The Whole Nine Months
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The Western Australian Preterm Birth Prevention Initiative

A joint collaboration between:

Government of Western Australia
Department of Health
WOMEN AND NEWBORN HEALTH SERVICE

THE UNIVERSITY OF WESTERN AUSTRALIA

KING EDWARD MEMORIAL HOSPITAL
WOMEN & NEWBORN HEALTH SERVICE

women & infants research foundation
Western Australia

AMA
WESTERN AUSTRALIA

The Royal Australian and New Zealand College of Obstetricians and Gynaecologists

In conjunction with:

- The Statewide Obstetric Support Unit
- Australian Medical Association

JULY 2015 • SECOND EDITION

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The Western Australian Preterm Birth Prevention Initiative

Preterm birth is the single greatest medical problem in human reproduction in our society. One in twelve Western Australian babies is born too early and for Aboriginal people the proportion is one in seven. Many of these children will go on to lead a healthy and productive life, but for too many others, there may be lifelong disability.

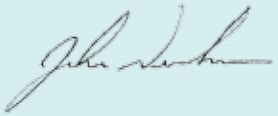
The Western Australian Preterm Birth Prevention Initiative aims to safely lower the rate of preterm birth in our state. Over the next year, *The Initiative* will commence with release of new evidence-based clinical guidelines and a dedicated Preterm Birth Prevention Clinic based at King Edward Memorial Hospital. Thereafter, there will be public health messages aiming to raise awareness in the women and families of our state. The entire process will be underpinned by on-going research and evaluation of the effects of implementation.

After many years of clinical and laboratory research, the field of preterm birth prevention has now come of age. The guidelines outlined in this document reflect the best evidence currently available. There is no doubt that clinical trials now in progress, and research studies yet to be initiated, will in due course enable expansion, refinement and improvement of these guidelines.

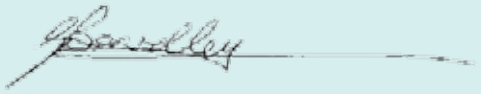
The Steering Committee of *The Initiative* will remain responsive to research findings, and vigilant and pro-active in altering and developing guidelines reflecting best practice. Every effort will be made to ensure that the health care workforce of our state has access to new information.

On behalf of the many clinicians and scientists who are contributing to *The Initiative*, we thank you for your role in reducing the rate of preterm birth and improving the health of the next generation of Western Australians.

On behalf of the Steering Committee,



Winthrop Professor John Newnham AM
Chair, WA PTB Prevention Initiative
Executive Director, WIRF



Mr Graeme Boardley
Acting Executive Director
Women and Newborn Health Service

Membership of the Steering Committee is shown in Appendix I.

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Key Practice Points

- Many cases of preterm birth may now be preventable. The antenatal care of all pregnant women needs to include an assessment of risk of preterm birth.
- Women with a history of spontaneous preterm birth between 20 and 34 weeks gestation should be prescribed natural progesterone vaginally, 200 mg daily, from 16 to 36 weeks gestation.
- Ultrasound measurement of the length of the cervix should be a routine component of the "anatomy" scan performed between 18 and 20 weeks gestation.
- Pregnant women with a shortened cervix measuring between 10 and 20 mm in mid-pregnancy should be prescribed natural progesterone vaginally, 200 mg daily, until 36 weeks gestation.
- Birth before 38 weeks' gestation may have important medical and behavioural implications for the child. Pregnancies should continue until at least 38 completed weeks' gestation unless there are medical or obstetric reasons justifying earlier intervention.
- Tobacco smoking remains an important and preventable cause of preterm birth. Practitioners need to harness the many strategies currently available to minimise the chance of pregnant women smoking, or being exposed to second-hand cigarette smoke.
- Cases at high risk of preterm birth, or where there is uncertainty, may benefit from referral to the Preterm Birth Prevention Clinic at King Edward Memorial Hospital. The Clinic staff will develop a management plan and the woman returned to her referring health care provider wherever suitable. For practitioners and patients at distant sites, this consultation may be by teleconference.

Further information go to www.**thewholeninemonths**.com.au

Preterm Birth
in Western Australia

Definition and Incidence

Preterm birth is defined as birth before 37 and after 20 completed weeks of gestation. In Western Australia, the rate of preterm birth is 8-9%, resulting in 2800 preterm infants each year from the state's total birth number of 34,000.

In Aboriginal Western Australians, the rate is approximately double.

Consequences

Preterm birth is the single greatest cause of death and disability in children up to five years of age in the developed world. In Western Australia, preterm birth is next to birth defects as the major known cause of perinatal loss.

The consequences of preterm birth are inversely proportional to the age at birth. Individuals born too early are at increased risk:

- **In the newborn period -** of death, respiratory disease, cerebral haemorrhage, necrosis of the bowel, infections and prolonged stay in an intensive care environment.
- **In childhood -** of cerebral palsy, chronic lung disease, deafness, blindness, learning difficulties and behavioural problems.
- **In adulthood -** of metabolic syndrome, diabetes and heart disease.

Prevention

Until recently, preterm birth was thought by many to be an unavoidable consequence of human reproduction. Times have changed and preterm birth is now considered to be preventable, at least in a proportion of cases.

There are many pathways to untimely early birth and recent advances mean that several of these pathways can be prevented at their onset. Research discoveries now enable clinical strategies to be developed that will safely prevent a variety of the causes.

The "interventions" which are feasible to be introduced into Western Australia and for which there is strong evidence of effectiveness are described in the following pages.

Interventions for the prevention of preterm birth

1 Pre-conception care

Ideally, all women should prepare for a future pregnancy by optimising their health. It is recommended that all women seek pre-conception counselling from their general practitioner.

Factors in a woman's history that increase her risk of subsequent preterm birth include:

- a personal or family history of early birth
- prior surgical intervention on the woman's cervix and
- recurrent miscarriages.

Risk stratification based on history is important for future pregnancy management.

Counselling should include:

- strategies to normalise body weight
- avoidance of smoking and exposure to second-hand cigarette smoke
- avoidance of recreational substance abuse
- education regarding alcohol consumption and
- assurance that supplementary folate is taken daily for at least three months before conception.

Women with medical conditions that affect pregnancy outcomes require diagnostic and therapeutic management in order that they enter pregnancy with the best possible health. Management should include:

- rigorous control of blood glucose levels in women with diabetes
- control of blood pressure in women with hypertension
- stabilisation of autoimmune conditions and
- referral to appropriate specialists when required.

Medications should be reviewed and altered if required to be suitable for use in pregnancy.

Where appropriate, women may benefit from being informed that preterm birth is more common at the extremes of maternal age and after inter-pregnancy intervals less than 18 months.

2 Progesterone treatment

Progesterone can be used in certain circumstances to prevent preterm birth. The exact mechanism of action is unknown but two mechanisms are proposed to underpin its effectiveness. First is an anti-inflammatory effect and second is a possible role in preventing functional withdrawal of the hormone at the receptor level.

Indications

There are two principal indications for use of progesterone treatment in the field of preterm birth prevention.

- In women with a history of preterm birth or a previous pregnancy loss between 20 and 34 weeks gestation. The treatment should commence at 16 weeks and continue until 36 weeks gestation. In this circumstance, the progesterone treatment will halve the risk of recurrence of a preterm birth.
- In pregnant women found on ultrasound imaging examination between 16 and 24 weeks gestation to have a shortened cervix with a length between 10 and 20 mm. This indication is based on the ultrasound measurement at 16-24 weeks and applies to all pregnant women with a singleton pregnancy, except of course those women who have already been prescribed progesterone based on their history. The incidence of shortened cervix at this gestational age in the general obstetric population is expected to be 2-3%. When prescribed on the basis of cervical shortening, vaginal progesterone will halve the risk of early preterm birth.

Progesterone treatment is not effective in preventing preterm birth in women with a multiple pregnancy and is not recommended in such cases.

(See next page for formulations)

Formulations

For preterm birth prevention only natural progestogens are used, and these are considered to be safe. There are two options:

- Vaginal progesterone which is used daily and has a half-life of 13 hours. This treatment is generally free of side effects although some women complain of local irritation. Studies have employed doses ranging from 90 to 400 mg each day, but there is no evidence that any one dose is superior to another. A dose of 200 mg inserted vaginally each evening is recommended. Vaginal progesterone is the first-line treatment option and is available on prescription.
- 17alpha hydroxyprogesterone caproate (17OHP) is a natural progesterone conjugate with a longer half-life of 7 days. 17OHP is administered by intra-muscular injection and is given weekly. In Australia, 17OHP is only available under the Special Access Scheme of the Australian Government Therapeutics Goods Administration.

3 Cervical cerclage

Cervical cerclage is the surgical placement of a suture or tape around the cervix in an attempt to prevent dilatation and preterm birth. The procedure requires anaesthesia.

Cerclage is recommended in two general circumstances.

- In women with a past history of spontaneous preterm birth prior to 34 weeks gestation, cervical cerclage significantly reduces the rate of spontaneous preterm birth prior to both 34 and 37 weeks' gestation. The effectiveness of this intervention in this group of women is similar to progesterone. The choice between progesterone and cervical cerclage should be individualised and based on clinician and patient preference and the woman's specific history.
- When transvaginal measurement of cervical length is less than 10 mm. In women with no past history of spontaneous preterm birth, cervical length less than 10mm is the only indication for cervical cerclage. When used for this indication, the relative effectiveness of cerclage versus progesterone remains uncertain.

There is no evidence that the combined use of both progesterone and cerclage is of benefit. The use of the two treatments together is best reserved for cases in which one of the two treatments appears to be failing, although evidence of effectiveness for the combined treatment is lacking.

4 Measurement of cervical length

Shortening of the length of the cervix in mid-pregnancy is predictive of subsequent preterm birth. The measurement is made by ultrasound imaging and requires special training and rigorous adherence to standards.

A brief description of the methodology to be employed is included in Appendix II

Many women will require a trans-vaginal scan to measure the cervical length as a full bladder may elongate the length and provide false reassurance. For women at low risk of preterm birth, the ultrasound measurement may be made by trans-abdominal scan as a part of the general imaging study, as long as the cervical length is found to be 35 mm or more. For those cases in which the length the less than 35 mm, of if the pregnancy is not at low risk of preterm birth, a trans-vaginal scan is recommended.

Measurement of cervical length is now recommended as part of the routine 18-20 week ultrasound scan and the result included in the report. This measurement is routine and therefore included in the imaging examination of all pregnant women, whether they be at low or high risk of preterm birth.

There is now Level I evidence that women found to have a cervix between 10 and 20 mm in length at this time of pregnancy will reduce by half their risk of early preterm birth if prescribed daily vaginal progesterone. Therefore, women found to have a cervical length between 10 and 20 mm should be prescribed natural vaginal progesterone 200 mg daily until 36 weeks gestation.

Ultrasound measurement of cervical length is predictive of preterm birth only in the 16 to 24 week gestational age window and measurements later in pregnancy are of decreasing predictive value. These measurements should not be performed after 28 weeks gestation.

There is little information to guide practice as regards repeat ultrasound measurements of cervical length in women in whom progesterone treatment has been commenced or cerclage inserted. Management of each case should be individualised and may be influenced by the presence of other clinical risk factors.

5 Individualised management guidelines

Management of individual cases is based on risk assessment. In this risk assessment, previous preterm birth refers to cases of spontaneous labour or labour following pre-labour rupture of membranes, rather than delivery resulting from late termination of pregnancy or intervention required for a medical disorder.

Women classified as **low risk** of preterm birth will have no personal or family history of previous preterm birth, no prior pregnancy loss between 16 and 24 weeks gestation and no previous cervical surgery or a uterine anomaly.

Women classified as **medium risk** will have a family history of preterm birth in a first degree relative, previous cervical surgery or a significant uterine anomaly.

Women classified as **high risk** will have a personal history of previous preterm birth or a prior pregnancy loss between 16 and 24 weeks gestation.

6 Prevention of non-medically indicated late preterm birth

Late preterm birth is defined as birth between 34 weeks and 0 days and 36 weeks and 6 days gestation. 70% of all preterm births occur in this time period.

In Western Australia, the percentage of live births between 32 and 36 completed weeks of gestation has increased 50% in the last 26 years. Similar increases in this gestational age period have been observed in other Western environments.

Late preterm birth is a potential danger to the child. Infants born in this age range are immature in their physiology and metabolism. In the neonatal period late preterm infants are at increased risk of death, admission to neonatal intensive care, respiratory distress and need for ventilation, apnoea, temperature instability, hypoglycaemia, jaundice, poor feeding, separation from the mother and re-admission after discharge. In childhood, there are increased risks of cerebral palsy, speech disorders, growth delay, learning problems and behavioural disorders including hyperactivity.

There is strong evidence that many of these risks extend into the 37 week 0 day to 37 week 6 day gestational age period.

Therefore, it is recommended that pregnancies continue until at least 38 weeks gestation unless there is a medical or obstetric reason justifying earlier intervention.

In cases in which there is reason for intervention before 38 completed weeks of gestation, prolongation of pregnancy may be achieved by more frequent visits to the obstetric health care provider and liberal use of fetal surveillance. In each case an individualised management plan is required and needs to balance the risks of early birth against the medical or obstetric condition that is prompting early delivery.

7 Reducing tobacco exposure

Cigarette smoking causes preterm birth and a dose-dependent reduction in birthweight. In Western Australia, the percentage of women who smoke during pregnancy has fallen to 12%. In Aboriginal women, however, the percentage has remained unchanged and is nearly 50%. Smoking cessation interventions in pregnancy have been shown to reduce both preterm birth and low birthweight.

Screening

Women who smoke, or have recently ceased smoking, should be identified at their first contact with a health care service, ideally in the preconception setting. Health care providers should enquire about smoking history and current smoking pattern and this information should be recorded so that it is available for the remainder of the pregnancy.

Counselling/behavioural support

All women who currently smoke or have recently quit should be advised of the risks of smoking and the value of smoking cessation. Health care providers should assess the patient's motivation and thoughts related to smoking cessation/reduction. They should advise patients to stop smoking and offer assistance with any smoking cessation attempts. Assistance can take the form of written information, referral to quit lines and/or referral to individual or group-based smoking cessation programs.

Phone and online resources for counselling and behavioural support are widely available in Australia. **Quitline** can provide telephone counselling assistance and make referrals to local services for the cost of a local phone call.

Quitline Phone Number Western Australia (WA) 13 78 48

The Commonwealth Department of Health has developed a website and a range of resources, including a phone app "Quit for you – Quit for two" to encourage smoking cessation in pregnant women.

The Royal Australian College of General Practitioners has developed clinical practice guidelines to aid the treatment of tobacco use and dependence. These guidelines include a widely-used 5-step process that can be used in all health care settings to aid smoking cessation.

The 5 A structure for smoking cessation

Ask about tobacco use	Identify and document tobacco use for every patient.
Assess readiness to quit and degree of nicotine dependence	Ask the patient how she feels about her smoking and if she is ready to stop. Willingness to quit can change with life circumstances such as pregnancy. Assessment can be made quickly by asking the patient: • How soon after waking does she have her first cigarette? • How many cigarettes are smoked daily? • Does she get cravings for a cigarette, or urges to smoke and withdrawals symptoms if/when she has tried to quit?
Advise all smokers to quit	Brief, repeated, consistent advice to quit smoking can increase success rates.
Assist	Provide advice and information appropriate to the patient's readiness to quit.
Arrange follow up	For the patient who is attempting to quit, arrange follow up visits and provide support and encouragement as appropriate.

Summarised from *Supporting smoking cessation: a guide for health professionals.*
Melbourne: The Royal Australian College of General Practitioners, 2011
[Updated July 2014]
http://www.racgp.org.au/download/Documents/Guidelines/smoking-cessation.pdf

Nicotine Replacement Therapy (NRT)

This information has been taken from *Supporting smoking cessation: a guide for health professionals.* (RACGP 2014).

There is limited evidence of the effectiveness of NRT in helping pregnant women stop smoking. The main benefits of using NRT are the removal of the other toxins contained in tobacco smoke and the lower dose of nicotine delivered by NRT than tobacco smoke. NRT can be used by pregnant and breastfeeding mothers, but the risks and benefits should be explained carefully to the woman by a suitably qualified health professional and the clinician supervising the pregnancy should be consulted.

In general, intermittent (oral) NRT should be used during pregnancy to deliver a lower total daily nicotine dose. However, larger doses or even combination therapy may be required to relieve cravings and withdrawal symptoms in pregnancy due to the faster clearance of nicotine. If patches are used by pregnant women, they should be removed before going to bed to protect the fetus from continuous exposure to nicotine.

Neither of the two prescription medicines for smoking cessation in Australia, varenicline and bupropion, has been shown to be effective or safe for smoking cessation treatment in pregnant smokers and they are not recommended. If a woman becomes pregnant while taking either agent, treatment should be ceased, and, if she agrees, reporting her pregnancy outcome to health authorities and the manufacturer may over time help us better understand any risk.

Partners

Partners of pregnant women should be asked about smoking status at points of contact with health professionals, including preconception, antenatal appointments, hospital admission and at follow up appointments. Partners of pregnant women should be identified and offered treatment for smoking cessation.

8 Judicious use of fertility treatments

Fertility treatments contribute to the risk of preterm birth both by increasing the incidence of multiple pregnancies and other obstetric and perinatal complications that are less clearly understood.

Counselling women who are considering fertility treatment should include discussion of the increased risk of preterm birth and its consequences. Practitioners involved in fertility care need to be aware of strategies that reduce the risk of multiple pregnancy and preterm birth.

9 The KEMH Preterm Birth Prevention Clinic

The KEMH Preterm Birth Prevention Clinic is a dedicated, multidisciplinary clinic with the aim of reducing the rate of preterm birth for women at increased risk. The clinic combines the benefits of evidence-based management, innovative care strategies and ongoing research to achieve reduction in the overall number preterm births and prolong pregnancies to reduce extreme preterm birth. The Preterm Birth Prevention Clinic commenced in November 2014.

The Clinic is primarily consultative and each woman can expect to have one, two or three visits enabling a treatment plan to be devised and documented. The Clinic will aim to refer women back to their usual health care provider with their personalised management plan and the remainder of their antenatal care and the birth to be conducted in the usual manner. A smaller number of women will need to have ongoing care at KEMH, possibly with ongoing involvement of the Clinic.

The Clinic will be staffed by obstetricians and midwives with a specialised interest in preterm birth prevention. In terms of administration, the Clinic will operate within the Maternal Fetal Medicine (Gold) Team, which in turn is within the Department of Obstetrics.

Referrals

The clinic will receive referrals from general practitioners, public obstetric and midwifery clinics from both metropolitan and rural locations, obstetricians and internally from clinics at King Edward Memorial Hospital.

It is estimated that the clinic will see 180 to 200 new patients annually. In addition, many other referrals will be managed by telehealth, or written and verbal communication.

Referrals will be received by the hospital through the usual referral system either into the general pool or direct referral to the Maternal Fetal Medicine Service.

General fax number: **08 9340 1031**

MFM fax number: **08 9340 1060**

Preterm Birth Prevention Clinic Midwives: **0466 329 638**
(Mon - Fri 8 – 4) **Fax No.** **9340 2469**

(See next page for referral criteria)

Referrals meeting the criteria will be collated by the Preterm Birth Prevention Clinic midwives and reviewed by the clinic doctors. Each referral will be triaged to receive either an appointment at the clinic, a telehealth consult, a phone call or letter to the referrer.

Referral criteria:

1. Previous preterm birth at 24 to 34 weeks' gestation
2. Two or more previous preterm births between 24 and 36+6 weeks' gestation
3. A pregnancy loss between 16+0 and 23+6 weeks' gestation
4. Significant uterine anomaly
5. History of cone biopsy of the cervix or more than one LLETZ procedure
6. Specific concern of referring clinician

Information to be provided with referral:

- A copy of the patient's booking blood test results and any ultrasound scan reports. Discharge summaries and operation reports from previous pregnancies
- Placental histopathology, post mortem examination results and relevant investigations from previous births
- Letters from other specialists involved in care.

APPENDIX I

The Western Australian Preterm Birth Prevention Initiative
Steering Committee

Professor John Newnham (Committee Chair and Executive Director Women and Infants Research Foundation)

Mr Graeme Boardley (Acting Executive Director, Women and Newborn Health Service)

Professor John Challis (Pro-Vice Chancellor of Health and Medical Research, The University of Western Australia)

Professor Jan Dickinson (Head, Maternal Fetal Medicine, Women and Newborns Health Service)

Professor Dorota Doherty (Head of Biostatistics and Study Design, Women and Infants Research Foundation)

Dr Michael Gannon (President, (WA) Australian Medical Association)

Dr Janet Hornbuckle (Head of Obstetrics, King Edward Memorial Hospital; Co-lead of WA Women and Newborn Health Network)

Dr Anne Karczub (Director of Obstetrics, King Edward Memorial Hospital, Medical Co-Director, State-wide Obstetric Support Unit, Western Australia - SOSU)

Professor Jeffrey Keelan (Director, Women and Newborns Health Research Network, King Edward Memorial Hospital)

Mrs Barbara Lourey (Clinical Midwifery Manager, King Edward Memorial Hospital)

Dr Chhaya Mehotra (Obstetrician, King Edward Memorial Hospital)

Dr Diane Mohen (Co-Director, State-wide Obstetric Support Unit, Western Australia - SOSU)

Associate Professor Craig Pennell (Head, Preterm Birth Prevention Clinic, King Edward Memorial Hospital)

Ms Bronwyn Rose (Chair and Co-Founder, Tiny Sparks WA)

Professor Tarun Weeramanthri (Executive Director, Public Health and Clinical Services Division, Health Department of Western Australia)

Dr Vicki Westoby (GP Liaison Officer, King Edward Memorial Hospital)

Mrs Tina Williams (Operations Manager, Women and Infants Research Foundation)

APPENDIX II

Ultrasound measurement of the cervix in mid-pregnancy

Cervical length is a strong predictor for preterm birth. This measurement is now standard practice at the 18-20 week ultrasound examination.

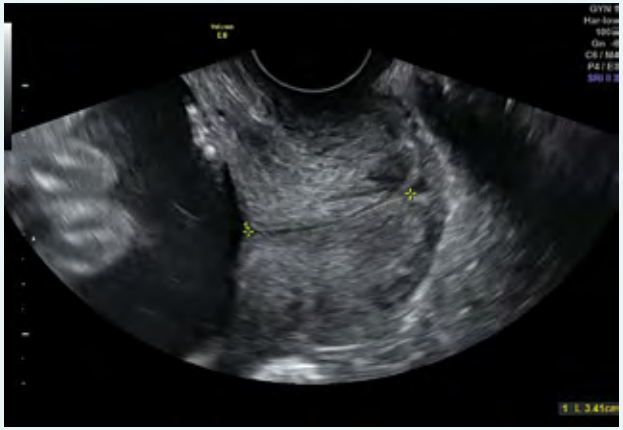
The transvaginal approach to cervical length assessment is the recommended method and an adequate image can be obtained in almost all cases.

The transabdominal approach is less invasive and may be more acceptable to some women, although this technique will tend to overestimate the cervical length and may fail to identify the cervical canal when the bladder is empty or if there is cervical shortening.

For women at low risk of preterm birth, transabdominal measurement may be the primary approach. A cervical length more than 35mm on transabdominal measurement will provide reassurance that the cervix is not shortened and that transvaginal measurement is not required. In all other circumstances, transvaginal measurement is recommended.

All sonographers performing cervical length screening need to have completed appropriate training and credentialing procedures.

An example of ultrasound measurement of transcervical length is shown below



Sagittal image of the cervix showing the cervical canal. The measurement of cervical length is made by caliper placement and includes the distance between the two yellow markers, which display the internal cervical os on the left and the external os on the right.

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