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THE SHORT CERVIX AND PROGESTERONE

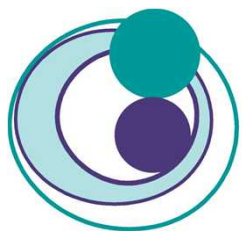
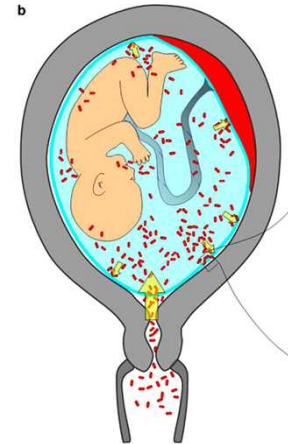
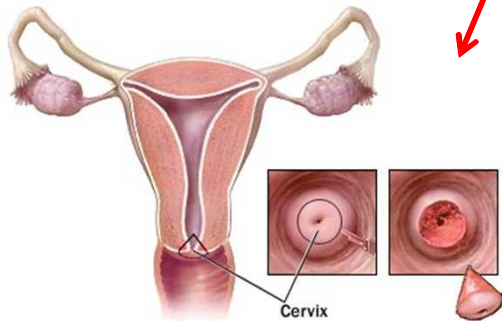
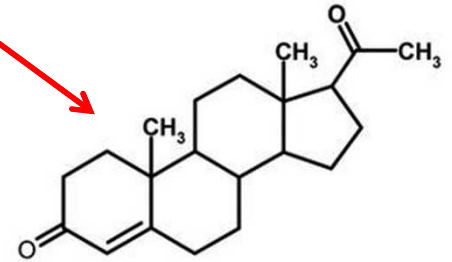
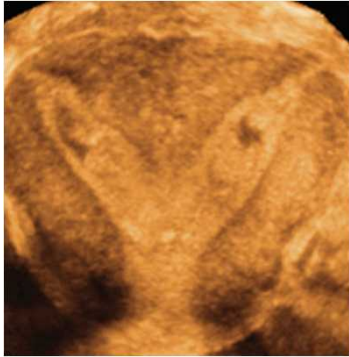
Overview

- Identifying the short cervix
- What does a short cervix mean?
 - Normal cervical length
 - Correlation with preterm delivery
- Management of a short cervix



Case

SHORT CERVIX



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Risk Factors

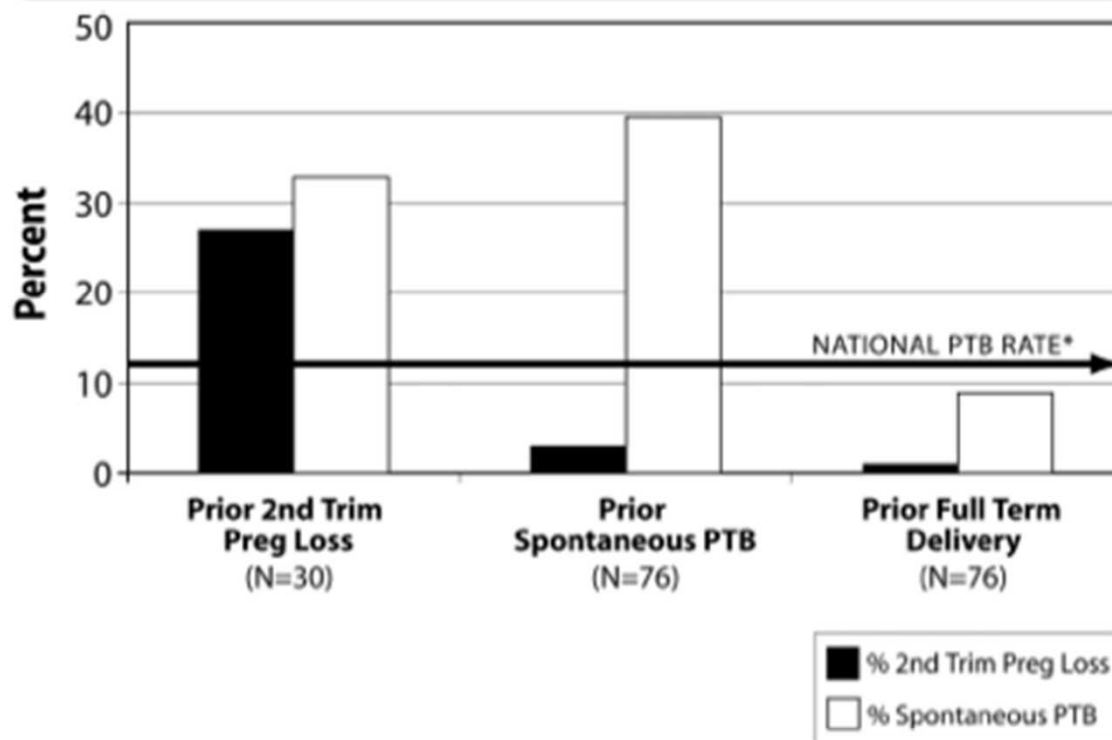
- Prior hx of PTB
- Maternal age <20, >35
- Low BMI <19.8 kg/m²
- Ethnicity: African-American

High Risk Groups

- Hx of spontaneous PTB in prior pregnancy
- Short Cx <25mm at <24 weeks current pregnancy
- Untreated
 - 15-20% recurrent PTB <28 weeks
 - 25-30% recurrent PTB <32 weeks
 - 50-60% recurrent PTB <37 weeks
 - *Iams et al AJOG 2010*
- Risks are higher:
 - The earlier the GA of PTB
 - The shorter the Cx length
 - Earlier in pregnancy the short Cx was diagnosed

FIGURE 1

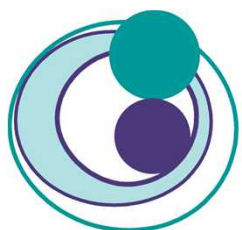
Pregnancy outcome after second trimester loss



Subsequent pregnancy outcome in women with prior second trimester loss, prior spontaneous preterm birth, and prior birth at term.

Reproduced, with permission, from Edlow et al.³²

Iams. Care for women with prior preterm birth. Am J Obstet Gynecol 2010.



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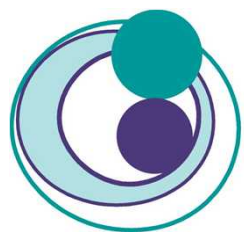
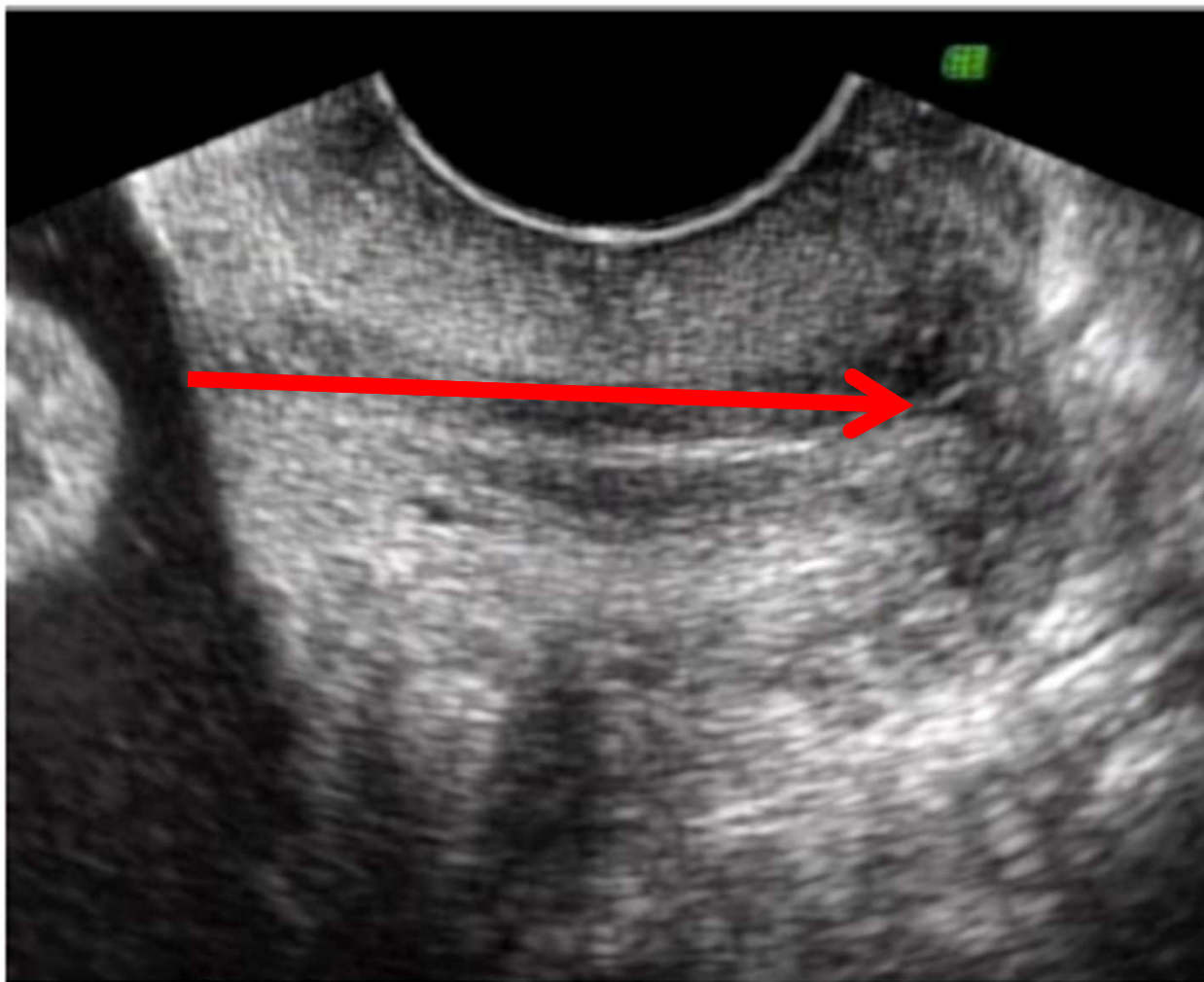
TVS Protocol

Mella MT and Berghella V. Prediction of Preterm Birth: Cervical Sonography. *Seminars in Perinatology*. 2009 33: 317-324

Table 1 Proper Technique of TVU Screening of The Cervix for Prediction of PTB (Figs. 1-3)

1. Have the woman empty her bladder just before ultrasound
2. Prepare the clean probe covered by a condom
3. Insert the probe (probe can be inserted by the woman for her comfort)
4. Guide the probe in the anterior fornix of the vagina
5. Obtain a sagittal long-axis view of the entire endocervical canal
6. Withdraw the probe until the image is blurred, and reapply just enough pressure to restore the image (to avoid excessive pressure on the cervix, which can elongate it)
7. Enlarge the image so that the cervix occupies at least 2/3 of the screen, and both external and internal os are seen
8. Measure the cervical length from the internal to the external os along the endocervical canal
9. Obtain at least three measurements, and record the shortest best measurement in millimeters
10. Apply transfundal pressure for 15 seconds, and record cervical length again at least 3 times, recording best measurement
11. Entire examination should last at least 5 minutes; record only the shortest best cervical length obtained for clinical management

Adapted from Berghella and Bega.³

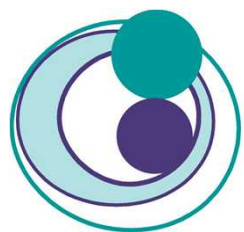
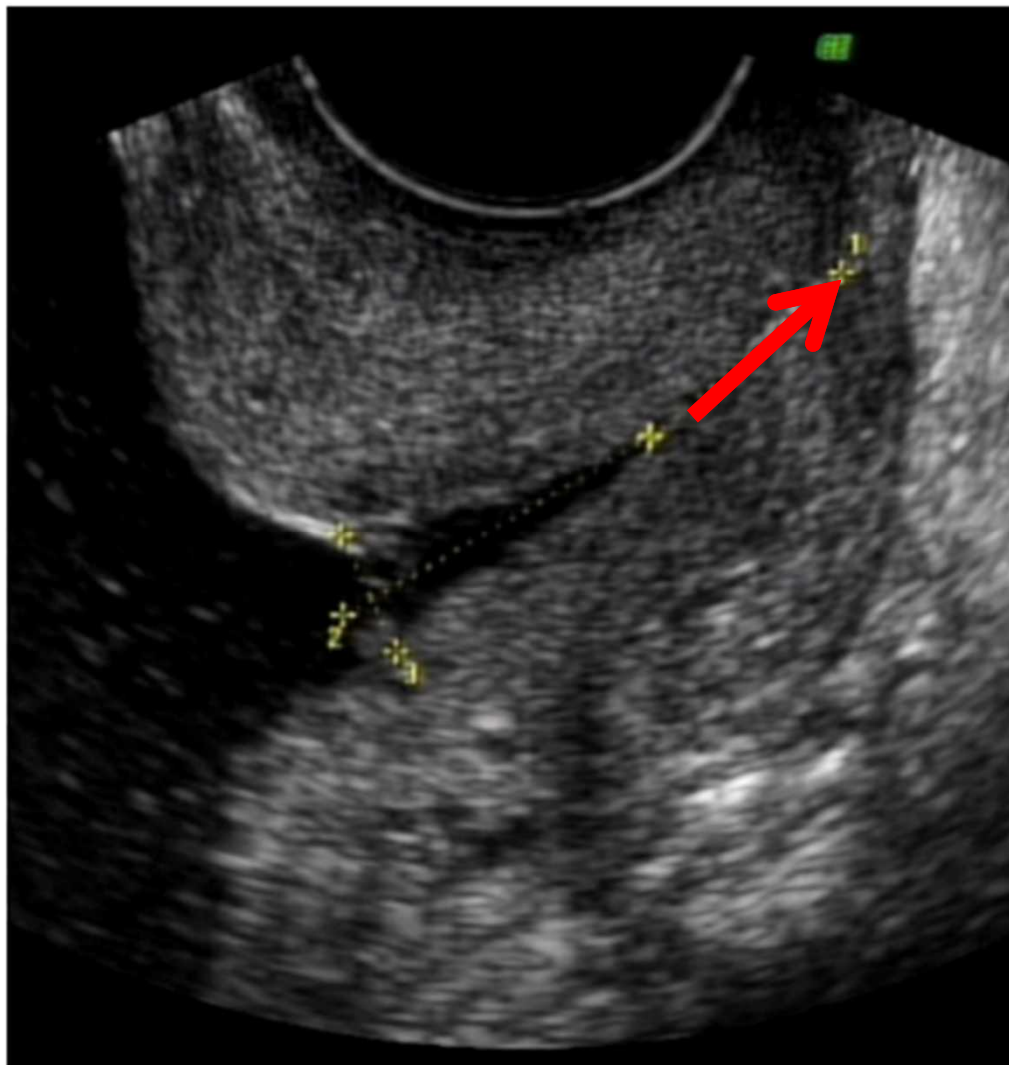


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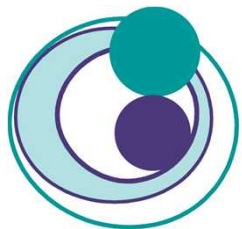
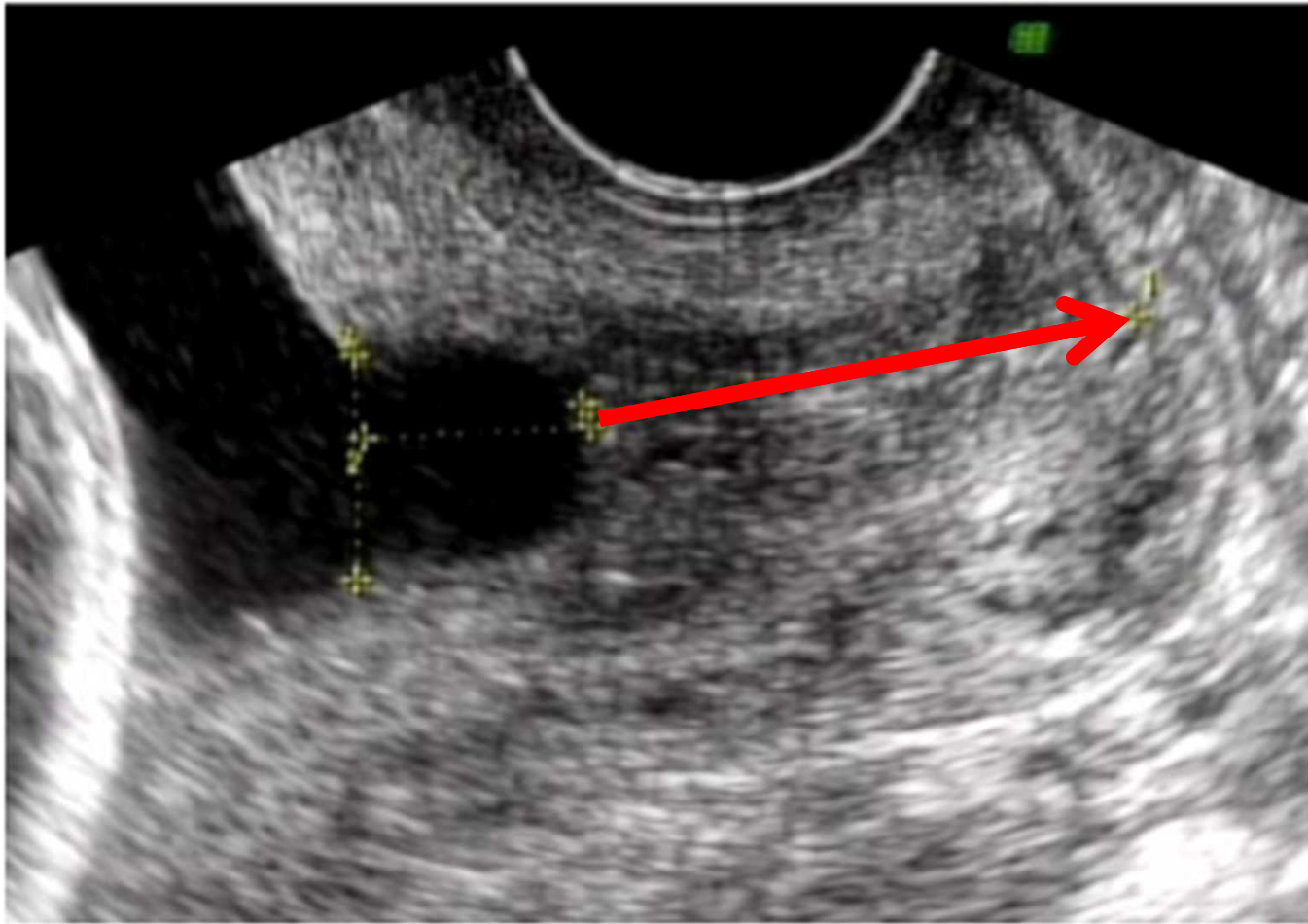


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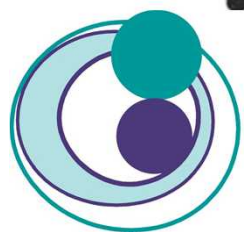
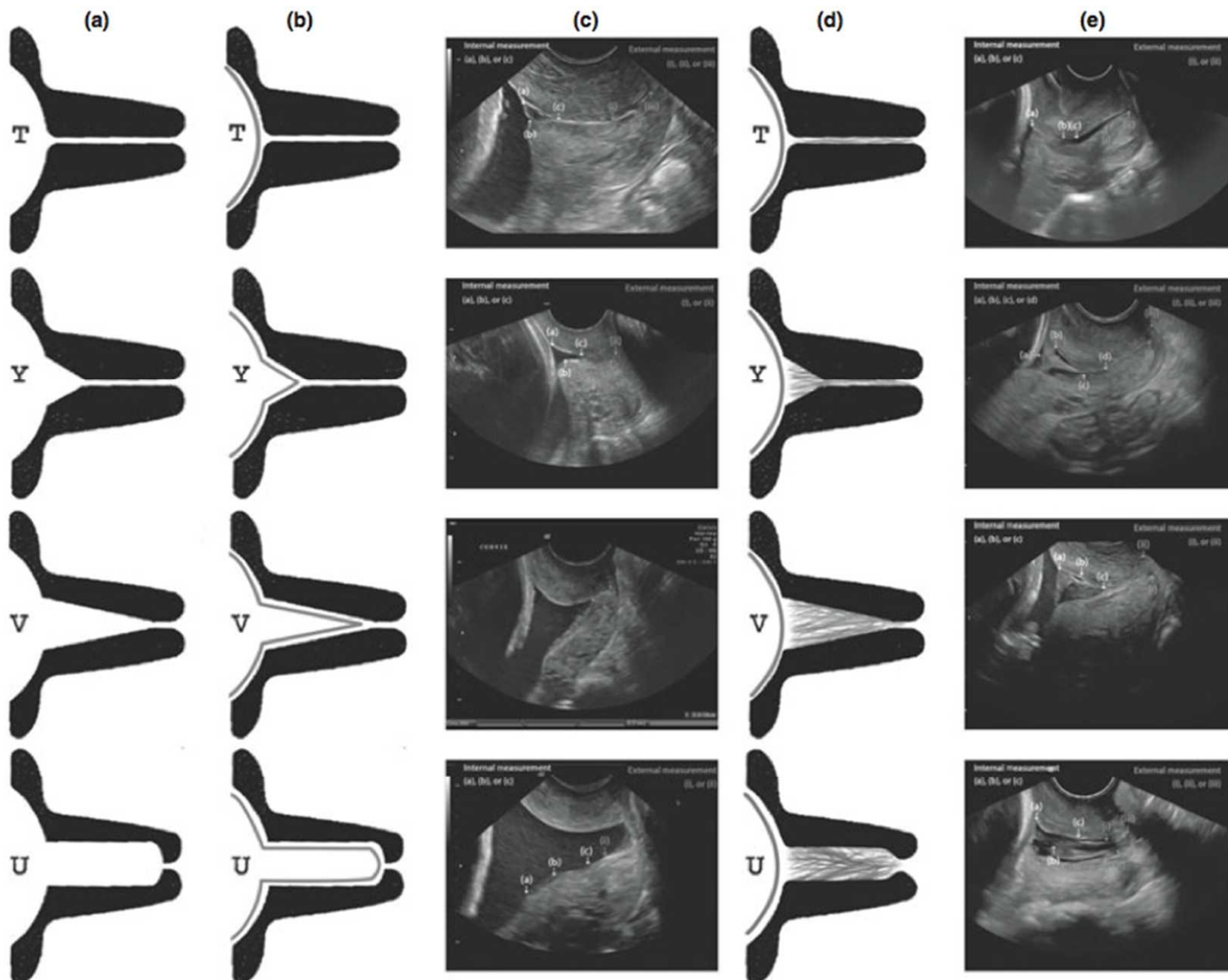


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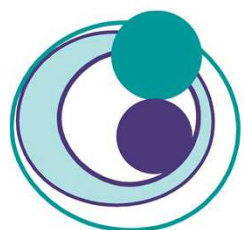
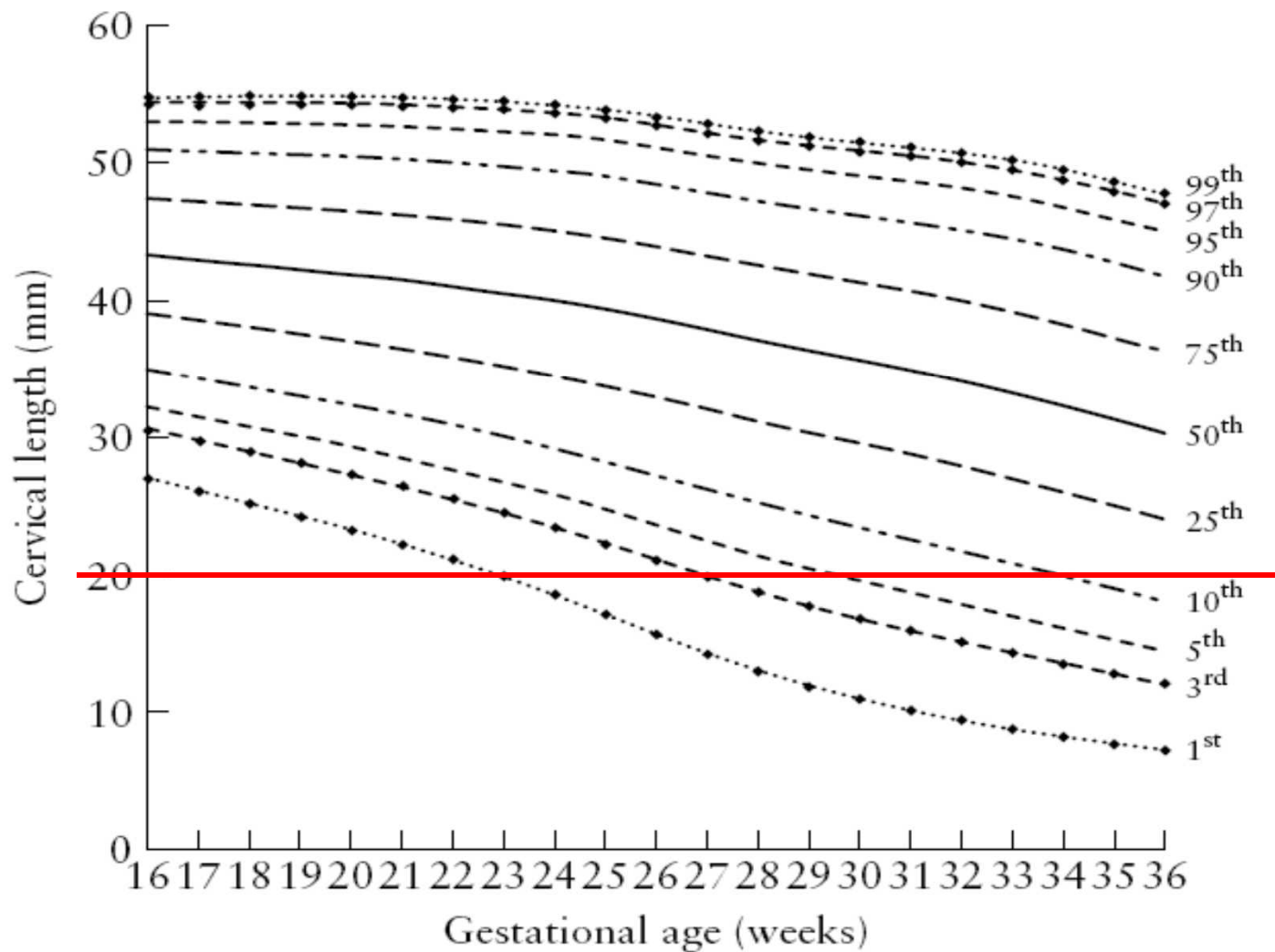


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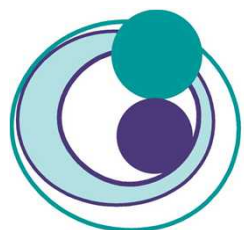
TABLE

Predicted probability of delivery before week 32 by cervical length (millimeters) and gestational age in weeks at time of measurement

| Cervical length, mm | Week of pregnancy | | | | | | | | | | | | | |
|---------------------|-------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 |
| 0 | 76.3 | 73.7 | 70.9 | 67.9 | 64.7 | 61.4 | 58.0 | 54.5 | 51.0 | 47.5 | 44.0 | 40.5 | 37.2 | 33.9 |
| 5 | 67.9 | 64.8 | 61.5 | 58.1 | 54.6 | 51.1 | 47.6 | 44.0 | 40.6 | 37.2 | 34.0 | 30.9 | 28.0 | 25.2 |
| 10 | 58.1 | 54.7 | 51.2 | 47.6 | 44.1 | 40.7 | 37.3 | 34.1 | 31.0 | 28.0 | 25.3 | 22.7 | 20.3 | 18.1 |
| 15 | 47.7 | 44.2 | 40.7 | 37.4 | 34.1 | 31.0 | 28.1 | 25.3 | 22.7 | 20.4 | 18.2 | 16.2 | 14.3 | 12.7 |
| 20 | 37.4 | 34.2 | 31.1 | 28.1 | 25.4 | 22.8 | 20.4 | 18.2 | 16.2 | 14.4 | 12.7 | 11.2 | 9.9 | 8.7 |
| 25 | 28.2 | 25.4 | 22.8 | 20.4 | 18.2 | 16.2 | 14.4 | 12.7 | 11.3 | 9.9 | 8.7 | 7.7 | 6.7 | 5.9 |
| 30 | 20.5 | 18.3 | 16.3 | 14.4 | 12.8 | 11.3 | 9.9 | 8.7 | 7.7 | 6.7 | 5.9 | 5.2 | 4.5 | 3.9 |
| 35 | 14.5 | 12.8 | 11.3 | 10.0 | 8.8 | 7.7 | 6.8 | 5.9 | 5.2 | 4.5 | 4.0 | 3.5 | 3.0 | 2.6 |
| 40 | 10.0 | 8.8 | 7.7 | 6.8 | 5.9 | 5.2 | 4.5 | 4.0 | 3.5 | 3.0 | 2.6 | 2.3 | 2.0 | 1.7 |
| 45 | 6.8 | 5.9 | 5.2 | 4.5 | 3.9 | 3.4 | 3.0 | 2.6 | 2.3 | 2.0 | 1.7 | 1.5 | 1.3 | 1.1 |
| 50 | 4.6 | 4.0 | 3.5 | 3.0 | 2.6 | 2.3 | 2.0 | 1.7 | 1.5 | 1.3 | 1.2 | 1.0 | 0.9 | 0.8 |
| 55 | 3.0 | 2.7 | 2.3 | 2.0 | 1.8 | 1.5 | 1.3 | 1.2 | 1.0 | 0.9 | 0.8 | 0.7 | 0.6 | 0.5 |
| 60 | 2.0 | 1.8 | 1.5 | 1.3 | 1.2 | 1.0 | 0.9 | 0.8 | 0.7 | 0.6 | 0.5 | 0.4 | 0.4 | 0.3 |

Reproduced, with permission, from Berghella et al.⁵⁹

Lancet. Care for women with prior preterm birth. Am J Obstet Gynecol 2010.



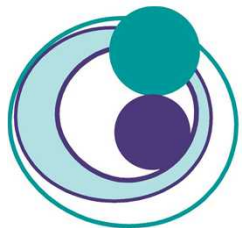
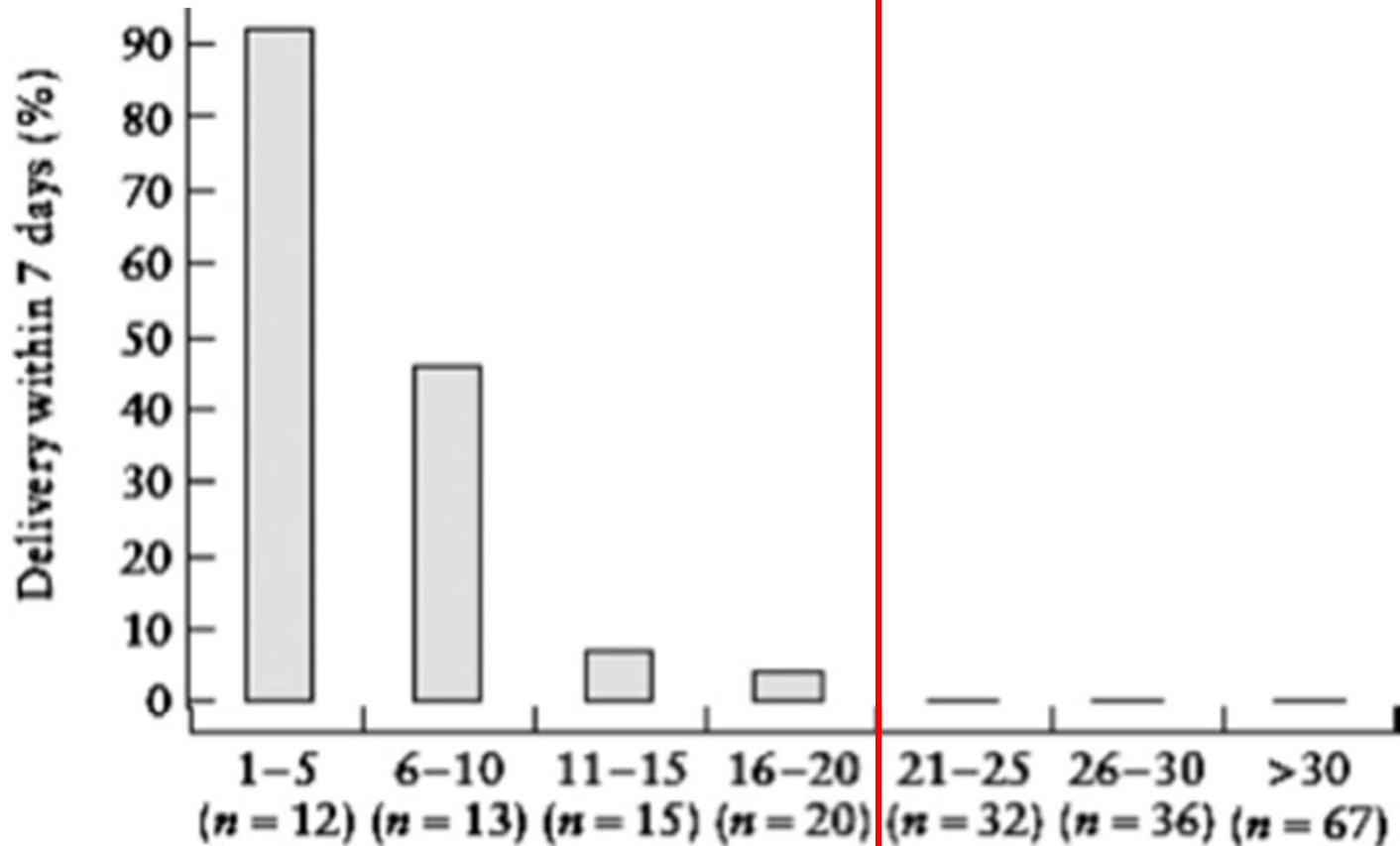
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Delivery within 7 days

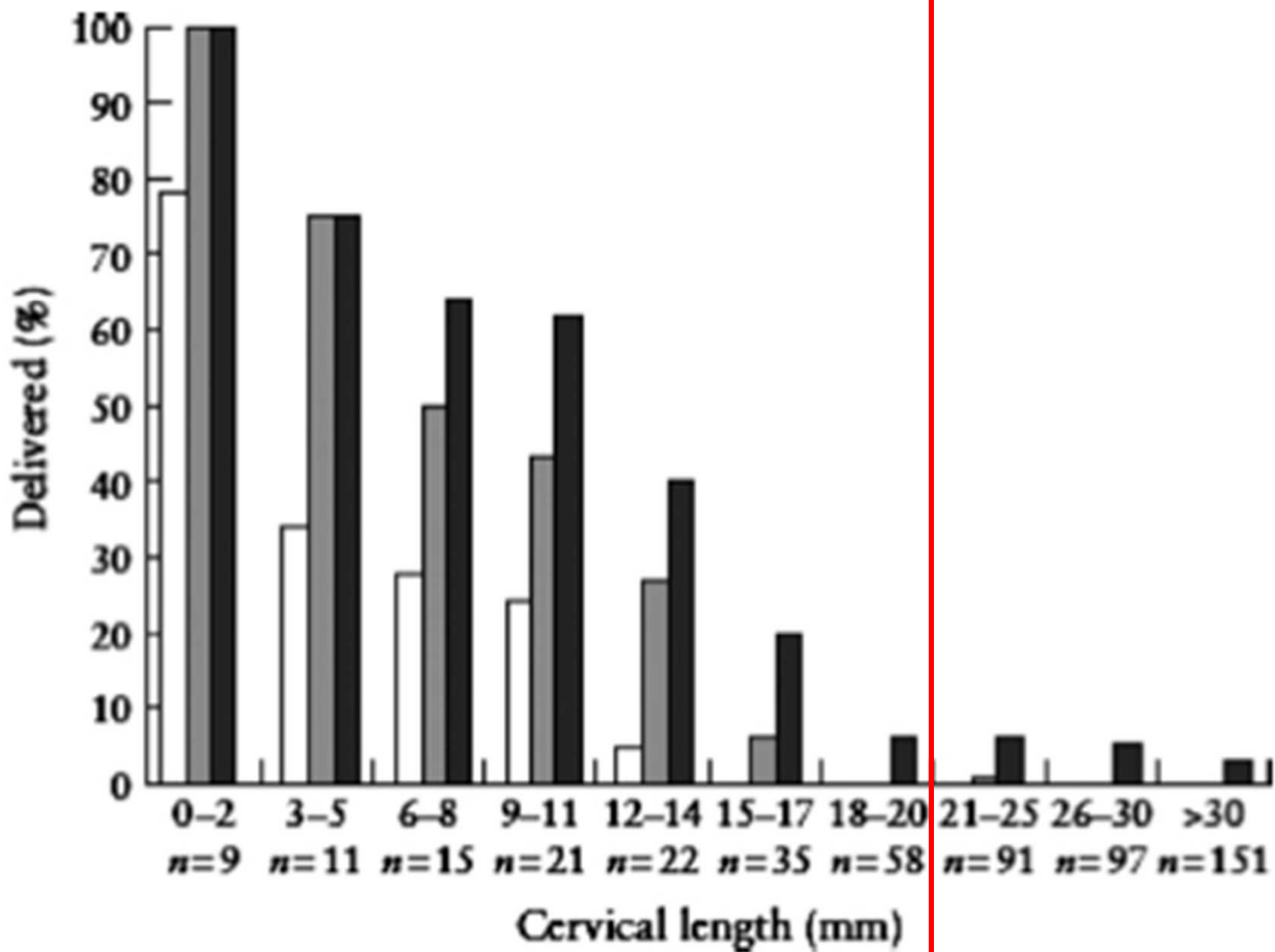


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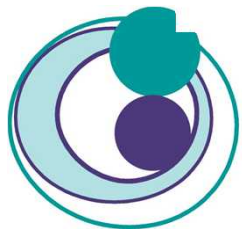
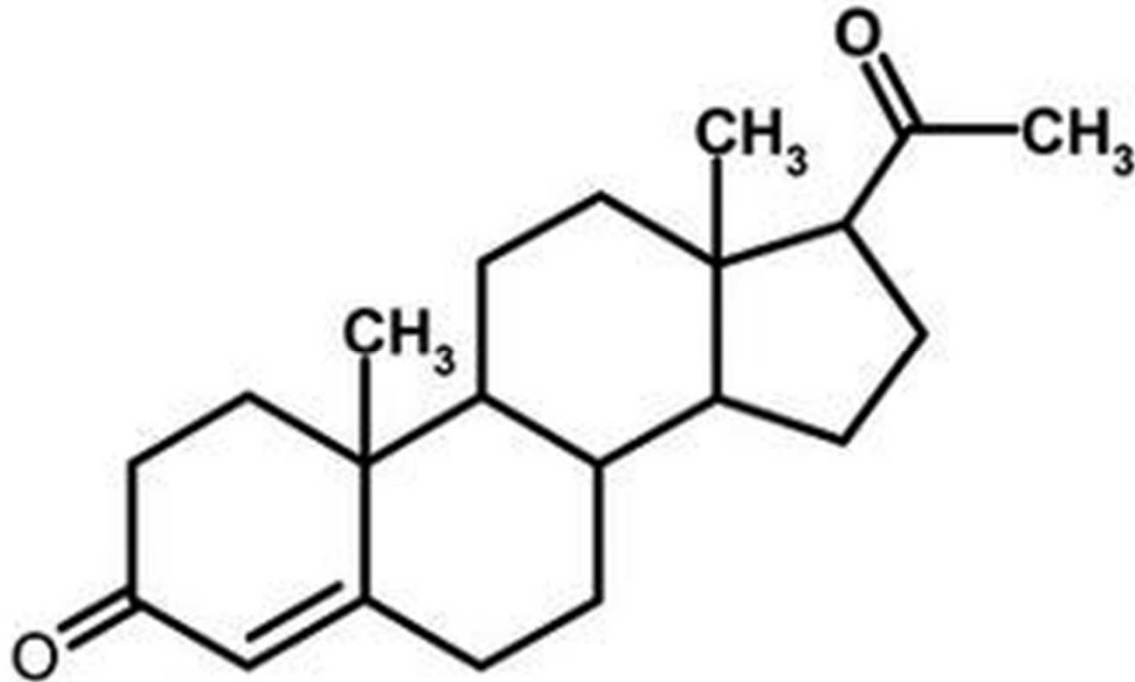
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Vaginal progesterone in women with an asymptomatic sonographic short cervix in the midtrimester decreases preterm delivery and neonatal morbidity: a systematic review and metaanalysis of individual patient data

Roberto Romero, MD; Kypros Nicolaides, MD; Agustin Conde-Agudelo, MD, MPH; Ann Tabor, MD; John M. O'Brien, MD; Elcin Cetingoz, MD; Eduardo Da Fonseca, MD; George W. Creasy, MD; Katharina Klein, MD; Line Rode, MD; Priya Soma-Pillay, MD; Shalini Fusey, MD; Cetin Cam, MD; Zarko Alfirevic, MD; Sonia S. Hassan, MD

OBJECTIVE: To determine whether the use of vaginal progesterone in asymptomatic women with a sonographic short cervix (≤ 25 mm) in the midtrimester reduces the risk of preterm birth and improves neonatal morbidity and mortality.

STUDY DESIGN: Individual patient data metaanalysis of randomized controlled trials.

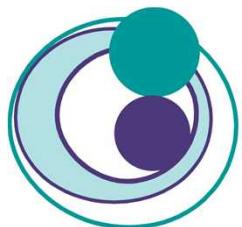
RESULTS: Five trials of high quality were included with a total of 775 women and 827 infants. Treatment with vaginal progesterone was associated with a significant reduction in the rate of preterm birth <33 weeks (relative risk [RR], 0.58; 95% confidence interval [CI], 0.42–0.80), <35 weeks (RR, 0.69; 95% CI, 0.55–0.88), and <28 weeks (RR, 0.50; 95% CI, 0.30–0.81); respiratory distress syndrome (RR, 0.48; 95% CI, 0.30–0.76); composite neonatal morbidity and mortality

(RR, 0.57; 95% CI, 0.40–0.81); birthweight <1500 g (RR, 0.55; 95% CI, 0.38–0.80); admission to neonatal intensive care unit (RR, 0.75; 95% CI, 0.59–0.94); and requirement for mechanical ventilation (RR, 0.66; 95% CI, 0.44–0.98). There were no significant differences between the vaginal progesterone and placebo groups in the rate of adverse maternal events or congenital anomalies.

CONCLUSION: Vaginal progesterone administration to asymptomatic women with a sonographic short cervix reduces the risk of preterm birth and neonatal morbidity and mortality.

Key words: admission to neonatal intensive care unit, birthweight <1500 g, mechanical ventilation, prematurity, preterm birth, progestin, respiratory distress syndrome, transvaginal ultrasound, uterine cervix, 17α -hydroxyprogesterone caproate

Cite this article as: Romero R, Nicolaides K, Conde-Agudelo A, et al. Vaginal progesterone in women with an asymptomatic sonographic short cervix in the midtrimester decreases preterm delivery and neonatal morbidity: a systematic review and metaanalysis of individual patient data. Am J Obstet Gynecol 2012;206:124.e1-19.



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Results

Preterm Birth

- Reduced
 - <28 weeks by 50%
 - <33 weeks by 40%
 - <35 weeks by 30%

Neonatal Outcomes

- Reduced
 - RDS
 - RR 0.48 (0.30-0.70)
 - NICU Admission
 - RR 0.75 (0.59-0.94)
 - Need for mechanical ventilation
 - RR 0.66 (0.44-0.98)
 - Lower rate of LBW <1500g
 - RR 0.55 (0.38-0.80)

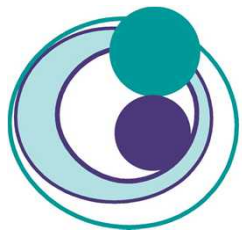
Recommendations

- Transvaginal cervical length
 - 19-24 weeks
 - Frequency?
 - Past Hx
 - Screening
 - Vaginal Progesterone
 - 90 mg/d
 - 20-36⁺⁶ weeks

Mechanism of action

- Anti-inflammatory
- Increased progesterone levels
- Decreases sensitivity of oxytocin receptors

What about a cerclage?



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Vaginal progesterone vs cervical cerclage for the prevention of preterm birth in women with a sonographic short cervix, previous preterm birth, and singleton gestation: a systematic review and indirect comparison metaanalysis

Agustin Conde-Agudelo, MD, MPH; Roberto Romero, MD, DMedSci; Kypros Nicolaides, MD; Tinnakorn Chaiworapongsa, MD; John M. O'Brien, MD; Elcin Cetingoz, MD; Eduardo da Fonseca, MD; George Creasy, MD; Priya Soma-Pillay, MD; Shalini Fusey, MD; Cetin Cam, MD; Zarko Alfirevic, MD; Sonia S. Hassan, MD

OBJECTIVE: No randomized controlled trial has compared vaginal progesterone and cervical cerclage directly for the prevention of preterm birth in women with a sonographic short cervix in the mid trimester, singleton gestation, and previous spontaneous preterm birth. We performed an indirect comparison of vaginal progesterone vs cerclage using placebo/no cerclage as the common comparator.

STUDY DESIGN: Adjusted indirect metaanalysis of randomized controlled trials.

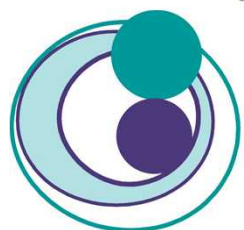
RESULTS: Four studies that evaluated vaginal progesterone vs placebo (158 patients) and 5 studies that evaluated cerclage vs no cerclage (504 patients) were included. Both interventions were associated with a statistically significant reduction in the risk of preterm birth at <32 weeks of gestation and composite perinatal morbidity and mortality

compared with placebo/no cerclage. Adjusted indirect metaanalyses did not show statistically significant differences between vaginal progesterone and cerclage in the reduction of preterm birth or adverse perinatal outcomes.

CONCLUSION: Based on state-of-the-art methods for indirect comparisons, either vaginal progesterone or cerclage are equally efficacious in the prevention of preterm birth in women with a sonographic short cervix in the mid trimester, singleton gestation, and previous preterm birth. Selection of the optimal treatment needs to consider adverse events, cost and patient/clinician preferences.

Key words: birthweight, cervix, neonatal intensive care unit, perinatal mortality, perinatal morbidity, premature, prematurity, progestin, 17 α -hydroxyprogesterone caproate, 17P

Cite this article as: Conde-Agudelo A, Romero R, Nicolaides K, et al. Vaginal progesterone vs cervical cerclage for the prevention of preterm birth in women with a sonographic short cervix, previous preterm birth, and singleton gestation: a systematic review and indirect comparison metaanalysis. Am J Obstet Gynecol 2013;208:42.e1-18.



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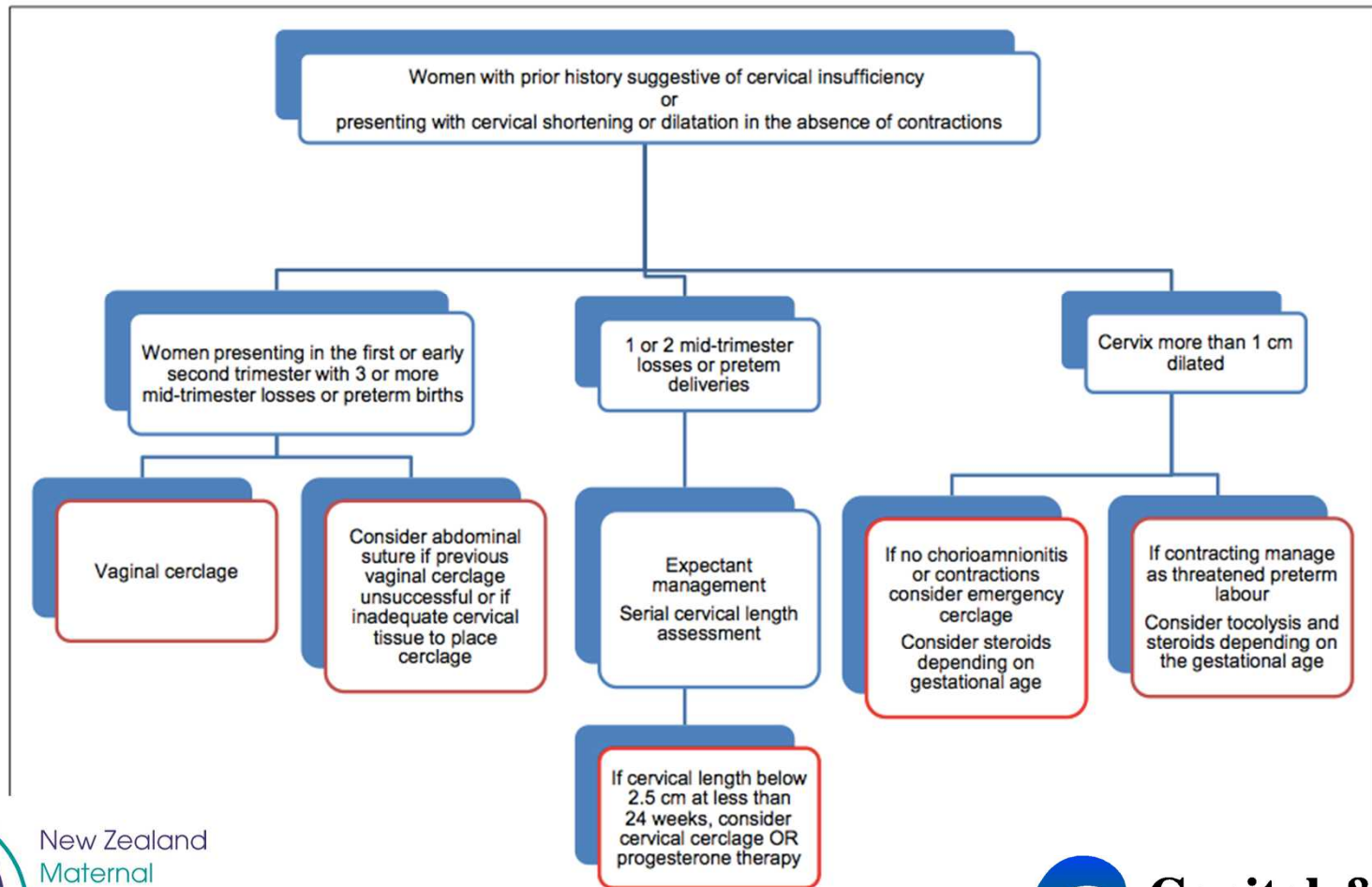
- Efficacy
 - Similar
- Considerations
 - Cost
 - Patient and physician preference
- Cerclage
 - Anesthetic
 - Surgical procedure
 - Complications
 - SROM
 - Bleeding
- Progesterone
 - Compliance

What about twins?

??????

What about an algorithm?

Flow diagram



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Prior PTB

- Serial Cx Lengths
 - 16-23 weeks
- Progesterone
 - 16-36 weeks
- Cerclage
 - Cx <25 mm
 - *Iams. AJOG*

What about Universal Screening?

1. The condition must be an important health problem
2. There should be an accepted treatment for patients with recognised disease
3. Must have facilities for diagnosis and treatment
4. There should be a recognised latent stage
5. There should be a suitable test or examination
6. The test should be acceptable to the population
7. The natural history of the disease should be understood
8. There should be an agreed policy on who to treat as patients
9. Cost of screening should be economically balanced in relation to possible expenditure on medical care
10. Case-finding should be a continual process and not a “once and for all” project

Guidelines

SOGC CLINICAL PRACTICE GUIDELINES

No. 301, December 2013

Cervical Insufficiency and Cervical Cerclage

This clinical practice guideline has been prepared by the Maternal Fetal Medicine Committee, reviewed by the Clinical Practice Obstetrics Committee, and approved by the Executive and Council of the Society of Obstetricians and Gynaecologists of Canada.

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Disclosure statements have been received from all contributors. The literature searches and bibliographic support for this guideline were undertaken by Becky Skidmore, Medical Research analyst, Society of Obstetricians and Gynaecologists of Canada.

Key words: Cervical insufficiency, cervical incompetence, cervical cerclage, preterm delivery, prematurity, Shirodkar cerclage, MacDonald cerclage, abdominal cerclage, rescue cerclage, cervical shortening, trans-vaginal ultrasound, cervical length

This document reflects emerging clinical and scientific advances on the date issued and is subject to change. The information should not be construed as dictating an exclusive course of treatment or procedure to be followed. Local institutions can dictate amendments to these opinions. They should be well documented if modified at the local level. None of these contents may be reproduced in any form without prior written permission of the SOGC.

Abstract

Objective: The purpose of this guideline is to provide a framework that clinicians can use to determine which women are at greatest risk of having cervical insufficiency and in which set of circumstances a cerclage is of potential value.

Evidence: Published literature was retrieved through searches of PubMed or MEDLINE, CINAHL, and The Cochrane Library in 2012 using appropriate controlled vocabulary (e.g., uterine cervical incompetence) and key words (e.g., cervical insufficiency, cerclage, Shirodkar, cerclage, MacDonald, cerclage, abdominal, cervical length, mid-trimester pregnancy loss). Results were restricted to systematic reviews, randomized control trials, controlled clinical trials, and observational studies. There were no date or language restrictions. Searches were updated on a regular basis and incorporated in the guideline to January 2011. Grey (unpublished) literature was identified through searching the websites of health technology assessment and health technology-related agencies, clinical practice guideline collections, clinical trial registries, and national and international medical specialty societies.

Values: The quality of evidence in this document was rated using the criteria described in the Report of the Canadian Task Force on Preventive Health Care (Table).

Recommendations

1. Women who are pregnant or planning pregnancy should be evaluated for risk factors for cervical insufficiency. A thorough medical history at initial evaluation may alert clinicians to risk factors in a first or index pregnancy. (B-B)
2. Detailed evaluation of risk factors should be undertaken in women following a mid-trimester pregnancy loss or early premature delivery, or in cases where such complications have occurred in a preceding pregnancy. (B-B)
3. In women with a history of cervical insufficiency, analysis for culture and sensitivity and vaginal cultures for bacterial vaginosis should be taken at the first obstetric visit and any infections so found should be treated. (A-A)
4. Women with a history of three or more second-trimester pregnancy losses or extreme premature deliveries, in whom no specific cause other than potential cervical insufficiency is identified, should be offered elective cerclage at 12 to 14 weeks of gestation. (A-A)

J Obstet Gynaecol Can 2013;35(12):1115-1127

Progesterone: Use in the second and third trimester of pregnancy for the prevention of preterm birth

This statement has been developed and reviewed by the Women's Health Committee and approved by the RANZCOG Board and Council.

A list of Women's Health Committee Members can be found in Appendix A.

Disclosure statements have been received from all members of this committee.

Disclaimer This information is intended to provide general advice to practitioners. This information should not be relied on as a substitute for proper assessment with respect to the particular circumstances of each case and the needs of any patient. This document reflects emerging clinical and scientific advances as of the date issued and is subject to change. The document has been prepared having regard to general circumstances.

First endorsed by RANZCOG: March 2010
Current: November 2013
Review due: November 2016

Objectives: To provide advice on the use of progesterone to prevent preterm birth.

Outcomes: Reduced risk of preterm birth for all women who have a history of previous spontaneous preterm birth or who are found to have a short cervix at the time of the routine morphology scan.

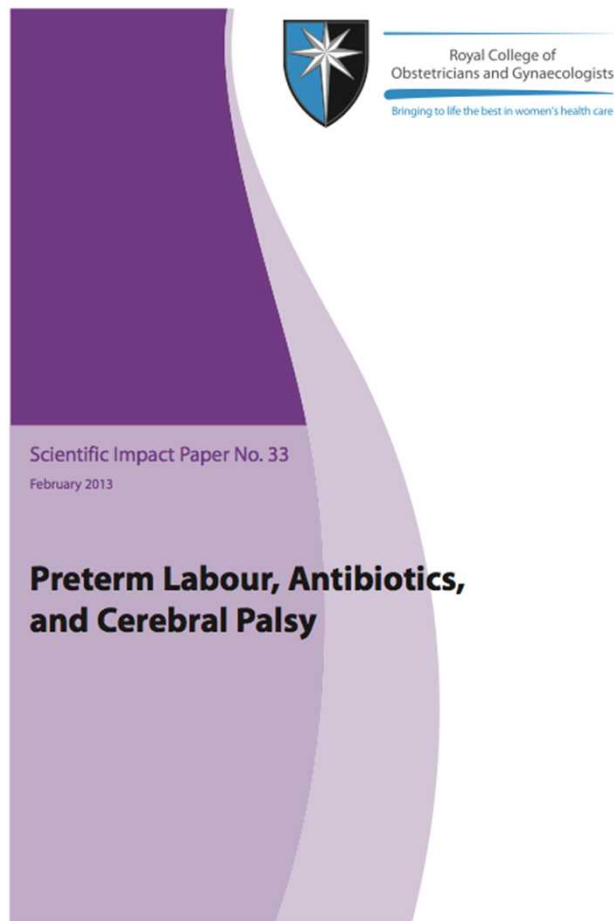
Target audience: All health practitioners providing maternity care and patients.

Evidence: Medline was searched for randomised trials and cohort studies.

Values: The evidence was reviewed by the Women's Health Committee (RANZCOG), and applied to local factors relating to Australia and New Zealand.

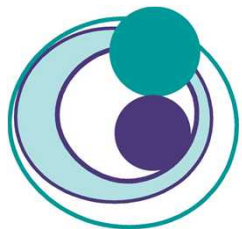
Background: This statement was first developed by Women's Health Committee in March 2010 and reviewed in March 2013.

Funding: The development and review of this statement was funded by RANZCOG.



- ORACLE Children Study (OCS)
 - followed-up surviving children at 7 years of age
 - parent-report postal questionnaire.
 - Spont PTL Rx erythromycin
 - children with any level of functional impairment 38% to 42%
 - cerebral palsy increased from 1.7% to 3.3%
 - (OR 1.93, 95% CI 1.21–3.09)
 - A continuing inflammatory environment could lead to fetal brain injury and thereby cerebral palsy

Are we leaving a fetus in a hostile intrauterine environment???



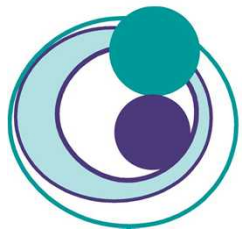
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Arabin Pessary

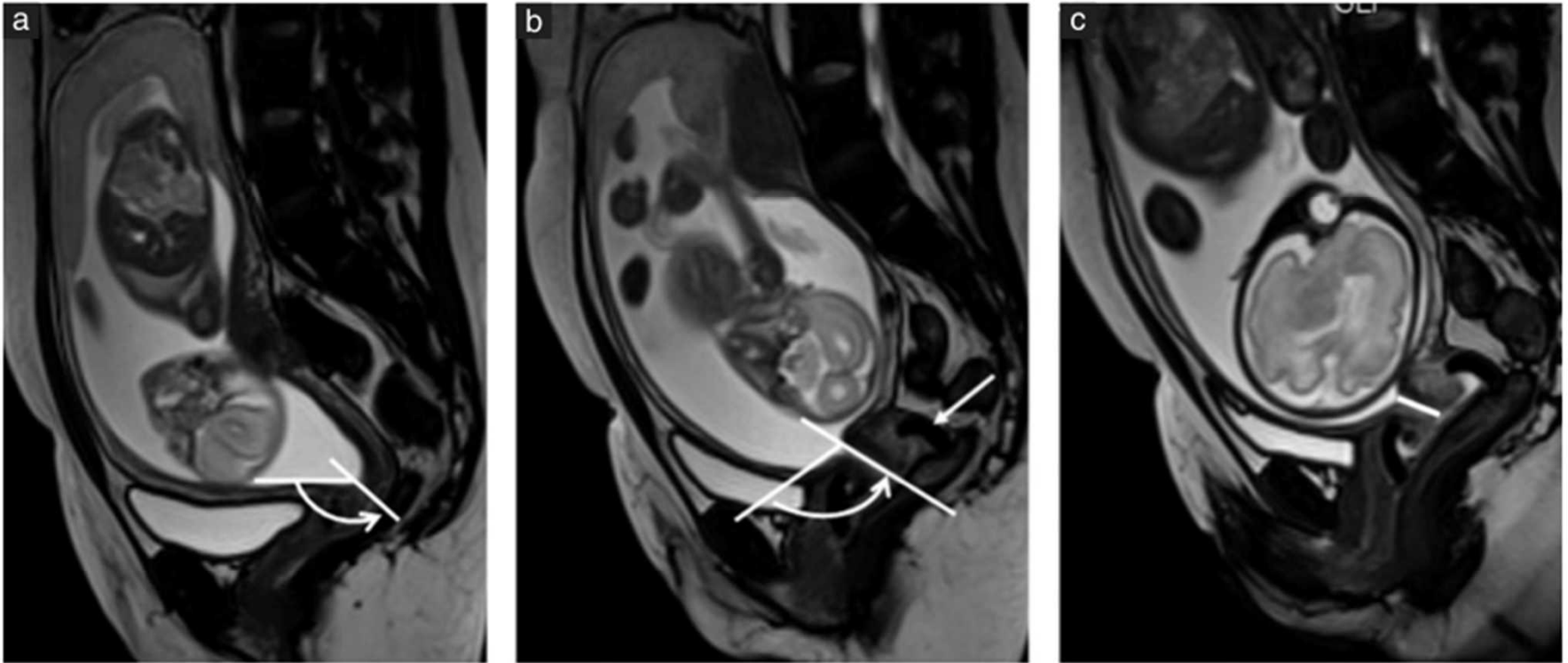


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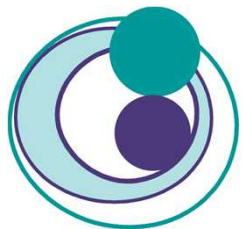
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