PHC Chapter 6: Obstetrics & gynaecology

OBSTETRICS

6.1 BLEEDING IN PREGNANCY

6.1.1 PREGNANCY, ECTOPIC

See Section 6.10: Pregnancy, ectopic.

6.2 MISCARRIAGE

O02.1/O03.4/O03.9

DESCRIPTION

Bleeding from the genital tract <22 weeks' gestation, which may or may not be associated with lower abdominal pain (LAP).

» Miscarriage is classified as follows:

Cervix closed on digital examination	Cervix dilated on digital examination
» Threatened miscarriage: – mild vaginal bleeding, usually no associated LAP » fetus is still in the uterus	» Inevitable miscarriage: – moderate vaginal bleeding with associated LAP » fetus is still in the uterus
» Complete miscarriage: – complete passage of all products of conception – bleeding and pain have settled – usually still requires referral for confirmation	» Incomplete miscarriage: – vaginal bleeding often with clots – partial expulsion of products of conception

» Miscarriage is considered to be safe or unsafe (septic) miscarriage:

Safe miscarriage	Unsafe (septic) miscarriage
– Normal vital signs: pulse, BP, temperature, respiratory rate, Hb – No clinical signs of infection, e.g. chills, malaise – Uterus <12 weeks in size – No offensive products of conception – No purulent vaginal discharge	– History of interference – Abnormal vital signs: any of tachycardia, hypotension, pyrexia, tachypnoea, pallor – Persistent heavy bleeding – Clinical signs of infections, e.g. chills, malaise – Uterus palpable abdominally (≥ 12 weeks in size) – Offensive vaginal discharge/ products of conception

For perinatal mortality audit and statistics (DHIS or PPIP), all fetuses ≥500 g are included.

GENERAL MEASURES

» Monitor vital parameters, e.g. Hb, pulse, BP, temperature.
» Treat for shock if indicated.
» Counselling and support.

» There is no specific treatment for threatened miscarriages: reassure the patient that bleeding usually stops spontaneously. Advise to return if bleeding worsens or persists or abdominal pain develops.

MEDICINE TREATMENT

For inevitable/incomplete miscarriages:

- Oxytocin, IV, 20 units, diluted in 1000 mL sodium chloride 0.9% and infused at 125 mL/hour (avoid where threatened miscarriage is suspected).

For all Rh-negative non-sensitised women who had a surgical procedure to manage a miscarriage:

- Anti-D immunoglobulin, IM, 50 mcg preferably within 72 hours but may be given up to 7 days following management of miscarriage.

Do not offer Anti-D prophylaxis to women who:

» only received medical management for a miscarriage, or
» had a threatened miscarriage, or
» had a complete miscarriage.

LoE:IVb[1]

If unsafe (septic) miscarriage is suspected, also give before referral:

O03.0/O08.0 + (A41.9/R57.2)

- Ceftriaxone, IV, 1 g as a single dose

CAUTION: USE OF CEFTRIAXONE

Do not administer calcium-containing fluids, e.g. Ringer's Lactate, concurrently with ceftriaxone.

AND

- Metronidazole, oral, 400 mg as a single dose.

REFERRAL

Urgent

» All patients with unsafe miscarriage
» Suspected ectopic pregnancy.
» Previous miscarriage or previously diagnosed incompetent cervix.

Note: For patients with safe miscarriage the need for referral is determined by skills and facilities at the primary health care level. A local referral policy should be in place. Ideally, midwife obstetric units and community health centres should be able to manage safe miscarriage using manual vacuum aspiration or medical management.

6.2.1 MANAGEMENT OF INCOMPLETE MISCARRIAGE IN THE 1ST TRIMESTER, AT PRIMARY HEALTH CARE LEVEL

O02.1/O03.4

Both Manual Vacuum Aspiration (MVA) and medical evacuation are equally effective for miscarriage.

GENERAL MEASURES

» Counselling.
» Evacuation of the uterus.

MEDICINE TREATMENT

Medical evacuation:

- Misoprostol, SL/PV/buccal, 800 mcg immediately as a single dose.
  - Repeat after 24 hours if necessary. *LoE:IIIb*[2]

Manual vacuum aspiration:

Routine analgesia for vacuum aspiration:

- Morphine, IM, 0.1 mg/kg 30 minutes before aspiration procedure, to a maximum of 10 mg (Doctor prescribed). *LoE:IVb*[3]

Alternatively, consider paracervical block if trained in technique. See the Adult Hospital Level STGs and EML, Section 5.9.1: TOP: Management of pregnancies up to the Twelfth week of gestation (12 weeks and 0 days)

Oral analgesia as required for 48 hours:

- Paracetamol, oral, 500 mg–1 g, 4–6 hourly as required (to a maximum of 4 g in 24 hours).
  - Maximum dose: 15 mg/kg/dose.

AND

- Ibuprofen, oral, 400 mg 8 hourly with or after a meal, for 2 to 3 days.

Follow up after one week to ensure that bleeding has stopped, or sooner if worsening symptoms.
Perform a pregnancy test three weeks after medical management.

LoE:IIIb[4]

REFERRAL

» Unsafe miscarriage.
» Miscarriage ≥13 weeks' gestation.
» Anaemia.
» Haemodynamic instability.
» Failed medical evacuation
» Positive pregnancy test 3 weeks after medical management.

6.2.2 ANTEPARTUM HAEMORRHAGE

O46.0/O46.8-9

DESCRIPTION

Vaginal bleeding in pregnancy from 22 weeks' gestation.
Important causes include the following:

» abruptio placentae,
» placenta praevia,
» uterine rupture (particularly when misoprostol was used to attempt an unlawful TOP).

GENERAL MEASURES

» Monitor vital parameters, e.g. Hb, pulse, BP, temperature.

» Treat for shock if indicated.
Avoid digital vaginal examination, unless placenta praevia excluded with ultrasound.

MEDICINE TREATMENT

- Sodium chloride 0.9%, IV.

REFERRAL

Urgent
All patients.

6.3 TERMINATION OF PREGNANCY (TOP)

DESCRIPTION

Under the Choice of Termination of Pregnancy Act, 1996, as amended, a TOP may be carried out in the following circumstances:

Women eligibility

If gestation ≤ 12 weeks and 0 days:
» On request.

If gestation 12 weeks and 1 day to 20 weeks and 0 days:
If Doctor is satisfied that:
» Pregnancy was from rape or incest, or
» There is a substantial risk that the fetus would suffer from a severe mental or physical abnormality, or
» The continued pregnancy would pose a risk to mother's physical or mental health, or
» Continued pregnancy will significantly affect the social or economic circumstances of the woman.

If gestation ≥20 weeks and 0 day:
» If the Doctor after consulting with a second Doctor or registered midwife or registered nurse is satisfied that continuing the pregnancy would endanger the mothers' life, pose a risk of injury to the fetus, or result in a severe fetal malformation.

Venue
Any facility that has a 24-hour maternity service can provide TOP service without specific designation - *The Choice on Termination of Pregnancy Act, 1996 (as amended by Act 38 of 2004), expanded access to abortions, allows registered nurses, as well as registered midwives, to perform abortions up to the twelfth week of pregnancy.*

Practitioner

If gestation ≤11 weeks and 6 days:
» Doctor, midwife or registered nurse with appropriate training.

If gestation ≥12 weeks and 0 day:
» Doctor is responsible for decision and prescription of medication. Registered nurse/midwife may administer medication according to prescription.

GENERAL MEASURES

» Pre- and post-termination counselling is essential.

» Consent for TOP and related procedures (e.g. laparotomy) may be given by minors. Minors are encouraged to consult parents or others, but parental consent is not mandatory.
» Consent of spouse/partner is not necessary.
» Offer contraception post TOP.

REFERRAL

» If service not available, refer to appropriate district or regional facility as soon as possible (within 2 weeks).
» If gestation ≥12 weeks and 0 day.

6.3.1 MANAGEMENT OF TERMINATION OF PREGNANCY AT PRIMARY HEALTH CARE LEVEL: GESTATION UP TO 12 WEEKS AND 0 DAYS

O04.9

GENERAL MEASURES

» Confirm pregnancy with urine pregnancy test.
» Determine gestational age with ultrasound. If ultrasound is unavailable, use dates (LMP) and bimanual (pelvic) examination.
» If unsure of dates, or examination disagrees with dates, or uterus palpable abdominally, or the woman is obese or difficult to examine, arrange pre-procedure ultrasound.
» Ultrasound is mandatory if suspected ectopic pregnancy – refer if uncertain.
» Counselling.
» Outpatient procedure by nursing staff with specific training.
» Screen for STIs (if treatment needed, do not delay TOP).
» Arrange Pap smear if needed.
» Check HIV status, Hb and blood group (Rh).
» Counsel and start contraception post TOP, before leaving facility. Arrange contraception follow-up.

MEDICINE TREATMENT

Medical TOP - if gestation ≤12 weeks and 0 days:

- Mifepristone, oral, 200 mg, immediately as a single dose. *LoE:IIIb*[5]

Followed 24 to 48 hours later by:

- Misoprostol, SL, 800 mcg by self-administration at home*.
  - If expulsion does not occur within 4 hours of misoprostol administration, a second dose of misoprostol 400 mcg, oral/PV may be given.
  - *From >9 weeks to ≤12 weeks- return to the facility within 48 hours to take misoprostol on-site (early morning) due to the risk of heavy bleeding.

LoE:IIIb[6]

Note: Bleeding may persist for up to 1 week. If there is no bleeding after the second dose of misoprostol, the woman must return to the facility as soon as possible as there is a possibility of an incomplete procedure or ectopic pregnancy. LoE:IIIb[7]

For pain:

After administration of mifepristone, start:

- Paracetamol, oral, 500 mg to 1 g, 4 to 6 hourly as required (to a maximum of 4 g in 24 hours).
  - Maximum dose: 15 mg/kg/dose.

LoE:IVb[8]

ADD

After expulsion is complete:

- Ibuprofen, oral, 400 mg 8 hourly with or after a meal, as needed for 2 to 3 days. LoE:IVb[9]

OR

TOP using manual vacuum aspiration (MVA) - if gestation ≤12 weeks and 0 days:

- Misoprostol, PV, 400 mcg 3 hours before vacuum aspiration of the uterus. LoE:IVb[10]

Routine analgesia for vacuum aspiration:

- Morphine, IM, 0.1 mg/kg 30 minutes before aspiration procedure, to a maximum of 10 mg (Doctor prescribed). LoE:IVb[11]

Alternatively, consider paracervical block if trained in technique. See the Adult Hospital Level STGs and EML, Section 5.9.1: TOP: Management of pregnancies up to the Twelfth week of gestation (12 weeks and 0 days)

Oral analgesia as required for 48 hours:

- Paracetamol, oral, 500 mg to 1 g, 4 to 6 hourly as required (to a maximum of 4 g in 24 hours).
  - Maximum dose: 15 mg/kg/dose.

LoE:IVb[12]

AND

- Ibuprofen, oral, 400 mg 8 hourly with or after a meal, as needed for 2 to 3 days. LoE:IVb[13]

For both medical and surgical TOPs (MVA):

In Rh-negative, non-sensitised women: (O36.0)

- Anti-D immunoglobulin, IM, 50 mcg preferably within 72 hours but may be given up to 7 days following TOP. LoE:IIIb[14]

Contraception:

Counsel all women on effective contraception, especially long-acting reversible methods.

All methods can be given at the time of the procedure, with the exception of the IUCD at a medical TOP. LoE:IVb[15]

Review all patients after 7 days: if bleeding persists, arrange urgent ultrasound.

REFERRAL

» If gestation ≥12 weeks and 1 day.

» If gestation uncertain.
» If any signs or symptoms of ectopic pregnancy or other early pregnancy complications.
» Co-morbid conditions (heart disease, asthma, diabetes, anaemia, clotting disorder, seizure disorder, substance abuse, hypertension).
» Large fibroids (may interfere with determining gestation age and/or MVA).
» Any signs of sepsis (tachycardia, hypotension, pyrexia, tachypnoea, offensive vaginal discharge).
» If gestation ≥9 weeks and 1 day and MVA not available or declined, refer.

6.4 ANTENATAL CARE

6.4.1 ANTENATAL SUPPLEMENTS

Z36.9 + (Z29.9)

DESCRIPTION

Supplements before and during pregnancy and lactation can help to prevent, or lessen the effect of, a number of conditions or complications associated with pregnancy. Specifically:

» Folic acid, given for at least one month before conception and during pregnancy (particularly the first 12 weeks) can help to prevent neural tube defects (abnormal development of spinal cord/brain).
» Iron can help to prevent anaemia.
» Calcium can help to prevent pre-eclampsia.
» Low dose aspirin can reduce the risk for early onset pre-eclampsia in women at risk.

GENERAL MEASURES

» Eat a balanced diet to prevent nutritional deficiency.
» Avoid unpasteurised milk, soft cheeses, raw or undercooked meat or poultry, raw eggs, and shellfish.
» Cut down on caffeine. Reduce intake of tea. Do not drink tea within 2 hours of taking iron tablets.

MEDICINE TREATMENT

Prevention of Neural Tube Defects (NTD)

- Folic acid, oral, 5 mg daily:
  - All women intending to become pregnant or pregnant women (first trimester of pregnancy).
  - If high risk, throughout pregnancy, i.e.:
    - on anticonvulsants - especially valproic acid and carbamazepine,
  - previous child with NTD, or
    - family history of NTD.

LoE:Ia[16]

CAUTION

Children born to women taking valproic acid are at significant risk of birth defects (10%) and persistent developmental disorders (40%).

Valproic acid is contra-indicated and should be avoided in pregnancy and women of child-bearing potential. *LoE:IIb*[17]

Prevention of anaemia:

During pregnancy, after delivery and during lactation:

- Ferrous sulfate compound BPC (dried), oral, 170 mg (± 55 mg elemental iron) 12 hourly with meals.

OR

- Ferrous fumarate, oral, 200 mg once daily (± 65 mg elemental iron).
  - Taking iron tablets with meals decreases iron absorption, but improves tolerability. (Note: Do not take iron tablets with milk).

If daily iron is poorly tolerated (e.g. epigastric pain, nausea, vomiting and constipation), intermittent iron supplementation may be administered:

- Ferrous sulfate compound BPC (dried), oral, 340 mg per week, (± 110 mg elemental iron), with meals.

OR

- Ferrous fumarate, oral, 400 mg per week (± 130 mg elemental iron).

Note: Established anaemia i.e. Hb <10 g/dL, see Sections 3.1: Anaemia and 6.4.3: Anaemia in pregnancy. *LoE:IVb*[18]

Prevention of pre-eclampsia:

From confirmation of pregnancy (all women):

- Calcium, elemental, oral, 1 g daily.
  - Although the benefit is greatest in high-risk women, consider use of this agent in all pregnant women.
  - Calcium reduces iron absorption from the gastro-intestinal tract. Take supplements 4 hours apart from each other. *LoE:IIIb*[19]

From confirmation of pregnancy (all women with risk factors. including: pre-eclampsia in a previous pregnancy, chronic hypertension, diabetes, antiphospholipid syndrome, or systemic lupus erythematosus (SLE)):

- Aspirin, oral, 150 mg, taken at bedtime, preferably not on an empty stomach, until 36 weeks.
  - Start at 6 weeks of gestation but preferably before 16 weeks.
  - Stop at 36 weeks to reduce risk of bleeding during labour.
  - Administration at bedtime reduces the risk of gastric irritation.

LoE:IVb[20]

» Refer to the next level of care as appropriate for the condition (see below). Women with a prior history of pre-eclampsia, but otherwise well, can be referred for the next available appointment, preferably around 20 weeks.

6.4.2 HYPERTENSIVE DISORDERS IN PREGNANCY

DESCRIPTION

Hypertension in pregnancy, pre-eclampsia and eclampsia may have very serious and fatal consequences for both the mother and the baby.

Hypertension is defined by:

» A systolic BP ≥140 and/or a diastolic BP ≥90 mmHg measured on 2 occasions, 4 hours apart.

OR

» A systolic BP ≥160 and/or a diastolic BP ≥110 mmHg measured on a single occasion.

(Always measure BP in the left lateral or sitting position (and not supine position).

Hypertensive disorders of pregnancy can be classified as:

» **Chronic hypertension:**
  - Hypertension diagnosed before pregnancy or <20 weeks of pregnancy.

» **Gestational hypertension:**
  - Hypertension without proteinuria, with onset ≥20 weeks of pregnancy.

» **Pre-eclampsia:**

» Hypertension with proteinuria, with onset ≥20 weeks of pregnancy (high risk patients include: nulliparity, obesity, multiple pregnancy, chronic hypertension, kidney disease, diabetes, pre-eclampsia in a previous pregnancy, advanced maternal age or adolescent pregnancy).

» **Eclampsia:**

» Generalised tonic-clonic seizures in women with pre-eclampsia.

» **Chronic kidney disease:**
  - Proteinuria with/without hypertension, diagnosed at <20 weeks of pregnancy.

Categorising hypertensive disease:

» A diastolic BP of 90 to 109 mmHg and/or systolic BP of 140 to 159 mmHg; but with **NO** symptoms or organ dysfunction is classified as hypertensive disease without severe features.

» Maternal features of severe hypertensive disease are any or more of the following:
  - Acute severe hypertension (diastolic BP of 110 mmHg and/or systolic >160 mmHg).

» Thrombocytopenia (platelet count <100 000/µL).
  - Impaired liver function (ALT or AST >40 IU/L).
  - Severe persistent right upper quadrant or epigastric pain.

» HELLP syndrome (platelets <100 000 and AST >70 µl and LDH >600 µl).

» Serum creatinine ≥120 micromol/L.
  - Pulmonary oedema.
  - New-onset severe headache unresponsive to medication.
  - Visual disturbances.

REFERRAL

Urgent

» Hypertension with severe features (refer to high risk labour ward urgently).

» Pre-eclampsia with or without severe features (refer to high risk labour ward, urgently if severe features present).

Non-urgent

» Chronic hypertension.
» Chronic kidney disease.

6.4.2.1 CHRONIC HYPERTENSION

O10.0

Stop oral antihypertensive medicines when pregnancy is planned or as soon as pregnancy is diagnosed, change to methyldopa and refer for assessment and management.

MEDICINE TREATMENT

- Methyldopa, oral, 250 mg 8 hourly.
  - Titrate to a maximum dose: 750 mg 8 hourly.
  - When using iron together with methyldopa, ensure that iron and methyldopa are not taken concurrently.

LoE:IIIb[21]

REFERRAL

Urgent (within 2 days)
All cases.

6.4.2.2 GESTATIONAL HYPERTENSION: NO SEVERE FEATURES

O13

DESCRIPTION

Hypertension occurring for the first time at ≥ 20 weeks' gestation with no proteinuria.

GENERAL MEASURES

» May be managed without admission <38 weeks' gestation, provided no proteinuria.
» Review the following on a weekly basis:
  - BP
  - weight
  - urine analysis
  - height of fundus (every two weeks)

» fetal heart rate and movements

» Educate on signs requiring urgent follow-up (headache, epigastric pain, visual disturbances, vaginal bleeding etc.).

MEDICINE TREATMENT

- Methyldopa, oral, 250 mg 8 hourly.
  - Titrate to a maximum dose: 750 mg 8 hourly.
  - When using iron together with methyldopa, ensure that iron and methyldopa are not taken concurrently.

LoE:IIIb[22]

REFERRAL

» All patients with gestational hypertension at 38 weeks for delivery.
» Pre-eclampsia (all levels of severity).
» Poor control of hypertension.
» Hypertension with severe features (urgent referral).

6.4.2.3 GESTATIONAL HYPERTENSION: WITH SEVERE FEATURES

O13

Management is the same as for treatment of pre-eclampsia with severe features – See Section 6.4.2.4: Pre-eclampsia.

6.4.2.4 PRE-ECLAMPSIA

O11/O14.0-2/O14.9

DESCRIPTION

» A systolic BP ≥140 and/or diastolic BP ≥90 mmHg with proteinuria, after 20 weeks of pregnancy (significant proteinuria defined as ≥1+ proteinuria).
» Pre-eclampsia with severe features is a life-threatenig condition and needs urgent stabilsation and referral.
» The following indicate a higher risk of developing pre-eclampsia: nulliparity, obesity, multiple pregnancy, chronic hypertension, kidney disease, diabetes, pre-eclampsia in a previous pregnancy, advanced maternal age or adolescent pregnancy.

GENERAL MEASURES

» Advise all pregnant patients to urgently visit the clinic if severe persistent headache, visual disturbances, epigastric pain (not discomfort).
» If severe features are present:
» Insert a Foley's catheter and monitor urine output hourly.
  - Monitor BP every 30 minutes.
  - Check reflexes every hour.

MEDICINE TREATMENT

Prevention of pre-eclampsia

See Section 6.4.1: Antenatal Supplements.

Treatment if severe features are present

- Magnesium sulfate, IV, 4 g as a loading dose diluted with 200 mL sodium chloride 0.9% and infused over 20 minutes.

FOLLOWED BY *LoE:Ia*[23]

- Magnesium sulfate, IM, 10 g given as 5 g in each buttock.
  - Then IM, 5 g every 4 hours in alternate buttocks.

CAUTION: USE OF MAGNESIUM SULFATE

Stop magnesium sulfate if knee reflexes become absent or if urine output <100 mL/4 hours or respiratory rate <16 breaths/minute.

If respiratory depression occurs:

- Calcium gluconate 10%, IV, 10 mL given slowly at a rate not >5 mL/minute.

AND

If systolic BP ≥ 160 and/or a diastolic BP ≥110 mmHg:

- Nifedipine, oral, 10 mg (not sublingual) as a single dose.
  - May be repeated after 30 minutes if diastolic BP remains ≥110 mmHg or if systolic BP remains ≥160 mmHg. *LoE:Ia*[24]

REFERRAL

Urgent

» Pre-eclampsia with severe features.

Non urgent

» Pre-eclampsia without severe features (within 24 hours).

6.4.2.5 ECLAMPSIA

O15.0-2/O15.9

GENERAL MEASURES

» Stabilise prior to urgent referral.
» Ensure safe airway.
» Place patient in left lateral position.
» Insert a Foley's catheter and monitor urine output hourly.
» Monitor BP and check reflexes every 30 minutes.

MEDICINE TREATMENT

- Administer oxygen.
- Magnesium sulfate, IV, 4 g as a loading dose diluted with 200 mL sodium chloride 0.9% and infused over 20 minutes.

AND

- Magnesium sulfate, IM, 10 g given as 5 g in each buttock
  - Then IM, 5 g every 4 hours in alternate buttocks.

CAUTION: USE OF MAGNESIUM SULFATE

Stop magnesium sulfate if knee reflexes become absent or if urine output <100 mL/4 hours or respiratory rate <16 breaths/minute.

If respiratory depression occurs:

- Calcium gluconate 10%, IV, 10 mL given slowly at a rate not >5 mL/minute. *LoE:IVb*[25]

If recurrent eclamptic seizures despite magnesium sulfate loading dose administration:

- Magnesium sulfate, IV, 2 g, diluted with 100 mL sodium chloride 0.9%, over 10 minutes. *LoE:IVb*[26]

If seizures still persist and are continuous, there may be another cause of the seizures: treat as for status epilepticus (see Section 21.2.11: Seizures and status epilepticus).
AND
If systolic BP ≥160 and/or a diastolic BP ≥110 mmHg and patient becomes alert:

- Nifedipine, oral, 10 mg (not sublingual) as a single dose.
  - May be repeated after 30 minutes if diastolic BP remains ≥ 110 mmHg or if systolic BP remains ≥160 mmHg.

LoE:Ia[27]

REFERRAL

Urgent
All cases.

6.4.3 ANAEMIA IN PREGNANCY

O99.0 + (D64.9)

DESCRIPTION

Anaemia in pregnancy is a Hb <11 g/dL, most commonly due to iron deficiency. Hb levels should be checked at the booking visit, between 28 and 32 weeks, and at ± 36 weeks.
Treatment is recommended when the Hb falls below 10 g/dL.
Women with iron deficiency often have 'pica', e.g. eating substances such as soil, charcoal, ice, etc.

GENERAL MEASURES

» A balanced diet to prevent nutritional deficiency.
» Reduce intake of tea.
» Do not drink tea within 2 hours of taking iron tablets.

MEDICINE TREATMENT

Established anaemia with Hb <10 g/dL:

Continue for 3 months after the Hb normalises in order to replenish body iron stores. Hb is expected to rise by at least 1.5 g/dL in two weeks.

- Ferrous sulfate compound BPC (dried), oral, 170 mg (± 55 mg elemental iron) 12 hourly with meals.
  - Taking iron tablets with meals decreases iron absorption, but improves tolerability (Note: Do not take iron tablets with milk).

OR

- Ferrous fumarate, oral, 200 mg (± 65 mg elemental iron) 12 hourly.
  - Taking iron tablets with meals decreases iron absorption, but improves tolerability. (Note: Do not take iron tablets with milk).

LoE:IIb[28]

REFERRAL

Urgent (same day)
» Hb <6 g/dL.
» Hb = 6-7.9 g/dL with symptoms (dizziness, tachycardia, shortness of breath at rest).

Non-urgent (within 1 week)

» Hb = 6-7.9 g/dL without symptoms (to high-risk clinic if available).
» Hb = 8-9.9 g/dL and no improvement after one month of treatment (to high-risk clinic, if available).
» Hb <10 g/dL at 36 weeks' gestation or more: transfer to hospital for further antenatal care and delivery.

6.4.4 SYPHILIS IN PREGNANCY

O98.1

DESCRIPTION

A sexually transmitted infection with many manifestations that has a latent phase and may be asymptomatic in pregnant women. It is caused by the spirochaete, T pallidum. Vertical transmission to the fetus occurs in up to 80% of cases in untreated mothers. Untreated maternal syphilis may lead to miscarriage, stillbirth, non-immune hydrops fetalis, or congenital syphilis in the newborn.

DIAGNOSIS

» All pregnant women should have a syphilis test at the first booking visit.
» Women who booked in the first trimester and tested negative should have a repeat test done around 32 weeks' gestation.
» Diagnosis is made by positive serology. Clinical signs and symptoms are most recognisable in secondary syphilis. These include rash on palms of the hand and/or soles of the feet; and condylomata lata on genital areas.
» There are 2 types of diagnostic tests:

Specific treponemal test (e.g. TPAb//TPHA/FTA-ABS):	Non-treponemal test (e.g. RPR):
» Specifically diagnoses syphilis. » Available as rapid on-site finger-prick syphilis tests or laboratory-based assays. » Dual HIV/syphilis rapid on-site test may be used when HIV status is negative/unknown. » Once positive, a specific treponemal test generally remains positive for life, and therefore the presence of specific treponemal antibodies cannot differentiate between current and past infections. » A person with previously successfully treated syphilis will retain lifelong positive specific treponemal test results. » Thus a positive test should be immediately followed by an RPR test to confirm active disease; however treatment can be started while awaiting the RPR result.	The RPR can be used: » To determine if the patient's syphilis disease is active or not, » To measure a successful response to therapy (at least a fourfold reduction in titre, e.g. 1:256 improving to 1:64), or » To determine a new re-infection. **Note:** » False RPR positive reactions may occur, notably in patients with connective tissue disorders (these are usually low titre <1:8). For this reason, positive RPR results should be confirmed as due to syphilis by further testing of the serum with a specific treponemal test; if the specific test result cannot be obtained the same day, start treatment while awaiting the result. » If specific treponemal test e.g. TPAb is performed first and gives a positive result, serum can be further tested for RPR to determine the presence of active syphilis (reverse testing algorithm). » Some patients, even with successful treatment for syphilis, may retain life-long positive RPR results at low titres (≤1:8), which does not change by more than one dilution difference over time (so-called serofast patients).

GENERAL MEASURES

» Encourage partner notification and treatment after confirmon the diagnosis.
» Provide counselling and promote HIV testing.
» Educate on treatment adherence.
» Promote condom use.

MEDICINE TREATMENT

Pregnant woman

- Benzathine benzylpenicillin, IM, 2.4 MU weekly for 3 weeks.
  - Reconstitute with 6 mL of lidocaine 1% without adrenaline (epinephrine).
  - Follow up at 3 months after the last injection to confirm a fourfold (i.e. 2 dilution) reduction in RPR titres, provided the initial titre was ≥1:8. If initial titre <1:8, further reductions may not occur (serofast reaction). *LoE:IVb*[29]

Severe penicillin allergy:

Z88.0

Refer for in-patient penicillin desensitisation.

Newborn baby

If baby asymptomatic, well and mother not fully treated >1 month before delivery, give:

- Benzathine benzylpenicillin (depot formulation), IM, 50 000 units/kg as a single dose into the lateral thigh.

CAUTION

Benzathine benzylpenicillin (depot formulation) must never be given intravenously.

REFERRAL (BABY)

» Mother was not treated.
» Mother has received <3 doses of benzathine benzylpenicillin.
» Mother delivered within 4 weeks of commencing treatment.
» Baby has any of the following:
  - Hepatosplenomegaly
  - Snuffles
  - Jaundice
  - Purpura
» Pseudoparesis
  - Oedema
  - Anaemia
  - Desquamative rash (especially involving palms and soles)

6.4.5 URINARY TRACT INFECTION, IN PREGNANCY

6.4.5.1 CYSTITIS

O23.1

DESCRIPTION

This condition usually presents with lower abdominal pain, frequency of micturition and/or dysuria. There are no features of sepsis, e.g. fever.
Urine dipstick testing usually shows nitrites and/or leukocytes; protein and/or blood may also be detected.

GENERAL MEASURES

» Encourage oral fluid intake.
» Midstream urine for microscopy, culture and sensitivity (start empiric treatment while awaiting results).

MEDICINE TREATMENT

See Section 8.4: Urinary tract infection.

REFERRAL

» No response to treatment, or resistant organism on culture.
» Features of pyelonephritis (see Section 6.4.5.2: Pyelonephritis)

6.4.5.2 PYELONEPHRITIS

O23.0

DESCRIPTION

Features of pyelonephritis include: temperature ≥38°C, renal angle tenderness, vomiting, tachypnoea, tachycardia, hypotension, confusion.
This condition is more serious and may result in preterm labour.

GENERAL MEASURES
» Collect midstream urine for microscopy and culture and sensitivity.
» Ensure adequate hydration with IV fluids while awaiting transfer.

MEDICINE TREATMENT
Empiric therapy:

- Ceftriaxone, IV, 1 g as a single dose. W

CAUTION: USE OF CEFTRIAXONE

Do not administer calcium-containing fluids, e.g. Ringer's Lactate, concurrently with ceftriaxone. *LoE:IVb*

REFERRAL
All cases.

6.4.6 LISTERIOSIS
A32.0-1/A32.7-9

Note: If you have any questions or concerns, visit www.nicd.ac.za or call the NCID hotline on 082 883 9920.

DESCRIPTION
Listeriosis is a preventable and treatable bacterial disease spread through food. Most listerial infections are sporadic but outbreaks do occur. Pregnancy is a predisposing factor for developing serious Listeriosis.
Patients present with a flu-like illness (with fever). They may also have sore joints, backache, diarrhoea and vomiting, and/or signs of meningitis (headache, neck stiffness, confusion).
Listeriosis has been added to the national list of notifiable diseases.

GENERAL MEASURES
Educate your patients on how to prevent it: wash hands, knives, and cutting boards after handling uncooked food, avoid luncheon meats/delicatessen meats, wash raw vegetables thoroughly, avoid unpasteurised milk, thoroughly cook raw food from animal sources.

MEDICINE TREATMENT
During outbreaks, if signs of meningitis are present, give pre-referral treatment (see Section 15.8.1: Acute Meningitis). *LoE:IVb*[30]

REFERRAL
All cases.

6.4.7 PRETERM LABOUR (PTL) AND PRETERM PRELABOUR RUPTURE OF MEMBRANES (PPROM)

6.4.7.1 PRETERM LABOUR (PTL)

O60.0

DESCRIPTION

Regular painful contractions: 3 per 10 minutes, occurring <37 weeks of gestation.

Note: Women with a previous spontaneous preterm delivery are at higher risk for preterm delivery in the next pregnancy. Refer the following high-risk cases for cervical screening:

» A history of 2nd trimester miscarriage (between 16 and 26 weeks).
» Previous history of spontaneous preterm birth between 27 and 34 weeks.
» No need to refer previous late preterm deliveries (34 to 37 weeks). *LoE:IVb*[31]

GENERAL MEASURES

<26 weeks:
» Refer without tocolysis (medicines to inhibit uterine contractions). *LoE:IVb*[32]

26–34 weeks of gestation:
» Refer with initial tocolysis and corticosteroids.

>34 weeks of gestation:
» Allow labour to continue at midwife obstetric unit.

MEDICINE TREATMENT

To improve fetal lung maturity at 26–34 weeks:

Z29.2

- Betamethasone, IM, 12 mg, 2 doses 24 hours apart. *LoE:Ia*[33]

If betamethasone is not available:

- Dexamethasone, IM, 8 mg, 3 doses 8 hours apart. *LoE:Ia*[34]

Note: Corticosteroids are maximally effective about 24 hours after administration of the first dose. Therefore, give as soon as possible following diagnosis of PTL or PPROM.

Tocolysis:

Z29.2

Preload with:

- Sodium chloride 0.9%, IV, 200 mL.

THEN

- Nifedipine, oral, 20 mg as a single dose.
  - Follow with 10 mg after 30 minutes, if contractions persist.
  - Then 10 mg every 4 hours until patient is transferred.
  - Maximum duration: 24 hours.

REFERRAL
All cases before 34 weeks.

6.4.7.2 PRETERM PRELABOUR RUPTURE OF MEMBRANES (PPROM)
O42.0-1/O42.9

DESCRIPTION
Rupture of the membranes before 37 weeks' gestation.
Confirmed with a sterile speculum examination demonstrating leakage of amniotic fluid.
If there is clinical uncertainty test for pH – liquor is alkaline.
Avoid digital vaginal examination.

MEDICINE TREATMENT
<u>To improve fetal lung maturity at 26 to 34 weeks: (Z29.2)</u>
- Betamethasone, IM, 12 mg, 2 doses 24 hours apart. *LoE:Ia*[35]

<u>Initiate antibiotic therapy:(Z29.2)</u>
- Ampicillin, IV, 1 g 6 hourly for 48 hours. A

Follow with:
- Amoxicillin, oral, 500 mg 8 hourly for a further 5 days. A

AND
- Azithromycin 1 g orally as a single dose. W *LoE:IIa*[36]

<u>Severe penicillin allergy:(Z88.0)</u>
- Azithromycin 1 g orally as a single dose and refer urgently. W

REFERRAL
All cases, but refer **urgently** if PPROM <34 weeks or cases of severe penicillin allergy.

6.4.7.3 PRELABOUR RUPTURE OF MEMBRANES AT TERM (PROM)
O42.0-1/O42.9

DESCRIPTION
Rupture of membranes before the onset of labour at term (>37 weeks).
A sterile speculum examination is required to visually confirm amniotic fluid draining through the cervical os.

GENERAL MEASURES
» If PROM is followed by uterine contractions at >34 weeks' gestation, allow labour to proceed.
» If the woman does not develop uterine contractions within 12 hours of PROM, commence antibiotics and transfer for induction of labour.

MEDICINE TREATMENT

Prolonged pre-labour rupture of membranes >12 hours/ suspected chorio-amnionitis:

Initiate antibiotic therapy and refer urgently:

O41.1

- Ampicillin, IV, 1 g as a single dose. A

AND

- Metronidazole, oral, 400 mg as a single dose and refer. A

Severe penicillin allergy:

Z88.0

- Azithromycin, oral, 500 mg as a single dose. W

AND

- Metronidazole, oral, 400 mg as a single dose and refer. A

LoE:IIa[37]

REFERRAL

Urgent

» Suspected chorio-amnionitis (refer after starting antibiotics).
» Prolonged pre-labour rupture of membranes (>12 hours).
» Meconium stained liquor.

6.5 INTRAPARTUM CARE

O80.0-1/O80.8-9

For the comprehensive management of women in labour refer to the most recent National Maternity Care and Intrapartum Care Guidelines.

DESCRIPTION

Labour is divided into 4 stages:

» First stage:
  - onset of regular painful uterine contractions at term to full dilatation of cervix.
» Second stage:
  - full dilatation to delivery of the baby.
» Third stage:
  - delivery of the baby to delivery of the placenta.
» Fourth stage:
  - 1 hour post-delivery of the placenta.

GENERAL MEASURES

» Encourage companion support.
» Ensure that the mother is adequately hydrated (can be done orally).
» Monitor progress of labour on partogram.

MEDICINE TREATMENT

First stage with cervical dilatation <10 cm:

Analgesia:

O62.9 + (Z51.2)

- Morphine, IM, 0.1 mg/kg to a maximum of 10 mg, 4 hourly. *LoE:IVb*[38]

OR

Especially in advanced first stage of labour:

- Nitrous oxide 50% mixed with oxygen 50%, given by mask.

AND

For nausea and sedation, if needed:

- Promethazine, IM, 25 mg 4 hourly.

Second stage

If episiotomy is needed, local anaesthetic:

O62.9 +(R10.2+Z51.2)

- Lidocaine1%.
  - Do not exceed 20 mL.

Fetal distress during labour

O68.0-3/O68.8-9/O75.9

Place the woman in the left lateral position.

Tocolysis, then refer:

- Salbutamol, IV, 0.5 mg/mL, 250 mcg administered slowly over 2 minutes.
  - Reconstitute as follows:
  - Salbutamol 1 mL (0.5 mg/mL) added to 9 mL of water for injection, to make a 50 mcg/mL solution. Monitor pulse.
  - Inject 5 mL (250 mcg) over at least 2 minutes. Monitor pulse.
  - If pulse increases >120 beats/minute, discontinue the injection.
  - Do not administer if mother has cardiac disease.

Third stage

Prevention of post-partum haemorrhage (PPH):

Z29.2

» Check for twins.

- Oxytocin, IM, 10 units.

» Clamp and cut cord after 1 minute.

» Controlled cord traction of the placenta.

If >500 mL blood loss, manage as postpartum haemorrhage (see Section 6.7.1: Postpartum haemorrhage (PPH)).

Rh-negative mother

O36.0

» Check baby's Rh status; do not given anti-D if the baby is Rh-negative, or if the mother has Anti-Rh antibodies.

Administer to Rh-negative mother, if baby is Rh-positive or baby's Rh group is unknown:

- Anti-D immunoglobulin, IM, 100 mcg, preferably within 72 hours but can be given up to 7 days after delivery.

Care of the newborn baby
If baby not crying/breathing well, see Section 6.6.2: Neonatal Resuscitation.
For routine care of the neonate, see Section 6.6.1: Routine care of the neonate.
Observe mother and neonate for 1–2 hours before transfer to the postnatal ward.

For pain after delivery
- Paracetamol, oral, 500 mg to 1 g, 4 to 6 hourly as required (to a maximum of 4 g in 24 hours).
  - Maximum dose: 15 mg/kg/dose.

If needed
- Ibuprofen, oral, 400 mg 8 hourly with or after a meal as needed for up to 5 days. *LoE:IVb*

REFERRAL
» Prolonged labour according to charting on partogram.
» Fetal distress during labour
» Post-partum haemorrhage.
» Retained placenta.
» Other complications of mother or baby.

6.6 CARE OF THE NEONATE

6.6.1 ROUTINE CARE OF THE NEONATE
Z76.2

For the comprehensive management of the newborn refer to the most recent Newborn Care Charts.

GENERAL MEASURES

Routine care for baby after delivery
» Dry the baby thoroughly at birth.
» If there is meconium, clear the airway first.
» **If baby is not crying**
  - Clear airway, stimulate.
  - If baby not breathing well, clamp and cut the cord and start resuscitation (see Section 6.6.2: Neonatal Resuscitation).
» **If the baby is crying and breathing well**
  - Place on mother's chest, keep warm and check breathing.
  - Clamp and cut cord after 1 minute.
  - Monitor with mother and initiate breastfeeding.

Check and record the Apgar score:

Apgar score	0	1	2
Heart rate	Absent	<100/min	>100/min

Respiration	Absent	Slow or irregular	Good, crying
Muscle tone	Limp	Slight flexion	Active, moves
Response to stimulation	No response	Grimace	Vigorous cry
Colour	Blue or pale	Body pink, limbs blue	Pink all over

Check baby from head to toe including baby's back

» Check weight and head circumference.
» If any of the following, provide immediate management (see Section 6.6.3: Care of sick and small neonates) and refer to a neonatal unit:
- Grunting or chest indrawing
- Central cyanosis
- Fast breathing
- Abnormal tone (floppy/stiff)
- Less than normal movements
- Major congenital abnormality
- Head circumference >39 cm
- Birth weight <2.0 kg

Identify the infant at risk or needing special treatment

» Birth weight <2.5 kg.
» Suspected chorio-amnionitis (membranes ruptured for >18 hours, offensive liquor at birth).
» Neurological or congenital problem.
» Hospital stay >3 days after delivery.
» Mother blood group O and/or Rh –ve.
» Possible social problem (mother has died or is ill, teenage caregiver, social deprivation).
» Mother diabetic.
» Mother syphilis positive (partially treated or untreated or treated <1 month before delivery).
» Mother HIV-infected.
» Infant not breastfed.
» Mother on TB treatment.

Initiate bonding and feeding

» Place the baby skin-to-skin with mother and initiate breastfeeding immediately.

Identify and record

» Formally identify the baby with the mother.
» Place a label with the mother's name and folder number, baby's sex, and time and date of birth on the baby's wrist and ankle.
» After giving vitamin K and chloramphenicol eye ointment, give the baby back to the mother, unless there is a reason for the baby to be transferred to a neonatal unit.

MEDICINE TREATMENT

Bleeding prophylaxis

Z29.2

- Vitamin K, IM, 1 mg immediately after birth routinely.
  - Administer in the antero lateral aspect of the mid-thigh.

Neonatal conjunctivitis prophylaxis

Z29.2

- Chloramphenicol ophthalmic ointment 1%, applied routinely to each eye after birth.

Routine EPI immunisation:

- BCG vaccination, intradermal, once neonate is stable. (Z23.2)
- bOPV (polio vaccine), oral, once neonate is stable. (Z24.0)

No baby must be sent home without immunisation.

REFERRAL

Refer to a neonatal unit if:

» Baby needed resuscitation.
» Apgar score <8 at 5 minutes.

6.6.2 NEONATAL RESUSCITATION

P29.8

Be prepared Be at the delivery Check the equipment and emergency medicines

» Follow the algorithm at the end of this section.
» Check that each step has been effectively applied before proceeding to the next step. The algorithm follows the assumption that the previous step was unsuccessful and the baby is deteriorating.
» Use oxygen concentration that alleviates central cyanosis, obtains target pulse oximetry readings (if pulse oximeter is available), and restores a heart rate >100 beats/minute. Bag and mask ventilation should be initially done with room air. (There is evidence that routine resuscitation with 100% oxygen is potentially harmful to the baby.)

An unsatisfctory response to resuscitation includes:

» A sustained slow heart rate, usually ≤60 beats/minute or a progressive decrease in heart rate until cardiac arrest occurs.
» Episodes of cardiac arrest, with a progressively weaker response to chest compressions, positive pressure ventilation and medicines.
» A decreasing blood pressure, increasing acidosis, severe hypotonia with central cyanosis or intense pallor.
» Apnoea or weak, irregular and inefficient respiratory efforts.

MEDICINE TREATMENT

If baby's response to resuscitation is inadequate once ventilation and circulation are adequately supported the following steps should be carried out:

If the mother is known or suspected to have had narcotic pain relief and the baby has normal heart rate and colour response to bag-mask ventilation, but has not initiated sustained regular respiratory effort:

- Naloxone, IV, 0.1 mg/kg.

Naloxone is not routinely indicated for neonatal resuscitation.

Check the blood glucose of the baby.If hypoglycaemia is present:

E16.0-2/P70.4

- Dextrose 10%, IV, 2.5 to 5 mL/kg.

Medicines used during neonatal resuscitation

Medicine and dose	Indications	Effect
• Adrenaline (epinephrine) ○ 0.1 mL/kg of a 1:10 000 dilution IV, (0.01 mg/kg/dose). ○ ET, up to 1 mL/kg of a 1:10 000 dilution (0.1 mg/kg/dose).	» Asystole. » Heart rate <60 beats/minute.	» ↑Heart rate. » ↑Myocardial contractility. » ↑Arterial pressure.
• Naloxone, IV/IM, 0.1 mg/kg. ○ May need repeating after 2 hours.	» Maternal administration of opiates with apnoeic infant.	» Corrects apnoea and/or hypoventilation.
• Dextrose,10% IV. ○ 2.5–5 mL/kg of 10% dextrose (250–500 mg/kg). ○ 10% solution: draw up 4 mL of 50% dextrose into a 20 mL syringe then draw up 16 mL water for injection – mix by agitating the syringe.	» Hypoglycaemia (usually only occurs after acute resuscitation).	» Corrects hypoglycaemia.
Fluid for volume expansion: • Sodium chloride 0.9%, IV, 10–20 mL/kg, slow IV (5–10 minutes).	» Hypovolaemia (usually history of blood loss, child pale shocked with poor pulses and perfusion).	» ↑Blood Pressure and improve tissue perfusion.

If no adequate response has occurred by this stage, a person skilled in neonatal resuscitation should be consulted and the baby transferred with ongoing resuscitation to a higher level of care:

» Discontinue resuscitation if the unsatisfactory response to resuscitation persists for >20 minutes and underlying conditions e.g. pneumothorax, diaphragmatic hernia has been excluded or >10 minutes of unresponsive cardiac arrest (asystole) and/or >20 minutes of unsustained respiration.

» Babies requiring minimal resuscitation with prompt and complete response may be watched with their mothers.

» Babies with a favourable response to resuscitation should be referred to a neonatal high or intensive care unit, if available, for post resuscitation care.

» Babies, who, after resuscitation, are not completely normal, should be referred to a higher level for care using transport with necessary support, e.g. oxygen, temperature control.

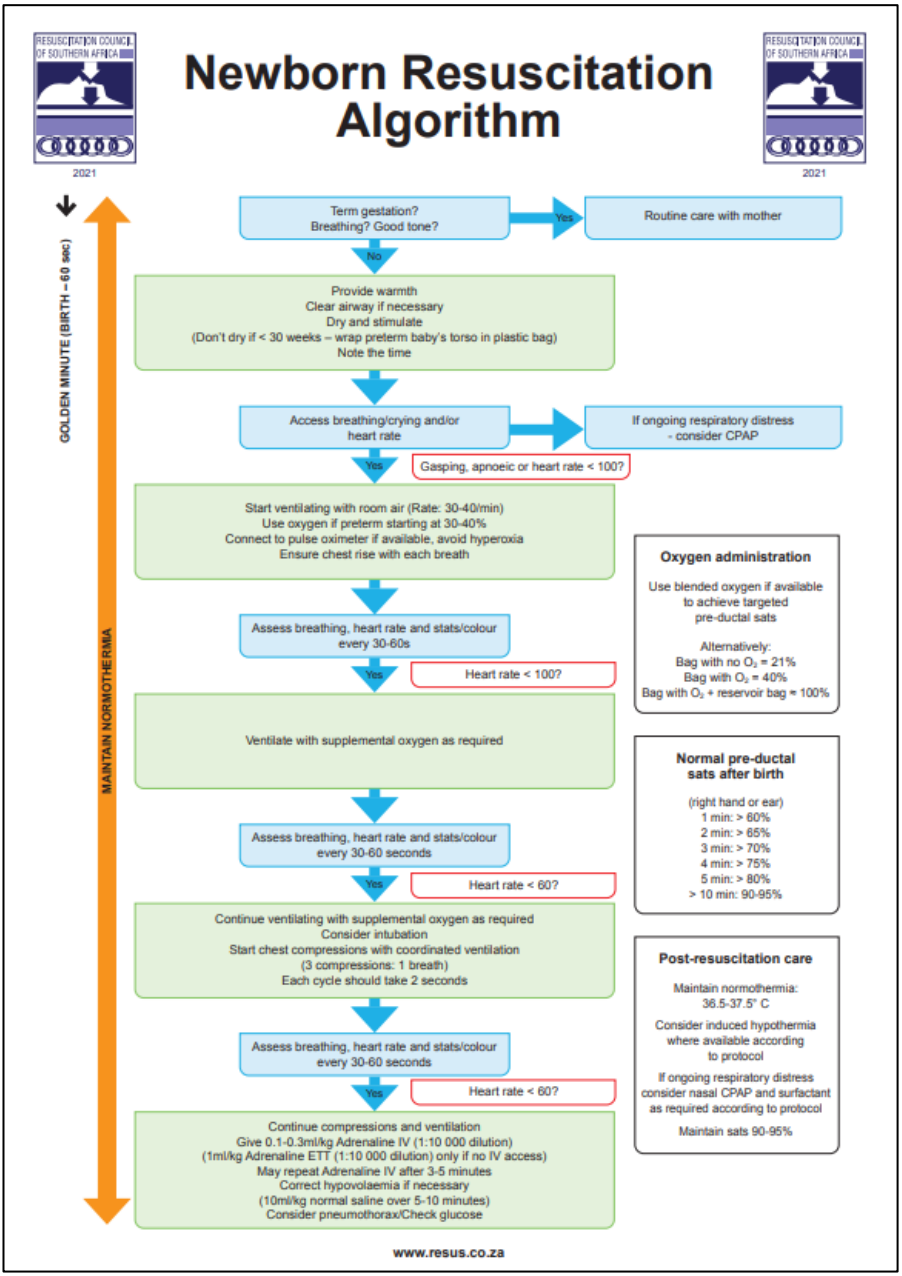

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Figure 6.1: Newborn resuscitation algorithm

6.6.3 CARE OF SICK AND SMALL NEONATES

DESCRIPTION

Neonates can become ill very rapidly and signs of disease are often not readily appreciated unless specifically looked for. Neonates should be referred urgently.
Neonates <2.5 kg are at higher risk of feeding and growth problems and need careful follow-up.

Urgently manage and refer neonates with any of the following signs of possible serious bacterial infection and/or jaundice:

- » Convulsions
- » Lethargic/ unconscious
- » Bulging fontanelle
- » Apnoea (<30 breaths/min)
- » Severe chest indrawing
- » Nasal flaring or grunting
- » Swollen eyes; pus draining from eye
- » Low or high temperature
- » Not able to feed
- » Passing blood per rectum
- » Pallor
- » Jaundice in 1st 24 hours of life
- » Diarrhoea
- » Many or severe skin pustules
- » Fast breathing (>60 breaths/min)
- » Vomiting everything/bile-stained vomitus
- » Only moves when stimulated
- » Umbilical redness extending to the skin and draining pus

GENERAL MEASURES

- » Keep the neonate warm (skin-to-skin/kangaroo mother care or in an incubator), the axillary temperature should be 36.5–37°C.
- » Check blood glucose concentration and treat if low (<2.6 mmol/L). Check blood glucose concentration again after 15 minutes. If normal, feed 2 to 3 hourly. If still low, treat as severe hypoglycaemia (see below).
- » Check mother able to successfully establish breastfeeding in the small neonate and check health and weight gain more frequently.

MEDICINE TREATMENT

If grunting or severe chest indrawing

P22.0-1/P22.8-9

- Oxygen, using nasal catheter at 1 L/minute.

If infection is suspected and jaundice has been excluded

Z29.2

- Ceftriaxone, IM, 80 mg/kg/dose immediately as a **single dose**. W
  - Administer into the lateral thigh.
  - Do not inject more than 1 g at one injection site.

CAUTION: USE OF CEFTRIAXONE IN NEONATES AND CHILDREN

- » If SUSPECTING SERIOUS BACTERIAL INFECTION in neonate, give ceftriaxone, even if jaundiced.
- » Avoid giving calcium-containing IV fluids (e.g. Ringer's Lactate) together with ceftriaxone:
  - If ≤28 days old, avoid calcium-containing IV fluids for 48 hours after ceftriaxone administered.

- If >28 days old, ceftriaxone and calcium-containing IV fluids may be given sequentially provided the giving set is flushed thoroughly with sodium chloride 0.9% before and after.
- Preferably administer IV fluids without calcium contents.

» Always include the dose and route of administration of ceftriaxone in the referral letter.

If blood glucose <2.6 mmol/L and baby able to suckle or take orally:

» Breastfeed or give expressed breastmilk (only if breastfeeding is not possible, give replacement milk feed 10 mL/kg).

» If unable to take orally consider nasogastric tube feeding. Check blood glucose concentration again after 15 minutes. If normal, feed 2 to 3 hourly. If still <2.6 mmol/L, manage as below.

If blood glucose <1.4 mmol/L or remains <2.6 mmol/L after an oral feed:

- Dextrose 10%, IV, 2 mL/kg as a bolus.

AND

- Dextrose 10%, IV, 3 mL/kg/hour. *LoE:IVb*[39]
  - Repeat in 15 minutes.
  - If blood glucose still low, repeat dextrose bolus.

REFERRAL

Urgent

» All neonates with a possible serious bacterial infection.

» All neonates with jaundice on the first day of life, with pallor or with poor feeding.

» All other neonates with increasing, deep or persistent (>10 days) jaundice should be referred as soon as possible.

» All small neonates (<2.5 kg) not able to feed.

» Persistent hypoglycaemia despite treatment.

(If possible, always send mother with the neonate as well as any clinical notes).

6.6.4 CARE OF THE HIV-EXPOSED INFANT

See Section 11.5: The HIV-exposed infant.

6.6.5 PERINATAL TRANSMISSION OF HEPATITIS B

P00.2

DESCRIPTION

Babies born to mothers with acute hepatitis B infection at the time of delivery or to mothers who are HBsAg-positive or HBeAg-positive.

MEDICINE TREATMENT

- Hepatitis B immunoglobulin, IM, 0.5 mL within 12 hours of delivery. *LoE:IVb*[40]

AND

- Hepatitis B vaccine, IM, 0.5 mL, first dose within 12 hours of delivery. *LoE:IVb*[41]
  - Continue hepatitis B immunisation according to the recommended immunisation schedule.

» Check the baby's hepatitis B surface antigen (HBsAg) and hepatitis B surface antibody (HBsAb) at 9 months:
  - If HBsAg positive: baby has hepatitis B infection – refer.
» If HBsAg negative and HBsAb negative: repeat vaccination with hepatitis B containing vaccine, with a repeat dose in 1 month. Repeat HBsAb one month after the second dose; if still HBsAb negative then refer.
» If HBsAb positive: baby is immune to hepatitis B. Reassure parents, no further testing required.

Note: Do not check hepatitis B serology before 9 months of age as antibodies from the birth dose of immunoglobulin might still be present. Refer if hepatitis B serology is not available.

6.7 POSTPARTUM CARE

6.7.1 POSTPARTUM HAEMORRHAGE (PPH)

O72.0-3

DESCRIPTION

Primary postpartum haemorrhage (PPH) is blood loss >500 mL that occurs within 24 hours of birth.
Secondary PPH occurs 24 hours to 12 weeks after delivery (late or delayed PPH).
The most common cause of primary PPH is an atonic uterus.

GENERAL MEASURES

» Massage fundus and expel clots from vagina.
» Empty the bladder.
» Two intravenous lines (wide bore if possible).
» Bimanually compress the uterus to stop the bleeding.
» If no response to medicine treatment, insert a condom catheter (an open condom slipped over a large Foley's catheter and secured at its base with string to provide a makeshift balloon catheter) into uterus, inflate with 400 to 500 mL of saline and clamp. Pack vagina with swabs to prevent expulsion and refer urgently.

MEDICINE TREATMENT

Replace fluids:

- Sodium chloride 0.9%, IV, infused as fast as possible in one IV line.

AND

- Oxytocin, IV 20 units in 1 000 mL sodium chloride 0.9% infused at 250 mL/hour in 2nd IV line. *LoE:IIb*[42]

AND

Tranexamic acid, IV, 1g in 200 mL sodium chloride 0.9% over 10 minutes, or 1 g by slow IV injection,

which may be initiated by a nurse, but only with prior approval of a medical practitioner. *LoE:IIIb*[43]

If no response:

- Ergometrine, IM, 0.5 mg. *LoE:IVb*

OR

- Oxytocin/ergometrine, IM, 5 units/0.5 mg.
  - Avoid ergometrine in hypertensive women and those with heart disease, unless haemorrhage is life threatening (woman haemodynamically unstable).
  - Repeat after 10 to 15 minutes if no response to 1st dose, while arranging referral.

Only in settings where oxytocin is not available:

- Misoprostol, sublingual/rectal, 600mcg as a single dose. *LoE:IIa*[44]

REFERRAL

All cases.

6.7.2 PUERPERAL SEPSIS

O85/O86.0-4/O86.8

DESCRIPTION

Clinical features include a temperature ≥38°C (usually ≥2 days after delivery), often accompanied by offensive vaginal discharge (lochia) and/or abdominal pain within the first 10 days postpartum. In post caesarean section (CS) cases, there may additionally be tenderness around the CS wound and offensive discharge from the wound.

GENERAL MEASURES

» Monitor vital parameters, e.g. Hb, pulse, BP, temperature.
» Treat for shock if indicated.

MEDICINE TREATMENT

- Ceftriaxone, IV, 1 g as a single dose. W

CAUTION: USE OF CEFTRIAXONE
Do not administer calcium-containing fluids, e.g. Ringer-Lactate, concurrently with ceftriaxone.

AND

- Metronidazole, oral, 400 mg as a single dose. A

REFERRAL

All cases.

6.7.3 CRACKED NIPPLES DURING BREASTFEEDING

O92.1

DESCRIPTION

The areola and nipple are protected by the secretion of a lubricant from Montgomery's glands. Cracked nipples may lead to infection and mastitis.

Causes of cracked nipples include:

» poor positioning of the baby and incorrect attachment to the breast,

» removing the baby from the breast before suction is broken,
» the four signs of good attachment are:
» chin touching breast (or very close),
  - mouth wide open,
  - lower lip turned outward,
  - more areola visible above than below the mouth.

GENERAL MEASURES

» Apply expressed breast milk to the nipples between feeds and air dry.
» If too painful, express the milk and nurse the baby on the other breast until improvement.
» Keep areola and nipple clean and dry.
» Avoid use of soap, creams and lotions on the nipples.

MEDICINE TREATMENT

- Zinc and castor oil ointment.
  - Apply between feeds.

If oral thrush is present, treat neonate with:

- Nystatin solution, oral. See Section 1.2: Candidiasis, oral (thrush).

REFERRAL

No improvement after 2 days.

6.7.4 MASTITIS

O91.2

DESCRIPTION

Inflammation of the breast tissue surrounding the milk ducts.
Risk factor includes retrograde infection from a fissured nipple and milk stasis.
Commonly isolated pathogens include *S. aureus* and *S. epidermidis*. Presentation includes painful breast(s), fever, erythema and malaise.

GENERAL MEASURES

Compresses.
Regular expressing of breast milk.
Do not stop breastfeeding, unless a breast abscess has developed.
If breast abscess present, refer for incision and drainage.

MEDICINE TREATMENT

- Flucloxacillin, oral, 500 mg 6 hourly for 5 days. A

Severe penicillin allergy:

Z88.0

Macrolide, e.g.:

- Azithromycin, oral, 500 mg daily for 3 days. W

Pain:

- Paracetamol, oral, 500 mg to 1 g, 4 to 6 hourly as required (to a maximum of 4 g in 24 hours).

- Maximum dose: 15 mg/kg/dose.

REFERRAL

» Breast abscess.
» No improvement after 2 days.

6.8 HIV IN PREGNANCY

O98.7

DESCRIPTION

HIV is currently the commonest cause of maternal deaths in South Africa. Transmission of HIV from mother to infant may occur during pregnancy, delivery and/or breastfeeding. Without intervention, 25–40% of infants born to women living with HIV may become infected. With appropriate interventions, maternal mortality as well as perinatal transmission of HIV can be substantially reduced. 4% of women who were initially HIV-negative become positive later during pregnancy. Repeat HIV testing is essential.
For comprehensive information on the care of HIV-infected pregnant women refer to the current National Consolidated Guidelines for the Prevention of Mother-to-Child Transmission of HIV (PMTCT) and the management of HIV in Children, Adolescents and Adults as well as the current Guidelines for Maternity Care in South Africa. See Chapter 11: HIV and AIDS.

GENERAL MEASURES

HCT in all pregnant and breastfeeding women

» Provide routine counselling and voluntary HIV testing to all pregnant women (if HIV status is negative or unknown) at their very first antenatal visit, and treat other STIs if necessary.
» All women who test negative must be offered repeat HIV testing at every routine visit throughout pregnancy, at labour/delivery, at the 6-week EPI visit and 3-monthly throughout breastfeeding.
» Perform a TB symptom screen at each visit.

Women who choose not to be tested

» Provide with individual 'post-refusal' counselling and offer HIV testing at every subsequent visit.
» Perform a TB symptom screen at each visit.
» Counsel on risks of MTCT to unborn baby, HIV risk reduction behaviour and offer HIV prevention services.

Pregnant women who test HIV positive

» Confirm result with a 2nd rapid HIV test of another type in compliance with current HCT policy.
» If results are discordant, repeat both first and confirmatory rapid HIV tests and if still discordant, send blood for a laboratory HIV ELISA.
  - All confirmed HIV-infected women must be fast-tracked for ART regardless of CD4 count.
» Perform clinical staging and TB symptom screen, and take a blood sample for CD4 cell count and creatinine, on the day of testing. Obtain results within a week.

» If CD4 <200 cells/mm^3, do a serum cryptococcal antigen (CrAg) test.
» Start ART on the day of diagnosis (unless there are symptoms of TB).
» Investigate all those with TB symptoms before ART initiation. If TB treatment is started, defer ART for 2 weeks.
» HIV-infected women (WLHIV) must return 1 week after their initial ANC visit to get their creatinine, and CD4 cell count results and be managed accordingly.
» Refer women with unwanted pregnancies <20 weeks' gestation for termination of pregnancy (TOP) services.
» Perform a TB symptom screen at each visit.

Pregnant women already known to be HIV-infected

» If not on ART, do clinical staging; take blood for CD4 count (to determine eligibility for cotrimoxazole prophylaxis) and creatinine. If CD4 <200 cells/mm^3, do a serum cryptococcal antigen (CrAg) test.
  - Start ART the same day if no contraindication.
» If already on ART for >3 months, take blood for viral load measurement irrespective of when it was last done.
» Perform a TB symptom screen at each visit.

Antenatal support

» Counsel about the importance of adherence and virological suppression for PMTCT.
» Counsel on infant feeding, safer sex, family planning, postnatal contraception, partner testing, routine cervical cancer screening.
» Provide appropriate nutritional care and support including iron, folate and calcium supplementation and Hb testing.

Postpartum support

» Provide adequate support and counselling, particularly addressing ART adherence during breastfeeding.
» Educate mothers about the benefits of breastfeeding. Only in circumstance where the mother has confirmed 2nd or 3rd line ART regimen failure, advise not to breastfeed and prescribe replacement feeds.
» Refer mother to appropriate services to continue lifelong ART as part of the general adult ART population.

MEDICINE TREATMENT

Opportunistic infection treatment and prophylaxis for HIV-infected pregnant women:

Pregnant women diagnosed with pulmonary TB:

» First line TB treatment is safe and effective in pregnant women.
» See Section 17.4.1: Pulmonary tuberculosis (TB) in adults.

Pregnant women on ART with no symptoms of TB:

» See Section 11.2.2: Tuberculosis preventive therapy (TPT).

Women with CD4 ≤ 200 cells/mm^3 or WHO clinical stage 3 or 4:

- Cotrimoxazole, oral, 160/800 mg daily, until CD4 >200 cells/mm^3. A

If CrAg-positive, consult an infectious disease expert, and refer.
See Section 11.3.4: Cryptococcosis.
Note: All CrAg positive women need a LP, unless contra-indicated, regardless of symptoms.

CAUTION	
» Although fluconazole should generally be avoided in the 1st trimester, pregnant women should be counselled that the benefits of fluconazole outweigh the risks in the management of cryptococcosis.	
» All pregnant women <20 weeks gestation exposed to fluconazole should have an ultrasound scan to detect congenital abnormalities.	*LoE:IIIb*[45]
» Fluconazole is present at concentrations similar to maternal plasma concentrations in breast milk.	*LoE:IVb*[46]

FIRST-LINE ART REGIMENS *(Also see Section 11.1: Antiretroviral therapy, adults and adolescents)*		
1ST ANC VISIT		
Pregnant women	• Tenofovir, oral 300 mg daily **AND** • Lamivudine, oral, 300 mg daily **AND** • Dolutegravir, oral, 50 mg daily **Note:** Provide as a fixed dose combination (FDC). *LoE:IIa*[47]	» Contraindication to TDF: renal insufficiency with creatinine >85 µmol/L.
If TDF contraindicated	Start alternative regimen (Doctor consult): • Abacavir, oral, 600 mg, daily **AND** • Lamivudine, oral, 300 mg, daily **AND** • Dolutegravir, oral, 50 mg daily *LoE:IIIb*[48]	
Pregnant women currently on ART	• Continue current ART regimen.	» Do a VL as soon as pregnancy is confirmed.
Pregnant women not currently on ART but ART exposed (previous PMTCT or ART loss to follow-up)	• Tenofovir, oral, 300 mg daily **AND** • Lamivudine, oral, 300 mg daily **AND** • Dolutegravir, oral, 50 mg daily **Note:** Provide as a fixed dose combination (FDC). If HBsAg positive: ensure patient is on TDF-containing regimen. *LoE:IIb*[49]	*LoE:IIIb*[50] » Resistance testing for WLHIV failing a DTG-based regimen and who meet the definition of confirmed virological failure may be authorized by an expert on a case-by-case basis.
2ND ANC VISIT (1 WEEK LATER)		
Creatinine ≤ 85 mmol/L	• Continue FDC: TDF+3TC+DTG	

Creatinine >85 mmol/L (TDF is contra-indicated)	• Stop tenofovir Start alternative regimen (Doctor consult): • Abacavir, oral, 600 mg, daily **AND** • Lamivudine, oral, 300 mg, daily **AND** • Dolutegravir, oral, 50 mg daily *LoE:IIIb*[51]	» High-risk pregnancy: change to alternate triple therapy within 2 weeks (Doctor consult) **and refer for renal dysfunction investigation**.
VL <50 c/mL (pregnant women currently on ART)	If still on EFV-based ART, offer switch to: • Tenofovir, oral, 300 mg daily **AND** • Lamivudine, oral, 300 mg daily **AND** • Dolutegravir, oral, 50 mg daily	
VL ≥ 50 c/mL (pregnant women currently on ART)	Continue current regimen whilst investigating and managing cause of elevated VL. Determine if the client should switch to 2nd line.	» Doctor/ expert consult or refer for expert advice. » Pregnant women with confirmed 2nd or 3rd line ART regimen failures should not breastfeed their infants, if they can safely formula feed.
WOMEN DIAGNOSED HIV POSITIVE IN LABOUR		
All unbooked women who test positive during labour should be given prophylactic ART during labour and initiated on lifelong ART before being discharged.	• Nevirapine, oral, 200 mg single dose as early as possible in labour. **AND** • Tenofovir, oral, 300 mg daily **AND** • Lamivudine, oral, 300 mg daily **AND** • Dolutegravir, oral, 50 mg daily **Note:** Provide TDF + 3TC + DTG as a FDC.	Before discharge: Start lifelong ART the day after delivery, if there are no contraindications, regardless of CD4: • TDF+3TC+DTG as a FDC.
POST-DELIVERY		
The mother should start ART within 24 hours of delivery to protect the baby during breastfeeding.	Start lifelong ART regardless of CD4: TDF+3TC+DTG as a FDC	
BABY		
See Section 11.5: The HIV-exposed infant, to decide whether infant is low risk or high risk and what HIV prophylactic management is needed.		

LoE:IIIb[52]

Note:

» eGFR and creatinine clearance are not reliable for diagnosing renal impairment in pregnancy.

» Monitor response to ART within 3 months of ART initiation with a plasma VL. If VL is not suppressed, refer or consult for expert advice.

Viral load monitoring for 1st line regimen in pregnant and breastfeeding women:
Newly diagnosed and initiated ART for the first time:
» Do 1st VL at 3 months on ART.
» If VL <50 c/mL, repeat VL at delivery.

Known HIV-positive women already on ART:
» Measure VL at first/booking visit in ANC,
» If VL <50 c/mL, repeat VL at delivery. *LoE:IIIb*[53]

Known HIV-positive women, who are not currently on ART, but are ART exposed (e.g. previous PMTCT, or ART loss to follow-up) and who are initiating a DTG-containing regimen:

» Do 1st VL at 3 months on ART.
» If VL <50 c/mL, repeat VL at delivery.

REFERRAL

» Refer mothers suspected of non-adherence early.

Urgent

» Creatinine >85 mmol/L.
» ALT >100 IU/L.
» Pregnant women who are CrAg+, and
  - LP cannot be performed, or
  - symptomatic (headache, confusion), or
  - asymptomatic, but in the 1st trimester.

6.9 MATERNAL MENTAL HEALTH

In vulnerable women, pregnancy exacerbates the risk of developing a mental illness. Approximately one in three women in South Africa have depression and/or anxiety in the perinatal period. Globally, postpartum psychosis affects 1 to 2 women in every 1000 after childbirth .

Risk factors for maternal mental illness include past history of mental illness, recent major life event, (e.g. bereavement) early childhood adversity/ abuse, domestic violence, a history of trauma, displacement from home of origin, low socio-economic status, food insecurity. Women who learn that they are HIV positive during pregnancy have a particular vulnerability to mental health conditions.

Untreated maternal mental illness is associated with the following:

» unplanned and unwanted pregnancy,
» poor adherence to health advice; poor uptake of antenatal services,
» tobacco, alcohol and other substance use,
» self-harm and suicide,
» relapse of the mental illness during the pregnancy or postpartum,
» gestational hypertension and/or diabetes,
» poor pregnancy outcomes, including preterm labour and low birth weight,

» increased risk of neonatal morbidity and stillbirth in mothers with bipolar and psychotic disorders,
» poor engagement with the infant,
» poor family relationships; paternal mental health conditions,
» behavioural and neurodevelopmental disorders in the offspring.

Suspect maternal mental illness if:

» unreliable antenatal clinic attendance,
» continued smoking and/or other substance use during pregnancy,
» any odd or eccentric speech or behaviour,
» screened positive using the 3-item tool in the Maternity Case Record.

Pre-conception care:

» Identify at-risk women – any current or past symptoms of mental illness, emotional problems, substance use, poor social support, abusive relationships, recent trauma, socio-economic deprivation.
» Initiate management for mental disorders/ substance use/ psychosocial stress as needed.
» Use medicines which are safe in pregnancy, unless benefit outweighs risk and patient consents to use (if valproate use, sign acknowledgement of risk form https://www.sahpra.org.za/wp-content/uploads/2025/05/GLF-CEM-PV-S01_v2-Valproate-Annual-Risk-Acknowledgement-Form-ARF.pdf.
» Discuss planning for pregnancy and initiate contraception according to individual choice.

6.9.1 PERINATAL DEPRESSION AND/OR ANXIETY

O28.8-9/ O90.9 + (F32.0-3/F32.8-9/ F33.0-4/F33.8-9/F34.1/F53.0-1/F53.8-9)

DESCRIPTION

See Sections 16.4.1: Depressive disorders and 16.3 Anxiety disorders, for symptoms of depression and/or anxiety. Note that these conditions may occur together in the same person.

» Depression and /or anxiety may be antenatal or postpartum. Postpartum depression usually begins within a month of delivery but can present up to a year after delivery.
» Anxiety disorders may present as fear of labour and childbirth, or other fears e.g. needle phobia. Such fears may interfere with antenatal and postnatal care if they are not addressed.
» Postpartum blues last less than a week, are characterised by irritability, tearfulness, anxiety beginning by day 3 to 5 postpartum. Usually resolve with gentle support but may progress to depression.

CAUTION: Suicide

» Highest risk period is from 6 weeks before to 12 weeks after delivery.
» Adolescent mothers are at particular risk.
» Those with a prior history of self-harm at particular risk.
» See Section 16.7: Suicide risk assessment.
» Inform all healthcare providers involved of suicide risk.
» Ensure psychosocial support – partner/ family/ NGO/ welfare support.

» Optimise treatment of mental illness.
» Do not leave unattended if high risk of self-harm.

GENERAL MEASURES

Antenatal

» Don't stop psychiatric medication if stable on treatment: assess course of illness, severity, and suicide risk. Refer if any or increasing signs of severity.
» Discuss potential benefits/harms of medication to patient and baby as well as alternatives (see Adult Hospital Level Sections 15.2: Anxiety and obsessive-compulsive disorders and 15.3.1: Depressive disorders).
» Antenatal care: provide active adherence support; provide regular, frequent CHW home visits; watch for preterm labour and/or SGA baby; follow-up on any up-referral.
» Explore and address psychosocial stressors: *LoE:IIIb*[54]
  - Mobilise patient's support system.
  - Stress management/coping skills – refer for counselling e.g. at www.sadag.org.
  - Relationship and family issues – refer for counselling, e.g. at www.famsa.org.za
  - Abuse or interpersonal violence - refer to a social worker and for support, e.g. by www.genderjustice.org.za or www.powa.co.za.

Postnatal

» Continue close home-based support of mother and baby for at least the first year.
» Encourage breastfeeding, if not contraindicated medically. (Breastfeeding difficulties may also be associated with depression and anxiety.)
» Optimise treatment of mental illness and co-morbid physical health conditions. *LoE:IIIb*[55]
» Optimise psychosocial and parenting support – utilise support groups e.g. at www.sadag.org Refer to Social Welfare if suspect child-care is seriously impaired.

MEDICINE TREATMENT

See Sections 16.4.1: Depressive disorders and 16.3: Anxiety disorders, for treatment of depression and/or anxiety.

» Mild to moderate anxiety – refer for psychotherapy if available (and/or psychosocial support from mothers' groups, NGOs, counsellors) and monitor response.
» Moderate – severe anxiety and/ or depression - antidepressant (SSRI) treatment for early symptom control and prevention of relapse is generally necessary.

REFERRAL

» All severe depression where functioning is severely impaired.

» Poor response to psychological and supportive medication.
» Poor response to first line SSRI (antidepressant) medication.
» Factors requiring urgent admission, invoke the MHCA if necessary:
  - Suicide risk.
  - Any possible psychotic features.
  - Risk to infant.

6.9.2 BIPOLAR, SCHIZOPHRENIA, AND RELATED DISORDERS

O28.8-9/ O90.9 + (F28/F29/F53.0-1/F53.8-9)

DESCRIPTION

Bipolar disorders (BD):

See Adult Hospital STG Sections 15.3.2: Bipolar and related disorders for description and management in the perinatal period.

Note that:

» BD may present with antenatal or postnatal depression, hypomania, mania or psychosis.
» the index episode often occurs postpartum – may be no prior history of mental illness.
» risk of relapse in those known to have BD is increased in pregnancy and postpartum.
» women with bipolar disorder have a 1 in 4 chance of postpartum psychosis.
» BD is associated with increased risk of pre-eclampsia, placental abnormalities, preterm delivery, LBW and SGA babies, neonatal morbidity, and maternal suicide.

Schizophrenia and related disorders:

See Section 16.5: Psychosis and Adult Hospital STG Section 15.5: Psychotic disorders for description and management.

Note that:

» Psychotic disorders are associated with poor pregnancy outcomes as with BD plus increased risk of diabetes, stillbirth, sudden infant death syndrome.
» The rate of deterioration from a non-psychotic to psychotic state may be more rapid in the postpartum period than usual. Take any reports of unusual behaviour by family members as serious and urgent.

CAUTION: Psychosis

» Is a medical emergency; requires urgent hospitalisation.
» Always exclude delirium due to puerperal sepsis.
» May present with subtle, odd behaviour and/or thoughts; women may be blunted, withdrawn, agitated, or aggressive.
» High risk for harm to self or others, suicide, infanticide.
» May severely impair mother-infant bonding and child-care.
» Manage aggressive or disruptive behaviour (see Section 16.1.2: Aggressive disruptive behaviour in adults).

GENERAL MEASURES

» Manage all pregnancies as high-risk in conjunction with obstetrician and psychiatrist.

» Don't stop psychiatric medication – discuss with Doctor/ psychiatrist.
» Actively monitor adherence to antenatal care and hospital referrals.
» Provide regular, frequent CHW home visits.
» Arrange for hospital delivery.
» Postpartum – keep in hospital, monitor mother and new-born, and ensure home-based care and outpatient follow-up before discharge.

Factors requiring urgent admission, invoke the MHCA if necessary:

» Suicide risk.
» Any possible psychotic features.
» Risk to infant.

REFERRAL

All patients.

GYNAECOLOGY

6.10 ECTOPIC PREGNANCY

O00.0-2/O00.8-9

DESCRIPTION

Pregnancy outside the uterus, usually presenting with the combination of:

» amenorrhoea (missed menstrual period),
» sudden lower abdominal pain/ pelvic pain,
» vaginal bleeding (os closed),
» dizziness,
» shock,
» anaemia,
» urine pregnancy test usually positive,
» shoulder tip pain.

Note: Consider ectopic pregnancy in young women who complain of lower abdominal pain.

GENERAL MEASURES

» Monitor vital parameters, e.g. Hb, pulse, BP, temperature.
» Treat for shock if indicated.

MEDICINE TREATMENT

- Sodium chloride 0.9%, IV.

REFERRAL

Urgent

All suspected cases of ectopic pregnancy.

6.11 VAGINAL BLEEDING

Note: Women should receive regular screening for cervical cancer after the age of 30 years. Any opportunity to perform screening should be taken; this includes taking pap smears during pregnancy.

6.11.1 ABNORMAL VAGINAL BLEEDING DURING REPRODUCTIVE YEARS

N92.0-2/3-6

DESCRIPTION

Increased vaginal blood flow in either volume, duration, and/or frequency, including menorrhagia or dysfunctional uterine bleeding.

GENERAL MEASURES

» Assess current contraceptives used.
» Exclude pregnancy complication or organic disease e.g. cervical cancer, fibroids.

MEDICINE TREATMENT

- Combined oral contraceptive pill (ethinylestradiol/levonorgestrel) for 3 to 6 months.
- Ibuprofen, oral, 400 mg 8 hourly with or after a meal as needed for 2 to 3 days.
  - Ibuprofen may reduce blood loss in menorrhagia associated with intrauterine contraceptive device (IUCD) or chronic salpingitis (see Chapter 12: Sexually transmitted infections).

If blood loss has been severe or there are signs of anaemia:

- Ferrous sulfate compound BPC (dried), oral, 170 mg (± 55 mg elemental iron) 12 hourly with meals.

OR

- Ferrous fumarate, oral, 200 mg (± 65 mg elemental iron) 12 hourly.

  - Continue for 3 months after Hb normalises - to replenish body iron stores.
  - Taking iron tablets with meals decreases iron absorption, but improves tolerability. (**Note:** Do not take iron tablets with milk.) *LoE:IIb*[56]

REFERRAL

» No improvement.
» Girls <12 years of age with vaginal bleeding before the development of their secondary sexual characteristics.
» For investigation of other causes such as:
  - sexual abuse,
  - foreign bodies,
  - tumours of the genital tract.
» Severe anaemia.

6.11.2 POST-MENOPAUSAL BLEEDING

N95.0

DESCRIPTION

Vaginal bleeding six months following the complete cessation of menstruation.
Note: If bleeding is profuse, stabilise before referral.

REFERRAL

All cases, to exclude underlying malignancy and other pathology.

6.12 DYSMENORRHOEA

N94.4-6

DESCRIPTION

Pain associated with menstrual cycles. In primary dysmenorrhoea there is no known cause. Secondary dysmenorrhoea usually has an organic cause.

GENERAL MEASURES

» Advise and reassure women with primary dysmenorrhoea about the nature of the condition.

» Encourage patient to carry on with normal everyday activities.

MEDICINE TREATMENT

- Ibuprofen, oral, 400 mg 8 hourly with or after a meal as needed for 2 to 3 days.

ADD

- Combined oral contraceptive pill, if symptoms still problematic, and if pregnancy is not planned.

Treat for pelvic infection when present.

REFERRAL

» Poor response to treatment.
» If an organic cause is suspected, e.g. fibroids.

6.13 HORMONE THERAPY (HT)

N95.1-2/N95.8-9

Indications:
Short-term symptomatic relief for severe menopausal symptoms.
For menopausal women, treatment should be ≤5 years.
Risk-benefit assessment should be individualised in all patients.

Contra-indications include:

» Known or suspected estrogen-dependent malignant tumours (such as endometrial cancer).
» Coronary heart disease.
» Active liver disease.
» Women ≥ 60 years of age.
» Current, past or suspected breast cancer.
» Thrombophilia.
» Undiagnosed genital bleeding.
» Previous idiopathic or current venous thromboembolism.
» Untreated endometrial hyperplasia.
» Porphyria cutanea tarda.

GENERAL MEASURES

Prior to starting HT:

» Do breast and gynaecological examination.
» Cervical screening.

MEDICINE TREATMENT (Doctor initiated)

Uterus present (no hysterectomy)
HT can be offered as sequentially opposed or continuous combined preparations. Continuous combined preparations are often preferred if the woman had her last menstrual period (menopause) over a year ago, as they will not usually cause bleeding then. For women who are still menstruating or have recently stopped, sequentially opposed preparations are preferred and will result in regular menstrual periods, whereas continuous combined may result in irregular bleeding.

CONTINUOUS COMBINED THERAPY
• Estradiol/norethisterone acetate, oral, 1mg/0.5mg for 28 days.
OR
• Estradiol/norethisterone acetate, oral, 2mg/1mg for 28 days.
OR
• Conjugated estrogens, oral, 0.3 to 0.625 mg for 28 days. **AND** • Medroxyprogesterone acetate, oral, 2.5 to 5mg daily for 28 days.

OR

SEQUENTIALLY OPPOSED THERAPY
• Estradiol valerate/cyproterone acetate, oral: • Estradiol valerate, oral, 2 mg for 11 days. • Estradiol valerate/cyproterone acetate, oral, 2mg/1mg for 10 days. • Placebo, oral, for 7 days.
OR
• Estradiol valerate, oral, 1 to 2 mg daily for 21 days. **ADD** • Medroxyprogesterone acetate, oral, 5 -10 mg daily from day 12 to 21. Followed by no therapy from day 22 to 28.
OR
• Conjugated estrogens, oral, 0.3 to 0.625 mg daily for 21 days. **ADD** • Medroxyprogesterone acetate, oral, 5–10 mg daily from day 12 to 21. Followed by no therapy from day 22 to 28.

LoE:IVb[57]

Note: Where a dose range is provided start at the lowest possible dose to alleviate symptoms. The need to continue HT should be reviewed annually.

Women with no uterus (post-hysterectomy)

- HT is given as estrogen only, e.g.:
- Estradiol valerate, oral, 1–2 mg daily.

OR

- Conjugated estrogens, oral, 0.3 mg daily to a maximum of 1.25 mg daily.

REFERRAL

» Premature menopause, i.e. <40 years of age.
» Severe osteoporosis
» Management difficulties, e.g. where oestrogen therapy is contra-indicated, poorly tolerated, or ineffective.
» Post-menopausal bleeding.
» If HT needed (symptoms persist) after 5 years of HT or woman ≥ 65 years.

6.14 VAGINAL ULCERS

See Section 12.5: Genital ulcer syndrome (GUS).

6.15 VAGINAL DISCHARGE/LOWER ABDOMINAL PAIN IN WOMEN

See Sections 12.1: Vaginal discharge syndrome (VDS) and 12.2: Lower abdominal pain (LAP).

References:

[1] Anti-D immunoglobulin, IM: Karanth L, JaafarSH, Kanagasabai S, Nair NS, Barua A. Anti-D administration after spontaneous miscarriage for preventing Rhesus alloimmunisation. The Cochrane database of systematic reviews. 2013(3): Cd009617. https://www.ncbi.nlm.nih.gov/pubmed/23543581

Anti-D immunoglobulin, IM: Hamel C, Esmaeilisaraji L, Thuku M, Michaud A, Sikora L, Fung-Kee-Fung K. Antenatal and postpartum prevention of Rh alloimmunization: A systematic review and GRADE analysis. PLoS One. 2020;15(9):e0238844. https://pubmed.ncbi.nlm.nih.gov/32913362/

Anti-D immunoglobulin, IM: Schmidt-Hansen M, Lord J, Hawkins J, Cameron S, Pandey A, Hasler E, et al. Anti-D prophylaxis for rhesus D (RhD)-negative women having an abortion of a pregnancy up to 13+6 weeks' gestation: a systematic review and new NICE consensus guidelines. BMJ Sex Reprod Health. 2020 Jan 20;bmjsrh-2019-200536. https://pubmed.ncbi.nlm.nih.gov/31959599/

Anti-D immunoglobulin, IM: NICE. Ectopic pregnancy and miscarriage: diagnosis and initial management, 24 November 2021. https://www.nice.org.uk/guidance/ng126

[2] Misoprostol (medical abortion): NICE. Guideline: Abortion Care, 25 September 2019. https://www.nice.org.uk/guidance/ng140

Misoprostol (medical abortion): WHO. Guideline: Medical management of abortion, 2018. https://www.who.int/reproductivehealth/publications/medical-management-abortion/en/

[3] Morphine, IM (Incomplete 1st trimester miscarriage): National Department of Health, Essential Drugs Programme: Adult Hospital Level STGs and EML, updated edition. https://www.knowledgehub.org.za/content/standard-treatment-guidelines-and-essential-medicines-list

[4] Medical abortion (follow-up pregnancy test): NICE. Guideline: Abortion Care, 25 September 2019. https://www.nice.org.uk/guidance/ng140

Medical abortion (follow-up pregnancy test): Barnhart K, Sammel MD, Chung K, Zhou L, Hummel AC, Guo W. Decline of serum human chorionic gonadotropin and spontaneous complete abortion: defining the normal curve. Obstet Gynecol. 2004 Nov;104(5 Pt 1):975–81. https://pubmed.ncbi.nlm.nih.gov/15516387/

[5] Mifepristone (Medical TOP): Royal College of Obstetrics and Gynaecology Guidelines.The Care of Women Requesting Induced Abortion (Evidence-based Clinical Guideline No. 7), 2011. https://www.rcog.org.uk/en/guidelines-research-services/guidelines/the-care-of-women-requesting-induced-abortion/

Mifepristone (Medical TOP): WHO.Safe abortion: technical and policy guidance for health systems, 2014. http://www.who.int/reproductivehealth/publications/unsafe_abortion/en/

Mifepristone (Medical TOP): National Department of Health, Essential Drugs Programme: Adult Hospital Level STGs and EML, updated version. https://www.knowledgehub.org.za/content/standard-treatment-guidelines-and-essential-medicines-list Mifepristone (Medical TOP): Republic of South Africa.Choice on Termination of Pregnancy Act Amendment 1 of 2008. http://www.gov.za/documents/choice-termination-pregnancy-amendment-act

Mifepristone (Medical TOP): National Department of Health: Affordable Medicines, EDP- Primary Health Care. Medicine Review: Can TOPs be accomplished safely and effectively without ultrasound, July 2016. https://www.knowledgehub.org.za/content/standard-treatment-guidelines-and-essential-medicines-list

[6] Misoprostol (Medical TOP): Royal College of Obstetrics and Gynaecology Guidelines. The Care of Women Requesting Induced Abortion (Evidence-based Clinical Guideline No. 7), 2011. https://www.rcog.org.uk/en/guidelines-research-services/guidelines/the-care-of-women-requesting-induced-abortion/

Misoprostol (Medical TOP): WHO.Safe abortion: technical and policy guidance for health systems, 2014. http://www.who.int/reproductivehealth/publications/unsafe_abortion/en/

Misoprostol (Medical TOP): National Department of Health, Essential Drugs Programme: Adult Hospital Level STGs and EML, updated version. https://www.knowledgehub.org.za/content/standard-treatment-guidelines-and-essential-medicines-list

Misoprostol (Medical TOP): National Department of Health: Affordable Medicines, EDP- Primary Health Care. Medicine Review: Can TOPs be accomplished safely and effectively without ultrasound, July 2016. https://www.knowledgehub.org.za/content/standard-treatment-guidelines-and-essential-medicines-list

[7] Misoprostol, oral/PV (TOP - Up to 12 weeks and 0 days): World Health Organisation. Medical management of abortion, 2018. http://www.who.int/reproductivehealth/publications/medical-management-abortion/en/

[8] Paracetamol, oral (Medical TOP): National Department of Health, Essential Drugs Programme: Adult Hospital Level STGs and EML, updated version. https://www.knowledgehub.org.za/content/standard-treatment-guidelines-and-essential-medicines-list

[9] Ibuprofen, oral (Medical TOP): National Department of Health, Essential Drugs Programme: Adult Hospital Level STGs and EML, updated version. https://www.knowledgehub.org.za/content/standard-treatment-guidelines-and-essential-medicines-list

[10] Misoprostol (MVA TOP): National Department of Health, Essential Drugs Programme: Adult Hospital Level STGs and EML, updated version. https://www.knowledgehub.org.za/content/standard-treatment-guidelines-and-essential-medicines-list

[11] Morphine, IM (MVA TOP): National Department of Health, Essential Drugs Programme: Adult Hospital Level STGs and EML, updated version. https://www.knowledgehub.org.za/content/standard-treatment-guidelines-and-essential-medicines-list

[12] Paracetamol, oral (MVA TOP): National Department of Health, Essential Drugs Programme: Adult Hospital Level STGs and EML, updated version. https://www.knowledgehub.org.za/content/standard-treatment-guidelines-and-essential-medicines-list

[13] Ibuprofen, oral (MVA TOP): National Department of Health, Essential Drugs Programme: Adult Hospital Level STGs and EML, updated version. https://www.knowledgehub.org.za/content/standard-treatment-guidelines-and-essential-medicines-list

[14] Anti-D immunoglobulin, IM (dose): NICE Clinical Guideline: 156 - Routine antenatal anti-D prophylaxis for women who are rhesus D negative, 2008. https://www.nice.org.uk/guidance/ta156/resources/routine-antenatal-antid-prophylaxis-for-women-who-are-rhesus-d-negative-pdf-82598318102725

[15] Contraception (TOP): WHO. Safe abortion: technical and policy guidance for health systems, 2012. http://www.who.int/reproductivehealth/publications/unsafe_abortion/9789241548434/en/

[16] Folic acid, oral: De-Regil LM, Peña-Rosas JP, Fernández-Gaxiola AC, Rayco-Solon P. Effects and safety of periconceptional oral folate supplementation for preventing birth defects. Cochrane Database Syst Rev. 2015 Dec 14;(12):CD007950. https://www.ncbi.nlm.nih.gov/pubmed/26662928

Folic acid, oral: Atta CA, Fiest KM, Frolkis AD, Jette N, Pringsheim T, St Germaine-Smith C, Rajapakse T, Kaplan GG, Metcalfe A. Global Birth Prevalence of Spina Bifida by Folic Acid Fortification Status: A Systematic Review and Meta-Analysis. Am J Public Health. 2016 Jan;106(1):e24-34. https://www.ncbi.nlm.nih.gov/pubmed/26562127

Folic acid, oral: Viswanathan M, Treiman KA, Kish-Doto J, Middleton JC, Coker-SchwimmerEJ, Nicholson WK. Folic Acid Supplementation for the Prevention of Neural Tube Defects: An Updated Evidence Report and Systematic Review for the US Preventive Services Task Force. JAMA. 2017 Jan 10;317(2):190-203. https://www.ncbi.nlm.nih.gov/pubmed/28097361

Folic acid, oral: RCOG. Nutrition in Pregnancy: Scientific Impact Paper No. 18. https://www.rcog.org.uk/en/guidelines

Folic acid, oral: ACOG Committee on Practice Bulletins. ACOG practice bulletin. Clinical management guidelines for obstetrician-gynecologists. Number 44, July 2003. (Replaces Committee Opinion Number 252, March 2001) Obstet. Gynecol. 2003;102(1):203–213. https://www.ncbi.nlm.nih.gov/pubmed/12850637

Folic acid, oral: U.S. Preventive Services Task Force.Folic acid for the prevention of neural tube defects: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med. 2009 May 5;150(9):626-31. https://www.ncbi.nlm.nih.gov/pubmed/19414842

Folic acid, oral: Wilson RD; Genetics Committee, Wilson RD, Audibert F, Brock JA, Carroll J, Cartier L, Gagnon A, Johnson JA, Langlois S, Murphy-Kaulbeck L, Okun N, Pastuck M; Special Contributors, Deb-Rinker P, Dodds L, Leon JA, Lowel HL, Luo W, MacFarlane A, McMillan R, Moore A, Mundle W, O'Connor D, Ray J, Van den Hof M. Pre-conception Folic Acid and Multivitamin Supplementation for the Primary and Secondary Prevention of Neural Tube Defects and Other Folic Acid-Sensitive Congenital Anomalies. J ObstetGynaecol Can. 2015 Jun;37(6):534-52. https://www.ncbi.nlm.nih.gov/pubmed/26334606

[17] Valproic acid – caution in pregnancy: European Medicines Agency - Pharmacovigilance Risk Assessment Committee. Assessment report EMA/198940/2018 - valproate exposure in pregnancy, 8 February 2018. https://www.sahpra.org.za/6-28_valproate_annual_risk_acknowledgement_form_dec18_v1/

Valproic acid – caution in pregnancy: Meador K, Reynolds MW, Crean S, Fahrbach K, Probst C. Pregnancy outcomes in women with epilepsy: a systematic review and meta-analysis of published pregnancy registries and cohorts. Epilepsy Res. 2008 Sep;81(1):1-13. https://www.ncbi.nlm.nih.gov/pubmed/18565732

[18] Ferrous (Iron) supplements, oral - intermittent dosing: National Department of Health: Affordable Medicines, EDP-Primary Health Care level. Medicine Review: Intermittent iron supplementation in pregnancy, 6 November 2017. https://www.knowledgehub.org.za/content/standard-treatment-guidelines-and-essential-medicines-list

Ferrous (Iron) supplements, oral - intermittent dosing:Peña-Rosas JP, De-Regil LM, Gomez Malave H, Flores-Urrutia MC, Dowswell T. Intermittent oral iron supplementation during pregnancy. Cochrane Database Syst Rev. 2015 Oct 19;(10):CD009997. https://www.ncbi.nlm.nih.gov/pubmed/26482110

[19] Calcium: Hofmeyr GJ, Lawrie TA, Atallah ÁN, Torloni MR. Calcium supplementation during pregnancy for preventing hypertensive disorders and related problems. Cochrane Database Syst Rev. 2018 Oct 1;10(10):CD001059. https://pubmed.ncbi.nlm.nih.gov/30277579/

Calcium: WHO. WHO recommendations for prevention and treatment of pre-eclampsia and eclampsia, 2011. http://www.who.int/reproductivehealth/publications/maternal_perinatal_health/9789241548335/en/

[20] Aspirin: National Department of Health: Affordable Medicines, EDP- Primary Health Care. Medicine Review: Initiation of aspirin at primary health care (PHC) level for reducing the risk of early onset pre-eclampsia in pregnant women with risk factors for the development of early onset pre-eclampsia (e.g. pre-eclampsia in a previous pregnancy, chronic hypertension, diabetes, antiphospholipid syndrome, or systemic lupus erythematosus (SLE)), as a nurse-initiated prescription prior to referral to secondary level of care, May 2024.
https://www.knowledgehub.org.za/content/standard-treatment-guidelines-and-essential-medicines-list

[21] Methyldopa, oral (iron interaction): Campbell NR, Campbell RR, Hasinoff BB. Ferrous sulfate reduces methyldopa absorption: methyldopa: iron complex formation as a likely mechanism. Clin Invest Med. 1990 Dec;13(6):329-32. https://pubmed.ncbi.nlm.nih.gov/2078911/

Methyldopa, oral (dosing): Wright JM, Orozco-Gonzalez M, Polak G, Dollery CT. Duration of effect of single daily dose methyldopa therapy. Br J Clin Pharmacol. 1982 Jun;13(6):847-54. https://www.ncbi.nlm.nih.gov/pubmed/7093115

[22] Methyldopa, oral (drug interaction with iron): Campbell N, Paddock V, and Sundaram R. Alteration of Methyldopa Absorption, Metabolism, and Blood Pressure Control Caused by Ferrous Sulphate and Ferrous Gluconate. ClinPharmacolTher, 1988, 43:381-6. https://www.ncbi.nlm.nih.gov/pubmed/3356082

[23] Magnesium sulfate, IV/IM (severe cases of preclampsia): Magee LA, Brown MA, Hall DR, Gupte S, Hennessy A, Ananth Karumanchi S et al. The Hypertensive Disorders of Pregnancy: The 2021 International Society for the Study of Hypertesion in Pregnancy Classification, Diagnosis & Management Recommendations for International Practice, Pregnancy Hypertension: An International Journal of Women's Cardiovascular Health (2021), doi: https://doi.org/10.1016/j.preghy.2021.09.008

Magnesium sulfate, IV/IM (severe cases of eclampsia): Which anticonvulsant for women with eclampsia? Evidence from the Collaborative Eclampsia Trial. Lancet. 1995 Jun 10;345(8963):1455-63. Erratum in: Lancet 1995 Jul 22;346(8969):258. https://pubmed.ncbi.nlm.nih.gov/7769899/

Magnesium sulfate, IV/IM (severe cases of eclampsia): Altman D, Carroli G, Duley L, Farrell B, Moodley J, Neilson J, Smith D; Magpie Trial Collaboration Group. Do women with pre-eclampsia, and their babies, benefit from magnesium sulphate? The Magpie Trial: a randomised placebo-controlled trial. Lancet. 2002 Jun 1;359(9321):1877-90. https://pubmed.ncbi.nlm.nih.gov/12057549/

[24] Nifedipine, oral: Magee LA, Brown MA, Hall DR, Gupte S, Hennessy A, Ananth Karumanchi S et al. The Hypertensive Disorders of Pregnancy: The 2021 International Society for the Study of Hypertesion in Pregnancy Classification, Diagnosis & Management Recommendations for International Practice, Pregnancy Hypertension: An International Journal of Women's Cardiovascular Health (2021), doi: https://doi.org/10.1016/j.preghy.2021.09.008

Nifedipine, oral: Sridharan K, Sequeira RP. Drugs for treating severe hypertension in pregnancy: a network meta-analysis and trial sequential analysis of randomized clinical trials. Br J Clin Pharmacol. 2018 Sep;84(9):1906-1916. https://pubmed.ncbi.nlm.nih.gov/29974489/

[25] Calcium gluconate 10%, IV: National Department of Health, Essential Drugs Programme: Adult Hospital level STG, updated version. https://www.knowledgehub.org.za/content/standard-treatment-guidelines-and-essential-medicines-list

[26] Magnesium sulfate, IV: National Department of Health, Essential Drugs Programme: Adult Hospital level STG, updated version. https://www.knowledgehub.org.za/content/standard-treatment-guidelines-and-essential-medicines-list

[27] Nifedipine, oral: Magee LA, Brown MA, Hall DR, Gupte S, Hennessy A, Ananth Karumanchi S et al. The Hypertensive Disorders of Pregnancy: The 2021 International Society for the Study of Hypertesion in Pregnancy Classification, Diagnosis & Management Recommendations for International Practice, Pregnancy Hypertension: An International Journal of Women's Cardiovascular Health (2021), doi: https://doi.org/10.1016/j.preghy.2021.09.008

[28] Ferrous (Iron) supplements: Reveiz L, Gyte GM, Cuervo LG, Casasbuenas A. Treatments for iron-deficiency anaemia in pregnancy. Cochrane Database Syst Rev. 2011 Oct 5;(10):CD003094. http://www.ncbi.nlm.nih.gov/pubmed/21975735

[29] Lidocaine 1% without adrenaline (epinephrine) - diluent:Kingston M, French P, Higgins S, McQuillanO,Sukthankar A, Stott C, McBrienB, Tipple C, Turner A, Sullivan AK; Members of the Syphilis guidelines revision group 2015, Radcliffe K, Cousins D, FitzGerald M, Fisher M, Grover D, Higgins S, Kingston M, Rayment M, Sullivan A. UK national guidelines on the management of syphilis 2015.Int J STD AIDS. 2016 May;27(6):421-46. https://www.ncbi.nlm.nih.gov/pubmed/26721608

[30] Listeriosis: National Institute of Communicable Diseases. Listeriosis: Clinical recommendations for diagnosis and treatment, 5 December 2017. http://www.nicd.ac.za/

[31] High-risk cases for preterm delivery: National Department of Health, Essential Drugs Programme: Adult Hospital Level STGs and EML, updated version. https://www.knowledgehub.org.za/content/standard-treatment-guidelines-and-essential-medicines-list

[32] <36 weeks PTL (no tocylosis): Department of Health, Republic of South Africa. 2015. Guidelines for Maternity care in South Africa, 5th edition. http://www.health.gov.za/

[33] Betamethasone, IM: McGoldrick E, Stewart F, Parker R, Dalziel SR. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. Cochrane Database Syst Rev. 2020 Dec 25;12(12):CD004454. https://pubmed.ncbi.nlm.nih.gov/33368142/

Betamethasone, IM: FIGO Working Group on Good Clinical Practice in Maternal-Fetal Medicine. Good clinical practice advice: Antenatal corticosteroids for fetal lung maturation. Int J Gynaecol Obstet. 2019 Mar;144(3):352-355. https://pubmed.ncbi.nlm.nih.gov/30710360/

[34] Dexamethasone, IM: McGoldrick E, Stewart F, Parker R, Dalziel SR. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. Cochrane Database Syst Rev. 2020 Dec 25;12(12):CD004454. https://pubmed.ncbi.nlm.nih.gov/33368142/

Dexamethasone, IM: FIGO Working Group on Good Clinical Practice in Maternal-Fetal Medicine. Good clinical practice advice: Antenatal corticosteroids for fetal lung maturation. Int J Gynaecol Obstet. 2019 Mar;144(3):352-355. https://pubmed.ncbi.nlm.nih.gov/30710360/

[35] Betamethasone, IM: McGoldrick E, Stewart F, Parker R, Dalziel SR. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. Cochrane Database Syst Rev. 2020 Dec 25;12(12):CD004454. https://pubmed.ncbi.nlm.nih.gov/33368142/

Betamethasone, IM: FIGO Working Group on Good Clinical Practice in Maternal-Fetal Medicine. Good clinical practice advice: Antenatal corticosteroids for fetal lung maturation. Int J Gynaecol Obstet. 2019 Mar;144(3):352-355. https://pubmed.ncbi.nlm.nih.gov/30710360/

[36] Antibiotic therapy (PROM): Kenyon S, Boulvain M, Neilson JP. Antibiotics for preterm rupture of membranes. Cochrane Database Syst Rev. 2013 Dec 2;(12):CD001058. https://pubmed.ncbi.nlm.nih.gov/24297389/

Antibiotic therapy (PROM): Verani JR, McGee L, Schrag SJ; Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention (CDC). Prevention of perinatal group B streptococcal disease--revised guidelines from CDC, 2010. MMWR Recomm Rep. 2010 Nov 19;59(RR-10):1-36. https://pubmed.ncbi.nlm.nih.gov/21088663/

Antibiotic therapy (PROM): ACOG. Prelabor Rupture of Membranes: ACOG Practice Bulletin, Number 217. Obstet Gynecol. 2020 Mar;135(3):e80-e97. https://pubmed.ncbi.nlm.nih.gov/32080050/

Antibiotic therapy (PROM): Navathe R, Schoen CN, Heidari P, Bachilova S, Ward A, Tepper J et al. Azithromycin vs erythromycin for the management of preterm premature rupture of membranes. Am J Obstet Gynecol. 2019 Aug;221(2):144.e1-144.e8. https://pubmed.ncbi.nlm.nih.gov/30904320/

[37] Antibiotic therapy (pre-referral dose with urgent referral: prolonged pre-labour rupture of membranes): Saccone G, Berghella V. Antibiotic prophylaxis for term or near-term premature rupture of membranes: metaanalysis of randomized trials. Am J Obstet Gynecol. 2015 May;212(5):627.e1-9. https://pubmed.ncbi.nlm.nih.gov/25555659/

[38] Morphine, IM (intrapartum care):. South African Medicines Formulary, 14th Edition. Division of Clinical Pharmacology. University of Cape Town, 2022.

[39] Dextrose, 10%, IV: National Department of Health: Integrated Management of Childhood Illness (IMCI) Guidelines, 2019 (updated). https://www.knowledgehub.org.za/e-library

Dextrose, 10%, IV: National Department of Health: Guidelines for the care of all newborns in District Hospitals, Health Centres and Midwife Obstetric Units in South Africa: Neonate care charts, March 2014. https://www.knowledgehub.org.za/e-library

[40] Hepatitis B immuniglobulin, neonatal transmission: National Department of Health, Essential Drugs Programme: Paediatric Hospital Level STGs and EML, 2023 draft version. https://www.knowledgehub.org.za/content/standard-treatment-guidelines-and-essential-medicines-list

[41] Hepatitis B vaccine, neonatal transmission: National Department of Health, Essential Drugs Programme: Paediatric Hospital Level STGs and EML, 2023 draft version. https://www.knowledgehub.org.za/content/standard-treatment-guidelines-and-essential-medicines-list

[42] Oxytocin, IV: HofmeyrGJ, Gülmezoglu AM, Novikova N, Linder V, Ferreira S, Piaggio G. Misoprostol to prevent and treat postpartum haemorrhage: a systematic review and meta-analysis of maternal deaths and dose-related effects. Bull World Health Organ. 2009 Sep;87(9):666-77. http://www.ncbi.nlm.nih.gov/pubmed/19784446

Oxytocin IV:Gülmezoglu AM, Villar J, Ngoc NT, Piaggio G, Carroli G, Adetoro L, Abdel-Aleem H, Cheng L, Hofmeyr G, Lumbiganon P, Unger C, Prendiville W, Pinol A, Elbourne D, El-Refaey H, Schulz K; WHO Collaborative Group To Evaluate Misoprostol in the Management of the Third Stage of Labour. WHO multicentre randomised trial of misoprostol in the management of the third stage of labour. Lancet. 2001 Sep 1;358(9283):689-95. http://www.ncbi.nlm.nih.gov/pubmed/11551574

[43] Tranexamic Acid, IV: Gallos I, Devall A, Martin J, Middleton L, Beeson L, Galadanci H, et al. Randomized Trial of Early Detection and Treatment of Postpartum Hemorrhage. New England Journal of Medicine. 2023 May 9;0(0):null.

[44] Misoprostol: Widmer M, Blum J, HofmeyrGJ, Carroli G, Abdel-Aleem H, Lumbiganon P, Nguyen TN, Wojdyla D, Thinkhamrop J, Singata M, Mignini LE, Abdel-Aleem MA, Tran ST, Winikoff B. Misoprostol as an adjunct to standard uterotonics for treatment of post-partum haemorrhage: a multicentre, double-blind randomised trial. Lancet. 2010 May 22;375(9728):1808-13. http://www.ncbi.nlm.nih.gov/pubmed/20494730

Misoprostol: World Health Organisation.WHO recommendations for the prevention and treatment of postpartum haemorrhage, 2012. http://apps.who.int/iris/bitstream/10665/75411/1/9789241548502_eng.pdf

[45] Fluconazole, oral (pregnancy): Mølgaard-Nielsen D, Pasternak B, Hviid A. Use of oral fluconazole during pregnancy and the risk of birth defects. N Engl J Med. 2013 Aug 29;369(9):830-9. http://www.ncbi.nlm.nih.gov/pubmed/23984730

Fluconazole, oral (pregnancy): Mølgaard-Nielsen D, Svanström H, Melbye M, Hviid A, Pasternak B. Association Between Use of Oral Fluconazole During Pregnancy and Risk of Spontaneous Abortion and Stillbirth. JAMA. 2016 Jan 5;315(1):58-67. http://www.ncbi.nlm.nih.gov/pubmed/26746458

Fluconazole, oral (pregnancy): Govender NP, Meintjes G (Chairpersons), Bicanic T, Dawood H, Harrison TS, Jarvis JN, Karstaedt AS, Maartens G, McCarthy KM, Rabie H, Variava E, Venter WDF(Expert panel members), Boulware DR, Chiller T, Meya DB, Scriven J (Reviewers). Guideline for the prevention, diagnosis and management of cryptococcal meningitis among HIV-infected persons: 2013 update. S Afr J HIV Med 2013;14(2):76-86. http://www.sajhivmed.org.za/index.php/hivmed/article/view/82/128

[46] Fluconazole, oral (breastfeeding): South African Medicines Formulary, 14th Edition. Division of Clinical Pharmacology. University of Cape Town, 2022.

Fluconazole, oral (breastfeeding): Govender NP, Meintjes G (Chairpersons), Bicanic T, Dawood H, Harrison TS, Jarvis JN, Karstaedt AS, Maartens G, McCarthy KM, Rabie H, Variava E, Venter WDF(Expert panel members), Boulware DR, Chiller T, Meya DB, Scriven J (Reviewers). Guideline for the prevention, diagnosis and management of cryptococcal meningitis among HIV-infected persons: 2013 update. S Afr J HIV Med 2013;14(2):76-86. http://www.sajhivmed.org.za/index.php/hivmed/article/view/82/128

[47] Dolutegravir (WOCP & pregnancy): National Department of Health: Affordable Medicines, EDP-PHC/Adult Hospital level. Medicine Review: Dolutegravir in pregnancy, Jun2 2021. https://www.knowledgehub.org.za/content/standard-treatment-guidelines-and-essential-medicines-list

Dolutegravir (WOCP & pregnancy): South African National Department of Health. 2023 Antiretroviral Therapy Clinical Guidelines for the Management of HIV in Adults, Pregnancy and Breastfeeding, Adolescents, Children, Infants and Neonates. April 2023.

[48] Abacavir: WHO. Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring: recommendations for a public health approach, July 2021. https://www.who.int/publications/i/item/9789240031593

Abacavir: National Department of Health: National Consolidated Guidelines for the Management of HIV in Adults, Adolescents, Children and Infants and Prevention of Mother-to-Child Transmission, June 2020. https://www.knowledgehub.org.za/elibrary/national-consolidated-guidelines-management-hiv-adults-adolescents-children-and-infants

[49] Second line (NNRTI-failure) and HbsAg positive: WHO. Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring: recommendations for a public health approach, July 2021. https://www.who.int/publications/i/item/9789240031593

Second line (NNRTI-failure) and HbsAg positive: National Department of Health: National Consolidated Guidelines for the Management of HIV in Adults, Adolescents, Children and Infants and Prevention of Mother-to-Child Transmission, June 2020. https://www.knowledgehub.org.za/elibrary/national-consolidated-guidelines-management-hiv-adults-adolescents-children-and-infants

[50] ART in pregnancy (Previous PMTCT or ART loss to follow-up): WHO. Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring: recommendations for a public health approach, July 2021. https://www.who.int/publications/i/item/9789240031593

ART in pregnancy (Previous PMTCT or ART loss to follow-up): National Department of Health: National Consolidated Guidelines for the Management of HIV in Adults, Adolescents, Children and Infants and Prevention of Mother-to-Child Transmission, June 2020. https://www.knowledgehub.org.za/elibrary/national-consolidated-guidelines-management-hiv-adults-adolescents-children-and-infants

[51] Abacavir: WHO. Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring: recommendations for a public health approach, July 2021. https://www.who.int/publications/i/item/9789240031593

Abacavir: National Department of Health: National Consolidated Guidelines for the Management of HIV in Adults, Adolescents, Children and Infants and Prevention of Mother-to-Child Transmission, June 2020. https://www.knowledgehub.org.za/elibrary/national-consolidated-guidelines-management-hiv-adults-adolescents-children-and-infants

[52] ART in pregnancy: WHO. Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring: recommendations for a public health approach, July 2021. https://www.who.int/publications/i/item/9789240031593

ART in pregnancy: National Department of Health: National Consolidated Guidelines for the Management of HIV in Adults, Adolescents, Children and Infants and Prevention of Mother-to-Child Transmission, June 2020. https://www.knowledgehub.org.za/elibrary/national-consolidated-guidelines-management-hiv-adults-adolescents-children-and-infants

[53] VL monitoring in pregnancy: WHO. Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring: recommendations for a public health approach, July 2021. https://www.who.int/publications/i/item/9789240031593

VL monitoring in pregnancy: National Department of Health: National Consolidated Guidelines for the Management of HIV in Adults, Adolescents, Children and Infants and Prevention of Mother-to-Child Transmission, June 2020. https://www.knowledgehub.org.za/elibrary/national-consolidated-guidelines-management-hiv-adults-adolescents-children-and-infants

VL monitoring in pregnancy: Wessels J, Sherman G, Bamford L, et al. The updated South African National Guideline for the Prevention of Mother to Child Transmission of Communicable Infections (2019). Southern African Journal of HIV Medicine [Internet]. AOSIS; 2020 Jul 8;21(1). Available from: http://dx.doi.org/10.4102/sajhivmed.v21i1.1079

[54] Antenatal care (actively support labour companionship): Bohren MA, Hofmeyr GJ, Sakala C, Fukuzawa RK, Cuthbert A. Continuous support for women during childbirth. Cochrane Database Syst Rev. 2017 Jul 6;7(7):CD003766. https://pubmed.ncbi.nlm.nih.gov/28681500/

[55] Breastfeeding practices (impacted by maternal health): Coo S, García MI, Mira A, Valdés V. The Role of Perinatal Anxiety and Depression in Breastfeeding Practices. Breastfeed Med. 2020 Aug;15(8):495-500. https://pubmed.ncbi.nlm.nih.gov/32522015/

[56] Ferrous sulfate, oral: South African Medicines Formulary, 14th Edition. Division of Clinical Pharmacology. University of Cape Town, 2022.

Ferrous sulfate, oral: Reveiz L, Gyte GM, Cuervo LG, Casasbuenas A. Treatments for iron-deficiency anaemia in pregnancy. Cochrane Database Syst Rev. 2011 Oct 5;(10):CD003094. https://www.ncbi.nlm.nih.gov/pubmed/21975735

Ferrous sulfate, oral : Rimon E, Kagansky N, Kagansky M, Mechnick L, Mashiah T, Namir M, Levy S. Are we giving too much iron? Low-dose iron therapy is effective in octogenarians. Am J Med. 2005 Oct;118(10):1142-7. https://www.ncbi.nlm.nih.gov/pubmed/16194646

Ferrous fumarate, oral: South African Medicines Formulary, 14th Edition. Division of Clinical Pharmacology. University of Cape Town, 2022.

[57] Hormone therapy (HT): National Department of Health, Essential Drugs Programme: Adult Hospital Level STGs and EML, updated version. https://www.knowledgehub.org.za/content/standard-treatment-guidelines-and-essential-medicines-list

SOUTH AFRICAN PRIMARY HEALTHCARE LEVEL ESSENTIAL MEDICINES LIST
CHAPTER 6: OBSTETRICS & GYNAECOLOGY
NEMLC RECOMMENDATIONS FOR MEDICINE AMENDMENTS (2020 -2024 REVIEW CYCLE)

Medicine amendment recommendations, with supporting evidence and rationale are listed below.
Kindly review the medicine amendments in the context of the respective standard treatment guideline (STG).

SECTION A

MEDICINE AMENDMENTS:

SECTION	MEDICINE/MANAGEMENT	ADDED/DELETED/AMENDED
6.2 Miscarriage	Anti-D immunoglobulin, IM	Amended
6.2.1 Management of incomplete miscarriage in the 1st trimester, at primary health care level - *medical evacuation*	Misoprostol, SL/PV/buccal	Directions for use amended
	Ibuprofen, oral	Directions for use amended
	Pregnancy test	Added
	Paracervical block (lidocaine 1%)	Added
6.3 Termination of pregnancy (TOP) - *venue*	TOP criteria	Amended
6.3.1 Management of termination of pregnancy at primary health care level: gestation up to 12 weeks and 0 days	Mifepristone, oral	Directions for use not amended
	Misoprostol, SL	Directions for use amended
	Paracervical block (lidocaine 1%)	Added (doctor only)
	Ibuprofen, oral	Directions for use amended
6.4.1 Antenatal supplements	Iron, oral	Not amended
	Calcium, oral	Retained, with an amendment showing only the elemental calcium requirement i.e. not the calcium carbonate salt dose
	Aspirin, oral	Added
6.4.2 Hypertensive disorders in pregnancy	Categories of gestational hypertension	Amended
6.4.2.1 Chronic hypertension	Methyldopa, oral	Dose and directions for use not amended
6.4.2.5 Eclampsia	Labetalol, IV	Not added
6.4.4 Syphilis in pregnancy	Lidocaine 1%, parenteral	Not amended
6.4.7.1 Preterm labour (PTL) *and*		
6.4.7.2 Preterm pre-labour rupture of membranes (PPROM)	Betamethasone, parenteral	Dosing amended
	Dexamethasone ,Parenteral	Added
6.4.7.2 Preterm prelabour rupture of membranes (PPROM) - *Antibiotic therapy*	Ampicillin, IV	Added
	Amoxicillin, oral	Retained
	Metronidazole, oral	Deleted
	Aztihromycin, oral	Added
- *Severe penicillin allergy*	Metronidazole, oral	Deleted
	Aztihromycin, oral	Dose amended
	Clindamycin, oral	Not added
6.4.7.3 Prelabour rupture of membranes at term (PROM): *>12 hours*	Antibiotic prophylaxis	Retained
6.5 Intrapartum care	Morphine, parenteral	Retained
	Pethidine, parenteral	Not added
	Anti-D immunoglobulin	Directions for use amended
6.6.2 Neonatal resuscitation	Naloxone, IV	Retained
	Resuscitation algorithm	Amended
6.8 HIV in pregnancy	Tenofovir + lamivudine + dolutegravir, oral	Indication amended
	HIV testing	Amended
- *CrAg positive*	Lumbar puncture	Added
6.13 Hormone therapy	Mammogram	Deleted

	Transdermal hormone therapy patches	Not added to the STG, but added to the therapeutic interchange database
Further change after publication of chapter: 6.7.1 Postpartum haemorrhage (PPH)	Tranexamic acid, parenteral	Added

**Throughout the chapter Paracetamol, oral dosing range has been aligned to AHL Chapter 25: Pain including a reiteration of the maximum dose.*

6.2 MISCARRIAGE

Anti-D immunoglobulin, IM: *amended*

Local resource constraints of Anti-D immunoglobulin warrants restricted use of Anti-D immunoglobulin, from "*all Rh-negative women who had a surgical procedure*" to "*only in Rh-negative, non-sensitised women who had surgical procedure for miscarriage*".

The STG was amended as follows:

~~For all miscarriages in Rh-negative, non-sensitised women:~~

For all Rh-negative non-sensitised women, who had a surgical procedure to manage a miscarriage:

- Anti-D immunoglobulin, IM, 50 mcg preferably within 72 hours but may be given up to 7 days following management of miscarriage.

~~Omit anti-D in the first trimester when there are supply constraints~~

Do not offer Anti-D prophylaxis to women who:

» only received medical management for a miscarriage or
» had a threatened miscarriage or
» had a complete miscarriage.

Level of Evidence: Low certainty evidence[1,2], Guidelines[3]

6.2.1 MANAGEMENT OF INCOMPLETE MISCARRIAGE IN THE 1ST TRIMESTER, AT PRIMARY HEALTH CARE LEVEL

Medical evacuation

Misoprostol, SL/PV/buccal: *directions for use amended*

The STG text was amended to align with NICE[4] and WHO[5] guidelines as follows:

- ~~Misoprostol, PV, 800 mcg every 3 hours for 2 doses.~~
  - ~~Repeat after 24 hours if necessary.~~

~~**OR**~~

- ~~Misoprostol, SL, 600 mcg every 3 hours for 2 doses~~
  - ~~Repeat after 24 hours if necessary~~
- Misoprostol, SL/PV/buccal, 800 mcg immediately as a single dose.
  - Repeat after 24 hours if necessary.

Level of Evidence: Low certainty evidence

Ibuprofen, oral: *directions for use amended*

The STG text was aligned with narrative within this chapter, noting harms associated with routine use of ibuprofen:

- Ibuprofen, oral, 400 mg 8 hourly with or after a meal, as needed for 2-3 days.

Pregnancy test: *added*

[1] Karanth L, Jaafar SH, Kanagasabai S, Nair NS, Barua A. Anti-D administration after spontaneous miscarriage for preventing Rhesus alloimmunisation. Cochrane Database Syst Rev. 2013 Mar 28;(3):CD009617. https://pubmed.ncbi.nlm.nih.gov/23543581/

[2] Hamel C, Esmaeilisaraji L, Thuku M, Michaud A, Sikora L, Fung-Kee-Fung K. Antenatal and postpartum prevention of Rh alloimmunization: A systematic review and GRADE analysis. PLoS One. 2020;15(9):e0238844.

[3] Schmidt-Hansen M, Lord J, Hawkins J, Cameron S, Pandey A, Hasler E, et al. Anti-D prophylaxis for rhesus D (RhD)-negative women having an abortion of a pregnancy up to 13+6 weeks' gestation: a systematic review and new NICE consensus guidelines. BMJ Sex Reprod Health. 2020 Jan 20;bmjsrh-2019-200536.

[4] NICE. Guideline: Abortion Care, 25 September 2019. https://www.nice.org.uk/guidance/ng140

[5] WHO. Guideline: Medical management of abortion, 2018. https://www.who.int/reproductivehealth/publications/medical-management-abortion/en/

Pregnancy test as follow up management was added, aligned with NICE guidance.[6]A 3-week period before testing is recommended to minimise false-positives (bHCG 25miu/ml is the cut-off for a positive pregnancy test).[7] Women with a positive pregnancy test to be referred, accordingly.

Perform a pregnancy test three weeks after medical management

Level of Evidence: Low certainty evidence

6.2.1 MANAGEMENT OF INCOMPLETE MISCARRIAGE IN THE 1ST TRIMESTER, AT PRIMARY HEALTH CARE LEVEL *and* **6.3.1 MANAGEMENT OF TERMINATION OF PREGNANCY AT PRIMARY HEALTH CARE LEVEL: GESTATION UP TO 12 WEEKS AND 0 DAYS**

Paracervical block (lidocaine 1%): *added*

Guidance was added for paracervical block with lidocaine 1%, parenteral with a cross-reference to the Adult Hospital Level STGs and EML, section 5.9.1: TOP: management of pregnancies ≤14 weeks of gestation, where detailed information is provided on directions for use.

The South African Nursing Council (SANC) *"maintains that Paracervical block is an invasive procedure which is outside the current Scope of Practice of Registered Nurses and Midwives. For this reason, training of nurses to perform such a procedure is not supported by SANC"*[8]*,* and thus guidance for paracervical block has been included as "doctor only".

6.3 TERMINATION OF PREGNANCY (TOP)

Venue

TOP criteria: *amended*

The Choice on Termination of Pregnancy Act, 1996 (as amended by Act 38 of 2004), provides expanded access to abortions; allows registered nurses, as well as registered midwives, to perform abortions up to the twelfth week of pregnancy. The following additional STG text was added:

~~An accredited facility with staff trained in performing TOP, designated by the Member of Executive Council at provincial level.~~ Any facility that has a 24-hour maternity service can provide TOP service without specific designation - *The Choice on Termination of Pregnancy Act, 1996 (as amended by Act 38 of 2004), expanded access to abortions, allowed registered nurses, as well as registered midwives, to perform abortions up to the twelfth week of pregnancy.*

6.3.1 MANAGEMENT OF TERMINATION OF PREGNANCY AT PRIMARY HEALTH CARE LEVEL: GESTATION UP TO 12 WEEKS AND 0 DAYS

Medical TOP

Mifepristone, oral: *directions for use not amended*

Timing of administration of misoprostol, following mifepristone is recommended by RCOG Best Practice guide[9] as 24-48 hours; whilst NICE guidelines[10] recommends 36-48 hours (and a shorter time interval, based on women's preference). However, for pragmatic purposes 24-48 hours was retained.

Level of Evidence: Low certainty evidence

Misoprostol, SL: *directions for use amended*

The RCOG Best Practice guide[11] recommends that > 14 weeks medical TOP should be performed in a facility, but it can

[6] Medical abortion (follow-up pregnancy test): NICE. Guideline: Abortion Care, 25 September 2019. https://www.nice.org.uk/guidance/ng140

[7] Barnhart K, Sammel MD, Chung K, Zhou L, Hummel AC, Guo W. Decline of serum human chorionic gonadotropin and spontaneous complete abortion: defining the normal curve. Obstet Gynecol. 2004 Nov;104(5 Pt 1):975–81. https://pubmed.ncbi.nlm.nih.gov/15516387/

[8] The SANC Circular 8/2019**:** https://www.sanc.co.za/2019/11/26/circular-30-84-2/

[9] Royal College of Obstetrics and Gynaecology Guidelines. The Care of Women Requesting Induced Abortion (Evidence-based Clinical Guideline No. 7), 2011. https://www.rcog.org.uk/en/guidelines-research-services/guidelines/the-care-of-women-requesting-induced-abortion/

[10] Medical abortion (follow-up pregnancy test): NICE. Guideline: Abortion Care, 25 September 2019. https://www.nice.org.uk/guidance/ng140

[11] Royal College of Obstetrics and Gynaecology Guidelines. The Care of Women Requesting Induced Abortion (Evidence-based Clinical Guideline No. 7), 2011. https://www.rcog.org.uk/en/guidelines-research-services/guidelines/the-care-of-women-requesting-induced-abortion/

be presumed that in South Africa it may be unsafe to abort 9-12 weeks at home or en-route to a hospital. Therefore, the STG text was amended to include the additional pragmatic guidance:

- Misoprostol, SL, 800 mcg by self-administration at home*.
  - If expulsion does not occur within 4 hours of misoprostol administration, a second dose of misoprostol 400 mcg, oral/PV may be given.
  - *From >9 weeks to ≤ 12 weeks - return to the facility within 48 hours to take misoprostol on-site (early morning) due to the risk of heavy bleeding.

Level of Evidence: Low certainty evidence

Pain

Ibuprofen, oral: *directions for use amended*

The STG text was aligned with narrative within this chapter, noting harms associated with routine use of ibuprofen:

- Ibuprofen, oral, 400 mg 8 hourly with or after a meal, as needed for 2-3 days.

6.4.1 ANTENATAL SUPPLEMENTS

Iron, oral: *not amended*

The STG currently provides guidance for dosing of oral iron in those with poor tolerance, supported by previously reviewed evidence.[12] [13]

Calcium, oral: *not amended*

Dosing for calcium was not amended. WHO guidance[14] recommends 1.5 - 2g in divided doses. The recent International Society for the Study of Hypertension in Pregnancy (ISSHP)[15] recommends 'at least 500g per day', assessed as 'weak evidence'. Authors of an updated Cochrane review[16] concluded, "*High-dose calcium supplementation (≥ 1 g/day) may reduce the risk of pre-eclampsia and preterm birth*", and that, "*The limited evidence on low-dose calcium supplementation suggests a reduction in pre-eclampsia, hypertension and admission to neonatal high care, but needs to be confirmed by larger, high-quality trials*".

Level of Evidence: Low certainty evidence

See also Section B for further changes after publication of chapter.

6.4.2 HYPERTENSIVE DISORDERS IN PREGNANCY

Categories of gestational hypertension: *amended*

Aligned with the Adult Hospital Level STGs and EML, 2019; Section 6.4: Hypertensive disorders in pregnancy.

STG text was amended from:

~~LEVELS OF SEVERITY OF HYPERTENSION~~

~~Level of hypertension~~	~~BP Level mmHg~~		
	~~Systolic~~		~~Diastolic~~
~~mild~~	~~140–149~~	~~or~~	~~90–99~~
~~moderate~~	~~150–159~~	~~or~~	~~100–109~~
~~severe~~	~~≥160~~	~~or~~	~~≥110~~

To:

[12] Ferrous (Iron) supplements, oral - intermittent dosing: National Department of Health: Affordable Medicines, EDP-Primary Health Care level. Medicine Review: Intermittent iron supplementation in pregnancy, 6 November 2017. https://www.knowledgehub.org.za/e-library

[13] Ferrous (Iron) supplements, oral - intermittent dosing:Peña-Rosas JP, De-Regil LM, Gomez Malave H, Flores-Urrutia MC, Dowswell T. Intermittent oral iron supplementation during pregnancy. Cochrane Database Syst Rev. 2015 Oct 19;(10):CD009997. https://www.ncbi.nlm.nih.gov/pubmed/26482110

[14] WHO recommendations for prevention and treatment of pre-eclampsia and eclampsia, 2011. http://www.who.int/reproductivehealth/publications/maternal_perinatal_health/9789241548335/en/

[15] Magee LA, Brown MA, Hall DR, Gupte S, Hennessy A, Ananth Karumanchi S et al. The Hypertensive Disorders of Pregnancy: The 2021 International Society for the Study of Hypertesion in Pregnancy Classification, Diagnosis & Management Recommendations for International Practice, Pregnancy Hypertension: An International Journal of Women's Cardiovascular Health (2021), doi: https://doi.org/10.1016/j.preghy.2021.09.008

[16] Hofmeyr GJ, Lawrie TA, Atallah ÁN, Torloni MR. Calcium supplementation during pregnancy for preventing hypertensive disorders and related problems. Cochrane Database Syst Rev. 2018 Oct 1;10(10):CD001059. https://pubmed.ncbi.nlm.nih.gov/30277579/

Categorising hypertensive disease:

» A diastolic BP of 90-109 mmHg and/or systolic BP of 140-159 mmHg; but with **NO** symptoms or organ dysfunction is classified as hypertensive disease without severe features.

» **Maternal features of severe hypertensive disease are any or more of the following:**

- Acute severe hypertension (diastolic BP of 110 mmHg and/or systolic >160 mmHg).
- Thrombocytopenia (platelet <100 000/µL).
- Impaired liver function (ALT or AST >40 IU/L).
- Severe persistent right upper quadrant or epigastric pain.
- HELLP syndrome (platelets <100 000 and AST >70 µl and LDH >600 µl).
- Serum creatinine ≥120 micromol/L.
- Pulmonary oedema.
- New-onset severe headache unresponsive to medication.
- Visual disturbances.

6.4.2.1 CHRONIC HYPERTENSION

Methyldopa, oral: *dose not amended*

The dose of methyldopa for chronic gestational hypertension was not amended, as this is aligned to the Adult Hospital Level STGs and EML, 2019 – refer to the extract from the NEMLC report for the Adult Hospital Level Obstetrics chapter (2017-19 review cycle), below:

Methyldopa, oral: dosing not amended
Query regarding the discrepancy between the NDoH Maternal Health Care Guidelines, 2012 and Adult Hospital Level STGs and EML, 2015 for methyldopa for management of hypertension in pregnancy, was received.
FIGO Guidelines: NDoH Maternal Care Guidelines aligned with International Federation of Gynecology and Obstetrics (FIGO) guidelines[17], recommending methyldopa 500 mg 8 hourly, oral.
Pharmacokinetic study: Adult Hospital STGs and EML, recommends, "Methyldopa, oral, 250 mg 8 hourly as a starting dose - increase to a maximum of 750 mg 8 hourly, according to response". It is noted that this aligns with the SAMF, 2016[18]; whilst a pharmacokinetic study[19] suggests that 12 hourly dosing is feasible.
***Recommendation:** Methyldopa, oral dosing retained as, "250 mg 8 hourly as a starting dose - increase to a maximum of 750 mg 8 hourly, according to response".*
Level of Evidence: III Pharmacokinetic study, Guidelines

Level of Evidence: Low certainty evidence

Methyldopa, oral: *directions for use not amended*

The STG text was not amended as iron supplements have been found to decrease methyldopa absorption[20]. Taking methyldopa two hours before or after iron-containing products can help avoid this interaction.

6.4.2.5 ECLAMPSIA

Labetalol, IV: *not added*

The NEMLC had not approved this in the previous review cycle, due to affordability and pragmatic implications at primary level of care.

NEMLC report for the 2016-2018 review of the PHC STGs and EML, 2018 edition:
The focus of management of eclampsia at primary level of care is to control the seizures with urgent referral. Emergency dosing with oral nifedipine was added to the STG in cases where patient is alert and BP ≥ 110/160 mmHg; whilst labetalol IV was not considered appropriate for primary level of care.
Level of Evidence: III Guidelines, Expert opinion

[17] International Federation of Gynecology and Obstetrics. The FIGO Textbook of Pregnancy Hypertension. http://www.safemotherhood.ucsf.edu/wpcontent/uploads/2013/01/FIGO-Pregnancy_Hypertension-Final.pdf
[18] SAMF, 2022
[19] Wright JM, Orozco-Gonzalez M, Polak G, Dollery CT. Duration of effect of single daily dose methyldopa therapy. Br J Clin Pharmacol. 1982 Jun;13(6):847-54. https://www.ncbi.nlm.nih.gov/pubmed/7093115
[20] Campbell NR, Campbell RR, Hasinoff BB. Ferrous sulfate reduces methyldopa absorption: methyldopa: iron complex formation as a likely mechanism. Clin Invest Med. 1990 Dec;13(6):329-32. https://pubmed.ncbi.nlm.nih.gov/2078911/

6.4.4 SYPHILIS IN PREGNANCY

Lidocaine 1%, parenteral*: not amended*

Recommendations for the administration of lidocaine 1% which is used as a diluent for less painful administration of intramuscular benzathine benzylpenicillin were not amended. The volume of lidocaine 1% as a diluent is aligned with Amir et al's study[21] and the UK 2008 STI guidelines[22] as previously cited.

6.4.7.1 PRETERM LABOUR (PTL) *and* 6.4.7.2 PRETERM PRELABOUR RUPTURE OF MEMBRANES (PPROM)

Betamethasone, parenteral: *dosing amended*

The administration of antenatal betamethasone has been shown to improve improve fetal lung maturity at 26–34 weeks, confirmed by the updated 2020 Cochrane review[23]. High certainty evidence showed that antenatal corticosteroids reduced the risk of:

- perinatal death (RR 0.85, 95% CI 0.77 to 0.93; 9833 infants; 14 RCTs; 2.3% fewer, 95% CI 1.1% to 3.6% fewer)
- neonatal death (RR 0.78, 95% CI 0.70to 0.87; 10,609 infants; 22 RCTs; 2.6% fewer, 95% CI 1.5% to 3.6% fewer)
- respiratory distress syndrome (RR 0.71, 95% CI 0.65 to 0.78; 11,183 infants; 26 RCTs; 4.3% fewer, 95% CI 3.2% to 5.2% fewer)

The dosing interval for commonly used regimen of two doses of betamethasone, IM 12 mg was corrected from "~~*12 hours apart"*~~ to "*24 hours apart*", aligned with the International Federation of Gynecology and Obstetrics clinical practice guide on maternal-fetal medicine[24].

Level of Evidence: High certainty evidence

6.4.7.2 PRETERM PRELABOUR RUPTURE OF MEMBRANES (PPROM)

Ampicillin, IV: *added*
Amoxicillin, oral: *retained*
Metronidazole, oral: *deleted*
Aztihromycin, oral: *added*

Antibiotics for PPROM reduces maternal and neonatal complications – a Cochrane review[25] showed that any antibiotic vs placebo results in:

- Less chorioamnionitis - any antibiotic vs placebo, RR 0.57; 95% CI 0.37 to 0.86.
- Less preterm birth - any antibiotics vs placebo; delivery within 7 days after admission RR 0.8; 95% CI 0.71 to 0.9.
- Less neonatal infection - any antibiotic vs placebo; neonatal infection RR 0.68; 95% CI 0.53 to 0.87.

However, women with PPROM have a high risk of group B streptococcal (GBS) infection. The recommended antibiotic for intrapartum GBS prophylaxis is penicillin.[26] Broad spectrum antibiotics are recommended to prolong latency (due to the colonization with vaginal and rectal organisms). [27]

Of note is that the Cochrane review[25] included 22 RCTs, of which only one RCT (from 1997) used metronidazole. From the available evidence, the Cochrane review recommends erythromycin as a better choice. When different regimens of azithromycin or erythromycin were compared, there was no difference in latency to delivery, incidence of

[21] Amir J, Ginat S, Cohen YH, Marcus TE, Keller N, Varsano I. Lidocaine as a diluent for administration of benzathine penicillin G. Pediatr Infect Dis J. 1998 Oct;17(10):890-3.
[22]Kingston M, French P, Goh B, Goold P, Higgins S, Sukthankar A, et al.; Syphilis Guidelines Revision Group 2008, Clinical Effectiveness Group. UK National Guidelines on the Management of Syphilis 2008. Int J STD AIDS. 2008 Nov;19(11):729-40. Erratum in: Int J STD AIDS. 2011 Oct;22(10):613-
[23] IM: McGoldrick E, Stewart F, Parker R, Dalziel SR. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. Cochrane Database Syst Rev. 2020 Dec 25;12(12):CD004454. https://pubmed.ncbi.nlm.nih.gov/33368142/
[24] FIGO Working Group on Good Clinical Practice in Maternal-Fetal Medicine. Good clinical practice advice: Antenatal corticosteroids for fetal lung maturation. Int J Gynaecol Obstet. 2019 Mar;144(3):352-355. https://pubmed.ncbi.nlm.nih.gov/30710360/
[25] Kenyon S, Boulvain M, Neilson JP. Antibiotics for preterm rupture of membranes. Cochrane Database Syst Rev. 2013 Dec 2;(12):CD001058. https://pubmed.ncbi.nlm.nih.gov/24297389/
[26] Verani JR, McGee L, Schrag SJ; Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention (CDC). Prevention of perinatal group B streptococcal disease--revised guidelines from CDC, 2010. MMWR Recomm Rep. 2010 Nov 19;59(RR-10):1-36. https://pubmed.ncbi.nlm.nih.gov/21088663/
[27] ACOG. Prelabor Rupture of Membranes: ACOG Practice Bulletin, Number 217. Obstet Gynecol. 2020 Mar;135(3):e80-e97. https://pubmed.ncbi.nlm.nih.gov/32080050/

chorioamnionitis, or neonatal outcomes. There also appears to be no additional benefit for an extended course of azithromycin beyond the single-day dosing.[28]
Level of Evidence: Moderate certainty evidence

Severe penicillin allergy
Metronidazole, oral: *deleted*
Aztihromycin, oral: *dose amended*
Clindamycin, oral: *not added*
As clindamycin is not currently included in the PHC EML, a single pre-referral dose of azithromycin 1 g is recommended with urgent referral (refer to discussion on azithromycin above).

6.4.7.3 PRELABOUR RUPTURE OF MEMBRANES AT TERM (PROM)

> 12 hours
Antibiotic prophylaxis*: retained*
Antibiotic prophylaxis for term or near-term premature rupture of membranes is not associated with any benefits in either maternal or neonatal outcomes. In women with latency longer than 12 hours, prophylactic antibiotics are associated with significantly lower rates of chorioamnionitis by 51% and endometritis by 88%.[29] The STG recommends a pre-referral dose of antibiotics with urgent referral.

6.5 INTRAPARTUM CARE

Morphine, parenteral: *retained*
Pethidine, parenteral: *not added*
Morphine was approved by NEMLC in the previous review cycle, as it has less side effects/less effect on the baby.

NEMLC report for the 2016-2018 review of the PHC STGs and EML, 2018 edition:
Analgesia:
Recommendation: *Morphine, IM replaces pethidine, IM as analgesia during first stage of labour with cervical dilatation < 10 cm.*
Rationale: Regulation 31 replaces regulation 47 of the Medicines and related substances Act 101 of 1965 i.e. access to pethidine is replaced by access to schedule 5 and 6 medicines in order to provide intrapartum care. In addition, there are safety concerns regarding pethidine's active metabolite, normeperidine that is potentially neurotoxic.
Level of Evidence: III Regulations[30], Guidelines[31]

Anti-D immunoglobulin: *directions for use amended*
Rational use of Anti-D immunoglobulin is warranted due to continual supply challenges. The following additional text was added to the STG:

» Check baby's Rh status; do not given anti-D if the baby is Rh-negative, or if the mother has Anti-Rh antibodies.

6.6.2 NEONATAL RESUSCITATION

Naloxone, IV: *retained*
The PHC/Adult Hospital Level Committee noted that naloxone, IV was not used in practice for initial neonatal resuscitation in the delivery room anymore. Maternally administered opioids in this clinical setting may cause neonatal respiratory depression, but evidence could not be sourced for naloxone, noting that ventilation and oxygenation may be sufficient for neonatal resuscitation.

[28] Navathe R, Schoen CN, Heidari P, Bachilova S, Ward A, Tepper J et al. Azithromycin vs erythromycin for the management of preterm premature rupture of membranes. Am J Obstet Gynecol. 2019 Aug;221(2):144.e1-144.e8. https://pubmed.ncbi.nlm.nih.gov/30904320/
[29] Saccone G, Berghella V. Antibiotic prophylaxis for term or near-term premature rupture of membranes: metaanalysis of randomized trials. Am J Obstet Gynecol. 2015 May;212(5):627.e1-9. https://pubmed.ncbi.nlm.nih.gov/25555659/
[30]Regulation 31 of the Medicines and related substances Act 101 of 1965.
[31] SAMF, 2022

NEMLC MEETING OF 24 JUNE 2021:

NEMLC Recommendation: *The NEMLC recommended that naloxone be retained for the indication stated in the STG: If the mother is known or suspected to have had narcotic pain relief and the baby has normal heart rate and colour response to bag-mask ventilation, but has not initiated sustained regular respiratory effort".*
However, concern of irrational use of naloxone in clinical practice was raised, and NEMLC deliberated on removing naloxone from the STG. However, as maternal opioid misuse was considered to be relatively common, the NEMLC recommended that naloxone be retained for the indication above, but that a statement be added that ***"Naloxone is not routinely indicated for neonatal resuscitation".***

The Resuscitation Council of Southern Africa's newborn resuscitation algorithm was updated from the 2015 version to the 2021 version.[32]

6.8 HIV IN PREGNANCY

(Note: Recommendations were aligned with updated[33] chapter 11: HIV and AIDs, as appropriate).

Tenofovir + lamivudine + dolutegravir, oral: *amended*
Indication expanded from ≥6 weeks gestation to ALL women
Refer to the medicine review: Dolutegravir in pregnancy, June 2021:

NDoH_PHC-Adult Medicine review_DT

Recommendation: The PHC/Adult Hospital Level Committee recommends that dolutegravir should be part of the preferred first line ART regimen for all adults and adolescents living with HIV, including pregnant women and women of child-bearing potential. The existing contra-indication in pregnancy should be removed from the STG.
Rationale: The risk of neural tube defects in infants exposed to dolutegravir in early pregnancy that was first identified in the Tsepamo observational study in Botswana has diminished over time, with the accumulation of further data. The risk difference between dolutegravir and efavirenz is no longer significant.
Dolutegravir (especially when combined with tenofovir alafenamide) is associated with more weight gain during pregnancy than efavirenz, but the difference is unlikely to be clinically relevant.
Randomised controlled trials have shown non-inferiority in terms of maternal viral suppression rates at 48 weeks. Dolutegravir causes more rapid viral suppression than efavirenz, resulting in increased viral suppression rates by time of delivery in randomised controlled trials of ART initiation in the second and third trimester of pregnancy. This has not yet translated into a demonstrable difference in mother-to-child transmission risk, but event rates are very low with both regimens.
A standardised regimen for all adults and adolescents living with HIV is likely to be easier for nurses to provide.
Based on those findings and observations, the PHC/Adult Hospital Level Committee feel that the potential long-term benefits to pregnant women and WOCP (Women of Child Bearing Potential), as well as potential short-term benefits to their infants, outweigh the risks.
Level of Evidence: Moderate certainty of evidence
Review indicator: New evidence of harms

NEMLC MEETING OF 24 JUNE 2021:
NEMLC Recommendation: The NEMLC accepted the recommendation as proposed by the PHC/Adult Hospital Level Committee, which would support the universal test-and-treat (UTT) strategy of the National HIV Programme.

[32] Published with permission from the Resuscitation Council of Southern Africa. https://resus.co.za/
[33] South African National Department of Health. 2023 Antiretroviral Therapy Clinical Guidelines for the Management of HIV in Adults, Pregnancy and Breastfeeding, Adolescents, Children, Infants and Neonates. April 2023.

It was also duly noted that the South African Health Products Regulatory Authority were currently reviewing the label of dolutegravir products registered on the South African market.

HIV testing: *amended*
Guidance for HIV-testing was amended to align with guidance recommended in the Prevention of Mother-to-Child Transmission of HIV (PMTCT) and the management of HIV in Children, Adolescents and Adults, current Guidelines for Maternity Care in South Africa - i.e. at every Basic Antenatal Care (BANC) visit (8 in total).

CrAg positive
Lumbar puncture: *added*
The following was added to the STG text:

Note: All CrAg positive women need a LP, unless contra-indicated, regardless of symptoms.

6.13 HORMONE THERAPY (HT)

Mammogram: *deleted*
The following STG text was deleted, specifically noting that no facilities are available at primary level of care:

» ~~Where the facility is available, arrange mammography before starting HT. However, lack of access to mammography should not delay HT if indicated for severe menopausal symptoms if the woman has no other special risk factors for breast cancer (e.g.: family history of breast cancer in first degree relative).~~

Transdermal hormone therapy patches: *not added to the STG, but added to the therapeutic interchange database*
Refer to the evidence summary on transdermal HT patches, July 2021, v2:

Transdermal HT Patches_Evidence Sum

Evidence for alternative routes for HT administration was reviewed, owing to reported supply constraints with oral HT. Oral and transdermal HT were both effective in terms of management of menopausal symptoms. Observational studies showed that the risk of thrombosis was higher with oral oestrogen compared to transdermal oestrogen. The PHC ERC therefore proposed that transdermal HT be added to the STG, but restricted to women at high risk of thrombosis, owing to cost. However, the two routes have not been compared directly in women with a high risk of thrombosis, and transdermal HT isn't specifically indicated/registered for this population.

NEMLC MEETING OF 19 DECEMBER 2021
Discussion: The risk for first time thrombosis was reported to be higher amongst women on oral HT compared to those using transdermal HT[34]. However, the number of women needing HT who have a high risk of thromboembolism was anticipated that this would be a small number[35]. Citalopram is recommended for treatment of menopausal symptoms in women at high risk of thromboembolism at secondary level of care. Furthermore, NEMLC raised concerns regarding the high price of transdermal HT.

Recommendation: NEMLC deliberated on the proposal suggested by the PHC/Adult Hospital Level Committee, and recommended that HT transdermal patches be removed from the STG, but be added to the therapeutic interchange database as an alternative to oral estrogens.
Rationale: The number of women requiring HT at high risk of thromboembolism is anticipated to be small. Transdermal HT is expensive compared to oral HT preparations. Citalopram is included on the secondary level EML for management of perimenopausal or menopausal syndrome where "oral" HT is contra-indicated, poorly tolerated or ineffective.

[34] Sweetland S, Beral V, Balkwill A, Liu B, Benson VS, Canonico M, et al.; Million Women Study Collaborators. Venous thromboembolism risk in relation to use of different types of postmenopausal hormone therapy in a large prospective study. J Thromb Haemost. 2012 Nov;10(11):2277-86. https://pubmed.ncbi.nlm.nih.gov/22963114/
[35] Previously, NEMLC had recommended venlafaxine, oral (for hormone with hormone-dependant cancers) not be included on the national EML for secondary level of care; but rather for consideration at tertiary and quaternary level of care – NEMLC minutes of the meeting of 14 December 2017.

Level of Evidence: Conditional recommendation, moderate certainty evidence

Review: equivalence of hormones

Hormone replacement therapy (HRT) reduce vasomotor symptoms in a dose-dependent fashion, and the standard treatment guidelines recommend that prescribers start with the lowest dose available and titrate upwards according to symptoms.[36] There are no head-to-head comparisons of the various formulations in relieving vasomotor symptoms.

Estrogens: Conjugated estrogen (CE) 0.625mg orally is considered a 'standard dose' of HRT and is equivalent to 1-2mg of oral estradiol.[3] A serum estradiol concentration of 76.8 pg/mL is achieved with CE 0.625 mg daily. For 1 mg and 2 mg doses of oral estradiol, serum concentrations of estradiol attained are 65.8 pg/mL and 107.6 pg/mL respectively. Although the optimal range for serum estradiol concentration to achieve therapeutic efficacy has not been established, a serum estradiol concentration of 60 pg/mL is needed to prevent osteoporosis[37] and reduce 50% of hot flashes.[38] During a normal menstrual cycle in the mid-follicular phase plasma estradiol concentrations are 60-150pg/ml.[4] Experimental studies in castrated animals and human studies in postmenopausal women suggest that a plasma estradiol concentration of approximately 100 pg/ml is optimal for treatment of hot flushes, prevention of bone loss and cardiovascular protection.[4]

Progestogens: Serum progesterone concentrations greater than 5 ng/mL must be achieved to inhibit endometrial mitosis and to induce a secretory change (endometrial protection). This threshold concentration is based on the observation that during a normal menstrual cycle, the corpus luteum produces circulating progesterone concentrations that are in the range of approximately 5 to 20 ng/mL.[39]

Norethisterone vs medroxyprogesterone acetate: The WHO 18th Expert Committee of the Selection and Use of Essential Medicines[40] systematically reviewed the evidence (1 systematic review[41] and 3 RCTs[42] [43] [44]) and concluded that low-dose HT be used to manage menopausal symptoms (doses of 5mg norethisterone not recommended as the risks outweigh the benefits). Combining estrogen with progestogen minimises the risk of endometrial hyperplasia which can develop into endometrial cancer in menopausal women with an intact uterus; and low dose estrogen plus progestogen (1 mg norethisterone or 1.5 mg medroxyprogesterone acetate) appears safe for the endometrium, taken either continuously or sequentially.[45]

The therapeutic interchange database for hormone therapy was updated as per the following table aligned with products currently available on the South African market listed in the SAMF, 2020 edition

NEMLC recommended that transdermal hormone therapy patches not be included on the PHC EML, but recommended that the patches should be added to the therapeutic interchange database and be grouped therapeutically with the other EML-recommended oral hormone preparations – the evidence (safety and efficacy) reviewed did not show value for

[36] Kim S-M, Kim SE, Lee D-Y, Choi D. Serum estradiol level according to dose and formulation of oral estrogens in postmenopausal women. Sci Rep. 2021 Feb 11;11:3585.

[37] de Lignieres B. Hormone replacement therapy: clinical benefits and side-effects. Maturitas. 1996 May;23 Suppl:S31-36.

[38] Steingold KA, Laufer L, Chetkowski RJ, DeFazio JD, Matt DW, Meldrum DR, et al. Treatment of hot flashes with transdermal estradiol administration. J Clin Endocrinol Metab. 1985 Oct;61(4):627–32.

[39] Stanczyk FZ, Paulson RJ, Roy S. Percutaneous administration of progesterone: blood levels and endometrial protection. Menopause. 2005 Apr;12(2):232–7.

[40] World Health Organization. 18th Expert Committee on the Selection and Use of Essential Medicines- Section 18.7: Progestogens, March 2011. [Accessed 17 March 2022] Available at: https://www.who.int/selection_medicines/committees/expert/18/applications/Norethisterone.pdf

[41] Zweifel JE, O'Brien WH. A meta-analysis of the effect of hormone replacement therapy upon depressed mood. Psychoneuroendocrinology. 1997 Apr;22(3):189-212. doi: 10.1016/s0306-4530(96)00034-0. Erratum in: Psychoneuroendocrinology 1997 Nov;22(8):655.

[42] Cagnacci A, Arangino S, Baldassari F, Alessandrini C, Landi S, Volpe A. A comparison of the central effects of different progestins used in hormone replacement therapy. Maturitas. 2004 Aug 20;48(4):456-62. doi: 10.1016/j.maturitas.2003.10.003.

[43] Magos AL, Brewster E, Singh R, O'Dowd T, Brincat M, Studd JW. The effects of norethisterone in postmenopausal women on oestrogen replacement therapy: a model for the premenstrual syndrome. Br J Obstet Gynaecol. 1986 Dec;93(12):1290-6. doi: 10.1111/j.1471-0528.1986.tb07868.x.

[44] Boschetti C, Cortellaro M, Nencioni T, Bertolli V, Della Volpe A, Zanussi C. Short- and long-term effects of hormone replacement therapy (transdermal estradiol vs oral conjugated equine estrogens, combined with medroxyprogesterone acetate) on blood coagulation factors in postmenopausal women. Thromb Res. 1991 Apr;62(1-2):1-8. doi: 10.1016/0049-3848(91)90663-h.

[45] Furness S, Roberts H, Marjoribanks J, Lethaby A. Hormone therapy in postmenopausal women and risk of endometrial hyperplasia. Cochrane Database Syst Rev. 2012 Aug 15;2012(8):CD000402. doi: 10.1002/14651858.CD000402.

investing in the transdermal HT patches, but could be considered as an alternative to the oral HT preparations when there are supply issues of the latter, or for scale of volume procurement purposes.

Indication	Therapeutic class	INN	Strength (mg)	formulation
Menstruation > 1 year ago	**Progestogens and estrogens, fixed combinations (lowdose)**	**Norethisterone/estrogen***	**0.5/1**	**oral**
Menstruation > 1 year ago	Progestogens and estrogens, fixed combinations (lowdose)	estradiol/ Norethisterone **	0.62/2.7	transdermal patches
Menstruation > 1 year ago	**Progestogens and estrogens, fixed combinations (standard dose)**	**Estradiol/Norethisterone ***	**1/1**	**oral**
Menstruation > 1 year ago	Progestogens and estrogens, fixed combinations (standard dose)	estradiol/Norethisterone **	3.2/11.2	transdermal patches
Menstruation > 1 year ago	**Progestogens (used with estrogens) - continuous combined therapy**	**Medroxyprogesterone acetate***	**2.5 to 5**	**oral**
Menstruation > 1 year ago	Progestogens (used with estrogens) - continuous combined therapy	Norethisterone**	1.25 to 2.5	oral
Menstruation > 1 year ago	**Estrogens (used with progestogens) - continuous combined therapy**	**Estradiol***	**1 to 2**	**oral**
Menstruation > 1 year ago	Estrogens (used with progestogens) - continuous combined therapy	Conjugated estrogens**	0.3 to 0.625	oral
Menstruation < 1 year ago/present	**Progestogens and estrogens, sequential preparations (low dose)**	**Norethisterone+estrogen/estrogen***	**1/2**	**oral**
Menstruation < 1 year ago/present	Progestogens and estrogens, sequential preparations (low dose)	Dydrogesterone+estrogen/estrogen**	10/1	oral
Menstruation < 1 year ago/present	**Progestogens and estrogens, sequential preparations (standard dose)**	**Norgestrel+estrogen/estrogen***	**0.5/2**	**oral**
Menstruation < 1 year ago/present	Progestogens and estrogens, sequential preparations (standard dose)	Cyproterone+estrogen/estrogen**	1/2	oral
Menstruation < 1 year ago/present	Progestogens and estrogens, sequential preparations (standard dose)	Norethisterone+estrogen/estrogen**	1/2	oral
Menstruation < 1 year ago/present	**Progestogens (used with estrogens) - sequential opposed therapy**	**Medroxyprogesterone acetate***	**5 to 10**	**oral**
Menstruation < 1 year ago/present	Progestogens (used with estrogens) - sequential opposed therapy	Norethisterone**	1.25 to 2.5	oral
Menstruation < 1 year ago/present	**Estrogens (used with progestogens) - sequential opposed therapy**	**Estradiol***	**1 to 2**	**oral**
Menstruation < 1 year ago/present	Estrogens (used with progestogens) - sequential opposed therapy	Conjugated estrogens**	0.3 to 0.625	oral
Uterus absent (post hysterectomy)	**Estrogens**	**Estradiol***	**1 to 2**	**oral**
Uterus absent (post hysterectomy)	Estrogens	Conjugated estrogens**	0.3 to 0.625	oral
Uterus absent (post hysterectomy)	Estrogens	Estradiol**	25 to 75	transdermal patches

**Listed in the STG*

***Listed in the therapeutic interchange database*

SECTION B

Further changes after publication of chapter:

6.4.1 ANTENATAL SUPPLEMENTS

Aspirin, oral: *Added*

Historically, the National Essential Medicines List Committee retained aspirin for secondary level initiation in all women with chronic hypertension, who are pregnant as the patient would require referral to the secondary level of care for evaluation and management.[46,47,48] NEMLC highlighted that pregnant women with chronic hypertension may have been on complex and teratogenic antihypertensive medication and ultrasound scanning to evaluate the foetus for abnormalities, and/or switching to safer medication would be appropriate for secondary level and therefore initiation of prophylactic aspirin and calcium for pre-eclampsia would also only be appropriate for secondary level of care. Expert opinion was cited as the evidence for strict secondary level aspirin initiation for prevention of pre-eclampsia.[49] However patients with historical risk factors (e.g. previous history of pre-eclampsia) might not be referred immediately to secondary care, but only at a scheduled appointment, which may be a few weeks later. These patients will then potentially miss out on the benefit of early initiation of aspirin prophylaxis.

[46] Duley L, Meher S, Hunter KE, Seidler AL, Askie LM. Antiplatelet agents for preventing pre-eclampsia and its complications. Cochrane Database Syst Rev. 2019 Oct 30;2019(10):CD004659. https://pubmed.ncbi.nlm.nih.gov/31684684/

[47] Hoffman MK, Goudar SS, Kodkany BS, Metgud M, Somannavar M, Okitawutshu J et al; ASPIRIN Study Group. Low-dose aspirin for the prevention of preterm delivery in nulliparous women with a singleton pregnancy (ASPIRIN): a randomised, double-blind, placebo-controlled trial. Lancet. 2020 Jan 25;395(10220):285-293. https://www.ncbi.nlm.nih.gov/pubmed/31982074

[48] National Department of Health: Affordable Medicines, EDP-Adult Hospital level. Review: Safety of aspirin in pregnancy, February 2020. https://www.knowledgehub.org.za/content/standard-treatment-guidelines-and-essential-medicines-list

[49] National Department of Health. South African Primary Healthcare Level Essential Medicines List Chapter 6: Obstetrics & Gynaecology Conditions. National Essential Medicines List Committee (NEMLC) Recommendations for Medicine Management (2016 – 2018)

The evidence for the use of aspirin in women at risk for early-onset pre-eclampsia is regarded as strong[50] and well documented.

Level of Evidence: Systematic Reviews, Randomised Control Trials & Guidelines

From a safety perspective the literature shows [50] low-dose aspirin has been widely regarded as safe in pregnancy, although there are small increases in bleeding risk; mostly intrapartum and postpartum bleeding and a small (0.06%) increase in neonatal intracranial bleeds. Most of these risks can be mitigated by discontinuing aspirin by 36 weeks, based on the lack of effectiveness for prevention of term pre-eclampsia.

Aspirin is widely available, inexpensive and has a favourable fetal and maternal safety profile and research shows that aspirin prophylaxis for women at risk of hypertensive related diseases of pregnancy particularly in low- and middle-income countries results in reduction in the risk of early onset preeclampsia.[50]

The Committee therefore recommended to alter the prescribing level of aspirin, 150mg, oral for reduction in the risk of early onset pre-eclampsia in pregnancy to PHC level for nurse initiation, in alignment with NDOH maternity and hypertension in pregnancy guidelines.

In line with local National Maternity Care Guideline[51] and the International Society for the Study of Hypertension in Pregnancy[52] the aspirin dosing is recommended at bedtime to prevent gastric irritation and initiated from 6 weeks of gestation (but preferably before 16 weeks) until 36 weeks. Additional guidance regarding taking aspirin preferably not an empty stomach was also added.

PHC/Adult ERC Recommendation: 2 May 2024
The PHC /AHL ERC supports the use of aspirin 150mg oral, until 36 weeks of pregnancy, for prevention of pre-eclampsia for all levels of care.

NEMLC Recommendation: 16 May 2024

NEMLC accepted the proposal as recommended by the PHC/Adult ERC (see above)

The description section of the STG was updated as follows:

DESCRIPTION
Supplements before and during pregnancy and lactation can help to prevent, or lessen the effect of, a number of conditions or complications associated with pregnancy. Specifically:
»Folic acid, given for at least one month before conception and during pregnancy (particularly the first 12 weeks) can help to prevent neural tube defects (abnormal development of spinal cord/brain).
» Iron can help to prevent anaemia.
» Calcium can help to prevent pre-eclampsia.
» Low dose aspirin can reduce the risk for early onset pre-eclampsia in women at risk.

Calcium, oral: *retained with an amendment showing only the elemental calcium requirement i.e. not the calcium carbonate salt dose*

[50] Ngene NC, Moodley J. Preventing maternal morbidity and mortality from preeclampsia and eclampsia particularly in low- and middle-income countries. Best Pract Res Clin Obstet Gynaecol. 2024 Feb 15;94:102473. doi: 10.1016/j.bpobgyn.2024.102473. Epub ahead of print. PMID: 38513504.
[51] NDOH. National Maternity Care Guidelines. Updated 2024.
[52] International Society for the Study of Hypertension in Pregnancy. Available at: https://isshp.org/guidelines/.

A provincial query was received by NDOH requesting clarity on the STG dose for calcium which was regarded as ambiguous as it contained both the calcium carbonate salt dose & elemental calcium dose. It was also raised that the that calcium doses are not standardized in the PHC (Obstetrics & Gynecology) AHL (Obstetrics) & AHL (Nephrology) chapters. Going forward, NEMLC has recommended that the STG recommendation should only contain the elemental calcium requirement as this is the actual calcium content contained in the tablet (i.e. the calcium carbonate salt dose, should not be included in the STG). Additionally, the recommended elemental calcium dose is now in line with how the peadiatric Hospital STG is currently phrased.

The medicine section for the prevention of pre-eclampsia of the STG was updated as follows:

Prevention of pre-eclampsia:
From confirmation of pregnancy (all women):

- Calcium, elemental, oral, 1 g daily ~~(given as calcium carbonate), 12 hourly~~.
  - Although the benefit is greatest in high-risk women, consider use of this agent in all pregnant women. ~~See Section 6.4.2.4: Pre-eclampsia.~~
  - Calcium reduces iron absorption from the gastro-intestinal tract. Take supplements 4 hours apart from each other.

From confirmation of pregnancy (all women with risk factors. including: pre-eclampsia in a previous pregnancy, chronic hypertension, diabetes, antiphospholipid syndrome, or systemic lupus erythematosus (SLE)):

- Aspirin, oral, 150 mg, taken at bedtime, preferably not on an empty stomach, until 36 weeks
  - Start at 6 weeks of gestation but preferably before 16 weeks
  - Stop at 36 weeks to reduce risk of bleeding during labour
  - Administration at bedtime reduces the risk of gastric irritation
- Refer to the next level of care as appropriate for the condition (see below). Women with a prior history of pre-eclampsia, but otherwise well, can be referred for the next available appointment, preferably around 20 weeks.

Editorially, the prevention of pre-eclampsia guidance was removed from section 6.4.2.2 pre-eclampsia, as it was updated under prevention of pre-eclampsia in section 6.4.1 antenatal supplements. A cross reference was added in section 6.4.2.2 pre-eclampsia to the updated prevention of pre-eclampsia guidance in section 6.4.1 antenatal supplements.

6.7.1 POSTPARTUM HAEMORRHAGE (PPH)

Tranexamic acid, parenteral: *Added*

Previously reviewed by NEMLC and not approved for inclusion on the PHC EML.

NEMLC report for the 2017-2019 review of the Adult Hospital Level STGs and EML, 2019 edition:
TXA, IV at primary level of care:
The National Committee of Confidential Enquires into Maternal Deaths (NCCEMD) requested that consideration be made to access TXA injection at primary level of care for PPH cases not responding to oxytocin and ergometrine. Currently, TXA IV is only included in the Adult Hospital Level EML.
WOMAN trial: E-mail communication from the investigators verified that risk factors for PPH were not collected and that the trial was done in the emergency situation.[53]

Rationale provided for inclusion of TXA, IV on the PHC EML:
Savings Mother report (2011-2013)[54] *reported that 15.9% (684) PPH cases caused maternal deaths; of which 2% occurred at primary level of care; whilst 36.7% occurred at secondary level facilities. The PHC STG recommends that where blood loss is greater than 500 mL, oxytocin/ergometrine to be administered with referral to secondary level of care.*
CRASH-2 study: Both the CRASH-2[55] *and the WOMAN studies showed a mortality benefit if TXA IV was administered within 3 hours of trauma or PPH. The WOMAN trial showed no additional statistical significant benefit or harm if TXA, IV was administered to women with PPH due to uterine atony beyond 3 hours.*

[53] E-mail communication from WOMAN trial investigator, 28 November 2017, on file.
[54] National Department of Health: National Committee for the Confidential Enquiries into Maternal Deaths Saving Mothers Report, 2011-2013.
[55] CRASH-2 Collaborators. Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in trauma patients with significant haemorrhage (CRASH-2): a randomised placebo-controlled trial. Lancet 2010; 376: 23-32. https://www.ncbi.nlm.nih.gov/pubmed/20554319

Pragmatic implications: From a pragmatic perspective, early access to TXA IV at primary level of care may be beneficial due to the quick onset and severity of PPH and early administration of TXA, once it is clear that there has been no response to initial oxytocin/ergometrine treatment. Access to TXA at midwife obstetric units (MOUs) may reduce referrals for PPH up to a higher level of care. Furthermore, there may be considerable delay in transferring women with PPH from an MOU to a higher level of care, either due to the long distance to the nearest hospital, or the from delay awaiting arrival of emergency medical services (EMS) at the MOU. This would necessitate additional training regarding intrapartum and emergency obstetric care for primary level healthcare workers.

NEMLC RECOMMENDATION:

The NEMLC did not accept the proposal to include TXA IV on the primary health care EML. (However, inclusion on the Adult Hospital Level EML was acceptable).

Rationale:

- "The **composite primary endpoint of death** from all causes or hysterectomy was not reduced with tranexamic acid (534 [5·3%] deaths or hysterectomies in the tranexamic acid group vs 546 [5·5%]in the placebo group, RR 0·97, 95% CI 0·87-1·09; p=0·65)"; **statistically not significant.** Death due to bleeding where tranexamic acid was administered within 3 hours of birth was a secondary endpoint. The effect size was small: ARR of 0.5% with NNT of 200 (1.2% in the tranexamic acid group vs 1.7% in the placebo group).
- Generalisability of the results of the WOMANS Trial to the local primary health care setting was not possible, as the trial was done in an emergency hospital setting.
- Referral to higher level of care for appropriate management from primary level may be delayed.

Level of Evidence: I RCT

Review indicator: Evidence of efficacy and safety in primary care setting**.**

In 2023, a motivation to include TXA, IV at PHC level was received arguing that it is reasonable to extrapolate the WOMAN trial findings to the PHC level and that the total price of the TXA, IV in the original review was incorrectly calculated.

At the NEMLC meeting, 30th March 2023, NEMLC recommended[56] that:

- Previous deliberations be revisited in response to the motivation received.
- PHC/Adult Hospital Level ERC review updated data (specifically safety and efficacy on use of TXA IV outside of hospitals i.e., extrapolatable for PHC use).

The E-MOTIVE (WHO) trial[57] published in May 2023 provides the updated evidence for the use of TXA, IV which can be extrapolated to PHC level. The E-MOTIVE trial was the Early detection of Postpartum Haemorrhage and treatment using the WHO MOTIVE 'first response' bundle: a parallel cluster-randomized trial that included a baseline control phase, along with mixed-methods evaluation in 210 132 low risk women undergoing vaginal delivery.

- E MOTIVE was performed mainly at Level one/district hospitals in South Africa (more than 18 000 women), Nigeria, Kenya and Tanzania (78 hospitals) and the Intervention included **E**arly detection with a calibrated blood collection drape. When 500mls was noted in the drape and/or clinical assessment of PPH, a bundle of care was immediately given with all components as close together as possible: Uterine **M**assage, **IV** fluids, **O**xytocin and **T**ranexamic acid and examination of the genital; tract with **E**scalation of care when needed. The control hospitals used an uncalibrated drape and usual care.
- Midwives were authorized to diagnose and treat PPH (including IV TXA) without the need for confirmation or authorization by a doctor. This would be similar to what would happen at a PHC level if TXA were available at PHC Level.
- A primary-outcome event (a composite of severe postpartum hemorrhage (blood loss, ≥1000 ml), laparotomy for bleeding, or maternal death from bleeding occurred in 794 of 48,678 patients (1.6%)

[56] National Department of Health. Minutes of the NEMLC Meeting. 30 March 2023.

[57] Gallos I, Devall A, Martin J, Middleton L, Beeson L, Galadanci H, et al. Randomized Trial of Early Detection and Treatment of Postpartum Hemorrhage. New England Journal of Medicine. 2023 May 9;0(0):null

in the intervention group and in 2139 of 50,044 (4.3%) in the usual-care group (risk ratio, 0.40; 95% confidence interval [CI], 0.32 to 0.50; P<0.001).

- This equates to a risk difference of 26 fewer per 1000 (2.6%), ranging from 55 to 40 fewer per 1000 for severe outcomes. This is based on the RR of 0.4 (95% CI from 0.32-0.5).
- For numbers needed to treat; you need to treat (apply the full bundle) to 37 cases of PPH to prevent one event of severe outcome (a composite of death, laparotomy, or severe blood loss). However, those 37 women will require treatment for PPH regardless.
- Compliance to the bundle was 92% in the E-MOTIVE group and 19% in the usual care group.
- The authors did not report on thrombotic events in the puerperium (not included in the trial design).

In summary, the WHO E-MOTIVE trial[57]has shown that a bundle of care that includes TXA given by midwives at district hospital level reduces PPH by 60%. The results of this study can be extrapolated to community health center/Midwifery Obstetrics Unit (MOU) level, as all the interventions in the trial were given by midwives without intervention from a doctor[57] and all women with a significant bleed will be urgently transferred to the next level of care, so further management will be under doctor or specialist care.

Cost and economic considerations:

Tranexamic Acid; 500mg/5ml; injection; 5 ml is R37,60.
Therefore, a 1-gram dose would cost R75,20 (2 x 500mg vials).

Additionally, an economic evaluation of the WOMAN trial in Nigeria and Pakistan concluded that early treatment of post-partum haemorrhage with tranexamic acid, IV, is cost-effective in Nigeria and Pakistan, and is likely to be cost-effective in countries in sub-Saharan Africa with similar incidence of PPH.[58]

Refer to the full evidence summary report below

Tranexamic_Acid_IV_
PHC_Summary_Final_

PHC/Adult ERC Recommendation: 8 June 2023
The PHC /AHL ERC supports the use of tranexamic acid (TXA) 1g IV (by slow injection or infusion in 200mls of N Saline over 10 minutes) for PPH for all levels of care.

NEMLC Recommendation: 20 July 2023
NEMLC supports the use of tranexamic acid (TXA) 1g IV (by slow injection or infusion in 200mls of N Saline over 10 minutes) for PPH for all levels of care, which may be initiated by a nurse, but only with prior approval of a medical practitioner.

Randomised Controlled Trial: GRADE IIIb

The STG was amended as follows:

[58] Li B, Miners A, Shakur H, Roberts I; WOMAN Trial Collaborators. Tranexamic acid for treatment of women with post-partum haemorrhage in Nigeria and Pakistan: a cost-effectiveness analysis of data from the WOMAN trial. Lancet Glob Health. 2018 Feb;6(2):e222-e228. doi: 10.1016/S2214-109X(17)30467-9. PMID: 29389542; PMCID: PMC5785366

MEDICINE TREATMENT

Replace fluids:
Sodium chloride 0.9%, IV, infused as fast as possible in one IV line.
AND
Oxytocin, IV 20 units in 1 000 mL sodium chloride 0.9% infused at 250 mL/hour in 2nd IV line.
AND
Tranexamic acid, IV, 1g in 200 mL sodium chloride 0.9% over 10 minutes, or 1g by slow IV injection,
which may be initiated by a nurse, but only with prior approval of a medical practitioner.

2026 Updates

Dexamethasone, parenteral: *Added*

The AHL Chapter 6 Obstetrics currently recommends betamethasone IM, 12 mg, 2 doses 24 hours for Preterm Labour (PTL) and Preterm Prelabour Rupture Of Membranes (PPROM) and recommends Dexamethasone IM as an alternative if Betamethasone Inj. is not available. Due to stock challenges experienced with betamethasone injection , dexamethasone injection has thus been added as an alternative in line with AHL Ch 6: Obstetrics. The STG has been amended as follows:

To improve fetal lung maturity at 26–34 weeks:
Z29.2
Betamethasone, IM, 12 mg, 2 doses 24 hours apart. — *LoE:Ia*[i]
If betamethasone is not available:

- Dexamethasone, IM, 8 mg, 3 doses 8 hours apart. — *LoE:Ia*[ii]

Note: Corticosteroids are maximally effective about 24 hours after administration of the first dose. Therefore, give as soon as possible following diagnosis of PTL or PPROM.

[i] Betamethasone, IM: McGoldrick E, Stewart F, Parker R, Dalziel SR. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. Cochrane Database Syst Rev. 2020 Dec 25;12(12):CD004454. https://pubmed.ncbi.nlm.nih.gov/33368142/

Betamethasone, IM: FIGO Working Group on Good Clinical Practice in Maternal-Fetal Medicine. Good clinical practice advice: Antenatal corticosteroids for fetal lung maturation. Int J Gynaecol Obstet. 2019 Mar;144(3):352-355. https://pubmed.ncbi.nlm.nih.gov/30710360/

[ii] Dexamethasone, IM: McGoldrick E, Stewart F, Parker R, Dalziel SR. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. Cochrane Database Syst Rev. 2020 Dec 25;12(12):CD004454. https://pubmed.ncbi.nlm.nih.gov/33368142/

Dexamethasone, IM: FIGO Working Group on Good Clinical Practice in Maternal-Fetal Medicine. Good clinical practice advice: Antenatal corticosteroids for fetal lung maturation. Int J Gynaecol Obstet. 2019 Mar;144(3):352-355. https://pubmed.ncbi.nlm.nih.gov/30710360/