Note:
This guideline provides advice of a general nature. This statewide guideline has been prepared to promote and facilitate standardisation and consistency of practice, using a multidisciplinary approach. The guideline is based on a review of published evidence and expert opinion.

Information in this statewide guideline is current at the time of publication.
SA Health does not accept responsibility for the quality or accuracy of material on websites linked from this site and does not sponsor, approve or endorse materials on such links.

Health practitioners in the South Australian public health sector are expected to review specific details of each patient and professionally assess the applicability of the relevant guideline to that clinical situation.

If for good clinical reasons, a decision is made to depart from the guideline, the responsible clinician must document in the patient’s medical record, the decision made, by whom, and detailed reasons for the departure from the guideline.

This statewide guideline does not address all the elements of clinical practice and assumes that the individual clinicians are responsible for discussing care with consumers in an environment that is culturally appropriate and which enables respectful confidential discussion. This includes:
- The use of interpreter services where necessary,
- Advising consumers of their choice and ensuring informed consent is obtained,
- Providing care within scope of practice, meeting all legislative requirements and maintaining standards of professional conduct, and
- Documenting all care in accordance with mandatory and local requirements.

Explanation of the aboriginal artwork:
The Aboriginal artwork used symbolises the connection to country and the circle shape shows the strong relationships amongst families and the aboriginal culture. The horse shoe shape design shown in front of the generic statement symbolises a woman and those enclosing a smaller horse shoe shape depicts a pregnant woman. The smaller horse shoe shape in this instance represents the unborn child. The artwork shown before the specific statements within the document symbolises a footprint and demonstrates the need to move forward together in unison.

Australian Aboriginal Culture is the oldest living culture in the world yet Aboriginal people continue to experience the poorest health outcomes when compared to non-Aboriginal Australians. In South Australia, Aboriginal women are 2-5 times more likely to die in childbirth and their babies are 2-3 times more likely to be of low birth weight. The accumulative effects of stress, low socio economic status, exposure to violence, historical trauma, culturally unsafe and discriminatory health services and health systems are all major contributors to the disparities in Aboriginal maternal and birthing outcomes. Despite these unacceptable statistics the birth of an Aboriginal baby is a celebration of life and an important cultural event bringing family together in celebration, obligation and responsibility. The diversity between Aboriginal cultures, language and practices differ greatly and so it is imperative that perinatal services prepare to respectfully manage Aboriginal protocol and provide a culturally positive health care experience for Aboriginal people to ensure the best maternal, neonatal and child health outcomes.

Purpose and Scope of PPG
This PPG is intended to guide primary care, emergency, specialist and midwifery practitioners in the care of women at risk of or experiencing preterm labour. It provides a standardised, evidence-based approach to the assessment and management of South Australian women presenting with threatened preterm labour and includes a statewide referral pathway for women presenting in regional/lower acuity centres. For the first time, this PPG includes recommendations for how to identify women at risk of preterm birth and strategies for prevention. It forms the basis of “The Whole Nine Months SA” campaign to safely reduce rates of preterm birth in South Australia.
Flowchart 1: Threatened Preterm Labour Assessment and Transfer – Regional Sites

**Signs & Symptoms of TPL**
- Lower abdominal or back pain
- Vaginal spotting or show
- Pelvic pressure
- Regular, palpable uterine activity

**History / Risk Factors**
- Surgical
  - LLETZ / cone biopsy
- Obstetric
  - Previous preterm birth / PPROM
  - Short cervix / cerclage
  - Multiple pregnancy
- Social
  - Smoking / substance misuse
  - Homelessness
  - Domestic violence

**Examination**
- Vital signs
- Abdominal examination, palpation and timing of contractions
- Urinalysis
  - Speculum examination (water only as lubricant)
    - Assess for ROM
    - Cervical appearance and dilatation
    - Collect IFN
    - Collect high vaginal swabs
    - Vaginal examination only if ROM & plexiform previa excluded

**Investigations**
- GTG (≥ 28 weeks)
- MSU for MOPS + PCR
- High vaginal swabs for MOPS, GBS + PCR
- Blood: FBC, CRP, Group and save

**≥ 3cm dilated or in active labour or ROM confirmed**

**YES**
- See PTL Management Pathway (Flowchart 3) and Consider maternal transfer if birth not imminent or neonate retrieved if birth anticipated. Phone the PAL on 137 827 for advice

**LOW RISK**
- IFN 0.49 ng/mL
- PTB unlikely within 2 weeks (<2%)
  - Reassure woman
  - Provide robust obstetric and midwifery education
  - Provide symptomatic management, encourage analgesia
  - Exclude other clinical causes of symptoms
  - Follow up MSU and vaginal swabs
  - Reassess if new/worsening symptoms
  - Document IFN result/risk of PTB <34 weeks on PRODAHR
  - Clinic follow-up with Senior Medical Officer in 1 week

**INTERMEDIATE RISK**
- IFN 50-199 ng/mL
- Risk of PTB within 2 weeks approx. 8%
  - Transfer to gestation appropriate maternity service
  - Provide symptomatic management, encourage analgesia
  - Consider antenatal corticosteroids and tocolytics if:
    - <34+6 weeks & planned vaginal birth
    - <37 weeks if planned CS
  - Symptomatic persist, cervical change
  - Intravenous birth likely within 1 week

**HIGH RISK**
- IFN ≥ 200 ng/mL
- Risk of PTB within 1 week: 14% if IFN 200-499 ng/mL
- 33% if IFN ≥ 500 ng/mL
  - Urgent transfer to gestation appropriate maternity service
  - Provide symptomatic management, encourage analgesia
  - Administer corticosteroids and tocolytics if:
    - <34+6 weeks & planned vaginal birth
    - <37 weeks if planned CS
  - Remain in gestation appropriate setting
Flowchart 2: Assessment of Threatened Preterm Labour – Metropolitan Sites

**Signs & Symptoms of TPL**
- Lower abdominal or back pain
- Vaginal spotting or show
- Pelvic pressure
- Regular, palpable uterine activity

**History / Risk Factors**
- Surgical
  - LLETZ / cone biopsy
  - Previous preterm birth / PPROM
- Obstetric
  - Short cervix / cerclage
  - Multiple pregnancy
- Social
  - Smoking / substance misuse
  - Homelessness
  - Domestic violence

**Examination**
- Vital signs
- Abdominal examination, palpation and timing of contractions
- Ultrasound
- Speculum examination (water only as lubricant)
- Access for ROM
- Cervical appearance and dilatation
- Collect IFN
  - Collect high vaginal swab
  - Vaginal examination only if ROM & placenta praevia excluded

≥ 3cm dilated or In active labour or ROM confirmed

**Investigations**
- CTG (≥ 28 weeks)
- MSU for MC&S +/- PCR
- High vaginal swabs for MC&S, GBS +/- PCR
- Blood: FBC, CRP, Group and save

**LOW RISK**
- IFN < 49 ng/mL
- PTB unlikely within 2 weeks (<2%)
  - Reassure women
  - Provide robust obstetric and midwifery education
  - Provide symptomatic management, encourage analgesia
  - Exclude other clinical causes of symptoms
  - Follow-up MSU and vaginal swabs
  - Represnt if new/worsening symptoms
  - Document IFN result/risk of PTB ≤34 weeks on PR20/H9R
  - Antenatal clinic follow up with Senior Medical Officer in 1 week

**INTERMEDIATE RISK**
- IFN 50-199 ng/mL
- Risk of PTB within 2 weeks approx. 8%
  - Admit to short stay unit or equivalent
  - Provide symptomatic management, encourage analgesia
  - Exclude other clinical causes of symptoms
  - Request formal ultrasound to be undertaken within 4 hours: 'TV cervical length only'
  - TV cervical length > 30mm
  - Antenatal clinic follow up with Senior Medical Officer in 1 week

**HIGH RISK**
- IFN ≥ 200 ng/mL
  - Risk of PTB within 1 week: 14% if IFN 200-499 ng/mL
  - 36% if IFN ≥ 500 ng/mL
  - Admit to antenatal ward
  - Provide symptomatic management, encourage analgesia
  - Administer corticosteroids if:
    - <34+6 weeks & planned vaginal birth
    - <37 weeks if planned CS
  - Follow-up MSU and vaginal swabs
  - Formal obstetric ultrasound
  - Consider discharge if asymptomatic or ≥72 hours
  - Document IFN result/risk of PTB <34 weeks on PR20/H9R
  - Antenatal clinic follow up with Senior Medical Officer in 1 week
Flowchart 3: Preterm Labour Management

**Active preterm labour or cervical dilatation present < 37 weeks gestation**

- Admit to Labour Ward
- IV access
- Bloods
  - Group & hold (G&H)
  - Full blood examination (FBE)
  - C-Reactive Protein (CRP)
- Commence IV GBS prophylaxis if GBS positive or unknown or triple IV antibiotics if chorioamnionitis suspected
- Continuous CTG (> 26 weeks)
- Check fetal presentation with US
- Discuss with obstetric consultant (via PAL if in rural site +/- organise transfer)
- Notify Neonatal Team (both local and via PAL if in rural site +/- organise retrieval)
- Consider antenatal corticosteroids

**If < 34+6 weeks:**
- Consider tocolysis if:
  - AN course of corticosteroids not completed OR
  - Woman requires transfer to a higher service level site AND
  - No contraindications

**If < 30 weeks:**
- Consider tocolysis if:
  - AN course of corticosteroids not completed OR
  - Woman requires transfer to a higher service level site AND
  - No contraindications
  - Administer magnesium sulphate for neuroprotection
  - Discuss plan for mode of birth with obstetrician and/or MFM

**If < 28 weeks:**
- Consider tocolysis if:
  - AN course of corticosteroids not completed OR
  - Woman requires transfer to a higher service level site AND
  - No contraindications
  - Administer magnesium sulphate for neuroprotection
  - Discuss with parents and obstetrician and/or MFM plan for monitoring in labour and indications for caesarean birth

**If < 26 weeks:**
- Consider tocolysis if:
  - AN course of corticosteroids not completed OR
  - Woman requires transfer to a higher service level site AND
  - No contraindications
  - Administer magnesium sulphate for neuroprotection
  - Discuss with parents and obstetrician and/or MFM and Neonatal team plan for monitoring in labour, indications for caesarean birth and plan for neonatal resuscitation and level of intervention

See body of PPG for detailed information and treatment regimens for:
- Antenatal Corticosteroids
- Tocolysis with nifedipine (first line) or salbutamol (second line)
- Magnesium Sulphate for Neuroprotection of the Fetus
# Table 1: Risk Factors for Preterm Birth and Recommended Actions – Quick Reference

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Action</th>
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<tr>
<td><strong>Maternal</strong></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>Continuity of Carer Postnatal LARC Consider aspirin (Appendix 1)</td>
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<td>Maternal Age</td>
<td></td>
</tr>
<tr>
<td>&lt;20</td>
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<tr>
<td>&gt;35</td>
<td></td>
</tr>
<tr>
<td>Ethnicity</td>
<td>Refer to AFBP Continuity of Carer</td>
</tr>
<tr>
<td>ATSI, Indian, African, Indo-Caribbean</td>
<td></td>
</tr>
<tr>
<td>Cervical Surgery</td>
<td>Cervical length at morphology</td>
</tr>
<tr>
<td>Especially &gt;10mm, repeated LLETZ or Cone Biopsy</td>
<td></td>
</tr>
<tr>
<td>Congenital Uterine Anomalies</td>
<td>Cervical length at morphology</td>
</tr>
<tr>
<td>BMI</td>
<td>Optimise BMI pre-pregnancy Consider aspirin (Appendix 1)</td>
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<tr>
<td>&lt;18 and &gt;30</td>
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<tr>
<td>Medical Comorbidities</td>
<td>Optimise pre-pregnancy Consider aspirin (Appendix 1) Multi-disciplinary Team Care</td>
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<td>Hypertension, DM, Renal Disease, SLE, APLS, Scleroderma</td>
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</tr>
<tr>
<td>Nutrition</td>
<td>Screen for Vitamin D deficiency</td>
</tr>
<tr>
<td>Vegetarian/Non-Fish Diet Malabsorption/Inflammatory Bowel Disease/Gastric Banding Previous PTB/At risk woman</td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td>Screen at booking &amp; every third visit as per SAPR Refer to Quitline</td>
</tr>
<tr>
<td>Obstetric History</td>
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</tr>
<tr>
<td>Previous preterm birth/PPROM/ cerclage/shortened cervix</td>
<td>Refer to Obstetrician/MFM</td>
</tr>
<tr>
<td>Previous fully dilated CS, STOP, GTOP</td>
<td>Cervical length at morphology</td>
</tr>
<tr>
<td>Pregnancy Features</td>
<td></td>
</tr>
<tr>
<td>Shortened Cervix</td>
<td>Urgent referral to Obstetrician/ MFM</td>
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<td>&lt;25mm on TVUS, especially &lt;10mm or funnelling</td>
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<tr>
<td>Short Interpregnancy Interval</td>
<td>Continuity of Carer Optmise nutrition &amp; medical comorbidities Postnatal LARC</td>
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<td>Especially &lt;6 but up to 18 months</td>
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<tr>
<td>ART/IVF</td>
<td>Single Embryo Transfer Consider aspirin (Appendix 1)</td>
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<tr>
<td>Urogenital Infections</td>
<td>Screen, culture &amp; treat UTI Culture &amp; treat urogenital infections</td>
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<tr>
<td>All Women</td>
<td>Refer to Obstetrician/MFM</td>
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<tr>
<td>Symptomatic Women</td>
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<tr>
<td>History of infection associated losses and PTB e.g. chorioamnionitis</td>
<td></td>
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<tr>
<td>Multiple pregnancy</td>
<td>Refer to Obstetrician. Refer to MFM if MCDA, DCDA complexity or higher multiple Consider aspirin (Appendix 1)</td>
</tr>
<tr>
<td>Social Factors</td>
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<tr>
<td>Low SES/Intimate Partner Violence</td>
<td>Continuity of Carer Any available enhanced antenatal care programs Refer to Social Work if indicated</td>
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<td>ATSI</td>
<td>Refer to AFBP</td>
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<tr>
<td>Substance abuse</td>
<td>Continuity of Carer Refer to Quitline/DASSA</td>
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Summary of Practice Recommendations

No pregnancy should be ended before 39 weeks without obstetric or medical indication.

Women with chronic hypertension, type 1 or type 2 diabetes, renal disease or autoimmune conditions such as antiphospholipid syndrome, systemic lupus erythematosus and scleroderma should commence low dose (100mg) oral aspirin nocte in early pregnancy.

Consider omega-3 and zinc supplementation in women at risk of dietary insufficiency.

Screen and treat vitamin D insufficiency in women at risk of preterm birth.

Ask about smoking in pregnancy initially and at every third visit if still smoking; refer women to Quitline and the “Quit for You, Quit for Two” app.

Vaginal progesterone from 16 to 36 weeks should be considered for women with a singleton pregnancy and a history of preterm birth.

Women with a history of preterm birth, PPROM, recurrent mid-trimester loss, shortened cervix and cervical cerclage should be referred to an obstetrician and/or MFM Unit, ideally for pre-conception counselling or as early as possible in pregnancy.

Measurement of cervical length is recommended at all mid-trimester morphology scans for women with risk factors. It should be considered for all other women.

- A closed length of ≥35mm is adequate.
- A closed cervical length of ≤25mm (via transvaginal ultrasound) is considered shortened and must be immediately referred to an obstetrician/MFM Unit.

Vaginal progesterone is recommended for women with a shortened cervix of ≤25mm at mid-trimester ultrasound screening.

Pregnancies should be spaced at least 12 months apart.

ART should be used carefully and judiciously, including single embryo transfer only, to minimise the risk of multiple pregnancy.

Routine urogenital antenatal screening for infection must include syphilis serology, a mid-stream urine sample to detect asymptomatic bacteriuria and screening for Chlamydia in women <25 years of age or otherwise at high risk.

There is insufficient evidence for routine screening and treatment of bacterial vaginosis; women at high risk of preterm birth should be referred to an obstetrician or MFM subspecialist to consider their individual risk profile.

All pregnant women should have the influenza vaccine.

Multiple pregnancies are at very high risk of preterm birth and should be managed by an obstetrician or MFM subspecialist.

Aboriginal and Torres Strait Islander women should be offered specialised and culturally appropriate antenatal care featuring continuity of carer and community stewardship.

Pregnant women with identified social risk factors for preterm birth such as young age, substance abuse and exposure to intimate partner violence should be allocated to enhanced models of antenatal care where available and referred for supporting services.

Women at high risk of preterm birth should be prioritised to receive antenatal care in a model that affords midwifery continuity of carer.

Antenatal corticosteroids are most effective if given between 48 hours and 7 days before birth.

A fFN reading of between 10-49ng/mL modestly increases the woman’s overall risk (8.2%) of experiencing a preterm birth before 34 weeks, therefore she should be counselled to represent with persistent, worsening or new symptoms.

Consider tocolysis for women who have not completed a full course of corticosteroids or for inutero transfer of a woman to a higher level service.

Do not continue nifedipine beyond 48 hours. A repeat course of nifedipine should only be considered if the woman represents with PTL. Nifedipine is NOT to be used prophylactically.

Commence IV antibiotic prophylaxis for GBS for women in active preterm labour.

Intravenous magnesium sulphate must be administered to any woman considered at imminent risk of preterm birth or where birth is planned at <30 weeks.
### Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>AFI</td>
<td>Amniotic Fluid Index</td>
</tr>
<tr>
<td>APH</td>
<td>Antepartum haemorrhage</td>
</tr>
<tr>
<td>APLS</td>
<td>Anti-Phospholipid Syndrome</td>
</tr>
<tr>
<td>ATSI</td>
<td>Aboriginal and Torres Strait Islander</td>
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<tr>
<td>BMI</td>
<td>Body Mass Index</td>
</tr>
<tr>
<td>BV</td>
<td>Bacterial vaginosis</td>
</tr>
<tr>
<td>CoC</td>
<td>Continuity of Care</td>
</tr>
<tr>
<td>CS</td>
<td>Caesarean Section</td>
</tr>
<tr>
<td>CTG</td>
<td>Cardiotocography</td>
</tr>
<tr>
<td>DASSA</td>
<td>Drug and Alcohol Services South Australia</td>
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<tr>
<td>DCDA</td>
<td>Dichorionic Diamniotic (Twin Pregnancy)</td>
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<td>DM</td>
<td>Diabetes Mellitus</td>
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<tr>
<td>fFN</td>
<td>Fetal fibronectin</td>
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<tr>
<td>GTOP</td>
<td>Genetic Termination of Pregnancy</td>
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<td>IBD</td>
<td>Inflammatory Bowel Disease e.g. Crohn’s, Ulcerative Colitis</td>
</tr>
<tr>
<td>IPV</td>
<td>Intimate Partner Violence</td>
</tr>
<tr>
<td>LARC</td>
<td>Long Acting Reversible Contraceptive</td>
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<tr>
<td>LLETZ</td>
<td>Large loop excision of the transformation zone</td>
</tr>
<tr>
<td>MC&amp;S</td>
<td>Microscopy, Culture and Sensitivities</td>
</tr>
<tr>
<td>MCDA</td>
<td>Monochorionic Diamniotic (Twin Pregnancy)</td>
</tr>
<tr>
<td>MDT</td>
<td>Multi-Disciplinary Team</td>
</tr>
<tr>
<td>MFM</td>
<td>Maternal Fetal Medicine</td>
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<td>MSU</td>
<td>Mid-stream urine</td>
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<tr>
<td>NAAT</td>
<td>Nucleic Acid Amplification Test</td>
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<tr>
<td>PPG</td>
<td>Perinatal Practice Guideline</td>
</tr>
<tr>
<td>PPH</td>
<td>Postpartum haemorrhage</td>
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<td>PPROM</td>
<td>Preterm prelabour rupture of membranes</td>
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<tr>
<td>PTB</td>
<td>Preterm Birth</td>
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<tr>
<td>RCT</td>
<td>Randomised controlled trial</td>
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<td>RDI</td>
<td>Recommended daily intake</td>
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<td>SALHN</td>
<td>Southern Adelaide Local Health Network</td>
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<td>SA PR</td>
<td>South Australian Pregnancy Record</td>
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<td>SES</td>
<td>Socioeconomic Status</td>
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<td>SET</td>
<td>Single Embryo Transfer</td>
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<tr>
<td>SLE</td>
<td>Systemic Lupus Erythematosus</td>
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<td>STOP</td>
<td>Surgical termination of pregnancy</td>
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<td>TVUS</td>
<td>Transvaginal Ultrasound</td>
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<tr>
<td>UTI</td>
<td>Urinary tract infection</td>
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<tr>
<td>WCHN</td>
<td>Women’s and Children’s Health Network</td>
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</table>

### Definition

**Preterm birth**  
A birth occurring before 37 weeks completed gestation
Background

Late preterm births, occurring between 34<sup>0</sup>-6<sup>6</sup> and 36<sup>0</sup>-6<sup>6</sup> weeks, account for over 70% of all preterm births, but early preterm births occurring before 34 weeks are responsible for the majority of associated morbidity and mortality.<sup>1</sup> The rate of preterm birth is steadily rising in most jurisdictions including South Australia, where 7.2% of live births and 9.6% of all births in 2017 were preterm; the rate of preterm birth in South Australian Aboriginal women is much higher at 19.1%.<sup>2</sup> It is important for clinicians to note that the rate of iatrogenic preterm births has doubled in the last 20 years.<sup>1</sup> This is despite the incidence of hypertensive disorders of pregnancy, small for gestational age babies and smoking in pregnancy all decreasing over the same time; instead, South Australian women are birthing at older ages with higher body mass indices (BMI’s) and we have a more ethnically diverse population.<sup>1</sup>

Prevention

A simple way of minimising the burden of prematurity in South Australia is to avoid further ‘obstetric creep’ or iatrogenic delivery at increasingly earlier gestations. Therefore:

No pregnancy should be ended before 39 weeks without obstetric or medical indication.

Spontaneous preterm birth by contrast, is the culmination of woman- and fetus-specific risk factors unique to each pregnancy and therefore, is more helpfully considered a syndrome rather than a diagnosis. By extension, the prevention of spontaneous preterm birth requires a multidisciplinary and multidimensional approach.

It is important for clinicians to be able to identify early in a woman’s pregnancy if she is at increased risk of preterm birth, in order to implement risk minimisation strategies and assign an appropriate model of care. Risk factors can be grouped by relation to the woman, her obstetric history, features of the current pregnancy and social determinants of health (see Table 1).

Maternal Risk Factors

Non-modifiable Maternal Risk Factors

Age

Young women (<18 years old) may be physiologically immature and are more likely to be experiencing disadvantageous social circumstances,<sup>4</sup> whilst older women (>35 years old) are more likely to have medical comorbidities such as diabetes and obesity contributing to their risk.<sup>4</sup>

Ethnicity

Aboriginal, South Asian, African, African American and Indo-Caribbean women are at higher risk of experiencing preterm and early preterm birth compared to other ethnicities.<sup>2,5</sup> Emerging evidence suggests at least some of this risk may be attributable to genetic polymorphic differences in immune response and differences in the vaginal microbiome.<sup>6,7</sup>

Cervical Surgery

A history of cervical procedures such as LLETZ and cervical conisation is associated with increased risk of preterm birth, especially with increased size of excision (>10mm), repeated procedures and conisation.<sup>8</sup> As a minimum standard of care these women should be identified and referred for a cervical length measurement at morphology ultrasound.
Congenital Uterine Anomalies

Women with congenital uterine anomalies are at increased risk of preterm birth and should have a mid-trimester cervical length measured.9 Whilst the risk of preterm birth appears greatest in women with major fusion defects (unicornuate, bicornuate and didelphys anomalies), the value of combined cervical length and fetal fibronectin (fFN) in predicting preterm birth is greater for those with resorptive anomalies (septate and arcuate anomalies).10

Modifiable Maternal Risk Factors

BMI

A powerful modifiable risk factor is BMI; women with low BMIs (<18) are at greater risk of spontaneous preterm birth, whereas women with high BMIs (>30) are more likely to experience an iatrogenic preterm birth secondary to oxidative stress-related complications such as preeclampsia and fetal growth restriction.11 Where possible, women should be encouraged and assisted to optimise their BMI before conceiving.

Medical Comorbidities

Medical comorbidities such as hypertension, diabetes, renal disease and autoimmune conditions should also be optimised prior to conception and managed in a multidisciplinary team, together with relevant specialists and obstetric physicians. A simple but powerful prevention strategy in addition to optimising these medical comorbidities is commencing low dose aspirin 100mg nocte once pregnancy is confirmed (preferably after confirmation of fetal heart beat), prior to 16 weeks’ gestation.12 (Appendix 1)

Nutrition

Nutrition is integral to a healthy pregnancy outcome and even in a high resource setting such as South Australia, some groups of women are at risk of malnutrition. Women with extremes of BMI (low and high), a history of bariatric procedures, inflammatory bowel disease, those who follow a vegan or vegetarian diet, recent migrants and women of low socioeconomic status are at particular risk of micronutrient insufficiencies in pregnancy. Specific nutrients that have been linked with preterm birth prevention include omega 3, vitamin D and zinc.

Omega 3

A Cochrane systematic review of omega 3 supplementation in pregnancy found an 11% reduction in preterm births and a 42% reduction in early preterm births, however, a single large randomised controlled trial (RCT) (Omega-3 to Reduce the Incidence of Preterm Birth – ORIP) in the Australian setting showed no benefit of universal high-dose omega 3 supplementation on preterm birth rates.13,14 Of note, ORIP enrolled multiple pregnancies, including triplets, as well as women who were already supplementing with low-dose omega 3. Further exploration of the ORIP data has revealed that in singleton pregnancies, a low baseline total omega 3 concentration (<4.2% total blood fatty acids) in early pregnancy was associated with increased risk of preterm birth and that targeted supplementation of these pregnancies significantly reduced the risk of preterm birth.15 As we do not routinely screen for total omega 3 concentrations in early pregnancy, we suggest that women who do not eat fatty fish such as salmon, herring, mackerel and sardines once a week or any fish 2-3 times a week should consider supplementing with a good quality marine (fish or algal) omega 3 source.
Zinc
A Cochrane systematic review of zinc supplementation in pregnancy showed a 14% relative reduction in preterm birth, though the majority of data came from resource poor settings, making general application in an Australian setting difficult. The Australian recommended daily intake (RDI) of zinc in pregnancy is 11mg/day, however, as absorption is greater from animal rather than plant sources, vegans and strict vegetarians require intakes that are 50% higher. The main sources of zinc are meat, fish and poultry and to a lesser extent, dairy, nuts and cereals.

Consider omega-3 and zinc supplementation in women at risk of dietary insufficiency.

Vitamin D
As regards vitamin D, the latest Cochrane systematic review has not shown universal supplementation in pregnancy to decrease preterm birth directly, however, there remains evidence that vitamin D adequacy decreases the risk of preeclampsia, gestational diabetes, low birth weight and postpartum haemorrhage (PPH). Therefore, we recommend screening for and optimising cholecalciferol levels in women at risk of preterm birth, particularly those with a history of prior preterm birth, in addition to women at risk of vitamin D insufficiency (see Vitamin D Status in Pregnancy PPG available at www.sahealth.sa.gov.au/perinatal).

Screen and treat vitamin D insufficiency in women at risk of preterm birth.

Smoking
Smoking remains an important modifiable risk factor for numerous pregnancy complications, including preterm birth. All pregnant women should be asked about their smoking status at booking and if still smoking, at every third antenatal visit in pregnancy as per the South Australian Pregnancy Record. Women who continue to smoke should be offered referral to the National Quitline Number (13 7848) (or complete the online referral form) and encouraged to use tools such as the “Quit for You, Quit for Two” app.

Ask about smoking in pregnancy initially and at every third visit if still smoking; refer women to Quitline and the “Quit for You, Quit for Two” app.

Obstetric History

Previous Preterm Birth
Clinically, the single greatest predictor of preterm birth is a history of preterm birth; the earlier the gestation at which birth occurred, the greater the risk. A woman with one previous preterm birth has a 4-fold increased risk in her second pregnancy, rising to 6.5-fold after two preterm births. Women with a history of preterm birth should be referred to an obstetrician and/or Maternal Fetal Medicine Unit, ideally preconceptionally, to assess contributing factors and optimise modifiable risk factors, as well as to identify women that may benefit from early interventions such as vaginal progesterone, serial cervical length measurement and prophylactic cervical cerclage.

There is much controversy regarding the use of vaginal progesterone for the prevention of preterm birth in women with a history of preterm birth, with two large recent RCTs contradicting the earlier results of systematic reviews and meta-analyses. Until updated meta-analyses are performed, current advice remains as per the Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG). Vaginal progesterone from 16 to 36 weeks should be considered for women with a singleton pregnancy and a history of preterm birth.

Vaginal progesterone from 16 to 36 weeks should be considered for women with a singleton pregnancy and a history of preterm birth.

Where a woman’s history of preterm birth is suggestive of cervical insufficiency, she should have serial ultrasound cervical length surveillance implemented from 14-16 weeks under the supervision of an obstetrician and/or MFM subspecialist. Further shortening may then justify an ultrasound indicated cervical cerclage.

Prophylactic cerclage is considered for some women with a history of recurrent mid-trimester losses and preterm birth but decisions around timing, approach and the implementation of a cervical cerclage should be undertaken by, or in consultation with, MFM.
Women with a history of preterm birth, PPROM, recurrent mid-trimester loss, shortened cervix and cervical cerclage should be referred to an obstetrician and/or MFM Unit, ideally for pre-conception counselling or as early as possible in pregnancy.

Obstetric Cervical Trauma

As with gynaecological cervical procedures, an obstetric history of cervical trauma including surgical termination of pregnancy (STOP), induced abortions, genetic terminations of pregnancy (GTOP) and previous fully dilated caesarean sections increase risk of preterm birth.26-28

Women with any history of obstetric cervical trauma are at increased risk of preterm birth and should have a cervical length measured at the mid-trimester morphology ultrasound.

Pregnancy Features

Shortened Cervix

Whilst this document has so far focused on women with risk factors to be specifically referred for a cervical length measurement at the mid-trimester morphology ultrasound, we know that many women experiencing pregnancy loss and preterm birth have no identifiable risk factors. Cervical length in mid-trimester is highly correlated with gestation at birth.25 We therefore strongly advocate that it become the standard of care that all South Australian radiology practices performing mid-trimester morphology scans report on the cervical length of all pregnant women.

Measurement of cervical length is recommended at all mid-trimester morphology scans.

Where the cervix can be imaged clearly on trans-abdominal scan, a closed length of \( \geq 35\text{mm} \) is adequate. In all other cases, trans-vaginal scanning is required, where a closed cervical length of \( \leq 25\text{mm} \) is considered shortened and must be immediately referred to an obstetrician/MFM Unit.

Trials have consistently shown that where a woman is found to have a shortened cervix on ultrasound, treatment with progesterone prolongs the duration of pregnancy and improves pregnancy outcomes. Vaginally administered progesterone appears to have better evidence than intramuscular formulations. As per RANZCOG23:

Vaginal progesterone is recommended for women with a shortened cervix of \( \leq 25\text{mm} \) at mid-trimester ultrasound screening.

Interpregnancy Interval

A short interpregnancy interval, particularly \(<6\) months but also between 6-18 months after the last, increases the risk of a subsequent preterm birth.29,30 Where possible, women should be counselled to delay subsequent pregnancies for 12 months and offered appropriate contraception to achieve this.

Pregnancies should be spaced at least 12 months apart from the end of one pregnancy to the beginning of the next.

Assisted Reproductive Technologies

Women who required assisted reproductive technology (ART) to conceive, in particular *in vitro* fertilisation (IVF) and intracytoplasmic sperm injection (ICSI), are at increased risk of preterm birth, however, other than limiting the number of embryos transferred (single embryo transfers only), there is no specific intervention to mitigate this risk.31 These technologies, including ovulation induction, should be used carefully and judiciously to minimise the numbers of multiple pregnancies that occur as a result. Optimisation of weight, nutrition and medical comorbidities should occur prior to use of ART and consideration be given to whether women meet criteria for low dose aspirin prophylaxis after conceiving.

**ART should be used carefully and judiciously, including single embryo transfer only, to minimise the risk of multiple pregnancy.**
Urogenital Infections

The initiation of labour is an inflammatory event and many cases of preterm birth are associated with systemic or urogenital infection. Urogenital infection is a strong risk factor for preterm birth. Routine screening and treatment of urogenital infection in pregnancy currently consists of:

- Syphilis serology screening with antenatal screening bloods (with additional screening in the third trimester (28 and 36 weeks), at birth and 6 weeks postnatally for women in outbreak areas or otherwise at high risk);
- A mid-stream urine (MSU) microscopy, culture and sensitivity performed together with antenatal screening bloods;
- Screening for chlamydia (+/- gonorrhoea) in pregnant women <25 years old or at high risk of a sexually transmitted infection.

Routine urogenital antenatal screening for infection must include syphilis serology, a mid-stream urine sample to detect asymptomatic bacteriuria and screening for Chlamydia in women <25 years of age or otherwise at high risk.

Whilst periodontal disease and bacterial vaginosis in pregnancy have been associated with preterm birth, causation has not been established and universal treatment of these conditions has not reduced the incidence of preterm birth. There is some evidence that for women with a history of preterm birth, prophylactic treatment with antibiotics from the mid-trimester where bacterial vaginosis is detected, may improve outcomes. Also, in a separate systematic review, treatment with oral clindamycin (rather than vaginal clindamycin or metronidazole) before 22 weeks of gestation for asymptomatic bacterial vaginosis decreased preterm births <37 weeks and late miscarriages. Women who are symptomatic with bacterial vaginosis or other genital tract infections should be treated.

Recent research has identified changes in the vaginal microbiome related to pregnancy, as well as ethnic variation. Some vaginal microbiomes and taxa are associated with increased risk of preterm birth, such as BV-associated bacterium 1, and may present a screening and therapeutic target, although this research is still underway.

There is insufficient evidence for routine screening and treatment of bacterial vaginosis; women at high risk of preterm birth should be referred to an obstetrician or MFM subspecialist to consider their individual risk profile.

Systemic Infections

Intercurrent systemic infections with pathogens such as malarial parasites or influenza are associated with preterm birth. These should be identified and treated. In the case of influenza, the Australian Government recommends and provides free vaccination to all pregnant women in recognition of their status as a vulnerable population.

All pregnant women should have the influenza vaccine.

Multiple Pregnancies

Three-quarters (75%) of multiple births are preterm in South Australia. The increased risk of general (hypertensive, cholestatic, diabetic) and multiple-specific (e.g. twin-twin transfusion, selective intra-uterine growth restriction) pregnancy complications, as well as the risk of stretch mechanoreceptor initiation of labour, contribute to both iatrogenic and spontaneous preterm births in multiple pregnancies, respectively. Aside from minimising the risk of multiple gestations arising from ART, twin and higher order multiple pregnancies require specialised care with either an obstetrician or MFM subspecialist.

Multiple pregnancies are at very high risk of preterm birth and should be managed by an obstetrician or MFM subspecialist.
Social Determinants

Social disadvantage has consistently been linked with preterm birth and is associated with a range of independent risk factors such as poor nutrition, substance abuse, periodontal disease, lower educational attainment and psychological stressors.40-42 Women in lower socioeconomic groups are also more likely to be over-represented in other at-risk groups related to ethnicity, extremes of age and BMI. High-grade evidence to support enhanced antenatal care programs for socially disadvantaged women to reduce preterm births in high-income countries is lacking and methodologically challenging, with many studies showing decreases in preterm birth outcomes that were not statistically significant or of borderline statistical significance when compared to standard care models.43 This, however, does not necessarily translate to a lack of clinical significance, particularly where individual outcomes and the cost, financial and otherwise, of a single early preterm birth are taken into account.

Aboriginal and Torres Strait Islander Women

Australian studies looking at antenatal care delivery to Aboriginal and Torres Strait Islander women have similarly suffered a lack of strong evidence, likely related to small sample sizes, heterogeneity of care delivery and reporting of outcomes.44 A recent prospective cohort study conducted in Brisbane, Australia, found an impressive 50% reduction in preterm birth in Aboriginal women receiving “culturally safe continuity of carer within a holistic service with high levels of community investment-ownership-activation and health service leadership across partner organisations.”45 We note that 25% of identified Indigenous births at the health service were excluded from the analysis, including women allocated to other specialised care such as MFM and drug and alcohol dependency services, nevertheless, the translatable absolute reduction in preterm births suggests this to be a worthwhile model of antenatal care for a group of women known to be at significantly increased risk of preterm birth.

Closer to home, Aboriginal women participating in the South Australian Aboriginal Family Birthing Program highly value receiving care from another Aboriginal woman, paving the way for greater engagement with antenatal care and improved outcomes. These women achieved similar birth outcomes, including preterm birth rates, to Aboriginal women in other models of care, despite having greater medical and social complexity.46

Socially Disadvantaged and Vulnerable Women

A lack of high-quality evidence similarly pertains to enhanced antenatal care provision to other socially disadvantaged women such as teenagers, pregnant women with substance abuse issues and women in low socioeconomic groups: whilst studies suggest improved outcomes including preterm birth rates, they suffer from selection bias and other methodological limitations.43 Women experiencing domestic or intimate partner violence (IPV) are represented among all socioeconomic groups and are at high risk of preterm birth; the importance of screening for IPV has been recognised by RANZCOG and the Australian Government by linking it to a number of antenatal (and postnatal) Medicare item numbers.47 Pragmatically, despite low grade evidence, socially vulnerable women should be offered enhanced antenatal and adjunct service provision including prioritisation to midwifery continuity of care models and other specialised antenatal care streams (e.g. Strengthening Links (WCHN), Early Links (SALHN)), as well as access to Drug and Alcohol Services South Australia (DASSA), social work and mental health services, to optimise their individual health and pregnancy outcomes, as any reduction in preterm births in terms of absolute numbers will still be clinically and economically meaningful.

Pregnant women with identified social risk factors for preterm birth such as young age, substance abuse and exposure to intimate partner violence should be allocated to enhanced models of antenatal care where available and referred for supporting services.
Antenatal Care Provision

Midwifery Continuity of Carer

There is good quality evidence that midwifery continuity of carer in pregnancy reduces preterm birth, with a reported risk reduction of 24%. Although none of the included studies had adequate blinding, this is unlikely to have affected outcomes, but only low-risk and mixed-risk women were included; women with ‘significant maternal disease and substance abuse’ were excluded from some trials, subgroups of women at high risk of experiencing preterm birth. Nevertheless, the findings raise important considerations regarding the value of therapeutic relationship continuity, which supersedes management and informational continuity, and how this may improve the pregnancy outcomes of women engaging in various models of antenatal care.

Women at high risk of preterm birth should be prioritised to receive antenatal care in a model that affords midwifery continuity of carer.

Dedicated Preterm Birth Clinics

The provision of antenatal care in dedicated preterm birth clinics helps to facilitate the streamlining of multidisciplinary care and predictive and preventive measures such as urogenital tract infections screening, second trimester alkaline phosphatase measurement, serial fetal fibronectin quantification, access to serial transvaginal cervical length measurement and midwifery and medical continuity of carers. Evidence from such clinics in the UK and Australia, both alone and as part of a comprehensive state-wide intervention, have demonstrated significant reductions in the incidence of preterm birth and improved prediction of women requiring inpatient management and timing of interventions such as antenatal corticosteroids. This despite systematic reviews failing to show statistically significant improvements in preterm birth prevention as with other models of antenatal care. The high personal and societal cost of each preterm birth together with the array of interventions requiring individualisation to each at-risk woman’s circumstances justify the need for dedicated preterm birth clinics and parent’s anxiety and satisfaction with care must be factored.

Women at high-risk of preterm birth benefit from specialised antenatal care to provide timely and evidenced access to predictive and preventive interventions; local health networks should strongly consider the establishment of dedicated preterm birth prevention clinics to facilitate this.
Threatened Preterm Labour

Presentations with threatened preterm labour are common and rarely result in preterm birth within 1-2 weeks.

Nevertheless, many of these women will remain at higher risk of delivering preterm later in pregnancy. The timing of interventions such as antenatal corticosteroids, magnesium sulphate and antibiotics is crucial to improving outcomes for those babies that do go on to be born prematurely – the earlier the gestation, the more important the timing of these interventions.53,54

Antenatal corticosteroids are most effective if given between 48 hours and 7 days before birth.

Repeated doses of antenatal corticosteroids are associated with less clear evidence of benefit and are associated with poorer long-term learning and behavioural outcomes; the optimal dosing regime is also uncertain. The greatest clinical challenge, therefore, is determining which women presenting with signs and symptoms of threatened preterm labour are at greatest risk of progressing to preterm birth in the next one to two weeks.

Cervical Length

Cervical length in the mid-trimester has now for some time been recognised as highly correlated with risk of preterm birth.55,56 Even in symptomatic women at later gestations, a longer cervical length is still protective in terms of predicting who will progress to preterm birth.57

Fetal Fibronectin

After identification of the glycoprotein fetal fibronectin (fFN) in 1988, it was quickly identified as being clinically useful in helping to predict which women presenting with symptoms of threatened preterm labour were at greatest risk of preterm birth.58 Fetal fibronectin promotes adhesion between the fetal chorion and maternal decidua and is typically absent from cervicovaginal secretions between 24 and 36 weeks’ gestation. In 2013 it was shown that quantifying the level of fFN in symptomatic women enhances its predictive value over qualitative measurement alone.59 Other biomarkers present in vaginal secretions are promoted as predictors of preterm birth but revert to a qualitative measurement and have not been found to have as high a negative predictive value, of great import when deciding not to administer interventions to improve neonatal outcomes.60

Combined Cervical Length and Fetal Fibronectin

Combining the use of cervical length measurement and quantitative fFN further improves the predictive ability of clinicians to determine which women are at highest risk of progressing to preterm birth in the next seven days and therefore more accurately and beneficially targeting interventions such as the administration of antenatal corticosteroids, magnesium sulphate and antibiotics.61-64 A risk threshold of 5% is generally used as a cut-off for determining who requires intervention, however, the gestation of the pregnancy and context may factor into clinical decision making.

Recognising that access to timely (<4 hours from presentation) and accurate cervical length measurement is challenging in most maternity settings and presentations, this guideline focuses on the use of quantitative fFN for triaging women presenting with signs and symptoms of threatened preterm labour to determine who requires transfer and intervention. Where available, the addition of cervical length can further assist with clinical decision making around administration of antenatal corticosteroids and magnesium sulphate and assist with discharge planning to local and distant settings.
Threatened Preterm Labour - Assessment (Flowcharts 1 & 2)

Signs and Symptoms

Women may present with:
- Lower abdominal cramping, regular, painful contractions or tightenings;
- Lower back pain;
- Vaginal or rectal pressure;
- Vaginal discharge including bleeding;
- PPROM: one-third of women will experience premature prelabour rupture of membranes (PPROM) before regular, painful tightenings. Intrauterine infection is a major concern – manage as per the Preterm Prelabour Rupture of Membranes PPG available at www.sahealth.sa.gov.au/perinatal

History and Risk Factors

A brief history should review the woman’s risk factors for preterm birth including:
- Congenital uterine anomalies;
- Previous LLETZ or cone biopsies;
- Any previous mid-trimester losses, PPROM and preterm births and the gestations at which these occurred;
- Women with a cervical cerclage, multiple pregnancy or polyhydramnios: these women are at higher risk of preterm birth and require MFM input;
- Women with social risk factors: a lower threshold for admission should be considered to obtain assistance and minimise ongoing risk where possible.

Examination

Initial triage and midwifery assessment should incorporate:
- Maternal vital signs including temperature;
- Fetal heart rate assessment either by Doppler auscultation or CTG at >28/40;
- Assessment of vaginal losses;
- Abdominal examination including presentation;
- Timing of uterine activity;
- Urinalysis.

Further assessment (within a midwife’s or doctor’s scope of practice) should incorporate:
- A speculum examination using only water as lubrication, assessing for:
  - PPROM, including any ancillary tests/glass slide for ferning;
  - Cervical length, dilatation and appearance;
  - Cervical and vaginal swabs for MC&S and Chlamydia/Gonorrhoea NAAT;
  - A fFN swab from the posterior fornix.

Please note that whilst recent digital or ultrasound vaginal examination, coitus and the presence of blood in the vagina are relative contraindications to performing a fFN measurement and increase the risk of both false and true positive results, a negative fFN in these situations is still clinically valid and should be performed if it will help appropriately time intervention and/or discharge planning.

If PPROM and placenta praevia have been excluded:
- A digital vaginal examination to assess the dilatation of the cervix; this may be repeated in 4 hours’ time to help determine if the woman is in active labour.

If bedside ultrasound is available:
- Confirm presenting part of fetus;
- Assess AFI and umbilical artery Dopplers.
Investigations

- Urine MC&S;
- Cervical and vaginal swabs for NAAT and MC&S, respectively;
- Bloods including full blood examination (FBE), group and hold and C reactive protein (CRP);
- fFN quantification
- TVUS cervical length if fFN >50 ng/mL
- A formal ultrasound assessment of growth should form part of the work up if the woman requires admission.

Threatened Preterm Labour Management (Flowcharts 1 & 2) (Appendix 2)

Fetal fibronectin 0-49 ng/mL

These women have a very low risk (<2%) of experiencing a preterm birth in the next 2 weeks and can therefore be managed symptomatically and discharged with timely (within 1 week) antenatal follow up.

Be aware that a reading of between 10-49ng/mL modestly increases the woman’s overall risk (8.2%) of experiencing a preterm birth before 34 weeks, therefore she should be counselled to represent with persistent, worsening or new symptoms and her antenatal care provider should remain vigilant to the risk of a preterm birth later in pregnancy.

Fetal fibronectin 50-199 ng/mL

These women are at a modestly increased risk (7.7%) of progressing to a preterm birth within 14 days. They should be transferred to a gestation appropriate maternity setting for a full assessment including growth ultrasound and transvaginal cervical length assessment (Flowchart 3). Antenatal corticosteroids should be considered but not automatically commenced as very few babies will benefit from them within 7 days. Any urogenital infections should be screened for and treated if clinically indicated or confirmed.

Fetal fibronectin >200 ng/mL

These women are increased risk of delivering within 1 week (14%) and must be transferred to a gestation appropriate maternity and nursery setting (Flowchart 3) with commencement of an antenatal corticosteroid course (with tocolysis) if less than 34+6 weeks gestation. They may need to remain in this setting even on discharge as their risk of delivery within 2 weeks is as high as 29%.

Fetal fibronectin >500 ng/mL

These women are at very high risk of preterm birth: 38% within 1 week and 47% within 2 weeks. They must be urgently transferred to a gestation appropriate maternity and nursery setting (Flowchart 3) and remain there for the duration of their pregnancy or until they attain a gestation suitable to be transferred to a lower acuity centre. Antenatal corticosteroids must be commenced as a priority with tocolysis if appropriate (see below).
Antenatal Corticosteroids

<table>
<thead>
<tr>
<th>Initial course</th>
<th>Indications:</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>• Gestational age is between 23(^{-0}) and 34(^{-6}) weeks;</td>
</tr>
<tr>
<td></td>
<td>• Risk of imminent preterm birth, even if within 24 hours;</td>
</tr>
<tr>
<td></td>
<td>• Preterm birth is planned or expected within the next seven days;</td>
</tr>
<tr>
<td></td>
<td>• Elective caesarean section at less than 37(^{-0}) weeks.</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Dosage:</th>
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<tbody>
<tr>
<td>• Administer IM betamethasone in two doses of 11.4 mg 24 hours apart to the woman;</td>
</tr>
<tr>
<td>• If betamethasone is unavailable, give IM dexamethasone in two doses of 12 mg, 24 hours apart.</td>
</tr>
</tbody>
</table>

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<tr>
<th>Repeat dose or course</th>
<th>Indications:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>When the gestational age is \textbf{32}^{6-0} \textbf{days or less}, a repeat antenatal corticosteroid dose may be given 7 days or more after the first course in women still considered at risk of early preterm birth</td>
</tr>
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<thead>
<tr>
<th>Dosage:</th>
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</thead>
<tbody>
<tr>
<td>• A \textbf{single repeat dose} of IM betamethasone 11.4 mg IM OR;</td>
</tr>
<tr>
<td>• A \textbf{repeat course} of IM betamethasone in two doses of 11.4 mg 24 hours apart.</td>
</tr>
<tr>
<td>• If betamethasone is unavailable, give IM dexamethasone 12 mg.</td>
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<th>Further doses</th>
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<tr>
<td></td>
<td>Seven days after the first, \textbf{single repeat dose} (and less than 14 days since the initial course), if the woman is still considered to be at risk of preterm birth at a gestation \textbf{32}^{6-0} \textbf{days or less} within the next seven days, a further, \textbf{single repeat dose} of antenatal corticosteroids (IM betamethasone 11.4 mg IM) can be given, up to a maximum of three, single repeat doses only.</td>
</tr>
</tbody>
</table>

|               | Do not give any further repeat courses if a repeat course of IM betamethasone in two doses (of 11.4 mg 24 hours apart) has already been given. |
Tocolysis (First Line) – Nifedipine

Oral nifedipine is the preferred available tocolytic for suppression of preterm labour (reduced side effects, ease of administration and greater efficacy compared to betamimetics).

**Indication:**
Tocolysis with nifedipine is **ONLY** indicated if:
- The woman is less than 34+6 weeks pregnant and;
- Requiring transfer to a gestation appropriate maternity service and/or;
- Yet to complete an initial course of antenatal corticosteroids.

**Contraindications:**
**Maternal:**
- A systolic blood pressure of <90mmHg
- Cervical dilatation >3cm, especially in the context of PPROM
- Hypersensitivity to nifedipine or any excipients within the formulation
- Cardiac comorbidities including congestive cardiac failure and aortic stenosis
- Hepatic dysfunction
- Preeclampsia/eclampsia
- Concurrent use of IV salbutamol.

**Fetal:**
- Chorioamnionitis
- Placental abruption/Antepartum Haemorrhage
- Fetal distress
- Severe IUGR
- IUFD
- Known lethal fetal anomalies.

**Administration and Dosage**
- Confirm threatened or actual preterm labour;
- Check systolic blood pressure >90 mmHg before administering nifedipine;
- Give stat oral dose nifedipine 20 mg; chew or crush* to aid the speed of absorption.

If uterine contractions persist after 30 minutes:
- Give stat oral dose nifedipine 20 mg; chew or crush* to aid the speed of absorption; the maximum dose of nifedipine in the first hour is 40 mg.

If uterine contractions persist after 3 hours:
- Give stat oral dose nifedipine 20 mg; chew or crush* to aid the speed of absorption.
- Administer oral nifedipine 20 mg every three hours for 48 hours (unless contractions cease or the woman establishes in labour).
- The maximum dose of nifedipine is 160 mg in 24 hours

**Do not continue nifedipine beyond 48 hours. A repeat course of nifedipine should only be considered if the woman represents with PTL and the same conditions are met.**

**Nifedipine is NOT to be used prophylactically.**

* Nifedipine tablets may be crushed to aid administration. Crushed tablets should be administered within 30-60 seconds of crushing to avoid significant loss of potency.
Observations:
- Maternal baseline BP, TPR, FHR before administering the first dose of nifedipine 20 mg
- Continue hourly BP and maternal pulse for four hours
- Temperature every 4 hours
- The rate of observations should be tapered according to the clinical situation
- Continuous CTG while contracting
- Recomence CTG in the presence of:
  - Regular abdominal pains or tenderness
  - Change in amount, colour of liquor
  - Antepartum haemorrhage
- And arrange medical review
- Stop nifedipine if:
  - There is marked hypotension e.g. systolic < 90 mm Hg
  - Significant dyspnoea

Tocolysis (Second Line) - Salbutamol

Betamimetics such as salbutamol have historically been used for tocolysis. A 2014 Cochrane review found that betamimetics can delay birth effectively, however are associated with serious (potentially life threatening) maternal side effects including pulmonary oedema.

However, in situations where nifedipine is unavailable, salbutamol may be used with caution as a second-line tocolytic. It is not to be used in conjunction with nifedipine due to a high degree of synergism.

The indication for IV salbutamol requires that:
- The woman is less than 34+6 weeks pregnant and;
- Requiring transfer to a gestation appropriate maternity service.

Contraindications include:
- Maternal:
  - A systolic blood pressure of <90mmHg
  - Cervical dilatation >3cm, especially in the context of PPROM
  - Hypersensitivity to salbutamol or any excipients within the formulation
  - Cardiac comorbidities including congestive cardiac failure and aortic stenosis
  - Hepatic dysfunction
  - Preeclampsia/eclampsia
  - Insulin-dependent diabetes
  - Thyroid disease
  - Multiple pregnancy (increased risk of pulmonary oedema)
- Fetal:
  - Chorioamnionitis
  - Placental abruption/Antepartum Haemorrhage
  - Fetal distress
  - Severe IUGR
  - IUFD
  - Known lethal fetal anomalies.
  - Cardiac anomalies

Adverse Reactions include:
- Tachycardia
- Hypotension
- Tremor
- Pulmonary oedema
- Hyperglycaemia
- Hypokalaemia.
## Salbutamol Intravenous Infusion Regimen for Tocolysis

> If salbutamol is to be used for tocolysis, **an IV infusion/syringe pump must be used for administration**

> Salbutamol should be used with care, as it is associated with maternal tachycardia, hypotension, tremor, pulmonary oedema, hyperglycaemia and hypokalaemia

### Preparation of Infusion

| > Add 5 mg of salbutamol (5mL ampoule, Ventolin Obstetric Injection®) to 100 mL of 0.9% sodium chloride to prepare a 50 microgram / mL solution |
| Using a medication added label write “salbutamol 50 micrograms per mL” and attach label to syringe |

### Administration

| > IV infusion/syringe pump must be used for administration |
| > **Initial rate**: 12 mL / hour (10 micrograms / minute) |
| > **Increments**: increase by 4 mL / hour (3.3 micrograms / minute) every 30 minutes until: |
| > Contractions cease or |
| > Maternal pulse rate reaches 120 beats/minute |
| > **Maximum**: 36 mL / hour (30 micrograms / minute) |
| > Maintain rate for 1 hour after contractions have stopped, then gradually reduce by half every 6 hour |

**Do not exceed 48 hours of salbutamol therapy.** Only in exceptional circumstances should the treatment be continued for more than 24 hours.

### Practice Points

| > The dose is determined by the woman’s tolerance (i.e. clinical indicators) of adverse effects against desired response; |
| > Women should be warned about tremors, anxiety, dizziness and headaches; |
| > Collect baseline electrolytes, urea, creatinine and maternal blood sugar level before commencement of infusion; repeat 4-hourly if abnormal; |
| > Perform half hourly maternal pulse, BP and respiratory rate until the maintenance dose is reached; |
| > Exercise caution with any additional intravenous fluids to avoid fluid overload; |
| > Perform cardiovascular examination including auscultation of lung bases once in the first 24 hours of therapy; |
| > **Reduce** the infusion if the maternal pulse >120bpm; |
| > **Cease** the infusion and request medical review immediately if there is chest pain, dyspnoea or the respiratory rate >30/min; |
| > Continuous electronic fetal heart rate monitoring >28/40; **cease** the infusion if the fetal heart rate >180bpm; |

Betamimetics can cause a fall in serum potassium (K⁺). This is related to the movement of K⁺ intracellularly and is usually limited and self-reversing. **No treatment is needed unless ECG changes occur or the serum potassium falls below 2.5 mmol/L**
Preterm Labour Management (Flowchart 3)

If a woman is more than 3cm dilated at presentation, or contracting regularly with progressive cervical effacement and dilatation, management of preterm labour must be initiated according to the gestational age of the baby and the setting. In units without neonatal facilities suitable for the gestation, consult with tertiary centre. Consider maternal transfer if birth is not imminent (telephone the Perinatal Advice Line on 137 827) or consult with neonatal retrieval service (also phone 137 827) if birth is anticipated (see Perinatal Advice and Emergency Transport PPG available at www.sahealth.sa.gov.au/perinatal).

Antibiotics

There is no role for the use of antibiotics to treat threatened preterm labour as doing so has been associated with an increased risk of cerebral palsy. If a woman, however, is in active preterm labour, IV antibiotics for GBS prophylaxis are recommended to reduce the risk of early onset GBS neonatal sepsis. See Antibiotics in the Peripartum Period PPG (available at www.sahealth.sa.gov.au/perinatal) for antibiotic choice.

| Commence IV antibiotic prophylaxis for GBS for women in active preterm labour. |

If there is a significant clinical suspicion of chorioamnionitis, birth should be expedited under intravenous antibiotic cover to improve maternal and neonatal outcomes. See Antibiotics in the Peripartum Period PPG (available at www.sahealth.sa.gov.au/perinatal) for antibiotic choices.

Chorioamnionitis:

- Signs including:
  - Maternal pyrexia;
  - Maternal tachycardia;
  - Fetal tachycardia;
  - Uterine tenderness;
  - Offensive and/or purulent vaginal discharge;
  - Elevated white cell count;
  - Raised C-Reactive Protein.

- Consult with senior obstetrician, MFM and/or Infectious Diseases physician when deciding whether or not to augment labour. Uncertainty in diagnosis, particularly at very preterm gestations may warrant amniocentesis to confirm the clinical suspicion of chorioamnionitis.

- Complete septic screen should include histological and microbiological examination of the fetal and maternal surfaces of the placenta and membranes after birth (see Histopathology Management of the Placenta PPG available at www.sahealth.sa.gov.au/perinatal).

Magnesium Sulphate

| Intravenous magnesium sulphate must be administered to any woman considered at imminent risk of preterm birth or where birth is planned at <30 weeks. |

The administration of a bolus of magnesium sulphate in women at imminent risk of preterm birth at less than 30 weeks’ gestation has been shown to reduce neonatal deaths and cerebral palsy by as much as 15% and cerebral palsy alone by almost 30% with numbers needed to treat of 42 and 63, respectively. This is a significant intervention clinicians can implement to reduce the burden of preterm birth and improve outcomes once preterm labour is established. We anticipate further advice from the MAGENTA study as to whether there is benefit for women and fetuses at risk of preterm birth between 30 and 34 weeks in the near future.

In women at risk of imminent preterm birth <30 weeks magnesium sulphate should be administered regardless of:

- Plurality (number of babies in utero);
- The reason the woman is considered to be at risk of preterm birth;
- Parity (number of previous births the woman has had);
- The anticipated mode of birth, and;
- Whether or not antenatal corticosteroids have been given.
When birth is planned, commence magnesium sulphate as close to **four hours before birth** as possible.

**Contraindications and Considerations**

- Allergy
- Concomitant use of nifedipine (increased risk of hypotension)
- **In situations where urgent birth is necessary because of maternal or fetal compromise, the birth should not be delayed to administer magnesium sulphate.**


**Mode of Birth**

There are few clinical trials and little high-quality evidence to guide mode of delivery for preterm birth. The exact gestation at which the birth is occurring, the presentation of the fetus and the clinical circumstances relating to maternal and fetal wellbeing all need to be taken into account. So too does the setting and plans for neonatal resuscitation and clinical experience of the obstetrician, GP obstetrician and/or midwife. A Cochrane systematic review included only 122 women whilst a recent retrospective analysis of WHO datasets did not include context and reasons for clinical decision making, making interpretation of the results challenging.

Generally, the available evidence suggests a trend to increased maternal morbidity and decreased neonatal death and morbidity with elective caesarean for very preterm births. See *Perinatal Care at the Threshold of Viability* PPG (available at [www.sahealth.sa.gov.au/perinatal](http://www.sahealth.sa.gov.au/perinatal)) for further information to guide decision making at very preterm gestations.

In each circumstance consider:

- Is there clinical justification for delivery by emergency caesarean section on maternal grounds?
- What is the agreed gestation of the fetus?
- Is aggressive neonatal resuscitation planned and available?
- What is the presentation of the fetus?
- Is the labour advanced and are the membranes intact? Emergency caesarean section can result in severe maternal and fetal injury where a preterm fetus with ruptured membranes is deep in the pelvis with little or no lower segment.
- What is the condition of the fetus? For example, is there growth restriction, or a known congenital anomaly or insult? Chorioamnionitis and suspected fetal acidosis are relative contraindications to delivery by caesarean section.
- What is the parity and age of the mother?
- What is the skill and experience of the most senior available accoucheur?

Involve a Senior Obstetrician and/or Maternal Fetal Medicine sub-specialist in your decision-making where possible.

**Principles to bear in mind:**

- Keeping the membranes intact the delivery of the extremely preterm fetus *en caul* will minimise fetal trauma, whether at vaginal or caesarean birth.
- Birth using vacuum extraction (ventouse) is contraindicated at less than 34 weeks’ gestation.
- Birth using forceps is relatively contraindicated at less than 34 weeks’ gestation.
- Preterm breech births are at greater risk of cervical head entrapment; if proceeding with a vaginal preterm breech delivery, be prepared to incise the cervix and aim to ensure adequate maternal analgesia i.e. epidural (see Table 2).
- A Classical caesarean section can facilitate ease of delivery, minimise fetal trauma and is preferable to an extended lower segment incision (*J* or *T* incision). This does however have implications for future pregnancy management, and a significantly increased risk of placenta accreta.
References


Appendix 1. Major Risk Factors for Preeclampsia and Aspirin Prophylaxis

**Major Risk Factors Present at First Assessment?**

- Preeclampsia in previous pregnancy & birth <37 weeks or HELLP Syndrome
- Predisposing medical conditions
  - Autoimmune
    - Systemic Lupus Erythematosus
    - Scleroderma
    - Anti-Phospholipid Syndrome
  - Chronic hypertension (especially severe)
  - Diabetes type 1 and 2
  - Chronic kidney disease
- Assisted conception with oocyte donation
- Family history of preeclampsia (mother and/or sister)

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**No**

No requirement for LDA

**Yes**

- Refer for prompt face-to-face specialist consultation
- Prescription for LDA and calcium to be provided by obstetric service (as early in pregnancy as possible but should be prior to 16 weeks)
- If timely access to specialist appointment is a barrier, telephone or telehealth consultation is recommended prior to prescribing

For women with any major risk factor for preeclampsia, meta-analysis suggests a reduction in risk of preeclampsia of 46% (95% CI 30% - 50%) when low dose aspirin (LDA) therapy is initiated in early pregnancy. These women may also benefit from calcium. LDA will reduce the risk from about 1 in 5 to 1 in 10 high risk women.

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Plan and document roles and responsibilities for ongoing antenatal care along with monitoring and timing for follow-up with specialist
Appendix 2: Stratification of Preterm Birth Risk by fFN Concentration in Symptomatic Women

<table>
<thead>
<tr>
<th>fFN Level</th>
<th>N (%)</th>
<th>Delivery ≤ 7 days</th>
<th>Delivery ≤ 14 days</th>
<th>Delivery before 34 wks. 0 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 10 ng/mL</td>
<td>170 (57%)</td>
<td>1%</td>
<td>1.8%</td>
<td>1.5%</td>
</tr>
<tr>
<td>10 to 49 ng/mL</td>
<td>62 (21%)</td>
<td>0%</td>
<td>1.6%</td>
<td>8.2%</td>
</tr>
<tr>
<td>50 to 199 ng/mL</td>
<td>41 (14%)</td>
<td>0%</td>
<td>7.7%</td>
<td>11.5%</td>
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<tr>
<td>200 to 499 ng/mL</td>
<td>14 (5%)</td>
<td>14%</td>
<td>29%</td>
<td>33%</td>
</tr>
<tr>
<td>≥ 500 ng/mL</td>
<td>13 (4%)</td>
<td>38%</td>
<td>46%</td>
<td>75%</td>
</tr>
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Appendix 3: Table 2. Management of Cervical Head Entrapment at Vaginal Breech Delivery

<table>
<thead>
<tr>
<th>Manoeuvres</th>
<th>Description</th>
<th>Risks</th>
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<tr>
<td>McRoberts position</td>
<td>Flexion of maternal knees so that the anterior aspect of the thighs are pressed against the abdomen</td>
<td>Maternal tachycardia, Uterine atony</td>
</tr>
<tr>
<td>Uterine relaxation</td>
<td>Beta adrenergic agonist (terbutaline 250 μg subcutaneous)</td>
<td>Uterine atony</td>
</tr>
<tr>
<td></td>
<td>Nitroglycerin (50-200 micrograms IV or one metered dose of sublingual spray (400 micrograms)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>General anaesthesia</td>
<td></td>
</tr>
<tr>
<td>Duhrssen’s incision</td>
<td>1–2 fingers placed between the partially dilated cervix and the presenting part, with incisions made along the length of the undilated cervix at 6, 2 and 10 o’clock</td>
<td>Extension of incision to the lower uterine segment or broad ligament</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Injury to uterine vessels, ureter and bladder</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Severe haemorrhage</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cervical incompetence in subsequent pregnancy</td>
</tr>
<tr>
<td>Symphysiotomy</td>
<td>Infiltration of the symphysis pubis and overlying skin with local anaesthesia</td>
<td>Pelvic instability, requiring delayed orthopaedic repair</td>
</tr>
<tr>
<td></td>
<td>Insertion of firm catheter into the urethra to displace it laterally</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Incision made over the symphysis to separate it just enough to deliver the head</td>
<td></td>
</tr>
<tr>
<td>Zavanelli manoeuvre and caesarean delivery</td>
<td>Administration of tocolytic and attempt to replace the fetal body into the uterus, followed by caesarean section</td>
<td>Complications of caesarean section, Cervical injury and subsequent cervical incompetence</td>
</tr>
</tbody>
</table>
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