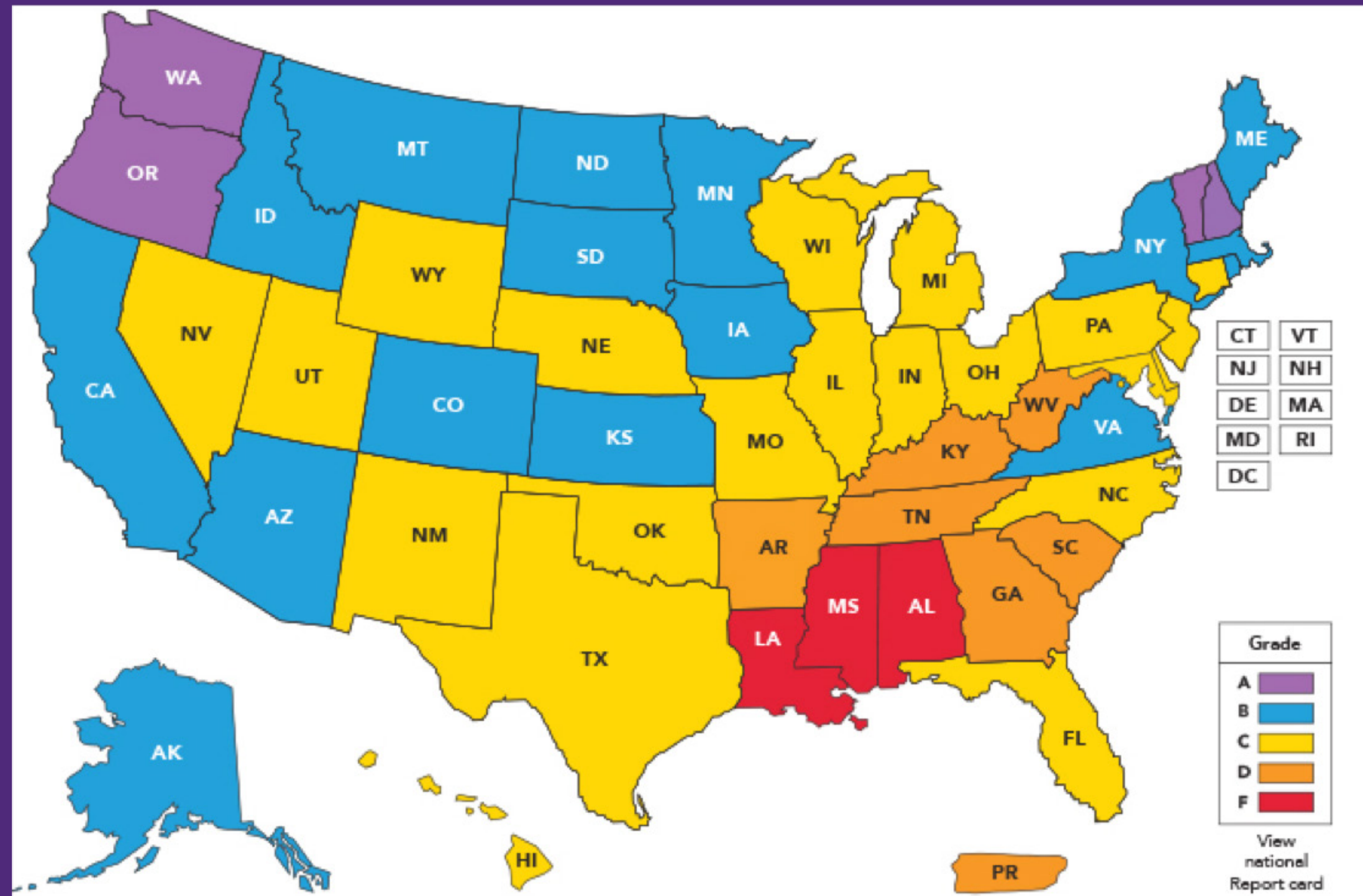


MARCH OF DIMES: 2016 PREMATURE BIRTH REPORT CARDS

Preterm birth increases in the U.S. for the first time in eight years!

The U.S. earned a
“C” grade



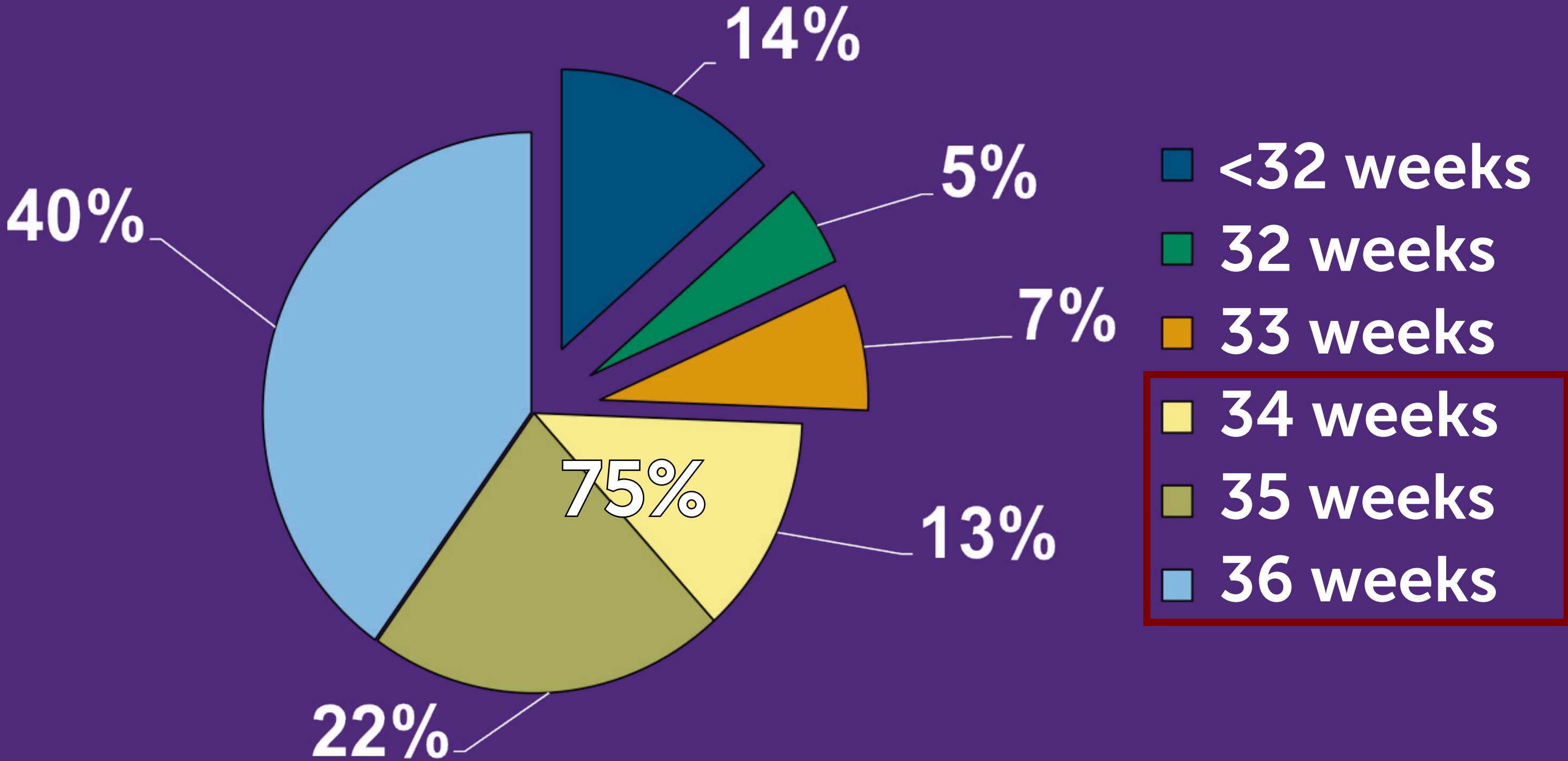
WHAT ARE THE CONSEQUENCES OF PTB?

- Health Impact
 - More than one-third of deaths during the first year of life are attributed to preterm birth-related causes
- Lifelong complications, including:
 - Developmental delays
 - Cerebral palsy
 - Chronic lung and vision problems

WHAT ARE THE CONSEQUENCES OF PTB? (CON'T)

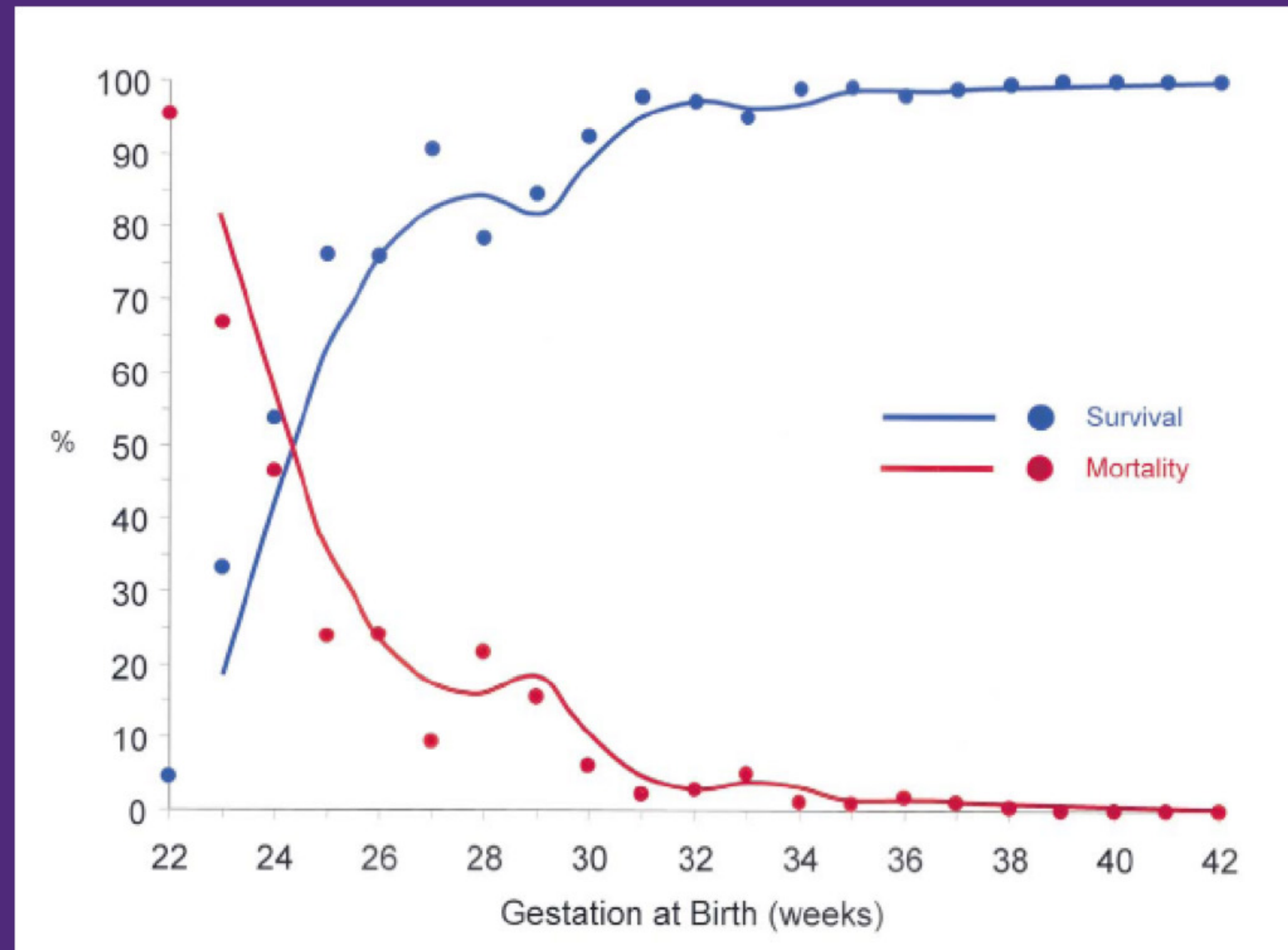
- Economic Impact
Annually, preterm birth costs:
 - An average of \$52,000 per premature infant
 - \$26 billion for the U.S.
 - Costs include health care, education and lost productivity
- U.S. preterm birth rate increased from 9.57 to 9.63 in 2015; then from 9.63 to 9.80 in 2016.
 - Rose for second year in a row!
 - 2017 rate?????

US PRETERM BIRTHS (SINGLETON)



"Vital Statistics Data Available Online." Data Access. Centers for Disease Control and Prevention, 14 May 2014. Web. 02 June 2014. Prepared by March of Dimes Perinatal Data Center, April 2006.

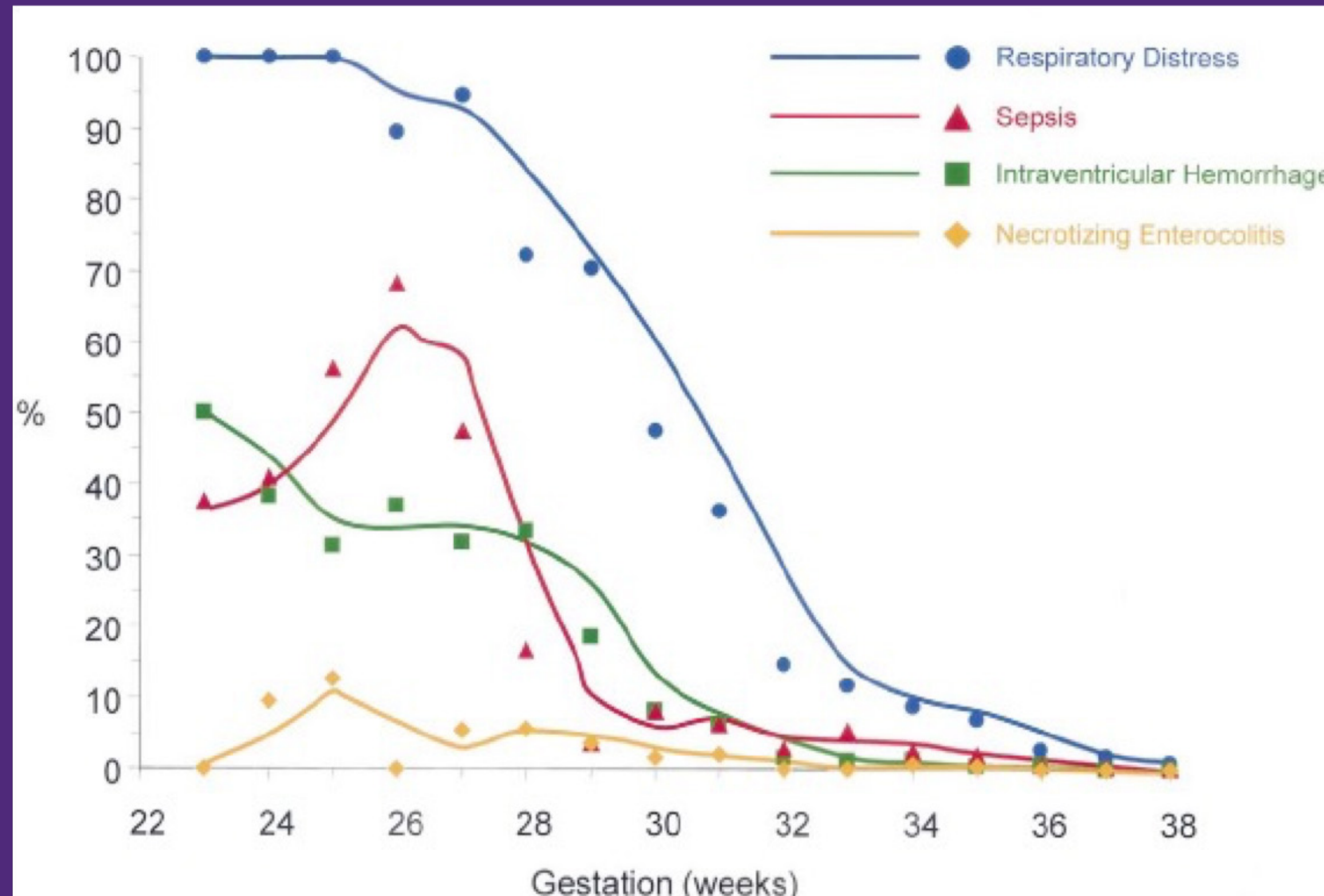
SURVIVAL BY GESTATIONAL AGE AMONG LIVE-BORN RESUSCITATED INFANTS



Results of a community-based evaluation of 8523 deliveries, 1997–1998, Shelby County, Tennessee

Mercer BM *Obstet Gynecol* 2003;101:178-93.

ACUTE MORBIDITY BY GESTATIONAL AGE AMONG SURVIVING INFANTS



Results of a community-based evaluation of 8523 deliveries, 1997–1998, Shelby County, Tennessee

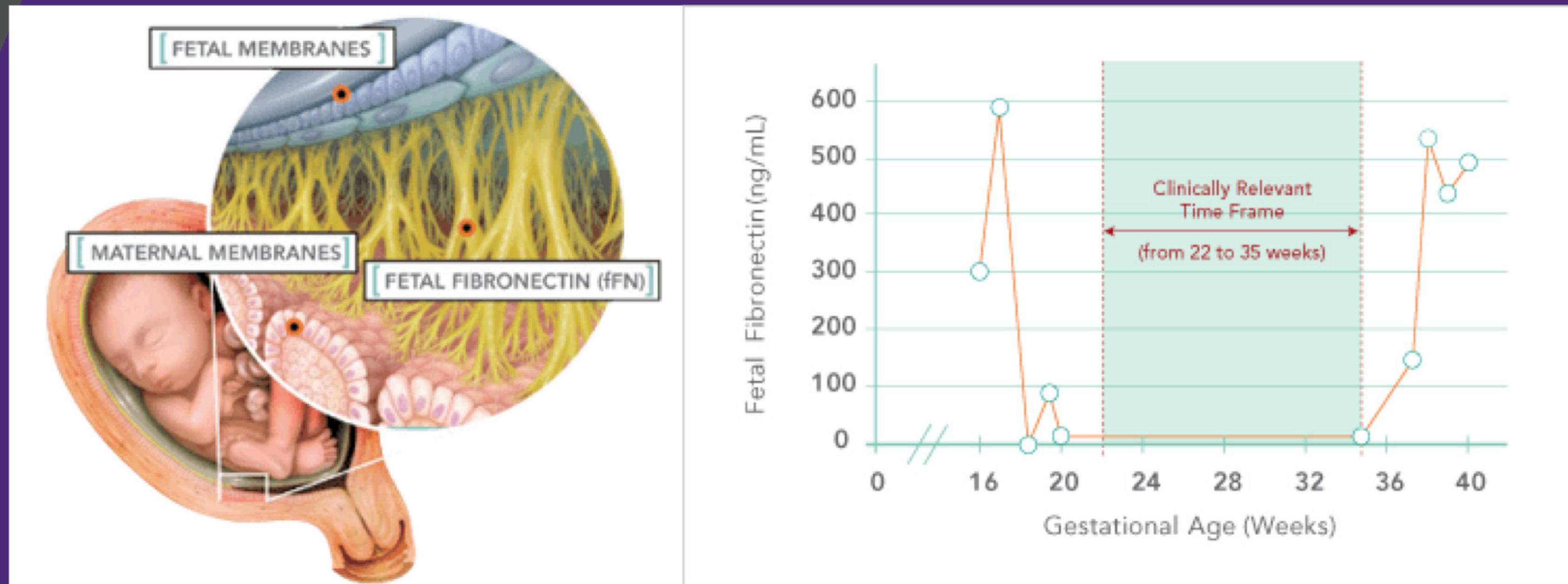
Mercer BM Obstet Gynecol 2003;101:178-93.

DHHS HEALTHY PEOPLE 2020

- Specific health objective: “Reduce preterm births”
- Sub-objectives:
 - Reduce total preterm births
 - Reduce late preterm or live births at 34 to 36 weeks gestation
 - Reduce live births at 32 to 33 weeks gestation
 - Reduce very preterm or live births at <32 weeks gestation
- Reduce annual cost of preterm birth in the U.S: \$51,000 per infant

FETAL FIBRONECTIN (fFN): CLINICAL RELEVANCE

Test performed between 22 and 34 weeks completed gestation



PREDICTIVE VALUES OF FETAL FIBRONECTIN

Sensitivity, Specificity, and Positive and Negative Predictive Values of Fetal Fibronectin for Delivery ≤ 7 and ≤ 14 Days among Symptomatic Women (n=763)^a

Delivery	n (%)	Sensitivity (95% CI)	Specificity (95% CI)	Pred Val + (95% CI)	Pred Val – (95% CI)
≤ 7 Days	22 (2.9%)	86.4% (66.4, 95.3)	82.3% (79.4, 84.9)	12.7% (4.2, 33.7)	99.5% (98.7, 99.8)
≤ 14 Days	30 (3.9%)	83.3% (66.3, 93.7)	82.9% (80.0, 85.4)	16.7% (7.3, 33.7)	99.2% (98.3, 99.6)

^aProportion of deliveries at each endpoint are calculated using 763 as the denominator

CLINICAL CASE #1: INITIAL PRESENTATION

Amy is a 26 y/o G2 P1001 @ 27 3/7 weeks with no significant medical history who presents to triage with back pain and contractions every 15 minutes. She is known not to have a previa. She is placed on continuous electronic fetal monitoring.

POLLING QUESTION #1: WHAT WOULD YOU DO NEXT?

- Vaginal exam
 - Using a sterile speculum exam to take swabs for:
 - Fetal fibronectin (fFN)
 - Group B streptococcus
 - Gonococcus
 - Chlamydia trachomatis
- Transabdominal ultrasound

CLINICAL CASE #1: CLINICAL COURSE (CON'T)

- Using a sterile speculum swabs were taken for:
 - Fetal fibronectin (fFN)
 - Group B streptococcus
 - Gonococcus
 - Chlamydia trachomatis
- On vaginal exam she was 1/60/-2
- Sterile vaginal ultrasound
- Transvaginal ultrasound was performed (TVUS)
- Cervical length (CL) is 3.1 cm

CLINICAL CASE #1: CLINICAL COURSE (CON'T)

- Amy is considered at low risk based on CL and absence of other symptoms of PTL
- No antenatal corticosteroids or other type of intervention is required
- fFN swab can be discarded as other factors were sufficient to make clinical decision
- Instructions provided to Amy to contact her physician and to be alert for any changes that might require medical attention

POLLING QUESTION #2: **WHAT WOULD YOU DO NEXT?**

- Antenatal corticosteroids
- Magnesium sulfate for neuroprotection
- Send fFN swab for more information

CLINICAL CASE #1: CLINICAL COURSE (CON'T)

- **Perform/send out fFN swab for testing**
- If fFN test returns negative, discharge Amy to home
- If the fFN test returns positive, consider:
 - Antenatal corticosteroids
 - No tocolysis required
 - 24-hour admission for observation, or
 - Next morning return for second corticosteroid injection

CLINICAL CASE #1: CLINICAL COURSE (CON'T)

- Consider:
 - Antenatal corticosteroids
 - No tocolysis required
 - 24-hour admission for observation, or
 - Next morning return for second corticosteroid injection
- fFN swab can be discarded as other factors were sufficient to make clinical decision

CLINICAL CASE #1: CLINICAL COURSE (CON'T)

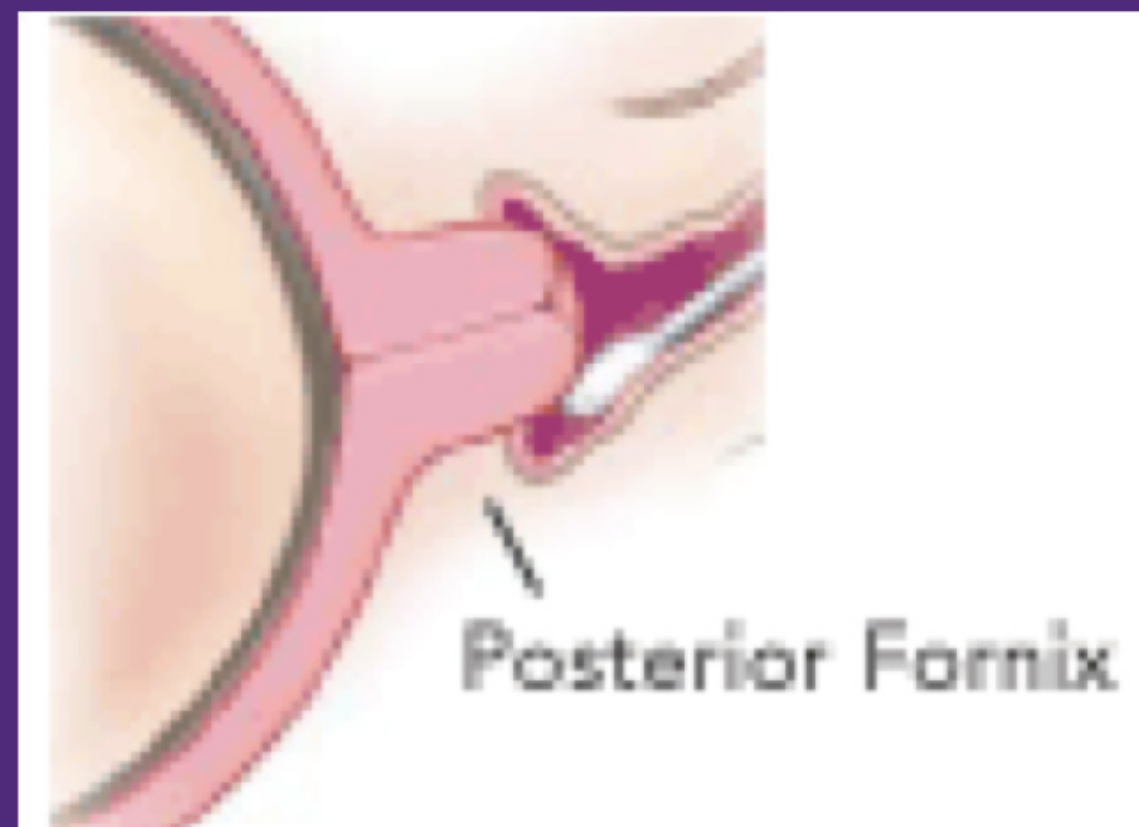
- Moreover:
 - If Amy's cervix was originally dilated ≥ 3 cm or $>80\%$ effaced during the sterile vaginal exam, she should be admitted to L&D
 - If Amy's cervix was originally dilated 2 to 3 cm, repeat the sterile vaginal exam in 30 to 60 minutes
 - If cervical change, move Amy to L&D
 - If no cervical change, perform TVUS and continue prior clinical algorithm

fFN ALGORITHMS IN PTB: A BROAD CONSENSUS

Source	Cervical Dilation	Cervical Length	fFN Test with TVU
Professional Society Guidance			
ACOG Practice Bulletin 171 (2016)	No guidance	No guidance	“The positive predictive value of a positive fetal fibronectin test result or a short cervix alone is poor and should not be used exclusively to direct management in the setting of acute symptoms”
ACOG Practice Bulletin 130 (2012)	No guidance	No guidance	Does not recommend fFN use for screening in asymptomatic women
SMFM	No guidance	20-29 mm	“fFN seems to be most helpful for women with a ‘borderline’ TVU CL of 20 to 29 mm”
Expert Opinion			
Lockwood 2017 (UpToDate)	<3 cm	20-30 mm	Yes
Published Algorithms			
Rose 2010	<2 cm	16-29 mm	Yes
Ness 2077	≤3 cm	20-29 mm	Yes
Iams 2003 (clinical + sonography data equivocal)	≤2 cm	20-30 mm	Yes
Iams 2003 (clinical + sonography data in conflict)	<3 cm and has changed	<35 mm	Yes

ENSURING VALID RESULTS WHEN TESTING FOR fFN

- **DO NOT** contaminate swab with any lubricants
- **DO NOT** use if sexual intercourse 24 hrs prior
- **DO NOT** use if moderate/gross blood present
- **DO NOT** use with advanced cervical dilation, >3cm
- **DO NOT** use with PPROM
- **DO NOT** use in placenta previa or abruption



CLINICAL CASE #2: INITIAL PRESENTATION

Cheryl is a 31 y/o G1 P0 @ 30 1/7 wks presenting to her community hospital c/o CTX. She has an unremarkable medical history and pregnancy course. She does not complain of leaking fluid. Her vital signs are WNL. Her medical history is unremarkable.

Continuous electronic fetal monitoring is begun.

CLINICAL CASE #2: INITIAL PRESENTATION

- Using a sterile speculum swabs were taken for:
 - Fetal fibronectin (fFN)
 - Group B streptococcus
 - Gonococcus
 - Chlamydia trachomatis
- Sterile vaginal exam performed
 - If no contractions/cervix not dilated, discharge; if dilated ≥ 3 cm, admit to L&D
- fFN swab can be discarded as other factors sufficient for clinical decision

What could you do if dilation is < 3 cm with contractions $> q15$ and no TVUS currently available?

POLLING QUESTION #3: WHAT WOULD YOU DO NEXT?

- Admit for observation
- Admit for antenatal corticosteroids and magnesium sulfate
- Send fFN test

CLINICAL CASE #2: CLINICAL COURSE (CON'T)

- **Send fFN swab for test**
- If fFN negative
 - Discharge Cheryl to home
 - Instruct that if contractions persist, F/U in clinic within week
- If fFN positive
 - Assess clinically if contractions persist, consider admission for corticosteroid or other intervention
 - If admitted, consider TVUS when available
 - If contractions cease or CL determined to be ≥ 3 cm, assess for near-term clinical risk and discharge if warranted

WHAT ARE THE LEARNING POINTS DEMONSTRATED BY THESE CASES?

- **When TVUS is available, incorporation of fFN results is:**
 - Not necessary if CL ≥ 3 cm, risk for PTB is very low, patient can be discharged
 - Valuable when CL 1.6 – 2.9 cm
 - Negative: discharge
 - Positive: manage to reduce PTB risk
 - Not necessary, if CL ≤ 1.5 cm, risk of PTB is very high, patient should be managed
- When TVUS is not available, fFN testing alone can help in decision making, especially if negative

ECONOMICS OF INCLUDING fFN ASSESSMENT IN PTB

- Giles and colleagues performed an 18-month prospective audit of fFN in 9 referral hospitals and one university maternal-fetal medicine unit (N=151 patients):

Overall, 90% of patients admitted to a referring hospital with threatened PTL and who had a negative fFN were not transferred, with cost savings of \$30,297

- Joffe and colleagues evaluated the impact of fFN testing:

Reported a significant reduction in the number of admissions, number of prescriptions for tocolytics, and LOS, with an estimated cost savings of \$486,000 over the 12 month study period

Giles W, Bisits A, Knox M, Madsen G, Smith R. *Am J Obstet Gynecol.* 2000;182:439-442; Joffe GM, Jacques D, Bemis-Heys R, Burton R, Skram B, Shelburne P. *Am J Obstet Gynecol.* 1999;180(3 Pt 1):581-586.

ECONOMICS OF INCLUDING fFN ASSESSMENT IN PTB (CON'T)

- Rose and colleagues conducted a 12-month retrospective observational study to look at the effect of a standardized evidence-based protocol for PTL evaluation on outcomes and resource use:

All 201 patients underwent triage evaluation per protocol with a combination of fFN and CL measurement. The hospital admission rate was reduced by 56% compared with the previous year, in which no standardized algorithm was used for PTL assessment.

This resulted in a total yearly cost savings of \$39,900.

ECONOMICS OF INCLUDING fFN ASSESSMENT IN PTB (CON'T)

- van Baaren and colleagues evaluated the cost-effectiveness of combining CL measurement and fFN for symptomatic women between 24 and 34 weeks gestation:

The authors concluded that fFN testing saved between €2.4 and 7.6 million per year compared with treating all symptomatic patients, resulting in a cost savings of €3,919 per patient.

van Baaren GJ, Vis JY, Wilms FF, et al. Ultrasound Obstet Gynecol. 2017 Mar 31 [Epub ahead of print].

ECONOMICS OF INCLUDING fFN ASSESSMENT IN PTB (CON'T)

- While multiple guidelines recommend the use of fFN testing under specified conditions, and there are both clinical and economic examples of benefit, available medical literature also presents conflicting results regarding the utility of fFN testing
- In a recent systematic review and meta-analysis of randomized clinical trials, women who underwent fFN testing experienced:
 - No difference in the incidence of preterm birth at <37; 34; 32 and 28 weeks of gestation
 - No differences in the number of delivery within 7 days, and gestational age at delivery
 - No difference in the rate of maternal hospitalization, in the use of tocolysis, antenatal steroids, in the mean time in the triage unit
 - No differences in neonatal outcomes
 - Management based on fFN test required higher hospitalization charges

Berghella V, Saccone G. Am J Obstet Gynecol. 2016;215:431-8.

LIMITATIONS

- Meta-analysis may have been underpowered
- Included studies were designed differently
 - Inconsistent application of fFN testing
 - Lack of adherence to standard protocols for PTL/PTB management
 - 3 studies used fFN as part of the protocol
 - Inappropriate use of fFN to positively identify women who will have a spontaneous PTB

Heyborne, KD. Letters to the Editors. Am J Obstet Gynecol. 2017;217:94

VALUE OF UNIVERSAL SCREENING

- Prospective cohort of nulliparous women (n= 9,410)
- Serial transvaginal cervical length and quantitative measurement of fetal fibronectin were performed during 2 study visits 4 or more weeks apart
- Results:
 - 474 PTB
 - Cervical length of 25mm or less occurred in 8.0% at 16 to 22 weeks and 23.3% at 22 to 30 weeks gestation
 - Fetal fibronectin levels of 50 ng/mL or greater at 16 to 22 weeks identified 7.3% and 8.1% at 22 to 30 weeks

Esplin, M.S. JAMA. 2017;317:1047-1056

THREE ESSENTIALS TO OPTIMIZING THE VALUE OF fFN TESTING IN ASSESSMENT OF RISK FOR PTB

- fFN testing is most valuable as a tool to help identify which women are at low risk for spontaneous PTB among those that present with symptoms of PTL.
- The lack of strict adherence to diagnostic and treatment protocols, as well as the expansion of the use of fFN beyond its core assessment strength, has resulted in literature-based evidence that has confounded understanding of the proper role of fFN testing.
- This has likely diminished fFN testing as a diagnostic tool in clinical settings, and is symptomatic of the failure to consistently employ algorithmic protocols when diagnosing a women's risk for PTB.

To download the algorithms mentioned in this activity,
please click on the link below.

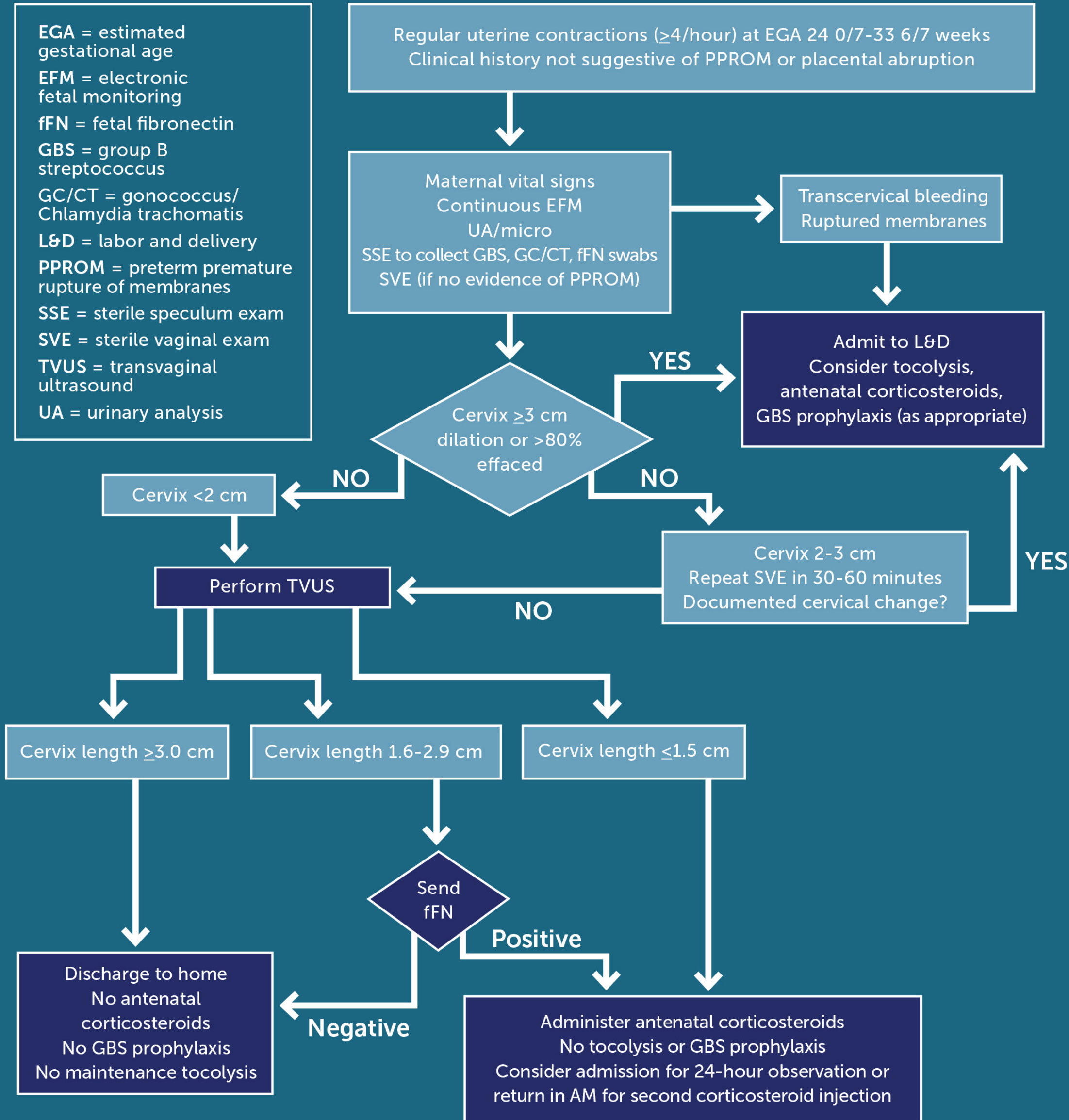
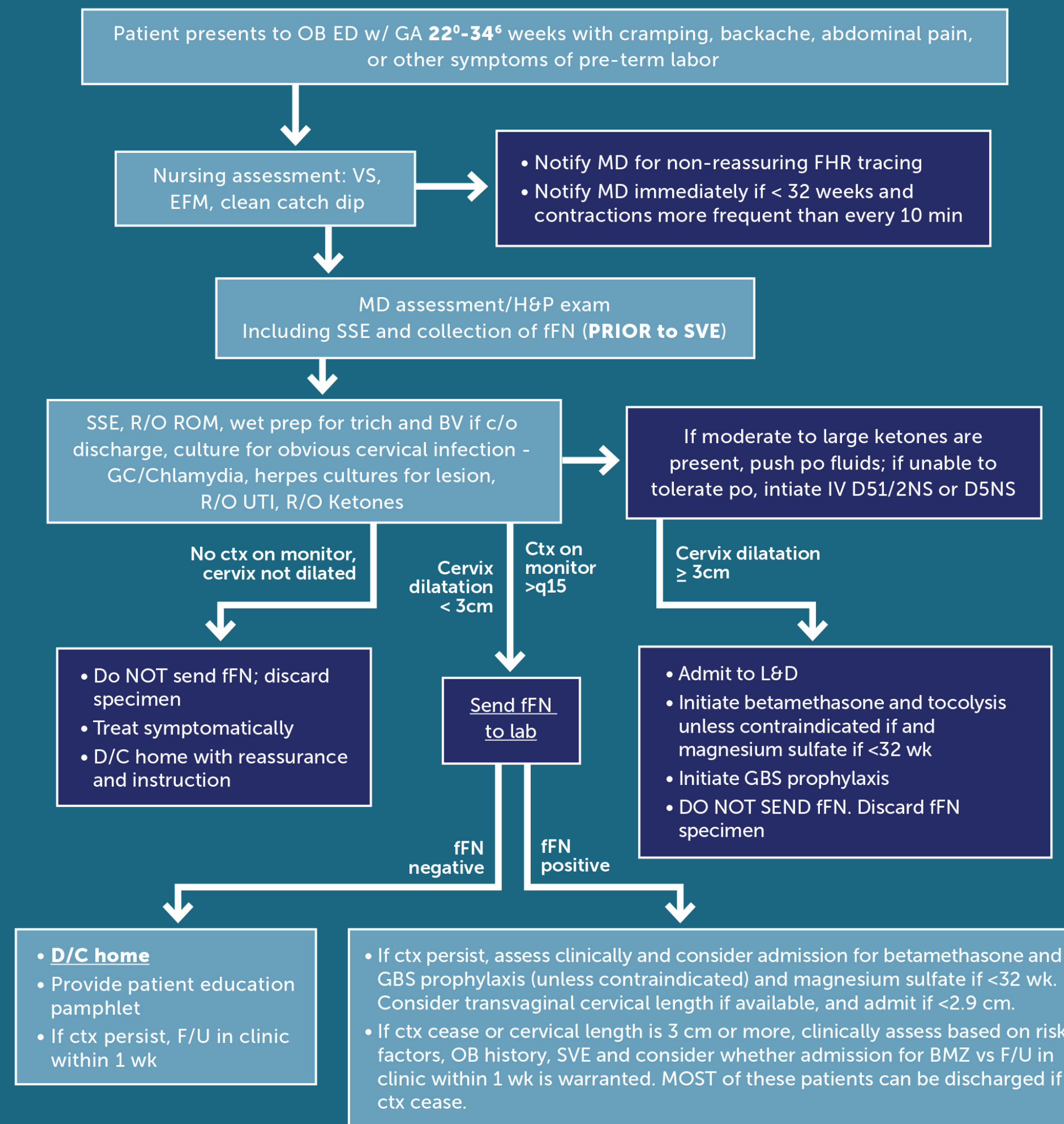


Figure 1
Protocol for Evaluation of Preterm Labor: Combined use of fFN + TVUS

(Permission granted by Rose, Mayo Clinic)

SUSPECTED PRETERM LABOR 22⁰-34⁶ WEEKS



BMZ = betamethasone
ctx = contractions
D/C = discharge
D&C = dilation and curettage
D51/2NS = dextrose 5% in 0.45% saline (crystalloid)
D5NS = dextrose 5% in 0.9% saline (crystalloid)
ED = emergency department

EFM = electronic fetal monitoring
FHR = fetal heart rate
fFN = fetal fibronectin
F/U = followup
GA = gestational age
GBS = group B streptococcus
GC = gonococcus
H&P = history and physical

MD, doctor, OB = obstetric
po = per orum
R/O = rule out
ROM = rupture of membranes
SSE = sterile speculum exam
SVE = sterile vaginal exam
UTI = urinary tract infection
VS = vital signs