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MINISTRY OF HEALTH MALAYSIA

GUIDELINES ON PREVENTION AND MANAGEMENT OF PRETERM BIRTH

MEDICAL DEVELOPMENT DIVISION
MINISTRY OF HEALTH MALAYSIA

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Guidelines on Prevention and Management of Preterm Birth

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LIST OF ABBREVIATIONS

ACOG	American College of Obstetricians and Gynecologists
C&S	Culture and Sensitivity
FEME	Full and Microscopic Examination
NICE	National Institute for Health and Care Excellence
O&G	Obstetrics and Gynaecology
PPROM	Preterm Prelabour Rupture of Membranes

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FOREWORD BY
DIRECTOR-GENERAL OF HEALTH MALAYSIA

Complications of prematurity are the single largest cause of neonatal death and the second leading cause of death among children under the age of 5 years. Global efforts to further reduce child mortality demand urgent action to address preterm birth.

To accomplish Goal 3 of the Sustainable Development Goals for 2030, the Ministry of Health, Malaysia (MOH) is committed to providing consistent, evidence-based, and high-quality maternity care to women nationwide. The creation of this Guideline on Prevention and Management of Preterm Birth is anticipated to improve patient care at MOH facilities as well as private facilities.

I would like to convey my gratitude to everyone who contributed, whether directly or indirectly, to the creation of this guideline, as their work will be appreciated by all parties involved. Let's hope that these efforts for reducing preterm birth will be met, followed by the goal of reducing perinatal morbidity and mortality in Malaysia.

DATUK DR. MUHAMMAD RADZI BIN ABU HASSAN
Director-General of Health Malaysia

FOREWORD BY
DEPUTY DIRECTOR-GENERAL OF HEALTH (MEDICAL) MALAYSIA

Preterm birth is increasingly common with substantial medical, economic and social impact as it is invariably associated with acute and chronic complications. Babies born preterm have high neonatal and infant mortality rates, and the risk of mortality increases as gestational age at birth decreases.

In Malaysia, approximately 500,000 babies are born each year, and the rate of preterm birth is about 12.3%. Thus, the development of this Guideline on Prevention and Management of Preterm Birth is to improve the prediction, prevention and management of preterm birth based on evidence obtained from published scientific literature, international guidelines and the experience of the guideline committee members.

I would like to congratulate and acknowledge the effort of the drafting committee especially the Medical Development Division of MOH and Jawatankuasa Pengurusan dan Perkembangan O&G KKM (JPPOBG) and members from all other disciplines for this great initiative in preparing this edition.

DATO' DR. ASMAYANI BINTI KHALIB
Deputy Director-General of Health (Medical) Malaysia

SECTION 1

INTRODUCTION AND BACKGROUND

SECTION 1: INTRODUCTION AND BACKGROUND

1.1 Definition of Preterm Birth

Preterm birth is defined as a birth that occurs between 22 weeks and before completed 37 weeks of gestation [1]. It is further classified into:

a. Extremely preterm (<28 weeks);
b. Very preterm (28 to <32 weeks); and
c. Moderate to late preterm (32 to <37 weeks).

1.2 Understanding the Burden of Preterm Birth

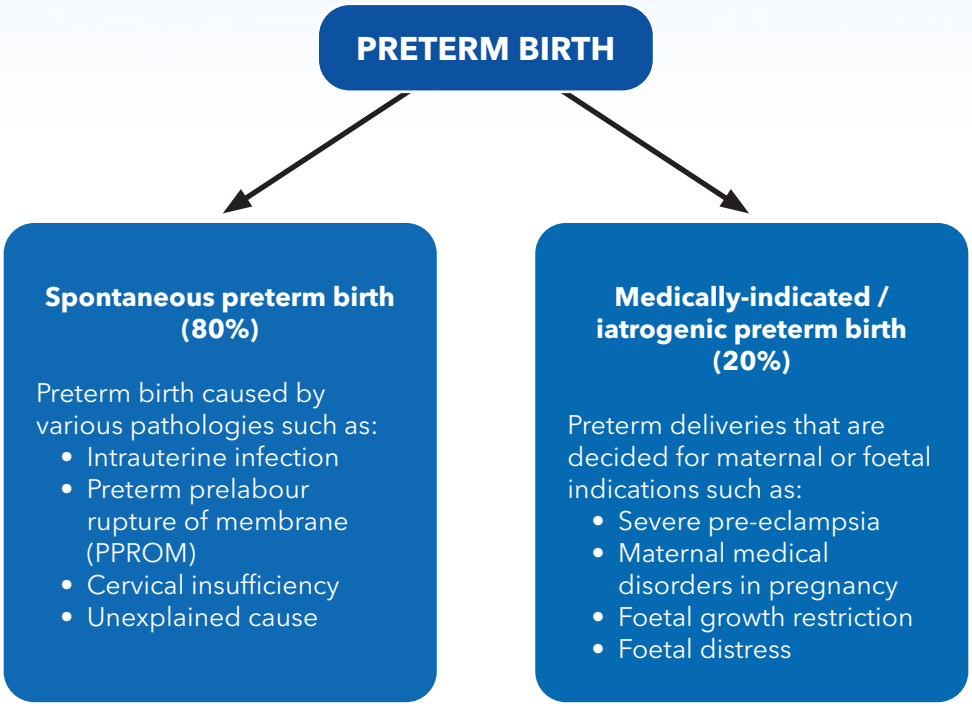
Preterm birth is a global problem. Approximately 15 million babies are born preterm worldwide annually, making up a global preterm birth rate of 10%[1,2], which is similar to the rate in developed countries like the United States (10.2% in 2019)[3]. Among preterm babies, more than 1 million of them die before the age of 5 years due to the complications of prematurity[2]. While children's mortality related to infection has declined in the last 2 decades, children's mortality related to prematurity has evolved into the leading cause of death in children below 5 years old. The risk of mortality increases as gestational age at birth decreases, and the preterm babies who survive also have higher rates of long-term neurodevelopmental disability.

In Malaysia, approximately 500,000 babies are born each year, and the rate of preterm birth is about 12.3%. Prematurity is also the second leading cause of under-five mortality. According to the Malaysia National Neonatal Registry 2016[4], among preterm babies, 23.3% were born below 32 weeks, and 25.5% were ≤1500g birthweight. The survival rates of babies born below 26 weeks were much lower as compared to babies born between 28 to 32 weeks (<50% versus 80 to 90%). Besides, 77.3% of premature babies <32 weeks suffered at least one major morbidity (e.g. patent ductus arteriosus requiring surgical ligation, stage 3,4 or 5 retinopathy of prematurity, oxygen dependency at 36 weeks or discharge, confirmed sepsis, or necrotizing enterocolitis).

Several prophylactic interventions such as cervical cerclage, progesterone and Arabin pessary have been assessed for women at high risk of preterm birth. There are research findings which reveal their effectiveness, however, due to the heterogeneity of preterm birth causes, there is still doubt about which intervention works best for the prevention of preterm birth. Recommendations made in international guidelines are based on the extrapolation of research findings [3,5].

1.3 Classification of Preterm Birth

Preterm birth is classified into spontaneous preterm birth and medically-indicated or iatrogenic preterm birth[6]



This guideline focuses on preventing and managing spontaneous preterm birth for singleton pregnancies. The management of medically-indicated / iatrogenic preterm birth and preterm birth related to multiple pregnancies is beyond the scope of this guideline.

1.4 Risk Factors of Preterm B irth

Previous studies have identified several important risk factors that link to spontaneous preterm birth, which are:

a. Previous spontaneous preterm birth
A history of preterm birth, especially if it had occurred at below 32 weeks of gestation, is a strong predictor for recurrent preterm birth in subsequent pregnancy [7,8].

b. Short cervix
The risk of spontaneous preterm birth increases fourfold when the cervical length of a pregnant woman measured between 18 and 24 weeks of gestation is <25 mm[9].

c. Previous cervical surgery/trauma
Previous excision of the cervix for cervical intraepithelial neoplasia (CIN) may increase the risk of preterm birth. The risk increases with increasing depth and volume of cervical excision.

Women with a medium (10-14 mm) (RR, 1.28; 95% CI, 0.98-1.68), large (15-19 mm) (RR, 2.04; 95% CI, 1.41-2.96) or very large (≥20 mm) (RR, 2.40; 95% CI, 1.53-3.75) excision of CIN have a higher risk of preterm birth than those with a small cervical excision (<10 mm)[10].

d. Smoking during pregnancy

Tobacco use during pregnancy is associated with an increased risk of preterm birth, and the risk increases with the higher number of cigarettes smoked. Second-hand smoke is also associated with an elevated risk of preterm birth.

The underlying mechanism could be related to nicotine-induced vasoconstriction and an elevated blood level of carbon monoxide [11,12,13]. Smoking cessation can lower the risk of preterm birth by 20%[14].

e. Bacteriuria / urinary tract infection (UTI)

Screening pregnant women for asymptomatic bacteriuria with urine culture during pregnancy and prompt antibiotic treatment may reduce the risk of pyelonephritis and preterm birth[6]. However, because of the low certainty of current evidence[15], universal screening for asymptomatic UTIs cannot be recommended as a routine practice for the time being. Otherwise, prompt investigation and treatment for pregnant women with symptomatic UTIs are recommended in this guideline.

f. Genital tract infection during pregnancy

Ascending infection in the female lower genital tract is the most common route of intrauterine infection that is responsible for the aetiology of spontaneous preterm birth. Microorganisms commonly isolated from infected amniotic fluid include Ureaplasma spp, Mycoplasma spp, Streptococcus, Fusobacterium and Enterobacteriaceae [11,13].

Other types of infections that are associated with preterm birth include Bacterial vaginosis, Trichomonas vaginalis, Neisseria gonorrhoea and Chlamydia trachomatis [6,11,13]. Treating symptomatic bacterial vaginosis can reduce the risk of preterm birth [16].

g. Low body mass index (BMI)

Preterm birth is also related to a maternal pre-pregnancy BMI below 18.5 kg/m^2, likely due to underlying malnutrition and eating disorders among underweight mothers [6,11,17]. The risk of preterm birth increases with the severity of underweight [17].

h. Teenage pregnancy

The increased risk of preterm birth among teenage mothers is attributable to gynaecological immaturity, being underweight, poor eating habits and unhealthy habits e.g. smoking and illicit drug abuse [6,13].

i. Uterine anomaly

Uterine anomalies, namely unicornuate, bicornuate and didelphys, are associated with preterm birth. The underlying mechanisms are uterine musculature deficiency, alternation of cervix and uterine malperfusion [6,13].

j. Multiple pregnancies

It is estimated that about 60% of twin pregnancies are born before 37 weeks and about 75% of triplet pregnancies are born before 35 weeks. The rise in the rate of multiple pregnancies is attributable to the increased use of assisted reproductive technology. To overcome this issue, single embryo transfer for a woman undergoing in-vitro fertilization is an effective strategy to reduce multiple pregnancies[11].

Noteworthily, the mechanism of preterm birth in multiple pregnancies is different from a singleton pregnancy[18]. Besides uterine overdistension, uterine contraction is also contributed by the increased secretion of uterotonic mediators, such as corticotrophin-releasing hormone from a larger placental mass and surfactant protein-A from foetal lungs.

1.5 The Role of Progesterone as a New Prophylactic Intervention

The quiescence of a gravid uterus, especially in the second half of pregnancy, is maintained by progesterone. Although the aetiology of preterm birth is heterogeneous, progesterone deficiency has been proven to be a significant causal factor associated with preterm birth[19]. Many randomized trials and meta-analyses have also revealed the beneficial effect of progesterone supplementation in pregnant women who are at risk of preterm birth[20-30]. Progesterone maintains uterine quiescence within the myometrium through several mechanism of actions, including reduction of stimulatory prostaglandins release, inhibition of contraction-associated protein genes (e.g. ion channel, oxytocin and prostaglandin receptors and gap junctions), maintenance of cervical integrity and anti-inflammatory effect [13].

1.6 Objectives of the Guideline

This guideline is developed for the prevention of spontaneous preterm birth in singleton pregnancies. As the pathophysiology of preterm birth in multiple pregnancies is different from singletons, the discussion about the prevention of preterm birth in multiple pregnancies is beyond the scope of this guideline.

a. General objective

i. To establish a guideline which aims to reduce the rates of spontaneous preterm birth.

b. Specific objectives

i. To develop a screening procedure to identify pregnant women at risk of preterm birth.

ii. To ensure health care providers can recognize preterm labour to enable them to commence appropriate management.

iii. To guide the use of progesterone supplementation and cervical cerclage for preventing preterm birth in singleton pregnancies.

SECTION 2

SCREENING STRATEGIES FOR PRETERM BIRTH

SECTION 2: SCREENING STRATEGIES FOR PRETERM BIRTH

2.1 Initial Risk Assessment

2.1.1 Perform an initial risk assessment at the time of booking to screen all pregnant women for the following risk factors of preterm birth:

a. Smoking;
b. Maternal age <20 years old;
c. Symptoms and signs of urinary tract infection (UTI);
d. Symptoms and signs of genital tract infection symptoms;
e. History of preterm birth;
f. History of cervical surgery; and
g. BMI <18.5 kg/m^2

Appropriate treatment can then be commenced to tackle the individual risk factor and help reduce the risk of preterm birth.

2.12 Send midstream urine (MSU) for FEME for pregnant women with UTI symptoms. If MSU FEME reveals a UTI, send an MSU C&S and start the woman on a seven-day course of antibiotics. A positive urine culture of ≥10^5 CFU/ml confirms the diagnosis of UTI. Once the completed treatment, repeat an MSU C&S to ensure the resolution of infection.

2.13 The relevant microorganisms to be screened for pregnant women who have symptoms of genital tract infection include Ureaplasma spp, Mycoplasma spp, Neisseria gonorrhoea, Chlamydia trachomatis, Trichomonas vaginalis, Bacterial vaginosis, and Group B Streptococcus (GBS). It is important to choose appropriate tests to accurately diagnose the types of genital tract infections.

2.2 Further Risk Assessment

2.2.1 Perform a further risk assessment to identify the following groups of pregnant women who are at higher risk for preterm birth:

a. History of mid-trimester loss or spontaneous preterm birth (between 16 and <37 weeks of gestation);
b. Previous preterm prelabour rupture of membranes (PPROM) excluding delivery at term or via an induction;
c. Previous cervical surgery, such as cone biopsy, large loop excision of the transformation zone or trachelectomy;
d. Cervical cerclage in a previous pregnancy; and
e. Known uterine anomalies, such as the bicornuate uterus and uterine didelphys.

2.2.2 Refer pregnant women with any of the above risk factors to the O&G specialist clinic for further evaluation and cervical length measurement.

2.2.3 The following groups of pregnant women DO NOT require a referral to an O&G specialist clinic for preterm birth risk assessment:specialist clinic for preterm birth risk assessment:

a. Previous iatrogenic preterm delivery for obstetric indications such as maternal medical disease, severe pre-eclampsia, placenta previa and intrauterine growth restriction;
b. Previous termination of pregnancy by either medical (gameprost) or surgical (dilatation and curettage) method;
c. Recurrent first trimester miscarriage;
d. Previous mid-trimester loss caused by a missed miscarriage; and
e. Previous preterm delivery related to multiple pregnancy.

2.3 Cervical Length Measurement

2.3.1 Pregnant women with a cervical length of ≤25 mm in the second trimester are 4.5 times more likely to end up with a preterm birth [9]. Transvaginal ultrasound is the recommended modality to assess cervical length because it is not affected by maternal obesity, the position of the cervix and shadowing from the foetal presenting part [3].

2.3.2 When measuring cervical length, the following precautions are necessary to ensure accurate measurement [3,31]:

a. Instruct the woman to empty her bladder before a transvaginal ultrasound.
b. Place the transvaginal probe in the anterior fornix of the vagina
c. Avoid undue pressure on the cervix that will falsely increase its length
d. Measure the cervical length between the internal os and external os (shown in **Figure 1**) three (3) times and take the shortest measurement. If the cervix is curved, cervical length is measured in two (2) or more segments to obtain an accurate length (shown in Figure 2).

2.3.3 Perform cervical length assessment every two (2) weeks from 16 weeks to 24 weeks of gestation on women at higher risk for preterm birth. A cervical length of ≤25 mm indicates a short cervix (shown in **Figure 3**), and subsequent management should be discussed with the patient. Apart from the measurement of cervical length, funnelling (shown in **Figure 4**) is also another sign of cervical shortening that should be looked for. If the cervical length remains normal i.e. >25 mm after 24 weeks, cervical length surveillance can be stopped thereafter.

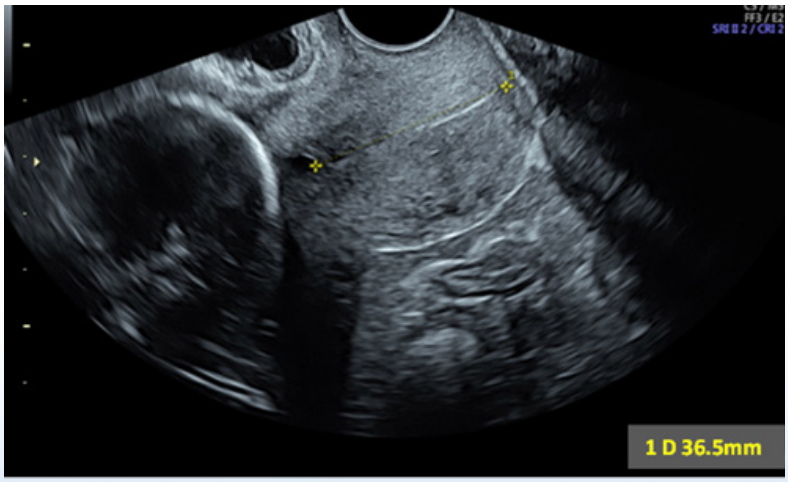


Figure 1 : Cervical length measurement during transvaginal ultrasound

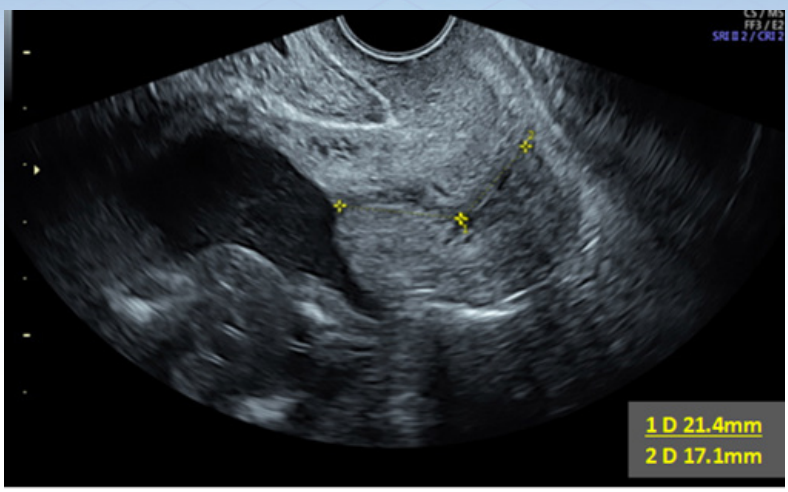


Figure 2 : If the cervix is curved, the cervical length is measured in two (2) or more segments.

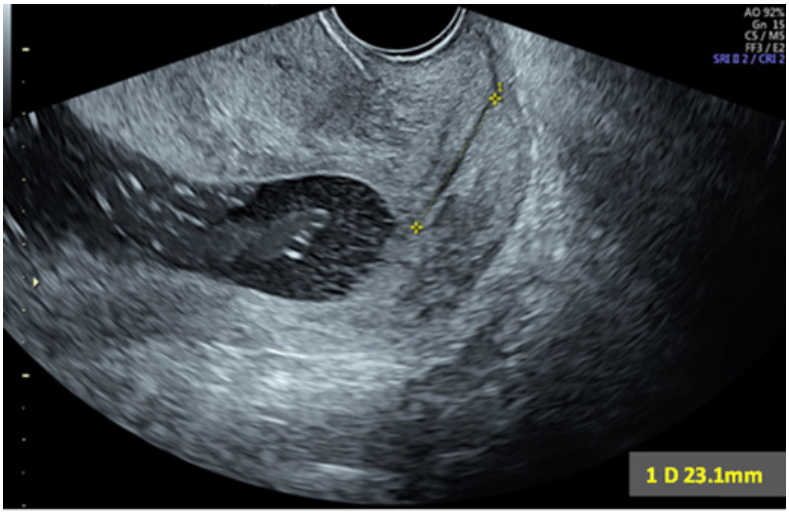


Figure 3 : A short cervix is detected during a transvaginal ultrasound

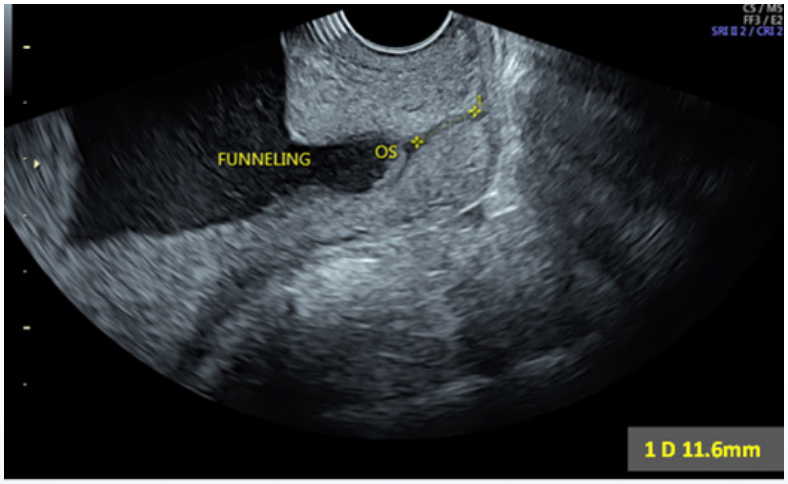


Figure 4 : A short cervix with funnelling is seen during a transvaginal Ultrasound

SECTION 3

PREVENTIVE STRATEGIES FOR PRETERM BIRTH

SECTION 3: PREVENTIVE STRATEGIES FOR PRETERM BIRTH

3.1 Progesterone

3.1.1 Two types of progesterone preparations that are used for the prevention of preterm birth are natural micronized progesterone and 17α-hydroxyprogesterone caproate (17α-OHPC) (shown in **Figure 5**).

3.1.2 Micronized progesterone comes in three preparations, i.e. vaginal suppository, vaginal gel and oral capsule. When micronized progesterone is administered through the vagina, it is absorbed quickly and exerts a direct local effect on the uterus with minimal systemic side effects. Vaginal progesterone also has higher bioavailability as it avoids hepatic first-pass metabolism[20,21]. For vaginal suppository preparation, a dose of 100 mg was used in trials that targeted pregnant women with a history of preterm birth [23,24,25], while 200 mg was used in trials of women with a short cervical length[26]. For vaginal progesterone gel, the recommended dosage is 90 mg once daily[27]. Oral micronized progesterone is less preferred because of its inconsistent bioavailability after ingestion and is metabolized in the liver. It is also associated with side effects such as dizziness, somnolence and vaginal dryness.

3.1.3 The 17α-OHPC is administered via intramuscular injection as this drug is inactivated when orally ingested. Due to its half-life of approximately 7.8 days[20], the suggested regime is, therefore, a once-weekly 250mg intramuscular injection to maintain the serum concentration[28,29].

3.1.4 The timing and duration of the prophylactic progesterone have also varied in the published trials [32]. The treatment can be initiated as early as 16 weeks of gestation and continuing until 34 weeks of gestation or delivery (whichever is earlier). Yet, research is still ongoing to determine the ideal gestational age for initiating the treatment, the optimal duration of treatment and the dosage of progesterone.

3.1.5 Many trials have demonstrated the efficacy of progesterone supplementation to prevent preterm birth. For women at high risk of preterm delivery (e.g. prior spontaneous preterm birth, prophylactic cervical cerclage and uterine malformation), the administration of vaginal progesterone has been shown to reduce the rate of preterm birth before 34 weeks[23] and 37 weeks[25] of gestation. A randomized trial conducted by Majhi et al. demonstrated that vaginal progesterone supplementation to pregnant women who have a history of one or more preterm birth significantly reduces the rate of preterm birth before 37 weeks of gestation[24]. On the other hand, 17α-OHPC also reveals a similar positive effect. One of the largest trials by Meis et al. showed that 17α-OHPC treatment to women with prior history of spontaneous preterm birth significantly reduced the rate of preterm birth below 37 weeks of gestation (relative risk: 0.66; 0.54 - 0.8]), preterm birth below 35 weeks of gestation (relative risk: 0.67; 0.48 -0.93), preterm birth below 32 weeks of gestation (relative risk: 0.58; 0.37-0.91) [28]. In addition, the rate of prematurity-related neonatal morbidities was also lower. The same finding about the efficacy of 17α-OHPC was also reported by Saghafi et al [29]. Knowing that a sonographic short cervix is an important predictor of preterm birth, several randomized trials had been conducted to assess the role of progesterone in this group of women to prevent preterm birth. Compared to

17α-OHPC, vaginal progesterone is more effective to reduce the risk of preterm birth in women with a short cervix [26,27]. A recent meta-analysis including the data from the OPPTIMUM study revealed that vaginal progesterone reduces the risk of preterm birth <33 weeks of gestation (relative risk: 0.62; 0.47-0.81; P = 0.0006) among pregnant women with a sonographic short cervix ≤25 mm [30].

3.1.6 In terms of the safety of progesterone use in pregnancy, the available evidence revealed that progesterone administration has not been associated with an elevated risk of a congenital anomaly or detrimental effects on childhood neurodevelopment and cognitive function [30,33].

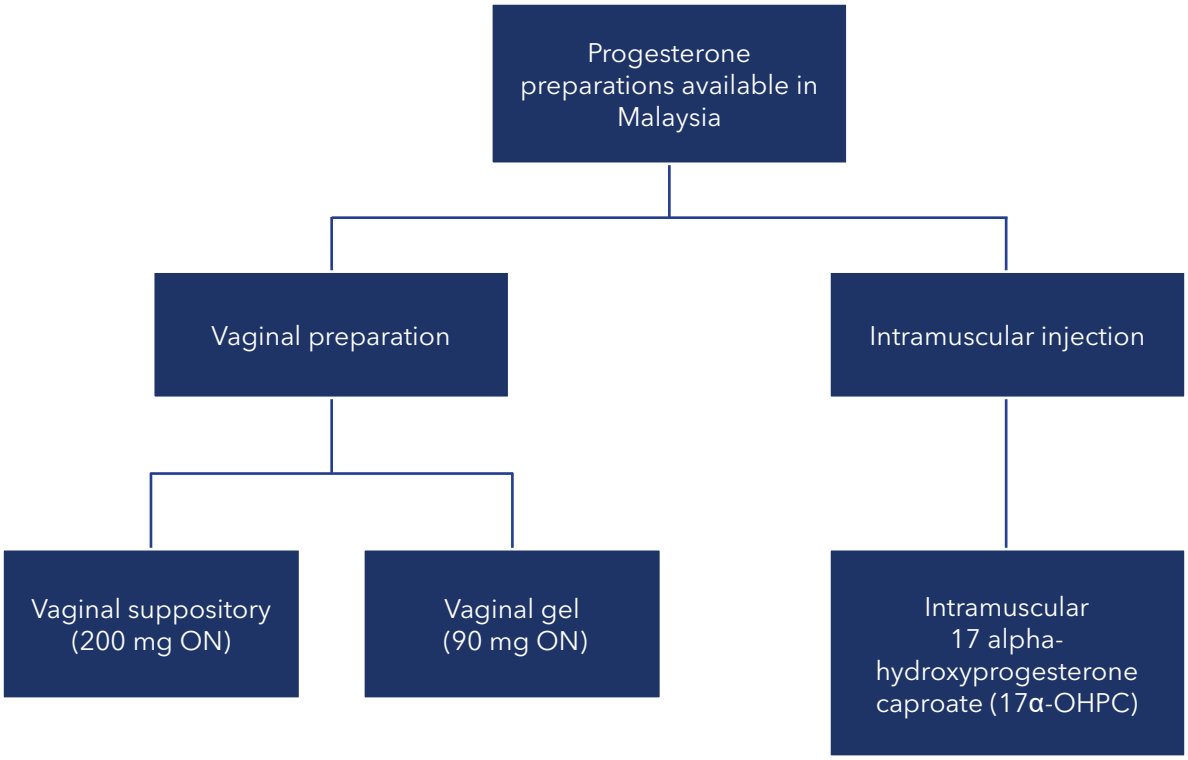


Figure 5: The types of progesterone preparation

3.2 Cervical Cerclage

3.2.1 Cervical cerclage is a surgical procedure that places a suture in the cervix under anaesthesia (shown in **Figure 6**). The transvaginal approach is more commonly performed than the transabdominal approach. A cervical cerclage provides mechanical support to the cervix and helps to retain the mucus plug within the cervical canal to prevent ascending infection. A closed cervical os that is maintained by the cerclage prevents the descent of foetal membranes from the lower uterus.

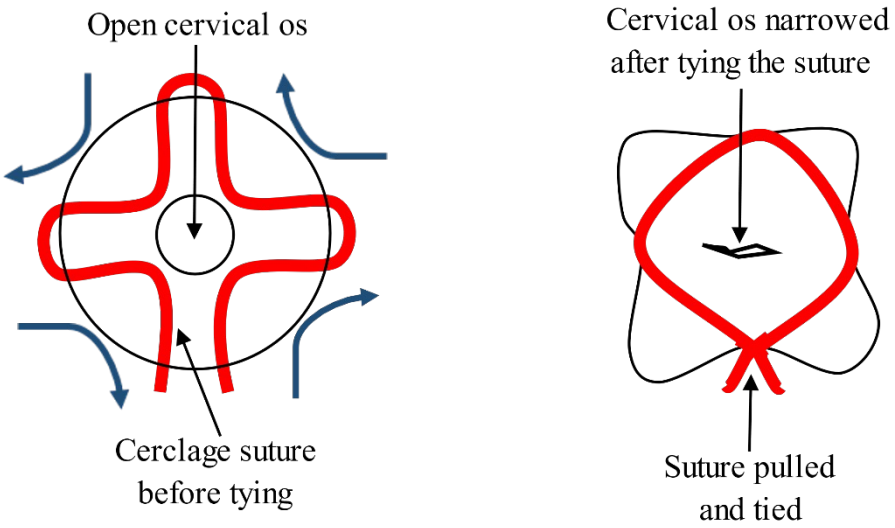


Figure 6: Transvaginal cervical cerclage

3.2.2 The International Federation of Gynaecology and Obstetrics (FIGO) has established the following indications of cervical cerclage [34]:

a. History-indicated cerclage: For women who have had three or more previous preterm births and/or second-trimester losses.
b. Ultrasound-indicated cerclage: For women with a short cervix <25 mm and previous preterm birth and/or second-trimester loss.
c. Rescue cerclage: For women who are in a condition where cervical dilatation and foetal membrane exposure have occurred.

3.2.3 Because of the low quality of evidence, the rationale of routine cervical cerclage to women with a short cervix but no history of preterm delivery is uncertain. However, a cervical cerclage might be potentially beneficial in this group of women with an extremely short cervix of <10 mm [35].

3.2.4 There is still uncertainty about the superiority of cervical cerclage over progesterone in preventing preterm births among women with previous preterm

birth and a short cervix between 16 and 24 weeks [3,5]. Therefore, ACOG and NICE advocate offering cervical cerclage as an equal option with progesterone in this group of pregnant women [3,5]. In addition, it is also acceptable to recommend a cervical cerclage as a conjunct to progesterone[36].

3.2.5 The two types of transvaginal cervical cerclage include McDonald and Shirodkar. In terms of which technique should be used, it is at the discretion of the obstetrician. Both techniques have shown similar effectiveness in terms of the prevention of preterm birth [37,38], though the latter involves more tissue dissection and can be technically challenging. Regardless of the technique of cervical cerclage, the key principle is to place the suture as high as possible[34].

3.2.6 Before a decision on cervical cerclage, it is crucial to ensure that genital tract infection, significant vaginal bleeding, placenta abruption and uterine contraction have been excluded.

3.2.7 The risks of cervical cerclage include:

a. Infection.
b. Vaginal bleeding.
c. Preterm contractions.
d. Rupture of membranes.
e. Miscarriage or preterm delivery if the cerclage is unsuccessful.

3.2.8 The contraindications for cervical cerclage are:

a. Uterine contractions.
b. Unexplained vaginal bleeding.
c. Intrauterine or vaginal infection.
d. Rupture of membranes.
e. Intrauterine foetal demise.
f. Major foetal anomaly.
g. Gestational age beyond 28 weeks.

3.2.9 A cervical cerclage should be removed at 36-37 weeks if preterm delivery has not occurred.

3.3 Cervical Pessary in the Prevention of Preterm Birth [39]

3.3.1 A pessary is a device made of synthetic material that is placed in the vagina and has been used for the prevention of preterm birth. It has been suggested that a potential mechanism of the pessary is an alteration of the cervical-uterine angle to a more posterior position, which reduces cervical compression in women with a singleton pregnancy and a short cervical length.

3.3.2 While some studies have shown benefits from the pessary, those benefits have often not been related to the a priori primary outcome or have been seen only after subgroup analysis in women with different cervical lengths. Other studies have shown statistically similar effects among women at risk of preterm birth regardless of whether they received a pessary. In some cases, the size of the trial has been small enough, and the confidence interval around the point estimate of the effect size sufficiently wide, that a clinically significant benefit remains possible. Interpretation of the results is further complicated because studies have varied concerning management among those enrolled, including whether vaginal progesterone was used.

3.3.3 This inconsistency in findings and lack of clear delineation of a specific group of individuals among whom pessary is efficacious is the basis upon which to conclude that, at this time, there is not sufficient evidence to suggest that pessary should be used as a standard treatment to prevent preterm birth. The usage can be considered on a case-to-case basis in the population.

3.4 Interventions That Have Limited or No Proven Benefit

Current evidence does not support the use of the following strategies for the prevention of preterm birth:[3,6,40]

a. Bed rest.
b. Sexual abstinence during pregnancy.
c. Screening and treatment of asymptomatic lower genital tract infections.
d. Treatment of gingival disease.
e. Empirical broad-spectrum antibiotic therapy.
f. Prophylactic tocolytic therapy.

SECTION 4

FIRST REVIEW AND FOLLOW-UP IN O&G SPECIALIST CLINIC

SECTION 4: FIRST REVIEW AND FOLLOW-UP IN O&G SPECIALIST CLINIC

4.1 Identify pregnant women who are at high risk of preterm birth during the initial and further risk assessment at peripheral health clinics (**Appendix 1 and 2**) and refer them to the O&G specialist clinic for further evaluation.

4.2 At the O&G specialist clinic, the following evaluation and decision of further management should be carried out (**Appendix 3**):

a. Patient assessment (includes a detailed medical and past obstetric history, reviewing risk factors, etc);
b. Cervical length measurement every two weeks between 16 and 24 weeks of gestation;
c. Screen for bacterial vaginosis for symptomatic cases;
d. Determine the suitability for prophylactic interventions, i.e. progesterone versus cervical cerclage; and
e. Patient counselling about the prophylactic interventions:
    i. The nature of each treatment (regular administration of progesterone versus a single operative surgery for cervical cerclage);
    ii. Advantages and disadvantages; and
    iii. Possible adverse effects.

4.3 Offer progesterone and/or cervical cerclage to pregnant women with a short cervix (≤25 mm) and prior spontaneous preterm birth or second-trimester loss (between 16 to <37 weeks of gestation).

4.4 Offer progesterone to pregnant women with any of the following conditions:

a. Previous spontaneous preterm birth or second-trimester loss (between 16 to <37 weeks gestation).
b. An isolated short cervix (≤25 mm) between 16 and 24 weeks of gestation without a history of spontaneous preterm birth, PPROM or cervical trauma.

4.5 Offer cervical cerclage to pregnant women with any of the following conditions:

a. A short cervix (≤25 mm) and PPROM in a previous pregnancy;
b. A short cervix (≤25 mm) related to previous cervical trauma; and/or
c. Previous successful cervical cerclage for cervical insufficiency in their previous pregnancy.

4.6 Start progesterone as early as 16 weeks and continued until 34 weeks of gestation or delivery (whichever is earlier). The choice of the types of progesterone to be used is at the discretion of the obstetrician. Having said that, different progesterone preparations seem to work differently in different situations. For asymptomatic women with a short cervix but no prior spontaneous preterm birth, vaginal progesterone rather than intramuscular 17α-OHPC has consistent evidence for preventing preterm birth in this group of women [22,30,41]. For women with a short cervix and a prior spontaneous preterm birth, both vaginal progesterone and intramuscular 17α-OHPC are effective at reducing the risk of recurrent preterm birth [22,42].

4.7 When women with a short cervix and previous spontaneous preterm birth who are on progesterone supplementation continue to be at significant risk of recurrent preterm birth, such as further shortening of cervix, it is reasonable to offer them a cervical cerclage while continuing progesterone treatment [3].

SECTION 5

DIAGNOSING AND TREATING PRETERM LABOUR

SECTION 5: DIAGNOSING AND TREATING PRETER LABOUR

5.1 Diagnosing Preterm Labour

5.1.1 A clinical diagnosis of preterm labour is made when a pregnant woman has:

a. Regular uterine contractions of 2 in every 10 minutes (Creasy and Herron criteria); and
b. had a speculum or vaginal examination that reveals os dilation and cervical effacement.

Treatment for preterm labour, in this context, should be commenced without further testing.

5.1.2 When the diagnosis of preterm labour is uncertain, the following diagnostic tests can be offered to predict the likelihood of birth within 48 hours (choose only **ONE**):

a. Measuring cervical length by a transvaginal ultrasound using the cut-off length of ≤15 mm for the diagnosis of preterm labour; or
b. Phosphorylated insulin-like growth factor-binding protein (IGFBP)-1 as a predictor of preterm delivery with a good negative predictive value of 99%.

5.2 Investigations

List of investigations that can be done:

a. Vagino-rectal swab.
b. MSU FEME and C&S.
c. Cardiotocograph.
d. Ultrasound assessment. (Note: It is important to exclude gross foetal anomaly during a scan)

5.3 Tocolysis

5.3.1 Use tocolysis in women with preterm labour that occurs between 24 weeks and 35 weeks 6 days of pregnancy. Tocolysis can delay delivery by 48 hours so that it allows the completion of a course of antenatal corticosteroids and in-utero transfer.

5.3.2 The options for a tocolytic agent are:

a. Nifedipine.
b. Oxytocin receptor antagonists, such as atosiban.
c. Terbutaline (Bricanyl).
d. Magnesium sulphate.

5.3.3 Regarding the cases of preterm labour at district hospitals and peripheral health clinics, it is preferable to administer s/c terbutaline 0.25mg stat for tocolysis to allow in-utero transfer.

5.3.4 Major side effects of tocolytic drugs:

a. Nifedipine: Maternal hypotension, dizziness, tachycardia.
b. Atosiban: Nausea, side effects are usually mild.

c. Terbutaline: Tachycardia, hypotension, hyperglycaemia, pulmonary oedema.
d. Magnesium sulphate: Flushing, respiratory depression, cardiac arrest.

5.3.5 Contraindications for tocolysis:

a. Antepartum haemorrhage.
b. Clinical features of infection.
c. Non-reassuring foetal heart rate.

5.4 Antenatal Corticosteroids

5.4.1 Administer antenatal corticosteroids to women between 24 weeks and 35 weeks 6 days of pregnancy who have preterm labour and PPROM. Antenatal corticosteroids are associated with a reduction in neonatal death, respiratory distress syndrome (RDS), intraventricular haemorrhage, necrotising enterocolitis and the need for mechanical ventilation [43].

5.4.2 The regime of corticosteroids is IM Dexamethasone 6mg bd for 2 days.

5.4.3 Perform blood sugar monitoring to anticipate steroids-induced hyperglycaemia, and consider additional insulin for diabetic mothers who receive antenatal corticosteroids.

5.4.4 A repeat course (rescue) of antenatal corticosteroids can be given to [5,44]:

a. Women who are ≤34 weeks 6 days of gestation with an imminent risk of preterm delivery if the initial course was administered more than seven (7) days previously.
b. The number of rescue corticosteroid courses should be limited to a maximum of two (2).

5.4.5 Rescue antenatal corticosteroids improve the short-term outcome by reducing the rate of RDS, the need for surfactant and composite morbidity, though there is no difference in long-term outcomes [45,46]. On the other hand, there is a concern about the association of repeat corticosteroids with a reduction of birth weight, length, and head circumference [45]. The reductions are larger with a higher number of repeated courses of corticosteroids. Therefore, repeat antenatal corticosteroids should be used with caution.

5.5 Magnesium Sulphate for Foetal Neuroprotection

5.5.1 Administer parenteral magnesium sulphate (MgSO4) to women between 24 weeks and 33 weeks 6 days of pregnancy who are in established preterm labour where delivery is likely to occur soon.

5.5.2 The regimes of MgSO4 are:

a. Specialist hospitals: A 4g intravenous bolus over 15 minutes, followed by an intravenous infusion of 1g per hour until the birth or for 24 hours (whichever is sooner).
b. District hospitals & peripheral health clinics: A 10g intramuscular bolus (5gm + 1 ml of lignocaine 2% each buttock), followed by 5g + 1 ml of lignocaine 2% in alternate buttocks 4 hourly until the birth or for 24 hours (whichever is sooner).

5.5.3 Monitor signs and symptoms of MgSO4 toxicity (hourly respiratory rate, urine output, deep patellar tendon reflexes). Consider reducing the dose of MgSO4 if the patient develops oliguria or has renal impairment.

5.5.4 MgSO4 has a modest neuroprotective effect and is currently recommended for use in preterm deliveries below 30 weeks of gestation or can be considered between 30 weeks and 33 weeks 6 days of gestation [5]. Antenatal MgSO4 therapy given to women at risk of preterm birth substantially reduced the risk of cerebral palsy (RR, 0.68; 95% CI, 0.54-0.87) and the rate of substantial gross motor dysfunction in their child (RR, 0.61; 95% CI, 0.44-0.85) [47].

5.6 Intrapartum Antibiotics

To start antibiotics if a patient progresses into preterm labour regardless of the status of GBS (refer to local guidelines for intrapartum antibiotics for GBS).

SECTION 6

REFERENCE

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APPENDIX

APPENDIX 1

Preterm Birth Screening Checklist

Initial Risk Assessment		Tick if done
1.	Smoking	
2.	Maternal age <20 years old	
3.	Screen for urinary tract infection symptoms	
4.	Screen for genital tract infection symptoms	
5.	History of preterm birth	
6.	History of cervical surgery	
7.	BMI <18.5kg/m2	
Further Risk Assessment		
1.	History of mid-trimester loss or spontaneous preterm birth (between 16 and <37 weeks of gestation)	
2.	Previous PPROM excluding delivery at term or via a labour induction	
3.	Previous cervical surgery e.g. cone biopsy, large loop excision of the transformation zone or trachelectomy	
4.	Cervical cerclage in previous pregnancy	
5.	Known uterine anomaly e.g. bicornuate uterus, uterine didelphys	

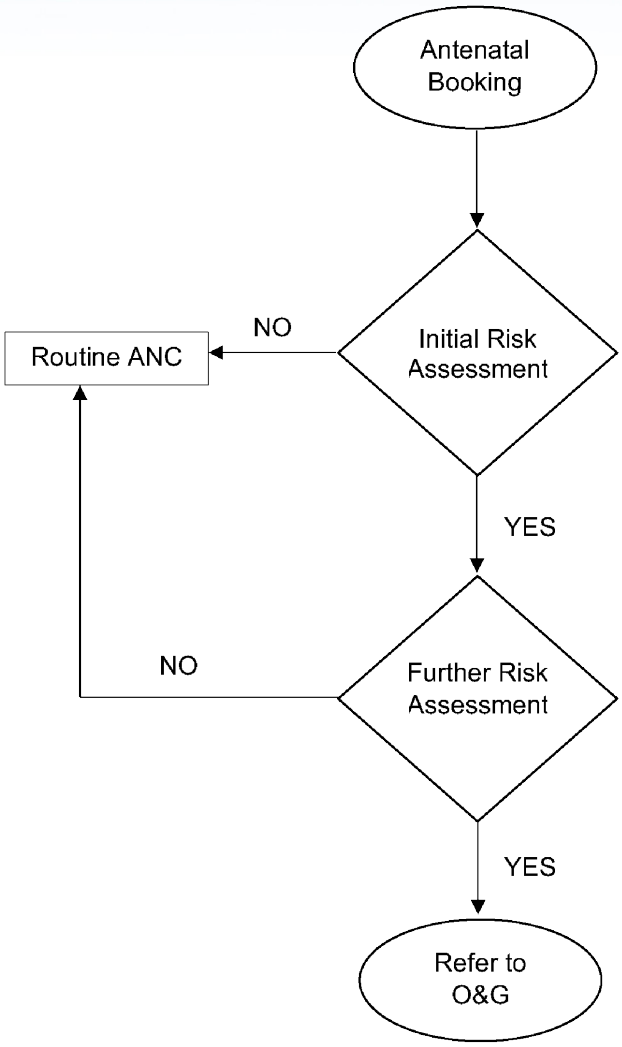
Refer the pregnant woman to the O&G specialist clinic if any risk factor as mentioned in Further Risk Assessment is detected.

**The following groups of pregnant women DO NOT require a referral to an O&G specialist clinic for preterm birth risk assessment:*

a. *Previous iatrogenic preterm delivery for obstetric indications (e.g. maternal medical disease, severe pre-eclampsia, placenta praevia, intrauterine growth restriction, etc).*
b. *Previous termination of pregnancy by either medical (e.g. gameprost) or surgical (e.g. dilatation and curettage) method.*
c. *Recurrent first trimester miscarriage.*
d. *Previous mid-trimester loss caused by a missed miscarriage.*
e. *Previous preterm delivery related to multiple pregnancy.*

APPENDIX 2

Flow Chart 1 : Algorithm for the prevention of spontaneous preterm birth: Initial and further risk assessment at peripheral health clinics



Initial Risk Assessment (Nurses):

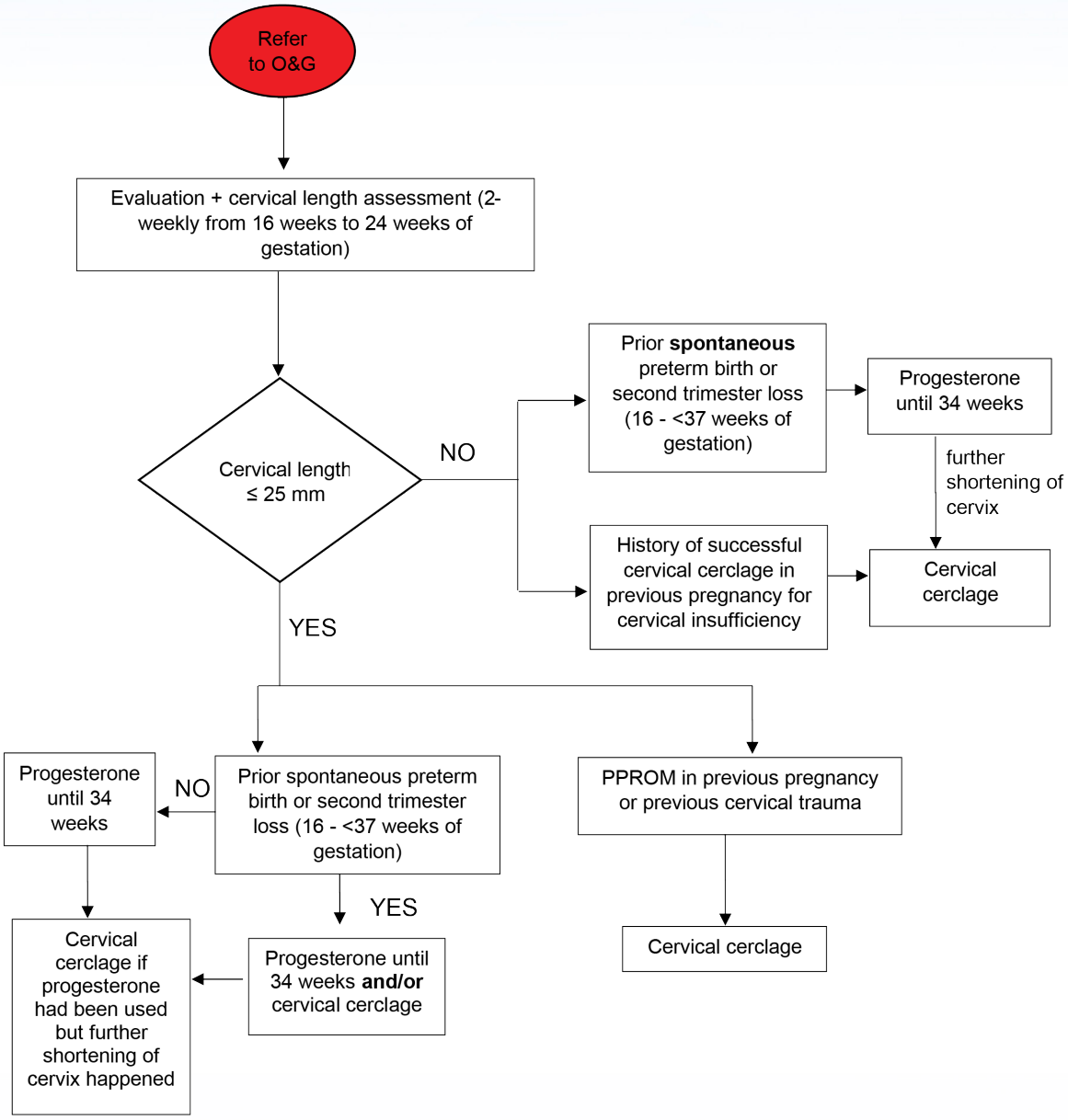
1. Smoking
2. Maternal Age < 20 years old
3. Screen for UTI symptoms
4. Screen for genital tract infection symptoms
5. History for preterm birth
6. History of cervical surgery
7. BMI < 18.5 kg/m²

Further Risk Assessment (Doctors):

1. History of mid-trimester loss or spontaneous preterm birth (between 16 and < 37 weeks of gestation)
2. Previous PPROM excluding delivery at term or via a labour induction
3. Previous cervical surgery and type
4. Previous cervical cerclage
5. Known uterine anomaly

APPENDIX 3

Flow Chart 2 : Algorithm for the prevention of spontaneous preterm birth: Evaluation and management at O&G specialist clinic



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