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Birth room transition support for term and near-term infants: a Cochrane overview (Protocol)

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[Overview of Reviews Protocol]

Birth room transition support for term and near-term infants: a Cochrane overview

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ABSTRACT

This is a protocol for a Cochrane Review (Overview). The objectives are as follows:

We will describe and summarise Cochrane Reviews of birth room interventions for term or near-term newborn infants, and assess their methodological quality and the validity of their findings. We will map the evidence from Cochrane Reviews and identify important gaps in the evidence base. We will not compare multiple interventions with the intention of drawing inferences about their comparative effectiveness.

BACKGROUND

This Cochrane overview will focus on interventions to support postnatal transition in term and near-term infants (those born at more than 34 weeks' gestation). A separate Cochrane overview will focus on transition-support interventions for preterm infants, particularly very preterm infants (those born at less than 32 weeks' gestation) in whom the need for support is driven primarily by surfactant insufficiency and respiratory distress syndrome (Brown 2019).

Description of the condition

One in ten newborn infants experiences delayed establishment of independent respiratory effort at birth that requires resuscitation or transition support. Reasons for ineffective or delayed transition to extra-uterine life, and the need for support, differ with gestational age. In preterm infants, particularly very preterm infants, the main cause is "respiratory distress syndrome" of prematurity,

primarily as a consequence of lung surfactant deficiency (Sweet 2019). In term and near-term newborn infants, surfactant deficiency is less common and the main reasons for delayed transition are respiratory distress due to incomplete clearance of lung fluid, and more serious perinatal complications including meconium aspiration, congenital infection, airway anomalies, or neonatal encephalopathy, which may be attributed to perinatal asphyxia (Vento 2010; Wyllie 2015; Wyllie 2016; Liley 2017).

Description of the interventions

For the purpose of this review, any intervention carried out within the birth room (also called delivery room or delivery suite) immediately after the birth of the baby (i.e., before the baby is transferred to the postnatal unit, nursery, or neonatal intensive care unit, as needed), will be considered a 'birth room intervention'. They are typically categorised as airway, breathing, and circulatory support; administration of supplemental oxygen or other drugs; and mea-

asures to prevent hypothermia or metabolic compromise (Davis 2012; Perlman 2012) and are delivered by any of the healthcare professionals attending the birth (doctors, nurses, or midwives) as appropriate to the circumstances and complexity of the intervention.

- Airway management includes optimising head, jaw, and tongue position to open the upper airway; removal of obstructing material such as mucus, blood, or meconium from the oro- or naso-pharynx; and use of devices to ensure and maintain upper airway patency (oropharyngeal airway, laryngeal airway, endotracheal tube).

- Breathing support, when the airway is patent, includes positive pressure ventilation that can be delivered via various devices, with the aim of clearing the alveolar regions of lung liquid to allow gas exchange to occur (Hooper 2016).

- Circulatory support, though rarely required when airway management and breathing support has been successful, may include measures such as cardiac compression and intravascular volume replacement.

- Drugs, with the exception of supplemental oxygen administered during respiratory support, are very rarely needed for transition support of newborn infants. They include adrenaline (epinephrine) and intravenous dextrose to correct hypoglycaemia during prolonged resuscitation.

- Temperature conservation measures - which aim to prevent hypothermia-induced suppression of postnatal metabolic and physiological transition processes - include maintaining a high ambient temperature in the birth room, and use of thermal mattresses, radiant warmers, hats and blankets (and use of occlusive wraps to minimise evaporative heat loss, particularly in preterm or low birth weight infants).

How the intervention might work

Assessment of the newborn infant (and intervention, if required) is performed to optimise metabolic and physiological transition from intra- to extra-uterine life. Birth room interventions aim to support respiration or ventilation to ensure pulmonary gas exchange and cardiac output sufficient for tissue oxygenation (Hooper 2016). Inadequate transition support may lead to worsening of hypoxia, with consequent metabolic acidosis and compromised cerebral perfusion and oxygen delivery that increases the risk of mortality and neurological morbidity.

Birth room interventions work in several different ways and, while some apply to most infants in most situations (e.g. positioning for the head or jaw to establish airway patency), other interventions may be disease-specific (e.g. early endotracheal airway placement to avoid intestinal gaseous distention for an infant with a congenital diaphragmatic hernia). Broadly, the level of support that may be needed is inversely related to the gestation of the newborn infant. Most term or near-term infants, who do not have additional complications such as meconium aspiration or infection, typically

need only basic transition-support measures such as airway positioning and stimulation.

Assessment and intervention at birth can vary by context and setting (Davis 2012; Perlman 2012). In low-income countries, lower levels of antenatal surveillance and care, and the prevalence of maternal conditions that affect both maternal health and fetal growth and well-being (e.g. maternal infection), influence the type of conditions that compromise the newborn infant and the type of interventions most appropriate to those settings (Singhal 2012; Umphrey 2018). Furthermore, the interventions available will differ according to health service resources, particularly in low-income countries where most infants are born at home and often without a trained birth attendant.

Why it is important to do this overview

International consensus guidelines for newborn resuscitation and transition support are aligned with participatory training programmes to standardise context-appropriate practices (Wyllie 2015; Wyllie 2016; Liley 2017). Evidence exists, however, of marked variation in the use of transition-support practices between neonatal centres internationally (El-Naggar 2012; Mann 2012; Singh 2013). Consensus guidelines and recommendations for birth room transition support are increasingly informed by evidence from Cochrane Reviews (Wyllie 2015; Wyllie 2016; Liley 2017). The validity and utility of guidelines and policy recommendations is dependent on the quality of the reviews. The methodological quality of Cochrane Reviews in several areas of health care, including perinatal and neonatal care, is variable (Al Faleh 2009; Wilhelm 2013). As with any other type of study, methodological weaknesses (low internal validity) may introduce bias and limit the external validity and applicability of the findings. Guidelines or policy recommendations based on evidence derived from flawed reviews, especially given the perceived status of Cochrane Reviews as “high-level evidence”, may drive or perpetuate poor practice and lead to adverse effects on outcomes for infants and families (Brok 2008; Meyer 2013).

Is an overview the correct approach?

Cochrane’s Comparing Multiple Interventions Methods Group’s “Editorial Decision Tree” suggests that an overview is an appropriate format to provide a “friendly front end” for users to access the synthesised evidence base (Methods Group’s Editorial Decision Tree). The overview will describe multiple reviews of birth room interventions for newborn infants, appraise their validity and applicability, and identify gaps within the current suite of Cochrane Reviews.

OBJECTIVES

We will describe and summarise Cochrane Reviews of birth room interventions for term or near-term newborn infants, and assess their methodological quality and the validity of their findings. We will map the evidence from Cochrane Reviews and identify important gaps in the evidence base. We will not compare multiple interventions with the intention of drawing inferences about their comparative effectiveness.

METHODS

Criteria for considering reviews for inclusion

We will include systematic reviews published in the *Cochrane Database of Systematic Reviews*, that assess birth room transition-support interventions (i.e. interventions delivered to the newborn in the same location as the birth took place) for term or near-term infants (those born at more than 34 weeks' gestation), including, but not limited to: airway support, ventilatory (breathing) support, circulatory support, drug interventions, and thermoregulatory interventions. Standard care, existing intervention, placebo, no treatment, an alternative intervention or any other comparator will be eligible.

We will assess reviews for inclusion based on the criteria specified by the review authors and we will report any discrepancies between inclusion criteria and trials included. Reviews including term and preterm infants will be eligible for inclusion and we will extract data on term and near-term infants where feasible. Reviews will be eligible for inclusion regardless of the number, type, and methodological quality of the studies included. Eligibility will not be restricted by outcomes reported. We will report the primary and secondary outcomes as defined in individual reviews; we anticipate that these will include mortality and major morbidity, including long-term neurodisability and impairment.

We will not include reviews of interventions that are more usually or feasibly delivered following admission of the newborn infant to the neonatal unit (if needed), or reviews of birth room interventions administered as part of routine practice to all infants.

Search methods for identification of reviews

We will search the lists of reviews published by Cochrane Neonatal and Cochrane Pregnancy & Childbirth, as available on their respective websites ([Cochrane Neonatal](#); [Cochrane Pregnancy and Childbirth](#)). No other databases will be searched. The search will be conducted independently by two overview authors (VW and JVEB). Any disagreements will be resolved through discussion. We will also consult the editorial teams of Cochrane Neonatal and Cochrane Pregnancy & Childbirth to ensure all relevant reviews are included. The study identification and selection process will be illustrated in a flowchart.

Data collection and analysis

We will use the standard methods of Cochrane for data collection and synthesis, according to the *Cochrane Handbook for Systematic Reviews of Interventions* ([Higgins 2011](#)).

Selection of reviews

Two overview authors (VW and JVEB) will assess the included systematic reviews independently. We will resolve any disagreement through discussion with a third author (WM) until consensus is reached.

“Out of date” reviews

Reviews will be assessed for eligibility regardless of publication date or date of the last search. For reviews older than five years (those published in 2013 or earlier), we will contact the corresponding author by email only to check if an update is planned or in progress, and inform them of our intention to include their review in our overview. We will make reasonable efforts to establish the current status of all reviews published before 2012. If two emails to the corresponding author (sent two weeks apart) do not receive a reply, we will contact the responsible editorial team to ascertain if the review in question is due to be updated or if an update is already in progress. We will document and publish the results of our enquiries. We will include a category of “status unclear” for any reviews older than five years for which we do not know the update status. If an update is planned or underway, we will include the review in a “being updated/update planned” category, and state a date when the update is expected whenever possible. If an update is not planned (as confirmed by the authors or editorial team, or both), we will distinguish between the following two categories of reviews.

- Reviews that are no longer being updated because the topic area is deemed to be fully understood or new evidence is highly unlikely to emerge: we will follow the authors' and editorial teams' assessment of this without running our own literature search for possible new evidence. For the purposes of our overview, these reviews will be deemed up-to-date (despite being older than five years old) and will be included in our synthesis.
- Reviews which the authors and editorial teams acknowledge should be updated but for which there are no current plans for updating: we will include these reviews in our overview in an “update needed” category and will include any updates in a future update of the overview. We will highlight these reviews to the responsible editorial team and urge them to prioritise these titles for updating.

Overlapping or competing reviews

We do not expect to find overlapping or competing reviews (i.e. reviews that address the same question or include some or all of the

same primary studies), as we are limiting our searches to Cochrane Reviews. Should we find two or more eligible reviews that address the same clinical question, we will only include the most recent one in our overview.

Protocols

Registered Cochrane protocols and titles will be identified and classified as “ongoing reviews”. We will contact the appropriate Cochrane editorial team to establish expected completion dates of any relevant reviews with published protocols.

Data extraction and management

We will extract the following data from each included Cochrane Review.

- Title, author, publication date, date of most recent search/update.
- Population (gestational age and birth weight, setting).
- Intervention(s) and comparator(s).
- Outcomes reported.
- Number of studies included.
- Number of participants included.
- Quality of the included studies (as assessed by the review authors).
- Results of the review, focusing on the following outcomes: death prior to hospital discharge, morbidity (necrotising enterocolitis, bronchopulmonary dysplasia, retinopathy of prematurity, infection), and neurodevelopmental outcomes at any time after discharge (most likely reported at 18 to 24 months and at school starting age).
 - Discrepancies between review protocol and publication (Page 2014).
 - Methodological quality, risk of bias, and any other limitations of the review.
 - GRADE assessments of certainty of evidence for review primary outcomes.

Data extraction will be carried out by one overview author and checked by another. Disagreements will be discussed or assessed by a third party until consensus is reached. Data will be extracted electronically into a piloted form and “Characteristics of included reviews” and “Overview of reviews” tables will be produced. We will contact the authors of eligible reviews to request any missing data, but will not attempt to make contact with authors of any of the primary studies included in eligible reviews.

Dual authorship

We may include Cochrane Reviews that were authored by members of the overview team. This is a potential source of bias (Büchter 2016). We will identify any Cochrane Reviews that share

one or more authors with this overview and ensure that the eligibility of such reviews is checked by a member of the of the overview team who is not affiliated with the review(s) in question. We will ensure similar procedures are in place for quality assessment of included reviews. The potential impact of including Cochrane Reviews affected by dual authorship will be addressed in the discussion of the overview.

Assessment of methodological quality of included reviews

We will use the AMSTAR 2 tool (Shea 2017; Appendix 1) to assess the methodological quality of the included reviews. To further assess the risk of bias of the systematic reviews, we will use the ROBIS tool (Whiting 2015; Appendix 2). Quality assessment will be carried out by one overview author and checked by another. Disagreements will be discussed until consensus is reached. In line with guidance provided by the developers of the AMSTAR 2 tool, we will not produce an overall quality score but will instead assess methodological quality as high/moderate/low/critically low (Shea 2017).

We will check included reviews against their protocols to enable assessment of methodological transparency and rigour. Particular attention will be paid to outcomes prespecified in the review protocol versus outcomes reported in the published review. Any discrepancies between protocols and published reviews that were not reported as amendments to the protocol in the publication will be reported.

We will not reassess the quality of included primary studies within reviews but instead will report study quality according to the review authors’ assessment. We will collect this information during the data extraction process, including the quality assessment tool used and the authors’ overall conclusions.

Data synthesis

We will provide a narrative description of the characteristics of the included Cochrane Reviews. We will organise the findings by group of neonates, wherever possible, as follows: interventions for neonates with perinatal asphyxia or with evidence of neonatal encephalopathy; interventions for neonates born near term; and interventions for other specific groups of ‘at risk’ neonates.

We will summarise the main results of the included reviews by categorising their findings using the framework adopted in a Cochrane overview of interventions to prevent cerebral palsy (Shepherd 2018), as follows.

- Effective interventions: the review found high-quality evidence of effectiveness for an intervention.
- Promising interventions (more evidence needed): the review found moderate-quality evidence of effectiveness for an intervention, but more evidence is needed.
- Ineffective interventions: the review found high-quality evidence of lack of effectiveness for an intervention.

- Probably ineffective interventions (more evidence needed): the review found moderate-quality evidence suggesting lack of effectiveness for an intervention, but more evidence is needed.

- No conclusions possible: the review found low- or very low-quality evidence, or insufficient evidence to comment on the effectiveness of an intervention.

We do not envisage undertaking indirect or mixed treatment comparisons within the overview but will assess if there is a need for a network meta-analysis to be undertaken at a later date.

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- * Indicates the major publication for the study

APPENDICES

Appendix I. AMSTAR 2

1. Did the research question and inclusion criteria for the review include the components of population, intervention, control group, and outcome (PICO)?
2. Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?
3. Did the review authors explain their selection of the study designs for inclusion in the review?
4. Did the review authors use a comprehensive literature search strategy?
5. Did the review authors perform study selection in duplicate?
6. Did the review authors perform data extraction in duplicate?
7. Did the review authors provide a list of excluded studies and justify the exclusions?
8. Did the review authors describe the included studies in adequate detail?
9. Did the review authors use a satisfactory technique for assessing the risk of bias in individual studies that were included in the review?
10. Did the review authors report on the sources of funding for the studies included in the review?
11. If meta-analysis was performed, did the review authors use appropriate methods for statistical combination of results?

12. If meta-analysis was performed, did the review authors assess the potential impact of risk of bias in individual studies on the results of the meta-analysis or other evidence synthesis?
13. Did the review authors account for risk of bias in individual studies when interpreting/discussing the results of the review?
14. Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?
15. If they performed quantitative synthesis, did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?
16. Did the review authors report any potential sources of conflict of interest, including any funding they received for the review?

Appendix 2. ROBIS

Phase 1: assessing relevance

Phase 2: identifying concerns with the review process

DOMAIN 1: study eligibility criteria

1. Did the review adhere to predefined objectives and eligibility criteria?
2. Were the eligibility criteria appropriate for the review question?
3. Were eligibility criteria unambiguous?
4. Were any restrictions in eligibility criteria based on study characteristics appropriate (e.g. date, sample size, study quality, outcomes measured)?
5. Were any restrictions in eligibility criteria based on sources of information appropriate (e.g. publication status or format, language, availability of data)?

DOMAIN 2: identification and selection of studies

1. Did the search include an appropriate range of databases/electronic sources for published and unpublished reports?
2. Were methods additional to database searching used to identify relevant reports?
3. Were the terms and structure of the search strategy likely to retrieve as many eligible studies as possible?
4. Were restrictions based on date, publication format, or language appropriate?
5. Were efforts made to minimise error in selection of studies?

DOMAIN 3: data collection and study appraisal

1. Were efforts made to minimise error in data collection?
2. Were sufficient study characteristics available for both review authors and readers to be able to interpret the results?
3. Were all relevant study results collected for use in the synthesis?
4. Was risk of bias (or methodological quality) formally assessed using appropriate criteria?
5. Were efforts made to minimise error in risk of bias assessment?

DOMAIN 4: synthesis and findings

1. Did the synthesis include all studies that it should?
2. Were all predefined analyses reported or departures explained?
3. Was the synthesis appropriate given the nature and similarity in the research questions, study design and outcomes across included studies?
4. Was between-study variation (heterogeneity) minimal or addressed in the synthesis?
5. Were the findings robust, e.g. as demonstrated through funnel plot or sensitivity analyses?
6. Were biases in primary studies minimal or addressed in the synthesis?

Phase 3: judging risk of bias

RISK OF BIAS IN THE REVIEW

1. Did the interpretation of findings address all of the concerns identified in Domains 1 to 4?
2. Was the relevance of identified studies to the review's research question appropriately considered?
3. Did the reviewers avoid emphasising results on the basis of their statistical significance?

CONTRIBUTIONS OF AUTHORS

All authors contributed to the development of the protocol.

DECLARATIONS OF INTEREST

JVEB: none known.

VW: none known.

WM: none known.

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Internal sources

- University of York, UK.

External sources

- Vermont Oxford Network, USA.

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