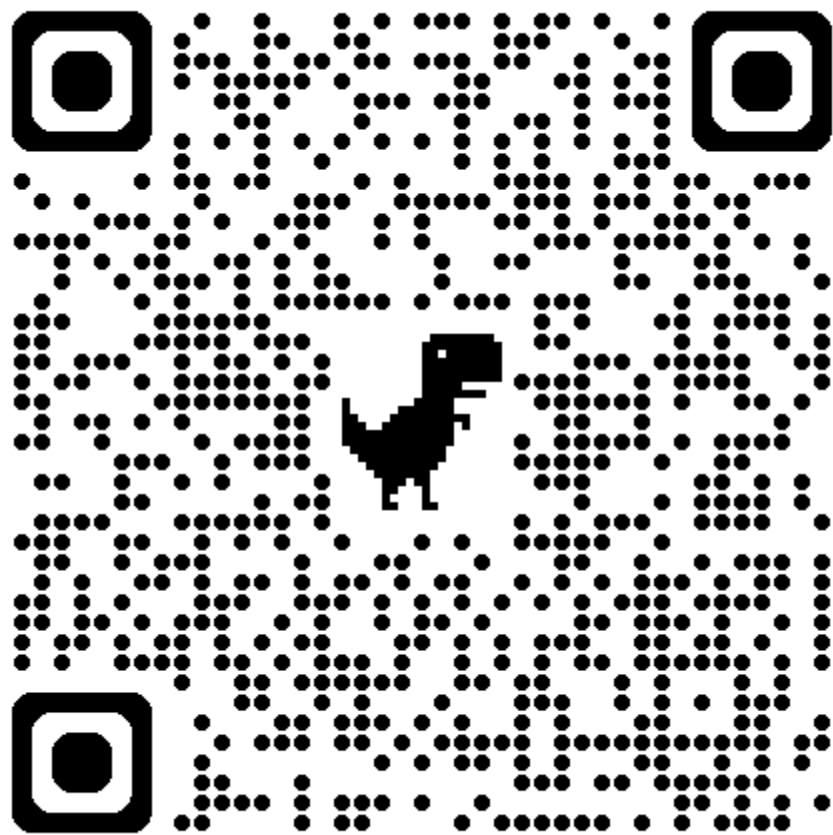




Prevention of Preterm Birth II: Without Progestins

Kerri Brackney, MD, FACOG
Maternal Fetal Medicine







I have no relevant disclosures.



Objectives

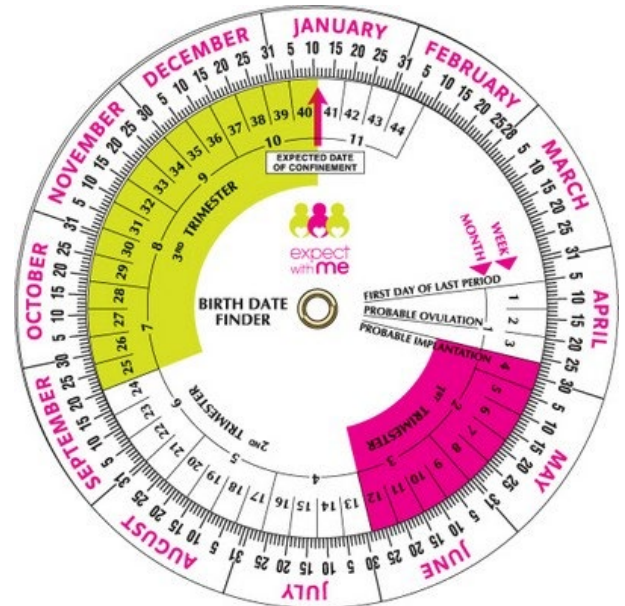
1. Assess risk for PTB.
2. Identify candidates for cervical length screening.
3. Apply interventions to reduce the risk of PTB.
4. Reduce regional rate of PTB.

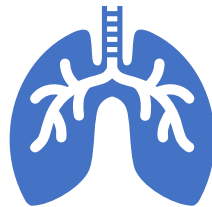
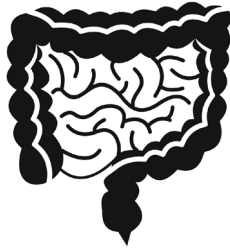
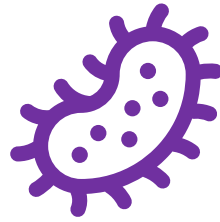
What is preterm birth?

Delivery **between 20.0 and 36.6 weeks** of gestation

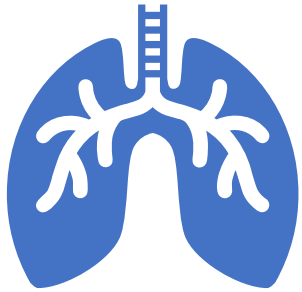
Late preterm = 34-36.6 weeks

Early preterm = 20-34 weeks



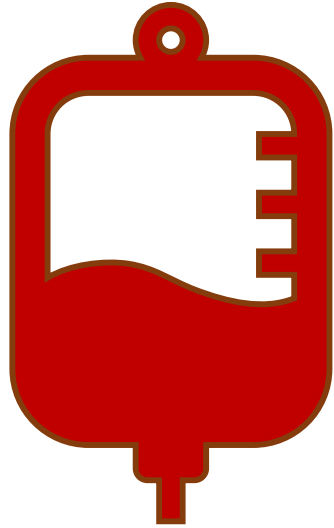


Neonatal Morbidity



Long-Term Morbidity





PTB = 8.6% risk of serious maternal complication

- Such as:
 - Hemorrhage
 - Infection
 - ICU admission
 - Death
- Classical CD increases the risk to **23%**

Spontaneous PTB

- **75% of PTB in the US**
- **Clinical diagnoses:**
 - **Preterm labor**
 - **PPROM**
 - **Cervical insufficiency**

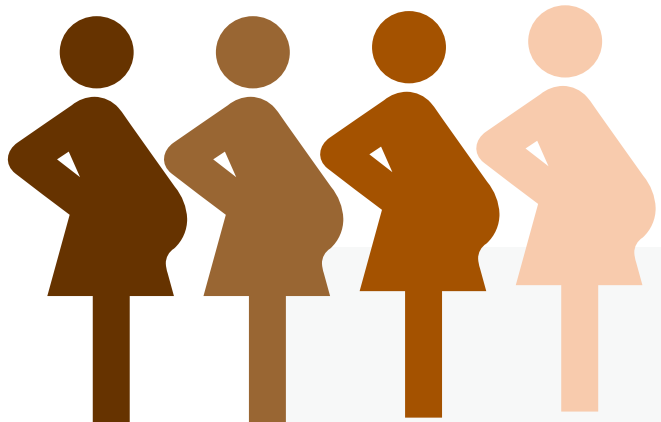
Indicated PTB

- **25% of PTB in the US**
- **Clinical diagnoses:**
 - **PreE (40%)**
 - **Abnl fetal status (25%)**
 - **FGR (10%)**
 - **Placental abruption (7%)**
 - **DM, GDM, renal disease, Rh sensitization, congenital anomalies**

Spontaneous PTB

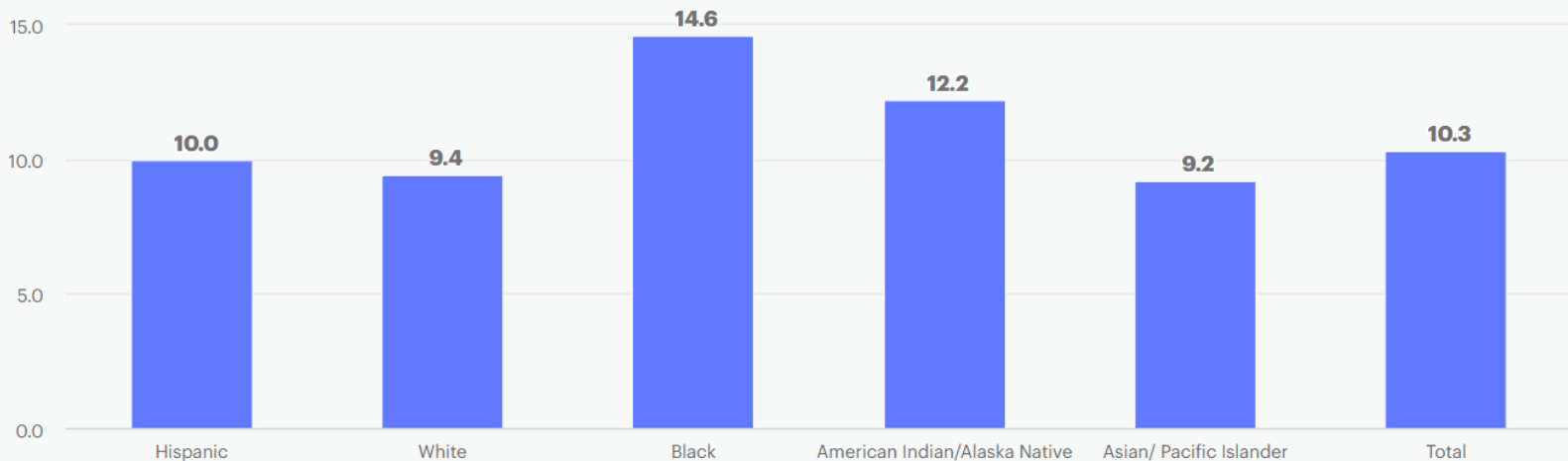
Risk Factors & Modifiers



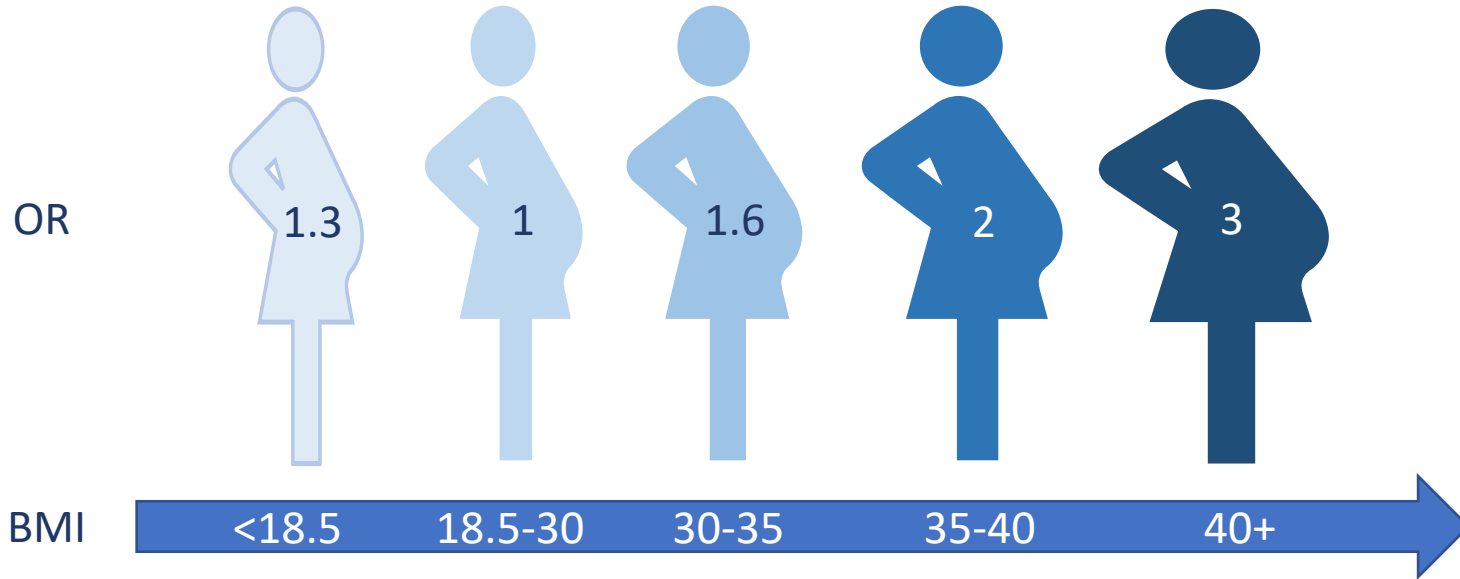


Preterm birth rate by race/ethnicity: United States, 2020-2022 Average

Percent of live births

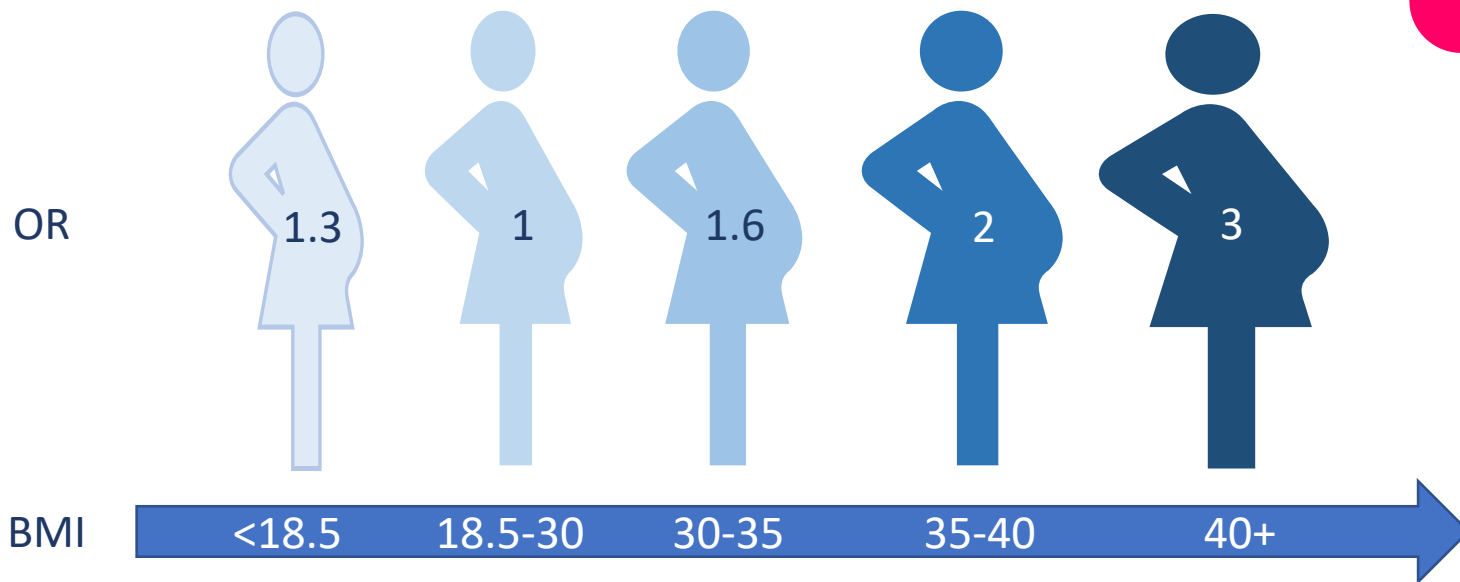
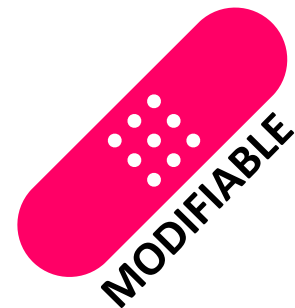


Odds of Spontaneous PTB by BMI



Cobo T, Kacerovsky M, Jacobsson B. Risk factors for spontaneous preterm delivery. *Int J Gynaecol Obstet.* 2020 Jul;150(1):17-23.

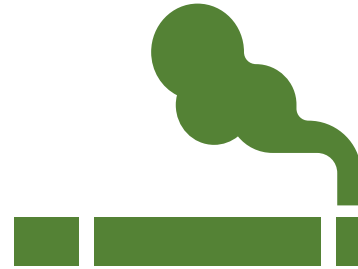
Odds of Spontaneous PTB by BMI



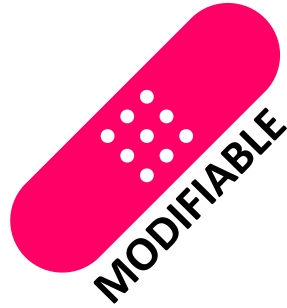
Cobo T, Kacerovsky M, Jacobsson B. Risk factors for spontaneous preterm delivery. *Int J Gynaecol Obstet.* 2020 Jul;150(1):17-23.

Smoking

OR of PTB = 1.4

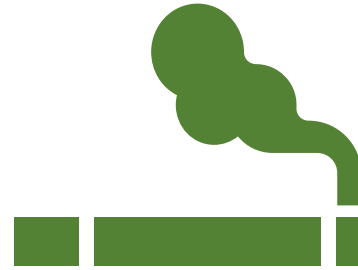


Cobo T, Kacerovsky M, Jacobsson B.
Risk factors for spontaneous preterm
delivery. *Int J Gynaecol Obstet.* 2020
Jul;150(1):17-23.



Smoking (& SUD)

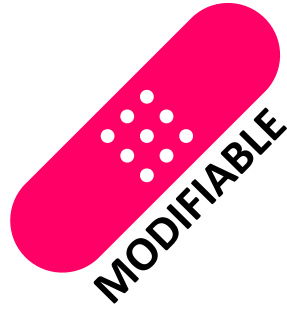
OR of PTB = 1.4



Cobo T, Kacerovsky M, Jacobsson B.
Risk factors for spontaneous preterm
delivery. *Int J Gynaecol Obstet.* 2020
Jul;150(1):17-23.

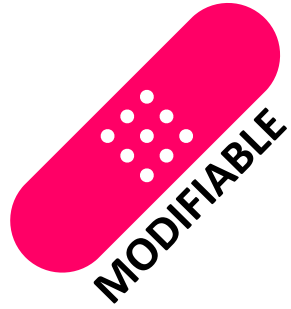
Short Inter- Pregnancy Interval



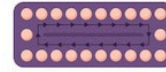


Short Inter- Pregnancy Interval





Short Inter- Pregnancy Interval



Contraceptive pill



Male condom



IUD
(Intrauterine Device)



Contraceptive
patch

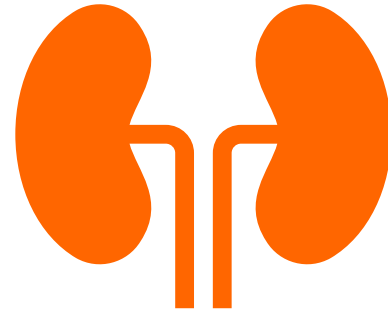


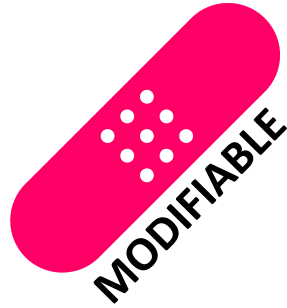
Contraceptive
injection



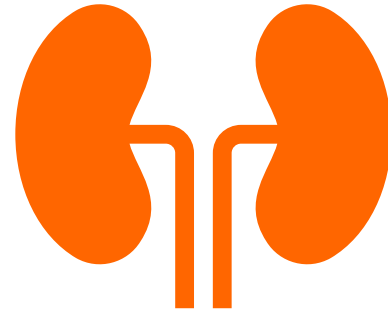
Female condom

Asymptomatic Bacteriuria





Asymptomatic Bacteriuria



Schieve LA, Handler A, Hershov R, Persky V, Davis F. Urinary tract infection during pregnancy: its association with maternal morbidity and perinatal outcome. *Am J Public Health* 1994;84:405–10.
Klein LL, Gibbs RS. Infection and preterm birth. *Obstet Gynecol Clin North Am* 2005;32:397–410.

Maternal Stress & Depression





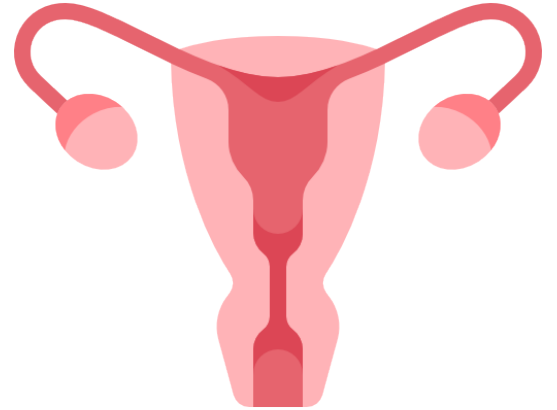
Maternal Stress & Depression



Previous D&C

OR of PTB = 1.29

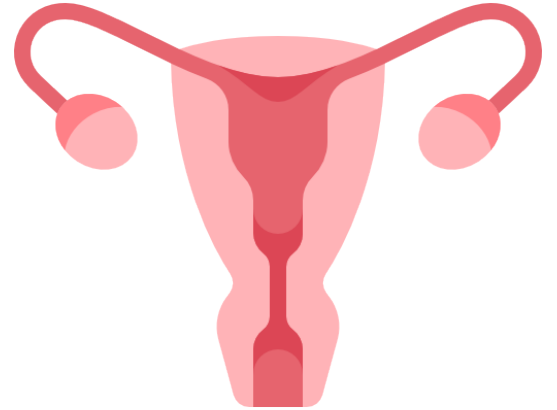
Multiple D&C OR = 1.74



Previous D&C

OR of PTB = 1.29

Multiple D&C OR = 1.74



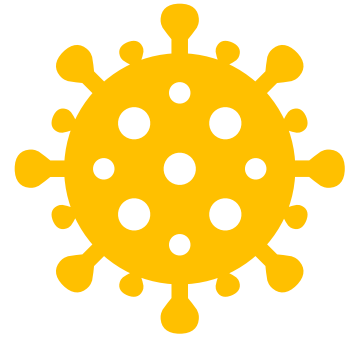
Lemmers M, Verschoor MA, Hooker AB, Opmeer BC, Limpens J, Huirne JA, et al. Dilatation and curettage increases the risk of subsequent preterm birth: a systematic review and meta-analysis. *Hum Reprod* 2016;31:34–45.

Hx LEEP/Cone for Cervical Dysplasia

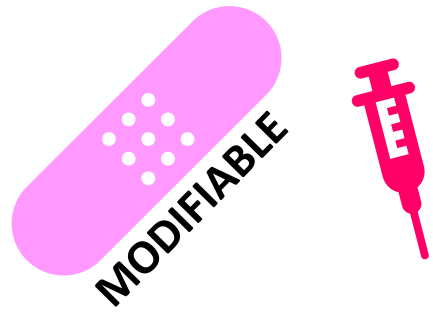
RR of PTB = 1.78

Higher for cone (2.7)

Higher for multiple excision (3.78)



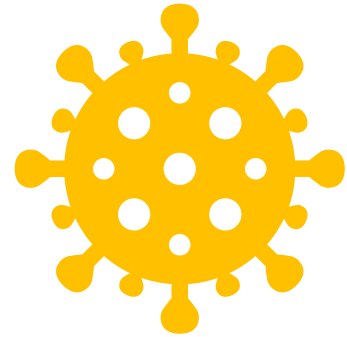
Hx LEEP/Cone for Cervical Dysplasia



RR of PTB = 1.78

Higher for cone (2.7)

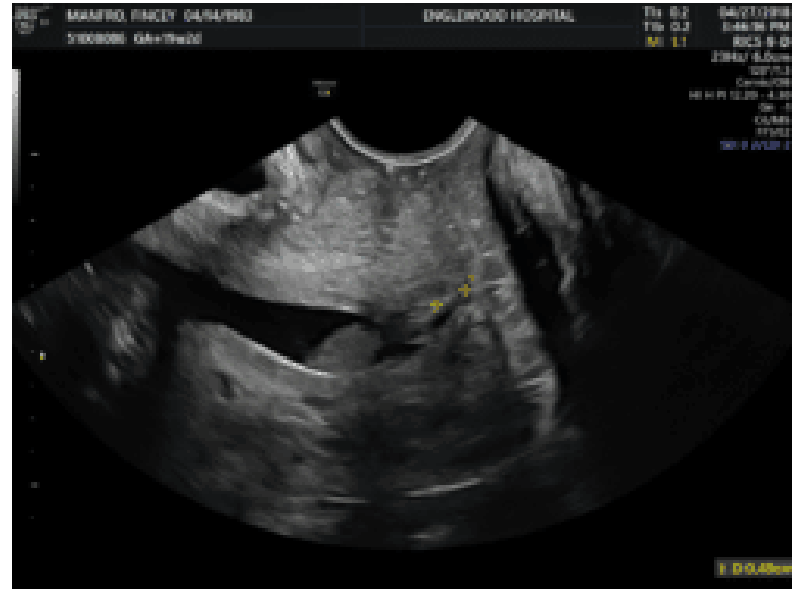
Higher for multiple excision (3.78)



Kyrgiou et al. Adverse obstetric outcomes after local treatment for cervical preinvasive and early invasive disease according to cone depth: systematic review and meta-analysis. *BMJ*. 2016 Jul 28;354:i3633.


Short cervix

At 16-24 weeks
<25 mm





Unsuccessful Risk Factor Modification

- Treatment of symptomatic UTI
 - Treatment of BV or trichomonas
 - Treatment of periodontal disease
 - Bedrest
- 

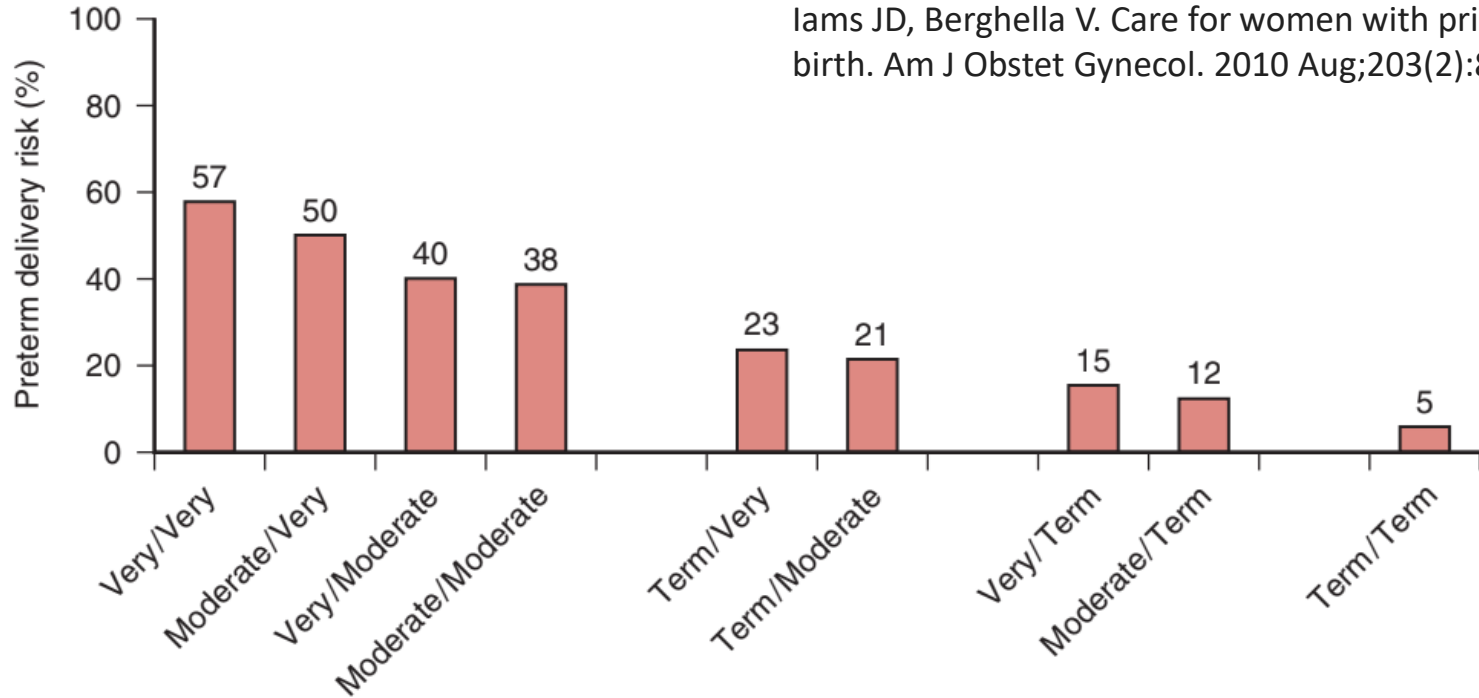
History Matters

it tends to repeat



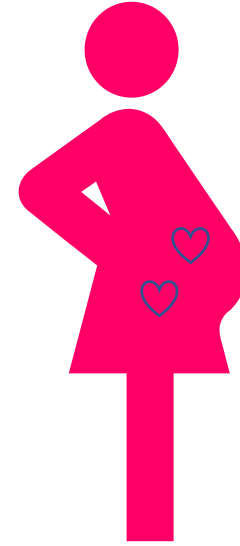
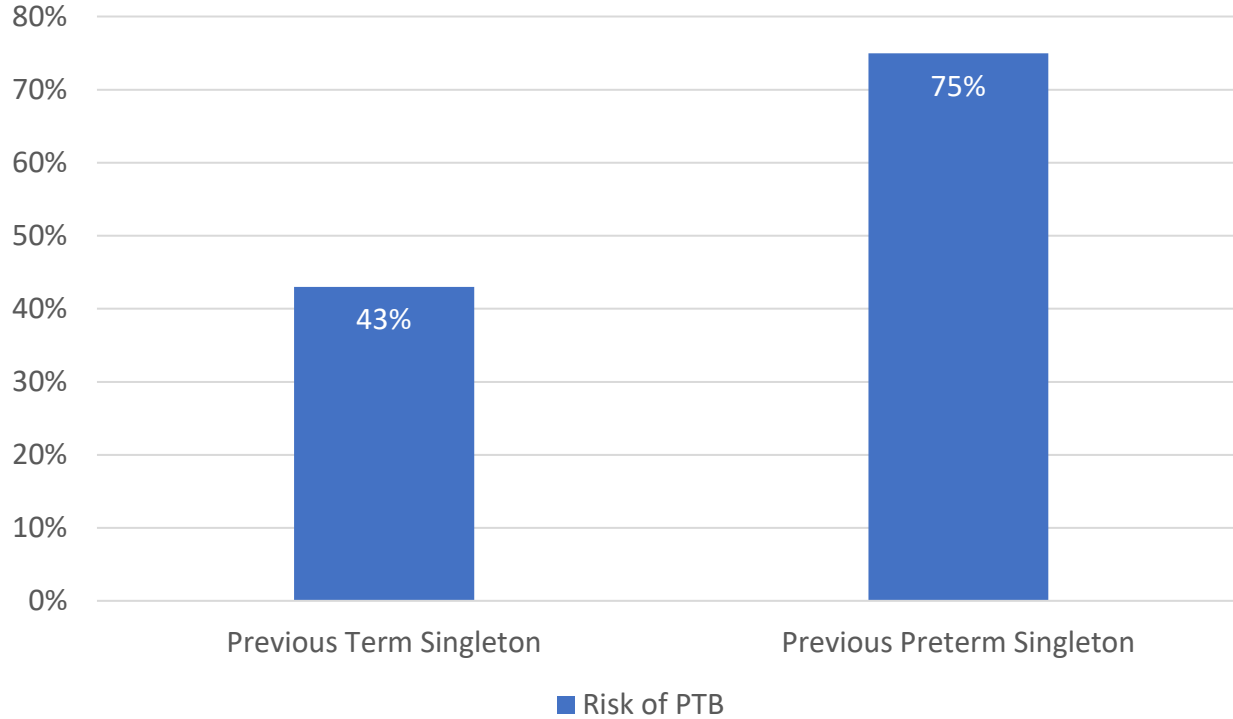
Risk of Preterm Birth at Third Delivery

Iams JD, Berghella V. Care for women with prior preterm birth. Am J Obstet Gynecol. 2010 Aug;203(2):89-100.

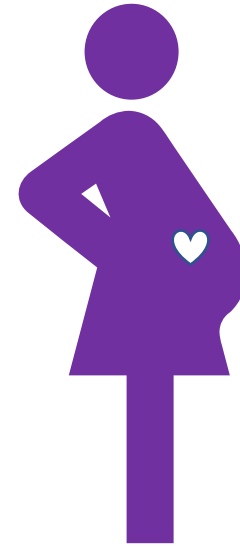
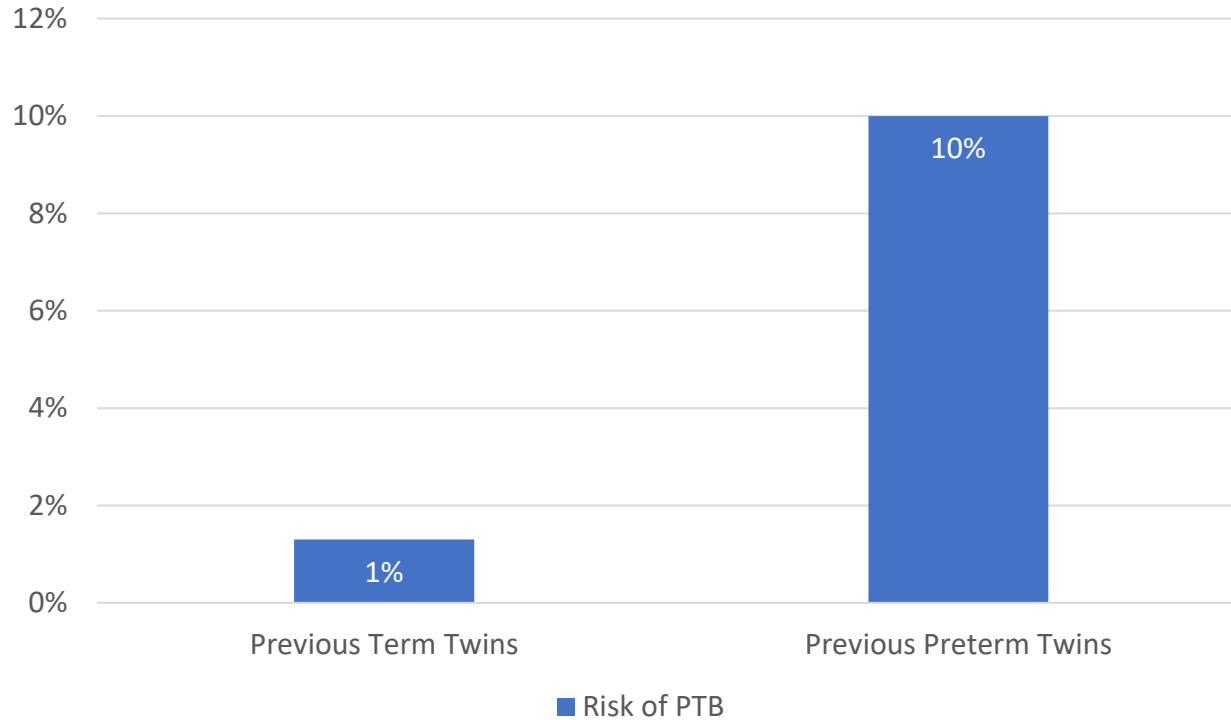


Prior preterm delivery status by order and gestational age at delivery

Risk of PTB in Twin Pregnancy



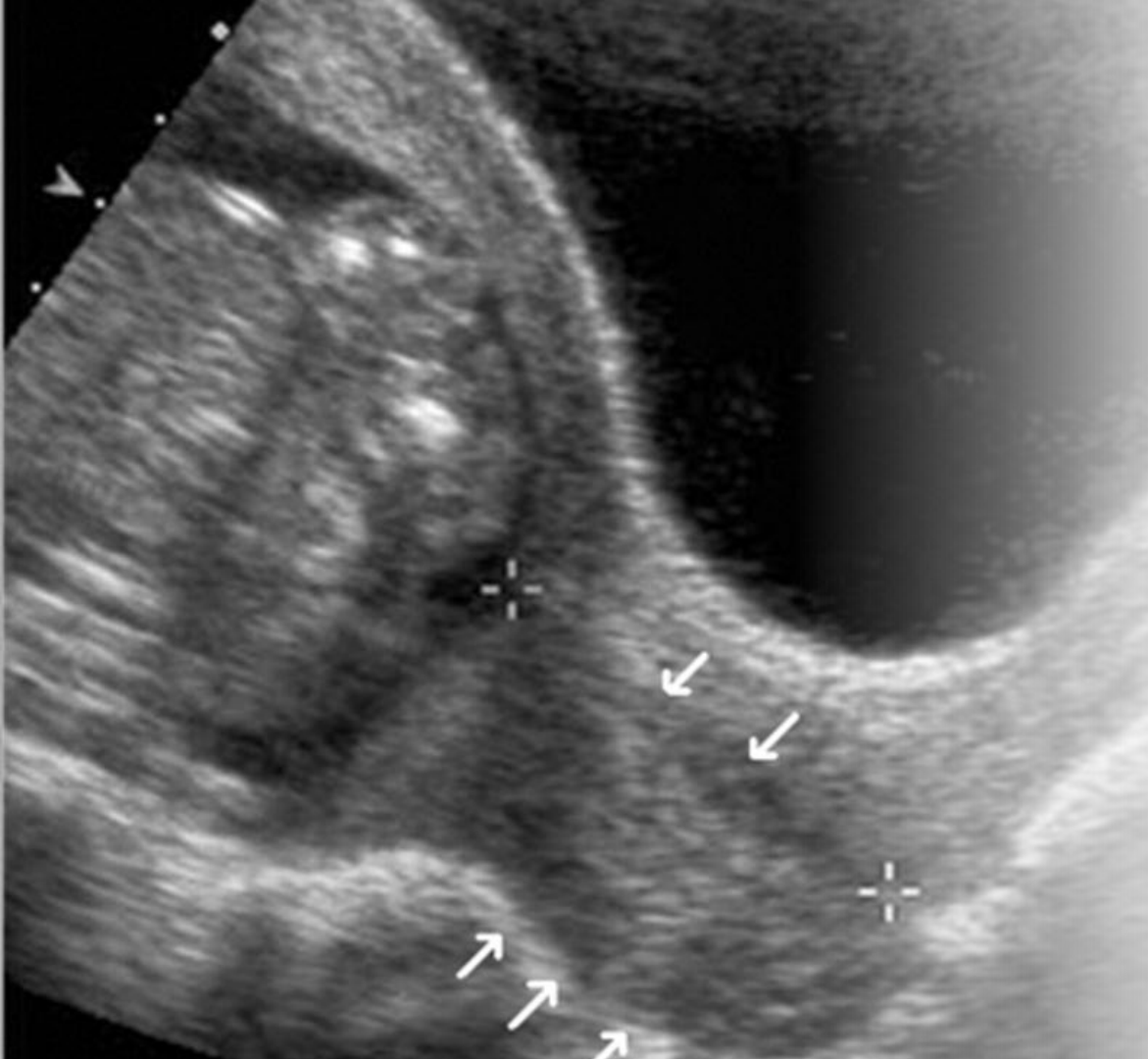
Risk of PTB in Singleton Pregnancy



Risk Assessment

Transabdominal Cervical Length

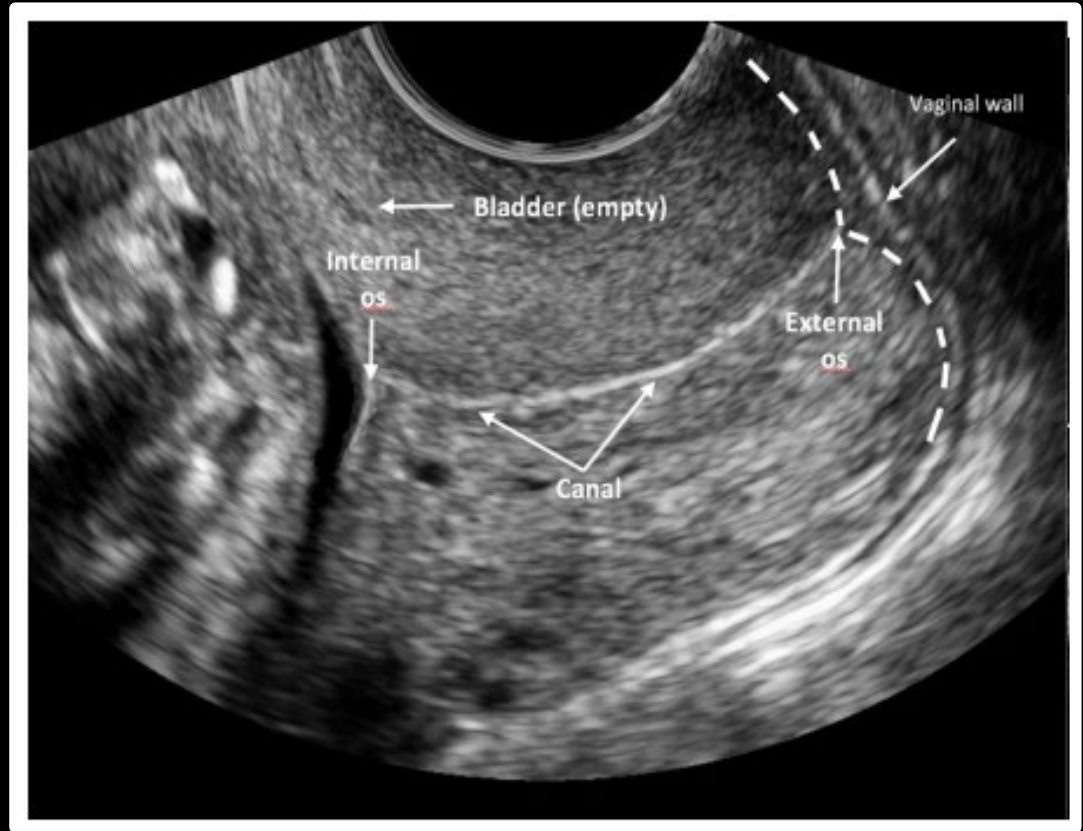
- Can be used as initial screen for short cervix
- Patients without prior sPTB
- Perform at 18-22.6w
- Threshold ≤ 36 mm
- Identifies 96% of patients with a TVCL ≤ 25 mm

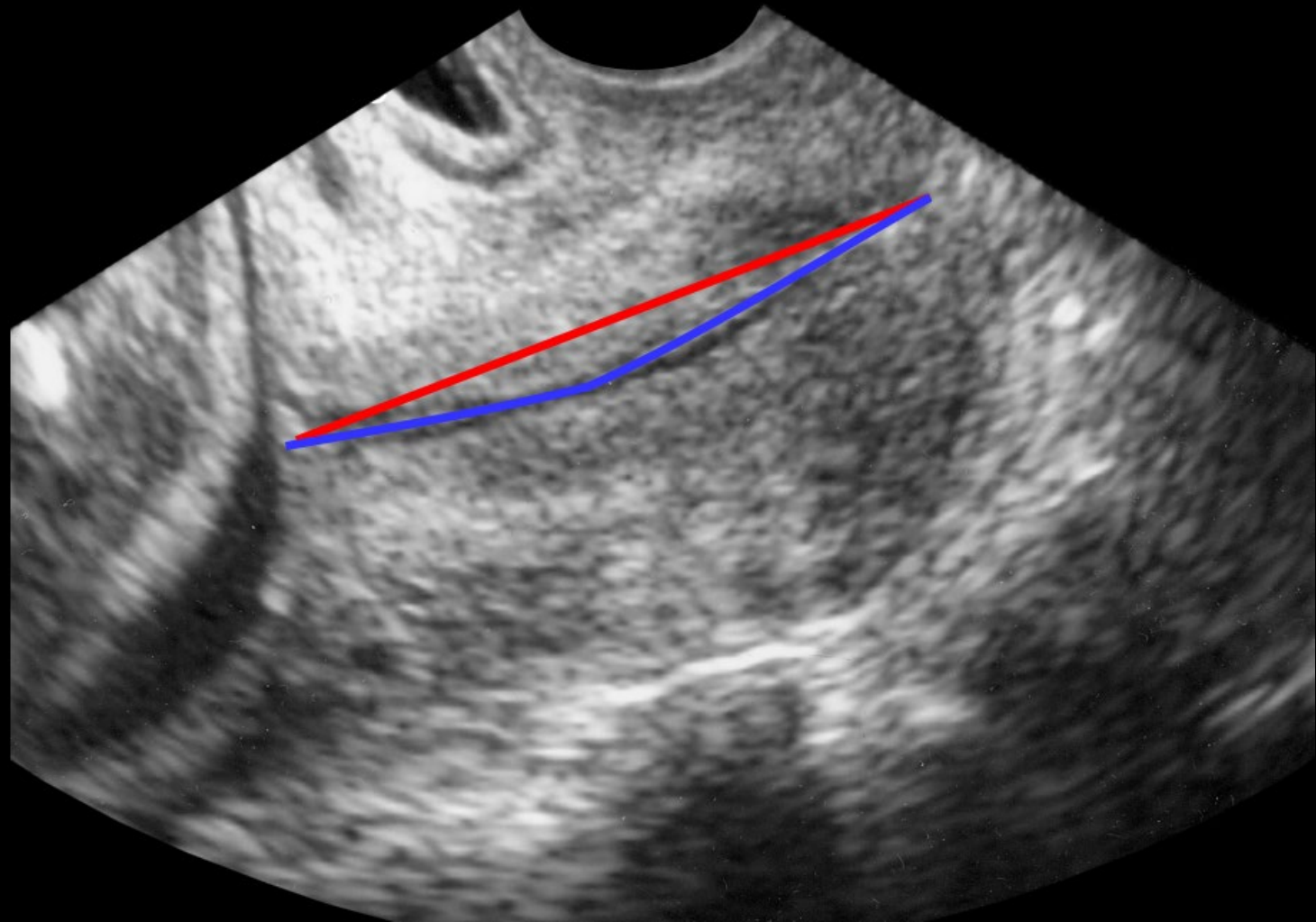




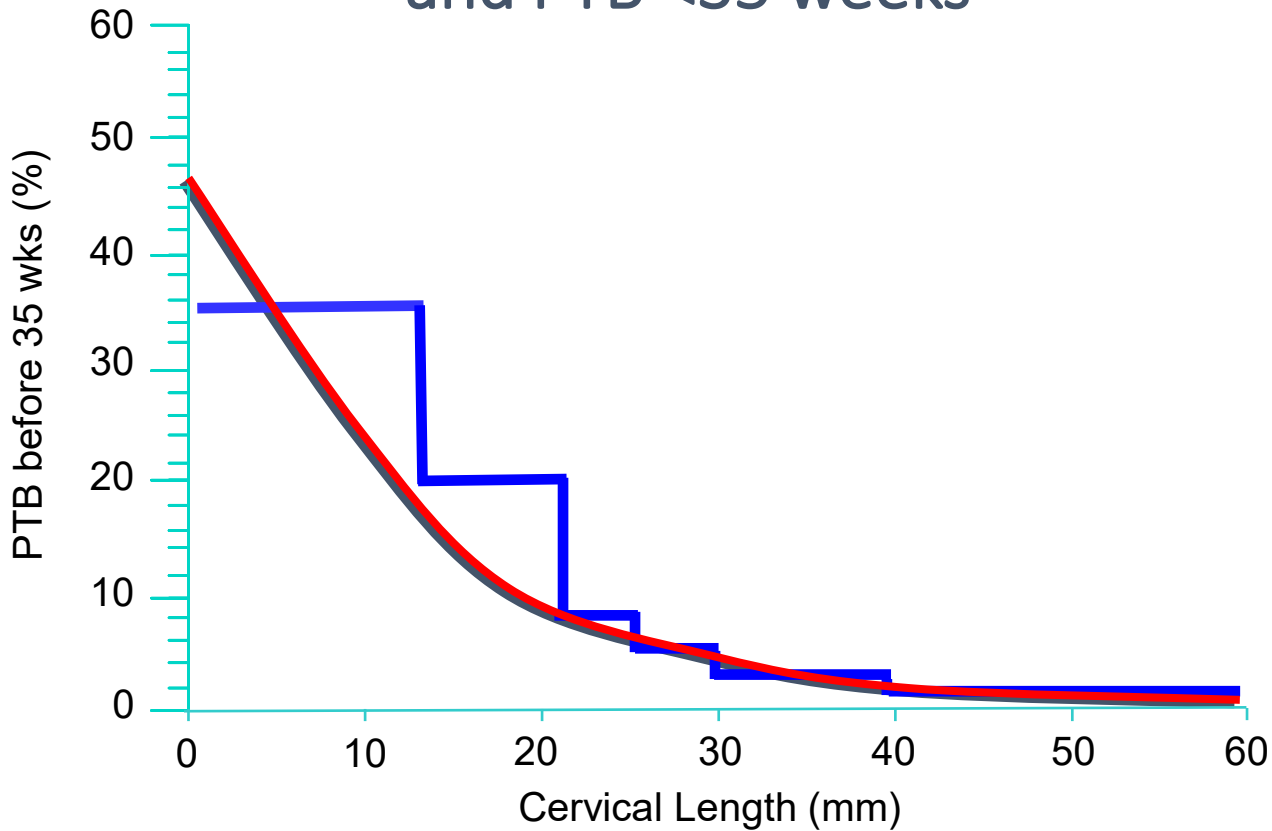
Cervical Length Education & Review

- **Transvaginal**
- **Empty bladder**
- **Zoom in (2/3 – 3/4 of field)**
- **Anterior = Posterior**
- **Internal + External Os visible**
- **Entire canal visualized**
- **Calipers at internal and external os**
- **Shortest, best of 3 measurements**

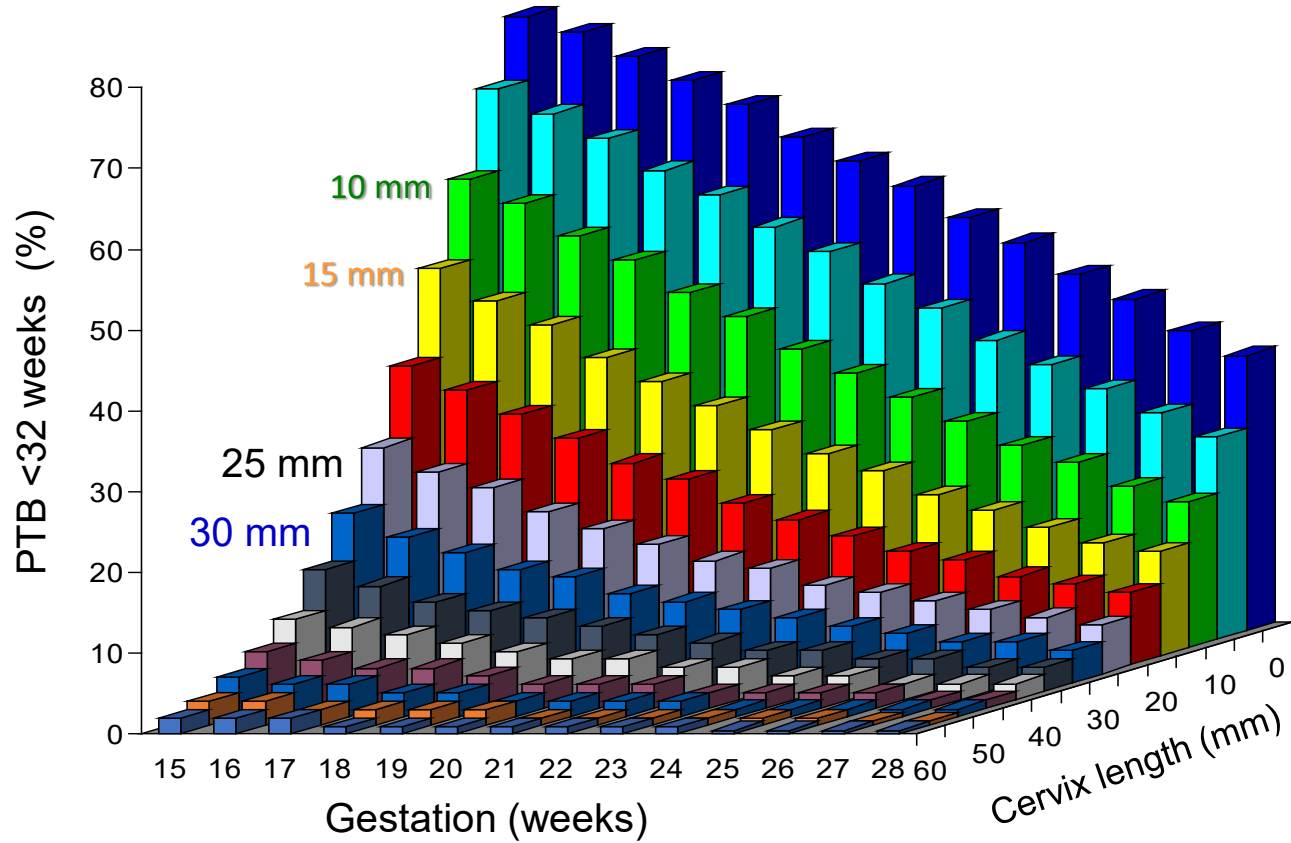


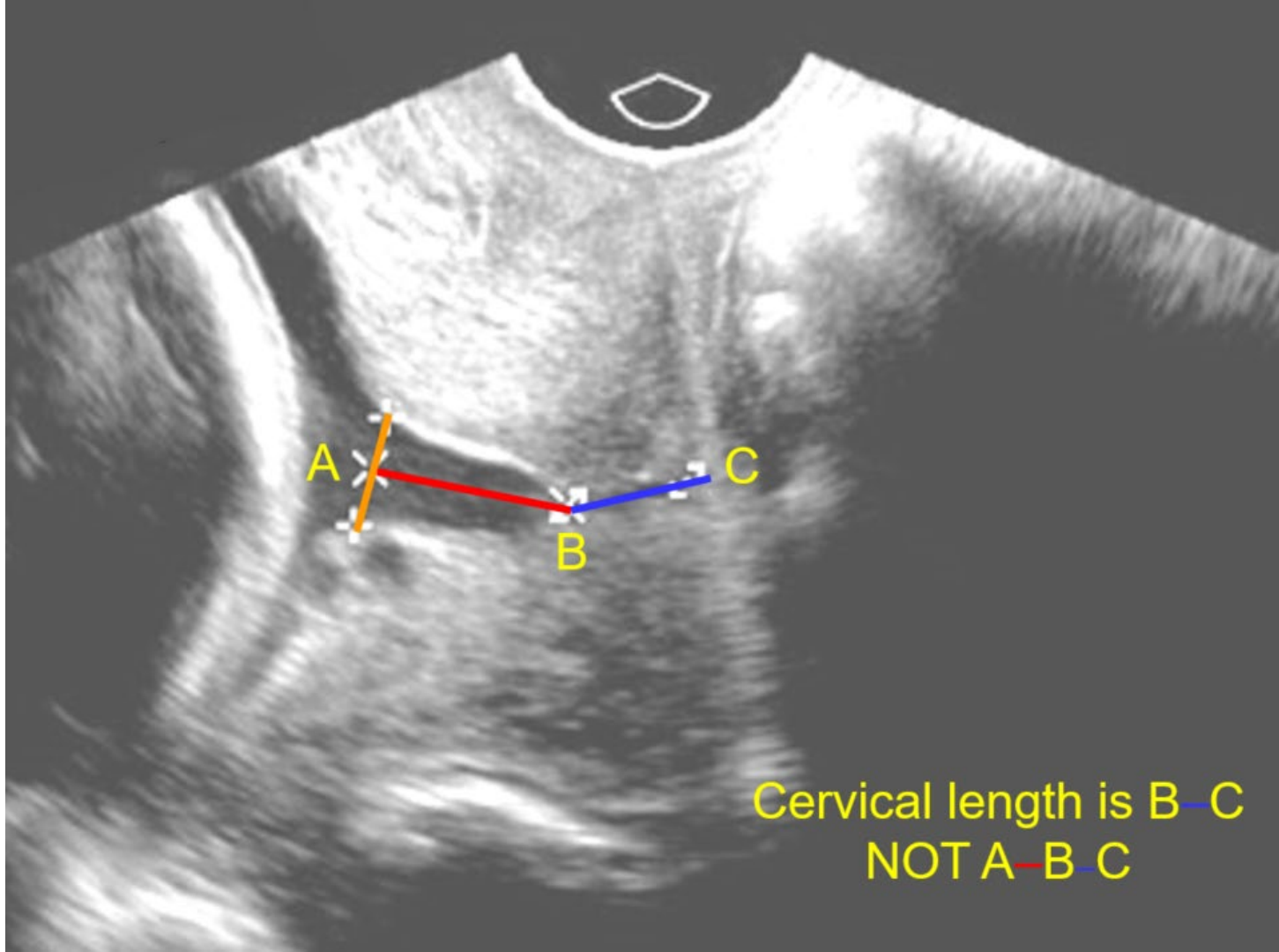


Vaginal Ultrasound at 22-24 Weeks Gestation and PTB <35 weeks



Gestational Age at Cervix Measurement and PTB Risk before 32 weeks (N= 2,601)





Cervical length is B-C
NOT A-B-C

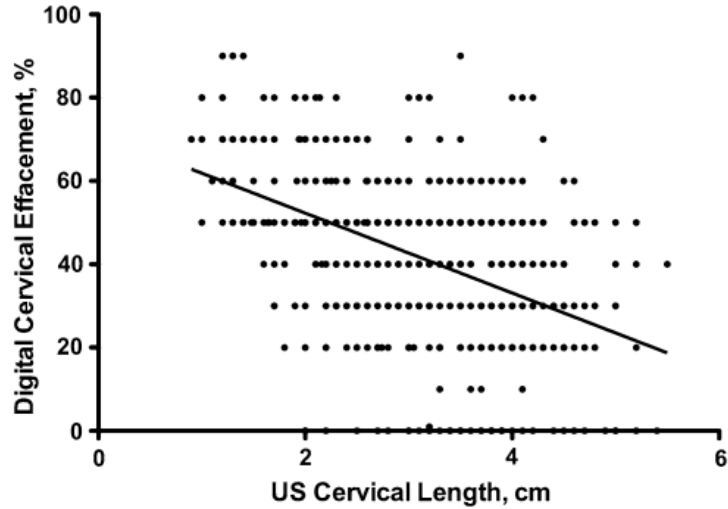
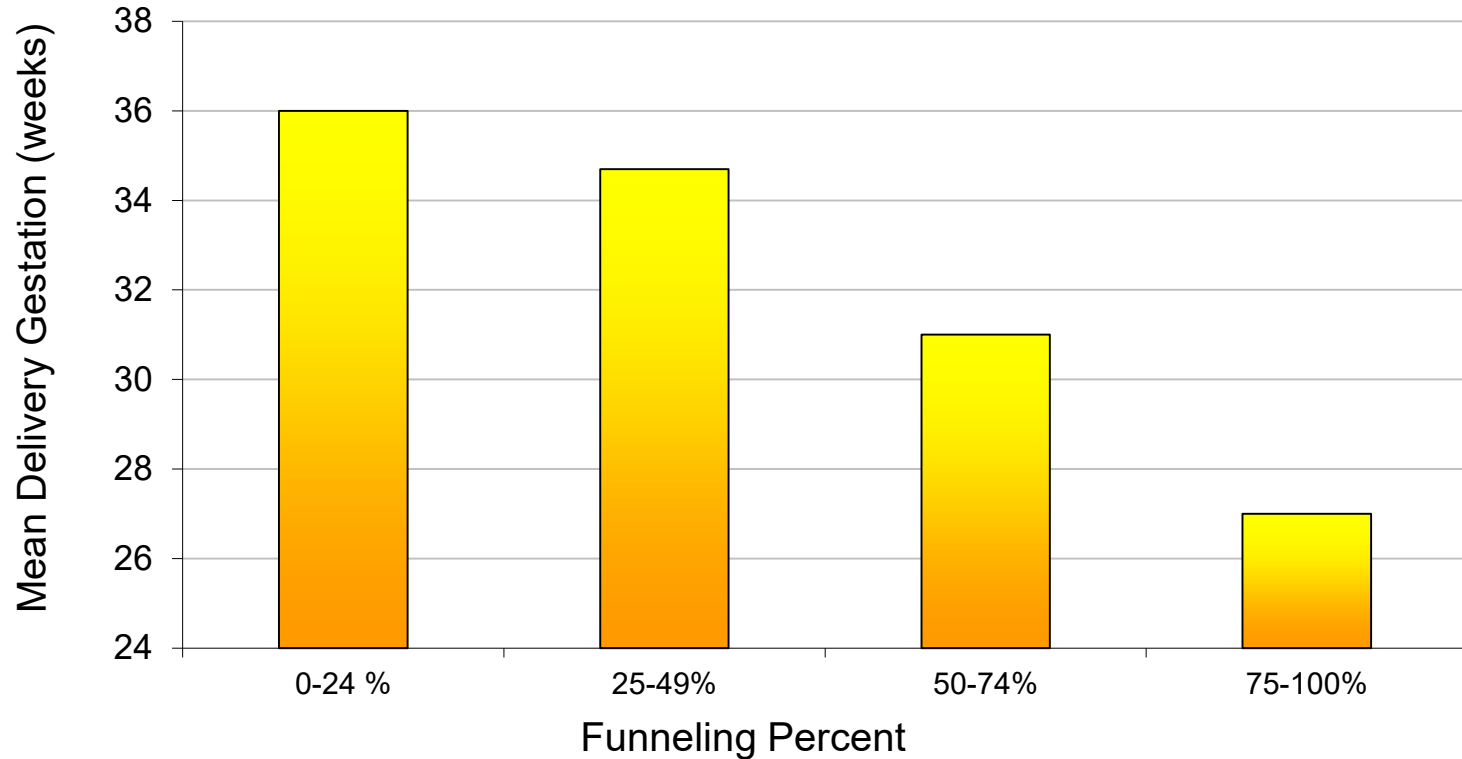


Fig. 1 Transvaginal ultrasound of cervical length compared to digital cervical effacement in 726 women demonstrates a significant linear relationship ($p < 0.001$) but poor correlation ($R^2 = 0.23$)

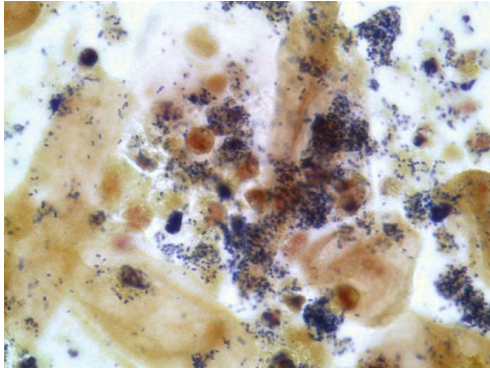
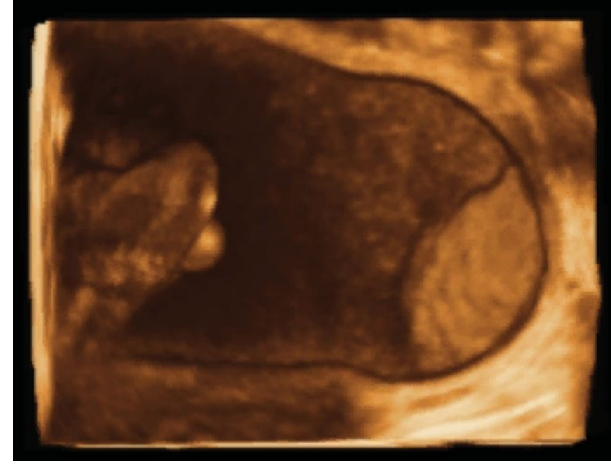


Cervical Funneling in Asymptomatic High-Risk Women

p = 0.049



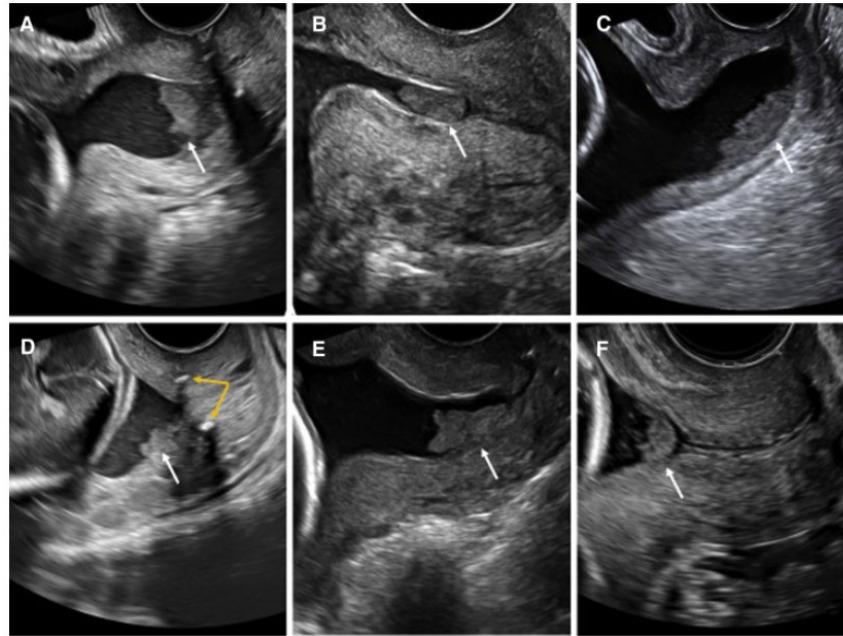
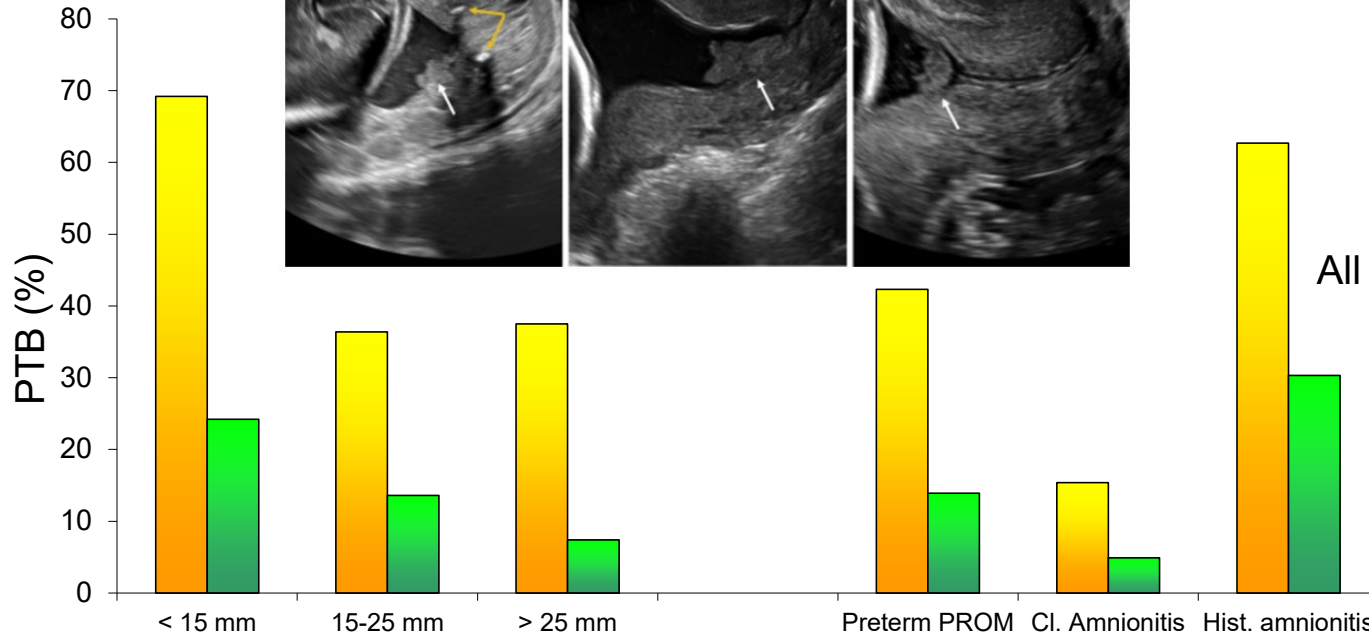
Amniotic Fluid Sludge



Amniotic Fluid Sludge

■ Sludge
■ No sludge

N = 281, Asymptomatic singletons at 13 – 29 weeks



All p-values < 0.05

Prevention of Spontaneous PTB



Screening & Interventions for PTB (ACOG 2021)

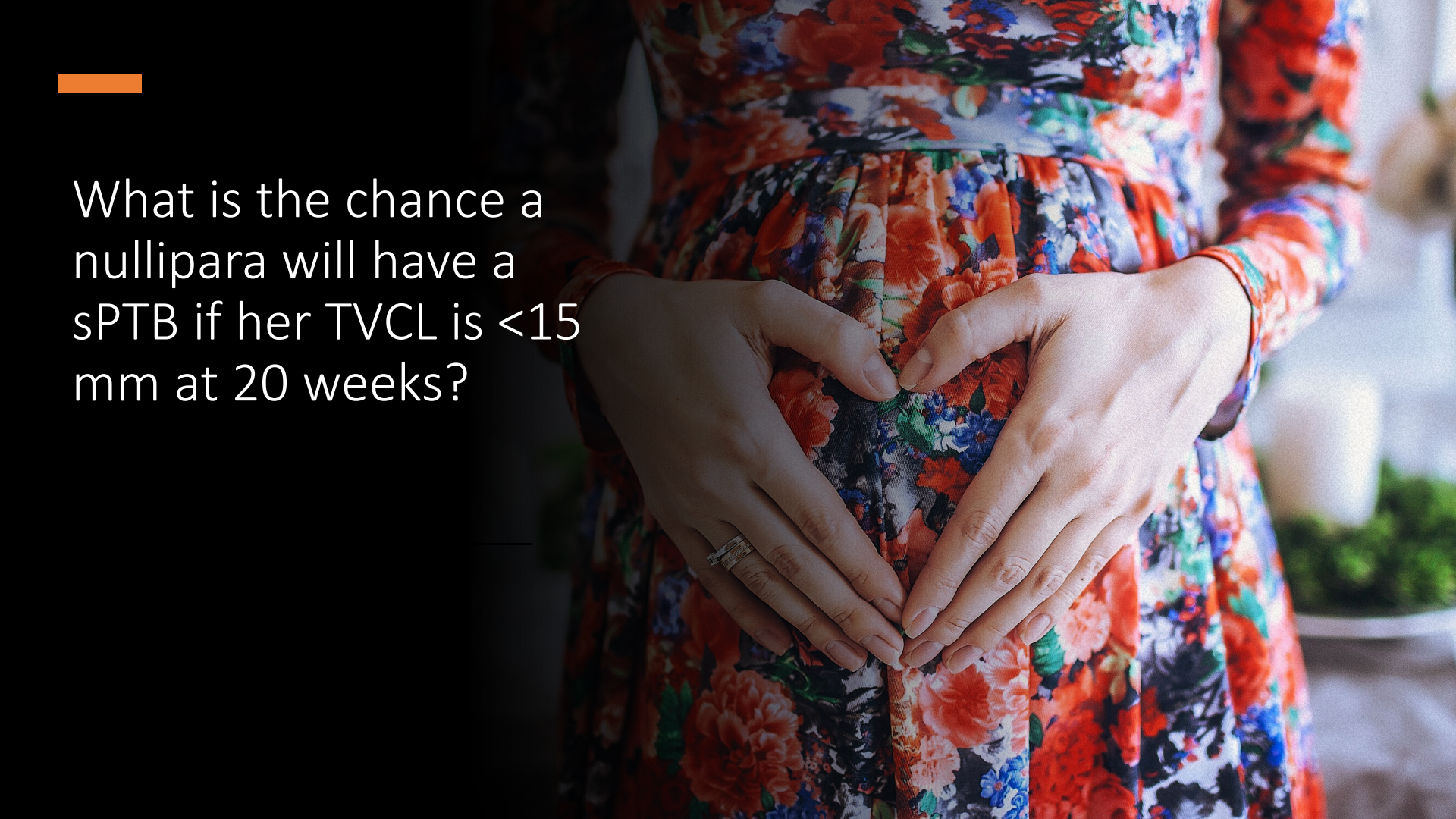
	CL Screen	Vaginal Prog	US-indicated Cerclage	Exam-indicated cerclage	Cervical Pessary, 17-OHP
Singleton, no prior sPTB	Single, at time of anatomy US	If TVCL <25 mm	Insufficient data, possible benefit if TVCL <10 mm	Consider	No
Singleton, with prior sPTB	Serial TVCL, 16-24.0w	Offer	Consider if TVCL <25 mm	Consider	No*
Multiple gestation	Single, at time of anatomy US	Insufficient data	Insufficient data	Consider	No

Singleton, No Prior sPTB

	CL Screen	Vaginal Prog	US-indicated Cerclage	Exam-indicated cerclage	Cervical Pessary, 17-OHP
Singleton, no prior sPTB	Single, at time of anatomy US	If TVCL <25 mm	Insufficient data, possible benefit if TVCL <10 mm	Consider	No

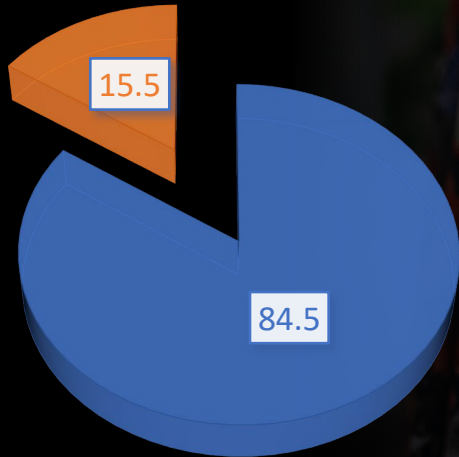
Singleton, No Prior sPTB

	CL Screen	Vaginal Prog	US-indicated Cerclage	Exam-indicated cerclage	Cervical Pessary, 17-OHP
Singleton, no prior sPTB	Single, at time of anatomy US	If TVCL <25 mm	Insufficient data, possible benefit if TVCL <10 mm	Consider	No

A pregnant woman wearing a vibrant, multi-colored floral dress is shown from the waist down. She is gently holding her belly with both hands. The background is softly blurred, showing a white candle and some greenery. The overall mood is calm and nurturing.

What is the chance a nullipara will have a sPTB if her TVCL is <15 mm at 20 weeks?

What is the chance a nullipara will have a sPTB if her TVCL is <15 mm at 20 weeks?





vaginal progesterone

200 mg micronized suppository daily

↓ risk of PTB before 34w
for low risk patients






vaginal progesterone

90 mg gel daily

↓ risk of PTB before 33w
for low risk patients



Singleton **With** Prior sPTB

	CL Screen	Vaginal Prog	US-indicated Cerclage	Exam-indicated cerclage	Cervical Pessary, 17-OHP
Singleton, with prior sPTB	Serial TVCL, 16-24.0w	Offer	Consider if TVCL <25 mm	Consider	No*

Updated Clinical Guidance for the Use of Progesterone Supplementation for the Prevention of Recurrent Preterm Birth

Practice Advisory ⓘ | April 2023

- Consider vaginal progesterone if cervix is short
- Vaginal progesterone is not proven effective in the absence of short cervix
- IM 17-OHPC is not recommended for primary prevention of recurrent sPTB

Original Investigation | Obstetrics and Gynecology

Association of Vaginal Progesterone Treatment With Prevention of Recurrent Preterm Birth

David B. Nelson, MD; Ashlyn Lafferty, BS; Chinmayee Venkatraman, BS; Jeffrey G. McDonald, PhD; Kaitlyn M. Eckert, BS; Donald D. McIntire, PhD; Catherine Y. Spong, MD

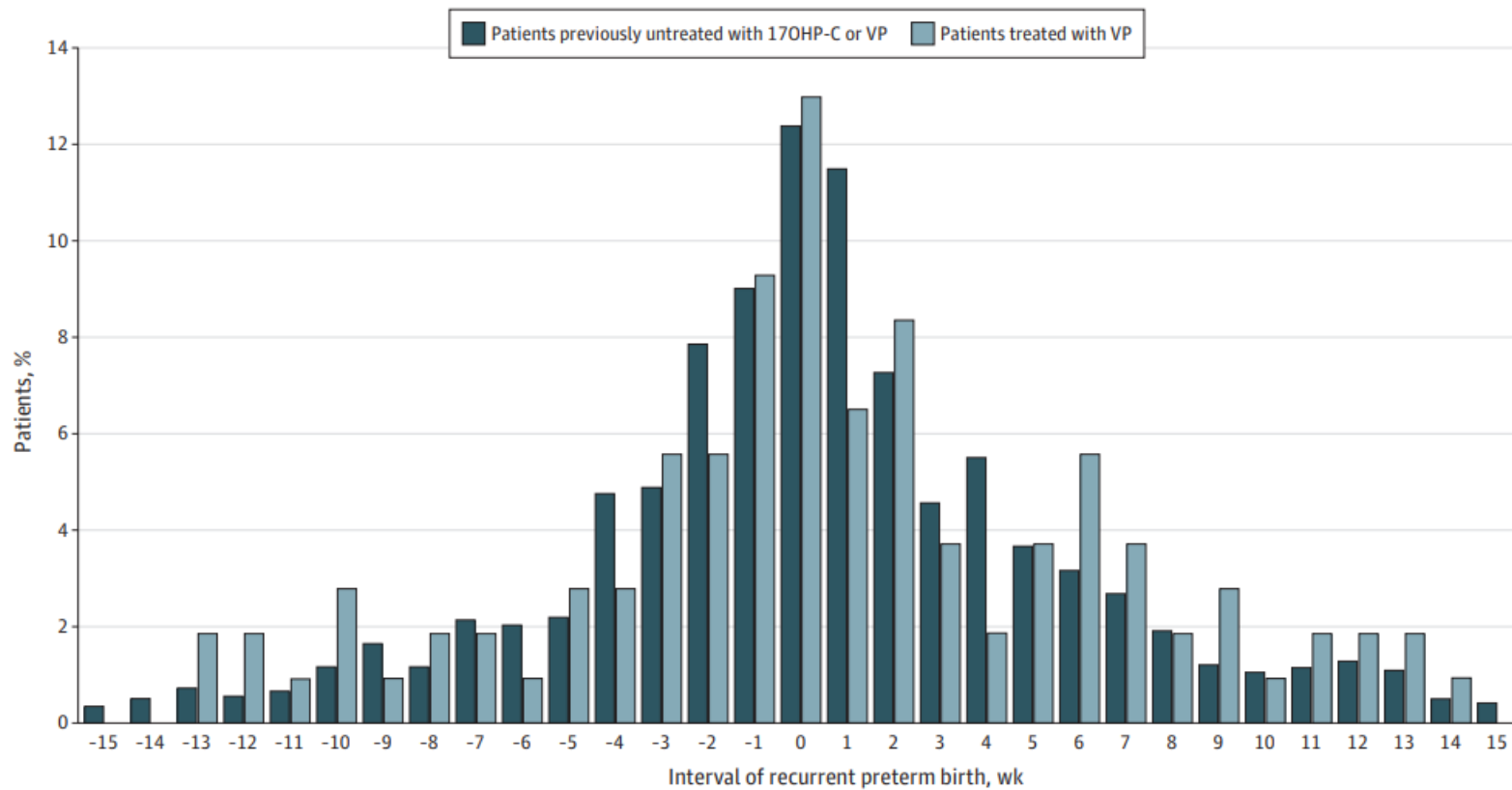
NO BENEFIT

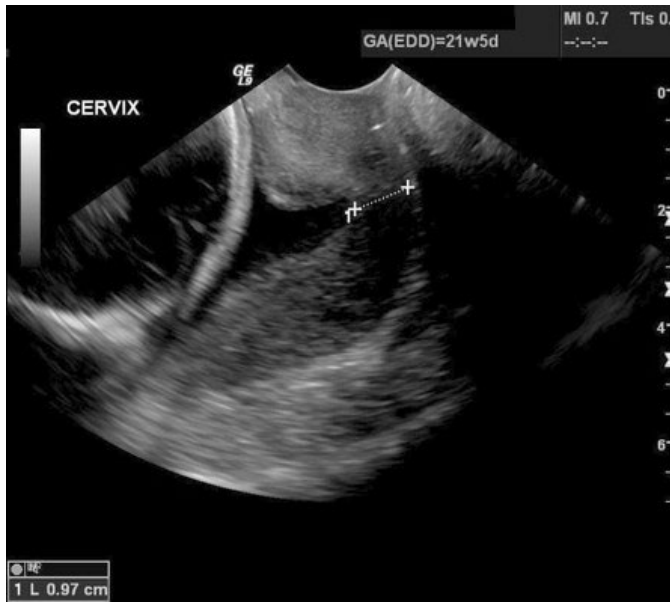
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Figure. Recurrent Preterm Birth From Proximate Birth Among Patients Treated With Vaginal Progesterone (VP) Compared With Matched Controls





Short Cervix

Preterm Labor

Clinical Presentation of Prior sPTB

Systematic Review
14 studies

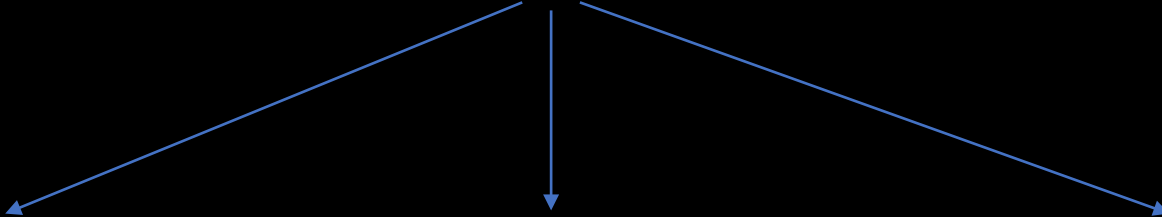
Pt at High Risk for PTB

Prior sPTB
LEEP or Cone



TVCL <25 mm

Before 24w




Sensitivity
65.4%

PPV
33.0%


NPV
92.0%

Multiple Gestation

	CL Screen	Vaginal Prog	US-indicated Cerclage	Exam-indicated cerclage	Cervical Pessary, 17-OHP
Multiple gestation	Single, at time of anatomy US	Insufficient data	Insufficient data	Consider	No

A pregnant woman with dark hair, wearing a white long-sleeved shirt with thin brown horizontal stripes, stands in a room. She is looking towards a mobile hanging over a wooden crib. Her right hand is near the mobile, and her left hand rests on the wooden railing of the crib. The room is brightly lit by a large window on the right, which shows a view of a building and a balcony. The overall atmosphere is calm and domestic.

What is the chance a
pt with twins will have
a sPTB if her TVCL is
<25 mm at 20 weeks?

A pregnant woman with dark hair, wearing a white and brown striped long-sleeved shirt, stands by a window. She is looking down and to the left with a thoughtful expression. Her right hand is near a mobile hanging over a crib, and her left hand rests on a wooden railing. The background shows a bright window with a view of a building outside.

What is the chance a
pt with twins will have
a sPTB if her TVCL is
<25 mm at 20 weeks?

75%

A pregnant woman with dark hair, wearing a white long-sleeved shirt with thin brown horizontal stripes, stands in a nursery. She is looking towards a mobile hanging over a wooden crib. Her right hand is resting on the railing of the crib, and her left hand is near the mobile. The room is dimly lit, with light coming from a window on the right. An orange horizontal bar is visible in the top left corner of the image.

What is her chance of
sPTB before 28w?

A pregnant woman with dark hair, wearing a white and brown striped long-sleeved shirt, stands in a nursery. She is looking towards a mobile hanging above a wooden crib. Her right hand is resting on the crib's railing, and her left hand is near the mobile. The room is brightly lit by a window on the right, showing a view of a building outside. A small orange horizontal bar is located in the top left corner of the image.

What is her chance of
sPTB before 28w?

25.8%



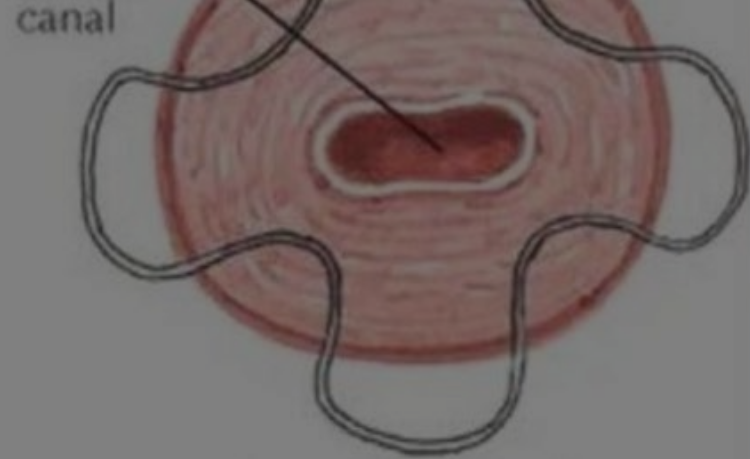
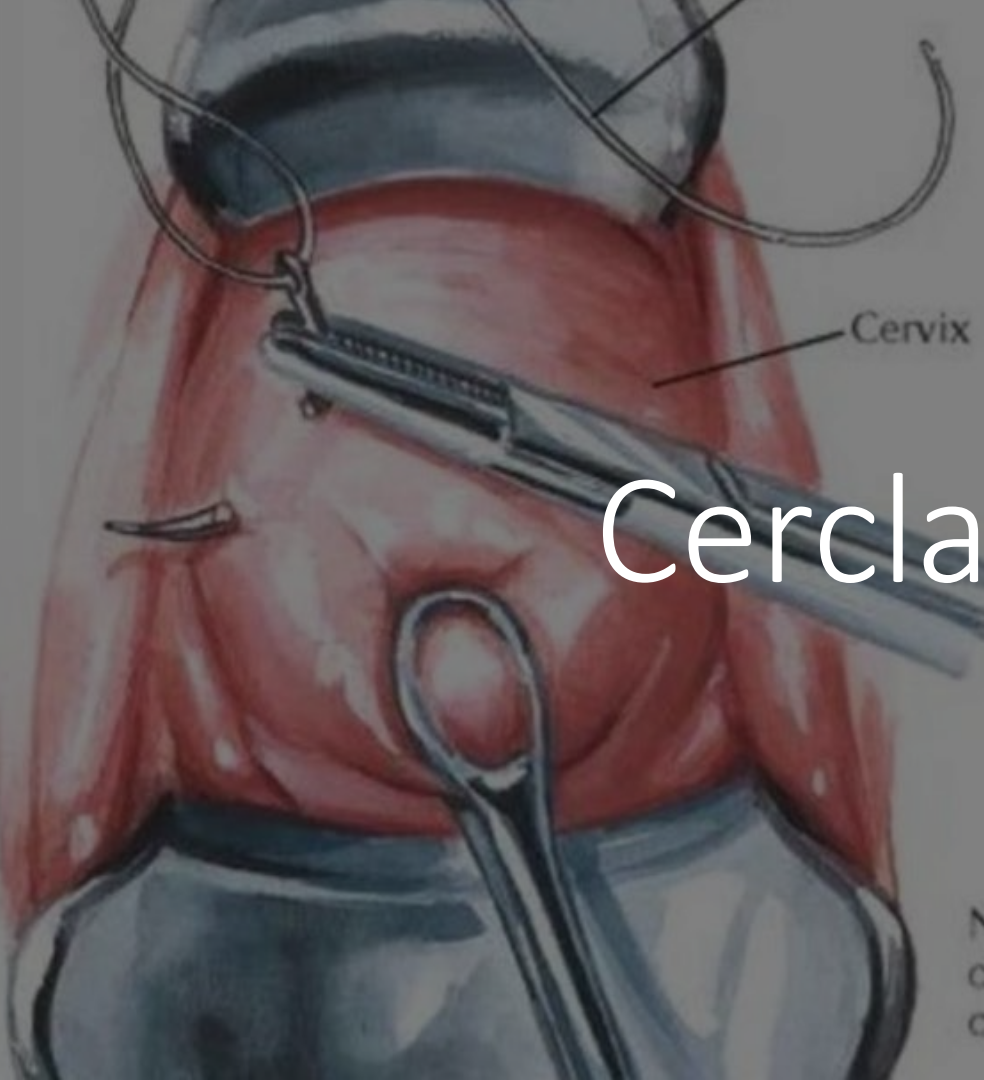
vaginal progesterone

various doses/preparations

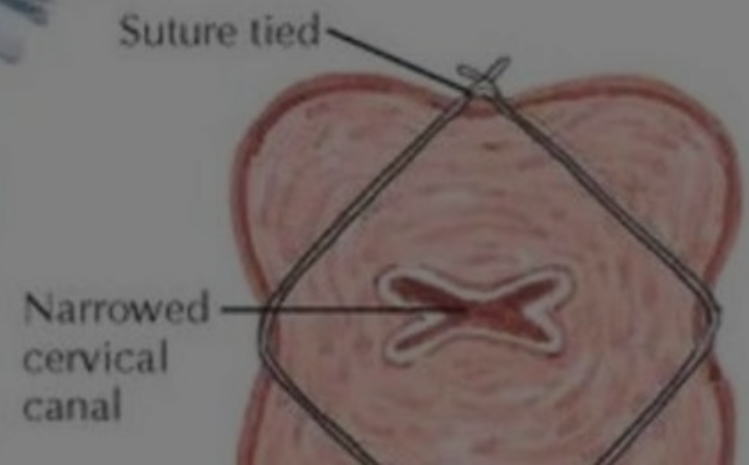
conflicting results



Cerclage



Purse-string (cerclage) suture prior to tying



Current Terminology

Cerclage Type	Replaced	Indication
History-indicated cerclage	Prophylactic cerclage Elective cerclage	Prior 2 nd tri losses and/or preterm births
Ultrasound-indicated cerclage		TVCL <25 mm with prior PTB TVCL <10 mm, no prior PTB
Physical exam-indicated cerclage	Rescue cerclage Emergency cerclage	Dilated cervix
Unindicated cerclage		None

Indications for Cerclage

(singletons)

History-Indicated

- Painless dilation leading to 2nd trimester birth
 - No PTL, PPROM or abruption
 - May have mild sx
- Prior cerclage for painless cervical dilation in the 2nd trimester

Ultrasound-Indicated

- Prior PTB before 34w
- AND
- TVCL <25 mm before 24w

Exam-Indicated

- Painless cervical dilation before viability

Cerclage Indication \neq Cervical Insufficiency

History-Indicated

- Painless dilation leading to 2nd trimester birth
 - No PTL, PPROM or abruption
 - May have mild sx

Indications for Cerclage

(singletons)

History-Indicated

- Painless dilation leading to 2nd trimester birth
 - No PTL, PPROM or abruption
 - May have mild sx
- Prior cerclage for painless cervical dilation in the 2nd trimester

Ultrasound-Indicated

- Prior PTB before 34w
- AND
- TVCL <25 mm before 24w

Exam-Indicated

- Painless cervical dilation before viability

Indications for Cerclage (singletons)

History-Indicated

- Painless dilation leading to 2nd trimester birth
 - No PTL, PPROM or abruption
 - May have mild sx
- Prior cerclage for painless cervical dilation in the 2nd trimester

- Place at 13-14 weeks
- Option: do serial TVCLs (ultrasound-indicated)

Indications for Cerclage (singletons)

- Contraindications:
Labor
Intraamniotic infection

Ultrasound-Indicated

- Prior PTB before 34w
AND
• TVCL <25 mm before 24w



Potential Indications for Cerclage (singletons)

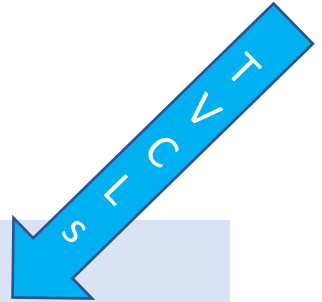
- Contraindications:
Labor
Intraamniotic infection

- TVCL <10 mm *without* a prior sPTB

Ultrasound-Indicated

- Prior PTB before 34w
AND
• TVCL <25 mm before 24w

- High risk for sPTB (conization, LEEP, uterine anomaly, etc.)
AND
• TVCL <25 mm before 24w



Indications for Cerclage (singletons)

- Contraindications
 - Labor
 - Infection
- Antibiotics/tocolytics
 - Indomethacin 50 mg postop q8h x 3 doses
 - Cefazolin 1-2 g (+/- 100 kg)

Exam-Indicated

- Painless cervical dilation before viability



Transabdominal Cerclage



Indications:

- Failed history-indicated or US-indicated cerclage (PTB <28w)
- Cervical cerclage technically impossible



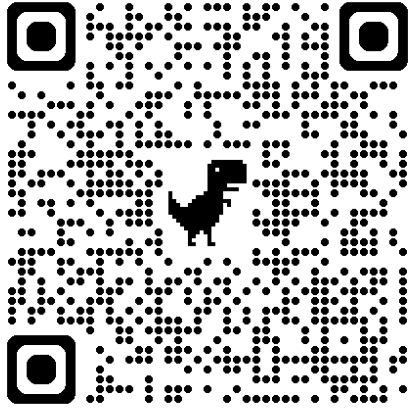
Interventions to Reduce PTB

- Pre-pregnancy weight modification
- Smoking cessation
- Treatment for SUD
- Contraception and interpregnancy interval >18 mos
- Screen for & treat lower genital tract infection
- Midwife-led continuity models of prenatal care
- Cerclage in appropriately selected patients
- Vaginal progesterone for nulliparas with TVCL <25 mm



Interventions that MAY Reduce PTB

- Manage miscarriage medically when possible
- Activity modification
- Treat depression



Thank you!

kbrackne@uthsc.edu

