



Management of Woman at high risk for Recurrent Second Trimester Miscarriage or Preterm Birth in Singleton Pregnancies

A guide to cervical length screening, cervical cerclage and vaginal progesterone

General comments:

- This guideline seeks to clarify the indications for cerclage and progesterone, within the context of counselling and shared decision making, after appropriate evaluation of specific high-risk cases at Tygerberg Hospital, namely:
 - women with ≥ 2 mid-trimester losses, irrespective of cervical length in the current pregnancy;
 - women with 1 mid-trimester loss and a short cervix (≤ 25 mm, measured between 16w0d and 24w0d) in the current pregnancy
 - women with ≥ 1 previous preterm births before 34 weeks' gestation and a short cervix (as above) in the current pregnancy.
- Ensure all other risk factors for preterm labour are addressed as well (do Urine MCS, treat symptomatic vaginal infections, inspect the cervix by speculum to rule out lateral tears, address smoking, check for IUGR etc.).
- Underlying medical conditions, such as poorly controlled diabetes, hypertension, thyroid disease and thrombophilia might have caused the adverse obstetric outcomes (rather than cervical insufficiency).
- In most cases, patients with the above-mentioned problems do not present with the classic combination of painful contractions and cervical changes. In the initial stage there is relatively asymptomatic "ripening" or activation of the cervix leading to effacement (shortening) and dilatation, with symptomatic contractions being a late sign. This emphasises the importance of appropriate measurement of the cervix in high-risk cases.
- However, all patients with any of the risk factors below should be counselled about the signs and symptoms of threatened preterm labour and encouraged to present ASAP if they occur. Patients should also be advised about abstinence. ["In populations at increased risk for preterm labour, there is no evidence to suggest a clear benefit from restricted sexual activity; however, this is a simple intervention that causes no harm and may be a reasonable recommendation until better evidence emerges"].

Cerclage or progesterone?

There are three broad categories of indications for transvaginal cerclage.

- History-indicated (prophylactic) cerclage.

This is typically performed at 12-14 weeks' gestation, for women with two or three previous second trimester losses, with a typical history (see below) of cervical incompetence/insufficiency,

regardless of the cervical length. Limited evidence suggests that the benefit is greatest for those with three preterm deliveries. Progesterone may also be considered.

- Ultrasound-indicated cerclage.

There is general consensus that progesterone or cerclage be considered in women with a history of spontaneous loss or preterm delivery (<34 weeks' gestation) and a short cervix (≤ 25 mm, measured between 16w0d and 24w0d). The cerclage is performed when indicated, but not beyond 23w6d. A short cervix without the relevant history does not automatically meet the criterion.

- Rescue (Emergency / clinically-indicated) cerclage.

In such cases there is also dilation of the vaginal cervix (<4 cm, membranes not prolapsed beyond the external os) without contractions, again before 24w. Rescue cerclage has been demonstrated to have benefit, but cases must be selected carefully. Progesterone is not effective with advanced effacement.

Progesterone may be offered for the first two categories above, starting at 16-24w until 34w0d.

The following high-risk women should undergo cervical screening and be offered a choice of cerclage (performed up to 23w6d) and/or progesterone, as appropriate, if cervical length is ≤ 25 mm:

- A history of 2nd trimester miscarriage (between 16 and 26 weeks) suggestive of cervical incompetence: Painless dilatation with a quick labour, and birth of a live baby or fresh stillbirth, after excluding other causes of mid-trimester losses, e.g. intra-uterine death that required induction, abruptio placentae, fetal abnormalities, polyhydramnios, and medical terminations. Take note of specific indications for history-indicated cerclage above.
- Previous history of spontaneous preterm birth of a live baby from 27w0d to 34w0d (exclude non-spontaneous causes e.g. iatrogenic delivery for pre-eclampsia, syphilis, intra-uterine death etc.).
- Women with a previous LLETZ or Cone biopsy, or previous cervical trauma/tears or known congenital uterine abnormality. Consider cerclage and/or progesterone.
- No need to workup previous late preterm deliveries (34-37 weeks).

Do not screen women at low-risk of preterm labour routinely, as it is not cost-effective.

Practical guide for cervical screening at HRC:

- Cervical length must be measured by a skilled operator using transvaginal ultrasound (see technique - Appendix A).
- Cervical measurement by ultrasound can be done every second week between 16 and 26 weeks (repeat in 1 week if significant shortening or borderline length not yet meeting criteria for intervention).
- The lengths should be recorded on the gravidogram so that shortening over the gestation can be appreciated.
- A cervical length of ≤ 25 mm indicates a higher risk for recurrent late miscarriage/preterm labour.

- Cervical length monitoring in high risk but asymptomatic women (with no signs of preterm labour) should DISCONTINUE after 26 weeks as there are no preventative strategies to treat a short cervix after this gestation (progesterone have been proven to be ineffective when initiated after this time).
- However, knowledge of a very short or dilated cervix (cervical ripening) in certain high risk women after 26 weeks may help with empiric management (altering activity level, work and travel, increased surveillance, relocation close to Tygerberg, and 'cooling down' of the cervix with antibiotics, anti-inflammatories and corticosteroids). Individualise care for women with specific risks (e.g. rural/farm workers, advanced age, very poor obstetric history etc.). Discuss with a consultant to continue cervical surveillance after 26 weeks.
- The only effective therapeutic interventions after 26 weeks are tocolytics and corticosteroids to advance fetal lung maturity in a patient with established preterm labour.
 - If the cervical length is still >25mm at the 26 weeks visit, and there are no symptoms of preterm labour, consider stepping down for routine care to a district hospital. The patient must be well educated on the signs and symptoms of preterm labour and return immediately if preterm labour is suspected. Discuss which labour ward to go to depending on the gestation at which the symptoms occur (e.g. before 33 weeks: come to TBH, 33 and 34 weeks can deliver at district hospital, 35 or more can deliver at MOU).
 - If a cervical cerclage was inserted, it is not necessary to perform serial ultrasound evaluation of the cervix.
 - If progesterone is being administered for a short cervix, continue with care at Tygerberg HRC every two weeks, until 34 weeks, after which progesterone can be stopped and care stepped down to MOU/BANC. It is generally not necessary to continue with cervical surveillance after 26 weeks, but see note above about individualisation.

TREATMENT FOR SHORT CERVIX (≤ 25 mm) IN HIGH RISK WOMEN

There is no evidence comparing progesterone and cerclage therefore the choice of cerclage or progesterone should be determined after discussion with the woman [NICE] and by the timing of the previous loss, with cerclage less effective in preventing third trimester deliveries. Women can be counselled that 17-20 cerclage procedures may prevent one preterm delivery (numbers needed to treat NNT 17 to 20) and that progesterone is successful in 1 out of every 8 cases (NNT 6 to 8), to assist them in making an informed decision (data from Cochrane review).

→ Placement and management of cerclage: see Appendix B.

→ Progesterone dose: 200 mg micronised progesterone vaginally at night, until 34 weeks.

- A. Consider history-indicated cervical cerclage (MacDonald suture) or progesterone
 - Typical history of ≥ 2 second trimester losses, even in absence of short cervix.
- B. Consider prophylactic vaginal progesterone **or** cervical cerclage (MacDonald suture) for women with:

- History of spontaneous preterm birth or PPRM (27-34 weeks) or a mid-trimester loss (16-26 weeks),
AND
- Cervical length \leq 25 mm confirmed on ultrasound (16w0d-23w6d).

C. Rescue cerclage:

- If the cervix is already open (< 4cm) and the membranes not prolapsed or ruptured, consider a rescue cervical cerclage (between 16-23w6d).
- Do not insert a rescue cerclage if there are contractions, active vaginal bleeding, prolapsed membranes, dilatation > 4cm, no workable cervix or signs of infection.
- In women already on progesterone present with continued shortening of the cervix and exposure of the membranes, consider a rescue cerclage as well (consultant decision).

Consideration of a trans-abdominal cerclage (TAC)

Women with a previous failed (the pregnancy was lost before viability) transvaginal cervical cerclage must be discussed with the MFM/Obstetric Special Care team, prior to pregnancy, or before 14w0d gestation (if already pregnant) for a possible TAC.

Criteria for consideration of transabdominal cerclage

- Previous failed, appropriately inserted transvaginal cerclage
- Significant damage to the cervix
- Insufficient vaginal portion of the cervix

AUTHORISED BY	S Gebhardt
COMPILED BY	S Gebhardt, Z Momberg
COMMITTEE RESPONSIBLE	S Gebhardt, L Geerts, D Hall, E Swart, L Muller
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Signed: GS Gebhardt

Head: General Specialist Services; Obstetrics and Gynaecology

Appendix A

Technique for cervical assessment:

How:

This should be performed according to ISUOG/FMF guidelines:

Empty bladder (full bladder can falsely elongate the cervix).

Lithotomy position.

Transvaginal probe (transabdominal assessment is inaccurate).

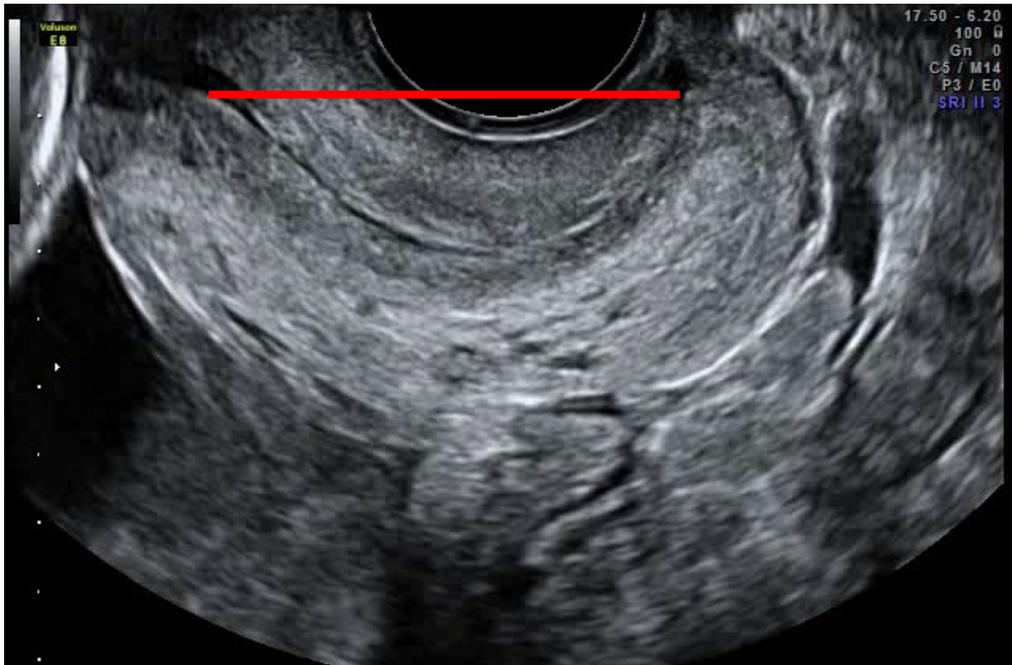
Avoid excessive pressure of the probe on the cervix.

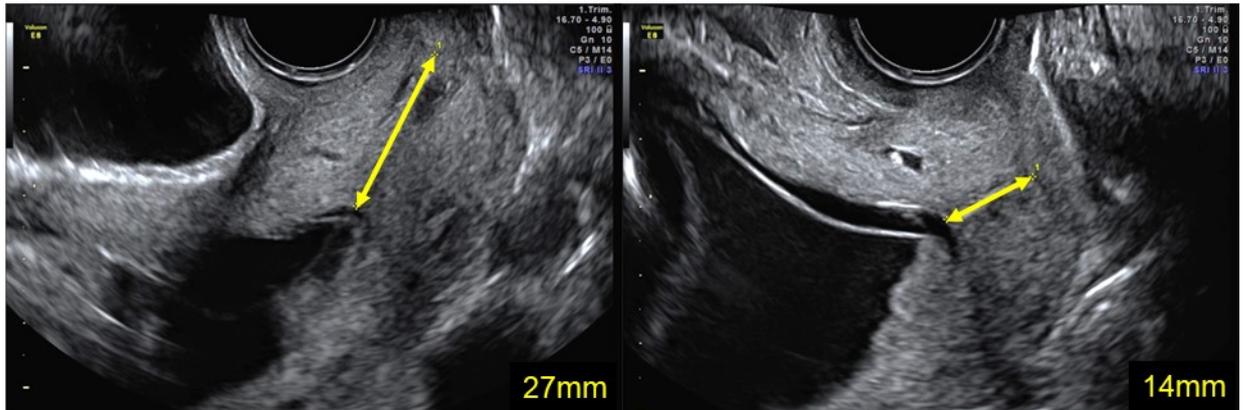
Cervix should be measured along its longitudinal axis. Cervix should be close to horizontal on the screen and occupy 50-75% of the image.

The cervical mucosa should be identified to help distinguish the upper cervix from the isthmus of the uterus. The cervix should be measured between the internal and external ora, using a straight caliper, even if the cervical canal appears curved (as in image below). The internal os is located where the cervical mucosa ends.

The examination should last 3-5 minutes as the cervix is dynamic and may shorten during the examination. Gentle fundal and then supra-pubic pressure should be applied to look for funneling.

Three measurements should be taken and the shortest used for counselling and decision making.

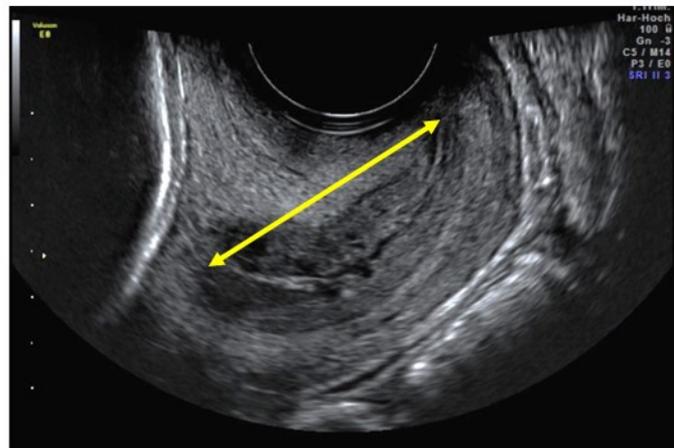




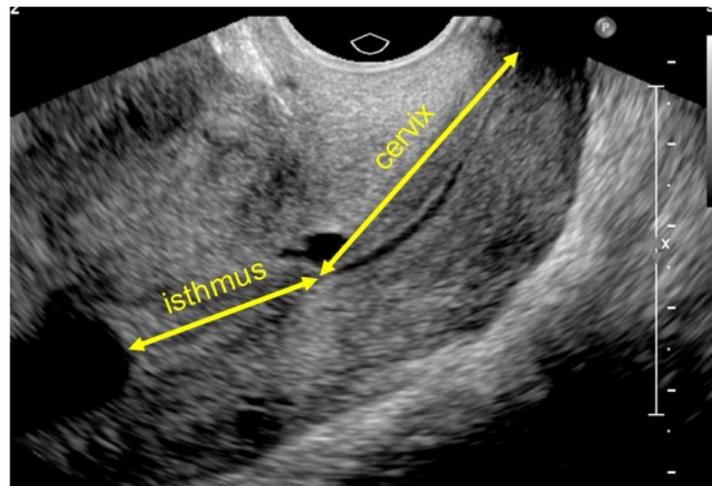
Full bladder

Empty bladder

A full bladder can artificially increase the cervical length. To *et al.* showed that mean difference between the cervical length measured with an empty and full bladder is about 4mm. In addition, a full bladder can obscure the presence of cervical funneling by compressing the two halves of the funnel together.



The cervical canal and the surrounding cervical mucosa need to be identified. In order to avoid inclusion of the isthmus into the cervical length measurement, care must be taken to identify the internal, as well as the cervical, os. The external cervical os is identified as the point where the anterior and posterior lips of the cervix come together. The identification of the internal cervical os can be more challenging. Identification of the cervical mucosa as a homogenous and hypoechoic structure, compared to the surrounding stroma, can be helpful in these cases, as the internal cervical os is located at the point where the cervical mucosa ends.

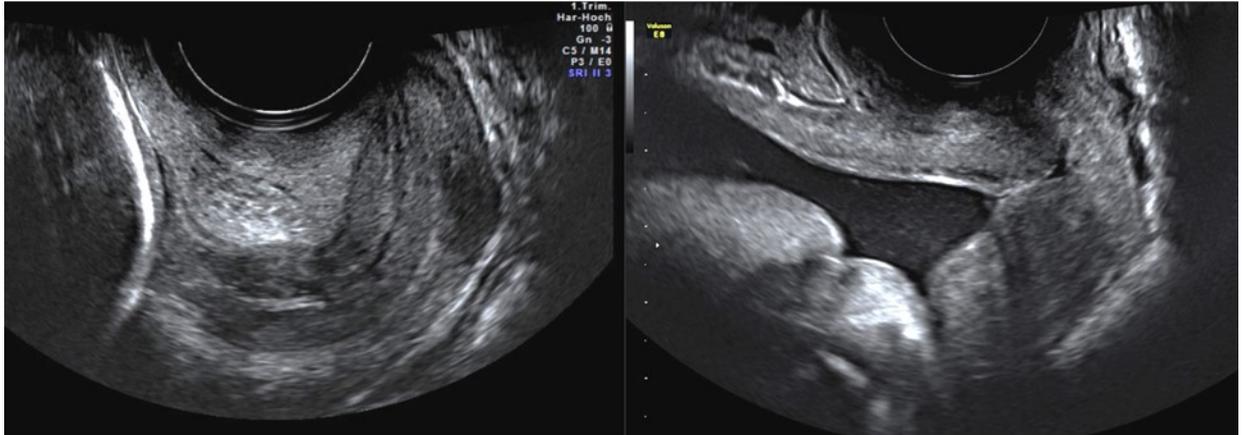


This is particularly important when measuring the cervical length in the first trimester.



Videoclip S2:
Ex_pressure.avi

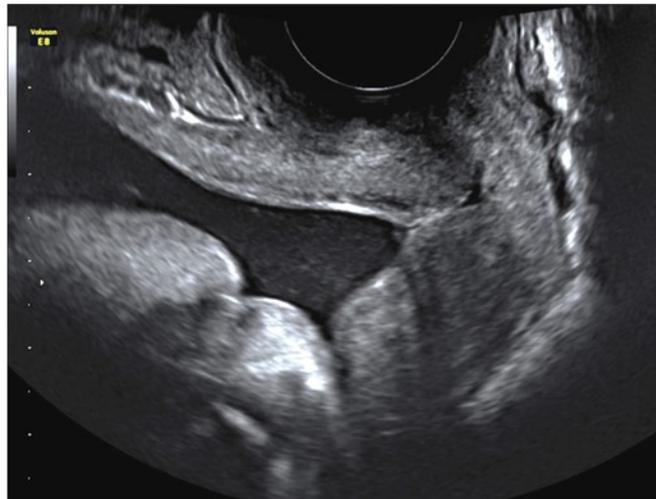
Excessive pressure on the cervix by the probe should be avoided, as the cervix artificially appears to be longer and the presence of a funnel will be obscured.



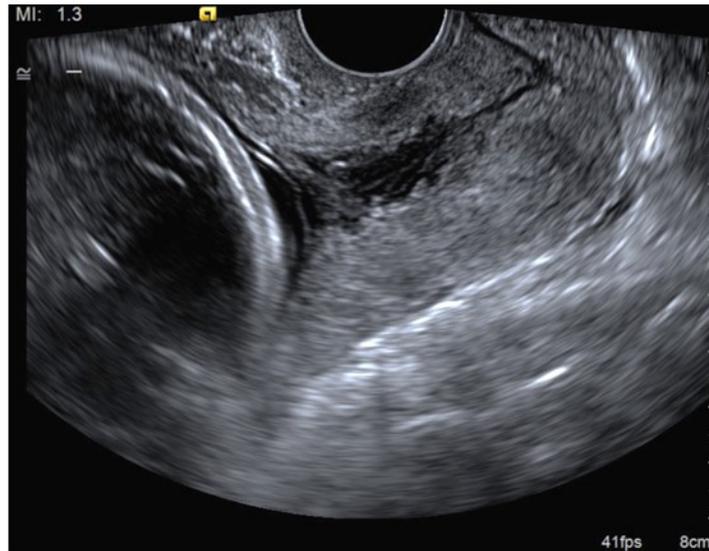
Long curved cervix

Short straight cervix

If the cervix exceeds 25mm, it will be curved in more than half of the cases. The standard method of measurement, using a straight line between the internal and the external *ora*, will underestimate the cervical length in these cases. However, this is of little clinical significance as these patients are at low risk regardless of the exact measurement. In the high-risk group of patients with a cervical length < 16mm, the cervix will always be a straight line.



Funneling, defined as protrusion of the amniotic membranes into the cervical canal, is considered by some as an additional risk factor of preterm delivery. Various criteria for the diagnosis of true funneling have been published. However, using a logistic regression analysis that includes both funneling and cervical length, funneling has been shown not to be an independent risk factor.



The cervical canal may have a thin layer of hypoechoic contents. This is especially true in the third trimester. In all likelihood, this represents accumulation of mucus. This finding needs to be differentiated from a thin cervical funnel. This is best done by delineating the course of the fetal membranes: if they are not prolapsing into the cervical canal and are located at the level of the internal cervical os, the presence of a true funnel is unlikely.

Appendix B

Cervical Cerclage

Contraindications for cervical cerclage:

- Absolute contraindications:
 - Active labour
 - Active vaginal bleeding
 - Rupture of membranes
 - Fetal compromise or death, lethal fetal anomalies
 - Suspected or clinically confirmed abruptio placenta
 - Suspected or clinically confirmed chorioamnionitis
- Relative contraindications include the following:
 - Prolapsed membranes or dilatation more than 4cm
 - Vaginal spotting
 - Immunosuppression (i.e. complicated DM, HIV etc.)
 - Multifetal gestations

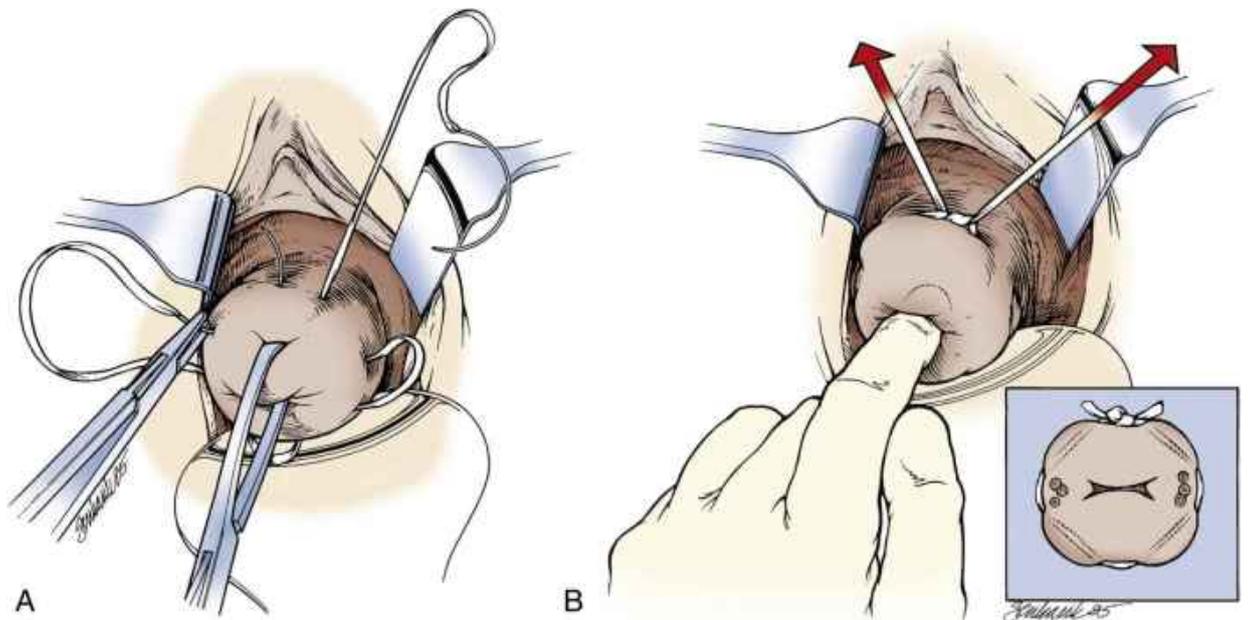
* If there is a valid indication for cerclage in the presence of a relative contraindication, a work up as stipulated below should be done and the case discussed with the consultant in the antenatal clinic or ward.

Clinical examination:

- Detailed obstetric and cervical evaluation
 - Vaginal speculum to visually inspect the cervix for previous scarring, deformity and length to ascertain the feasibility of placing a transvaginal cerclage.
 - A wet mount smear must be performed on all patients to exclude bacterial vaginosis (if present metronidazole 400 mg orally twice a day for 7 days or clindamycin 300 mg orally twice daily for 7 days), trichomonas vaginalis (if present single dose metronidazole 2g orally) or chronic cervicitis (individualize management on suspected underlying cause).
 - Urinary dipstix specifically to evaluate for the presence of proteinuria, glycosuria and haematuria.
- Special investigations:
 - Ensure that routine antenatal screening investigation results are noted on the card and managed appropriately (syphilis, HIV, Rhesus). If HIV positive the timing and results of the last CD4 and viral load and type and duration of current treatment should be documented in the maternity case record.
 - A midstream urine specimen for urine culture and ideally treat ASB prior to cerclage insertion.

- Ultrasound to confirm a single intrauterine viable pregnancy and to exclude any major anomalies – a formal anomaly scan can be arranged at a GA dependant on the indication and urgency of the cerclage. In all surgical cases, fetal life should be documented before and after the procedure.
- Counselling: Patients should be thoroughly counselled regarding the following risk groups:
 - Disease-related risks: premature rupture of membranes; pregnancy loss; infection (chorioamnionitis); preterm labour requiring hospitalization; extreme prematurity.
 - Immediate procedure-related risks: usual anaesthetic risks (minor with spinal anaesthesia which is preferable); minor vaginal bleeding; maternal soft tissue injury (rare); cervical trauma and injury during placement, rupture of membranes.
 - Ongoing procedure-related risks: cervical injury from the suture in case of uncontrollable preterm labour; chronic cervical irritation and inflammation with possible intra-amniotic infection, suture displacement/migration, increased incidence of caesarean section (soft tissue dystocia from scar tissue).
- Preoperative Management
 - Tocolytic drugs are not routinely given to women undergoing placement of a cerclage however indomethacin has been reported to improve outcome in the rescue cerclage where cervical activation has commenced.
 - Use of antibiotic prior to or after cerclage is controversial. The following conditions may warrant antibiotics prior to the cerclage placement:
 - Patients with evidence of chronic cervicitis (on speculum examination and wet mount).
 - Patients with copious and malodorous vaginal discharge.
 - Emergency cerclage with exposure of the membranes to the vaginal environment. Allow 48 hours of “cooling off” then re-evaluate cervix.
 - If antibiotics are indicated then complete treatment prior to cerclage placement, if possible.
- Placement of a transvaginal cervical cerclage
 - The following description is applicable to a McDonald's technique with a good vaginal portio (>1.5cm) and no old tears or trauma.
 - Anaesthesia: Regional anaesthesia is preferred.
 - Equipment needed:
 - 5mm Mercilene tape suture on 48mm ½ circle taper-cut or cutting needle

- Aseptic syringe for irrigation
 - Suction tubing with Yankauer suction tip
 - Wertheim vaginal retractors
 - Allis (soft tissue) forceps/clamps
 - Doyen retractors
 - Extra-long blade weighted speculum
 - Straight needle holders
- Positioning:
 - Patient in a dorsal lithotomy position. The surgeon must protect vulnerable neurologic, vascular, and bony points of the lower extremities and padding should be used at all potential pressure points. The buttocks should be positioned at the end of the table, with the table level. Hyperflexion of the hips should be avoided, as this can cause femoral neuropathy. Final positioning of the legs should be such to allow for assistants to be able to visualize the operative field.
 - The patient is then prepped and draped and the vagina should be gently cleansed with a water-based antiseptic solution.
- Procedure:
 - The bladder must be emptied with aseptic technique and the cervix is visualised by placing a long weighted speculum posteriorly, and curved or right angle retractors anteriorly and laterally as needed.
 - An Allis clamp is used to grasp the anterior and posterior lips of the cervix as high in the vagina as possible to mobilise the cervix in a gentle downward and lateral direction. The cervix can also be exposed and mobilized by Babcock forceps but care should be taken not to traumatise the tissue.
 - Ensure that only cervical stromal tissue is included in the suture and that the cervical canal is not entered.
 - The suture is placed above the Allis clamp, curving through the cervical stroma of the right lower quadrant. In order to place the suture as high as possible; the junction of the rugated vaginal epithelium and the smooth cervix just distal to the cervical reflection is used as a landmark (note that the suture is placed too low in the illustration below).



- This manoeuvre is then repeated in the right upper quadrant in the same fashion and the process is repeated with the second needle on the left and the knot is placed at 12 o'clock. Care should be taken to avoid the paracervical vessels (at 3 and 9 o'clock), the bladder and the rectum. Additional bites are sometimes necessary when the cervix is damaged/friable or anteriorly in order to ensure that the knot does not slip down.
 - The stitch is pulled tight enough to close the internal os, the knot being made anterior to the cervix and the end left long enough to facilitate subsequent removal.
 - The higher a cerclage is placed within a shortened cervix, the lower the subsequent odds of preterm birth.
- Post-Operative management
 - Despite a lack of evidence, excessive physical activity should be avoided. Routine abstinence for intercourse is unnecessary.
 - Paracetamol alone provides adequate analgesia for most women.
 - Cerclage can be done as a day procedure and the patient can be discharged after recovery from the anaesthetic and when ambulant to void.
 - ⊖ For emergency cerclage placement: admit for bed rest until next day.
 - After discharge women are followed up as outpatients on 2-weekly basis (from 24w onwards) with assessments of cervical length by vaginal examination. In the event of preterm labour after 26w prompt admission with administration of antenatal corticosteroids, magnesium sulphate and tocolysis is indicated (see departmental protocol on spontaneous preterm labour). Removal of the cerclage

upon suspected or confirmed preterm labour, or PPROM before 34w should be discussed with the consultant on duty.

- Patients should be informed that they should present immediately to their health care facility if they experience any of the following symptoms after cerclage insertion: contractions or cramping, lower abdominal or back pain that comes and goes like labour pain, any vaginal bleeding, fever or chills, nausea and vomiting, foul-smelling vaginal discharge, water breaking or leaking (rupture of membranes).

- Cerclage removal:
 - Elective cerclage removal is done at 36w gestation in the antenatal clinic during a routine visit.
 - Immediate removal if the women presents in advanced labour at any gestation.
 - Immediate removal upon onset of preterm labour or PPROM after 34 weeks.