Guideline

Management of Threatened Preterm Labour

Summary To provide guidance on the assessment and management of women who present with signs and symptoms of threatened preterm labour prior to 37 weeks gestation.

Document type Guideline

Document number GL2022_006

Publication date 08 July 2022

Author branch Agency for Clinical Innovation

Branch contact (02) 9464 4711

Replaces GL2020_009

Review date 08 July 2027

Policy manual Not applicable

File number H22/12021

Status Active

Functional group Clinical/Patient Services - Baby and Child, Maternity

Applies to Local Health Districts, Chief Executive Governed Statutory Health Corporations, Specialty Network Governed Statutory Health Corporations, NSW Ambulance Service, Public Hospitals

Distributed to Ministry of Health, Public Health System, Divisions of General Practice, Government Medical Officers, NSW Ambulance Service, Private Hospitals and Day Procedure Centres, Tertiary Education Institutes

Audience Maternity Clinicians;Aboriginal Maternity Infant Health Services;Emergency Department

NSW Health

GUIDELINE

Management of Threatened Preterm Labour

GUIDELINE SUMMARY

This Guideline applies to all NSW Health Organisations and/or maternity services where women may present with signs and/or symptoms of threatened preterm labour.

The screening for risk factors associated with prevention and the management of preterm birth are outside the scope of this document.

KEY PRINCIPLES

NSW Health organisations are responsible for the implementation of this Guideline within their services / facilities to ensure local protocols or operating procedures are in place and aligned and consistent with this Guideline.

A comprehensive clinical assessment must be reviewed by the most senior obstetric clinician available and is essential to differentiate threatened preterm labour from preterm labour. The clinician must assess maternal and fetal wellbeing and to develop a comprehensive management plan.

Interventions for threatened preterm labour may include the use of corticosteroids, tocolytics, magnesium sulphate and antibiotics.

The use of tocolytic agents is restricted to when there is benefit from delaying preterm birth. There is greater benefit in delaying birth under 34 weeks' gestation.

Care at 23-25^{+6} weeks should be individualised and will depend on the risk to the woman from continuing the pregnancy and the management approach to care of the fetus after birth.

Women and their families must be provided with information and resources to guide shared decision making.

The Maternal Transfer Decision Making Tool is to be used to determine when an in-utero transfer is required and the subsequent process for effective transfer.

REVISION HISTORY

Version	Approved By	Amendment Notes
GL2022_006 July-2022	Deputy Secretary, Health System Strategy and Planning	Clarification of the preferred presentation of nifedipine and access to the preparation under the Special Access Scheme (SAS).
GL2020_009 April-2020	Deputy Secretary, Health System Strategy and Planning	Advice on clinical assessment and management of threatened preterm labour, administration of corticosteroid, tocolytics, magnesium sulphate and antibiotics, a maternal transfer decision making too.
PD2011_025 May-2011	Deputy Director, General Strategic Development	Updates and replaces PD2005_029.
PD2005_249 April-2002	Director General	Originally issues as a new policy under Circular 2002/49.

CONTENTS

1. BACKGROUND

Maternity care is coordinated across NSW and the ACT through formalised arrangements of Tiered Perinatal Networks (TPNs), local endorsed operational plans and escalation pathways in line with the NSW Health Policy Directive *Tiered Networking Arrangements for Perinatal Care in NSW* (PD2020_014) and NSW Health Guideline *Maternity and Neonatal Service Capability* (GL2022_022). These elements ensure care is provided at a facility with designated service capability for the woman's gestation and clinical complexity as close as possible to her home and supports.

Women who present with threatened preterm labour (TPL) may require transfer to higher level care. Transfer may be within or across tiered perinatal networks and optimal management of threatened preterm labour is essential to prevent preterm birth (PTB) at a maternity service with an inappropriate service capability.

A timely, coordinated multidisciplinary approach is required to optimise outcomes for the woman and fetus. Care must include rigorous clinical assessment, consultation and referral, and discussions with the woman specifically addressing the gestational age and any co-morbidities.

Preterm birth remains a major cause of perinatal morbidity and mortality especially at lower gestational ages. The incidence of preterm birth in NSW in 2018 was 7.5%, with a higher rate for Aboriginal women (11.1%)[1]. Approximately 65-75% of preterm births are spontaneous, and the majority are not preventable.

1.1. About this document

This document provides guidance on the assessment and management of women who present with signs and symptoms of threatened preterm labour. A consistent approach to the management of preterm labour could reduce the incidence of preterm birth and the associated consequences.

1.2. Key definitions

Fetal Fibronectin	A glycoprotein normally present in low concentrations in the cervico-vaginal secretions between 18 and 34 weeks' gestation, rising as term approaches.
Preterm	Preterm is gestational age less than 37^{+0} completed weeks with subcategories based on weeks of gestational age: • extremely preterm: less than 28 weeks gestational age • very preterm: 28 to less than 32 weeks gestational age • moderate to late preterm: 32 to less than 36^{+6} weeks gestational age.

Preterm birth	Occurs between 20^{+0} - 36^{+6} weeks' gestation.
Preterm Labour (PTL)	The presence of regular painful contractions, associated with cervical dilatation, between 20^{+0} - 36^{+6} weeks' gestation.
Preterm prelabour rupture of membranes	The spontaneous rupture of membranes, between 20^{+0} - 36^{+6} weeks' gestation.
Service capability	The scope of planned activity and clinical complexity a service is capable of safely providing. Each maternity and neonatal service has a designated service capability from Level 1 (no planned Maternity) to Level 6 (Tertiary Care). Local Health Districts are responsible for determining and maintaining the service capability of their maternity and neonatal services.
Threatened Preterm Labour (TPL)	The presence of regular uterine contractions and other signs and symptoms of labour (for example backache, pelvic pressure, or vaginal loss), between 20^{+0} - 36^{+6} weeks' gestation.
Tiered Perinatal Network (TPN)	A formalised arrangement between maternity and neonatal services within and across Local Health Districts in NSW and ACT that are linked with a tertiary (Level 6) hospital to provide support where higher level care is required. The tiered perinatal network recognises the capability, capacity, responsibilities and expertise of each facility in the network.

1.3. Relevant NSW Health Policies and Guidelines

This Guideline is to be read in conjunction with the following documents

Policy Number	NSW Health document
(PD2012_069)	Health Care Records - Documentation and Management
(GL2018_025)	Maternity - Fetal heart rate Monitoring
(PD2020_008)	Maternity - National Midwifery Guidelines for Consultation and Referral
(PD2020_014)	Tiered Networking Arrangements for Perinatal Care in NSW
(PD2020_018)	Recognition and management of patients who are deteriorating
(PD2020_047)	Incident Management
(GL2022_022)	Maternity and Neonatal Service Capability
Safety Notice 001/21	Discontinuation of nifedipine immediate release products (update)

2. RISK ASSESSMENT

There are known risk factors that increase the incidence of threatened preterm labour and preterm birth (Table 1). Despite this knowledge, threatened preterm labour remains largely unpredictable. For up to 50% of women who experience threatened preterm labour there is no identified cause[3]. Vigilant surveillance is essential in all pregnancies. Women are to be given information to help them recognise any variation from progress in a normal pregnancy, and when to seek advice from their maternity care provider.

Table 1: Risk factors for threatened preterm labour

Aspect	Risk factors associated with threatened preterm labour and preterm birth may include the following
Maternal characteristics	Age younger than 18 years or older than 35 years Ethnicity particularly indigenous, African and South East Asian, Maori / Pacific Islander populations Cigarette smoking and/or other substance use High levels of psychological stress Late or no health care during pregnancy Low socio-economic status Body mass index (BMI) <18 or >35
Medical and pregnancy conditions	Short cervical length Previous preterm birth Urinary tract infections Antepartum haemorrhage Assisted reproduction Preterm premature rupture of membranes (PPROM) Surgical procedures involving the cervix Polyhydramnios/ oligohydramnios Multiple gestation - N.B. 60% of twins are born preterm Chronic medical conditions Acute medical conditions (e.g., preeclampsia, antepartum haemorrhage) Fetal anomalies

The comprehensive antenatal assessment performed at the commencement of maternity care is the basis of ongoing care planning for the pregnancy.

Reference is to be made throughout the assessment to the NSW Health Policy *Maternity - National Midwifery Guidelines for Consultation and Referral* (PD2020_008).

Any risk factors identified for threatened preterm labour must be discussed with the woman and her family (as defined by the woman) to recommend the most appropriate lead maternity care provider, model and place of care. Risk assessment must occur at each episode of care.

3. COMMUNICATION

3.1. Information for women and shared decision making

All assessment and management strategies for threatened preterm labour are to be implemented in an environment that supports informed choice and shared decision making. A woman's decisions about her care must reflect her self-determination, autonomy and control.

There will be occasions where the gestation of the pregnancy and/or the clinical complexity may contradict active efforts to suppress preterm labour. These situations will require a multidisciplinary discussion with the woman and her family. This will inform them of the options and aid the development of an agreed care plan for mother and fetus. This plan must be reviewed regularly as the clinical situation evolves.

Women describe threatened preterm labour as a stressful experience especially when it involves a transfer away from their family and support structures[21]. Women may require additional support through social work, Aboriginal liaison, multicultural or other support services during or after the decision-making process. Social work services can provide advice and assistance for families about accommodation and travel support.

Maternal transfer must be a shared decision between clinicians, the women and her family. It must consider the risks and benefits for the mother and fetus. Where a maternal transfer is clinically appropriate the destination hospital is to be selected taking into consideration the women and her family's preference.

Providing women and their families with culturally appropriate, evidence-based information can improve their experience and guide shared decision making. A valuable resource for women and their families is *Birth Before 32 Weeks: What to expect when your baby is born prematurely* (Pregnancy and newborn Services Network, Sydney Children's Hospital Network, 2018).

3.2. Aboriginal women

Aboriginal women have a higher rate of threatened preterm labour and/or preterm birth than non-Aboriginal women[4]. When clinical risks are identified for an Aboriginal woman and she needs to be transferred to another facility for assessment of threatened preterm labour and preterm birth she may require additional support. This may include Aboriginal health professionals such as Aboriginal liaison officers, health workers or other culturally specific services.

It is important to discuss all aspects of care with Aboriginal women in a culturally sensitive, respectful and supportive manner. It is also important to engage and work in partnership with Aboriginal women and where appropriate involve their family.

3.3. Documentation

The management of threatened preterm labour will involve a multidisciplinary team and consultation with the responsible tiered perinatal network when higher level care is required. All clinical assessments and discussions between care providers and the woman must be documented.

This must be current, accurate and available to provide adequate information between maternity care providers. If this is unable to be shared electronically between facilities a written document with all required information is to accompany the woman if transfer occurs.

4. CLINICAL ASSESSMENT OF THREATENED PRETERM LABOUR

Many of the signs of threatened preterm labour are common in pregnancy and may be benign. These signs may include mild irregular uterine tightening / contractions, changes in vaginal discharge, backache, loose bowel motions, vaginal or pelvic pressure, and cramping.

The accurate identification of women in preterm labour will direct appropriate management and care. Just as importantly, the accurate identification of women not in preterm labour and with a low likelihood of birth, prevents unnecessary interventions and transfers.

4.1. Clinical assessment for diagnosis of threatened preterm labour

A comprehensive clinical assessment is essential to differentiate threatened preterm labour from preterm labour and to determine the likelihood of birth within the next seven days. The assessment must also determine maternal and fetal wellbeing (Appendix 1).

The most senior obstetric clinician available is to review the comprehensive clinical assessment of the woman, review fetal wellbeing and document an ongoing management plan. When there is a high likelihood of birth and the clinical presentation is outside the service capability of that facility, the management plan is to include consideration for transfer to higher level care.

4.1.1. Fetal fibronectin testing

Fetal fibronectin (fFN) is a glycoprotein, thought to promote adhesion between the fetal chorion and maternal decidua. It is normally present in low concentrations in the cervico-vaginal secretions between 18 and 34 weeks' gestation, rising as term approaches.

Quantitative fetal fibronectin testing may improve assessment of risk of preterm birth, reduce transfer where there is a low likelihood of birth and reduce longer term costs and burden for women and families[5].

Levels of maternity services are defined in NSW Health Policy Directive *Tiered Networking Arrangements for Perinatal Care in NSW* (PD2020_014) and NSW Health Guideline *Maternity and Neonatal Service Capability* (GL2022_022). Facilities of Level 4, 5 and 6 service capability must utilise the quantitative fetal fibronectin testing method. For facilities of Level 3 service capability either qualitative or quantitative testing may be considered. Facilities in more rural and isolated locations, consideration are to be given to adopting quantitative testing to inform decision making where transfer requirements are more complex.

Contraindications to fetal fibronectin testing include vaginal bleeding, cervical cerclage in-situ, following rupture of membranes, or in the presence of soaps, gels, lubricants or semen in the vagina.

When a woman is assessed for threatened preterm labour using point of care testing, she must be admitted. This will ensure the result of fetal fibronectin is uploaded to the electronic medical record.

Clinical management planning is to be guided by the fetal fibronectin results (Appendix 3):

- A result >50 nanogram/mL with signs of threatened preterm labour is considered positive and the woman must be admitted. Management planning is to be directed by gestation, clinical presentation, facility location and service capability.
- A result <=50 nanogram/mL is considered negative with a low likelihood of birth within 7 days (<5%). Ongoing admission following point of care testing is not required provided there are no other risk factors / indications.

The Maternal Transfer Decision Making Tool in the NSW Health Policy Directive *Tiered Networking Arrangements for Perinatal Care in NSW* (PD2020_014) is to be used to determine the priority rating to guide decision making for timing of transfer if required. (Appendix 2).

4.1.2. Cervical length assessment

Assessment of cervical length can be a useful adjunct in the assessment of threatened preterm labour especially when assessment using fetal fibronectin is contraindicated.

If cervical length assessment is available and utilised, the following principles are to be considered:

- Assessment of measurements is to be performed by qualified or credentialed clinicians.
- Reliable recording of images and reporting of the results are to occur.
- Local procedures must be available to guide decision making using cervical length.

4.1.3. Assessing the need for admission

The decision regarding the need for ongoing inpatient admission or transfer of a woman must consider her history, results of clinical assessments and investigations and service capability of the facility. Differential diagnoses with similar clinical signs and symptoms are to be considered during management and decision making.

Clinical judgement is to be combined with multidisciplinary consultation (including tiered perinatal network clinicians if appropriate) and discussion with the woman to make a management plan. The woman must be provided with clear advice about threatened preterm labour. The management plan and the woman's choices are to be documented in the medical record.

5. MANAGEMENT OF THREATENED PRETERM LABOUR

Maternal transfer must be a shared decision between clinicians, the woman and her family.

5.1. Planning care

Antenatal steroids, magnesium sulphate and appropriate transfer are the main strategies to prevent adverse neonatal outcomes. Tocolysis may be utilised to facilitate steroid / magnesium treatment and/or transfer. Management options will depend on:

- gestational age
- availability of facility resources (equipment and staff)
- service level of the facility, and availability and timeliness of transfer options
- individual clinical circumstances and the woman's preferences.

If further advice is required, consultation with a senior obstetrician from the tiered perinatal network must occur as per the tiered perinatal network operational plan.

Administration of tocolytic agents are to be restricted to women when there is benefit from delaying preterm birth. Generally, there is greater benefit in delaying birth under 34 weeks' gestation.

5.2. In-utero transfer

If preterm labour is diagnosed the woman must be admitted for ongoing care and may require transfer to higher level care. The tiered perinatal network operational plan must be referred to if transfer is required and the maternal decision making tool (refer to NSW Health Policy Directive *Tiered Networking Arrangements for Perinatal Care in NSW* (PD2020_014)) used to determine the level of urgency of the transfer (Appendix 2).

Women and their families are to be actively involved in the transfer decision and informed of the approximate travel time to the receiving facility and the risk of birth during transfer. The woman may benefit from the company of family and support people (Appendix 4).

5.3. Administration of corticosteroids

Administration of corticosteroids is known to reduce fetal mortality and morbidity; specifically relating to, neonatal respiratory distress syndrome (RDS), intraventricular haemorrhage, early sepsis and necrotising enterocolitis[8].

Corticosteroids are recommended for women under 34^{+6} weeks' gestation with preterm labour, where active neonatal care is planned, and birth is likely within the next 7 days. A single course of corticosteroids reduces the risk of respiratory distress syndrome from 26% to 17% [8,9,10].

Exceptions to these gestational limits are to be considered after consultation in the tiered perinatal network with a senior obstetric consultant, neonatologist and the woman and her family (Appendix 5).

5.4. Tocolysis

Administration of tocolytic agents must be restricted to women when there is benefit from delaying preterm birth. Generally, there is greater benefit in delaying birth under 34 weeks' gestation.

The approach to tocolysis at 23 - 25^{+6} weeks are to be individualised and will depend on the risk to the woman from continuing the pregnancy and the management approach to care of the fetus after birth. The management approach for the fetus is made after the options for interventions are discussed by the neonatal intensive care team, the maternity team and the woman and her family.

The primary aim for the use of tocolytics is to delay preterm birth for up to 48 hours. This provides time for: administration of maternal corticosteroid therapy to promote fetal lung maturation, maternal transfer for higher level care and for the administration of magnesium sulphate for fetal neuro-protection if indicated. Maternal corticosteroids and birth at an appropriate facility significantly improve neonatal outcomes[12] (Appendix 6).

5.4.1. Contraindications to tocolytics

Supressing preterm labour may be potentially harmful if there are adverse maternal and/or fetal conditions. Maternal conditions include significant antepartum haemorrhage, severe pre-eclampsia, severe maternal cardiac disease, or evidence of chorioamnionitis. When there is cervical dilatation greater than three centimetres, suppression of labour may be less effective. Tocolysis must be individualised according to gestation and maternity service capability.

There may be contraindications to tocolysis in the presence of the following fetal conditions: proven intrauterine growth restriction, fetal death in-utero, lethal fetal conditions, preterm premature rupture of the membranes without uterine activity, a gestation less than 23 weeks[2] and when active neonatal care is not being considered. Discussions must occur within the tiered perinatal network and with the woman and her family.

5.4.2. Choice of tocolytic

If tocolysis is considered of benefit in the management of threatened preterm labour a calcium channel blocker that relaxes smooth muscle is considered first line therapy and nifedipine is most commonly used.

Compared to Beta Agonists nifedipine is associated with fewer side effects and improved neonatal outcomes[11,12]. Nifedipine is only to be used for up to 48 hours as evidence indicates maintenance treatment after threatened preterm labour does not prevent preterm birth or improve maternal or infant outcomes[13,14] (Appendix 6).

For further information see Safety Notice 001/21 *Discontinuation of nifedipine immediate release products (update*).

Note: Tocolysis is not an approved indication for use of nifedipine. Its use is therefore considered off-label i.e., the use of a registered medication that is not included in the TGA approved product information or which is disclaimed in the product information.

For further information refer to *Rethinking Medicines Decision-Making in Australian Hospitals: Guiding Principles for the quality use of off-label medicines* (Council of Australian Therapeutic Advisory Groups. November 2013).

5.5. Magnesium sulphate for neuroprotection

Evidence suggests that magnesium sulphate, when given to women shortly before birth reduces the risk of cerebral palsy and protects gross motor function in infants born preterm[15,16,17]. The effect may be greatest at early gestations and is not associated with adverse long-term fetal or maternal outcomes[16,18]. Therefore, magnesium sulphate is recommended for women prior to 30^{+0} weeks' gestation where preterm birth is expected or planned within 24 hours (Appendix 7).

5.6. Antibiotics

Routine administration of prophylactic antibiotics is not recommended for women in threatened preterm labour with intact membranes and without evidence of infection[17,19,20].

For women with ruptured membranes, clinical chorioamnionitis and/or preterm labour when Group B Streptococcus (GBS) status is unknown, antibiotics must be given as per local clinical guidelines.

6. SUBSEQUENT MANAGEMENT

When preterm birth does not occur following admission for preterm labour, coordination of ongoing care and discharge planning with the women and her family, relevant health care professionals and the referring hospital (as required) is essential (Appendix 8).

7. REFERENCES

1. Centre for Epidemiology and Evidence 2019, *Centre for Epidemiology and Evidence: Services and Programs*, NSW Ministry of Health, Sydney.
2. Meertens, L., van Montfort, P., Scheepers, H., et al. 2018, 'Prediction models for the risk of spontaneous preterm birth based on maternal characteristics: a systematic review and independent external validation.', *Acta Obstet Gynecol Scand*.
3. Iams, J. 2014, 'Prevention of preterm parturition.', *New England Journal Medicine.*, vol. 370, no. 19
4. Centre for Epidemiology and Evidence. 2018, *New South Wales Mothers and Babies 2017*, NSW Ministry of Health, Sydney.
5. Abbott, D., Radford, S.K., Seed, P.T., Tribe, R.M., Shennan, A.H. 2013, 'Evaluation of a quantitative fetal fibronectin test for spontaneous preterm birth in symptomatic women. ', *Am J Obstet Gynecol*, vol. 208, no. 2.
6. Kagan, K., Sonek, J. 2015, 'How to measure cervical length', *Ultrasound Obstet Gynecol* vol. 45, pp. 358-62
7. Di Renzo, G.C., Cabero Roura, L., Facchinetti, F., Helmer, H., Hubinont, C., Jacobsson, B., Jørgensen, J.S., Lamont, R.F., Mikhailov, A., Papantoniou, N., Radzinsky, V., Shennan, A., Ville, Y., Wielgos, M. & Visser, G. 2017, 'Preterm Labor and Birth Management: Recommendations from the European Association of Perinatal Medicine', *The Journal of Maternal-Fetal & Neonatal Medicine*, vol. 30, no. 17, pp. 2011-30.

8. Roberts, D., Brown, J., Medley, N., Dalziel, S. 2017, 'Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth.', Cochrane Database Syst Rev. CD004454 (3).

9. Antenatal Corticosteroid Clinical Practice Guidelines Panel 2015, Antenatal corticosteroids given to women prior to birth to improve fetal, infant, child and adult health: Clinical Practice Guidelines., Liggins Institute, The University of Auckland, Auckland New Zealand.

10. Lawn, J., Segre, J., Buekens, P., Althabe, F., Belizan, J.M., Jobe, A.H., Brooke, S., Hodkins, S., de Graft Johnson, J. 2012, 'Case study for the United Nations Commission for Life-Saving Commodities for Women and Children', *Antenatal Corticosteroids for the Reduction of Deaths in Preterm Babies*.

11. Conde-Agudelo, A., Romero, R., & Kusanovic, J.P. 2011, 'Nifedipine in the management of preterm labor: a systematic review and metaanalysis', *Am J Obstet Gynecol*, vol. 204, no. 2, pp. 131-20.

12. Flenady, V., Wojcieszek, A.M., Papatsonis, N.M.D., Stock, O.M., Murray, L., Jardine, L.A., & Carbonne, B. 2014, 'Calcium channel blockers for inhibiting preterm labour and birth', *Cochrane Database of Systematic Reviews (7)*.

13. Gaunekar, N.N., Raman, P., Bain, E., & Crowther, C. 2013, 'Maintenance therapy with calcium channel blockers for preventing preterm birth after threatened preterm labour', *Cochrane Database of Systematic Reviews, CD004071(10)*

14. van Vliet, E., Dijkema, G., Schuit, E., Heida, K., Roos, C., van der Post, J., Parry, E., McCowan, L., Lyell, DJ., El-Sayed,YY., Carr, D., Clark, AL., Mahdy, ZA., Uma, M., Sayin, N.C., Varol, G.F., Mol, B.W., Oudijk, M.A. 2016, 'Nifedipine maintenance tocolysis and perinatal outcome: an individual participant data meta-analysis', *BJOG: An International Journal of Obstetrics & Gynaecology*, vol. 123, pp. 1753-60.

15. Crowther, C., Middleton, P.F., Voysey, M., Askie, L., Duley, L., Pryde, P.G., Marret, S., Doyle, L.W. 2017, 'Assessing the neuroprotective benefits for babies of antenatal magnesium sulphate: An individual participant data meta-analysis.', *PLoS Med.*, vol. 14, no. 10.

16. Doyle, L., Crowther, C.A., Middleton, P., Marret, S., Rouse, D. 2009, 'Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus', *Cochrane Database of Systematic Reviews, CD004661.pub3*

17. Shepherd, E., Salam, R.A., Middleton, P., Makrides, M., McIntyre, S., Badawi, N., Crowther, C.A. 2017, 'Antenatal and intrapartum interventions for preventing cerebral palsy: an overview of Cochrane systematic reviews.', *Cochrane Database Syst Review CD005528.* no. 6.

18. Doyle, L., Anderson, P.J., Haslam, R., Lee, KJ., Crowther, C. 2014, 'School-age outcomes of very preterm infants after antenatal treatment with magnesium sulfate vs placebo ', JAMA, vol. 312, no. 11, pp. 1105-13.

19. Flenady, V., Hawley, G., Stock, O.M., Kenyon, S., Badawi, N. 2013, 'Prophylactic antibiotics for inhibiting preterm labour with intact membranes ', *Cochrane Database of Systematic Reviews*, no. 12.

20. The Royal Australian and New Zealand College of Obstetricians and Gynaecologists. 2016, 'Maternal Group B Streptococcus in pregnancy: screening and management.', vol. C-Obs-19

21. Lewis, M., Passant, L., Cooke, H., Challis, D. 2019. Women's antenatal transfer experience study (WANTe) – exploring women's experience of in-utero transfer for threatened preterm labour in NSW. Women and Birth, Vol 32, Supp 1.

8. APPENDIX LIST

1. Clinical Assessment of Threatened Preterm Labour
2. Maternal Transfer Decision Making Tool
3. Fetal Fibronectin Testing
4. In-utero Transfer: 23 – 28 Weeks Gestational Age
5. Administration of Corticosteroids
6. Tocolysis – Use of Nifedipine for Suppression of Preterm Labour
7. Magnesium Sulphate for Neuroprotection
8. Subsequent Management

8.1. Appendix 1: Clinical Assessment of Threatened Preterm Labour

Aspect	Consideration
Context	Threatened preterm labour is diagnosed by: • the presence of regular painful uterine contractions >2 contractions every 10 minutes that last more than 30 seconds • contractions are accompanied by cervical change: dilatation <3 cm and/or effacement • Positive fFN >50ng/mL. The most senior obstetric clinician available are to review the comprehensive clinical assessment of the woman, fetal wellbeing and document an ongoing management plan.
History	Medical, surgical, obstetric, psychosocial and lifestyle risk factors associated with preterm birth
Signs and symptoms	Shortening of the cervix is the most common sequence preceding preterm birth, followed by decidual membrane activation, then contractions characterised by: • Cervical effacement / dilatation • Pelvic pressure / low back pain • Lower abdominal cramping • Vaginal loss (mucous, blood or fluid) • Regular uterine activity

Physical examination	• Maternal vital signs
	• Abdominal examination to assess tone, tenderness, fetal size and position
	• Assessment of contraction frequency, duration and intensity
	• Speculum examination using an aseptic technique (using a wet, non-lubricated speculum) to:
	  ○ visualise cervix and estimate cervical dilation; more than 3 cm differentiates the diagnosis between threatened and actual preterm labour
	  ○ evaluate membrane status (intact or ruptured) and assess liquor
	  ○ obtain cervico-vaginal fluid for fFN testing (see Section 4.1.1)

Fetal surveillance	• Preterm uterine activity requires continuous electronic fetal monitoring (EFM) in line with NSW Health Guideline *Maternity – Fetal Heart Rate Monitoring* (GL2018_025). • Concerns for fetal wellbeing may require ultrasound assessment if feasible, accessible and will not delay required treatment. • Electronic fetal monitoring and interpretation of fetal heart rate features at very early gestations (<25 weeks) are to be in consultation within the tiered perinatal network and due consideration of the woman's decision.
Investigations	• High vaginal swabs for microscopy, culture and sensitivity (MC&S). • Combined low vaginal / anorectal swab for Group B Streptococcus in line with NSW Health Guideline *Maternity – Maternal Group B Streptococcus (GBS) and minimisation of neonatal early-onset GBS sepsis* (GL2017_002). • Obtain cervico-vaginal fluid for fFN testing, refer to Appendix 3 Fetal Fibronectin Testing • Midstream specimen of urine for bacteriology (MC&S).

Considerations	• Avoid digital examination unless the cervix cannot be adequately visualised or if the information is urgently needed (e.g., abnormal fetal heart rate pattern, probable advanced phase of active labour) and where placenta praevia is unlikely. • Obstetric ultrasound examination for fetal, placental, and maternal anatomic abnormalities; confirmation of fetal presentation; estimation of amniotic fluid volume and fetal weight. This information may be used for counselling the woman about the potential causes and outcomes of preterm birth and determining the best mode of birth. • Clinical care and management of preterm birth must not be delayed if appropriately skilled personnel or equipment are not immediately available.

8.2. Appendix 2: Maternal Transfer Decision Making Tool

MATERNAL TRANSFERS DECISION MAKING TOOL					
Maternity Priority	MP1*	MP2*	MP3	MP4	MP5
Medically Agreed time frame (Time by which woman should be receiving higher level care)	Immediate Midwifery/ Medical escort required	< 3 hours Midwifery/ Medical escort required	< 12 hours Midwifery escort required	24 hours	72+ hours Consultation or referral or back transfer
Transport determined by local LHD	NSW Ambulance/ ACC immediate dispatch	NSW Ambulance/ ACC	NSW Ambulance/ ACC/ PTS	PTS/ Private Provider	PTS/ Private Provider
Preterm Labour (PTL)	>26 progressive dilation >3 cm (if safe)**	Dilated 1-3cm	Dilated <1 cm and labour suppressed		
(Regular contractions with any cervical change)	23^{+0} – 26^{+0} With imminent birth	Gestation as per tiered perinatal network operational plan			<23 weeks
Threatened preterm labour (TPL), closed cervix – quantitative fFN			≥200 ng/mL	50-199 ng/mL	< 50 ng/mL or short cervix without symptoms
APH (stable) in absence of uterine activity				≥ 23 weeks as per operational plan	Consult / referral
PPROM (without labour)				≥ 23 weeks as per operational plan	< 23 weeks
Multiple pregnancies	The above conditions in multiple pregnancies should be considered as one MP category higher than for singleton pregnancy				Consult / referral
Maternal condition	Deteriorating +/- Planned urgent birth**	Maternal Deterioration whereby birth likely required within 12-24 hours			Consult / referral
Fetal condition	Deteriorating +/- Planned urgent birth**	Fetal Deterioration whereby birth likely required within 12-24 hours			Consult / referral

***Requires consultation with Obstetric Consultant**

ACC – Aeromedical Control Centre
APH – Antepartum Haemorrhage
Fetal Condition – e.g., growth restriction
FFN – Fetal Fibronectin
Maternal Condition – deterioration may increase MP
Medically Agreed timeframe – transfer to higher care may be impacted by geographical conditions

****May benefit from advice with the SOC Statewide Obstetric Consultant**

Multiple Pregnancy – twins, triplets, quadruplets
PTL – Preterm labour
PPROM – Preterm premature rupture of membranes
PTS – Patient Transport Service
TPL – Threatened Preterm Labour – if cervical changes overtime becomes PTL.

8.3. Appendix 3: Fetal Fibronectin Testing

Quantitative fetal fibronectin testing may improve assessment of overall risk, reduce transfer where there is a low / very low likelihood of birth and ultimately reduce longer term costs and burden for women and families.

Aspect	Consideration
Context	• Fetal fibronectin (fFN) is normally present in low concentrations in the cervico-vaginal secretions between 18 and 34 weeks' gestation, rising as term approaches. • The risk of preterm birth is increased with elevated levels of Fetal fibronectin (typically > 50 ng/mL) in cervico-vaginal secretions after 22 weeks' gestation
Indications	Symptomatic threatened preterm labour between 23^{+0} and 36^{+0} weeks' gestation **and** Intact membranes **and** Cervical dilatation less than or equal to 3 cm **and** Where knowledge of result will change the clinical management
Contraindications	• Cervical dilatation more than 3 cm • Ruptured membranes • Bleeding • Cervical cerclage in-situ • Presence of soaps, gels, lubricants, disinfectants, semen in the vagina
Relative contraindications	Potential for **FALSE NEGATIVE RESULT** • After the use of lubricants or antiseptics Potential for **FALSE POSITVE RESULT** • Within 24 hours of sexual intercourse or digital cervical examination
Procedure	• Performed during sterile speculum examination prior to any examination or manipulation of the cervix or vagina • Use only sterile water as a lubricant • Obtain the sample for testing from the posterior fornix of the vagina as per test kit instructions
Quantitative fetal fibronectin testing	Quantitative Fetal fibronectin testing can: • Quantify the likelihood of preterm birth • Assist with risk assessment and planning • Avoid unnecessary interventions • Identify women for targeted interventions • Provide reassurance to health care providers and the woman Admit the woman undergoing assessment for threatened preterm labour using point of care testing to ensure the result of Fetal fibronectin is uploaded into the electronic medical records.
Imminent birth	Fetal fibronectin assessment is **not required** when birth is imminent **(*MP1 category – see Appendix 2** Maternal Transfer Decision Making Tool)

Interpreting fetal fibronectin results	Action
Fetal fibronectin ≥200 ng/mL (29% chance birth WILL occur <14 days)	As for all women requiring admission **and** Commence tocolysis if delay of birth indicated and no contraindications **(*MP3 category – see Appendix 2** Maternal Transfer Decision Making Tool)
Fetal fibronectin 50 – 199 ng/mL (8% chance birth WILL occur <14 days)	As for all women requiring admission **and** • Consider tocolysis if delay of birth indicated and no contraindications • Consider all clinical circumstances including previous history of PTB (***MP4 category – see Appendix 2:** Maternal Transfer Decision Making Tool)
Fetal fibronectin <50 ng/mL (negative) (98% chance birth will NOT occur <14 days)	Ongoing admission following point of care testing is not required provided there are no other risk factors / indications. Arrange follow up and provide the women with targeted information (***MP5 category – see Appendix 2:** Maternal Transfer Decision Making Tool)

8.4. Appendix 4: In-utero Transfer: 23 – 26 weeks Gestational Age

Context	• If transfer is required, reference should be made to the tiered perinatal network operation plan and escalation pathways to coordinate advice and/or transfer arrangements. • Refer to Appendix 2 Maternal Transfer Decision Making Tool during discussions to determine the need for transfer, the most appropriate facility for transfer and the time frame that this should occur within. • All decision-making should be between the most senior obstetric clinician at both the referring and the accepting facilities. • The Patient Flow Portal (PFP) should be accessed to determine bed capacity at the most suitable facility for the presenting clinical situation.
Principles for transfer **23 – 26 weeks' gestational age**	• Accept a greater level of risk of birth occurring en-route when gestational age is 23–26 weeks because the benefit of birth in a tertiary hospital is substantial. • Intubation and/or full resuscitation is not generally feasible within a transport vehicle, especially aircraft. Neonatal care should include keeping baby warm using skin to skin care (if possible) and respiratory support.
	• Accountability and responsibility for transfer decisions and their outcomes reside with the transferring and receiving consultants.
	• Recognise that retrieval support may not be immediately available (e.g. due to traffic, pilot and crew hours, weather or aircraft service needs).
	• Decisions about transfer may be escalated by receiving or transferring clinicians as required. • Reassess the woman after initial stabilisation to review timelines around transfer decisions, particularly if there are delays in transfer or transfer is not immediately feasible.

	The transferring obstetrician is responsible for ensuring:
	• the risks and benefits of in-utero transfer are discussed with the woman and her family including the limited resuscitation that may be provided should birth occur en-route.
	• comprehensive documentation in the health record and transfer documents regarding:
	  ○ discussions with the woman and her family about the transfer including limited resuscitation if birth occurs en-route
	  ○ clinical assessment of the woman and the assessed risk of preterm birth
	  ○ discussions between receiving and transferring clinicians about the planned transfer.

	The tiered perinatal network will coordinate a combined services audit of births of 23 – 26 weeks' gestational age occurring outside a Level 6 neonatal unit
Recommendation	• When transfer is indicated, aim for in-utero transfer wherever possible. If gestational age is 23–26 weeks, accept a high level of risk for birth en-route unless such transfer puts the mother's life at risk
	• If clinically appropriate, use tocolysis to allow in-utero transfer

8.5. Appendix 5: Prescription and Administration of Corticosteroids

Administration of corticosteroids is known to reduce fetal mortality and morbidity; specifically relating to neonatal respiratory distress syndrome (RDS), intraventricular haemorrhage, early sepsis and necrotising enterocolitis[8]. A single course of corticosteroids reduces the risk of respiratory distress syndrome from 26% to 17%[8,9,10].

Purpose	To facilitate lung maturation to reduce neonatal morbidity and mortality associated with prematurity.
Recommendation	• Corticosteroids **are** recommended for women under 34^{+6} weeks gestation with threatened preterm labour and where neonatal resuscitation is planned and birth is likely within the next 7 days. • Where there is a low likelihood of birth with a negative fetal fibronectin of <50 ng/mL routine prophylactic administration of corticosteroids is **not** recommended

Betamethasone Injection
***Celestone Chronodose®**
	• **Presentation**: Injection is a sterile aqueous suspension
	• **Administration**: Betamethasone 22.8 mg by intramuscular injection (IM) in divided doses completed between 12 and 36 hours
	  ○ **1st dose**: Betamethasone 11.4mgs IM
	  ○ **2nd dose**: Betamethasone 11.4mgs IM 24 hours later, if birth has not occurred.
	Full corticosteroid cover is achieved 24 hours after administration of the second dose of betamethasone, although some benefit is achieved within 8 hours of the initial dose.

Repeat antenatal corticosteroids	• The clinical decision to use a repeat course of corticosteroids should be based on an assessment of ongoing risk for preterm birth. • Where appropriate, estimate the risk of preterm birth by considering the use of additional prediction tests including fetal fibronectin and assessment of cervical length.
Special considerations	Women with pre-existing or gestational diabetes are at risk of altered blood glucose levels with the administration of corticosteroids. Endocrinologist/ obstetric medicine advice should be sought to guide optimal control of blood glucose levels.
***Alternatively, if Celestone Chronodose® is not available**	
Dexamethasone	• Give dexamethasone phosphate 24 mg in divided doses (dexamethasone 6mg IMI 6th hourly). • Full corticosteroids cover is achieved 48 hours after administration of the fourth dose of Dexamethasone.

8.6. Appendix 6: Tocolysis – Use of Nifedipine for Suppression of Threatened Preterm Labour

Nifedipine has potential to cause fetal hypoxia associated with maternal hypotension. This effect is exacerbated when other blood pressure lowering medicines are being taken by the mother.

Caution must be exercised if nifedipine and magnesium sulphate are used at the same time as nifedipine may increase the effects of magnesium sulphate and the risk of hypotension. These circumstances will require monitoring of BP, deep tendon reflexes and respiratory function.

Purpose	To delay the progress of preterm labour and birth to facilitate: • administration of corticosteroids • transfer to higher level care as required. • administration of magnesium sulphate for neuro protection.
Drug committee approval	Tocolysis is an off-label indication for use of nifedipine and informed consent should be obtained.
Presentation	10mg nifedipine immediate release tablet (medium acting) is the preferred presentation. See Safety Notice 001/21 *Discontinuation of nifedipine immediate release products (update).*
Administration	• Nifedipine tablets should be swallowed whole. • Onset of tocolysis usually occurs within 30-60 minutes. • Dose may vary with clinical situations and should be titrated against tocolytic effect.
Initial Dose	20mg nifedipine orally stat
If contractions persist after 60 minutes	20 mg nifedipine orally may be given at 30 minute intervals for a total of three (3) doses if required and the BP is stable.
Maintenance dose	• A maintenance dose of 20 to 40mg every 6 hours may be given, depending on uterine activity and other clinical circumstances. • **Maximum dose of 160 mg in 24 hours.** • Continue maintenance dose for 48 hours or until 24 hours after second dose of corticosteroids, whichever is sooner. Decisions about cessation of treatment will be made on an individual basis and need to consider location, steroid cover and gestational age.
Maximum dose	**160mg in 24 hours**
Adverse effects	Hypotension, tachycardia, palpitations, flushing, headache, dizziness, nausea.

Maternal observations	**Acute Phase** (uterine activity detected): • Observations every 30 minutes: blood pressure, temperature, pulse, respiratory rate. **Maintenance Phase** (when contractions have ceased) • Observations may be reduced to minimum of 4 hourly during tocolytic maintenance. • Report systolic BP <100mm Hg, pulse rate >100bpm, temperature >37.5 Celsius. Document on SMOC and implement local CERS as required for any observations that are not *Between the Flags.*
Fetal monitoring	• Continuous EFM during acute phase. • If the fetal heart rate (FHR) pattern is normal, FHR can be recorded hourly with doppler during maintenance phase.

Contraindications	These include situations where prolonging the pregnancy is contraindicated, including but not limited to the following:
	• Known sensitivity to nifedipine.
	• In-utero fetal death / lethal fetal abnormalities / suspected fetal compromise.
	• Severe maternal cardiac disease.
	• Where maternal condition is compromised:
	  ○ bleeding with haemodynamic instability
	  ○ placental abruption
	  ○ severe pre-eclampsia
	  ○ chorioamnionitis.

Overdose symptoms	The most common symptoms of overdose are: • disturbed consciousness • hypotension • tachycardia / bradycardia • hyperglycaemia • metabolic acidosis • cardiogenic shock with pulmonary oedema.
Caution	**This guidance is based on administration of the immediate release tablet (medium acting) is the preferred preparation.** **If alternate preparations (immediate release capsules, or slow / extended-release tablets) are used the same safety and efficacy described cannot be guaranteed.**
NB: Nifedipine is only available for use in Australia under the Special Access Scheme (SAS). Hospitals will need to make arrangements through their individual Pharmacy Departments for availability and access to either of these products for emergency use. The prescriber will be required to complete a Category A form and obtain patient informed consent for use.	

8.7. Appendix 7: Magnesium Sulphate for Neuroprotection

Magnesium sulphate given to mothers shortly before birth is believed to reduce the risk of cerebral palsy and protect gross motor function in those infants born preterm[15]. The effect may be greatest at early gestations and is not associated with adverse long-term fetal or maternal outcome[16,18].

Magnesium Sulphate Heptahydrate	
Indications	• Magnesium sulphate are to be recommended to women between 24^{+0} and 30^{+0} weeks' gestation when birth is expected or planned within 24 hours
Recommendations	• When birth is planned, commence administration as close to four (4) hours prior to birth as possible • Best effect when given for at least four (4) hours and within the six (6) hours prior to birth • If birth is expected to occur within four (4) hours, give magnesium sulphate immediately, as there may still be benefit from administration • In situations where urgent birth is necessary, do not delay birth to administer magnesium sulphate.
	• If birth does not occur after giving magnesium sulphate (less than 30 weeks' gestation) and preterm birth again appears imminent (planned or expected within 24 hours), a repeat dose of magnesium sulphate may be considered at the discretion of the obstetrician[16].
Presentation	Pre-mixed solutions of magnesium sulphate heptahydrate are commercially available and recommended as pre-mixed solutions. Confer safety benefits over manually prepared solutions.
Administration	**Loading dose:** 4 grams (16 mmol) magnesium sulphate heptahydrate over 20-30 minutes. • Always administered via infusion pump. • The intravenous line should not be used to inject other drugs. • Magnesium sulphate should be ceased for transfer (except in exceptional circumstances where the mothers clinical condition overrides this concern). **Maintenance dose:** 1 gram per hour via intravenous route. Continue maintenance dose until birth or for 24 hours, whichever comes first. **NOTE**: The evidence for the maintenance dose is not clear. Some clinicians / facilities may elect to give a loading dose only and omit the maintenance infusion.
Contraindications	**NOTE:** Magnesium sulphate may be extremely hazardous in the following circumstances: renal failure, severe renal compromise or if oliguria is present (as elimination of magnesium is predominantly renal). Half dose magnesium sulphate should be considered if there is: • renal compromise • in association with hypocalcaemic states • myasthenia gravis • cardiac conditions, especially conduction problems or myocardial damage.
Complications	Magnesium sulphate may: • lower blood pressure (secondary to vasodilatation) • require adjustment of concomitant antihypertensive medication

	• have some tocolytic effect • decrease fetal heart rate variability • cause loss of reflexes (patellar reflexes will be absent well before toxic serum levels of magnesium are reached) • be used with caution in the presence of calcium antagonists or other respiratory depressants (e.g., diazepam).
Common maternal adverse effects	• Sensation of pain and warmth in arm • Flushing of hands, face and neck • Nausea, vomiting
Signs of maternal toxicity	• Loss of patellar reflexes • Respiratory rate <10 breaths/minute • Slurred speech, weakness, feeling extremely sleepy, double vision • Muscle paralysis • Respiratory / cardiac arrest
Antidote	Calcium gluconate 1 gram (10 mL of 10% solution) slowly via intravenous route over 10 minutes; can be given by slow intravenous injection over 3 minutes if there is clinical concern over respiratory depression.
Care and observations during infusion	Close observation and assessment (maternal and fetal) are required for the duration of the infusion. If the woman's condition is unstable, the frequency of observation will need to be increased. **Routine observations** • Before starting infusion check that knee or other tendon reflex is present, respiratory rate is >16 respirations/minute and urine output is >100 mL during the previous 4 hours (or >25 mL/hour). • 1- 2 hourly recording of maternal blood pressure, respiratory rate, heart rate and urine output. (Cease infusion if respiratory rate is <12 breaths/minute or if urine output is <100 mLs over four hours). • Patellar reflexes at completion of loading dose and then every 2 hours. (Cease infusion if unable to elicit reflexes). • Fetal heart rate monitoring as clinically indicated. • Serum magnesium monitoring is recommended in cases of renal compromise. • Calcium gluconate injection should be available in case of hypermagnesaemia requiring treatment.
Example 1: Premixed commercial solution (8 grams magnesium sulphate in 100 mLs water for injection)	
Loading Dose 50 mLs (4 grams) magnesium sulphate premixed solution (8 grams magnesium sulphate heptahydrate in 100 mL water for injection; each 100 mL contains approximately 32 millimoles magnesium) Infuse over 20 - 30 minutes	

8.8. Appendix 8: Subsequent Management

When preterm birth does not occur following admission for threatened preterm labour, a management plan for ongoing care and discharge planning must be coordinated with the woman and her family, relevant health care professionals and the referring hospital (as required).

Clinical judgement is to be used to individualise care. A woman's management plan must consider gestation, the treatment required for threatened preterm labour, whether transfer to higher level care is required and the presence of any underlying clinical considerations (e.g., PPROM). The following information is to be used as a guide to influence management planning.

Aspect	Considerations
Ongoing admission	• Maternal observations including but not limited to uterine activity and signs of infection. • Daily EFM or minimum fetal heart rate assessment (as appropriate to gestational age) and as maternal clinical condition changes. • Review of management plan for woman and fetus. • Psycho-social support for the woman and her family.
Back transfer	• If a woman has been transferred for higher level care, discharge home **may not** be an option after presentation with threatened preterm labour. This may be in circumstances where transfer and suppression of labour with a fetal fibronectin>50 ng/mL was required. • Transfer back to the referring facility or another facility with appropriate service capability for the gestation must be considered. • The tiered perinatal network operational plan must be used to guide decision making for the most appropriate location for back transfer considering the woman's clinical presentation and logistics. • The aim is for discharge or transfer back as soon as clinically safe and operationally feasible.
Discharge	When the woman's condition is clinically stable with no ongoing signs or symptoms of threatened preterm labour the management plan is to be for discharge home. This is appropriate when: • maternal vital signs are between the flags • there are no signs of chorioamnionitis • membranes are intact or the woman is suitable for expectant management at home • contractions have ceased or are infrequent / irregular • there has been no ongoing cervical change / cervical length (if measured) • there is a normal fetal heart rate pattern relevant to gestational age • fetal fibronectin test result <50ng/mL • the woman and her family have no ongoing concerns for wellbeing and/or safety.
	The woman must be provided with information that: • aids her recognition of the signs and symptoms of preterm labour • Identifies risk reduction measures appropriate to the circumstances (e.g., fluids, sexual activity) • Provides instruction about when to seek clinical advice

Referral and follow-up	Ensure the ongoing lead clinician / facility where care will be provided is aware of recommended care especially where that care will be provided at the referring facility. • Inform the General Practitioner about the episode of care and recommended care. • Provide the woman and her family with information about her plan of care including the regime of antenatal visits. • Offer social worker referral as indicated.