ATHABASCA UNIVERSITY

# DEXTROSE GEL FOR THE TREATMENT OF NEONATAL HYPOGLYCEMIA: A RAPID REVIEW

BY

HEATHER KENNEDY

A THESIS

SUBMITTED TO THE FACULTY OF GRADUATE STUDIES

IN PARTIAL FULLFILMENT OF THE REQUIREMENTS FOR THE DEGREE OF

MASTER OF HEALTH STUDIES

FACULTY OF HEALTH DISCIPLINES

ATHABASCA, ALBERTA

NOVEMBER, 2024

Athabasca University
Faculty of Graduate Studies

**Approval of Thesis**

The undersigned certify that they have read the thesis entitled

**DEXTROSE GEL FOR THE TREATMENT OF NEONATAL HYPOGLYCEMIA: A RAPID REVIEW**

Submitted by

**Heather Kennedy**

In partial fulfillment of the requirements for the degree of

**Master of Health Studies**

The thesis examination committee certifies that the thesis
and the oral examination is approved

**Supervisors:**
Dr. Debbie Fraser
Athabasca University

Dr. Gina Martin
Athabasca University

**External Examiner:**
Dr. Michelle Butt
Athabasca University

November 1, 2024

1 University Drive, Athabasca, AB, T9S 3A3 Canada
Toll-free (CAN/U.S.) 1.800.788.9041 ex. 6821
fgs@athabascau.ca | fgs.athabascau.ca | athabascau.ca

**Abstract**

Neonatal hypoglycemia (NH) is a common issue for newborns that can lead to brain damage or death if not promptly treated. NH can often be treated with feeding-based methods such as breastfeeding or formula supplementation, however, if this is not successful, the newborn must be separated from their family and admitted to a neonatal intensive care unit (NICU) for intravenous (IV) dextrose therapy. Oral dextrose gel is an alternate treatment to IV dextrose therapy that may help to prevent NICU admissions and is currently being used in many hospitals, however, the evidence from existing systematic reviews to support this therapy is mixed. Using a rapid review, literature published since 2021 was examined to assess the efficacy of dextrose gel and to create updated recommendations for practice. Data from nine eligible studies were synthesized narratively. The majority of the included studies found data that supports the use of dextrose gel in newborns, with six studies (three of high-quality evidence, one moderate-quality, two low-quality) demonstrating a significant decrease in NICU admissions and/or IV dextrose use. One of the studies showed no significant differences (low-quality evidence) and two were deemed to be inconclusive (both low-quality evidence). The implementation of a dextrose gel treatment protocol in hospitals that have not already done so may help to prevent NICU admissions for NH and keep more newborns in the care of their families on postpartum wards.

*Keywords:* Hypoglycemia, hypoglycaemia, newborn, neonatal, infant, dextrose gel, glucose gel, NICU, neonatal intensive care unit

## Table of Contents

## List of Tables

## List of Figures and Illustrations

## Chapter 1. Introduction

NH is the most common metabolic disorder in newborns, affecting an estimated 15% of infants within hours after birth (Hegarty et al., 2017). Without adequate treatment, NH can result in brain damage or death (Hegarty et al., 2017), particularly when experienced for a prolonged period (Narvey & Marks, 2019). Therefore, infants at risk of developing NH should have timely glucose screening after birth and appropriate treatment if necessary (Edwards & Harding, 2021). NH can often be treated using feeding-based methods such as breastfeeding or supplementary formula, however, in severe or prolonged cases, infants are admitted to NICU for close monitoring and nasogastric tube feeding or intravenous (IV) dextrose infusion to regulate blood glucose levels (Narvey & Marks, 2019). An IV dextrose infusion delivers sugar directly to the bloodstream, treating NH by raising the blood glucose levels of the newborn (Narvey & Marks, 2019). IV infusions in newborns must be monitored by nursing staff with specialized training beyond standard postpartum care, therefore it is necessary in most hospitals for newborns receiving IV treatment to be admitted to a NICU.

NICU admission results in separation of the infant from their family, which can disrupt bonding and negatively impact the infant's psychological and physical development as well as contribute to higher rates of depression and anxiety in parents (Hames, 2020). Separation of infants from their families due to NICU admission and treatments for NH can also delay the establishment of breastfeeding and impact exclusive breastfeeding rates (Harris, 2013). Breastfeeding opportunities while the infant is in NICU care may be limited due to the physical separation of mother and baby receiving care in different units, or may be discouraged during glucose stabilization with IV dextrose therapy to avoid stimulation of insulin release (Alsaleem, 2019). In addition, treatment of NH in the NICU involves frequent heel pokes for blood glucose

testing and, often, insertion of an IV (Narvey & Marks, 2019), which can cause pain and stress in the infant.

Due to the increase in prevalence of certain risk factors for NH in Canada such as gestational diabetes and small for gestational age births (El Adam et al., 2022; Feig et al., 2014; Government of Canada, 2016), the incidence of NH is thought to be increasing. Thus, there is a need to explore treatment options for NH that can be administered outside of the NICU environment to help prevent the negative repercussions of NH and preserve the bonding experience and psychological health of the infant and their family. There is also a need to address other impacts that a potential rise in NICU admissions could cause, such as the financial strain this may have on a hospital if more babies were to require a higher level of care (Hegarty et al., 2017; Rios et al., 2021).

Dextrose gel is a treatment used for NH in some institutions that can be administered to the newborn's oral mucosa in a standard newborn care setting, potentially preventing the need for NICU admission (Harris, 2013). Systematic reviews of randomized controlled trials (RCTs) and cohort studies that have been conducted to assess the efficacy of dextrose gel for NH in term and near-term newborns have had mixed results, with one review (Edwards et al., 2022) concluding that dextrose gel is probably an effective treatment for NH, another review (Wang et al., 2023) concluding that dextrose gel may not be effective in reducing the incidence of NH, and a third review (Roberts et al., 2023) concluding that dextrose gel reduces the risk of NH but does not reduce the risk of NICU admission or the need for IV dextrose treatment. Thus, there may be hesitancy from stakeholders and policymakers when considering this treatment for implementation in hospitals. There also has been recent literature published on the use of dextrose gel in newborns that has not yet been included in a review, as previous systematic

reviews included studies published up until 2020. The purpose of this rapid review is to explore the recent literature published on the use of dextrose gel in treating NH in term and near-term (≥ 35 weeks gestation) infants and synthesize the findings, with the goal of building on the existing literature to provide recommendations for practice.

**Context and Motivation**

As a nurse in the Women's and Infants' Program at. Joseph's Healthcare Hamilton, a hospital in Hamilton, Ontario, Canada, I have witnessed the impact that NH can have on newborns and their families. Staff within this program perceive NH as being a very prevalent issue, reporting a high workload and staffing pressures due to many babies requiring screening and treatment for NH. Babies at risk for NH must have blood samples checked multiple times, which involves a painful poke on their heel with a lancet. If hypoglycemia occurs and persists despite treatment with breastfeeding and/or bottle feeding, the baby must leave their mother's room and they are brought to the NICU, where they receive either feedings via a nasogastric tube or IV dextrose treatment as per the decision of the pediatrician. This process is often quite emotional for the parents, who may be worried that their baby is feeling pain during these procedures or concerned about their baby's health status. Additionally, no longer having the newborn in their room to care for and bond with in the first hours after birth can be very distressing. The initial interest in this issue as a thesis topic was inspired by the concerns of the staff and families at St. Joseph's and the desire to explore possible interventions to address the rate of NICU admissions for NH in this population. Dextrose gel is not currently being used at St. Joseph's as an intervention for NH and could potentially be introduced. The results of the review study undertaken in this thesis could help to assist policymakers and clinicians at St.

Joseph's in deciding if dextrose gel should be a treatment option to be implemented in the newborn population.

## Chapter 2. Background

### Neonatal Hypoglycemia

At birth, the placental supply of glucose to the neonate is stopped abruptly, resulting in a physiologic decrease in blood glucose levels within the first hours of life during the transition to the extrauterine environment (Chen et al., 2022). Most healthy newborns can regulate their blood glucose quickly after birth; however, certain infants have an increased risk of more severe or prolonged hypoglycemia during this transitional period (Chen et al., 2022). A lack of glucose available for consumption by the brain caused by hypoglycemia can lead to adverse neurodevelopmental outcomes (Narvey & Marks, 2019). In a study by Wickström et al. (2018), 101,060 infants born in Sweden between 2008 and 2012, otherwise healthy infants who had a diagnosis of NH (defined in this study as at least one blood sugar level of less than 2.2 mmol/L) during their stay in the postnatal ward were compared to babies who had been euglycemic during this period. During a follow-up in 2014, when participants were two to six years old, babies who had NH were found to have higher rates of adverse neurodevelopmental outcomes when compared to euglycemic babies, with more than double the adjusted risk of developmental delay (OR 2.53, 95% CI 1.71-3.73). These results highlight the importance of proper identification and screening of babies at risk for NH and prompt and effective treatment if NH is to occur.

Common symptoms of NH include tremors, lethargy, convulsions, apneic spells, tachypnea, and difficulty feeding; however, many newborns remain asymptomatic despite markedly low blood sugar levels (Narvey & Marks, 2019). Asymptomatic infants with risk factors for NH should have their blood glucose levels tested regularly during the first hours after birth as per institutional protocols (Narvey & Marks, 2019). The primary approach to NH treatment involves increasing energy intake either orally or intravenously to raise blood glucose

levels (Narvey & Marks, 2019). Asymptomatic NH may be managed initially with feeding-based treatment methods such as breastfeeding or formula supplementation before advancing to treatment via IV dextrose infusion for more severe or prolonged cases (Narvey & Marks, 2019). Most hospitals require that the newborn be transferred from the postpartum ward with their mother to a NICU or special care nursery for IV administration. This separation may disrupt bonding and the establishment of breastfeeding, causing stress on the newborn and family, as well as incurring additional costs on the healthcare system (Hegardy et al., 2017).

***Prevalence***

Differences in screening protocols and definitions make the prevalence of NH difficult to estimate. The threshold for NH treatment according to the Canadian Paediatric Society is < 2.6 mmol/L for the first 72 hours of life (Narvey & Marks, 2019), whereas the American Academy of Pediatrics' (AAP) standard is < 2.2 mmol/L within the first 4 hours of life and 2.5 mmol/L between 4-24 hours of life (Adamkin, 2017). The Pediatric Endocrine Society's definition is more conservative at ≤ 2.8 mmol/L for the first 48 hours of life (Thornton et al., 2015). Glucose testing is not routinely performed on all babies within a population, as it is only indicated in babies at risk for NH, so the true prevalence rate among the newborn population is not well established. Estimates of the incidence of NH among all newborns range from 5-15% (Edwards & Harding, 2021), however, this estimate may have to be updated to reflect the increasing prevalence of certain risk factors for NH. For example, the rate of gestational diabetes in Canada is rising, with a 33.6% increase between 2004/2005 and 2010/2011 (Government of Canada, 2016). Feig et al. (2014) found that the rate of gestational diabetes doubled in Ontario women between 1996 (2.7%) and 2010 (5.6%). The rate of small for gestational age births is also

increasing in Canada (El Adam et al., 2022), which could impact the prevalence of NH.

### *Risk Factors*

Infants that are preterm, have intrauterine growth restriction, or are small for gestational age have reduced amounts of adipose tissue and glycogen stores, potentially impairing the production of glucose via gluconeogenesis and affecting an infant's ability to self-regulate their blood glucose levels (Abramowski et al., 2022). Infants of diabetic mothers and those who are large for gestational age experience prolonged elevations of maternal glucose concentrations while in utero, resulting in increased fetal insulin production (Abramowski et al., 2022). These elevated insulin levels persist after birth and can result in severe or prolonged NH (Abramowski et al., 2022). Other risk factors for NH include cold stress (Laptook & Jackson, 2006), medications taken during pregnancy such as beta-blockers or steroids (Abramowski et al., 2022; Narvey & Marks, 2019), perinatal asphyxia (Narvey & Marks, 2019), other perinatal stress such as preeclampsia/eclampsia and sepsis (Abramowski et al., 2022), and certain congenital and metabolic disorders (Abramowski et al., 2022; Narvey & Marks, 2019). Maternal obesity may be associated with an increased risk of NH, as it is plausible that obesity may lead to subclinical insulin resistance and predispose the infant to NH (Turner et al., 2019). Maternal obesity also increases the likelihood of gestational diabetes and having a macrosomic infant (Neumann et al., 2017). Birth by caesarean section may also increase the risk of NH, as it is associated with delayed lactogenesis, delayed skin-to-skin contact, and impaired thermoregulation (Turner et al., 2019). Also, not all C-section deliveries coincide with labour, which is thought to be associated with a lower risk of NH as the newborn has time to undergo hormonal transition prior to birth (Turner et al., 2019). When determining if a newborn is at risk for NH, the full maternal history,

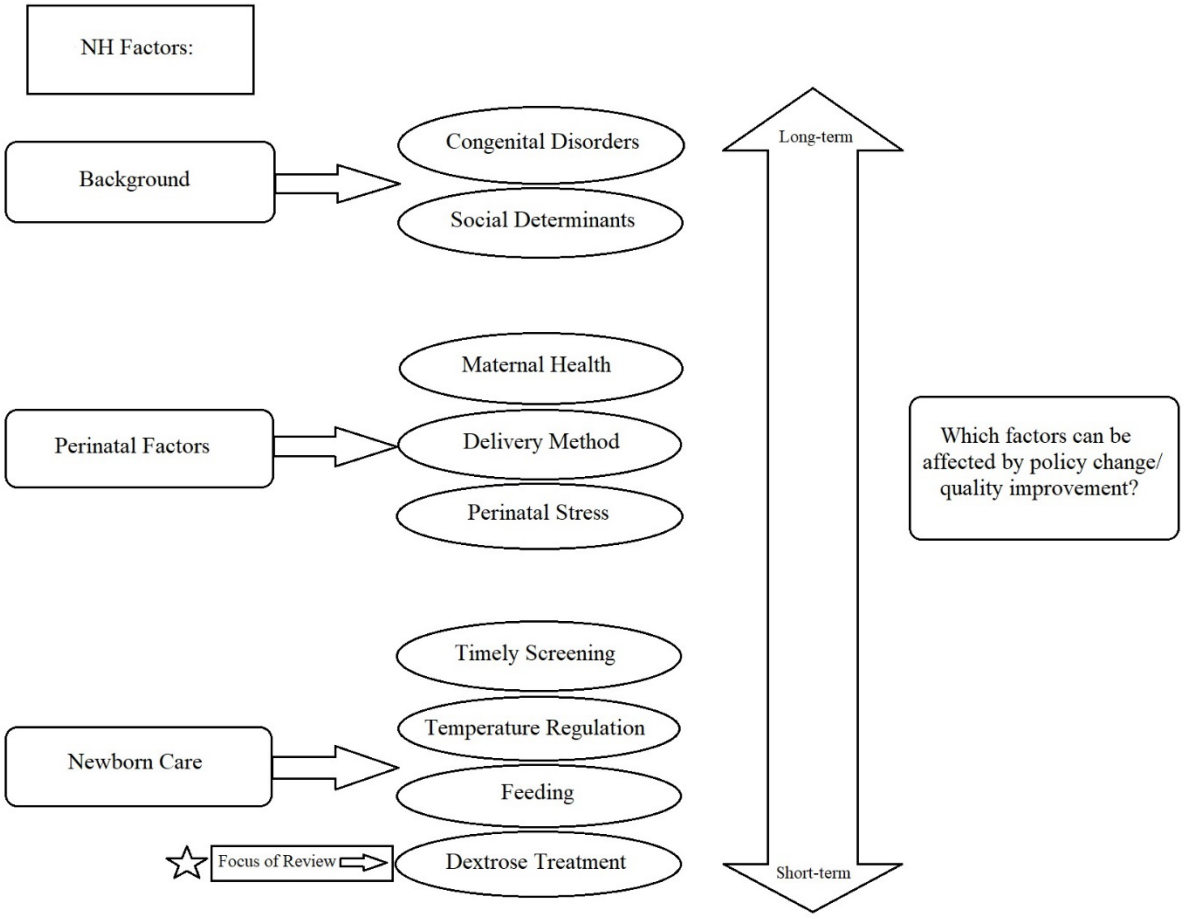
birth history, and the newborn's weight and clinical status should be carefully considered.

### *Conceptual Framework: Factors Contributing to Neonatal Hypoglycemia*

There are many factors throughout the pregnancy, birth, and care of the newborn that can contribute to the development of NH. Due to the possible increase in prevalence of NH in Canada and the negative repercussions that this could have on the newborn population and their families, research efforts targeting both prevention and treatment of NH are valuable. Factors contributing to NH can be divided into the following categories: background, perinatal factors, and newborn care (see Figure 1). Background factors such as social determinants of health are present before pregnancy begins and would require long-term policy changes to address. Perinatal factors are those present during pregnancy and birth, such as maternal health and diet, perinatal stress, and method of delivery. Interventions to target these factors could include maternal education throughout pregnancy to promote health and prevent cases of gestational diabetes and gestational hypertension. Lastly, interventions during newborn care to prevent and manage NH include regulating the newborn's temperature, early skin-to-skin contact and breastfeeding, timely screening for NH beginning within 2 hours after birth, and prompt and appropriate management of NH through supplementation with expressed breast milk or formula, dextrose gel, or IV dextrose administration if needed. This review will focus on intervention targeting the newborn care portion of this framework, specifically, the administration of dextrose gel to treat NH.

***Figure 1***

*Conceptual Framework: Factors Contributing to Neonatal Hypoglycemia*




***Dextrose Gel***

Factors related to management of NH after birth can be addressed through more short-term policy changes, such as incorporating the use of oral dextrose gel into a treatment algorithm for newborns. Forty percent dextrose gel is a simple carbohydrate in concentrated thickened aqueous solution, which can be administered directly to the oral mucosa (Harris et al., 2013). When administered to the buccal cavity, the area between the gums and cheek, the drug is absorbed via the lingual vein and directly enters the systemic circulation, bypassing the first pass

effect of the hepatic portal system that occurs during oral-gastrointestinal administration (Edwards & Harding, 2021). Therefore, dextrose gel can potentially act faster than carbohydrates taken orally and is commonly used to treat hypoglycemia in adults (De Buck et al., 2019). Dextrose gel is readily available in many hospital pharmacies, inexpensive and easy to administer (Harris et al., 2013), making it a possible alternative treatment to the more-invasive IV dextrose for treatment of asymptomatic NH. In addition, it can be administered to newborns without admission to NICU, potentially allowing more newborns to stay together with their families during treatment for hypoglycemia (Harris et al., 2013).

The first RCT on the use of dextrose gel in treating NH was conducted by Troughton et al. (2000) in Northern Ireland. They used a small sample size of 75 babies, who were assigned to receive either 400 mg/kg of dextrose gel plus a feeding for treatment group babies or a feeding alone for control group babies. This study found no significant difference in blood glucose levels between the two groups at 15 minutes and 30 minutes post treatment. This study is referenced in much of the literature on dextrose gel, however, it is not available to read online. The authors' contact information is also not available and thus the text was not able to be reviewed.

In 2013, Harris et al. published the now well-known Sugar Babies study, a double-blind RCT with a sample size of 242 babies that was conducted in New Zealand. Babies were randomized and treated for hypoglycemia with either dextrose gel or a similar-looking placebo gel massaged into their gums and then were encouraged to feed. Treatment failure was defined as a blood glucose level of less than 2.6 after two consecutive doses. They found that treatment failure was significantly ($p = 0.04$) less likely in the dextrose gel group, with 16 (14%) babies failing treatment in the treatment group versus 29 (24%) in the control group. Additionally, 16 babies (14%) in the dextrose gel group were admitted to NICU for hypoglycemia versus 30

(25%) in the control group. The authors also noted that the treatment was inexpensive, easy to apply, and was found to be acceptable by the majority of the mothers of babies in the study.

Rather than using dextrose gel to treat NH once it occurs, an alternate method used in several studies is the prophylactic administration of dextrose gel to all at-risk babies to help prevent NH before it arises. Hegarty et al. (2016) sought to find the most effective dextrose gel dosing regimen for preventing NH when administered after birth to all at-risk newborns within a group. Using a sample size of 416 babies, they randomly assigned participants into one of four dextrose gel treatment groups: 200 mg/kg at one hour after birth, 400 mg/kg at one hour after birth, one 200 mg/kg dose at one hour of life and then a 200 mg/kg dose before the next three feeds, one 400 mg/kg dose at one hour after birth and then three 200 mg/kg before the next three feeds, or to one of four corresponding control groups where babies received an identical-appearing placebo gel. They found that babies who received any dose of dextrose gel were less likely to develop hypoglycemia than those who received placebo gel (RR 0.79, 95% CI 0.64–0.98, $p = 0.03$), and were less likely to be admitted to NICU for hypoglycemia (RR 0.46, 95% CI 0.21– 1.01, $p = 0.05$); however, overall rates of NICU admission for all reasons were similar between groups. The authors selected a single dose of 200 mg/kg dextrose gel as the ideal dosing regimen, due to both its efficacy and its tolerance by participants. They found that larger and more frequent doses were more likely to spill from the baby's mouth and took more time to administer.

Harding et al. (2021) continued to test the efficacy of prophylactic dextrose gel in preventing NH and NICU admissions, using the work by Hegarty et al. (2016) to inform their dosing regimen of a single dose of 200 mg/kg gel. They conducted an RCT in 18 New Zealand and Australian maternity hospitals from 2015 to 2019. A total of 2,149 babies at risk for

hypoglycemia without other indications for NICU care were given either a single dose of dextrose gel or placebo gel at 1 hour of age. The results showed that babies in the dextrose gel group were significantly less likely to develop hypoglycemia (37% vs. 42%, $p = 0.02$), but were not significantly less likely to be admitted to the NICU. They also found that 21 babies needed to be treated with dextrose gel to prevent one case of hypoglycemia. Since the dose of dextrose gel was administered at 1 hour of age, it appears that it may have helped prevent some of the transient cases of hypoglycemia that occur soon after birth, but it was not effective in preventing the more persistent cases of hypoglycemia that result in NICU admissions later on. The mean age of babies admitted to NICU for NH was 11 hours, suggesting that a single dose of dextrose gel at 2 hours of age is not sufficient to maintain blood glucose levels for long enough to prevent NICU admissions.

### *Systematic Reviews on Dextrose Gel for Neonatal Hypoglycemia*

Given the increasingly widespread use of dextrose gel in the neonatal population, there have been at least three systematic reviews published that examine the use of dextrose gel in preventing and treating NH. A systematic review by Edwards et al. (2022) of RCTs compared the use of dextrose gel in treating NH versus a control group. These authors limited their inclusion criteria to RCTs, therefore there were only two studies published prior to 2022 available for analysis. Specifically, only the two studies discussed earlier by Troughton et al. (2000) and Harris et al. (2013) were included in the review. Due to the small sample size used in the Troughton et al. study, most of the data in the meta-analysis comes from the Harris et al. study. Only the study by Harris et al. (2013) included data on the separation of the infant from the mother for hypoglycemia treatment as an outcome, which favored the use of dextrose gel over placebo with a 0.54 risk ratio (95% CI 0.31, 0.93). When looking at receipt of IV treatment

for NH as an outcome, the two studies showed conflicting results, with a 1.33 risk ratio (CI 95% 0.65, 2.74) for the Troughton et al. (2000) study and 0.47 risk ratio (CI 95% 0.21, 1.06) for the Harris et al. (2013) study, with combined results of 0.78 (CI 95% 0.46, 1.32). While the authors cautioned that the evidence in this review was "very uncertain", they concluded that dextrose gel is probably a safe and effective first-line treatment for infants with NH in high-income settings due to the populations included in the studies. In addition, certain factors contributing to NH such as rates of gestational diabetes may have changed since these studies were published in 2000 and 2013 respectively, and thus there is a need for an updated review that captures studies published since their search in October 2021.

A second systematic review by Wang et al. (2023) explored the efficacy of dextrose gel in preventing NH. This review included RCTs, quasi-experimental studies, and cohort studies published up until December 2020. They included 10 studies in their meta-analysis with a combined total of 4801 newborn participants. Although the authors stated that their goal was to determine whether dextrose gel can prevent NH, only two of the included studies used a dextrose gel dose as prophylaxis and the remaining eight studies used dextrose gel as a treatment. Thus, there was some heterogeneity in the interventions used in the included studies. Additionally, one of the studies (Coors et al., 2018) used a 77% dextrose gel instead of the standard 40% used in neonatal populations, which the authors noted may have caused a hyperinsulinemic response to the increased carbohydrate concentration and affected NH rates. Only two of the studies included data on the efficacy of dextrose gel in preventing IV dextrose use, which were the same two studies used in the meta-analysis by Edwards et al. (2022) (Troughton et al., 2000 & Harris et al., 2013). The meta-analysis by Wang et al. was consistent with the work by Edwards et al. and found that dextrose gel did not contribute to a statistically significant difference in the need for

IV dextrose treatment. Seven of the included studies (Harris et al., 2013, Hegarty et al., 2016, Ter et al., 2017, Scheans et al., 2017, Coors et al., 2018, Makker et al., 2018, & Stanzo et al., 2020) looked at the efficacy of dextrose gel in preventing NICU admissions for NH. Wang and colleagues found that the combined results through meta-analysis showed no statistically significant difference in NICU admission rates between dextrose gel and control groups. However, on inspection of their findings, it was noted that there is a potential error in their analysis. A study by Makker et al. (2018) looked at the rates of NICU admission before and after implementation of a dextrose gel protocol in a hospital, assigning year 1 as the control group (pre-implementation) and year 2 as the treatment group (post-implementation), however, Wang and colleagues have assigned year 1 as the treatment group and year 2 as the control. Thus, they found that the relative risk of NICU admission for the treatment versus control group was 2.21 (95% CI 1.20, 4.05), with the data from the groups appearing to be reversed. The authors were contacted via email to discuss this possible error and no response was received. When looking at the data from the study in question directly, Makker et al. found that NICU admissions for hypoglycemia decreased from 8.1% in the pre-dextrose gel implementation period to 3.7% in the post-implementation period *(p* = 0.01).

A third systematic review was conducted by Roberts et al. (2023), examining the efficacy of prophylactic dextrose gel in preventing NH. They included only RCTs and quasi-RCTs in their analysis. The authors did not include studies that used dextrose as a treatment to reverse NH. Two studies, by Hegarty et al. (2016) and Harding et al. (2021), met their inclusion criteria and were used in their analysis. Meta-analysis of the two studies found that prophylactic dextrose gel does reduce the risk of NH (defined as blood glucose < 2.6 mmol/L) when compared to placebo gel, but that it probably does not reduce the rate of NICU admission for NH and

probably does not reduce the rate of IV dextrose administration. Most of the data used in the meta-analysis comes from the Harding et al. (2021) study, as it had a much larger sample size than the Hegarty et al. (2016) study (n = 416 vs. n = 2,149). Thus, most of these participants only received one dose of dextrose gel. As stated earlier, it appears that one prophylactic dose of dextrose gel given soon after birth can help prevent some transient cases of NH that would have resolved on their own with time, but it is not effective for the more persistent cases of NH that result in NICU admissions.

It is difficult to compare the results of the reviews due to the differences in study interventions used (see Table 1). A one-time prophylactic dose of dextrose gel should be considered a distinct intervention from multiple doses administered throughout the hospital stay to reverse NH as needed, as the physiology of the newborn during the initial transition to extrauterine life versus several hours later may differ (Chen et al., 2022). Edwards et al. looked at studies using dextrose gel as a treatment for NH, Roberts et al. looked at studies using it as prophylaxis, and Wang et al. looked at a combination of the two. There was not a high degree of certainty about the results found in any of the three reviews and none of the authors were able to make strong recommendations for practice. Edwards et al. concluded that dextrose gel treatment for NH is probably effective, Wang et al. concluded that it may not be effective in preventing NH, and Roberts et al. concluded that it is probably effective in reducing the risk of NH but probably not effective in reducing the rates of NICU admission or IV dextrose treatment. These statements may leave practitioners and policymakers looking to these three reviews for guidance with feelings of uncertainty about the efficacy of NH and whether it should be used in newborns. For example, Edwards et al. and Wang et al. included two of the same studies (Troughton et al., 2000 & Harris et al., 2013) on the use of dextrose gel as treatment for NH in their analyses and

came to opposite conclusions about its efficacy. A goal of this rapid review is to provide more clarity on the efficacy of dextrose gel treatment in reducing the rates of NICU admission and IV dextrose treatment for NH.

Due to the limited amount of data available from RCTs in the review by Edwards et al., the potential error in the review by Wang et al. that could impact their conclusions, and the inconsistent conclusions between the reviews, there is a need for further review of the recent literature on the evidence surrounding the use of dextrose gel in treating NH. This may help to assist policymakers and clinicians in their decision-making regarding the use of dextrose gel in newborns. Also, there has been no review that includes more recently published studies on dextrose gel used as treatment rather than prophylaxis, as the reviews by Edwards et al. and Wang et al. included treatment-based studies published up until 2013 and 2020, respectively. Accordingly, the objective of this rapid review is to assess the efficacy of dextrose gel in *treating* NH in term and near-term (≥ 35 weeks gestation) newborns, and its impact on the rates of NICU admission and IV dextrose administration for NH. Specifically, this review will provide an update to the literature on dextrose gel for treatment of NH and will include studies that were published worldwide from 2021 onward and were not included in the previous systematic reviews.

**Table 1**

*Comparison of Systematic Reviews*

| Author | Research Questions | Types of Studies | Number of studies | Analysis Methods |
|---|---|---|---|---|
| Edwards et al. (2022) | Can dextrose gel correct NH and reduce long-term neurodevelopment impairment? | RCTs, quasi-RCTs | 2 | Fixed-effect meta-analysis |
| Wang et. al (2023) | Can dextrose gel prevent NH? | RCTs, quasi-RCTs, cohort studies | 10 | Fixed-effect & random-effect meta-analysis |
| Roberts et al. (2023) | Can dextrose gel safely prevent NH and reduce long-term neurodevelopment impairment? | RCTs, quasi-RCTs | 2 | Fixed-effect meta-analysis |

**Table 1 (continued)**

*Comparison of Systematic Reviews*

| Author | Strengths and Limitations | Key Conclusions |
|---|---|---|
| Edwards et al. (2022) | Strengths: Rigorous search and data analysis methods<br>Limitations: Authors graded the certainty of evidence as moderate to very low, one study had an unclear to high risk of bias, small sample size | Dextrose gel is probably an effective and safe first-line treatment for infants with NH in high-income settings and may result in a slight reduction in the risk of major neurological disability at 4.5 years of age |
| Wang et al. (2023) | Strengths: Large sample size and number of studies<br>Limitations: Heterogeneity in intervention methods, possible flaws in data analysis | Preventative dextrose gel may not be effective in reducing the incidence of NH |
| Roberts et al. (2023) | Strengths: Rigorous search and data analysis methods, large sample size<br>Limitations: Authors were not confident in the evidence due to only including two studies | Prophylactic dextrose gel reduces the risk of NH, probably does not reduce the risk of NICU admission or IV dextrose treatment for NH |

# Chapter 3. Methods

## Objectives

Dextrose gel is possibly an effective treatment for NH, however, the results of previous systematic reviews are mixed and there is a need for an updated review. There is a specific need to clarify the efficacy of dextrose gel as a treatment versus prophylaxis and to consider types of studies other than RCTs due to the existing gaps in the literature. The purpose of this rapid review is to explore the recent literature published on the use of dextrose gel in treating NH in term and near-term infants and synthesize the findings, with the goal of building on the current literature to provide clearer recommendations for practice.

Research Objective:

To determine the efficacy of oral dextrose gel in treating NH in term and near-term (≥ 35 weeks gestation) infants when compared to feeding-based treatment methods alone.

Research Questions:

1. Does the use of oral dextrose gel for treatment of NH affect the rates of NICU admission in term and near-term infants?
2. Does the use of oral dextrose gel for treatment of NH affect the rates of IV dextrose use in term and near-term infants?

The population chosen for this review is newborns born at ≥ 35 weeks gestation. Many institutions automatically admit babies born at less than 35 weeks gestation to NICU, therefore there is less of a need to investigate strategies to decrease NICU admission rates in the premature population. The two treatment outcomes being used to assess the efficacy of dextrose gel are NICU admission and IV dextrose treatment. If a newborn who receives dextrose gel requires NICU admission or IV dextrose treatment for NH, this indicates that dextrose gel was not effective in treating NH for that particular participant.

## A Rapid Review Approach

A rapid review is a form of knowledge synthesis that provides timely information to decision-makers by simplifying the evidence synthesis process (Tricco et al., 2022). Compared to a traditional systematic review, rapid reviews can be completed in a much shorter timeframe, making them favorable when decision-makers need access to evidence to inform policy development or planning when time constraints are present (Tricco et al., 2022). Full scale systematic reviews require a team of researchers and can take up to 18 months to complete (Simon Fraser University, 2023). In contrast, a rapid review can be completed by an individual researcher and can be completed in under six months (Simon Fraser University, 2023). Rapid reviews have similar characteristics to systematic reviews, including a clearly defined objective and eligibility criteria for studies, a systematic search that seeks to find all eligible studies available, an assessment of the validity of the studies, and a synthesis of the findings in the included studies; however, some steps may be adapted or omitted (James Cook University Library, 2024). Another type of review is a scoping review, which aims to address an exploratory research question, map key concepts, and identify gaps in research (James Cook University Library, 2024). Scoping reviews involve more broad research questions than systematic or rapid reviews and do not involve critical appraisal of literature (James Cook University Library, 2024).

Out of the options of a systematic review, rapid review, and scoping review, a rapid review was chosen for this study because there is a specific research question to be answered and evidence is needed within a limited time frame. With the rates of NH in Canada potentially on the rise, given the increase in known risk factors, and the need for a timely update to existing evidence to inform decision-making, conducting a rapid review on the use of dextrose gel for NH treatment is an appropriate methodology to use. In addition, this approach is feasible within the

scope of a Master's thesis as the student is the sole screener of the literature. In order to build on previous reviews rather than replace existing data, the review will only include studies that were published after the Wang et al. (2023) review search in 2021 and therefore not included in the previous analyses. Critical analysis of the most up-to-date data published worldwide from 2021 onwards will help to inform policymaking decisions regarding the use of dextrose gel and its potential impact on NICU admission rates. Details of the protocol on this rapid review were registered on PROSPERO under ID number 545880 and can be accessed at: https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=545880

## Search Approach

### *Inclusion Criteria*

All types of studies evaluating the efficacy of dextrose gel in treating newborns with NH versus standard feeding-based methods were considered for inclusion. This could include RCTs, quasi-RCTs, or cohort studies. Included studies must involve term and near-term (≥ 35 weeks gestation) newborns with NH as their study population and include NICU admission and/or IV dextrose therapy as treatment outcomes. Only studies published in English from 2021 onwards were considered.

### *Exclusion Criteria*

Studies using prophylactic dextrose gel were excluded, as this review is focusing on dextrose gel as a treatment. Studies without full texts available were excluded. Systematic reviews were excluded.

### *Search Strategy*

The search was done with assistance from a librarian at the University of Manitoba, who helped to determine the search terms used, ran the search on the databases, and imported the

search results into Covidence. The search was conducted on 06 March 2024 using Medline, Embase, Cumulated Index in Nursing and Allied Health Literature (CINAHL), & Cochrane Central databases, which were selected as they focus on health care evidence. The search was limited to studies published in English from 01 January 2021 to current date. Table 2 shows an example of the search terms used for the Medline database. See Appendix for a full list of search terms to be used in each database.

**Table 2**

*List of Medline Database Search Terms*

| Search Number | Search Terms |
|---|---|
| 1 | exp infant, newborn/ or nurseries, infant/ or nurseries, hospital/ or infant care/ or rooming-in care/ or infant health/ or intensive care, neonatal/ or neonatal nursing/ or nurses, neonatal/ or neonatology/ or neonatologists/ |
| 2 | (baby* or babies or infan* or neonat* or newborn* or new born* or late preterm* or nurser*).ti,ab,kf. |
| 3 | 1 or 2 |
| 4 | exp hypoglycemia/ |
| 5 | (hypoglyc* or hypo glyc* or hyperinsulin* or hyper insulin* or glycopeni*).ti,ab,kf. |
| 6 | ((low* or reduc*) adj2 (blood sugar* or blood glucose*)).ti,ab,kf. |
| 7 | or/4-6 |

| | |
|---|---|
| 8 | (glucogel or glucagon or dextrogel or dex4 or Glutose or Hypostop or InstaGlucose or insta glucose or rapilose or sweet cheek*).ti,ab,kf. |
| 9 | exp glucose/ and (gels/ or administration, oral/ or administration, buccal/ or administration, sublingual/) |
| 10 | (glucose or dextrose).ti,ab,kf. |
| 11 | (gels or gel or jelly or jellies or sublingual* or lingual* or buccal* or oral* or mouth* or gum or gums or gingiva* or cheek* or tongue*).ti,ab,kf. |
| 12 | 10 and 11 |
| 13 | 8 or 9 or 12 |
| 14 | 3 and 7 and 13 |
| 15 | limit 14 to (english language and yr="2021 -Current") |

***Data Extraction***

The following data was extracted and organized in Covidence for each study: author(s), year of publication, country in which the study was conducted, the aim of the study, study design, start and end dates, study funding sources, possible conflicts of interest, population description, inclusion/exclusion criteria, number of participants, intervention descriptions, and results. The characteristics of each study was organized into a table, which includes the author, date of publication, country, type of study, study population, and number of participants. A table with a summary of strengths, limitations, and quality ratings was also constructed.

***Critical Appraisal***

Studies included in the review were each assessed using Critical Appraisal Skills Programme (CASP) checklists, which can be accessed on their website (CASP, 2024). Using a CASP checklist can help to assess if a study is valid, if it is methodologically sound, and if it is at risk of bias (CASP, 2024). Other commonly used critical appraisal tools include JBI's critical appraisal checklists (JBI, 2020), which are similar to the CASP checklists and ask a lot of the same questions. The CASP checklists were ultimately chosen for critical appraisal as they are the tools recommended by McMaster University's Rapid Review Guidebook (Dobbins, 2017) for appraising single studies. There are different CASP checklists available for each type of study (RCT, cohort, etc.), and the appropriate tool was used for each individual study.

***Analysis***

The results of each study were synthesized narratively, with commentary on the overall impressions of the findings. Narrative synthesis was chosen over meta-analysis, as the studies included in the review were conducted in different hospitals with slight variations in study procedures and cut-off values for blood glucose levels. Rather than combine these diverse studies with a meta-analysis, the differences were acknowledged and analyzed through discussion and comparison. Studies rated as low-quality through the CASP assessment process were not removed from the analysis, as discussion of these studies and identification of which procedures used were effective or ineffective may still help to add insight into the development of a clinical algorithm for dextrose gel in a postpartum ward.

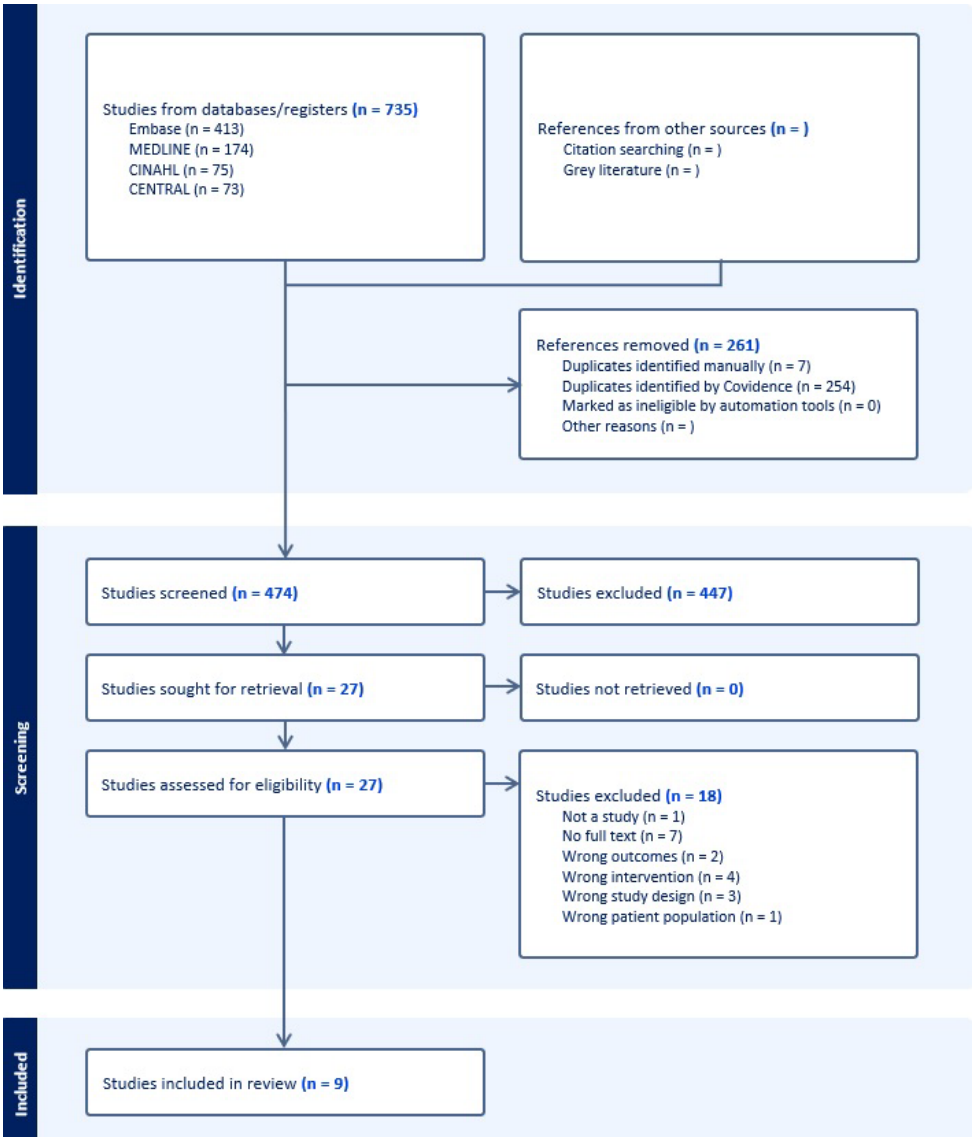
# Chapter 4. Results

## Screening

The search yielded 735 studies that were imported into Covidence, with 261 studies identified as duplicates, leaving 474 studies to be screened. First, the titles of these 474 studies were screened for relevance, paying close attention to the topics and the study populations used. Studies not related to the use of dextrose gel in newborns were excluded. From there, the abstracts were reviewed and studies were screened further for topics related to the treatment of NH with dextrose gel. There were 27 studies found to be relevant and the full texts were reviewed. Of these 27 studies, 18 were excluded after reviewing full texts:

- Seven were conference abstracts with no full-text versions available
- Three were the previous systematic reviews
- One was the study by Harding (2021) on prophylactic dextrose gel
- One study was a secondary analysis of the Harding (2021) study
- One study was a quality improvement project that implemented several interventions at once
- One study was a quality improvement project with the goal of increasing the use of dextrose gel
- One study included only premature (< 34 weeks) babies
- One study looked at length of stay as the primary outcome and had no full text available
- One study implemented a guideline that did not include dextrose gel as one of the new interventions
- One article was a commentary

***Figure 2:*** **Search results**




## Included Studies

Nine studies were eligible and were included in the review. One was an RCT and eight were cohort studies comparing groups before and after implementation of dextrose gel treatment.

**Table 3**

*Characteristics of Studies Included in the Rapid Review*

| Author | Year | Country | Type of study | Study Population | *N* |
|---|---|---|---|---|---|
| Deyo-Svendsen | 2021 | USA | Cohort | Newborns screened for NH[1] | 230 |
| Gibson | 2021 | USA | Cohort | Newborns ≥ 36 weeks with NH | 64 |
| Meneghin | 2021 | Italy | Cohort | Newborns ≥ 35 weeks with NH | 69 |
| Washer | 2021 | USA | Cohort | Newborns ≥ 35 weeks with NH | 188[2] |
| Desai | 2022 | USA | Cohort | Newborns ≥ 35 weeks & ≥ 2kg with NH | 1329 |
| Gupta | 2022 | India | RCT | Newborns ≥ 35 weeks with NH | 291 |
| Plummer | 2022 | USA | Cohort | Newborns ≥ 36 weeks screened for NH | 4666 |
| Parappil | 2023 | Qatar | Cohort | Newborns ≥ 35 weeks with NH | 3584 |
| Walravens | 2023 | USA | Cohort | Newborns ≥ 35 weeks screened for NH | 4299 |

[1]Gestational age not specified, however, this is a level 1 nursery that cares for babies ≥ 35 weeks gestation

[2]Number of participants in treatment group only. Number of controls not reported

**Table 4**

*Key Results of Studies Included in the Rapid Review*

| Author | NICU Admission Rate | | | IV Dextrose Rate | | |
|---|---|---|---|---|---|---|
| | Control | Dextrose Gel | *p*-value | Control | Dextrose Gel | *p*-value |
| Deyo-Svendsen | 7/122 (2.25%)[1] | 0/108 (0%) | 0.029 | - | - | - |
| Gibson | 4/29 (13.8%) | 4/35 (11.4%) | 0.534 | 3/29 (10.3%) | 4/35 (11.4%) | 0.607 |
| Meneghin | 19/39 (48.7%) | 3/30 (10%) | 0.001 | 14/39 (35.9%) | 3/30 (10%) | 0.01 |
| Washer | 54 admissions | 25 admissions | - | - | - | - |
| Desai | 153/548 (27.9%) | 126/781(16.1%) | < 0.001 | 60/548 (10.9%) | 51/781 (6.5%) | 0.004 |
| Gupta | - | - | - | 58/140 (41.4%) | 17/147 (11.5%) | < 0.001 |
| Plummer | - | - | - | 2.5%[2] | 1.0% | < 0.001 |
| Parappil | 396/1801 (22%) | 329/1783 (18.5%) | 0.008 | 277/1801 (15.4%) | 182/1783 (10.2%) | < 0.001 |
| Walravens | - | - | - | 77/1596 (4.8%) | 110/2703 (4.1%) | 0.242[3] |

[1] NICU admissions and IV dextrose use were combined into one value in this study

[2] Percentages reported only

[3] After a special cause shift, dextrose gel rate decreased to 3.5% and *p*-value is 0.05

**Table 5**

*Quality Assessment of Included Studies*

| Author | Strengths | Limitations | Quality Rating |
|---|---|---|---|
| Deyo-Svendsen | | Retrospective data, small sample size, very imprecise odds ratio | Low |
| Gibson | Study addressed a poignant and clearly focused issue | Retrospective data, very small sample size, baseline differences between groups | Low |
| Meneghin | Study addressed a poignant and clearly focused issue | Retrospective data, very small sample size, baseline differences between groups | Low |
| Washer | Very detailed implementation procedures | Retrospective data, small sample size, number of participants not specified | Low |
| Desai | Large sample size, multivariate analysis performed | Retrospective data, difference in NH protocol between groups apart from gel | Moderate |
| Gupta | RCT, both groups treated the same apart from intervention | Inability to do blinding | High |

**Table 5 (continued)**

*Quality Assessment of Included Studies*

| Author | Strengths | Limitations | Quality Rating |
|---|---|---|---|
| Plummer | Large sample size, regression analysis performed | Retrospective data | High |
| Parappil | Large sample size, regression analysis performed | Retrospective data, difference in NH threshold between groups | High |
| Walravens | Large sample size | Retrospective data, baseline differences between groups, changes in procedures throughout study | Low |

## Quality Assessment

See the appendix for the CASP checklists completed for each study. After completion of the CASP checklists and careful consideration of each assessment point, the nine reviewed studies were assigned a quality rating of "high", "moderate", or "low". In order to assign a quality rating to a study, the strengths and limitations of each study were weighed subjectively. If a study was methodologically strong overall but may have had minor limitations that did not appear to affect the results, it was given a "high" quality rating. If a study was strong but had more considerable limitations, it was given a "moderate" rating. If a study had major limitations, had a large possible source of bias, or did not make a valuable contribution to the literature, it was assigned a "low" rating. Three studies (Gupta, 2022; Parappil, 2023; & Plummer, 2022) were rated as "high", one (Desai, 2022) was rated as "moderate", and five (Deyo-Svendsen, 2021; Gibson, 2021; Meneghin, 2021; Washer, 2021; & Walravens, 2023) were rated as "low". A summary of strengths, limitations, and ratings can be seen in Table 5.

## Study Characteristics

Of the nine included studies, six were conducted in the United States, one in India, one in Italy, and one in Qatar. Eight were cohort studies comparing data from a pre-gel implementation period where breast- and/or formula-feeding was the first-line treatment for NH to a post-implementation period where dextrose gel was used in combination with feeding methods. One study was an RCT that compared breastfeeding and dextrose gel treatment to breastfeeding alone. All of the studies included NICU admission and/or IV dextrose treatment as an outcome of interest.

## Synthesis

1. *Does the use of oral dextrose gel for treatment of NH affect the rates of NICU admission in term and near-term infants?*

There is evidence that the use of oral dextrose gel for treatment of NH decreases the rate of NICU admission in term and near-term infants. Of the nine studies included in the review, six examined NICU admissions as an outcome of interest. Four of these studies (one high-quality, one moderate-quality, two low-quality [Desai et al., 2022; Deyo-Svendsen et al., 2021; Meneghin et al., 2021; & Parappil et al., 2023]) found a significant decrease in NICU admission rates between the dextrose gel group and control group. In the study by Desai et al. (2022), the authors noted a decrease in NICU admission rates from 27.9% to 16.1% ($p < 0.001$) after implementation of dextrose gel treatment among a sample size of 1,329 babies (moderate-quality evidence). Deyo-Svendsen et al. (2021) found a decrease in NICU admission/IV dextrose treatment rates (combined as one value) from 2.25% to 0% ($p = 0.029$) among a sample size of 230 babies (low-quality evidence). In the study by Meneghin et al. (2021), there was a decrease in NICU admission rates from 48.7% to 10% ($p = 0.001$), however, this was among a very small sample size of 69 participants and the study was rated as low-quality evidence. Parappil et al. (2023) found a decrease in NICU admission rates from 22% to 18.5% ($p = 0.008$) among a sample size of 3,584 babies.

A study by Gibson et al. (2021) found no significant difference between groups, with NICU admission rates of 13.8% and 11.4% before and after implementation of dextrose gel treatment, respectively ($p = 0.534$). However, this study used a very small sample size of 64 babies and was assigned a low-quality assessment rating. Gibson et al. (2021) and Meneghin et al (2021) used very similar sample sizes and study protocols and found very different results, illustrating the possible limitations that can arise with small study populations. Additionally,

Gibson et al. (2021) changed their blood glucose treatment threshold from 40 mg/dL (2.0 mmol/L) in the control group to 50 mg/dL (2.8 mmol/L) in the dextrose gel group, creating a more conservative treatment protocol and making it harder for the newborns to avoid NICU admissions, which may have affected results.

In study by Washer et al. (2021), the number of NICU admissions for NH was tracked for a year before and after the implementation of a dextrose gel treatment protocol. The authors found that the number of NICU admissions for NH within a year decreased from 54 to 25, however, the total number of newborns screened in the control group year is not included and thus the NICU admission rate is unknown. The lead author was contacted for more information, and they confirmed that this number was not known. Due to this uncertainty, the effects of the dextrose gel treatment in this study will be treated as anecdotal evidence and the results as inconclusive.

In summary, four of the studies examined in this review found a significant decrease in NICU admission rates when dextrose gel was used for treatment of NH, one study found no significant difference in NICU admission rates, and one study was deemed to be inconclusive. All of the treatment groups in these studies followed an algorithm where blood glucose was drawn at certain times after birth, and a weight-based dose of 0.5 mL/kg of dextrose gel was administered with the infant's feeding if certain criteria were met. Desai et al. (2022) also tested a standard dosing regimen of 2 mL of dextrose gel and found that it appeared to be safe and effective (moderate-quality evidence). A similar algorithm was followed by the control group with timed blood glucose checks and feeding times without the administration of dextrose gel. If the blood glucose fell below a certain level, defined as per institutional protocols, the algorithm was stopped, and the newborn was admitted to the NICU. The implementation of a treatment

algorithm for NH that includes oral dextrose gel appears to reduce the rate of NICU admissions in term and near-term infants, however, not all evidence supporting this is from high-quality sources.

2. *Does the use of oral dextrose gel for treatment of NH affect the rates of IV dextrose use in term and near-term infants?*

There is evidence that the use of oral dextrose gel for treatment of NH decreases the rate of IV dextrose use for treatment of NH in term and near-term infants. Of the nine studies included in the review, eight examined IV dextrose use as an outcome of interest. Six of these studies (three high-quality, one moderate-quality, two low-quality [Desai et al., 2022; Deyo-Svendsen et al., 2021; Gupta et al., 2022; Meneghin et al., 2021; Parappil et al., 2023; & Plummer et al., 2022]) found a significant decrease in IV dextrose use rates between the dextrose gel group and control group. Desai et al. (2022) found a decrease in IV dextrose treatment rates from 10.9% to 6.5% ($p = 0.004$) after implementation of dextrose gel treatment among a sample size of 1,329 babies (moderate-quality evidence). As mentioned in the previous section, Deyo-Svendsen et al. (2021) noted a decrease in NICU admission/IV dextrose treatment rates (the outcome used was either NICU admission or IV dextrose treatment, combined as one value) in their study from 2.25% to 0% ($p = 0.029$). In a study by Gupta et al. (2022), 291 infants who developed NH were randomized to receive treatment with either dextrose gel plus breastfeeding or breastfeeding alone (control). The rate of IV dextrose treatment was 41.4% in the control group versus 11.5% in the dextrose gel group ($p < 0.001$) (high-quality evidence). Meneghin et al. (2021) found a decrease in IV dextrose treatment rates from 35.9% to 10% ($p = 0.01$) (low-quality evidence). Parappil et al. (2023) found that the rate of IV dextrose treatment decreased from 15.4% to 10.2% ($p < 0.001$) (high-quality evidence). In a study by Plummer et al. (2022),

the authors noted a decrease in IV dextrose treatment rates from 2.5% to 1.0% ($p < 0.001$) with dextrose gel treatment among a large study population of 4,666 babies (high-quality evidence).

The study by Gibson et al. (2021) also found no significant difference between the dextrose gel and control groups in the rates of IV dextrose treatment for NH, with a slight but non-significant increase from 10.3% to 11.4% ($p = 0.607$) after dextrose gel implementation. As noted earlier, the change to a more conservative treatment cut-off for blood glucose values in the NH algorithm for the dextrose gel group (2.8 mmol/L versus 2.0 mmol/L in the control group) may have explained this slight increase in the necessity of IV dextrose.

A study by Walravens et al. (2023) was deemed to be inconclusive, as results were initially statistically insignificant and then became significant after the study protocol was changed. Authors found a decrease in the rate of IV dextrose treatment for NH from 4.8% to 4.1% ($p = 0.242$) after implementation of dextrose gel treatment among a sample size of 4,299 babies, however, after making some changes to the feeding protocol and providing additional education to staff, the IV dextrose rate dropped to 3.5% ($p = 0.05$). Due to the changes made partway through the study and the ambiguity of the results, this study was assigned a "low" quality assessment rating. The authors also noted that they were unsure if the decrease in IV dextrose could be attributed to the dextrose gel or possibly due to the others changes that were made.

In summary, data from six of the studies examined in this review, including three high-quality studies, one moderate-quality study, and two low-quality studies, showed a significant decrease in the need for IV dextrose when dextrose gel was used as a first-line treatment of NH. One study found no significant difference in IV dextrose rates, and one study was deemed to be inconclusive. As with standard practice in most North American hospitals (Adamkin, 2017;

Narvey & Marks, 2019), formula supplementation was used when NH was not managed with breastfeeding alone in most of the included studies. One exception is the study by Gupta (2022), conducted in India, where exclusive breastfeeding was practiced in the first two days of life as per hospital policy and no formula was given to treat NH. This may explain why the baseline rates of IV dextrose treatment for NH were markedly higher than in other studies and why the dextrose gel had such a dramatic effect, as exclusively breastfed infants may have lower blood glucose levels in the first hours after birth than formula-fed babies (Rozance & Hay Jr., 2010). In the study protocol by Gupta et al. (2022), dextrose gel was used more as an alternate treatment to formula supplementation, whereas in the other studies reviewed dextrose gel was used in combination with breastfeeding and formula treatment to manage NH. In the study by Parappil et al. (2023), which, like the study by Gupta et al., had a large study population and was assigned a "high" quality appraisal score, a more modest decrease in IV dextrose treatment rates was seen. Should dextrose gel treatment be implemented in a North American hospital where formula supplementation is standard policy, a more modest decrease like this may be likely. A decrease in the IV dextrose treatment rate from 15.4% to 10.2%, however, was still clinically significant and resulted in the prevention of a painful IV insertion for many babies.

To revisit the overall research objective of this rapid review, oral dextrose gel appears to be effective in treating NH in term and near-term infants when compared to feeding-based treatment methods alone. Using NICU admission rates and IV dextrose treatment rates as measures of efficacy, dextrose gel was shown to be effective in a clinically significant degree in six of the nine studies included in the review. Additionally, two of the nine studies demonstrated results in favor of the use of dextrose gel but were deemed to be inconclusive due to

methodological issues. One study showed no significant difference in outcomes for newborns with NH with the use of dextrose gel.

**Limitations of Included Studies**

Many of the studies included in the review were limited by overall quality of evidence assigned, with three rated as high-quality evidence, one rated as moderate-quality, and five rated as low-quality. Some studies were limited by the small sample sizes used. Meneghin et al. (2021) and Gibson et al. (2021) used a sample size of only 69 and 64 newborns, respectively, which may have limited the accuracy of the results. Although Deyo-Svendsen et al. (2021) used a slightly larger sample of 230 newborns, the rate of NICU admission/IV dextrose use in their population was already very low, with only seven newborns requiring these interventions in their control group. Thus, the reduction in these interventions from 2.25% to 0% was a reduction from seven babies to none.

Although the study by Desai et al. (2022) used a large sample size and was otherwise methodologically strong, the decision to change the criteria for NICU admission from three glucose values less than 40 mg/dL (< 2.2 mmol/L) in the control group to two glucose values less than 40 mg/dL in the dextrose gel group created a difference between the groups apart from the intervention. However, this protocol led to more conservative treatment in the dextrose gel group and thus the positive effects of dextrose gel may have appeared to be even larger without this change. Similarly, in the study by Gibson et al. (2021) the threshold for treatment was changed from 40 mg/dL (2.2 mmol/L) in the control group to 50 mg/dL (2.8 mmol/L) in the dextrose gel group, and in the study by Parappil et al. (2023) it was changed from 2.6 mmol/L to 2.8 mmol/L. Parappil et al. (2023) noted that only seven babies in the dextrose gel group were affected by this difference and it did not affect the overall results.

Some studies had other baseline differences between groups that may have affected the results, for example, in the study by Meneghin et al. (2021) there were significantly more premature babies in the control group versus the dextrose gel group and this was not considered during analysis. In the study by Walravens et al. (2023), there was a large difference in the rate of NH between groups (41% vs. 34.4%) despite the robust sample size ($n = 4299$), however, the authors did adjust the results to account for the difference.

## Chapter 5. Policy and Practice Recommendations

From the results of the rapid review, recommendations can be made for policymakers who wish to implement the use of dextrose gel for the treatment of NH at a hospital. These recommendations were developed by considering the steps in treatment protocol that were found to be effective in the reviewed studies, with emphasis on methods found in studies with higher quality ratings.

1. If the newborn experiences asymptomatic NH with blood glucose levels within a range that may be treatable by feeding (1.4-2.5 mmol/L or as defined by the institution), administer dextrose gel prior to a feeding through the following steps:
    a) Dry the newborn's mouth with gauze to promote buccal absorption (based on one high-quality study and one low-quality study [Deyo-Svendsen et al., 2021; Plummer et al. 2022]).
    b) Administer 0.5 mL/kg of 40% dextrose gel via syringe into the buccal cavity (three high-quality studies and two low-quality studies [Deyo-Svendsen et al., 2021; Gupta et al., 2022; Meneghin et al., 2021; Parappil et al., 2023; & Plummer et al., 2022]).
    c) Massage gel into the gums with a gloved finger (one high-quality study and one low-quality study [Deyo-Svendsen et al., 2021; Plummer et al. 2022]).
2. If the newborn shows symptoms of NH or their blood glucose level drops to 1.3 mmol/L or lower (or as defined by institutional protocol), abandon the dextrose gel protocol and admit the newborn to the NICU for IV dextrose treatment (two high-quality studies [Gupta et al., 2022; Parappil et al., 2023]).
3. In an attempt to treat NH, dextrose gel may be administered:

a) Up to two consecutive times (one high-quality and one moderate-quality study [Gupta et al., 2022; Meneghin et al., 2021]).
b) Up to six doses within 48 hours (two high-quality and one moderate-quality study [Gupta et al., 2022; Meneghin et al., 2021; & Plummer et al., 2022]). If euglycemia is not achieved within these limits, the newborn should be admitted to the NICU for further treatment.
c) Newborns who require NICU admission for NH should receive a dose of dextrose gel while waiting for transfer or if IV access is not readily available (one high-quality study [Parappil et al., 2023]).

Recommendations on the steps of the implementation process of dextrose gel in a newborn unit were suggested in two low-quality studies (Washer et al., 2021; Walravens et al., 2023), which are summarized here:

1. Prior to the implementation of a dextrose gel protocol for NH, representatives from all relevant disciplines (pediatrics, neonatology, nursing, management, pharmacy, etc.) should meet to create a task force and discuss topics such as current knowledge gaps on dextrose gel, decisions about the specifics of the protocol as per recommendations from the literature and expert opinions, and to determine the steps that will be taken towards implementation.
2. The task force should work together to create a dextrose gel order set and to determine the specific product that will be dispensed and how it will be drawn up for administration. The gel may either be squeezed into a cup and drawn up into a syringe by the nurse before administration, or premeasured syringes may be used that can be directly applied to the baby's mouth.

3. Staff education on dextrose gel and the changes that will be occurring to practice must be provided to the interprofessional team. A short educational session with a discussion, or a slideshow presentation viewed at the participant's own pace are suggested ideas for presenting the information. Additionally, posters hung on the unit for staff to reference and for parents to read could help to reinforce this education and disperse the information.
4. After the initial implementation of a new protocol, it is important to check in with staff, review what they feel is effective and what is not, and make changes as necessary to improve practice and ensure that important factors are not being overlooked.

## Chapter 6. Discussion

With the inclusion of all types of studies published since 2021 evaluating dextrose gel as a treatment for NH, this review has provided an updated look at the evidence since the previous three rapid reviews were published and may help to provide clearer recommendations for practice. When deciding to begin the implementation of a dextrose gel protocol for newborns in a hospital, clinicians should consider the information presented in both this review and previous reviews in order to make a broadly informed decision.

With the rates of NH possibly on the rise in Canada (El Adam et al., 2022; Feig et al., 2014; Government of Canada, 2016) and the negative impacts that NH may have on the newborn, family, and hospital system, it is pertinent to explore treatment options for NH that may improve these issues. After examination of the studies included in this review, the synthesized evidence shows improved outcomes for patients with NH with the use of oral dextrose gel treatment over feeding-based treatment alone. When using dextrose gel in conjunction with feeding-based treatment methods for NH, the majority of the studies reviewed found a statistically significant decrease in the rate of NICU admissions and/or IV dextrose treatment for NH.

The experience of having a newborn in the NICU may cause mothers to have feelings of stress, anxiety, depression, loss of control, and fear (Obeidat et al. 2009), and postpartum stress has been shown to have negative impacts on infant growth, nutrition, bonding, temperament, and childhood mental wellbeing (Oyetunji & Chandra, 2020). The evidence synthesized in this review has demonstrated the efficacy of oral dextrose gel in helping to resolve NH while newborns are in the comfort of their mother's postpartum room, appearing to prevent the need for NICU transfer for many of the babies included in the studies. Thus, in addition to treating NH

and helping to prevent the negative effects that this can have on the newborn's neurodevelopment, dextrose gel may result in positive impacts to the child and family's long-term well-being.

NICU care in Canada is expensive (Rios et al., 2021), as there are many associated costs such as an increased level of nursing care, supplies, monitors, and medications that are not used in a postpartum ward; therefore, high rates of NICU admissions can place economic stress on a hospital (Hegarty et al., 2017). Another potential benefit of dextrose gel that two (Gibson et al., 2021 & Parappil et al., 2023) of the included studies noted was an associated reduction in hospital spending after the gel treatment protocol was implemented. Gibson et al. (2021) found that there was a decrease in spending by 14.5% per patient in their dextrose gel group versus control group, a savings of $1,190.60 US dollars (approximately $1,600 Canadian). A cost analysis by Parappil et al. (2023) estimated that dextrose gel implementation would save an average of 2.83 million Qatari riyals (approximately $1.05 million Canadian) per year. Gupta et al. (2022) also noted that dextrose gel treatment was very inexpensive, with an estimated cost during their study of only 20 Indian rupees (approximately 32 cents Canadian) per dose, and a number needed to treat of 3.5 babies to prevent one NICU admission. Thus, implementation of dextrose gel treatment for NH may help to decrease healthcare spending by cutting costs associated with expensive NICU admissions.

Breastfeeding has a number of potential long-term health benefits for the baby, including improved cognitive development, a decreased risk of sudden infant death, and protective effects against several diseases such as leukemia, celiac disease, and inflammatory bowel disease (Brahm & Valdés, 2017). Breastfeeding is also associated with a number of health benefits for the mother, including a decreased risk of breast and ovarian cancers and type II diabetes

(Chowdhury et al., 2015). NICU admission for NH may impact the establishment of breastfeeding, as the mother and newborn are physically separated and the newborn may not be allowed to orally feed (Hegarty et al., 2017). Five of the studies included in the rapid review (Desai et al., 2022; Gibson et al., 2022; Meneghin et al., 2021; Parappil et al., 2023; & Plummer et al., 2022) also looked at exclusive breastfeeding rates at discharge as an outcome of interest, and all five found a statistically significant improvement in the dextrose gel group versus control group. Therefore, dextrose gel treatment may also lead to benefits for the long-term health of the newborn and mother in these numerous other ways.

Authors of the reviewed studies have identified a number of positive outcomes associated with the use of dextrose gel treatment for NH, such as a decrease in NICU admission rates, lower hospital spending costs, and improved exclusive breastfeeding rates at discharge. A point of particular interest in this review was the highly statistically significant ($p < 0.001$) difference in the need for IV dextrose treatment when dextrose gel was used in three high-quality studies (Gupta et al., 2022; Parappil et al., 2023; & Plummer et al., 2022), indicating strong evidence for its use.

**Strengths and Limitations**

Key strengths of this rapid review are the focused research questions and clearly defined populations and outcomes of interest, which streamlined the study screening process and allowed for the questions to be answered precisely with the gathered evidence. Another strength was the use of multiple databases and the assistance of a research librarian to run the literature search to ensure that it was thorough. A limitation of this review was that studies were screened for inclusion/exclusion criteria and critically appraised by only one person, creating a potential for bias. Also, studies in languages other than English were not included.

## Next Steps

There is evidence to support the use of dextrose gel in treating NH from the studies examined in this review, however, there has not yet been an RCT conducted on this topic within a North American population. Although the Sugar Babies study (Harris et al., 2013) helped lead to groundbreaking advancements in newborn care, there may be some baseline differences such as ethnicity between the population used in this study in New Zealand over a decade ago and newborns in Canada today that could affect outcomes (James-Todd et al., 2018; Nguyen et al., 2012; Yuen & Wong, 2015). Likewise, although the RCT conducted in India by Gupta et al. (2022) showed that dextrose gel greatly improves outcomes in infants with NH, this may not be able to translate effectively to a Canadian setting where baseline differences are present in both socioeconomic factors and hospital protocols. An up-to-date RCT conducted in Canada could potentially reveal the effects that dextrose gel has on newborn outcomes within this specific population and if there are any differences from past studies.

## Conclusion

The evidence synthesized from this rapid review supports the use of oral dextrose gel for treatment of NH in term and near-term newborns while in hospital. Introduction of a treatment protocol for NH that includes the use of dextrose gel in addition to feeding-based treatment methods may reduce NICU admissions and IV dextrose use rates for NH. Additionally, dextrose gel treatment may have positive impacts on hospital spending and exclusive breastfeeding rates at discharge. Further research, including an up-to-date RCT conducted in a Canadian setting, may help to build on existing evidence.

## References


Abramowski, A., Ward, R., & Hamdan, A. F. (2022). *Neonatal hypoglycemia.* StatPearls Publishing.

Adamkin, D. H. (2017). Review: Neonatal hypoglycemia. *Seminars in Fetal & Neonatal Medicine, 22,* 36-41.

Alsaleem, M., Saadeh, L., Kumar, V. H. S., Wilding, G. E., Miller, L., & Mathew, B. (2019). Continued enteral feeding is beneficial in hypoglycemic infants admitted to intensive care for parenteral dextrose therapy. *Global Pediatric Health, 6,* 1-6.

Brahm, P. & Valdés, V. (2017). Benefits of breastfeeding and risks associated with not breastfeeding. *Chilean Journal of Pediatrics, 88*(1), 15-21.

CASP. (2024). *CASP checklists*. Critical appraisal skills programme. https://casp-uk.net/casp-tools-checklists/

Chen, Y. S., Ho, C. H., Lin, S. J., & Tsai, W. H. (2022). Identifying additional risk factors for early asymptomatic neonatal hypoglycemia in term and late preterm babies. *Pediatrics and Neonatology, 63*(6), 625-632.

Chowdhury, R., Sinha, B., Sankar, M. J., Taneja, S., Bhandari, N., Rollins, N., Bahl, R., & Martines, J. (2015). Breastfeeding and maternal health outcomes: A systematic review and meta-analysis. *Acta Paediatrica, 104,* 96-113.

Coors, S. M., Cousin, J. J., Hagan, J. L., & Kaiser, J. R. (2018). Prophylactic dextrose gel does not prevent neonatal hypoglycemia: a quasi-experimental pilot study. *The Journal of Pediatrics, 198,* 156-161.

De Buck, E., Borra, V., Carlson, J. N., Zideman, D. A., Singletary, E. M., & Djärv, T. (2019). First aid glucose administration routes for symptomatic hypoglycaemia. *Cochrane*

*Database of Systematic Reviews,* 3. https://doi.org/10.1002/14651858.CD012152.pub3

Desai, P., Verma, S., Bhargava, S., Rice, M., Tracy, J., & Bradshaw, C. (2022). Implementation and outcomes of a standard dose dextrose gel protocol for management of transient neonatal hypoglycemia. *Journal of Perinatology, 42*(8), 1097-1102.

Deyo-Svendsen, M., Herrmann, S., Andrist, C., Phillips, M., Svendsen, M. C., & Svendsen, R. O. (2021). Prevention of neonatal hypoglycemia with oral glucose gel for high-risk newborns. *Wisconsin Medical Journal, 120*(1), 51-53.

Dobbins, M. (2017). *Rapid Review Guidebook.* National Collaborating Centre for Methods and Tools. https://www.nccmt.ca/uploads/media/media/0001/02/800fe34eaedbad09edf80ad5081b9291acf1c0c2.pdf

Edwards, T. & Harding, J. E. (2021). Clinical aspects of neonatal hypoglycemia: A mini review. *Frontiers in Pediatrics, 8*(562251). https://doi.org/10.3389/fped.2020.562251

Edwards, T., Liu, G., Battin, M., Harris, D. L., Hegarty, J. E., Weston, P. J., & Harding, J. E. (2022). Oral dextrose gel for the treatment of hypoglycaemia in newborn infants. *Cochrane Database of Systematic Reviews, 3*. https://doi.org/10.1002/14651858.CD011027.pub3

El Adam, S., Hutcheon, J. A., McLeod, C., & McGrail, K. (2022, January 19). Health Reports: Why are babies in Canada getting smaller? Statistics Canada. https://www.doi.org/10.25318/82-003-x202200100001-eng

Feig, D. S., Hwee, J., Shah, B. R., Booth, G. L., Bierman, A. S., & Lipscombe, L. L. (2014). Trends in incidence of diabetes in pregnancy and serious perinatal outcomes: A large, population-based study in Ontario, Canada, 1996-2010. *Diabetes Care, 37,* 1590-1596.

Gibson, B. L., Carter, B. M., LeDuff, L. D. 3rd, & Wallace, A. (2021). 40% glucose gel for the

treatment of asymptomatic neonatal hypoglycemia. *Advances in Neonatal Care, 21*(5), 371-378.

Glascow, M. J., Harding, J. E., & Edlin, R. (2018). Cost analysis of treating neonatal hypoglycemia with dextrose gel. *The Journal of Pediatrics, 198,* 151-155. https://doi.org/10.1016/j.jpeds.2018.02.036

Government of Canada. (2016, May 17). *Maternal diabetes in Canada*. https://www.canada.ca/en/public-health/services/publications/healthy-living/maternal-diabetes-canada.html

Gupta, K., Amboiram, P., Balakrishnan, U., Ashok, C., Abiramalatha, T., & Devi, U. (2022). Dextrose gel for neonates at risk with asymptomatic hypoglycemia: A randomized clinical trial. *Pediatrics, 149*(6).

Hames, J. L., Gasteiger, C., McKenzie, M. R., Rowley, S., Serlachius, A. S., Juth, V., & Petrie, K. J. (2020). Predictors of parental stress from admission to discharge in the neonatal special care unit. *Child: Care, Health, Development, 47,* 243-251.

Harding, J. E., Hegarty, J. E., Crowther, C. A., Edlin, R. P., Gamble, G. D., & Alsweiler, J. M. (2021). Evaluation of oral dextrose gel for prevention of neonatal hypoglycemia (hPOD): A multicenter, double-blind randomized controlled trial. *PLoS Medicine, 18*(1).

Harris, D. L., Weston, P. J., Signal, M., Chase, J. G., & Harding, J. E. (2013). Dextrose gel for neonatal hypoglycaemia (the sugar babies study): A randomised, double-blind, placebo-controlled trial. *Lancet, 382*, 2077-2083.

Hegarty, J. E., Harding, J. E., Crowther, C. A., Brown, J. & Alsweiler, J. (2017). Oral dextrose gel to prevent hypoglycaemia in at-risk neonates (Review). *Cochrane Database of Systematic Reviews, 7.* https://doi.org/10.1002/14651858.CD012152.pub2

Hegarty, J. E., Harding, J. E., Gamble, G. D., Crowther, C. A., Edlin, R., & Alsweiler, J. M.

(2016). Prophylactic oral dextrose gel for newborn babies at risk of neonatal hypoglycaemia: A randomised controlled dose-finding trial (the pre-hPOD study). *PLoS Medicine, 13*(10). https://doi.org/10.1371/journal.pmed.1002155

James Cook University Library. (2024, Jan 16). *Rapid reviews.* James Cook University Australia. https://libguides.jcu.edu.au/rapidreview/introduction

James-Todd, T., March, M. I., Seiglie, J., Gupta, M., Brown, F. M., & Majzoub, J. A. (2018). Racial differences in neonatal hypoglycemia among very early preterm births. *Journal of Perinatology, 38,* 258-263.

JBI. (2020). *Critical appraisal tools.* https://jbi.global/critical-appraisal-tools

Laptook, A. L., & Jackson, G. L. (2006). Cold stress and hypoglycemia in the late preterm ("near-term") infant: Impact on nursery of admission. *Seminars in Perinatology, 30*(1), 24-27.

Makker, K., Alissa, R., Dudek, C., Travers, L., Smotherman, C., & Hudak, M. L. (2018). Glucose gel in infants at risk for transitional neonatal hypoglycemia. *American Journal of Perinatology, 35,* 1050-1056.

Meneghin, F., Manzalini, M., Acunzo, M., Daniele, I., Bastrenta, P., Castoldi, F., Cavigioli, F., Zuccotti, G. V., & Lista, G. (2021). Management of asymptomatic hypoglycemia with 40% oral dextrose gel in near term at-risk infants to reduce intensive care need and promote breastfeeding. *Italian Journal of Pediatrics, 47*(1), 201.

Narvey, M. R., & Marks, S. D. (2019, November 20). *Position statement: The screening and management of newborns at risk for low blood glucose.* Canadian Paediatric Society. https://cps.ca/en/documents/position/newborns-at-risk-for-low-blood-glucose

Neumann, K., Indorf, I., Härtel, C., Cirkel, C., Rody, A., & Beyer, D. A. (2017). C-section

prevalence among obese mothers and neonatal hypoglycemia: A cohort analysis of the Department of Gynecology and Obstetrics of the University of Lübeck. *Geburtsh Frauenheilk, 77,* 487-494.

Nguyen, B. T., Cheng, Y. W., Snowden, J. M., Esakoff, T. F., Frias, A. E., & Caughey, A. B. (2012). The effect of race/ethnicity on adverse perinatal outcomes among patients with gestational diabetes mellitus. *American Journal of Obstetrics and Gynecology, 207*(4), 322.e1-322.e6

Obeidat, H. M., Bond, E. A., & Callister, L. C. (2009). The parental experience of having an infant in the newborn intensive care unit. *Journal of Perinatal Education, 18*(3), 23-29.

Oyetunji, A. & Chandra, P. (2020). Postpartum stress and infant outcome: A review of current literature. *Psychiatry Research, 284.*

Parappil, H., Gaffari, M., Ahmed, J., Skaria, S., Rijims, M., Chandra, P., & Babu, K. T. S. (2023). Oral dextrose gel use in asymptomatic hypoglycemic newborns decreases NICU admissions and parenteral dextrose therapy: A retrospective study. *Journal of Neonatal-Perinatal Medicine, 16*(1), 111-117.

Plummer, E. A., Ninkovic, I., Rees, A., Rao, R., Bendel, C. M., & Stepka, E. C. (2022). Neonatal hypoglycemia algorithms improve hospital outcomes. *The Journal of Maternal-Fetal & Neonatal Medicine, 35*(12), 2278-2285.

Rios, J. D., Shah, P. S., Beltempo, M., Louis, D., Mukerji, A., Premji, S., Shah, V., Lee, S. K., & Pechlivanoglou, P. (2021). Costs of neonatal intensive care for Canadian infants with preterm birth. *The Journal of Pediatrics, 229,* P161-167.

Roberts, L., Lin, L., Alsweiler, J., Edwards, T., Liu, G., & Harding, J. E. (2023). Oral dextrose gel to prevent hypoglycaemia in at-risk neonates (review). *Cochrane Database of*

*Systematic Reviews, 11*. https://doi.org/10.1002%2F14651858.CD012152.pub4

Rönö, K., Masalin, S., Kautiainen, H., Gissler, M. Raina, M., Eriksson, J. G., & Laine, M. G. (2018). Impact of maternal income on the risk of gestational diabetes mellitus in primiparous women. *Diabetic Medicine, 36*(2), 214-220.

Rozance, P. J., & Hay Jr., W. W. (2010). Describing hypoglycemia—Definition or operational threshold? *Early Human Development, 86,* 275-280.

Scheans, P., Bennett, C., Harris, D. (2017). Using dextrose (glucose) gel to reverse neonatal hypoglycemia. *Neonatal Network, 36,* 233–238.

Simon Fraser University. (2023, September 06). *Systematic, scoping, and rapid reviews: An overview.* Library Research Commons. https://www.lib.sfu.ca/about/branches-depts/rc/writing-theses/writing/literature-reviews/systematic-scoping-rapid-reviews

Stanzo, K., Desai, S., & Chiruvolu, A. (2020). Effects of dextrose gel in newborns at risk for neonatal hypoglycemia in a baby-friendly hospital. *Journal of Obstetrical, Gynecological & Neonatal Nursing, 49,* 55-64.

Stanzo, K., Kumar, V., Gallegos, A., & Chirovolu, A. (2023). How much glucose is in Sweet Cheeks oral glucose gel? *Journal of Perinatology, 43,* 1181-1182.

Ter, M., Halibullah, I., & Leung, L., & Jacobs, S. (2017). Implementation of dextrose gel in the management of neonatal hypoglycaemia. *Journal of Pediatrics and Child Health, 53,* 408-411.

Thornton, P. S., Stanley, C. A., De Leon, D. D., Harris, D., Haymond, M. W., Hussain, K., Levitsky, L. L., Murad, M. H., Rozance, P. J., Simmons, R. A., Sperling, M. A., Weinstein, D. A., White, N. H., & Wolfsdorf, J. I. (2015). Recommendations from the Pediatric Endocrine Society for evaluation and management of persistent hypoglycemia

in neonates, infants, and children. *Journal of Pediatrics, 167*(2), 238-245.

Tricco, A. C., Khalil, H., Holly, C., Feyissa, G., Godfrey, C., Evans, C., Sawchuck, D., Sudhakar, M., Asahngwa, C., Stannard, D., Abdulahi, M., Bonnano, L., Aromataris, E., McInerney, P., Wilson, R., Pang, D., Wang, Z., Cardoso, A. F., Peters, M. D. J.,… Munn, Z. (2022). Rapid reviews and the methodological rigor of evidence synthesis: a JBI position statement. *JBI Evidence Synthesis, 20*(4), 944-949.

Troughton, K. E. V., Corrigan, N.P., Tait, R. M. E. (2000). Hypostop gel in the treatment of neonatal hypoglycaemia: A randomised controlled trial. *Archives of Disease in Childhood, 82(supp 1),* A30.

Turner, D., Monthé-Drèze, C., Cherkerzian, S., Gregory, K., & Sen, S. (2019). Maternal obesity and cesarean section delivery: additional risk factors for neonatal hypoglycemia? *Journal of Perinatology, 39,* 1057-1064.

Walravens, C., Gupta, A., Cohen, R. S., Kim, J. L., & Frymoyer, A. (2023). Fewer glucose checks and decreased supplementation using dextrose gel for asymptomatic neonatal hypoglycemia. *Journal of Perinatology, 43*(4), 532-537.

Wang, M. Q., Zheng, Y. N., Zhuang, Y. (2023). Oral glucose gel in the prevention of neonatal hypoglycemia: A systematic review and meta-analysis. *Medicine, 102*(48), e36137.

Washer, A., Di Fiore, T., & Siegmund, L. A. (2021). A project to implement use of 40% dextrose gel for transient neonatal hypoglycemia. *Nursing for Women's Health, 25*(2), 122-128.

Wickström, R., Skiöld, B., Petersson, G., Stephansson, O., & Altman, M. (2018). Moderate neonatal hypoglycemia and adverse neurological development at 2-6 years of age. *European Journal of Epidemiology, 33,* 1011-1020.

Yuen, L., & Wong, V. W. (2015). Gestational diabetes mellitus: Challenges for different ethnic groups. *World Journal of Diabetes, 6*(8), 1024-1032

## Appendix A: Search Terms

Medline:

1 exp infant, newborn/ or nurseries, infant/ or nurseries, hospital/ or infant care/ or rooming-in care/ or infant health/ or intensive care, neonatal/ or neonatal nursing/ or nurses, neonatal/ or neonatology/ or neonatologists/

2 (baby* or babies or infan* or neonat* or newborn* or new born* or late preterm* or nurser*).ti,ab,kf.

3 1 or 2

4 exp hypoglycemia/

5 (hypoglyc* or hypo glyc* or hyperinsulin* or hyper insulin* or glycopeni*).ti,ab,kf.

6 ((low* or reduc*) adj2 (blood sugar* or blood glucose*)).ti,ab,kf.

7 or/4-6

8 (glucogel or glucagon or dextrogel or dex4 or Glutose or Hypostop or InstaGlucose or insta glucose or rapilose or sweet cheek*).ti,ab,kf.

9 exp glucose/ and (gels/ or administration, oral/ or administration, buccal/ or administration, sublingual/)

10 (glucose or dextrose).ti,ab,kf.

11 (gels or gel or jelly or jellies or sublingual* or lingual* or buccal* or oral* or mouth* or gum or gums or gingiva* or cheek* or tongue*).ti,ab,kf.

12 10 and 11

13 8 or 9 or 12

14 3 and 7 and 13

15 limit 14 to (english language and yr="2021 -Current")

Embase:

1 newborn/ or hospitalized infant/ or high risk infant/ or nursery/ or infant care/ or exp newborn care/ or neonatal nurse practitioner/ or neonatal nurse/ or neonatology/ or neonatologist/

2 (baby* or babies or infan* or neonat* or newborn* or new born* or late preterm* or nurser*).ti,ab,kf.

3 1 or 2

4 exp hypoglycemia/

5 (hypoglyc* or hypo glyc* or hyperinsulin* or hyper insulin* or glycopeni*).ti,ab,kf.

6 ((low* or reduc*) adj2 (blood sugar* or blood glucose*)).ti,ab,kf.

7 or/4-6

8 (glucogel or glucagon or dextrogel or dex4 or Glutose or Hypostop or InstaGlucose or insta glucose or rapilose or sweet cheek*).ti,ab,kf.

9 glucose/ and (exp gel/ or oral drug administration/ or exp buccal drug administration/ or po.fs. or bd.fs. or li.fs.)

10 (glucose or dextrose).ti,ab,kf.

11 (gels or gel or jelly or jellies or sublingual* or lingual* or buccal* or oral* or mouth* or gum or gums or gingiva* or cheek* or tongue*).ti,ab,kf.

12 10 and 11

13 8 or 9 or 12

14 3 and 7 and 13

15 limit 14 to (english language and yr="2021 -Current")

CINAHL:

(MH "infant, newborn+") or (MH "nurseries, hospital") or (MH "infant care") or (MH "rooming in") or (MH "intensive care, neonatal") or (MH "neonatal nurses+") or (MH "neonatal nursing+") or (MH "neonatal nurse practitioners") or (MH neonatology) or (MH neonatologists)

(baby* or babies or infan* or neonat* or newborn* or "new born*" or "late preterm*" or nurser*)

S1 or S2

(MH hypoglycemia+)

(hypoglyc* or "hypo glyc*" or hyperinsulin* or "hyper insulin*" or glycopeni*)

((low* or reduc*) N2 (blood sugar* or blood glucose*))

S4 or S5 or S6

(glucogel or glucagon or dextrogel or dex4 or Glutose or Hypostop or InstaGlucose or "insta glucose" or rapilose or "sweet cheek*")

(MH glucose) and ((MH gels) or (MH "administration, oral+"))

(glucose or dextrose)

(gels or gel or jelly or jellies or sublingual* or lingual* or buccal* or oral* or mouth* or gum or gums or gingiva* or cheek* or tongue*)

S10 and S11

S8 or S9 or S12

S3 and S7 and S13

S14 Limiters - Publication Date: 20210101-; English Language

Cochrane Central:

1 exp infant, newborn/ or nurseries, infant/ or nurseries, hospital/ or infant care/ or rooming-in care/ or infant health/ or intensive care, neonatal/ or neonatal nursing/ or nurses, neonatal/ or neonatology/ or neonatologists/

2 (baby* or babies or infan* or neonat* or newborn* or new born* or late preterm* or nurser*).ti,ab,kw.

3 1 or 2

4 exp hypoglycemia/

5 (hypoglyc* or hypo glyc* or hyperinsulin* or hyper insulin* or glycopeni*).ti,ab,kw.

6 ((low* or reduc*) adj2 (blood sugar* or blood glucose*)).ti,ab,kw.

7 or/4-6

8 (glucogel or glucagon or dextrogel or dex4 or Glutose or Hypostop or InstaGlucose or insta glucose or rapilose or sweet cheek*).ti,ab,kw.

9 exp glucose/ and (gels/ or administration, oral/ or administration, buccal/ or administration, sublingual/)

10 (glucose or dextrose).ti,ab,kw.

11 (gels or gel or jelly or jellies or sublingual* or lingual* or buccal* or oral* or mouth* or gum or gums or gingiva* or cheek* or tongue*).ti,ab,kw.

12 10 and 11

13 8 or 9 or 12

14 3 and 7 and 13

15 limit 14 to (english language and yr="2021 -Current")

## Appendix B: CASP Checklists

Cohort Studies

*Deyo-Svendsen (2021)*

| Question | Answer |
|---|---|
| Did the study address a clearly focused issue? | Yes—to assess the effects of the implementation of a dextrose gel protocol on IV dextrose administration and NICU transfer rates in newborns with NH |
| What the cohort recruited in an acceptable way? | Yes—data was collected through chart review of all infants who met inclusion criteria |
| Was the exposure accurately measured to minimize bias? | Yes—newborns were treated with 0.5 mL/kg of dextrose gel as per protocol |
| Was the outcome accurately measured to minimize bias? | Yes—blood glucose levels were measured objectively and NICU admission/IV dextrose administration occurred if the newborn met criteria as per a treatment algorithm |
| Have the authors identified all important confounding factors? | Yes—results may have been skewed if patients who were admitted to NICU for reasons unrelated to NH were included in analysis |
| Have they taken account of the confounding factors in the design and/or analysis? | Yes—symptomatic newborns and those transferred to NICU for reasons unrelated to NH were excluded from analysis |

| | |
|---|---|
| Was the follow up of subjects complete enough? | Many participants (37 of 122 newborns in year 1 and 22 of 108 in year 2) had symptomatic NH and were excluded from the study |
| Was the follow up of subjects long enough? | Yes—eligible newborns were followed for their hospital stay |
| What are the results of the study? | Dextrose gel significantly decreased NICU/IV dextrose rate:<br>Year 1 (control): 7/122 (2.25%) NICU or IV dextrose<br>Year 2 (dextrose gel): 0/108 (0%) NICU or IV dextrose ($p = 0.029$) |
| How precise are the results? | Very imprecise: odds ratio of needing NICU or IV dextrose was 0.07 (95% CI 0.004 to 1.25) between |
| Do you believe the results? | Yes—a reduction to zero NICU admissions is remarkable, but there were only seven admissions in the control group |
| Can the results be applied to the local population? | Can't tell—study was conducted in the United States and there may be some socioeconomic differences in populations that could affect results. Also, gestational age of participants was not specified |
| Do the results of the study fit with other available evidence? | Yes—most of the other studies show a decrease in NICU admissions/IV dextrose with use of dextrose gel |
| What are the implications of this study for practice? | The use of dextrose gel in newborns may help prevent NICU admissions/IV dextrose use—a larger study |

| | |
|---|---|
| | population with more precise results may be necessary to make practice recommendations |

*Gibson et al. (2021)*

| Question | Answer |
|---|---|
| Did the study address a clearly focused issue? | Yes—to assess the effects of dextrose gel on exclusive human milk diet rates, time on protocol, NICU admission rates, length of stay, and total hospital costs for newborns ≥ 36 weeks with asymptomatic NH |
| What the cohort recruited in an acceptable way? | Yes—data was collected through chart review of all infants who met criteria |
| Was the exposure accurately measured to minimize bias? | Yes—newborns were treated with 0.5 mL/kg of dextrose gel as per protocol |
| Was the outcome accurately measured to minimize bias? | Yes—blood glucose levels were measured objectively and NICU admission/IV dextrose administration occurred if the newborn met criteria as per a treatment algorithm |
| Have the authors identified all important confounding factors? | No—there is a large difference between groups for delivery mode that was not addressed—control: 14/29 (48.3%) vaginal, 15/29 (51.7%) C-section; treatment: 29/35 (82.9%) vaginal, 6/35 (17.1%) C-section |
| Have they taken account of the confounding factors in the design and/or analysis? | No—(see above); authors also note that the change in treatment threshold level from 40 mg/dL to 50 mg/dL |

| | |
|---|---|
| | created a difference between groups apart from the intervention (more conservative in dextrose gel group) |
| Was the follow up of subjects complete enough? | Yes—all participants were included in analysis |
| Was the follow up of subjects long enough? | Yes—newborns were followed for their hospital stay |
| What are the results of the study? | No significant differences between groups:<br>NICU admissions: 4/29 (13.8%) in control group vs. 4/35 (11.4%) in dextrose gel group (p = 0.534)<br>IV dextrose use: 3/29 (10.3%) in control group vs. 4/35 (11.4%) in dextrose gel group (p = 0.607) |
| How precise are the results? | OR 0.80 (95% CI 0.18 to 3.55) |
| Do you believe the results? | Yes |
| Can the results be applied to the local population? | Can't tell—study was conducted in the United States and there may be some socioeconomic differences in populations that could affect results |
| Do the results of the study fit with other available evidence? | No—most other studies show a difference between dextrose gel and control groups |
| What are the implications of this study for practice? | The use of dextrose gel in newborns may not help to prevent NICU admissions or IV dextrose gel in newborns—a larger study population with more precise results may be necessary to make practice recommendations |

*Meneghin et al. (2021)*

| Question | Answer |
|---|---|
| Did the study address a clearly focused issue? | Yes—to compare the effect of a new NH protocol using dextrose gel on NICU admission and IV dextrose rates versus old protocol (controls) in newborns ≥ 35 weeks gestation at risk for hypoglycemia |
| What the cohort recruited in an acceptable way? | Yes—data was collected through chart review of all infants who met criteria |
| Was the exposure accurately measured to minimize bias? | Yes—newborns were treated with 0.5 mL/kg dextrose gel as per protocol |
| Was the outcome accurately measured to minimize bias? | Yes—blood glucose levels were measured objectively and NICU admission/IV dextrose administration occurred if the newborn met criteria as per a treatment algorithm |
| Have the authors identified all important confounding factors? | Yes—the authors note that there is some heterogeneity in baseline characteristics between groups in discussion section |
| Have they taken account of the confounding factors in the design and/or analysis? | No—authors only note that there is some heterogeneity between groups and do not take this into account during analysis. For example, there were 73/389 (18.8%) premature babies in control vs. 36/308 |

| | |
|---|---|
| | (11.2%) in treatment group and this may have affected results |
| Was the follow up of subjects complete enough? | Yes—7/308 infants in the dextrose gel group were excluded; all other infants were accounted for in analysis |
| Was the follow up of subjects long enough? | Yes—infants were followed throughout their hospital stay |
| What are the results of the study? | Dextrose gel use significantly decreased NICU admissions: 19/39 (48.7%) in control group vs. 3/30 (10%) in dextrose gel group (p = 0.001)<br>Dextrose gel significantly decreased IV dextrose use: 14/39 (35.9) in control group vs. 3/30 (10%) in dextrose gel group (p = 0.01) |
| How precise are the results? | NICU admissions: OR 0.12 (95% CI 0.03, 0.45)<br>IV dextrose: OR 0.20 (95% CI 0.05, 0.77) |
| Do you believe the results? | Yes, but they may have been influenced by baseline differences between groups |
| Can the results be applied to the local population? | Can't tell—study was conducted in the Italy and there may be some socioeconomic differences in populations that could affect results |
| Do the results of the study fit with other available evidence? | Yes—most of the other studies show a decrease in NICU admissions/IV dextrose with use of dextrose gel |

| | |
|---|---|
| What are the implications of this study for practice? | The use of dextrose gel in newborns may help prevent NICU admissions/IV dextrose use—a larger study population with more precise results may be necessary to make practice recommendations |

*Washer et al. (2021)*

| Question | Answer |
|---|---|
| Did the study address a clearly focused issue? | Yes—to assess the effects of oral dextrose gel and oral feedings on blood sugar homeostasis in term and late preterm (≥ 35 weeks gestation) newborns in the first day of life in an effort to decrease transfers to the NICU |
| What the cohort recruited in an acceptable way? | Yes—all infants who had blood glucose monitoring within a certain timeframe were included |
| Was the exposure accurately measured to minimize bias? | Yes—dextrose gel was administered as per treatment algorithm |
| Was the outcome accurately measured to minimize bias? | Yes—blood glucose levels were measured objectively and NICU admission/IV dextrose administration occurred if the newborn met criteria as per the treatment algorithm |
| Have the authors identified all important confounding factors? | Yes—the authors have not included the number of participants in the control group (only the number of |

| | |
|---|---|
| | NICU admissions pre- and post-dextrose gel use), and thus they identify that their study has strict limitations |
| Have they taken account of the confounding factors in the design and/or analysis? | Yes—no inferential statistics were used due to limitations in design |
| Was the follow up of subjects complete enough? | Unsure—total number of newborns in control group was not provided |
| Was the follow up of subjects long enough? | Yes—eligible newborns were followed until the hypoglycemia algorithm was complete or they were admitted to NICU |
| What are the results of the study? | Dextrose gel reduced NICU admissions for NH: 54 in year 1 (control) vs. 25 in year 2 (dextrose gel) |
| How precise are the results? | No statistics provided |
| Do you believe the results? | Can't tell—unsure without seeing total number of participants in each group |
| Can the results be applied to the local population? | No—the authors advise that the results cannot be generalized to other hospitals or units |
| Do the results of the study fit with other available evidence? | Yes—most of the other studies show a decrease in NICU admissions with dextrose gel use |
| What are the implications of this study for practice? | The authors advise that this specific algorithm worked for their unit but cannot be generalized to other hospitals or units |

*Desai et al. (2022)*

| Question | Answer |
|---|---|
| Did the study address a clearly focused issue? | Yes—to assess the impact of dextrose gel on the rates of IV dextrose use, NICU admission, breastfeeding, and adverse events in infants ≥ 35 weeks and ≥ 2000 g with hypoglycemia |
| What the cohort recruited in an acceptable way? | Yes—data was collected through chart review of all infants who met criteria |
| Was the exposure accurately measured to minimize bias? | Yes—infants were given 0.5 mL/kg of dextrose gel during the weight-based dose intervention period or 2 mL of gel during the standard dose intervention period |
| Was the outcome accurately measured to minimize bias? | Yes—blood glucose levels were measured objectively and NICU admission/IV dextrose administration occurred if the newborn met criteria |
| Have the authors identified all important confounding factors? | No—infants were admitted to NICU after two glucoses less than 40 mg/dL in the control group and after three glucoses less than 40 mg/dL in the dextrose gel groups. This could have affected NICU admission rates and was not addressed |
| Have they taken account of the confounding factors in the design and/or analysis? | No—differences in protocol between groups apart from dextrose gel was not addressed |

| | |
|---|---|
| Was the follow up of subjects complete enough? | Yes—it appears that all participants were included in analysis |
| Was the follow up of subjects long enough? | Yes—newborns were followed for their hospital stay |
| What are the results of the study? | Dextrose gel significantly reduced NICU admissions: 27.9% in control group vs. 16.1% in dextrose gel group ($p < 0.001$)<br>Dextrose gel significantly reduced IV dextrose use: 10.9% in control group vs. 6.5% in dextrose gel group ($p = 0.004$) |
| How precise are the results? | Unadjusted OR for IV dextrose use: 0.57 (95% CI, 0.39 to 0.84) |
| Do you believe the results? | Yes |
| Can the results be applied to the local population? | Can't tell—study was conducted in the United States and there may be some socioeconomic differences in populations that could affect results |
| Do the results of the study fit with other available evidence? | Yes—most of the other studies show a decrease in NICU admissions/IV dextrose with use of dextrose gel |
| What are the implications of this study for practice? | The use of dextrose gel in newborns may help prevent NICU admissions/IV dextrose use |

*Plummer et al. (2022)*

| Question | Answer |
|---|---|

| | |
|---|---|
| Did the study address a clearly focused issue? | Yes—to assess if implementation of hypoglycemia algorithms improved outcomes for newborns ≥ 36 weeks with asymptomatic NH including decreased IV dextrose use, decreased NICU admissions, increased breastfeeding rates, and decreased length of stay within the hospital system |
| What the cohort recruited in an acceptable way? | Yes—retrospective data from all infants who met criteria were included in the study |
| Was the exposure accurately measured to minimize bias? | Yes—infants received 0.5 mL/kg of dextrose gel per dose as per a hypoglycemia algorithm |
| Was the outcome accurately measured to minimize bias? | Yes—blood glucose levels were measured objectively and NICU admission/IV dextrose administration occurred if the newborn met criteria |
| Have the authors identified all important confounding factors? | Yes—authors note that differences are seen in sex, gestational ages, and distribution of hypoglycemia risk factors between groups |
| Have they taken account of the confounding factors in the design and/or analysis? | Yes—risk factors were adjusted for using logistic regression |
| Was the follow up of subjects complete enough? | Yes—it appears that all participants were included in analysis |
| Was the follow up of subjects long enough? | Yes—newborns were followed for their hospital stay |

| | |
|---|---|
| What are the results of the study? | When comparing algorithm 1 (control) to algorithm 2 (dextrose gel), IV dextrose use rates for NH fell from 2.5% to 1.0% ($p < 0.001$) |
| How precise are the results? | Unadjusted OR for IV dextrose use: 0.57 (95% CI, 0.39 to 0.84) |
| Do you believe the results? | Yes |
| Can the results be applied to the local population? | Can't tell—study was conducted in the United States and there may be some socioeconomic differences in populations that could affect results |
| Do the results of the study fit with other available evidence? | Yes—most of the other studies show a decrease in NICU admissions/IV dextrose with use of dextrose gel |
| What are the implications of this study for practice? | The use of dextrose gel in newborns may help prevent IV dextrose use |

*Parappil et al. (2023)*

| Question | Answer |
|---|---|
| Did the study address a clearly focused issue? | Yes—to assess the effect of dextrose gel supplementation for asymptomatic NH in reducing NICU admissions and IV dextrose use in newborns ≥ 35 weeks gestation |
| What the cohort recruited in an acceptable way? | Yes—retrospective data from all infants who met criteria were included in the study |

| | |
|---|---|
| Was the exposure accurately measured to minimize bias? | Yes—infants received 0.5 mL/kg of dextrose gel per dose as per a hypoglycemia algorithm |
| Was the outcome accurately measured to minimize bias? | Yes—blood glucose levels were measured objectively and NICU admission/IV dextrose administration occurred if the newborn met criteria |
| Have the authors identified all important confounding factors? | Yes—authors note that baseline characteristics were similar between groups |
| Have they taken account of the confounding factors in the design and/or analysis? | Yes—authors explain in their analysis that differences in hypoglycemia thresholds (2.6 vs. 2.8 mmol/L) between groups may be a potential limitation to the study, but they explain why they feel that this did not affect the results |
| Was the follow up of subjects complete enough? | Yes—it appears that all participants were included in analysis |
| Was the follow up of subjects long enough? | Yes—newborns were followed for the first 48 hours of life |
| What are the results of the study? | Dextrose gel significantly reduced NICU admissions: 396/1801 (22%) in control group vs. 329/1783 (18.5%) in dextrose gel group ($p = 0.008$)<br>Dextrose gel significantly reduced IV dextrose use: 277/1801 (15.4%) in control group vs. 182/1783 (10.2%) in dextrose gel group ($p < 0.001$) |
| How precise are the results? | NICU admissions: OR 0.80 (95% CI, 0.68 to 0.95) |

| | |
|---|---|
| | IV dextrose: OR 0.63 (95% CI, 0.51 to 0.76) |
| Do you believe the results? | Yes |
| Can the results be applied to the local population? | Can't tell—this study was done in Qatar and there may be socioeconomic differences that may affect results |
| Do the results of the study fit with other available evidence? | Yes—most of the other studies show a decrease in NICU admissions/IV dextrose with use of dextrose gel |
| What are the implications of this study for practice? | The use of dextrose gel in newborns may help prevent NICU admissions/IV dextrose use |

*Walravens et al. (2023)*

| Question | Answer |
|---|---|
| Did the study address a clearly focused issue? | Yes—to evaluate the impact of a NH clinical pathway including dextrose gel on factors such as the number of blood glucose measurements taken, the use of milk supplementation, and the need for IV dextrose in newborns ≥ 35 weeks gestation |
| What the cohort recruited in an acceptable way? | Yes—all infants who met criteria were included in the study |
| Was the exposure accurately measured to minimize bias? | Yes—infants received 0.5 mL/kg of dextrose gel per dose as per a hypoglycemia algorithm |
| Was the outcome accurately measured to minimize bias? | Yes—blood glucose levels were measured objectively and interventions occurred if the newborn met criteria |

| | |
|---|---|
| Have the authors identified all important confounding factors? | Yes—the authors identified that the dextrose gel group had a significantly lower baseline rate of NH than the control group. They also noticed that nurses were feeding the newborns in the dextrose gel group less than those in the control group |
| Have they taken account of the confounding factors in the design and/or analysis? | Yes—post-hoc analysis was done to adjust the results to account for the differences in baseline rates of NH. Nurses were provided additional education on appropriate feeding after administering dextrose gel and a "special cause shift" was created within the results |
| Was the follow up of subjects complete enough? | Yes—it appears that all participants were included in analysis |
| Was the follow up of subjects long enough? | Yes—newborns were followed for the first 48 hours of life |
| What are the results of the study? | IV dextrose use for NH decreased from 4.8% to 4.1% (3.5% after special cause shift) |
| How precise are the results? | OR 0.84 (95% CI, 0.62 to 1.13) |
| Do you believe the results? | Can't tell—the large difference in baseline NH rates between groups (41% vs. 34.4%) indicate that there may have been other differences between groups that were not accounted for |

| | |
|---|---|
| Can the results be applied to the local population? | Can't tell—this study was done in United States and there may be socioeconomic differences that may affect results |
| Do the results of the study fit with other available evidence? | Yes—most of the other studies show a decrease in IV dextrose with use of dextrose gel |
| What are the implications of this study for practice? | The use of dextrose gel in newborns may help prevent IV dextrose use |

Randomized Controlled Trials

*Gupta et al. (2022)*

| Question | Answer |
|---|---|
| Did the study address a clearly focused research question? | Yes—aimed to study the efficacy of 40% dextrose gel plus breastfeeding versus breastfeeding alone for treating asymptomatic NH in babies ≥ 35 weeks gestation at risk for NH |
| Was the assignment of the participants to interventions randomized? | Yes—a computer generated variable block randomization sequence was used and allocation concealment was by serially numbered, opaque, sealed envelopes at a 1:1 allocation ratio |
| Were all participants who entered the study accounted for at its conclusion? | Yes |
| Were the participants "blind" to interventions they were given | No—blinding was not done due to the unavailability of a similar-looking placebo |

| | |
|---|---|
| Were the investigators “blind” to the intervention they were giving to participants? | No—blinding was not done due to the unavailability of a similar-looking placebo |
| Were the people assessing/analyzing outcomes “blinded”? | No—blinding was not done due to the unavailability of a similar-looking placebo |
| Were the study groups similar at the start of the RCT? | Yes—maternal and neonatal baseline characteristics were similar in both groups |
| Apart from the experimental intervention, did each study group receive the same level of care? | Yes |
| Were the effects of intervention reported comprehensively? | Yes—power calculation was done, risk ratio, p-values and NNT were calculated for “treatment failure” (IV dextrose) between treatment and control groups. One potential error was made: the number of participants who received dextrose gel was reported as 147 in one place and 141 in another (either way, significant difference between groups for both numbers) |
| Was the precision of the estimate of the intervention or treatment effected reported? | Yes—confidence intervals were reported |

| | |
|---|---|
| Do the benefits of the experimental intervention outweigh the harms and costs? | Yes—no adverse events reported. NNT to prevent one NICU admission was 3.5 patients. Gel had a very minimal cost: approximately 20 rupees ($0.32 CAD) per dose |
| Can the results be applied to your local population/in your context? | Can't tell—this study was done in India and there may be socioeconomic differences that may affect results |
| Would the experimental intervention provide greater value to the people in your care than any of the existing interventions? | Can't tell—this study compares the use of dextrose gel and breastfeeding to breastfeeding alone, does not compare dextrose gel to formula supplementation |