartum period to promote optimal health outcomes. Family-centred maternity care promotes the provider-patient-family relationship as a collaboration that shares information and fosters family unity through sensitivity to beliefs, values, and customs of the mother's culture, ethnic group, and religion (Zwelling & Phillips, 2001). In addition, family-centred maternity care recognizes the importance of encouraging family support, participation, and choice to empower

mothers and their families (Phillips, 2003). FCMNC in Canada is based on 17 principles to improve care and health outcomes for childbearing individuals, their newborns, and their families (PHAC, 2017; see Table 1). The principles respond to the physical, emotional, psychological, and spiritual needs of pregnant individuals and their families, consider pregnancy and birth as healthy life events, and recognize the significance of family support, participation, and informed choice (PHAC, 2017, p. 5).

Table 1

17 Principles of the Family-Centred Maternity and Newborn Care (Public Health Agency of Canada, 2017)

Family-Centred Maternity and Newborn Care Principles
1. A family-centered approach to maternal and newborn care is optimal.
2. Pregnancy and birth are normal, healthy processes.
3. Early parent-infant attachment is critical for newborn and child development and the growth of healthy families.
4. Family-centred maternal and newborn care applies to all care environments.
5. Family-centred maternal and newborn care is informed by research evidence.
6. Family-centred maternal and newborn care requires a holistic approach.
7. Family-centred maternal and newborn care involves collaboration among care providers.
8. Culturally appropriate care is important in a multicultural society.
9. Indigenous peoples have distinctive needs during pregnancy and birth.
10. Care as close to home as possible is ideal.
11. Individualized maternal and newborn care is recommended.
12. To make informed choices, women and their families require knowledge about their care.
13. Women and their families play an integral role in decision making.
14. The attitudes and language of health care providers have an impact on family's experience of maternal and newborn care.
15. Family-centred maternal and newborn care respects reproductive rights.
16. Family-centred maternal and newborn care functions within a system that requires ongoing evaluation.
17. Family-centred maternal and newborn care best practices from global settings may offer valuable options for Canadian consideration.

Benefits of Family-Centred Care Models

There are various models of FCC in hospitals. I discuss a few examples of FCC models used in the NICU that have been evaluated. Family Integrated Care (FiCare) is one model of FCC in the NICU. FiCare is an extension of the principles of FCC as the model promotes parents to be the true partners in their infants' care during hospitalization (FiCare, 2023). O'Brien et al. (2018) conducted a cluster randomized control trial in 26 NICUs (19 Canadian, six Australian, and one New Zealand level three NICUs) from April 1st, 2013, to August 31st, 2015. O'Brien et al. (2018) compared neonatal and parental outcomes of dyads receiving FiCare to dyads receiving standard care. Dyads receiving FiCare required caregivers to be at the bedside for at least six hours daily, participate in caring for their baby and attend educational sessions (O'Brien et al., 2018). O'Brien et al. (2018) found that premature infants who had received FiCare (n = 895), had a greater weight gain, greater exclusive breastmilk feeding rate, lower mean stress and anxiety scores in parents, compared to those who were receiving standard care (n = 891; $p < .001$).

The *March of Dimes NICU Family Support* is a national program in the United States which aims to provide information, comfort, and support to NICU families during their stay in the hospital, transition home, or in the event of a newborn death (Cooper et al., 2007). The program provides direct face-to-face support to families with an on-site specialist and promotes FCC throughout the NICU (Cooper et al., 2007). Cooper et al. (2007) conducted a quasi-experimental study interviewing NICU staff and families to evaluate the impact of this program. Cooper et al.'s (2007) study demonstrated that the FCC model (March of Dimes) reduces family stress levels in the NICU and improves parenting confidence. When NICU staff were asked about the impact of the program on parents (actual or anticipated impacts), 81% indicated that

parents were more informed, 80% said that parents were less stressed, 75% indicated that parents had more confidence at discharge, and 74% said that there was an enhanced bonding between the parents and their infant ($N = 502$; Cooper et al., 2007). In addition, based on the results from 216 family respondents to a survey of the March of Dimes model of care, families who had this program fully implemented in their NICU reported more opportunities for involvement in the care of their baby and a higher level of comfort for caring for their baby compared to sites that did not have this program (93% compared to 74% respectively). For example, parent's understanding of what to expect of their infant's medical condition was greater in fully implemented family centred-care sites ($n = 63$, 73.5% $p < .001$) compared to centers that did not have this program ($n = 8$, 50.0%, $p < 0.03$)

Over a decade ago, Ortenstrand et al. (2010) conducted a randomized controlled trial in two NICUs in Stockholm to compare the outcomes of premature infants receiving care in a FCC ward to those receiving standard care. In the FCC ward, at least one family member was expected to stay 24 hours a day from admission to discharge (Ortenstrand et al., 2010). In contrast, on the standard ward, parents were encouraged to visit their infant daily (but not required). For families receiving standard care, the option to stay overnight was only offered a few days before their infant's discharge (Ortenstrand et al., 2010). Recruitment occurred between September 2006 and March 2008, and 366 infants were randomly assigned to the receiving FCC or standard care (Ortenstrand et al., 2010). A reduced risk of moderate to severe bronchopulmonary dysplasia (BPD; described as moderate if requiring < 30% oxygen or severe if requiring > 30% oxygen at 36 weeks corrected) was evident for those receiving family care compared to infants in the control group (3/183 in FCC group had moderate to severe BPD compared to 11/183 in standard group; 1.6 % vs 6.0% respectively; adjusted odds ratio: 0.18

[95% CI: 0.04-0.7]). In addition, a five-day reduction in hospital stay was found for infants receiving FCC compared to the standard group (a mean of 27.4 days [95% CI: 23.2-31.7] compared to 32.8 in the standard group [95% CI: 29.6-35.9]; p = .05).

Family-Centred Care: Where Are We Today?

Although published over a decade ago, Kuo et al. (2012) stated that FCC is a widely used model across various areas of healthcare, with growing evidence supporting its use in practice. There has been growing momentum within the past two decades to apply the principles of FCC beyond pediatric care and into adult settings (Johnson, 2000). Although most pediatric healthcare workers believe FCC is the best way to deliver care to children, FCC is not always implemented effectively and is not universally implemented (Abraham & Moretz, 2012; Coyne, 2008; Jolley & Shields, 2009). Kuo et al. (2012) stated that FCC is at a crossroads. Many misunderstandings about FCC remain, including how to implement FCC and how to determine the efficacy of FCC (Kuo et al., 2012). Furthermore, outdated policies may limit the opportunities for families to be involved in a collaborative role, an essential attribute of FCC (Abraham & Moretz, 2012).

Family-centred maternity care in Canada needs improvement and requires systematic changes aligned with Canadian women's and their families' needs (Jimenez et al., 2010). Jimenez et al. (2010) conducted semi-structured interviews on the birth experiences and prenatal and postpartum care for 36 Canadian women. Participants in this study felt that information-sharing and collaborative decision-making had been lacking during their hospital stay for birth (Jimenez et al., 2010). Consequentially, misunderstandings and misinformation resulted in anxiety and mistrust in health care professionals (Jimenez et al., 2010).

Sigurdson et al. (2020) conducted an analysis to explore the experiences of NICU families. Focus groups and interviews were conducted with 18 family members who had their

infants cared for in a California NICU (Sigurdson et al., 2020). Several emerging challenges were identified from these interviews, including a lack of knowledge or conflict between families and social work, staff judgement, unmet family-identified needs for continuity of care, meaningful relationships with nurses, and inconsistent access to adequate linguistic services (Sigurdson et al., 2020). Based on the FCC principles, researchers identified a lack of mutual trust and power sharing for NICU families (Sigurdson et al., 2020).

Larocque et al. (2021) conducted a concept analysis and literature review of FCC to conceptualize what FCC means in the NICU. Larocque et al. (2021) identified four antecedents that create the foundational concept of FCC in the NICU: (a) family and healthcare provider collaboration; (b) education support for parents, (c) support from institutional leadership, and (d) physical environments that support parent-infant attachments. Next, Larocque et al. (2021) described the attributes of FCC as (a) individualized and developmentally sensitive; (b) physical and emotional closeness between families and infants; (c) genuine partnership; (d) parent empowerment through education and knowledge translation; and (e) supporting and taking care of families. Outcomes when FCC attributes are used within clinical practice include an enhanced bio-psychosocial well-being, improved neonatal outcomes, increased family satisfaction, enhanced parental confidence, and improved role clarity (Larocque et al., 2021). Larocque et al. (2021) highlighted the need for quality improvement projects and interventions to target FCC in the NICU.

Reid et al. (2021) conducted a narrative literature review about FCC in the NICU. The principles of neonatal FCC includes dignity and respect, communication, information sharing, partnership and collaboration (Reid et al., 2021). Reid et al. (2021) noted that there may be possible misperceptions that FCC only regards the interactions between NICU staff members and

families, which may lead to the unsuccessful implementation of FCC when other key components are overlooked. Reid et al. (2021) emphasized that FCC is a comprehensive care approach, and encompasses the healthcare system, infrastructure, hospital services and resources. Although FCC in the NICU has evolved and made great advances over the past six decades (see Appendix H), FCC in the NICU is still not fully implemented, and current implementation may be inconsistent (Benzies et al., 2016; Reid et al., 2021; Staniszewska et al., 2021).

Family-Centred Care in Clinical Practice Guidelines

Implementing FCC requires a total and comprehensive organizational commitment; otherwise, there may be challenges in shifting healthcare culture (Abraham & Moretz, 2012). Johnson (2000) stated that to make FCC a complete reality, it is necessary to change attitudes and practices, develop collaborative approaches, and change how families are viewed. Kokorelias et al. (2019) identified that concrete steps are required to implement a universal FCC model of care into practice. As Kuo et al. (2012) stated: "The principles of family-centered care should be acknowledged and actively incorporated within all care delivery and practice guidelines" (p. 302).

Guideline and policy transformations are required to strengthen family-centred perinatal care in the healthcare system. Although CPGs may be of high quality in their development, if they are not supported by FCC values, healthcare providers may unintentionally revert to delivering traditional and institutional approaches to care. Over 20 years ago, Johnson (2000) highlighted that healthcare institutions could support FCC by incorporating FCC principles into policies and practices. More recently, Maree & Downes (2016) also acknowledged the importance of evidence-based policies and that parents and family members are essential to their development. FCC should be at the root of all clinical decisions and care, which requires FCC to

be reflected in CPGs. Kuo et al. (2012) encouraged the development and validation of evaluation tools for FCC. Currently, however, no tools are available to provide a metric for the degree and quality of FCC values reflected in CPGs. Responding to this gap, I led the development of a tool to measure the degree and quality of FCC within maternal-newborn CPGs.

Methods for the Development and Pilot of Family-Centred Maternal Newborn Care Appraisal Tool (FCMNC-T)

Whiting et al. (2017) proposed a comprehensive framework for developers of quality assessment tools to refer to and outlined a systematic approach to ensure that a robust development method is followed throughout a tool's development. This framework is grouped into three stages, including (a) five initial steps, (b) four steps for tool development, and (c) four steps for dissemination (Whiting et al., 2017; see Appendix I). Whiting et al.'s (2017) three-stage framework was developed through discussion among team members with extensive experience in developing various quality assessment tools and study designs. Features from the three-stage framework proposed by Whiting et al. (2017) were used in the planning, development, and piloting of this FCMNC-T.

Methods for the Development of the FCMNC-Tool

Stage 1: Initial Steps

The first stage of the Whiting et al. framework (2017) consists of five initial steps to organize and manage the plan for the tool development:

1) Identify the need for a new tool.

2) Obtain funding for the tool development.

3) Assemble a team.

4) Manage the project.

5) Define the scope.

As previously stated in this chapter, there is a need to develop a tool to assess the quality of FCC values within perinatal CPGs to optimize health outcomes for families. No funding had been obtained to develop this appraisal tool. I (CF) am responsible for managing drafts, pilot results, and communication between team members involved in the tool development. The working group involved in the development of the FCMNC-T consists of members of various academic backgrounds and expertise, including CF (novice researcher and NICU RN); IG (senior researcher and knowledge translation expert); DH (senior researcher and expert in maternal-newborn health); WP (senior researcher and expert in maternal-newborn health); CC (perinatal expert/RN); and MB (novice researcher and NICU RN). The scope of this tool is the quality assessment (defined as FCC) in perinatal CPGs.

Stage 2: Tool Development

Tool development is the second stage of Whiting et al.'s (2017) framework. This stage consists of four steps:

1) Generate items.
2) Agree on items.
3) Produce the first draft and develop guidance.
4) Pilot/refine.

In the following paragraphs, I will briefly describe the first three steps, including the generation of items from a thematic analysis of purposefully selected literature and consultation with team members, followed by the drafting of the tool. The refined final tool and the pilot will be discussed in the results section of this chapter.

A literature review of FCC was conducted to identify the attributes of FCC. This literature informed our understanding of the central aspects of clinical care that reflect FCC in maternal-newborn settings (i.e., rooming in, skin-to-skin, participation in rounds, etc.). Through the literature review, we also identified several appraisal tools for families that measure FCC in various clinical settings (Arslan et al., 2019; Simione et al., 2020; Wells et al., 2015). The articles were thoroughly reviewed to identify key attributes of FCC, clinical examples, and the methodology for tool development.

Three publications relating to FCC principles identified from the literature review were purposefully selected and used to inform the development of the tool. The first selected article is the *Family-centred Maternity and Newborn Care National Guidelines (*PHAC, 2017). This guideline includes 17 evidence-based principles of family-centred maternity newborn care developed by Canadian experts to improve FCC in Canadian clinical practice (PHAC, 2017). Next, the Institute for Patient and Family-Centered Care definition of FCC was also used to guide the tool development (Johnson et al., 2008). Johnson's four core principles of FCC are well-known in clinical practice and are used by many institutions and organizations to define FCC in their practice (2008). Finally, Larocque et al.'s (2021) FCC concept analysis was selected as this recent Canadian study provides insights into the attributes and components of FCC in the NICU.

Thematic analysis of 17 Principles of Family-Centred Maternity Newborn Care (PHAC, 2017). Thematic analysis is a method for analyzing qualitative data. Thematic analysis entails searching written content (data) to identify, analyze and report patterns (Braun & Clarke, 2006). Thematic analysis of the three selected documents was conducted using Braun and Clarke's six-step framework to identify the themes of FCC (2006). This six-step framework

comprises familiarizing self with data, generating initial codes, searching for themes, reviewing themes, defining, and naming themes, and producing the report.

The PHAC's (2017) 17 evidence-based principles of family-centred maternity newborn care was purposely selected for a thematic analysis as it governs maternity and newborn care in Canada. First, the 17 principles were compared with each other for similar wording, underlying values, and intended outcomes. The 17 principles were then grouped based on their similarities. This was a dynamic process of coding and matching principles, as often one principle would share similarities with more than one of the other principles. After careful analysis of the 17 principles, eight main themes were identified (see Table 2).

The eight themes that emerged from PHAC's (2017) 17 principles were compared to Johnson et al. (2008) and Larocque's (2021) interpretation of FCC to validate the eight themes. For example, Larocque et al. (2021) described attributes of FCC, which include (a) individualized and developmentally sensitive; (b) physical and emotional closeness between families and infants; (c) genuine partnership; (d) parent empowerment through education and knowledge translation; and (e) supporting and taking care of families. Johnson et al. (2008) core concepts include respect and dignity, information sharing, participation, and collaboration. The eight themes were then reviewed with the tool development team members.

The various clinical examples of FCC that were identified in the literature review were matched to one of the eight themes that it best reflected. CF and members of the tool development team agreed upon the matching of the clinical examples to the themes, at which point the structure of the first draft was developed.

Table 2

Eight Emerging Themes of Family-Centred Maternity-Newborn Care

Eight Themes of Family-Centred Care	**PHAC (2017) Principles**	**Johnson et al. (2008) Core Concepts**	**Larocque et al. (2021) Attributes of FCC**
1) Normalization of pregnancy and birth	Pregnancy and birth are normal, healthy processes (Principle 2).	Dignity and Respect	Physical and emotional closeness between families and infants Supporting and taking care of families
2) Inclusive and equitable healthcare	Culturally appropriate care is important in a multicultural society (Principle 8). Indigenous peoples have distinctive needs during pregnancy and birth (Principle 9). The attitudes and language of health care providers have an impact on a family's experience of care (Principle 14). Family-centered maternal and newborn care respects reproductive rights (Principle 15).	Dignity and Respect	Individualized and developmentally sensitive Supporting and taking care of families
3) Providing evidence-based information	Family-centered maternal and newborn care is informed by research evidence (Principle 5). Family-centered maternal newborn care best practices from global settings may offer valuable options for Canadian consideration (Principle 17	Information Sharing	Parent empowerment through education and knowledge translation
4) Dynamic information sharing between patient-family-providers	Women and their families require knowledge about their care (Principle 12).	Information Sharing	Parent empowerment through education and knowledge translation

5) Participation	A family-centered approach to maternal and newborn care is optimal (Principle 1). Family-centered maternal and newborn care applies to all care environments (Principle 4). Women and their families play an integral role in decision making (Principle 13).	Participation	Genuine partnership Supporting and taking care of families
6) Keeping families together	Early parent-infant attachment is critical for newborn and child development and the growth of healthy families (Principle 3). Care as close to home as possible is ideal (Principle 10).	Participation	Physical and emotional closeness between families and infants
7) Well-rounded and individualized family care	Family-centered maternal and newborn care requires a holistic approach (Principle 6). Family-centered newborn care involves collaboration among care providers (Principle 7). Individualized maternal and newborn care is recommended (Principle 11).	Collaboration	Individualized and developmentally sensitive Genuine partnership Supporting and taking care of families
8) Recognition that families have valuable knowledge and feedback	Family-centered maternal and newborn care functions within a system that requires ongoing evaluation (Principle 16).	Collaboration	Parent empowerment through education and knowledge translation Genuine partnership

The Development of First Draft. The eight themes were placed in the table's first column and labelled as “criteria items” (see Appendix J). The eight criteria items were sub-grouped into one of four of Johnson et al.’s principles of FCC (2008) that the item best reflected. Next to the criteria item, the PHAC principle(s) aligned with each criteria item was placed in a second column. Finally, a third column listed examples of how a CPG could reflect the corresponding criterion item. Each criteria item is scored out of 1. If there is no evidence of the CPG demonstrating any of the provided examples, the criteria item would be scored 0. If there is some evidence, the appraiser would give a score of 0.5. Finally, if there is outstanding evidence of the criteria, the appraiser would give a score of 1. The appraiser is instructed to do this for each of the eight criteria items and to give the guideline a total score out of eight.

The first draft of the appraisal tool was reviewed by five members of the maternal-newborn community in the Ottawa region and the thesis advisory committee for expert feedback. CF purposely asked this group to provide feedback on the tool's structure, the clinical examples, and the clarity of instructions. Based on their initial feedback, the scoring method was adjusted to make it clearer for users. For example, some of the clinical examples were rearranged to another criteria item that it better aligned with. A discussion that arose from the group’s feedback is that some examples may provide a “higher level” of FCC than others. Some examples may also have more evidence to support the implementation in practice. For example, encouraging skin-to-skin and rooming-in may provide more bonding and attachment opportunities compared to other FCC approaches. Therefore, the scoring instructions of the tool were modified so that the higher-level family-centred recommendations are bolded and reflect a greater weight for scoring purposes. The scoring instructions were changed for the second draft so that the appraiser must identify at least one of the bolded clinical examples for each criteria item to

receive a total score of 1. A score of 0.5 is given if there is some evidence of support for the criteria item, and a score of 0 is given if there is no evidence to support the criteria item.

Pilot of the Second Draft. WP and CF piloted the second draft of the tool using five maternal-newborn CPGs on various maternal-newborn topics (refer to Table 3). Each guideline was scored for the quality of FCC for each criteria item and scored out of 8. Weighted Cohen's Kappa (linear) was used to determine the inter-rater reliability between the two appraisers. IBM SPSS was used for calculations (IBM SPSS Statistics Version 28.0).

Table 3

Results from FCMNC Pilot of Second Draft.

Guideline	Cohen's Kappa (Weighted)	Asymptotic Standard Error	Z	P	Lower 95% Asymptotic CI Bound	Upper 95% Asymptotic CI Bound
1	0.556	0.231	2.108	.035	0.103	1.008
2	1.000	0.000	3.544	.000	1.000	1.000
3	0.310	0.220	1.247	.213	-0.120	0.741
4	0.429	0.350	1.852	.064	-0.257	1.114
5	1.000	0.000	2.828	.005	1.000	1.000

Kappa values ≤ 0 indicate no agreement between appraisers, 0.01-0.20 as none to slight, 0.21-0.40 as fair, 0.41-0.60 as moderate, 0.61-0.80 as substantial, and 0.81-1.00 as almost perfect agreement (McHugh, 2012). In the pilot of the second draft, there is moderate-substantial inter-rater reliability amongst the two appraisers for 4/5 appraised guidelines. After piloting the second draft, the tool was sent to IG, DH, and CC for final feedback.

Development of Third Draft. After a discussion of the tool's user-friendliness, the FCMNC-T was further refined. The first change was that the 17 PHAC principles were re-arranged and placed into column A (see Table 4) before the criteria item (column B). With this arrangement, appraisers can see that the PHAC principle established the criteria item. Next, a

few examples of FCC (column C) were more clearly defined and re-arranged to better align with the criteria item to ensure face validity.

Finally, Column E was added in order to ensure that endorsement statements are being scored separately from clinical examples. For example, a guideline could have an endorsement statement saying they support the criterion item (e.g., "we believe that pregnancy and birth are normal and healthy life processes") but may have limited or conflicting recommendations to support the statement (e.g., recommends invasive interventions before non-invasive, does not support breastfeeding or skin to skin, etc.). In contrast, the guideline could have excellent FCC clinical recommendations, but developers do not explicitly state the value. In response, column E (see Table 2) was added to score endorsement statements separately from the content examples. With this arrangement, appraisers may differentiate between what the guideline developers say they support (column E; endorsement statement) and what they recommend clinically (column C; content). Appraisers may decide which is more or less important to them (guideline developer's values versus clinical practice examples). For example, suppose the guideline authors explicitly state they support the criteria item. In that case, the appraiser will give a score of 1 for the criteria item in column E. If there is no endorsement statement for the criteria item, a score of 0 is given. This is done for the eight criteria items and is given a final score of 8 for endorsement appraisal, separate from the content scoring. The instructions for scoring the content (column C) remain the same as in the second draft. Column D (content score) was added so that appraisers can record the score for the criteria item and write the rationale for the content score.

Piloting of the FCMNC-T

Two graduate students, CF and MB, independently piloted the final version of the FCMNC-T on 11 neonatal abstinence syndrome guidelines (NAS). The 11 NAS guidelines were randomly selected from the guidelines retrieved for appraisal in Chapter 2. Reading and appraising the guidelines with the FCMNC-T took approximately 30 minutes each.

Data Analysis

In order to evaluate if the criteria items were interpreted and scored the same way by two appraisers, the weighted Cohen's kappa was used to test inter-rater reliability for each individual criteria item based on the content and endorsement scores from the 11 guidelines. The content scores and endorsement scores results will be displayed separately as they are measuring two distinct aspects of the FCC tool. Considering that Cohen's kappa requires integers for data analysis, the scores were coded on SPSS as follows: a score of 0 (no evidence) = 1; a score of 0.5 (some evidence) = 2; and a score of 1 (substantial evidence) = 3.

Next, the weighted Cohen's kappa was calculated for each guideline's total content and endorsement scores to determine the inter-rater reliability between the appraisers. This was done to evaluate how well the appraisers agreed on the scoring for each guideline. Finally, the intra-class correlation (ICC) was conducted on both the cumulative content and endorsement scores of the 11 guidelines to provide two overall inter-rater reliability scores for the content and endorsement appraisals. This analysis provided insight into how well the appraisers can agree and identify low-quality versus high-quality FCC guidelines. The ICC was selected as the total guidelines scores are presented as interval data; therefore, the weighted Cohen's kappa would no longer be appropriate to use for this purpose.

Results of Pilot Testing of Family-Centred Maternal Newborn Care Appraisal Tool (FCMNC-T)

The FCMNC-T was developed after several meticulous steps, including a literature review of FCC in maternal-newborn care settings, a thematic analysis of the 17 principles of the FCMNC in Canada, and applying expert feedback. The final version of the FCMNC-T consists of eight criteria of FCC that are used to appraise a guideline's content and endorsement of FCC (see Table 4).

Table 4

Family-Centred Maternal Newborn Care Tool

A Tool for Assessing Family-Centred Care Values in Maternal-Newborn Clinical Practice Guidelines

Explanation of columns in the table below:
A: PHAC principle - All 17 principles are from the Public Health Agency of Canada's Family-centred Maternity and Newborn Care (FCMNC), from which thematic groupings were created (1-5 principles/group).
B: Criteria item -These criteria items have been developed from the thematic groupings of PHAC principles listed in column A, and are also listed according to the four core concepts of patient and family-centred care (indicated by blue rows) as follows: Dignity and respect, information sharing, participation and collaboration (Johnson et al., 2008). You will provide a content score for each of these items in column D.
C: Examples of guideline content – To look for to determine your content score in column D. This is a list of examples that reflects the criteria item.
D: Content score – To record the score examples in guideline content for each criteria item.
E: Endorsement score – To score the endorsement statement for each criteria item.

Instructions:
CONTENT SCORE*:*

1. Rate each of the eight criteria items (column B) by finding examples of content in the guideline (see column C) and give a content score in column D.
   Give a score of:
   - **1** if there is *outstanding evidence* in the guideline to support the item. There must be at least **one bolded example** identified in the guideline to receive a full score of **1.**
   - **0.5** if there is *some evidence* in the guideline to support the item.
   - **0** if there is *no evidence* in the guideline to support the item.
2. Write the rationale for each item's content score in column D. You may choose to add your own examples.
3. Add all scores together for a final content score out of 8.

ENDORSEMENT SCORE:

4. Indicate if there is an endorsing statement for each of the criteria items.
   - This can be an explicit statement or a statement that implies that the guideline developers value and support the item.

- If there is an endorsing statement, give 1 point.
- If there is not an endorsing statement, 0 point.

5. Add all scores together for a final endorsement score out of 8.

A ***PHAC Principle***	B **Criteria Item**	C **Examples of content in the guideline that meet this criteria item**	D ***CONTENT SCORE***	E ***ENDORSEMENT SCORE***
		Dignity and Respect		
Pregnancy and birth are normal, healthy processes (Principle 2)	**1. Pregnancy and birth are normalized.**	□ **Parents/caregivers are viewed as essential primary caregivers.** □ **Skin to skin and/or breastfeeding are encouraged.** □ Medical interventions should only be used when necessary. □ Least invasive/interventions with the least risk are recommended first (e.g., non-pharmacological interventions). □ Is clear on who required specific tests/procedures/therapy (e.g., not all babies require [specific intervention]).	**/1**	Does the guideline provide a statement that endorses the criteria item "Pregnancy and Birth are Normalized"? Yes = 1 point No = 0 point **/1**
Culturally appropriate care is important in a multicultural society (Principle 8)	**2. Inclusive and equitable healthcare for families is a priority.**	□ **Guideline includes recommendations that are consistent with the equity, diversity and inclusion principles.** □ **The words "respect" and/or "dignity" are used.** □ **Traditional practices, ceremonies, and rituals are encouraged and welcomed.**		Does the guideline provide a statement that endorses the criteria item "Inclusive and Equitable healthcare for families is a priority"?

A ***PHAC Principle***	B **Criteria Item**	C **Examples of content in the guideline that meet this criteria item**	D ***CONTENT SCORE***	E ***ENDORSEMENT SCORE***
Indigenous peoples have distinctive needs during pregnancy and birth (Principle 9) *The attitudes and language of health care providers have an impact on a family's experience of care (Principle* 14) *Family-centered maternal and newborn care respects reproductive rights (Principle 15)*		□ Recommendations include the ability to provide culturally safe care that is acceptable to Indigenous individuals and congruent with their needs. □ Guideline promotes strategies that address health disparities. □ Guideline recommends use of translation services. □ Language of guideline and recommendations are inclusive for LGBTQ2S+ individuals. □ Guideline uses appropriate language of inclusion for all family members (e.g., wording such as partner, caregiver, etc.). □ Guideline suggests strategies to eliminate barriers in the healthcare system; recognizes the stigma and attitudes of health care workers as barriers. □ Guideline recommends that reproductive information is offered to families (when applicable). Families' reproductive rights and decisions are respected.	**/1**	Yes = 1 point No = 0 point **/1**
	Evidence-based Practice and Information Sharing			

A *PHAC Principle*	B Criteria Item	C Examples of content in the guideline that meet this criteria item	D *CONTENT SCORE*	E *ENDORSEMENT SCORE*
Family-centered maternal and newborn care is informed by research evidence (Principle 5) *Family-centered maternal newborn care best practices from global settings may offer valuable options for Canadian consideration (Principle 17)*	**3. Families receive information that is evidence based.**	**Recommendations are supported by up-to-date, reliable and valid research evidence when possible, and referenced appropriately.** Development and attachment theories are referenced (e.g., Erikson's Stages of Development). References to family-centered care are evidence-based. There is evidence and best practices from global settings.	**/1**	Does the guideline provide a statement that endorses the criteria item "Families receive information that is evidence based"? Yes = 1 point No = 0 point **/1**
Women and their families require knowledge about their care (Principle 12)	**4. Families receive timely and complete information allowing for an open**	**Families receive information about diagnosis and treatment options are identified.**		Does the guideline provide a statement that endorses the criteria item "Families receive timely and complete

A *PHAC Principle*	B Criteria Item	C Examples of content in the guideline that meet this criteria item	D *CONTENT SCORE*	E *ENDORSEMENT SCORE*
	conversation with healthcare providers.	□ **Families receive explanation on the benefits and risks for interventions, and rational for any tests/procedures/therapies.** □ **Communication with families is encouraged.** □ Recommendations suggest when to call families and/or how to communicate sensitive information. □ Guideline includes strategies on how to communicate information in a timely and effective way to support informed decision making. □ Guidelines suggests that health literacy of family is considered and information is presented through various means (e.g., pamphlets, audio, and presentations). □ Guideline states that decision support is offered to families. □ Guideline offers strategies on how to support making an informed decision (e.g., decision aids).	**/1**	information allowing for an open conversation with healthcare providers"? Yes = 1 point No = 0 point **/1**
		Participation		
A family-centered approach to maternal and newborn care is	**5. Families are encouraged to participate in decision making and care in all settings.**	□ **Guideline uses "family-centered," "family-centered care," and/or "team" in vocabulary.**		Does the guideline provide a statement that endorses the criteria item "Families are encouraged to participate in

A ***PHAC Principle***	B **Criteria Item**	C **Examples of content in the guideline that meet this criteria item**	D ***CONTENT SCORE***	E ***ENDORSEMENT SCORE***
optimal (Principle 1). *Family-centered maternal and newborn care applies to all care environments (Principle 4)* *Women and their families play an integral role in decision making (Principle 13)*		□ **Guideline includes a discussion or recommendation about how parents/caregivers should be actively involved in decision making.** □ **Parents/caregivers are encouraged to voice their preferences and wishes.** □ **Goals and priorities are decided in collaboration with family.** □ **Recommendations include the participation of caregivers in all aspects of care** (e.g., mother to hold baby while newborn blood work is being performed). □ Guideline states that family is an important part of the mother-newborn dyad. □ Recommendations that support family centered care in various environments (e.g., Labor and Delivery, Postpartum, NICU/SCN, Pediatrics). For example, skin to skin is supported in the NICU/SCN.	**/1**	decision making and in care in all settings"? Yes = 1 point No = 0 point **/1**
Early parent-infant attachment is critical for newborn and child	**6. Families are kept together.**	□ **Guideline uses language such as "attachment" and "bonding" or highlights the importance of parent-infant attachment.** □ **24/7 rooming in is recommended/no parental separation during hospitalization.**		Does the guideline provide a statement that endorses the criteria item "Families are kept together"?

A ***PHAC Principle***	B **Criteria Item**	C **Examples of content in the guideline that meet this criteria item**	D ***CONTENT SCORE***	E ***ENDORSEMENT SCORE***
development and the growth of healthy families (Principle 3). *Care as close to home as possible is ideal (Principle 10)*		□ Guideline consists of recommendations that: 1) Screens for healthy attachment, 2) Educates families of healthy attachment, 3) Identifies barriers in attachment (e.g., PPD), and 4) Interventions to support healthy attachment. □ Family strengths are assessed and should be utilized □ Recommendations include parents to participate in the care of their infant in the NICU/SCN. □ Recommendations support services close to home/at home. □ Recommendations are provided that may reduce separation from home/families (e.g., virtual appointments).	**/1**	Yes = 1 point No = 0 point **/1**
		Collaboration		
Family-centered maternal and newborn care requires a holistic approach (Principle 6) *Family-centered newborn care involves collaboration among care*	**7. All aspects of a families' potential needs are addressed.**	□ **Most, if not all aspects of care are addressed for the patient/family (e.g., physical, spiritual, emotional needs).** □ **Guideline discusses various health care providers such as midwives, physicians, nurses, lactation consultants, social service providers (e.g., social workers, family therapists), and allied health professionals (e.g., respiratory therapists, pharmacists, audiologists) that can be involved in care.**		Does the guideline provide a statement that endorses the criteria item "All aspects of a families' needs are addressed"? Yes = 1 point No = 0 point

A ***PHAC Principle***	B **Criteria Item**	C **Examples of content in the guideline that meet this criteria item**	D ***CONTENT SCORE***	E ***ENDORSEMENT SCORE***
providers (Principle 7) *Individualized maternal and newborn care is recommended (Principle 11)*		**Guideline recognizes the uniqueness of every individual and their needs.** Healthcare team makes effort to maintain families' routines and preferences in hospital. Guideline indicates when referrals are recommended. Interdisciplinary team collaborates with families in regards to continuity of care (e.g., transfers, discharge planning, community supports).	**/1**	**/1**
Family-centered maternal and newborn care functions within a system that requires ongoing evaluation (Principle 16)	**8. Families are viewed as an important part of an interdisciplinary team and have valuable feedback.**	**Family/ies or a patient advisory committee have been engaged in the development of the guideline (e.g. providing input/feedback).** All health care providers introduce themselves and their role. Guideline recommends that families are encouraged to provide their feedback on their experiences for quality improvement/research. Families are encouraged to participate in research. Patient and family perspectives have been integrated into the development of guideline recommendations.	**/1**	Does the guideline provide a statement that endorses the criteria item "Families are viewed as an important part of an interdisciplinary team and have valuable feedback"? Yes = 1 point No = 0 point **/1**

A *PHAC Principle*	B Criteria Item	C Examples of content in the guideline that meet this criteria item	D *CONTENT SCORE*	E *ENDORSEMENT SCORE*
			Content Score TOTAL: **/8**	**Endorsement Score TOTAL:** **/8**

Inter-Rater Reliability of Criteria Items (Themes)

Criteria Items and Content Scores

The weighted Cohen's kappa for the content score ranges from 0.029-0.807 for criteria items 2-8 (Table 5). Cohen's kappa was not identified for criteria 1, as there was a lack of variance between the scores (of note, the appraisers agreed on 10/11 of scores for this item). One criteria item demonstrated substantial reliability (criteria item 2), and three criteria items demonstrated moderate reliability (criteria item 3,4,8). The remainder of the criteria items falls at or below fair agreement (criteria items 5,6,7). Scores from both appraisers can be found in Appendix K.

Table 5

Inter-rater reliability of Criteria Items (Themes) for Content Score (Column C/D)

Criteria Item	Weighted Cohen's Kappa	Asymptotic Standard Error	Z	P	Lower 95% Asymptotic CI Bound	Upper 95% Asymptotic CI Bound
1	*All ratings are the same for at least one rater. This command is not executed.*					
2	0.807	0.123	3.424	.001	0.565	1.049
3	0.421	0.261	2.327	.020	-0.090	0.932
4	0.468	0.181	2.085	.037	0.113	0.823
5	0.029	0.211	0.117	.907	-0.384	0.442
6	0.247	0.218	1.030	.303	-0.182	0.675
7	0.075	0.073	0.494	.621	-0.068	0.218
8	0.507	0.310	2.073	.038	-0.100	1.115

Criteria Items and Endorsement Scores

The weighted Cohen's Kappa for the criteria items relating to the endorsement scores ranged from 0.377-1.000 (see Table 6). A weighted Cohen's kappa for many of the criteria items could not be calculated due to the lack of variance amongst the appraisers' scores.

Table 6

Inter-rater reliability of Criteria Items (Themes) for Endorsement Scores (Column E)

Criteria Item	Weighted Cohen's Kappa	Asymptotic Standard Error	Z	P	Lower 95% Asymptotic CI Bound	Upper 95% Asymptotic CI Bound
1	*All ratings are the same for at least one rater. This command is not executed.*					
2	1.000	0.000	3.317	.001	1.000	1.000
3	*All ratings are the same for at least one rater. This command is not executed.*					
4	*All ratings are the same for at least one rater. This command is not executed.*					
5	0.377	0.291	1.279	.201	-0.192	0.947
6	0.377	0.291	1.279	.201	-0.192	0.947
7	*All ratings are the same for at least one rater. This command is not executed.*					
8	*All ratings are the same for at least one rater. This command is not executed.*					

Inter-rater Reliability of the Content Score and Endorsement Scores

The weighted Cohen's kappa for the content scores for each guideline ranges from 0.125-0.875 (see Table 7). Out of the 11 guidelines, one guideline demonstrated almost perfect reliability (guideline 5), three demonstrated substantial reliability (guidelines 3,8,9), three demonstrated moderate reliability (guidelines 6,7,10), two demonstrated fair reliability (guidelines 4,11), and two demonstrated none to slight reliability (guidelines 1,2).

Table 7

Inter-rater Reliability of Guideline's Content Scores

Guideline	Kappa	Asymptotic Standard Error	Z	P	Lower 95% Asymptotic CI Bound	Upper 95% Asymptotic CI Bound
1	0.125	0.166	0.730	.465	-0.201	0.451
2	0.172	0.269	0.662	.508	-0.355	0.699
3	0.692	0.182	2.533	.011	0.335	1.050
4	0.385	0.297	1.380	.168	-0.198	0.967
5	0.875	0.115	2.670	.008	0.650	1.100
6	0.412	0.198	1.717	.086	0.024	0.800
7	0.600	0.189	2.533	.011	0.229	0.971
8	0.636	0.031	2.828	.005	0.576	0.697

9	0.652	0.233	2.496	.013	0.195	1.110
10	0.600	0.280	2.268	.023	0.051	1.149
11	0.231	0.315	0.880	.379	-0.386	0.848

The weighted Cohen's kappa for the endorsement scores ranges from -0.200 to 1.000 (see Table 8). There was a lack of variance in the appraisers' scores to calculate the weighted Cohen's kappa for six guidelines (guidelines 1,4,5,6,7,10). Out of the six guidelines that have a Cohen's kappa available, two guidelines demonstrate almost perfect agreement (guidelines 3,11), two guidelines demonstrate moderate agreement (guidelines 8,9), and one guideline demonstrates no agreement (guideline 2).

Table 8

Inter-rater Reliability of Guideline's Endorsement Scores

Guideline	Kappa	Asymptotic Standard Error	Z	P	Lower 95% Asymptotic CI Bound	Upper 95% Asymptotic CI Bound
1	*All ratings are the same for at least one rater. This command is not executed.*					
2	-0.200	0.147	-0.617	.537	-0.488	0.088
3	1.000	0.000	2.828	.005	1.000	1.000
4	*All ratings are the same for at least one rater. This command is not executed.*					
5	*All ratings are the same for at least one rater. This command is not executed.*					
6	*All ratings are the same for at least one rater. This command is not executed.*					
7	*All ratings are the same for at least one rater. This command is not executed.*					
8	0.529	0.254	1.697	.090	0.031	1.028
9	0.600	0.343	1.852	.064	-0.072	1.272
10	*All ratings are the same for at least one rater. This command is not executed.*					
11	1.00	0.000	2.828	.005	1.000	1.000

Cumulative Content and Endorsement Scores Amongst 11 Guidelines

An ICC of less than 0.5 represents poor reliability, values between 0.5-0.75 represent moderate reliability, values between 0.75-0.9 indicate good reliability, and values greater than 0.9 indicate excellent reliability (Portney & Watkins, 2000). Out of all the eleven appraised

guidelines for content, the two appraisers overall had an ICC of 0.751 (good reliability; see Table 9) for the content scores and an ICC of 0.763 for the endorsement scores (good reliability; see Table 10).

Table 9

Cumulative Content Scores

ICC (Single Measures)	95% Confidence Interval		Value	F Test with True Value 0		
	Lower Bound	Upper Bound		Df1	Df2	Sig
0.751	0.308	0.926	7.024	10	10	0.002

Table 10

Cumulative Endorsement Scores

ICC (Single Measures)	95% Confidence Interval		Value	F Test with True Value 0		
	Lower Bound	Upper Bound		Df1	Df2	Sig
0.763	0.333	0.930	7.432	10	10	0.002

Discussion

This study aimed to develop and pilot the first-ever tool for the appraisal of FCC in CPGs. The pilot demonstrates good agreement between the two appraisers for the cumulative guideline scores appraised for content and endorsement statements (see Tables 9 and 10). The high inter-rater reliability found from the cumulative content scores and endorsement scores shows that the two appraisers tend to have similar total scores for each guideline. Although the total guideline scores are similar for both the content and endorsement scores of the tool, where the appraisers assigned scores varied. This is reflected by the low agreement seen in certain criteria items for both the content and endorsement scores. This finding highlights the need to

refine the content examples and endorsement statement in order to ensure that it properly reflects that criteria item. However, it is important to note that the tool allows appraisers to provide their own examples and flexibility for interpretation. Overall, appraisers had a moderate-almost perfect agreement for 7/11 for the individual guideline content scores, reflecting that the appraisers can agree and may identify between "high quality" versus "low quality" FCC guidelines (see Table 7). Further testing on the construct validity is required to validate the criteria items.

User Feedback and Areas for Improvement

After appraising the eleven guidelines, a few areas for improvement were identified. First, a common challenge among appraisers was deciding between what warrants a half score versus a full score. Although the appraisers had identified the same clinical examples throughout the guidelines, there remained a discrepancy in how they were scored. For example, one appraiser may have decided that a guideline with one bolded clinical example and one non-bolded example was enough to provide the criteria item with a full score, whereas the second appraiser may have found that to be insufficient for a full score. A consensus-based approach to scoring may be helpful to facilitate discussion between appraisers in these situations.

Secondly, the endorsement scoring in the pilot could have been more consistent between appraisers. For example, sometimes a guideline would not explicitly have the exact wording as the endorsement statement in the tool, but it may say something similar that endorses that value. In these instances, there were inconsistencies between appraisers when determining whether or not to assign a point. The development team discussed the need for flexibility in interpreting the endorsement statement to ensure the guideline developer's values are accurately captured.

Overall, the appraisers agreed that this tool was easy to use and recognized its capacity for it to measure FCC values in CPGs.

Strengths

A strength of this study was our use of the Whiting et al. framework (2017) to guide the development of this tool. This framework provided a robust methodology to follow and reduced the risk of bias during the development of the tools. Next, the team members who provided feedback on this tool were experts on various maternal-newborn health topics, which allowed for improved content and face validity of the provided examples in the tool.

Limitations

There were several limitations to the development and piloting of the tool. Only two appraisers assessed the final tool with 11 guidelines, and minimal training prior to the piloting was completed. Although scores were similar among the two appraisers, a greater number of appraisers are required to validate the FCMNC-T. The next step for this tool includes piloting at a greater scale with a power analysis conducted to determine the number of guidelines required to be appraised. In future piloting studies of this tool, the appraisers should not only consist of maternal-newborn care providers but include those who work in other clinical areas, administration, and/or research. To ensure that this tool is valid across maternal-newborn settings, there should be further piloting with guidelines of a large range of maternal-newborn topics (i.e., Labour and Delivery, Postpartum, Antepartum). Finally, a training module must be developed before this tool can be used.

There are limitations when using the weighted Cohen's kappa under certain circumstances. For example, Cohen's kappa is influenced by prevalence (distribution) rates, which brings forth the kappa paradox (Feinstein & Cicchetti, 1990; Thompson & Walter, 1988).

The kappa paradox occurs when the evaluators tend to assign a subject more frequently to one outcome (Zec et al., 2017). In our pilot study, there were some instances that a weighted Cohen's kappa could not be calculated due to a lack of variance between the appraisers (e.g., see Table 6). In these instances, the appraisers scored the same or nearly the same for each guideline (refer to Appendix K). Furthermore, there were some instances where the kappa resulted in a low inter-rater reliability despite an overall good agreement in scores between the appraisers (e.g., see Table 8, guideline 2). Morris et al. (2018) indicated that the failure to acknowledge how prevalence may be impacting kappa scores may cause misinterpretation of the true reliability of the measurement tool. The percentage agreement or odds ratio may be used and reported alongside the Cohen's kappa when there are circumstances of similar or identical proportion of agreements (Hoehler, 2000). Therefore, the inter-rater reliability determined by the weighted Cohen's kappa in this pilot may be lower due to the low distributions between the appraisers' scores.

Implications for Practice

The Family-Centred Maternal Newborn Care Tool (FCMNC-T) is an instrument developed to identify and evaluate the degree of FCC in perinatal CPGs. This tool can appraise existing perinatal CPGs for their degree of FCC. Policy and guideline developers may also use this tool to ensure that their CPGs reflect FCC during development. The FCMNC-T should be used in conjunction with another quality appraisal tool that evaluates the external, internal, and reporting factors of CPGs, such as the AGREE-II tool (Brouwers et al., 2010).

Implications for Research

The FCMNC-T requires a review and evaluation by patients and family advisors in the maternal-newborn community as the next phase of its development. For this tool to be fully

family-centred, the true experts (families) must be involved in the development of this tool. Based on their feedback, this tool requires further refinement, piloting, and validity testing on a greater scale. Instructions require re-wording for clarity purposes, and content examples require additional refinement to ensure adequate internal consistency. The development and piloting of the tool can be published and serve as a starting point for addressing the need for family-centred clinical practice guidelines in maternal newborn care.

Whiting et al.'s (2017) final stage of tool development concerns dissemination. After further refinement and piloting of the tool, this tool may be considered for a manuscript. No publication strategy, website, encouragement of tool uptake, or translation will be considered until further refinement and piloting of this tool have been completed.

Conclusion

Over the past century, significant progress has been made in implementing FCC practices in healthcare. FCC, however, is still not fully implemented and lacks standardization in healthcare. For FCC to be effectively implemented in practice, FCC must be considered and valued when making clinical decisions. CPGs that serve as the foundation for clinical decision-making must therefore be rooted in and reflect FCC values. A *Family-Centred Maternity-Newborn Care Tool* (FCMNC-T) was developed and piloted to evaluate FCC values within guidelines. The preliminary findings from the pilot of the FCMNC-T suggest that this tool may be a promising metric to evaluate FCC values in maternal-newborn CPGs. This tool may help ensure that FCC is grounded in all clinical decisions, ultimately supporting positive health outcomes and satisfaction for maternal-newborn dyads and their families. Further testing at a greater scale to evaluate the reliability and validity of this tool is warranted.

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Chapter Four: Integrated Discussion

In this chapter, I first summarize the main findings from our systematic review of clinical practice guidelines (CPGs) for the management of neonatal abstinence syndrome (NAS). Next, using a social-ecological model of care for NAS, I critically examine the implications of these findings for infants with NAS, their families, nursing practice and research. Throughout the implication sections, I identify areas that may benefit from further research while also discussing how my findings compare and contrast with existing literature. Furthermore, I identify how CPGs for NAS may be improved and integrate my findings from Chapter three (Family-Centred Maternal-Newborn Care Tool [FCMNC-T]). I then critically analyze the strengths and limitations of this research. Finally, I conclude this chapter by synthesizing the various aspects of this research, summarizing my overall recommendations, and revisiting a quote introduced at the beginning of this thesis.

Summary of Findings

Our systematic review of CPGs for the management of NAS addressed four research questions. The main findings for each research question are summarized below:

1: What CPGs for the management of NAS are available for use by clinicians?

Based on our eligibility criteria (refer to Appendix B), we identified 20 CPGs for the management of NAS that are available for clinicians to use. All were published in English and originated from the United States (U.S.; 6), Australia (6), Canada (3), England (3), Switzerland (1), and Scotland (1). All guidelines are free for clinicians to access on the internet.

2: What is the quality of currently available CPGs for the management of NAS?

Two appraisers evaluated the 20 guidelines that met our eligibility criteria using the AGREE-II tool (AGREE Next Steps Consortium, 2017). The majority of the guidelines were

found to be low quality based on the AGREE-II appraisal (16/20 had two or less domain scores of ≥ 60%). Most guidelines had a clear presentation and formatting; however, a significant number of guidelines lacked a rigorous development process. This reflects insufficiencies in the developers' process of gathering and synthesizing the evidence, the methods used to formulate the recommendations and the process for updating (AGREE Next Steps Consortium, 2017, p. 7). The top three guidelines appraised using the AGREE-II instrument were *Guidelines for the Identification and Management of Substance Use and Substance Use Disorders in Pregnancy* (high-quality A [five domains ≥ 60% including *rigour of development*]; World Health Organization [WHO], 2014), *Clinical Guidance for Treating Pregnant and Parenting Women with Opioids Use Disorders and Their infants* (moderate-quality A [four domains ≥ 60% including *rigour of development*; Substance Abuse and Mental Health Services Administration [SAMHSA], 2018), and *Perinatal Substance Use: Neonatal* (moderate-quality B [four domains ≥ 60% not including *rigour of development*]; Queensland Health, 2021).

3: What are the recommendations for the non-pharmacological and pharmacological management of NAS?

Two appraisers evaluated the 20 CPGs using the AGREE-REX tool (AGREE-REX Research Team, 2019). Despite the variation in quality between guidelines, most recommended similar non-pharmacological therapies, including skin-to-skin, rooming in, breastfeeding, swaddling, decreasing noise and light, and using a pacifier. Non-pharmacological interventions were consistently recommended before the use of pharmacological therapies. We found variations between CPGs on when pharmacological treatment should be started, what medication should be used, the dose range, and the weaning process.

4: What is the quality and applicability of the non-pharmacological and pharmacological recommendations for the management of NAS?

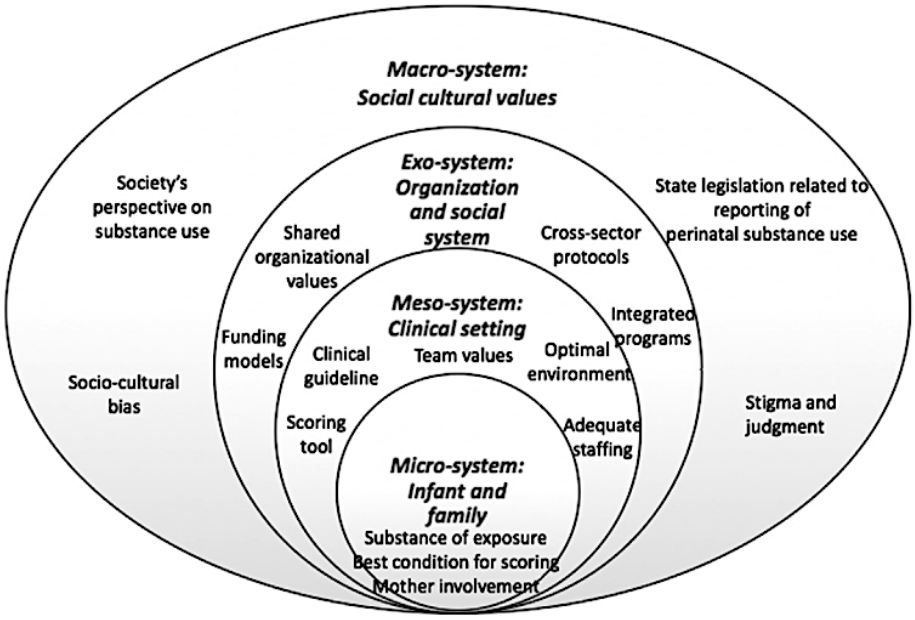
Similar to the quality assessment conducted on the guidelines using the AGREE-II appraisal tool, the appraisal of the recommendations using the AGREE-REX also revealed low scores for most CPGs. Overall, there was consistency between the two appraisal tools. For example, if a guideline scored "moderate" range on the AGREE-II tool, it would likely also score in the "moderate" on the overall AGREE-REX score (see p. 63).

Implications of Research

Marcellus (2018) used Bronfenbrenner's Social-Ecological Framework (1979) to identify and describe various factors that influence the treatment of infants with NAS. Marcellus (2018) encourages mapping clinical practices across the multilevel and intersections within this framework to identify areas for practice improvement. Therefore, my discussion of the implications of the findings from our systematic review is organized based on the four levels within Marcellus' (2018)/Bronfenbrenner's (1979) integrated framework and recommendations for future research will be examined throughout**.**

Figure 1

Marcellus (2018) Summary of Social-ecological System Factors that Influence the Care of Infants with Neonatal Abstinence Syndrome



Micro-system (Infant, Mother/Caregiver and Family)

At this first level, clinical processes that may influence the type of care provided to infants with NAS and their families are explored.

Implications for Infants with NAS.

Scoring Tools. In our systematic review, we found variations in the scoring tools used to score the severity of infants' withdrawal symptoms and in the cut-off scores for the initiation of pharmacological treatment. Standardized guidelines for treating NAS can decrease the variations in care, ultimately improving outcomes (Wood et al., 2019). The use of a standardized tool is recommended in the top two guidelines (SAMSHA, 2018; WHO, 2014), while the Finnegan scoring tool, in its modified and original version, is the most commonly recommended tool throughout the 20 appraised guidelines (Finnegan et al., 1975; Jansson & Patrick., 2019; Mehta

et al., 2013). We identified slight variations, however, in the interpretations of the Finnegan tool, particularly for the defined threshold for starting pharmacological treatment. An infant who may meet the threshold for pharmacological treatment using one guideline may not meet the threshold with the use of another guideline, which raises concerns that some infants may be started on pharmacological therapy too early without exhausting non-pharmacological measures. On the other hand, infants may be started on pharmacological therapy too late, resulting in several negative consequences including an increased severity of symptoms, risk of seizures, long-term health effects, and prolonged hospitalization.

The Finnegan tool and modified versions of the Finnegan tool have not been validated and may have poor inter-rater reliability due to the subjectiveness of the assessment (Bagley et al., 2014; Singh & Davis, 2021). Although most institutions use a cut-off score of eight on the Finnegan tool to initiate pharmacological treatment, there has been little evaluation of the effectiveness of this score as a threshold (Schiff & Grossman, 2019). A quality improvement initiative performed by Wachman et al. (2018) modified their protocol for starting pharmacological therapy to two scores ≥ 8 or one score ≥12, which differed from the standard protocol of three greater than 8 or two greater than 12 (Finnegan,1975; Kocherlakota, 2014). Wachman et al. (2018) found that with their modified protocol, pharmacological therapy was therefore initiated earlier, and there was a lack of consideration for additional non-pharmacological interventions prior to initiation. When their protocol (pre-intervention group) was compared to a function-based assessment (post-intervention group) using the *Eat Sleep Console Tool* (ESC; Grossman et al., 2017), Wachman et al. (2018) found that the proportion of infants requiring pharmacological treatment decreased from 87.1% (n = 101) in the pre-intervention group to 40.0% in the post-intervention group (n = 85; $p < .05$). Morphine was the

primary line of treatment for infants in the pre-intervention group, and methadone was the primary treatment for those in the post-intervention group. Wachman et al. (2018) found that the proportion of adjunct medication use (either phenobarbital or clonidine) decreased for those who received ESC assessments and methadone in the post-intervention group compared to those who received Finnegan scoring and morphine as the primary line of treatment in the pre-intervention group (2.4%, $n = 85$ and 33.6 %, $n = 101$ respectively; $p < .05$).

The ESC assesses the infant's disturbances in feeding, sleeping, and their ability to be consoled (Grossman et al., 2018). Pharmacologic treatment should only begin if there are disturbances in these functions which non-pharmacological interventions cannot alleviate (Grossman et al., 2018). Several studies have reported that when the ESC approach is used as a part of an infant's care, there is a reduced hospital length of stay for the infant, along with a decrease in the need for and duration of pharmacological treatment (Hein et al., 2021; Miller & Willier, 2021; Ryan et al., 2021). Hein et al. (2021) found a decrease in NICU admissions when an ESC model was implemented, from 50% preintervention (27/54) to 31% post-intervention (44/137). Furthermore, for infants requiring admission to the NICU for opioid withdrawal, Hein et al. (2021) found a decrease in the need for pharmacotherapy in the post-intervention group (24% [32/137] compared to 31%, [17/54] in pre-intervention), and the average length of treatment decreased from 14 days in the preintervention group to 10 days in the post-intervention group. In Miller & Willier's (2021) retrospective chart review of infants with NAS, 34 charts pre-ESC implementation and 37 post-ESC implementation were reviewed. Miller & Willier (2021) found a reduced requirement for morphine treatment in the post-ESC group compared to the pre-ESC group (58% [20/34] in pre-ESC group to 2.7% [1/37] in post-ESC group; $p < .05$) and a reduced mean length of stay from 17.7 days in pre-ESC compared to 5.9 days in post-ESC

($p < .05$). Ryan et al. (2021) conducted a retrospective cohort study evaluating outcomes with the Modified Finnegan Neonatal Abstinence Scoring System compared to ESC ($N = 158$). Ryan et al. (2021) found a reduced length of stay for infants who were assessed with the ESC (median of 9.6 days with the modified Finnegan [$n = 118$] compared to 5 days with ESC [$n = 40$]; $p < .05$) and a reduced need for pharmacologic treatment (53% with the modified Finnegan compared to 33% with the ESC; $p = .018$). For those who required pharmacological treatment, Ryan et al. (2021) found that the duration of treatment was reduced for infants managed with the ESC approach (median 11 days with modified Finnegan compared to 7 days with ESC; $p < .05$). A literature review conducted by Nicholson & Waskosky (2022) identified that among studies that reported length of stay and medication use, all studies reported a decreased length of stay with the use of the ESC compared to the Finnegan tool (pre-implementation length of stay between 9.5-31.8 days with Finnegan compared to 4.5-21.3 days with ESC).

The ESC is a promising and valuable tool for clinical practice supported by high-quality research. The ESC also aligns with the second principle of Canada's Principles of Family-Maternity and Newborn Care (FCMNC; PHAC, 2017). This principle defines normal birth, minimizes unnecessary interventions, and optimizes effective and proven interventions (PHAC, 2017). Using the ESC may decrease unnecessary interventions (pharmacological interventions and prolonged length of stay), and maternal-newborn bonding may be optimized as it encourages family as active members in care. Buczkowski et al. (2020) conducted a qualitative study interviewing 15 families receiving care for their infant in a Northern New England level II/III NICU and examined themes including NAS management, communication, preparation and education, family resources and maternal guilt. Buczkowski et al. (2020) identified that families expressed frustrations with the Finnegan tool and the variability of being involved with scoring.

According to Buczkowski et al. (2020), “one mother expressed that the Finnegan scoring system was not clear and was too subjective to accurately capture the clinical picture of her child” (p. 186).

The ESC is a family-centred intervention that should be recommended by guidelines and adopted into the hospital setting. Despite the existing body of evidence to support the ESC (Hein et al., 2021; Miller & Willier, 2021; Ryan et al., 2021), only two guidelines identified in our systematic review recommended the ESC (Alaska Native Medical Centre, 2020; Queensland Health, 2021). Two other guidelines recognized the use of ESC in practice but did not clearly recommend its use (Children’s Hospital at Westmead, 2021; Government of South Australia, 2022). Guideline developers may not recommend the ESC if their institution does not have the infrastructure that supports family involvement (e.g., care by parent rooms), a key component of the ESC model. Further research is needed to explore the facilitators and barriers of the ESC in practice, and family experiences with using the ESC.

Non-Pharmacologic Therapy. Systematic reviews conducted on the non-pharmacological management of NAS have identified several effective non-pharmacological interventions, including rooming in, breastfeeding, environmental modifications (i.e., decrease in light and noise), positioning and swaddling (Bagley et al., 2014; Edwards & Brown, 2016; MacMillan et al., 2018; MacVicar & Kelly, 2019; McQueen et al., 2019; Oostlander et al., 2019; Ryan et al., 2019; Wachman et al., 2018). A Cochrane review of the non-pharmacological care for infants with NAS revealed that interventions including environment modification, feeding practices and support for the dyad have low certainty of evidence (Pahl et al., 2020). Although systematic reviews have identified that many non-pharmacological interventions are based on

low-quality evidence, the possible benefits outweigh the very minimal risks of these interventions (Bagley et al., 2014; Edwards & Brown, 2016; Pahl et al., 2020).

In our systematic review, all 20 guidelines recommend similar non-pharmacological interventions despite varying quality scores on the AGREE-REX. There are some conflicting recommendations between the 20 guidelines, often related to the type of artificial milk used (e.g. starting sensitive/lactose-free formula versus standard term formula) and the volume and frequency in feeding (feeding on demand or providing smaller frequent volumes). These findings align with Bogen et al. (2017) study, where they identified a wide variation in the feeding practices used for infants with NAS across 76 hospitals across the United States. Furthermore, Bogen et al. (2017) found that 70% of hospitals included in their study had established policies/guidelines pertaining to breastfeeding. The policies indicated certain conditions required for mothers to meet prior to initiating breastfeeding, including having a negative drug screen at delivery (50%), enrolled in a treatment program (40%) or confirmed adherence to a drug treatment program (36%; Bogen et al. 2017). In Murphy et al. (2017) study of 65 Canadian NICUs, 53.8% of units reported that breastfeeding is always encouraged, 44.6% discourage breastfeeding if the mother is using illicit drugs, and 1.5% make breastfeeding recommendations on a case-by-case basis. In our review, we found that all guidelines recommended breastfeeding/providing breastmilk, with most guidelines indicating that it is safe to do so while on methadone/buprenorphine. The bed type used was another conflicting recommendation between guidelines. Several guidelines advised caution when using oscillating beds as it may worsen NAS symptoms if the infant becomes overstimulated.

Six of the 20 guidelines included recommendations for the skin care of infants with NAS. Infants with NAS are more susceptible to diaper dermatitis and excoriation in other areas of their

body (Glashan, 2022). Skin breakdown or diaper dermatitis can be painful for infants, and their discomfort may be mistakenly attributed to increased withdrawal symptoms. Infants with diaper dermatitis may exhibit more periods of agitation/crying and changes in feeding and sleeping patterns (Atherton et al., 2004; Burdall et al., 2019). Therefore, diaper dermatitis can ultimately appear as a worsening of withdrawal symptoms, which may affect the infant's course of treatment and hospital length of stay (Glashan, 2022). Protecting the skin of a newborn should be a priority in the care of the infant with NAS; however, it is not included in many NAS guidelines.

The appraised guidelines are aligned with current research on the recommendations for non-pharmacological treatment identified in the literature. However, some recommendations may not be effectively implemented into practice. For example, most guidelines scored poorly on the "implementation" of the AGREE-REX instrument, demonstrating room for improvement for guideline developers to provide practical strategies for guideline users on how to implement a recommendation. Most of the evidence for non-pharmacological therapy is based on low-quality or consensus-based evidence. Future research should investigate the effectiveness of various non-pharmacological treatments (i.e., bed type, massage, acupuncture) to better understand their therapeutic benefits. A scoping review conducted by Jackson et al. (2019), for example, identified that acupuncture is a non-invasive, feasible and safe intervention that may alleviate withdrawal symptoms.

Pharmacological Therapy. In our systematic review, we found variations in the type of medications recommended for use, dosing protocols, and weaning regimes for pharmacological treatments across the 20 guidelines. Notably, even when the same medication was recommended between guidelines, we found discrepancies between guidelines for their recommended

maximum dose. This raises concerns regarding the potential safety and toxicity risks between the guideline recommendations. On the other hand, infants may be subjected to the start of adjuvant therapies without reaching the maximum dose of the primary medication that they could have had. For example, one guideline indicates that the maximum daily dose of morphine is 1.2mg/kg/day (Kilpatrick et al., 2017). In contrast, another guideline indicates the maximum morphine dose is 100mcg/kg/dose q4h (equivalent to 0.6mg/kg/day; Royal Cornwall Hospitals, 2022). Variability of the pharmacological interventions being used for the management of NAS has also been reported in other studies across institutions in United States and Canada with no universally accepted treatment protocol (Bogen et al., 2017; Byerley et al., 2021; Murphy et al., 2017; Wood et al., 2019; Young et al., 2021).

Ghazanfarpour et al. (2019) systematic review of pharmacological treatment for NAS included 13 randomized control trials. Ghazanfarpour et al. (2019) review found that studies have shown that methadone, buprenorphine, and clonidine for NAS are more effective than morphine (Bada et al., 2015; Brown et al., 2014; Davis et al., 2018; Kraft et al., 2017). In Davis et al.'s (2018) randomized clinical trial, 117 term infants requiring pharmacological treatment for NAS from eight U.S. newborn units were randomized to receive morphine or methadone pharmacological treatment. Davis et al. (2018) found that methadone was associated with a reduced median length of stay (16 days with methadone compared to 20 days with morphine; $p = .005$). Lee et al. (2019) conducted a systematic review and meta-analysis on morphine, methadone, and buprenorphine treatments for NAS. Lee et al. (2019) identified eight studies (two randomized control trials and six cohort studies, $n = 8876$ infants) comparing methadone and morphine. Lee et al. (2019) found no difference in the length of treatment (weighted mean differences = -1.39; 95% CI: -5.79 to 3.01 days) or length of stay (weighted mean differences = -

1.38; 95% CI: -5.75 to 2.79 days) for infants primarily treated with morphine compared to methadone. However, Lee et al. (2019) did find a 1.5-fold increase in the rate of adjuvant drug required for infants using morphine compared to methadone (Risk Ratio = 1.51; 95% CI: 1.35-1.69). Lee et al. (2019) concluded that this finding alone is a compelling rationale to use methadone over morphine, as adjuvant drugs such as phenobarbital are associated with cognitive deficits. Of the 20 guidelines appraised in our systematic review, 14 recommended specifically using morphine as a primary medication for therapy, four recommended using either morphine or methadone/general opioid, one recommended using methadone, and one recommended using morphine in combination with clonidine. Literature on pharmacological treatment for NAS suggests that methadone may be superior to morphine (Davis et al., 2018). Sutter et al. (2022), on the other hand, conducted a small pilot study and indicated that they did not find any trends - in length of stay (17.9 days on morphine vs. 16.1 days on methadone; p = .5) or treatment duration (14.7 days on morphine vs. 12.8 days on methadone; p = .54) between infants who received methadone compared to morphine (N = 61). High-quality studies with larger sample sizes evaluating various medications and the most appropriate dosing are warranted so clinicians can make informed decisions about the medication regime for NAS.

Implications for Infants and Their Families.

Family-Centred Care as a Management Strategy for NAS. The most robust recommendation from the 20 included CPGs supported by strong evidence is to prioritize keeping families of infants with NAS together. MacMillan et al. (2018) systematic review and meta-analysis identified “strong and robust consistency” between results that rooming-in can reduce the need for pharmacological therapy and length of stay for infants with NAS (p. 5). Howard et al.’s (2017) retrospective study demonstrated that the more time families spend with

their infant with NAS, the severity of an infant's withdrawal, the need for pharmacological treatment, and the hospital length of stay is reduced. A Canadian study by Cooney et al. (2023) found that when caregivers had limited ability to leave the postpartum unit during the COVID-19 pandemic, there was a reduced number of transfers to the NICU for NAS pharmacological treatment. Other recommendations, including breastfeeding and skin-to-skin, further promote the notion of keeping families together. Non-pharmacological interventions that engage the participation of family caregivers are an essential foundation for the care of an infant with NAS (Patrick et al., 2020). Although our quality appraisal demonstrates varying quality among the guidelines and recommendations, strategies including rooming in, skin-to-skin, and breastfeeding are consistently recommended interventions by the appraised guidelines.

Family Involvement in Scoring. The ESC strongly focuses on promoting families as the primary caregivers for the infant with NAS. A qualitative study investigating 18 parents' experiences with the ESC tool in the United States found that parents felt they were active participants in their infant's care and had been encouraged by the staff members to lead their infant's care (McRae et al., 2021). The ESC, therefore, should not only be considered as a scoring tool but also as an intervention for supporting FCC. When families are involved in their infants' symptom scoring, parents' confidence in recognizing their newborns' withdrawal symptoms, identifying between normal and abnormal newborn behaviours, and their overall confidence in providing newborn care may be enhanced. This dynamic, collaborative relationship between family-facilitated care and clinician care encourages families to be active participants in their infants' care, which may foster families' trust and satisfaction in the healthcare team (McRae et al., 2021).

Maternal-Newborn Bonding. Rooming in, skin-to-skin and breastfeeding collectively support newborn bonding and attachment, which can be compromised when an infant is hospitalized and separated from their family. Despite existing research on strategies to foster secure attachments between at-risk mothers and their infants, limited studies investigate the impact of attachment-based interventions for newborns with NAS (Kondili & Duryea, 2019). This presents an opportunity to explore attachment-based inventions for NAS care, which could subsequently be incorporated into practice recommendations within CPGs.

Supporting Families. A qualitative study conducted by Atwood et al. (2016) collected interview data from 20 families in the United States regarding their experience with hospitalization for their infant with NAS. Atwood et al. (2016) identified several domains that influenced families' experiences during their infants' hospitalizations, including education and preparation (e.g., prenatal/postnatal education on NAS); partners in care (e.g., involvement with care and scoring); interpersonal interactions and communication (e.g., support from staff); hospital environment and transitions (e.g., different unit routines), and external factors (e.g., economic limitations that affected their ability to visit their infant). Similarly, a qualitative study conducted in the United States involving 15 families of hospitalized infants with NAS highlights the families' desire to participate in caring for their infant and for further education on NAS during the prenatal and postpartum period (Buczkowski et al., 2020).

Further research is required to explore the experiences of families of NAS, particularly during hospitalization. This research could help to create knowledge about the facilitators and barriers in creating a hospital environment that supports these families' psychosocial needs. Understanding their unique needs could help institutions and guideline developers create resources and educational materials and link families to required support (i.e., social work,

lactation consultant, etc.) while reducing barriers to participation in care. While these aspects of care are often considered within the appraised NAS guidelines, a more significant consideration of families' needs may improve the quality score on the *applicability* domain of the AGREE-II tool, as well as the three domains of *clinical applicability*, *values and preferences*, and *implementability* on the AGREE-REX tool.

Meso-system (Clinical Setting)

The next level of the social-ecological framework describes the meso-system as the link between the infant and the clinical setting, including the care team, physical environment, and CPGs (Marcellus, 2018).

Implications for Clinicians and Nursing Staff (Care Team). The findings of our systematic review of CPGs can be valuable to physicians, nurses, midwives, and other interdisciplinary team members caring for an infant with NAS as it offers a quality assessment of several guidelines they may be referring to in their practice. Clinicians may consider the overall AGREE-II guideline score utilizing our quality threshold definition, or may prioritize a specific domain of interest. Our review presents a comprehensive compilation of some well-known guidelines for NAS, guidelines that are used by large hospitals and institutions, along with some lesser-known guidelines available for free, on the internet. The recommendation matrix (see Chapter 2, p. 70) provides a practical visual layout comparing worldwide practices for NAS management. Our systematic review enables healthcare professionals to reflect on their current practice and consider adopting other practices as recommended in other guidelines into their practice. With the knowledge generated from the various global recommendations for NAS management, clinicians may continually enhance their care, optimize treatment outcomes, and stay current with recommendations for care. This directly relates to the FCMNC principles,

indicating that care is informed by research evidence and functions with ongoing evaluation (PHAC, 2017).

Healthcare professionals may consider the recommendations provided in our review and the facilitators and barriers when implementing a NAS-friendly and FCC unit. For example, self-reflection on any stigma or biases towards people who use illicit substances during pregnancy can help healthcare workers overcome potential barriers impeding them from providing optimal FCC. The understanding amongst the care team that providing FCC also encompasses trauma-informed care is essential when caring for this specific population. SAMSHA (2014) provides a concept of trauma-informed care that is grounded in four assumptions:

1) All levels of an organization have a realization of how trauma can affect families, groups, communities, and individuals.
2) People in the organization can recognize the signs of trauma.
3) The organization responds by applying principles of a trauma approach.
4) Care seeks to resist-re traumatization of clients and staff (p. 9-10).

Hospitals can further support staff training by offering trauma-informed courses in orientations to better recognize and care for the specific needs of families. These implications support the Canadian FCMNC principles, which indicate that the family-centred approach is optimal, maternal-newborn care requires a holistic approach, and care is individualized (PHAC, 2017).

Physical Environment. An additional barrier that is noteworthy to consider when caring for an infant with NAS is the physical environment. Non-pharmacological recommendations consistently reported in the NAS guidelines include decreasing noise and light in the NICU/SCN and keeping families together, emphasizing the importance of a non-stimulating and family-

centred environment for optimal NAS care. Unit nursing managers, leaders and organizations must therefore assess how their physical environment may impact an infant with NAS and take appropriate measures to ensure a conducive space for healing and family bonding. This implication directly aligns with the Canadian FCMNC principle that FCC applies to all environments and that early parent-infant attachment is critical for the growth of healthy families (PHAC, 2017). Finally, providing optimal nurse-patient ratios and training is essential to support nurses in fostering therapeutic relationships with families. By prioritizing these considerations, healthcare facilities can create an environment that fosters FCC for infants with NAS, leading to improved outcomes for infants and their families.

Improvement in Clinical Practice Guidelines. As indicated above, providing FCC is integral to managing NAS and should be reflected in all clinical decisions and CPGs. Healthcare professionals should use the FCMNC-T to ensure their recommendations are family-centred and reflect their other values as an institution. We identified an overall low quality of NAS guidelines and their corresponding recommendations. Currently, available NAS guidelines scored poorly on *rigour of development* domain on the AGREE-II. Although many recommendations for NAS are based on lower-quality research or consensus opinion, guideline developers may take steps to improve the quality of the guideline development by clearly addressing various items on the *rigour of development* domain of the AGREE-II (e.g., the methods used to search for evidence, explaining how recommendations were formulated, weighing the benefits versus the risks, and linking the recommendations with supporting evidence; Brouwers et al., 2010a). It is important for guideline developers to clearly explain their attempts to minimize bias, as scientific evidence to support guidelines is rarely available (Brouwers et al., 2010a). Furthermore, there is a need for practical suggestions identified within the NAS CPGs on how to implement recommendations

into practice. Additionally, addressing the barriers and facilitators that a guideline user may encounter when adopting a recommendation into practice may enhance the success of guideline implementation. Guideline developers are encouraged to use the AGREE-II and AGREE-REX when developing NAS guidelines to ensure that the guidelines and their content are credible and trustworthy.

Exo-system and Organizational Social System

The next level of the social-ecological framework describes the exo-system within the broader context of the NICU (Marcellus, 2018). I will explain how findings from our systematic review relate to healthcare models, institutional values, policy, and funding.

Healthcare Models: Continuum of Care for Neonatal Abstinence Syndrome. This thesis focuses on evaluating the in-hospital management of infants with NAS. However, it is essential to recognize that in-hospital management represents a minor facet of the comprehensive care required for infants with NAS and their families. According to Williams et al. (2008), many health problems in individuals occur long before they access healthcare. Interventions are therefore needed both within and outside the healthcare system. Interventions outside the healthcare system may have a superior effect in reducing the incidence and severity of illness (Williams et al., 2008). To establish a continuum of care for infants with NAS and their families under a public health upstream approach, supportive care must be initiated long before the infant's birth while encompassing the mother's/family's health and psychosocial needs. Whalen et al. (2019) emphasized that an optimal care model for opioid-exposed infants should include the mother, family, society, and the larger healthcare system. An upstream care approach addresses the root causes of population health illnesses, often by addressing social, economic, and

environmental conditions (PHAC, 2016). An upstream care approach to NAS may therefore reduce the occurrence and/or severity of NAS seen within NICU/SCN.

The continuum of care for infants with NAS should begin with supporting individuals with substance use disorders, ensuring they can access and receive appropriate healthcare services for their unique needs. In particular, this support is critical for pregnant individuals in their prenatal and postpartum periods. Ordean & Kahan (2011) described their retrospective chart review of 121 women in Toronto who had received care from the *Toronto Centre for Substance Use in Pregnancy* (T-CUP) program. T-CUP is a "one-stop access model" that provides comprehensive services for pregnant individuals supported by an interdisciplinary team. Services offered include prenatal and postnatal medical care, counselling, and assistance with psychosocial needs (Ordean & Kahan, 2011). Ordean & Kahan (2011) found a significant decrease in the use of prescribed opioids, cocaine, marijuana, benzodiazepines, and alcohol from the first trimester to the third trimester ($p < .05$). Furthermore, those who enrolled in this program earlier in their pregnancy had a shorter hospital length of stay for their infant, suggesting a lesser severity of NAS (mean of 6.6 days when women enrolled in the program in their first trimester [$n = 34$] compared to 11.5 days when enrolled in the third trimester [$n = 28$]; Ordean & Kahan, 2011). Odrean & Kahan (2011) also found greater breastfeeding rates among those who started the program earlier in their pregnancy (64.7% for those presenting in the first trimester compared to 39.5% presenting in the third) and an increased likelihood of retaining custody over their infant (94% of women who started in the program in the first trimester retained custody at discharge compared to 64.3% who came in during the third trimester). Other similar models of care, including the *New Choices* program in Hamilton, Canada (Sword et al., 2004), the *Sheway Program* in Vancouver, Canada (Garm, 1999; Marcellus, 2016) and the *Moms*

in Recovery program in Dartmouth-Hitchcock, United States (Goodman, 2015) demonstrated similar improved maternal and neonatal outcomes with a comprehensive model of care.

Comprehensive care models can open a vital opportunity to identify and manage various maternal co-morbidities that, left untreated, may lead to significant consequences for mothers and their infants. For example, untreated maternal mental health conditions are associated with an increased likelihood of preterm birth, decreased maternal-infant attachment, and poorer neurodevelopmental outcomes for the infant (Hoffman et al., 2017; Männistö et al., 2016; Ohoka et al., 2014; Whalen et al., 2019). A retrospective study in the United States of 338 maternal-newborn dyads found that mothers of infants with NAS were more likely to have claims on their insurance for major depression compared to mothers whose infants did not have NAS (33% vs. 15% respectively, $p < .01$), postpartum depression (7% vs. 3%, $p = .04$) and anxiety (27% vs. 13%, $p < .001$; Corr et al., 2020). Cigarette use is another prevalent health concern in pregnant individuals with substance use disorders (Akerman et al., 2015). In Chisolm et al. (2013) secondary data analysis, Chisolm et al. found that 95% of their sample of opioid-dependent pregnant individuals reported current cigarette use ($N = 124$ participants from across the United States, Canada, and Austria). Research has shown a link to greater NAS symptoms, longer hospital length of stays, and higher doses of morphine required for symptom relief when opioids and cigarettes are used together during pregnancy (Choo et al., 2004; Jones et al., 2013; Kaltenbach et al., 2012; Winklbaur et al., 2009).

Prenatal support is critical to improve the health outcomes for infants with NAS and their families. However, there is currently an insufficient number of programs that provide this comprehensive care to dyads. According to Rizk et al. (2019), only 19 states in the United States have substance treatment programs that are designed and targeted specifically for pregnant

individuals. Further research is required on how harm reduction services (e.g., methadone/buprenorphine treatment for opioid use disorders) in the prenatal period and postnatal support influence maternal and newborn health outcomes. There is limited knowledge about the prevalence of individuals with substance use disorders who do not access prenatal care and the various barriers to accessing healthcare. This presents a unique area for future research in prenatal nursing research.

Many of the guidelines appraised in our systematic review have recommendations regarding preparing families for their infant's hospital discharge and recommendations for follow-up care in the community for their infant. The first year after a person's delivery is the most likely time for opioid use relapse and fatal and nonfatal overdoses to occur (Schiff et al., 2018). Schiff et al.'s (2018) review of 4,158 births to women with an opioid use disorder (OUD) in Massachusetts, United States, found 242 opioid overdose events either in the first year before or after delivery, with most occurring 7-12 months after delivery. Unfortunately, many mothers/caregivers may not be receiving optimal support for their OUD. In Faherty et al.'s (2021) descriptive study of mother-infant dyads in three states in the United States, Medicaid insurance claims were linked to newborns who had in-utero substance exposure. Faherty et al. (2021) found that of Medicaid-insured mothers who had an infant with in-utero substance exposure, only 15% of women received any postpartum substance use treatment. The findings from Schiff et al.'s (2018) and Faherty et al.'s (2021) studies highlight the critical need for accessible and individualized postpartum care to support optimal health outcomes for postpartum individuals/caregivers and their infants. I was unable to find any Canadian literature on postpartum OUD management.

Evaluating Institutional/Organizational Values. Providing FCC is a common philosophy in many maternal-newborn healthcare settings. For FCC to be fully adopted, it must be at the root of all clinical decisions and supported within CPGs. In Chapter three of this thesis, I described a newly developed and piloted tool (FCMNC-T) to evaluate the quality of FCC in maternal-newborn CPGs. The preliminary results of the FCMNC-T pilot demonstrated a moderate-almost perfect agreement between two appraisers for 7/11 guidelines that were appraised for content (refer to Chapter three). Using a standardized tool to evaluate FCC in CPGs may help ensure that recommendations reflect family-centred values.

Two appraisers used the FCMNC-T to assess FCC values within the 20 NAS guidelines identified in our systematic review. The results of this appraisal will be analyzed and interpreted at a subsequent time as it goes beyond the scope of this thesis. As per the integrated framework presented in Chapter 1 this future research will compare the *quality of family-centred values* within NAS guidelines to the *confidence of evidence* based on the AGREE-II and AGREE-REX results. This would answer the following research question: *What is the quality of family centred-care in NAS Clinical Practice Guidelines?* Results from this research will provide clinicians with knowledge of the family-centred values within NAS guidelines. Although a guideline may be "high quality" based on the AGREE-II and AGREE-REX appraisal tools, a clinician may decide not to implement the guideline if it does not have "high quality" FCC values.

Implications for Policy and Quality Improvement Initiatives. In Chapter 1, I present an integrated framework that conceptualizes the "quality" of CPGs (see p. 24). This framework draws upon the principles of FCC and the AGREE-II tool. This framework aligns with various attributes encompassing the definition of "quality" as recognized by various organizations. For example, WHO (2020) states that quality health services should be effective (providing

evidence-based healthcare services) and people-centred (providing care that responds to individual preferences, needs, and values). This integrated framework can be helpful when designing, implementing, or evaluating policies or quality improvement initiatives in maternal-newborn settings. When family-centred values are embraced while promoting credible, trustworthy, and evidence-based care, organizations may be able to enhance the quality of their healthcare.

Cost-Effective Management for NAS and Funding Allocation. The increase in the incidence of NAS has burdened the healthcare system, with the most recent Canadian literature demonstrating that total costs of care increased from CAN$ 15.7 million in 2010 to CAN$ 26.9 million in 2014 (Filteau et al., 2018). In our systematic review, we have identified several cost-effective non-pharmacological recommendations for the management of NAS. Non-pharmacological interventions are not only cost-effective, but also often easy to implement (Kocherlakota, 2014; Mangat et al., 2019). For example, the ESC tool for scoring and promoting family in the care of the infant has been shown to reduce costs and improve infant health outcomes. Specifically, the ESC model has been found to reduce hospital length of stay for the infant and decrease the need for and duration of pharmacological treatment (Hein et al., 2021; Miller & Willier, 2021; Ryan et al., 2021). These outcomes may provide significant cost savings for healthcare. Furthermore, standardized treatment protocols improve health outcomes for infants with NAS and may help to decrease healthcare costs (Burnette et al., 2019).

Funding is essential to support the implementation of comprehensive models of care in the community for individuals with substance use disorders during their prenatal and postpartum periods. Greater funding directed toward community and primary care services for this population, in turn, may proactively help reduce the duration of the hospital management of

NAS, the severity of NAS, and other adverse health outcomes for the mother/caregiver-infant dyad. This upstream approach to care may reduce the overall health expenditure required for the care of an infant with NAS and their family. Currently, however, there is a notable lack of research evaluating the cost-effectiveness of these models. Future research is necessary to evaluate the economic impact of these types of models of care. This research may provide vital support to secure funding for harm reduction programs.

Macro-system

Regarding this level of the social-ecological framework, I will describe how the findings of our systematic review relate to government and the societal context.

Canadian Government - National Guidelines. In an evaluation of the management of NAS in Canada, Murphy et al. (2017) acknowledged the need to develop a national guideline for the management of NAS. Although Canada has a 'practice point' (Lacaze-Masmonteil, 2020), no Canadian national CPG for managing NAS has been developed. There is an urgency for the development of a national guideline in order to ensure that care across Canada is consistent and evidence-based. Throughout this discussion, I recommend a comprehensive model of care for infants with NAS. I propose that a national NAS guideline should therefore encompass the prenatal and postpartum care of the mother and appropriate recommendations to manage the infant's health after discharge from the hospital. Marcellus (2018) identifies that "individual and biomedically orientated clinical practices are required but are not sufficient on their own to holistically address the care of neonates with neonatal opioid withdrawal (NOW)" (p. 516). A current high-quality guideline may optimize the health outcomes for infants and their families while providing more efficient resource allocation and cost savings.

Societal Implications. Societal factors play a significant role in how individuals access health care services. The societal factors for care, however, may not always be adequately addressed in clinical guidelines. For example, there may be legal implications and consequences when individuals with substance use disorders access prenatal health services. In several states in the United States, substance use is considered a crime during pregnancy or child abuse (Rizk et al., 2019). According to Hui et al. (2017) over one-third of the United States will punish pregnant individuals for substance use, while "co-opting the medical profession through mandatory testing and reporting" (p. 112). These varying state laws may impact how healthcare providers care for individuals with substance use disorders and may cause fear or mistrust between the family and healthcare provider. Families may avoid seeking health services due to fear of child custody and the stigma associated with drug use (Howard et al., 2017; Ordean & Kahan, 2011). This threat to the patient-provider relationship and resulting legal consequences may cause pregnant individuals to avoid seeking prenatal care or care for their infant experiencing NAS symptoms (Rizk et al., 2019). Furthermore, there is no evidence that punishing pregnant individuals improves maternal or fetal outcomes (Hui et al., 2017). Punishment for substance use will only consequentially further exacerbate both the medical and social challenges this population faces (Rizk et al., 2019). In Canada, substance use during pregnancy is not illegal, nor can a pregnant individual be mandated to receive addiction treatment (Canada FASD Research Network's Action Team, 2014). Prenatal substance use is not considered an indicator of an individual's ability to parent and care for their child in Canada (Canada FASD Research Network's Action Team, 2014). Healthcare professionals do not have a legal obligation to report prenatal substance use; however, they do have a duty to report to child welfare when there is a concern for the

individual's ability to parent their child (Canada FASD Research Network's Action Team, 2014).

CPGs for NAS may provide some excellent high-quality, evidence-based recommendations for managing NAS. However, in the future, guideline developers must also consider how socio-economic factors may result in poor implementation of these recommendations. Research has shown that families in the lower income quartiles have the highest prevalence of NAS and are more likely to reside in rural areas/lower income areas compared to urban areas (Cairncross et al., 2018; Dookeran et al., 2023; Villapiano et al., 2017). Our systematic review identified that parental presence is an important strategy in reducing NAS severity. However, socioeconomic factors such as transportation may be a significant barrier for families' ability to be present and involved in their infant's care in the NICU, particularly when hospitals do not offer rooming-in. Models of care such as the *T-CUP* (Ordean & Kahan, 2011) that provide parents with substance use disorders with resources and community links to housing, social assistance, etc., may help facilitate parental presence in the NICU.

Strengths

Methodology

A strength of our systematic review is that it followed a rigorous methodology. For example, the protocol was developed using PRISMA (Page et al., 2021) to identify and select the guidelines for review, and the search strategy was peer-reviewed to capture the most appropriate guidelines. Next, a grey literature review was conducted in a systematic manner which allowed additional guidelines to have been identified. Two reviewers reviewed each link from the grey literature to ensure that appropriate guidelines that met our eligibility criteria were selected, which reduced the risk of selection bias. The methodology in which we conducted the grey

literature screening on Google Scholar may be helpful for other researchers to use in their reviews. Currently, there is no "gold standard" on how to complete a rigorous grey literature review, and Cochrane provides minimal guidance on how to successfully conduct a grey literature review (Godin et al., 2015; Higgins et al., 2022). This method of screening for grey literature opens the discussion for the development of a platform (similar to Distiller Systematic Review) that captures findings from the grey literature review into a database allowing for a systematic screening process.

AGREE-II and AGREE-REX Instruments

Prior to completing the quality appraisals, four appraisers completed training on the AGREE-II and AGREE-REX instruments. The four appraisers demonstrated a good inter-rater reliability on the AGREE-II and AGREE-REX training document scores. Rather than only using the AGREE-II to appraise the guidelines, incorporating the AGREE-REX instrument complimented and expanded on the results from the AGREE-II instrument by allowing for the consideration of values, evidence within the recommendations, how applicable, and how implementable the recommendations are. When the AGREE-II instrument is used alone, the results may identify high quality guidelines, but these guidelines may not include high quality recommendations that are useful for clinicians (Brouwers et al., 2020). By incorporating the AGREE-REX instrument in this appraisal, clinicians may have a fuller understanding of the quality of the guideline, in both its development process and recommendations.

FCMNC-T

The FCMNC-T is the first developed tool for clinicians and guideline developers to appraise FCC values within maternal-newborn guidelines. Results from the pilot showed a good inter-rater reliability among the two appraisers.

Limitations

There are several limitations to our systematic review. Some guidelines and commonly referred to documents by clinicians for NAS management were not included in our review. For example, due to the restriction of having the word "guideline" in the text, the Canadian Pediatric Society Practice *Point* (Lacaze-Masmontiel et al., 2018) and the *American Academy of Pediatric Clinical Report* (Hudak et al., 2012) were not included in our review. From the time the search was initially conducted in April 2022 to the present, there may be further CPGs published, or updated versions of the guidelines we appraised. Additionally, some of the guidelines included in our review had properties that indicated it may be a policy document. However, because some of these documents were referred to as a "guideline" and met the other inclusion criteria, they were therefore screened as eligible for the review.

The relatively lower quality scores from the AGREE-II and AGREE-REX appraisals may be attributed to inadequate reporting rather than poor methodological execution (Brouwers et al., 2010b; Florez et al., 2020). Therefore, the quality of the development and its recommendations of the guidelines may be higher than what we had scored. However, like all clinicians coming across these guidelines, we only had what was accessible to review.

Conclusion

Our systematic review is the first to evaluate the quality of NAS management guidelines and their recommendations using the AGREE-II and AGREE-REX appraisal tools while also considering FCC values. The highest scored guidelines on the AGREE-II and AGREE-REX appraisals were achieved from WHO (2014), SAMSHA (2018) followed by Queensland Health (2021). Findings indicated that while non-pharmacological recommendations are fairly consistent between the guidelines, there is considerable variability in recommendations for

pharmacological management. Our review sheds light on areas that need improvement and potential changes in NAS CPGs. For example, growing evidence supports new management interventions, such as the ESC, which can be integrated into future NAS guidelines. Comprehensive models of care encompassing the mother/caregiver-infant dyad in managing NAS may provide optimal health and economic outcomes. Guideline developers must address various socioeconomic factors that may facilitate the successful implementation and sustainability of recommendations within clinical practice. The FCMNC-T provides a promising resource for nurses and other healthcare professionals in maternal-newborn settings to critically appraise the degree of family-centred values included in their own CPGs. Research priorities identified in our review include further validation of the ESC, optimal pharmacological medications (particularly comparing the efficacy of morphine compared to methadone) and investigating the impact of comprehensive models of care on maternal-newborn health and economic outcomes.

As I conclude this chapter, I would like to reflect on a quote introduced at the start of this thesis: *"You can't go back and change the beginning, but you can start where you are and change the ending"* (C.S. Lewis). It is my hope that these findings will be used to improve the quality of NAS guidelines and pave the way for greater comprehensive FCC models to help create a "happily ever after" for infants with NAS and their families.

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Appendix A

PRISMA Checklist (Chapter 2)

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	44
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	49
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	46-48
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	49
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	49-50 Appendix B
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	50 Appendix D
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Appendix C
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	51-52
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	51-52
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	49-50
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	52-53
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	53-54
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	54
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	/

Section and Topic	Item #	Checklist item	Location where item is reported
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	52
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	52-55
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	/
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	/
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	/
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	/
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	/
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	56
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	56
Study characteristics	17	Cite each included study and present its characteristics.	58-61
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	63-66
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	/
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	/
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	63
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	/
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	/
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	/
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	/
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	81-83
	23b	Discuss any limitations of the evidence included in the review.	/

Section and Topic	Item #	Checklist item	Location where item is reported
	23c	Discuss any limitations of the review processes used.	84
	23d	Discuss implications of the results for practice, policy, and future research.	83
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	49
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	49
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	/
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	/
Competing interests	26	Declare any competing interests of review authors.	/
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	/

Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. *BMJ* 2021;372:n71. doi: 10.1136/bmj.n71

Appendix B

Clinical Practice Guideline Eligibility Criteria Using PICAR Framework (Chapter 2)

PICAR Item	Eligibility	
	Inclusion Criteria	**Exclusion Criteria**
P: Population, clinical indication(s), and conditions (s)	Hospital inpatient newborns with neonatal abstinence syndrome as a result from in-utero opioid exposure.	1) Outpatient newborn with NAS. 2) Withdrawal from opioid wean or cessation in critically ill neonates for analgesia and sedation purposes (withdrawal from opioids not from in-utero exposure). 3) CPGs focusing on the management of withdrawal not from opioids (from benzodiazepines, antidepressants).
I: Interventions	CPGs that include pharmacological and/or non-pharmacological management for NAS, and that adhere to IOM (2011) of CPGs.	CPGs that do not make recommendations on the management (either nonpharmacological or pharmacological) of NAS
C: Comparator(s), comparison(s), and (key) content	Not applicable	
A: Attributes of the CPG	**Language:** Available in English or French **Year:** Published > January 1st, 2011 (past ten years). **Country:** National or international CPGs will be included. **Version:** Latest and most up to date version only. **Availability:** CPGs that are accessible to the public (i.e. does not require membership) or which can be obtained through the University of Ottawa library databases. **Publication Type:** Must be published by a professional organization, association, peer reviewed journal, hospitals or health care/research institutes. **Development Process:** Evidence and/or consensus-based **Text:** Must have the key word "guideline" in the text. **Recommendations:** At least one eligible recommendation is reported.	1) Recommendations for the management of NAS from systematic reviews, clinical reports, clinical trials, case series, conference posters, presentations, abstracts, thesis or institutional policies. 2) Unpublished CPGs, or currently under development.
R: Recommendation characteristics and "other" considerations	Eligible CPG is dependent on the presence of eligible recommendations, as follows:	

	• There must be at least one recommendation that discusses pharmacological or non-pharmacological management of NAS. Aligned to key content, recommendations must pertain to the management of NAS related to opioid exposure. • Recommendations can be found within the text of the CPGs.	

Appendix C

MEDLINE Search Strategy (Chapter 2)

Ovid MEDLINE(R) ALL <1946 to April 22, 2022>

1 exp infant, newborn/ or Intensive Care, Neonatal/ or Intensive Care Units, Neonatal/ or Neonatology/ 654215
2 (baby* or babies or infant or infants or infant? or infantile or infancy or neonat* or newborn* or new born or new borns or newly born or NICU or premature or pre-mature or prenatal).ti,ab,kw,kf. 1008640
3 or/1-2 [Filter: Neonatal Population 04-2022-OVID MEDLINE] 1295020
4 neonatal abstinence syndrome/ 1627
5 "NAS".tw,kf. 8559
6 substance withdrawal syndrome/ or exp opioid-related disorders/ 50112
7 ((drug or drugs or opi* or heroin or morphine or substance*) adj3 (withdraw* or addict* or disorder* or dependen* or abstinence or abstain*)).tw,kf. 92634
8 or/4-7 130674
9 exp clinical pathway/ 7476
10 exp clinical protocol/ 184223
11 clinical protocols/ 29658
12 exp consensus/ 18303
13 exp consensus development conference/ 12605
14 exp consensus development conferences as topic/ 2997
15 critical pathways/ 7476
16 exp guideline/ 36971
17 guidelines as topic/ 42004
18 exp practice guideline/ 29766
19 practice guidelines as topic/ 127254
20 health planning guidelines/ 4164
21 Clinical Decision Rules/ 861
22 (guideline or practice guideline or consensus development conference or consensus development conference, NIH).pt. 46816
23 (position statement* or policy statement* or practice parameter* or best practice*).ti,ab,kf,kw. 41115
24 (standards or guideline or guidelines).ti,kf,kw. 125898
25 ((practice or treatment* or clinical) adj guideline*).ab. 47764
26 (CPG or CPGs).ti. 6179
27 consensus*.ti,kf,kw. 31404
28 consensus*.ab. /freq=2 30549
29 ((critical or clinical or practice) adj2 (path or paths or pathway or pathways or protocol*)).ti,ab,kf,kw. 24128
30 recommendat*.ti,kf,kw. or guideline recommendation*.ab. 53163
31 (care adj2 (standard or path or paths or pathway or pathways or map or maps or plan or plans)).ti,ab,kf,kw. 73721

32 (algorithm* adj2 (screening or examination or test or tested or testing or assessment* or diagnosis or diagnoses or diagnosed or diagnosing)).ti,ab,kf,kw. 9282
33 (algorithm* adj2 (pharmacotherap* or chemotherap* or chemotreatment* or therap* or treatment* or intervention*)).ti,ab,kf,kw. 11779
34 (guideline* or standards or consensus* or recommendat*).au. 548
35 (guideline* or standards or consensus* or recommendat*).ca. 1167
36 (practice adj1 point*).ti,ab,kf,kw. 601
37 or/9-36 704067
38 3 and 8 and 37 288
39 limit 38 to (yr="2011 -Current" and (english or french)) 219

Appendix D

Grey Literature Search (Chapter 2)

Clinical Practice Guideline Databases: Agency for Healthcare Research and Quality (https://www.ahrq.gov/gam/index.html), Canada's Drug and Health Technology Agency (CADTH; https://www.cadth.ca/), ECRI Guidelines (https://guidelines.ecri.org/), Dynamed, National Institute of Health and Clinical Excellence (https://www.nice.org.uk/), Guidelines International Network (https://g-i-n.net/), Guideline Central (https://www.guidelinecentral.com/), Joanna Briggs Institute EDP Database, The National Health and Medical Research Council Australia (www.nhmrc.gov.au), The New Zealand Guideline Group (www.health.govt.nz/about-ministry/ministry-health-websites/new-zealand-guidelines-group), The Scottish Intercollegiate Guidelines Network (https://www.sign.ac.uk/), Strategy for Patient Orientated Research (https://sporevidencealliance.ca/key-activities/cpg-asset-map/cpg-database/) and World Health Organization (https://www.who.int).

Societies and Associations Websites: Canadian Paediatric Society (https://www.cps.ca/), American Academy of Pediatrics (https://www.aap.org/en-us/Pages/Default.aspx), European Academy of Pediatrics (https://www.eapaediatrics.eu/), The Society of Obstetricians and Gynaecologists of Canada (https://sogc.org/), The Canadian Association of Perinatal and Women's Health Nurses (https://capwhn.ca/), The Association of Women's Health, Obstetric and Neonatal Nurses (https://www.awhonn.org/), National Association of Neonatal Nurses (http://nann.org/), American College of Obstetricians and Gynecologists (https://www.acog.org/), Canadian Association of Midwives (https://canadianmidwives.org/), Canadian Provincial Perinatal/Maternal/Child Health Councils (i.e., http://www.perinatalservicesbc.ca/).

Appendix E

Training Scores: AGREE-REX and AGREE-II Appraisal (Chapter 2)

Table 1

Guideline 1 Appraisal Scores

Guideline 1: Major Depression in Adults (BC Ministry of Health, 2013)								
	AGREE II				AGREE REX			
	CF	WP	CC	MB	CF	WP	CC	MB
1	5	6	5	5	1	1	1	1
2	1	5	5	3	6	4	6	3
3	4	6	7	6	3	2	3	4
4	2	1	2	2	5	1	5	3
5	1	1	1	1	2	1	2	3
6	7	5	7	7	2	1	2	1
7	1	1	1	1	1	1	1	2
8	1	1	1	4	4	3	4	3
9	1	1	1	1	2	1	2	2
10	1	1	1	1				
11	2	2	2	4				
12	1	1	1	1				
13	2	1	2	2				
14	1	1	1	1				
15	4	2	5	3				
16	7	3	7	7				
17	7	7	7	7				
18	1	1	1	1				
19	5	4	5	5				
20	1	2	4	2				
21	1	3	1	1				
22	1	1	1	1				
23	1	1	1	1				
TOTAL	58/161	57/61	69/161	67/161	26/63	15/63	26/63	22/63

Table 2

Guideline 2 Appraisal Scores

Guideline 2: Prevention, Diagnosis and Treatment of Lyme Disease (American College of Rheumatology, 2021)								
	AGREE II				AGREE REX			
	CF	WP	CC	MB	CF	WP	CC	MB
1	7	4	7	5	7	4	7	5
2	7	5	7	3	7	7	7	7
3	7	7	7	6	5	7	5	5
4	7	7	7	7	7	5	5	4
5	7	7	1	3	2	5	2	3
6	7	7	7	6	3	2	3	1
7	7	7	7	6	5	4	1	4
8	7	5	7	7	7	6	7	5
9	7	6	7	1	4	1	4	2
10	7	7	7	5				
11	7	7	7	3				
12	7	7	7	5				
13	6	7	6	4				
14	5	7	5	7				
15	7	7	7	5				
16	7	7	7	6				
17	7	7	7	5				
18	6	2	1	2				
19	2	3	1	2				
20	5	2	5	1				
21	3	1	1	1				
22	5	5	5	3				
23	7	6	7	4				
TOTAL	**144/161**	**130/161**	**130/161**	**97/161**	**47/63**	**41/63**	**41/63**	**36/63**

Table 3

Guideline 3 Appraisal Scores

Guideline 3: Breastfeeding (RNAO, 2018)								
	AGREE II				AGREE REX			
	CF	WP	CC	MB	CF	WP	CC	MB
1	7	7	7	7	7	5	7	5
2	7	7	7	6	7	7	7	6
3	7	7	7	7	6	7	6	7
4	7	7	7	7	5	7	5	5
5	6	7	5	6	5	5	5	2
6	7	7	7	7	5	7	5	6
7	7	7	7	7	5	7	5	5
8	7	7	7	7	7	7	7	7
9	7	6	7	7	5	6	5	5
10	7	5	7	7				
11	7	7	7	7				
12	7	7	7	7				
13	7	7	7	7				
14	7	7	7	7				
15	7	7	7	7				
16	7	7	7	7				
17	7	7	7	5				
18	6	7	5	5				
19	7	6	7	6				
20	6	5	5	4				
21	7	7	7	7				
22	7	7	7	7				
23	7	7	7	7				
TOTAL	158/161	155/161	155/161	151/161	52/63	58/63	52/63	48/63

Table 4

Training Scores: ICC Results

Guideline 1 – (Major Depression in Adults)			
Appraiser 1	**Appraiser 2**	**AGREE-II**	**AGREE-REX**
CF	CC	Single Measure: 0.860 ICC Average Measure 0.925 ICC Sig <0.001	Single Measure: 1.000 ICC Average Measure: 1.000 ICC
CF	MB	Single Measure: 0.900 ICC Average Measure: 0.947 ICC Sig <0.001	Single Measure: 0.514 ICC Average Measure: 0.679 ICC Sig 0.066
CF	WP	Single Measure: 0.729 ICC Average Measure:0.843 ICC Sig <0.001	Single Measure: 0.512 ICC Average Measure: 0.677 ICC Sig 0.017
CF/CC/MB/WP		Single Measure: 0.842 ICC Average Measure: 0.955 ICC Sig 0.000	Single Measure: 0.607 ICC Average Measure: 0.861 Sig <0.001
Guideline 2 – (Lyme Disease)			
Appraiser 1	**Appraiser 2**	**AGREE-II**	**AGREE-REX**
CF	CC	Single Measure:0.613 ICC Average Measure:0.760 ICC Sig <0.001	Single Measure: 0.752 ICC Average Measure: 0.858 ICC Sig 0.005
CF	MB	Single Measure: 0.273 ICC Average Measure: 0.429 ICC Sig 0.011	Single Measure: 0.636 ICC Average Measure:0.778 ICC Sig 0.006
CF	WP	Single Measure: 0.608 ICC Average Measure:0.756 ICC Sig <0.001	Single Measure: 0.467 ICC Average Measure: 0.637 ICC Sig 0.087
CF CC MB WP		Single Measure:0.507 ICC Average Measure: 0.804 ICC Sig <0.001	Single Measure: 0.641 ICC Average Measure: 0.877 ICC Sig <0.001
Guideline 3 – (Breastfeeding)			
Appraiser 1	**Appraiser 2**	**AGREE-II**	**AGREE-REX**
CF	CC	Single Measure: 0.854 ICC Average Measure: 0.921 ICC Sig <0.001	Single Measure 1.0 ICC Average Measure: 1.0 ICC
CF	MB	Single Measure: 0.472 ICC Average Measure: 0.641 ICC Sig 0.005	Single Measure: 0.443 ICC Average Measure: 0.614 ICC Sig 0.100

CF	WP	Single Measure: 0.220 ICC Average Measure: 0.361 ICC Sig 0.150	*Single Measure: -0.014 ICC* *Average Measure: -0.029 ICC* *Sig 0.518*
CF CC MB WP		Single Measure: 0.484 ICC Average Measure: 0.789 ICC Sig <0.001	Single Measure: 0.402 ICC Average Measure: 0.729 ICC Sig 0.003

Appendix F

Recommendation Matrix of Lowest 10 Guidelines from AGREE-REX Appraisal (Chapter 2)

CATEGORY ⇓	Guideline ⇒ *(presented in order of the highest AGREE-REX scores)* / SUBCATEGORY ⇓	Guideline 4[49]	Guideline 7[52]	Guideline 10[55]	Guideline 14[59]	Guideline 12[57]	Guideline 13[58]	Guideline 9[54]	Guideline 3[48]	Guideline 15[60]	Guideline 11[56]
SCREENING/SCORING	**Toxicology Screening** (Urine/Meconium/Hair)	Y!			Y!	Y	Y				
	Scoring Tool										
	Recommends a standardized scoring system										
	Finnegan Neonatal Abstinence Scoring (FNAS)		Y			Y					
	Modified Finnegan Neonatal Abstinence Syndrome Tool	Y		Y	Y			Y		Y10*	
	Eat, Sleep, Console (ESC)										
	Other						Y8*		Y		Y12*
	Initiation of Screening										
	2 hr after birth		Y	Y						Y	
	4-6 hr after birth					Y	Y				
	6+ hr after birth										
	When NAS is suspected							Y			
	Observation Period										
	2 days										
	3 days		Y1*		Y4*				Y9*		
	4-7 days			Y							
	5+ days	Y	Y1*		Y4*	Y7*					Y
FEEDING	**Breastfeeding**										
	Breastfeeding on drugs/alcohol										
	Breastfeeding on Methadone/Buprenorphine	Y	Y	Y	Y	Y	Y	Y	Y	Y11*	Y
	Hypercaloric Feeds	Y	Y		Y	Y		Y		Y	
	Sensitive Formula				Y5*	Y		Y			
	Frequent, Small Volume Feeds		Y	Y	Y	Y	Y		Y		

CATEGORY ⇓	Guideline ⇒ *(presented in order of the highest AGREE-REX scores)*	Guideline 4[49]	Guideline 7[52]	Guideline 10[55]	Guideline 14[59]	Guideline 12[57]	Guideline 13[58]	Guideline 9[54]	Guideline 3[48]	Guideline 15[60]	Guideline 11[56]
	SUBCATEGORY ⇓										
NON-PHARMACOLOGICAL RECOMMENDATIONS	**Rooming In**		Y	Y				Y			Y
	Kangaroo Care/Skin to Skin	Y	Y	Y	Y	Y		Y		Y	
	Swaddling	Y	Y	Y	Y	Y	Y	Y	Y		Y
	Pacifier/Hand to Mouth	Y	Y	Y	Y	Y	Y				Y
	Vertical Rocking		Y			Y					
	Gentle Handlings, Firm Pressure		Y		Y		Y	Y			
	Electric Swing				Y	Y!		(vibrating mats)			
	Decrease Light/Noise	Y	Y	Y	Y		Y	Y	Y	Y	
	Positional Support Water Beds				(prone)			(prone)			
	Skin Protection										
	Skin Barriers					Y	Y				
	Padding					Y	Y				
	Infant Massage	Y									
	Laser Acupuncture (adjuvant to pharmacological therapy)										
	Bathing	Y					Y				
	Music Therapy				Y						
PHARMACOLOGICAL RECOMMENDATIONS	**Initiation of Medication:**										
	Average of 3 consecutive scores ≥ 8, or 2 average scores ≥ 12.	Y	Y2*					Y		Y	
	> 8 for 3 consecutive readings or >12 for 2 consecutive readings		Y2*								
	3 consecutive scores ≥ than 9, or two scores ≥ 12.					Y					
	Average of 8 or more for 3 consecutives scores or averaging 11 or more for 2 consecutive scores.			Y							
	First Line Treatment										
	An Opioid (Unclear)										
	Morphine	Y	Y	Y	Y6*	Y	Y	Y	Y?	Y	Y
	Phenobarbital										
	Methadone		Y3*								
	Buprenorphine										
	Second Line Treatment										
	Clonidine	Y	Y(1^{st})		Y6*	Y(1^{st})				Y (1^{st})	
	Phenobarbital	Y	Y	Y		Y(2^{nd})		Y			Y

1* At least 3 days the infant should be monitored but up to 5 days or more for methadone/buprenorphine exposure.
2* Considers both
3* Methadone has been occasionally used as the first-line treatment, but morphine is more common.
4* 3 days minimum for an infant born to mother on low-dose opiate with short half-life. For a longer half-life (methadone) babe should be observed for 5-7 days.
5*reserve lactose-free formula for infants with persistent diarrhea
6* morphine AND clonidine together
7* 4 days for short-acting prescribed narcotics, 5-6 days for buprenorphine, Suboxone, and 5-7 days for heroin or methadone.
8* neonatal drug withdrawal chart.
9* minimum
10* also uses Finnegan short form
11* does not state if ok to breastfeed with methadone
12* Modified Lipsitz Score Tool

Appendix G

Canadian Pediatric Society and American Academy of Pediatric Recommendations (Chapter 2)

Table 1

Recommendation Matrix

		Guideline	
	Recommendations ⬇	**Canadian Pediatric Society (2018)**	**APP (Hudak et al., 2012)**
SCREENING/SCORING	**Toxicology Screening** *(Urine/Meconium/Hair)*	!	Y
	Scoring Tool:		
	Recommends a standardized scoring system	Y	Y
	Finnegan Neonatal Abstinence Scoring (FNAS)		
	Modified Finnegan Neonatal Abstinence Syndrome Tool		
	Eat, Sleep, Console (ESC)		
	Other (system disturbance)		
	Initiation Of Screening:		
	2 hr after birth	Y (1-2hr)	
	4-6 hr after birth		
	When NAS is suspected		
	Observation Period:		
	2 days		
	3 days	Y (minimum)	
	4-7 days		Y
	5+ days		
FEEDING	**Breastfeeding:**		
	Breastfeeding	Y	Y!
	Breastfeeding on drugs/alcohol		
	Breastfeeding on Methadone/Buprenorphine	Y	
	Hypercaloric Feeds		
	Sensitive Formula		
	Frequent, Small Volume Feeds		
NON-PHARMACOLOGICAL RECOMMENDATIONS	**Rooming In**	Y	
	Kangaroo Care/Skin to Skin	Y	
	Swaddling	Y	
	Pacifier/Hand to Mouth		
	Vertical Rocking		
	Gentle Handlings, Firm Pressure	Y	
	Electric Swing		
	Decrease Light/Noise	Y	Y
	Positional Support **Water Beds**	Y	
	Skin Protection Skin Barriers Padding		
	Infant Massage	Y	
	Laser Acupuncture/Acupuncture (adjuvant to pharmacological therapy)		
	Bathing		

	Music Therapy	Y	
PHARMACOLOGICAL RECOMMENDATIONS	**Initiation of Medication:**		
	3 consecutive scores >8 or the average of two scores or score for two consecutive intervals is >12		
	3 consecutive scores average ≥ than 8, or two consecutive scores ≥ 12 on FNAS		
	3 consecutive scores ≥ 8, or 1 score ≥ 12		
	Eat Sleep Console: Any question answered "YES" or consoling score of "3" required.		
	Other		
	First Line Treatment:		
	An Opioid (unspecified)	Y	
	Morphine		Y
	Phenobarbital		
	Methadone		Y
	Buprenorphine		
	Second Line Treatment:		
	Clonidine	Y	
	Phenobarbital	Y	
EDUCATION	***Antenatal Education***		
	Admission Education		
	Family Discharge Preparation		
	Community Follow-Up	Y	

Table 2

Canadian Pediatric Society (2018) Medication Guideline

MEDICATION	INITIATION	DOSE	MEDICATION INCREASE	MEDICATION WEAN
MORPHINE	Finnegan score is ≥ 8 on 3 (or ≥ 12 on 2) consecutive evaluations	Start at 0.32 mg/kg/day, divided every 4 h–6 h, orally.	If score persists ≥ 8 on 3 (or ≥ 12 on 2) consecutive evaluations, increase by 0.16 mg/kg/day every 4 h–6 h Maximum of 1.0 mg/kg/day.	Decrease dose by 10% of the total daily dose, every 48 h–72 h
METHADONE		0.05-0.1mg/kg/dose every 6h-12h	Increase by 0.05mg/kg every 48 h Maximum dose 1mg/kg/day	
PHENOARBITAL	May be used in addition to morphine	Loading dose: 10mg/kg PO every 12 h for 3 doses Maintenance dose: 5mg/kg/day orally		Wean by 10% to 20% every day or two days
CLONIDINE	May be used in addition to morphine	Start at 0.5mcg/kg for the first dose. Recommended maintenance dose is 3-5mcg/kg/day every 4-6h		Wean by 25% of the total daily dose every over day (q4h to q6h x48h, to q8h x 48h, to q12h x 48h to HS, then D/C)
BUPRENIRPHINE		4-5mcg/kg/dose every 8 h	Maximum dose 60mcg/kg/day	

Appendix H

Models of Care (Chapter 3)

Traditional Healthcare Model

Traditional or medical healthcare models adopt a health system-centric approach, where physicians direct patient care and care is acuity-oriented and hospital-based (Barnsteiner et al., 2014). Traditional healthcare models are grounded on beneficence and authoritarianism, are disease-oriented rather than patient-oriented, and aim to treat the illness rather than the patient with the disease (Sacristán, 2013). The primary purpose of traditional healthcare models is to improve the outcomes for the average patient, yet it frequently overlooks the patient's preferences and perspectives while doing so (Sacristán, 2013).

Patient/Person Centred Care Model or Patient/Person and Family-Centred Care Model

Patient/Person-Centred Care is an evolving concept, with various organizations adopting different definitions (Santana et al., 2018). Patient/person-centred care considers "patients' individual needs and ensures that patients are active participants in all aspects of their health care decisions" (College of Nurses of Ontario [CNO], 2022, para. 2). Patient/person-centred medicine is founded on the principle of patient autonomy (Sacristán, 2013). The IOM (2001) describes patient-centred care as "providing care that is respectful of, and responsive to, individual patients' preferences, needs and values, and ensuring that patient values guide all clinical decisions" (p. 6). Epstein & Street (2011) described the philosophical grounds of patient-centred care as "an approach to care and perceived as the right thing to do" (p. 2). Patient/person-centred care is not limited solely to the patient, but also includes their families and caregivers (Santana et al., 2018). Patient/person-centred care may also be referred to as the "patient/person and family-centred care model." The Registered Nurses' Association of Ontario (RNAO, 2015) describes

"person and family-centred care," in which the "person" is inclusive of the individual and their family. The main difference between family-centred and patient-centred care is that in family-centred care, the family should be the centre and the unit of care (Coyne et al., 2018).

History of Family-Centred Care

FCC is believed by many healthcare providers as the best way to deliver care in hospitals and health services (Jolley & Shields, 2009). However, healthcare providers have faced many barriers and resistance to the implementation of FCC models (Kuo et al., 2012). Nevertheless, the implementation of FCC healthcare models became more predominant towards the end of the 20th century as research and advocacy in maternal-newborn attachment and health flourished (Jolley & Shields, 2009).

Dr. Stéphane Tarnier was an early leader in providing medical care for premature newborns (Dunn, 2002). In the late 1800s, Dr. Tarnier introduced the concept of thermoregulation and the incubator, which was revolutionary for the care of premature infants (Dunn, 2002). Dr. Martin Couney used the incubators to exhibit premature newborns across Europe and the United States at fairs and other events for profit (L.M Gartner & C Gartner, 1992). If the premature infants survived the travelling and were no longer eligible for exhibitions, they would be returned to their mothers (Maree & Downes, 2016). Unfortunately, it was challenging for parents to take over the responsibilities and care for their infants after hospital discharge (Maree & Downes, 2016; Silverman, 1979). It would be fair to hypothesize that it would be challenging for parents to care for their infant at home when they had not been involved in their infant's care during hospitalization. Therefore, it is with no surprise that infants were often brought back to the hospital for idiopathic failure to thrive (Duxbury & Adams, 1992). The first centre for premature newborns in the United States opened in Chicago in 1914,

although the first true Neonatal Intensive Care Unit (NICU) was not established until 1960 in the United States at the Yale New Haven Hospital (Gluck, 1992; L.M Gartner & C. Gartner, 1992). In Canada, the first NICU was established at Sick Kids Hospital in 1961 (C.N. Reese & J. Reese, 2018).

In the early 1900s, hospitals were portrayed as industrialized environments, remarkably evident in children's hospitals (Jolley & Shields, 2009). Between the 1920s and the end of World War II, nursing was depicted by Jolley & Shields (2009) as "the battle of science against infectious diseases and against cross-infection in hospitals" (p. 3). For this reason, parents were restricted from visiting their children due to the hospital staff's fear of spreading infections and causing outbreaks in pediatric hospitals (Jolley & Shields, 2009; Philip, 2005). Unfortunately, during this time, the hospital requirements were prioritized over the emotional needs of children and their families (Jolley & Shields, 2009). This type of institutionalized approach to care was not without consequences for hospitalized children. In Jolley's doctoral study, Jolley demonstrated striking evidence of the trauma that remains in adults from their experience being hospitalized during their childhood (less than 12 years old) in the UK between 1920-1970 (Jolley, 2004; Jolley & Shields, 2009). The individuals interviewed in Jolley's study described the hospital environment during their childhood as affectionless and scary and the staff as uncaring and nonhuman (Jolley, 2004).

Childbirth was also profoundly industrialized and medicalized at the start of the 20th century. In an attempt to support perinatal health outcomes during the early 1900s, birthing shifted away from families' homes into the hospital environment (Gooding et al., 2011). Phillips et al. (2003) describe this as a period in which "impersonal bureaucracy, efficiency, and medical professionalism dominated the hospital birth experience" (p. 8). By the 1940s, approximately

80% of women birthed their infants in hospitals (Phillips et al., 2003). In the first volume of the *American Journal of Obstetrics and Gynecology*, Dr. Lee wrote that childbirth was not a normal function (Phillips, 1999; Speert, 1980). In response, Dr. Lee encouraged the routine use of forceps, episiotomy and anesthesia to prevent complications due to what he described as a pathologic process and encouraged giving birth under general anesthesia (Phillips, 1999; Speert, 1980). After childbirth, newborns were customarily separated from their mothers and placed in a large nursery (Phillips et al., 1999). Newborns were brought to their mothers for 20-minute intervals every 3-4 hours for feedings, then swiftly returned to the nursery so the mother could rest (Phillips et al., 1999). Families were not allowed to visit their newborns in the nursery, as families were considered a source of infection, and fathers were excluded from care (Phillips et al., 1999).

Both premature and term infants had lower survival rates at the start of the 20th century compared to the present. At the start of the 20th century in Canada, the total number of infant deaths for children under the age of one was 187 deaths per 1,000 births, compared to 4.5/1000 live births in 2020 (O'Neill, 2022; Statistics Canada, 2022). Throughout the mid-20th century, physicians became increasingly interested in the care of premature infants, and more attempts were made to save these infants (Philip, 2005). However, there was no trace of FCC in nurseries for premature infants (Maree & Downes, 2016). Parents could only see their infants through a glass divider (Philip, 2005). Unfortunately, most premature infants in the nursery deceased within a few days after birth, and doctors often attributed parents to the cause of their newborn's death due to parents' "germs" (Maree & Downes, 2016).

The paradigm shift towards integrating FCC philosophies began to be more thoughtfully implemented after World War II. During this time, greater attention was placed on the effects of

child-parent separation caused by home evacuations and separations caused by the war (Burlingham & Freud, 1942; Jolley & Shields, 2009). John Bowlby and James Robertson's research on attachment and separation was vital in changing pediatric and maternal-newborn care (Alsop-Shields & Mohay, 2001; Jolley & Shields, 2009). Bowlby, a British psychiatrist, recognized that children may suffer "catastrophically" when they experience maternal deprivation (Bowlby et al., 1965). Bowlby identified that for children to grow up healthy, they must experience a "warm, intimate, and continuous relationship with his mother" (Bowlby, 1951, p. 13). In Robertson's research, Robertson found that even minor adverse events can be traumatic for children when they are separated from their families (Alsop-Shields & Mohay, 2001). John Kennell and Marshall Klaus developed the concept of "bonding," which was a driving force for the paradigm shift in healthcare (1998). Kennell & Klaus (1998) recognized that the period after birth is critical for bonding and therefore emphasized the need for close maternal-newborn contact during this time. Klaus et al. (1986) discovered reduced perinatal complications when birthing women have social support during their labour compared to mothers who did not receive support from a companion.

Moreover, research in the mid-to-late-1900s on the importance of maternal-newborn bonding and attachment led to more emphasis on keeping the dyad together. Attitudes were slowly changing during this time to include parents as essential team members in their infant's care (Philip, 2005). One of the first pieces of evidence of FCC in the NICU was identified in the mid-20th century. Dr. Edith Jackson introduced rooming-in (allowing mothers to stay with their newborns) in 1944 at the Yale Hospital (Gluck, 1992). Although the terms "kangaroo care" and "skin-to-skin" were not yet used, Dr. Edith Jackson began these practices by placing babies on their mothers' chests soon after birth (Gluck, 1992). Dr. Edith Jackson allowed parents to handle

their babies in the nursery in 1955, although it was against the law at this time (Gluck, 1992). Today, “care-by-parent rooms” are designated rooms within a hospital that allow parents to be with their children 24/7 and provide care. Care-by-parent rooms were first introduced in the United States in the 1960s and in Britain in 1980 (Clearly, 1992; Goodband & Jennings, 1992; Jolley & Shields, 2009). In Canada, evidence of “rooming in” occurred in 1971 in Winnipeg (Health Sciences Centre, Winnipeg; n.d.). When mothers were informed of the importance of newborn attachment, more mothers requested to room in with their infant (Phillips et al., 1999). The use of formula was a popular and well-known substitute for breastmilk (Stevens et al., 2009), and breastfeeding was on a steady decline until the 1970s (Fomon, 2001). Breastfeeding and providing human milk to infants began to be encouraged in the 1980s, as research identified the contribution of breastfeeding to bonding (Johnson, 2013; Maree & Downes, 2016).

Family advocates and family-centred health organizations also played a significant role in deinstitutionalizing hospitals and changing hospital care for children and families (Bergman & Singer, 1996; Kuo et al., 2012; Zwelling & Phillips, 2001). By 2003, the American Academy of Pediatrics had incorporated FCC into policy statements and affirmed that FCC is the standard of healthcare for all children (AAP, 2003).

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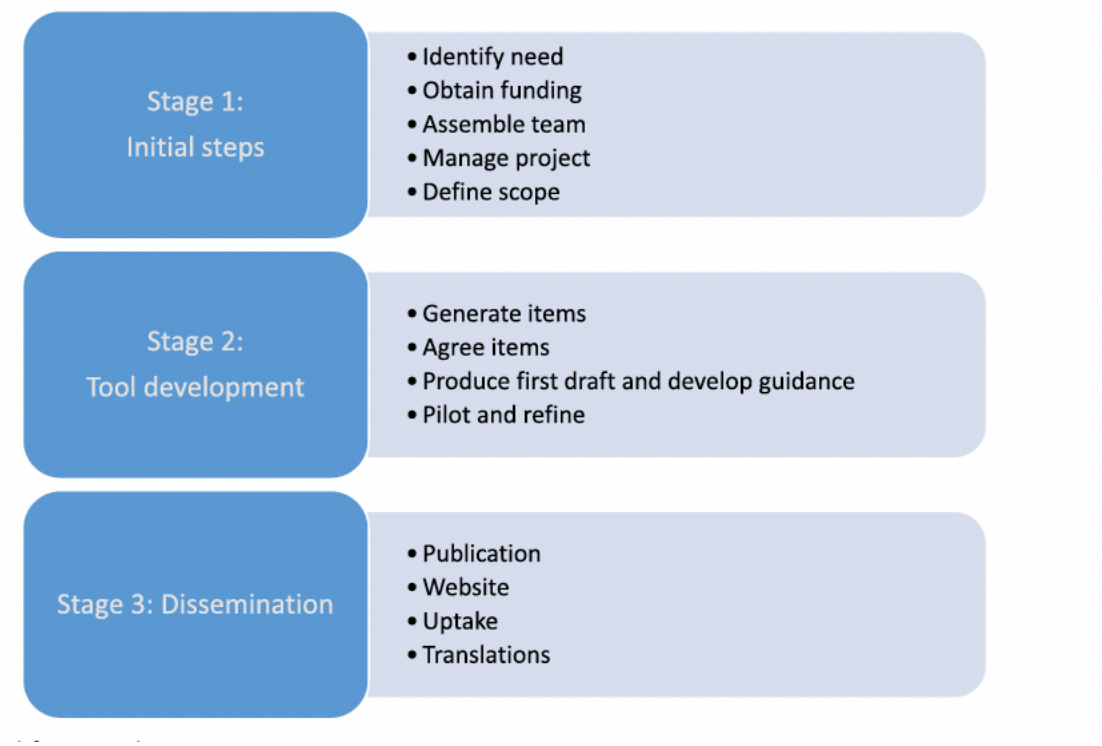
Appendix I

Whiting et al. (2017) Proposed Framework for Developing Quality Assessment Tools (Chapter 3)



Appendix J

Draft of the FCMNC-T (Chapter 3)

Family-Centered Maternal-Newborn Care: A Reporting Tool For Family-Centered Care Values in Maternal-Newborn Clinical Practice Guidelines

Instructions: Please rate each criteria item a score of **1** if there is outstanding evidence in the guideline to support the item, **0.5** if there is some evidence, and **0** if there is no evidence.

- There must be at least **one bolded example** identified in the guideline to receive a full score of **1.**
- You may choose to add your own examples. Please indicate the rationale for each item score.
- Add all scores together for a final score out of 8.

Dignity and Respect			
Criteria Item	**PHAC Principle**	**Examples**	**Score**
2. Pregnancy and birth are normalized.	*Pregnancy and birth are normal, healthy processes (principle 2).*	• **Key words such as "healthy," "normal," and/or "empowerment" are used to discuss pregnancy, birth and the postnatal transition period.** • **Parents/caregivers are viewed as essential primary caregivers.** • **Skin to skin and/or breastfeeding are encouraged.** • Medical interventions should only be used when necessary. • Least invasive/interventions with the least risk are recommended first (e.g., non-pharmacological interventions). • Explains the reasons for any tests/procedures/therapies. • Is clear on who required specific tests/procedures/therapy (e.g., not all babies require [specific intervention]).	
3. Inclusive and equitable healthcare for families is a priority.	*Culturally-appropriate care is important in a multicultural society (principle 8).*	• **Guideline includes recommendations that are consistent with the equity, diversity and inclusion principles.** • **The words "respect" and/or "dignity" are used.**	

	Indigenous peoples have distinctive needs during pregnancy and birth (principle 9). *The attitudes and language of health care providers have an impact on a family's experience of care (principle* 14). *Family-centered maternal and newborn care respects reproductive rights (principle 15).*	• **Traditional practices, ceremonies, and rituals are encouraged and welcomed.** • Recommendations include the ability to provide culturally safe care that is acceptable to Indigenous individuals and congruent with their needs. • Guideline promotes strategies that address health disparities. • Professional translation services are recommended. • Language of guideline and recommendations are inclusive for LGBTQ2S+ individuals. For example, guideline uses appropriate language of inclusion for all family members (e.g., wording such as "partner, caregiver" etc.). • Guideline suggests strategies to eliminate barriers in the healthcare system; recognizes the stigma and attitudes of health care workers as barriers. • Reproductive information is offered to families (when applicable). Families' reproductive rights and decisions are respected.	
Information Sharing			
4. Families receive information that is evidence based.	*Family-centered maternal and newborn care is informed by research evidence (principle 5).* *Family-centered maternal newborn care best practices from global settings may offer valuable options for Canadian consideration (principle 17).*	• **Recommendations are supported by up-to-date research from high grade evidence when possible, and referenced appropriately.** • Development and attachment theories are referenced (e.g., Erikson's Stages of Development). • References to family-centered care are evidence-based. • There is evidence and best practices from global settings.	
5. Families receive timely and complete information allowing for an open conversation with healthcare providers.	*Women and their families require knowledge about their care (principle 12).*	• **Families receive all information about diagnosis and treatment options.** • **Families receive explanation on the benefits and risks for interventions.**	

		• **The importance of communication with families/updating/keeping families informed is recognized.** • **Communication with families is encouraged.** • Recommendations suggest when to call families and/or how to communicate sensitive information. • Guideline includes strategies on how to communicate information in a timely and effective way to support informed decision making. • Health literacy of family is considered and information is presented through various means (pamphlets, audio, presentations). • Decision support is offered to families. • Guideline has strategies on how to support making an informed decision (e.g. decision aids).	
Participation			
6. Families are encouraged to participate in decision making and in care in all settings.	*A family-centered approach to maternal and newborn care is optimal (principle 1).* *Family-centered maternal and newborn care applies to all care environments (principle 4).* *Women and their families play an integral role in decision making (principle 13).*	• **Guideline uses "family-centered," "family-centered care," and/or "team" in vocabulary.** • **Guideline states that family-centered care should be provided.** • **Parents/caregivers are actively involved in decision making.** • **Parents/caregivers are encouraged to voice their preferences and wishes.** • **Goals and priorities are decided in collaboration with family.** • **Recommendations include the participation of caregivers in all aspects of care** (e.g., mother to hold baby while newborn blood work is being performed). • Guideline states that family is an important part of the mother-newborn dyad. • Recommendations that support family centered care in various environments (e.g., Labor and Delivery, Postpartum, NICU/SCN, Pediatrics). For example, skin to skin is supported in NICU/SCN.	

7. Families are kept together.	*Early parent-infant attachment is critical for newborn and child development and the growth of healthy families (principle 3).* *Care as close to home as possible is ideal (principle 10).*	• **Guideline uses language such as "attachment" and "bonding" or highlights the importance of parent-infant attachment.** • **24/7 rooming in is recommended/no parental separation during hospitalization.** • Guideline consists of recommendations that: 1) screens for healthy attachment, 2) educates families of healthy attachment, 3) identifies barriers in attachment (e.g., PPD), and 4) interventions to support healthy attachment. • Family strengths are assessed and should be utilized • Recommendations include parents to participate in the care of their infant in the NICU/SCN. • Recommendations support for services close to home/at home. • Recommendations are provided that may reduce separation from home/families (e.g., virtual appointments).	
Collaboration			
8. All aspects of a families' potential needs are addressed.	*Family-centered maternal and newborn care requires a holistic approach (principle 6).* *Family-centered newborn care involves collaboration among care providers (principle 7).* *Individualized maternal and newborn care is recommended (principle 11).*	• **Most, if not all aspects of care are addressed for the patient/family (e.g., physical, spiritual, emotional needs).** • **Guideline discusses various health care providers such as midwives, physicians, nurses, lactation consultants, social service providers (e.g. social workers, family therapists), and allied health professionals (e.g. respiratory therapists, pharmacists, audiologists) that can be involved in care.** • **Guideline recognizes the uniqueness of every individual and their needs.** • Healthcare team makes effort to maintain routines and preferences in hospital. • Guideline indicates when referrals are recommended.	

		• Families collaborate with interdisciplinary team in regards to continuity of care (e.g., transfers, discharge planning, community supports).	
9. Families are viewed as an important part of an interdisciplinary team and have valuable feedback.	*Family-centered maternal and newborn care functions within a system that requires ongoing evaluation (principle 16).*	• **The guideline has been evaluated by a family or patient advisory committee.** • All health care providers introduce themselves and their role. • Families are encouraged to provide their feedback on their experiences for quality improvement. Families are encouraged to participate in research. • Patient and family perspectives have been integrated into the development of guideline recommendations.	

Final Score: /8

Appendix K

Guideline Scores from FCMNC-T Pilot (Chapter 3)

Guideline 1					
		Content Score		Endorsement Score	
FCC Pillar	Criteria Item	CF	MB	CF	MB
Dignity and Respect	1	0.5	1	0	0
	2	1	1	0	0
Evidence Based Practice & Information Sharing	3	1	1	0	0
	4	0.5	0	0	0
Participation	5	0.5	0	0	0
	6	0.5	1	0	0
Collaboration	7	0.5	0	0	0
	8	1	0	0	0
Total Score:		5.5	4/8	0/8	0/8

Guideline 2					
		Content Score		Endorsement Score	
FCC Pillar	Criteria Item	CF	MB	CF	MB
Dignity and Respect	1	1	1	0	0
	2	0	0.5	0	0
Evidence Based Practice & Information Sharing	3	0.5	1	0	0
	4	1	1	1	0
Participation	5	1	0.5	1	0
	6	1	0.5	0	1
Collaboration	7	0	1	0	0
	8	0	0	0	0
Total Score:		4.5/8	5.5/8	2/8	1/8

Guideline 3					
		Content Score		Endorsement Score	
FCC Pillar	Criteria Item	CF	MB	CF	MB
Dignity and Respect	1	1	1	0	0
	2	0	0	0	0
Evidence Based Practice & Information Sharing	3	0	0	0	0
	4	0	0	0	0
Participation	5	0.5	1	0	0
	6	0.5	0.5	1	1
Collaboration	7	0	0.5	0	0
	8	0	0	0	0
Total Score:		2/8	3/8	1/8	1/8

Guideline 4					
		Content Score		Endorsement Score	
FCC Pillar	Criteria Item	CF	MB	CF	MB
Dignity and Respect	1	1	1	0	0
	2	0.5	0.5	0	0
Evidence Based Practice & Information Sharing	3	1	1	0	0
	4	0.5	1	0	0
Participation	5	1	1	0	1
	6	0.5	1	0	0
Collaboration	7	1	1	0	0
	8	1	1	0	0
Total Score:		6.5/8	7.5	0/8	1/8

Guideline 5					
		Content Score		Endorsement Score	
FCC Pillar	Criteria Item	CF	MB	CF	MB
Dignity and Respect	1	1	1	0	0
	2	0	0	0	0
Evidence Based Practice & Information Sharing	3	1	1	0	0
	4	0	0	1	0
Participation	5	1	1	0	0
	6	0	0.5	0	0
Collaboration	7	1	1	0	0
	8	0	0	0	0
Total Score:		4/8	4.5/8	1/8	0/8

Guideline 6					
		Content Score		Endorsement Score	
FCC Pillar	Criteria Item	CF	MB	CF	MB
Dignity and Respect	1	1	1	0	0
	2	0	0.5	0	0
Evidence Based Practice & Information Sharing	3	0.5	1	0	0
	4	0	0	0	0
Participation	5	0	1	0	0
	6	1	1	1	0
Collaboration	7	0.5	1	0	0
	8	0	0	0	0
Total Score:		3/8	5.5/8	1/8	0/8

Guideline 7					
		Content Score		Endorsement Score	
FCC Pillar	Criteria Item	CF	MB	CF	MB
Dignity and Respect	1	1	1	0	0
	2	0	0	0	0
Evidence Based Practice & Information Sharing	3	0.5	1	0	0
	4	0.5	1	0	0
Participation	5	1	1	0	0
	6	0.5	0.5	0	0
Collaboration	7	0.5	1	0	0
	8	0	0	0	0
Total Score:		4/8	5.5/8	0/8	0/8

Guideline 8					
		Content Score		Endorsement Score	
FCC Pillar	Criteria Item	CF	MB	CF	MB
Dignity and Respect	1	1	1	0	0
	2	1	1	1	1
Evidence Based Practice & Information Sharing	3	1	1	0	0
	4	1	1	1	0
Participation	5	1	1	1	1
	6	1	1	1	1
Collaboration	7	1	1	1	0
	8	0.5	0	0	0
Total Score:		7.5/8	7/8	5/8	3/8

Guideline 9					
		Content Score		Endorsement Score	
FCC Pillar	Criteria Item	CF	MB	CF	MB
Dignity and Respect	1	1	1	0	0
	2	0.5	0.5	0	0
Evidence Based Practice & Information Sharing	3	0.5	1	0	0
	4	1	1	0	0
Participation	5	1	1	1	1
	6	1	1	1	0
Collaboration	7	0.5	1	0	0
	8	0	0	0	0
Total Score:		5.5/8	6.5/8	2/8	1/8

Guideline 10					
		Content Score		Endorsement Score	
FCC Pillar	Criteria Item	CF	MB	CF	MB
Dignity and Respect	1	1	1	0	0
	2	1	1	0	0
Evidence Based Practice & Information Sharing	3	1	1	0	0
	4	0.5	1	0	0
Participation	5	1	1	1	0
	6	1	1	0	0
Collaboration	7	0.5	1	0	0
	8	0	0	0	0
Total Score:		6/8	7/8	1/8	0/8

Guideline 11					
		Content Score		Endorsement Score	
FCC Pillar	Criteria Item	CF	MB	CF	MB
Dignity and Respect	1	1	1	0	0
	2	1	1	1	1
Evidence Based Practice & Information Sharing	3	1	1	0	0
	4	0	1	0	0
Participation	5	1	0.5	0	0
	6	0.5	1	0	0
Collaboration	7	0.5	1	0	0
	8	0	0	0	0
Total Score:		5/8	6.5/8	1/8	1/8