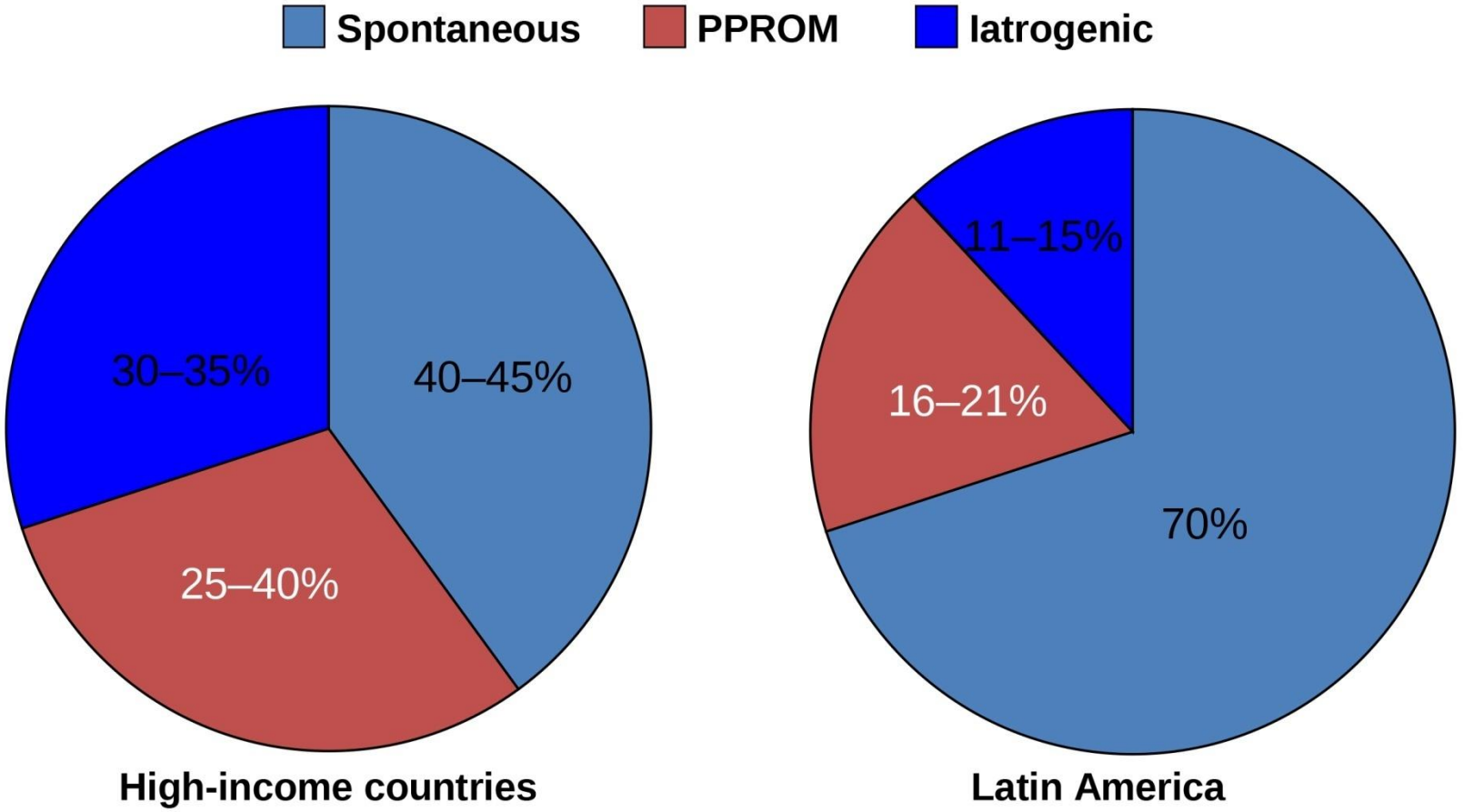
Preterm Labour

- 7-12 % of all deliveries.
- Accounts for > 85% of perinatal mortality and morbidity.

The majority of preterm births are spontaneous



Gravett MG, et al. BMC Pregnancy and Childbirth 2010;10(Suppl 1):S2. (Link)

Preterm Labor

-The occurrence of regular uterine contraction associated with cervical changes (dilatation &effacement) after the age of viability and before 37 completed wks from the last menstrual period.

-Threatened PTL---regular uterine contractions but no evidence of cx changes.

Preterm Labor

The World Health Organization (WHO) defines preterm birth as being born before 37 weeks of gestation

Preterm births (PTB) can be subdivided into categories according to gestational age

- Preterm category Gestational age (weeks)

Moderately	33–36
Very	<32
Extremely	<28

Three categories of preterm birth

Iatrogenic

Medically indicated

Maternal complications
- severe hypertension
- abruptio placentae

Endangered fetus
- IUGR
- Fetal distress

PPROM

Preterm premature rupture of membranes

- Rupture of amniotic membranes prior to the onset of labour <37 weeks' gestation
- Infection usually the main cause

Spontaneous

Idiopathic

- Birth occurs after preterm labour
- Risk factors include obstetrical history, social factors and lifestyle

IUGR=intrauterine growth restriction

Moutquin JM, et al. BJOG 2003; 110(Suppl 20):30–33. (Link)

Risk Factors

- Maternal characteristics:
  - -Age ⇨ Lowest 25-29 years
    Highest < 15 or first child
    > 35 yrs.
  - -Race ⇨ Twice in blacks
  - -weight ⇨ 3 fold increase if <50kg.
  - -Habits ⇨ smoking, alcohol, coitus

Risk Factors---cont

- Past Reproductive History:
  - -Previous history
  - -History of abortions(2nd trimester)
  - -Uterine abnormalities.
  - -Previous pregnancy bleeding.

Risk factors---cont

- **Present Pregnancy complications:**

  -Uterine over distention.

  -Congenital abnormalities: multiple,cns,renal

  -APH or threatened abortion

  -Maternal illness

  -Miscellaneous –retained IUCD

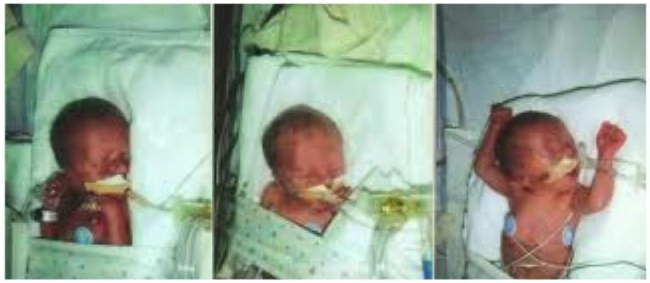
  - IUFD -PROM

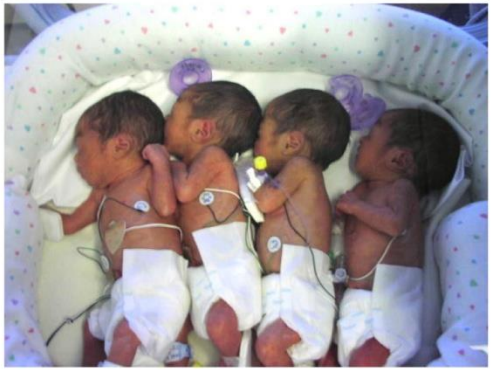
- **Genital tract infection.**

Multiple pregnancy is the biggest single risk factor for preterm birth

- 15–20% of all preterm births are from multiple pregnancies
- 60% of twins are born preterm
  - 40% have spontaneous labour or PPROM before 37 weeks' gestation
  - 20% indicated preterm delivery

- Nearly all higher multiple gestations result in preterm birth

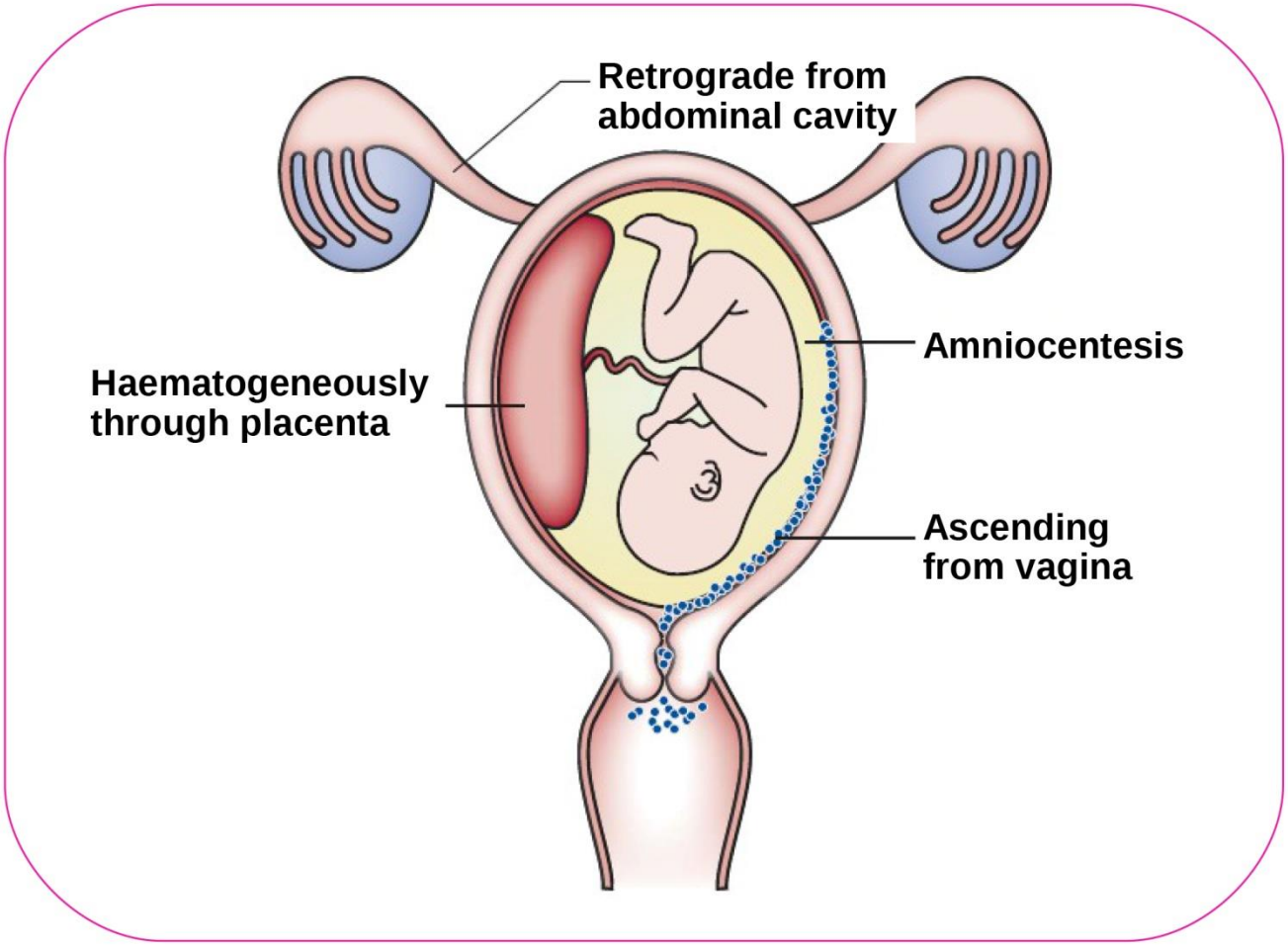




Goldenberg RL, et al. Lancet 2008;371:75–84. (Pubmed)

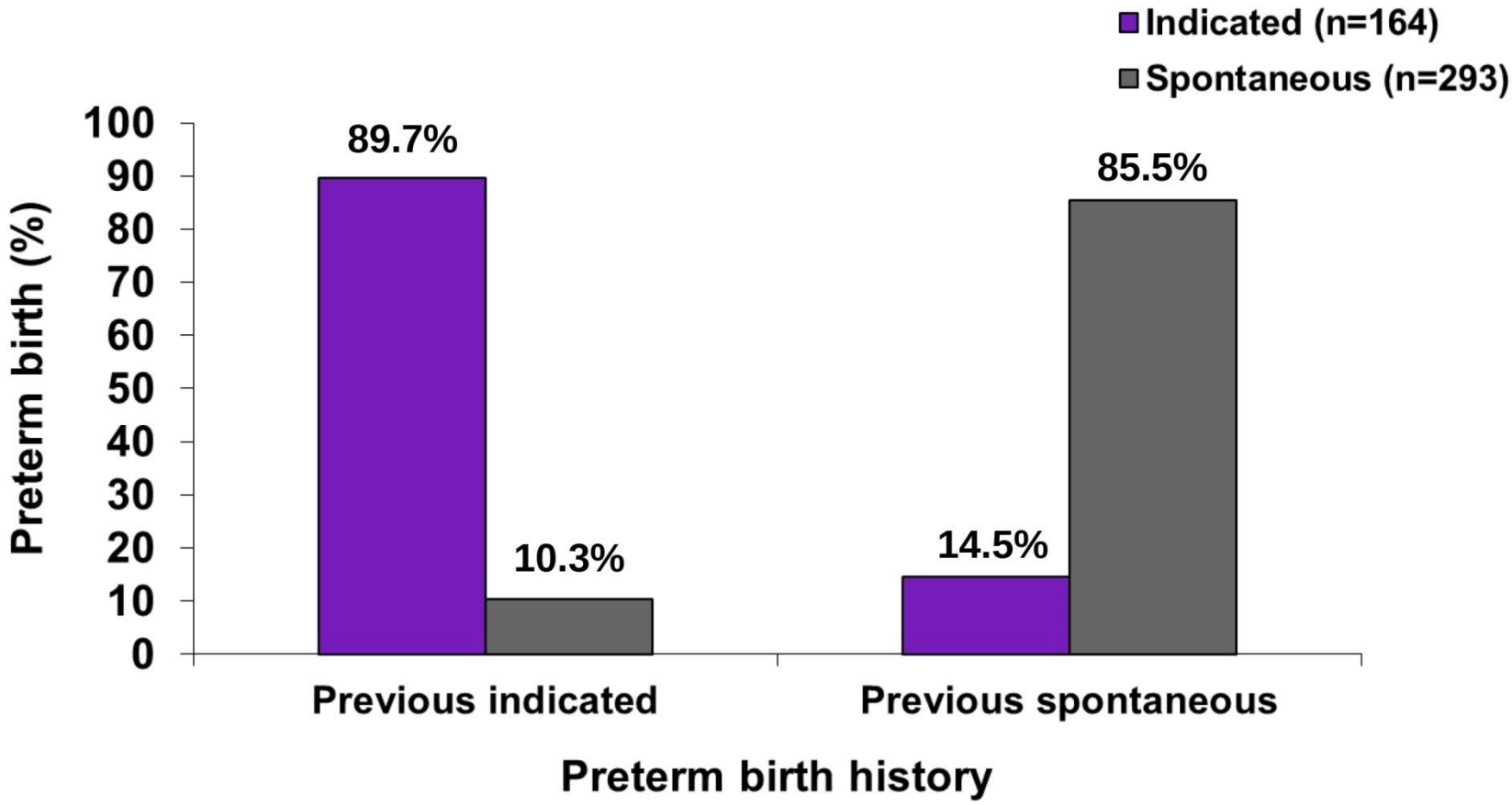
Infection can originate from different sources

- Vagina or cervix
- Placenta
- Invasive procedures
- Fallopian tubes



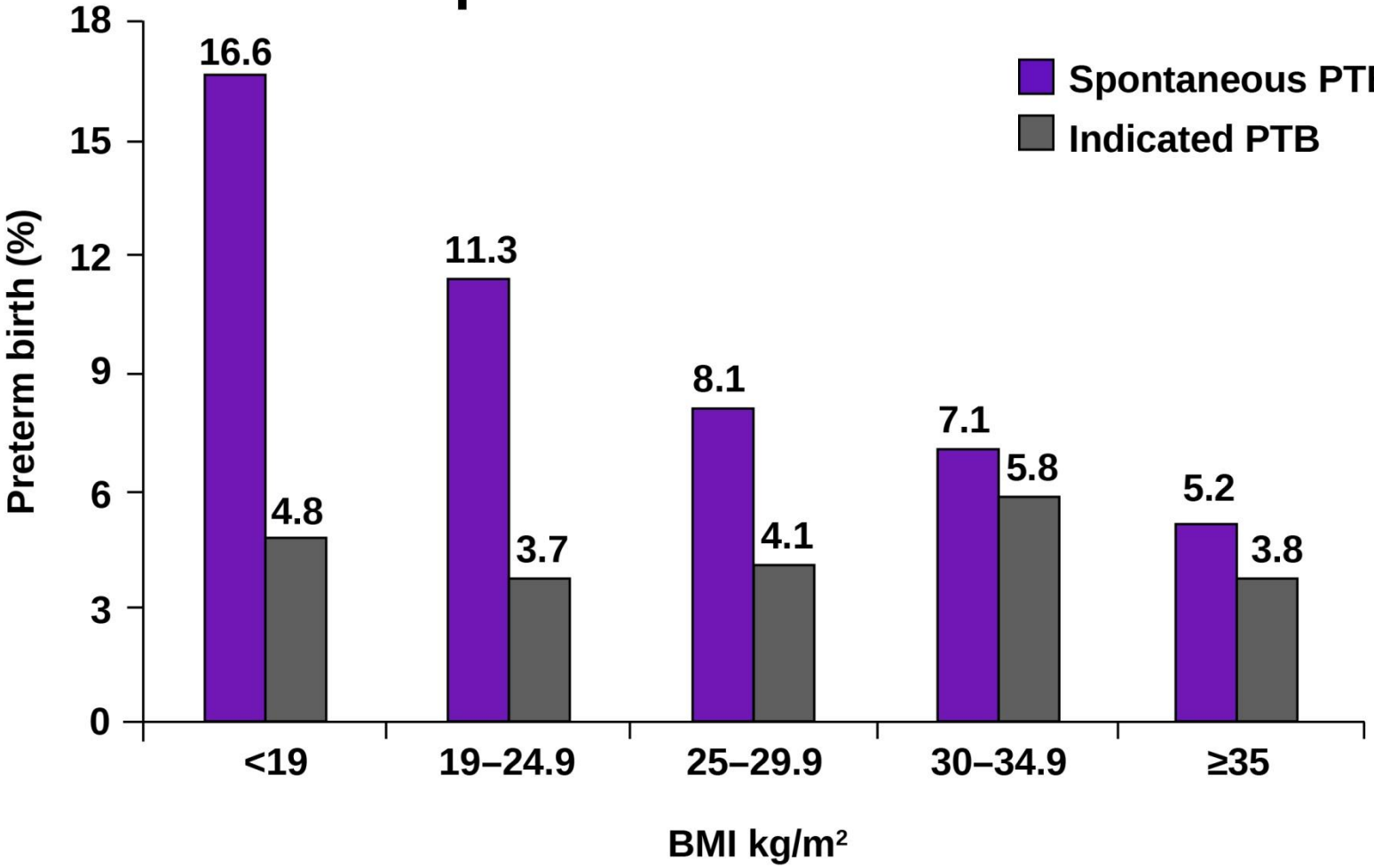
Goldenberg RL, et al. Lancet 2008;371:75–84. (Pubmed)

A history of preterm birth greatly increases likelihood of reccurrence



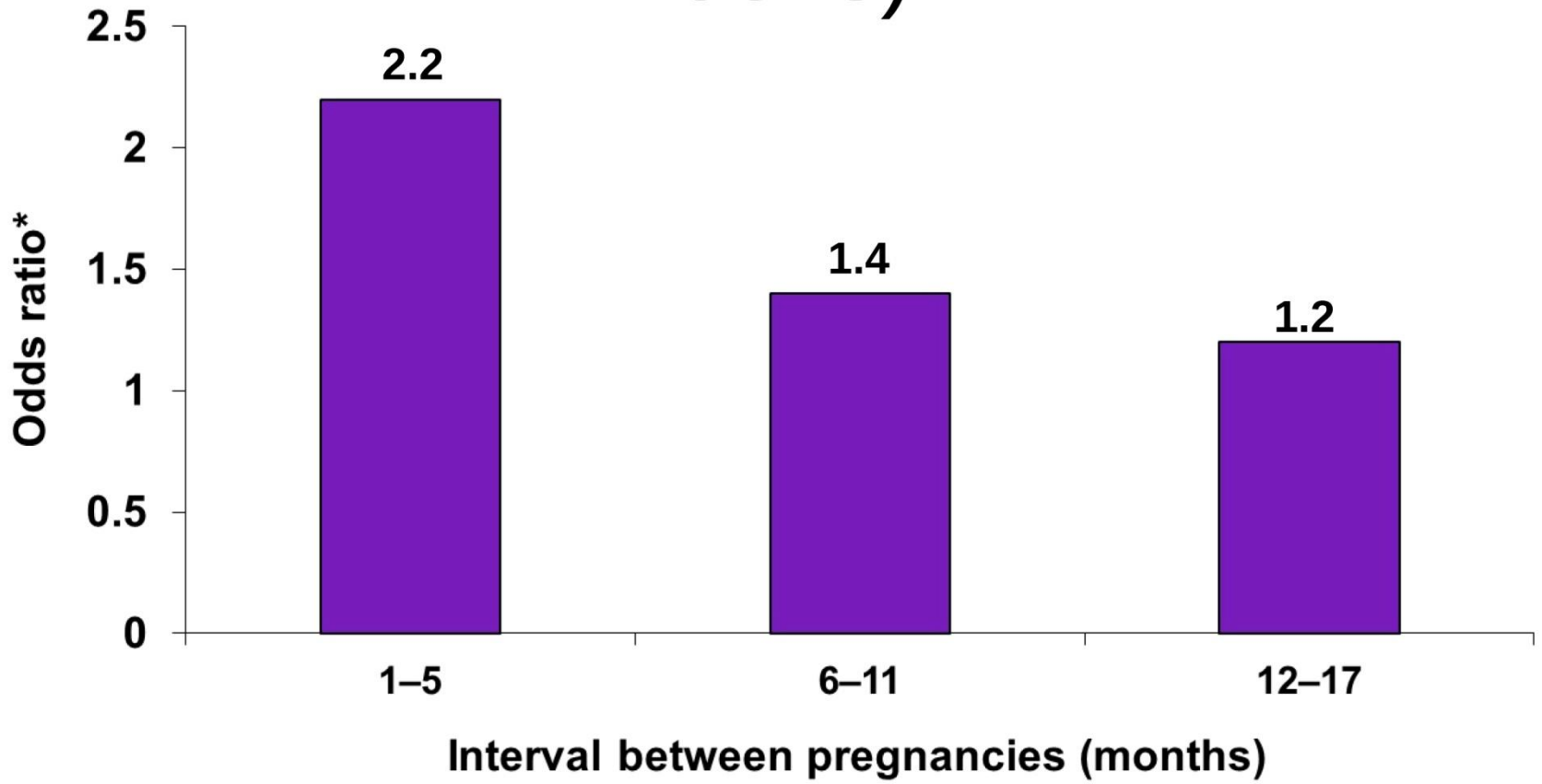
Goldenberg RL, et al. Am J Obstet Gynecol 2006;195:792–796. (Pubmed)

Extremely low maternal body mass index (BMI) increases risk of preterm birth



Hendler I, et al. Am J Obstet Gynecol 2005;192:882–886. (Pubmed)

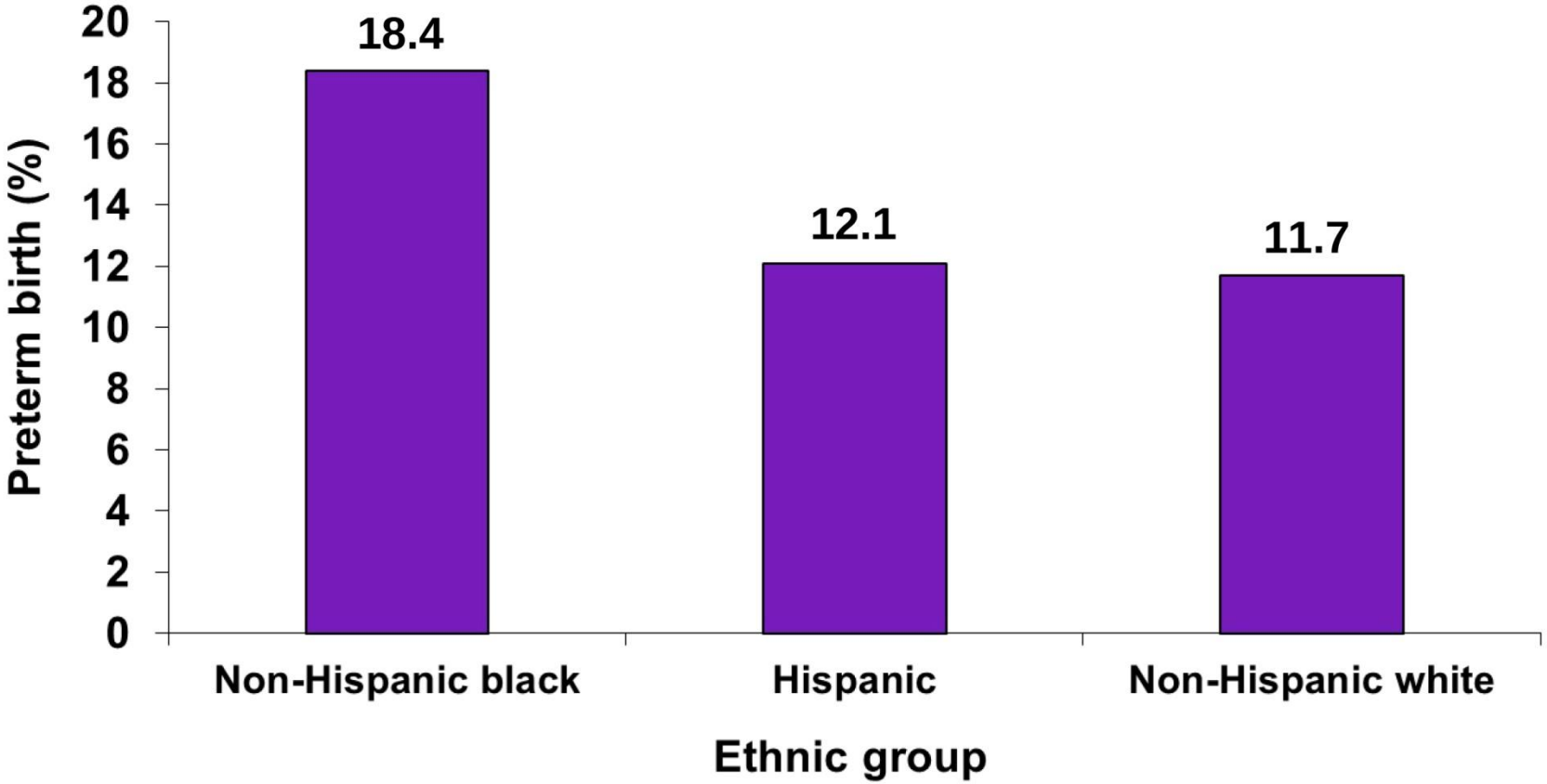
Short interval between pregnancies doubles risk of preterm birth (24–32 weeks)



*Relative to women with interpregnancy interval of 18–23 months
Data adjusted for maternal age, marital status, height, socioeconomic deprivation category, smoking, previous birth weight, and previous caesarean section.

Smith GC, et al. BMJ 2003;327:313. (Link)

Risk of preterm birth is highest in black women



Hamilton BE, et al. Pediatrics 2007;119:345–360. (Pubmed)

Other maternal risk factors may be important

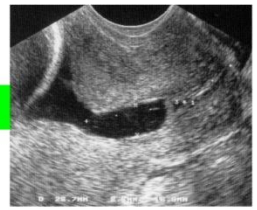
- Peridontal infection[1]
- Bleeding in second trimester[1,2]
- Psychiatric disorder[1]
- Smoking[1,2]
- Diabetes[1,2]
- Thyroid disease[2]
- Asthma[2]
- Hypertension[2]
- Psychological stress[2]
- Depression[2]

1. Ables AZ. J Fam Pract 2005;54:245–252. (Pubmed).
2. Goldenberg RL, et al. Lancet 2008;371:75–84. (Pubmed).

Prediction of spontaneous preterm birth

<u>Cervix or vagina</u>
Bacterial vaginosis
IL-6
IL-8
IL1β
fetal fibronectin (fFN)
ferritin
α-fetoprotein
human chorionic gonadotropin
prolactin
C-terminal propeptide of procollagen
pIGFBP-1

Cervical length (TVUS)
EMG
Maternal BMI
Previous History

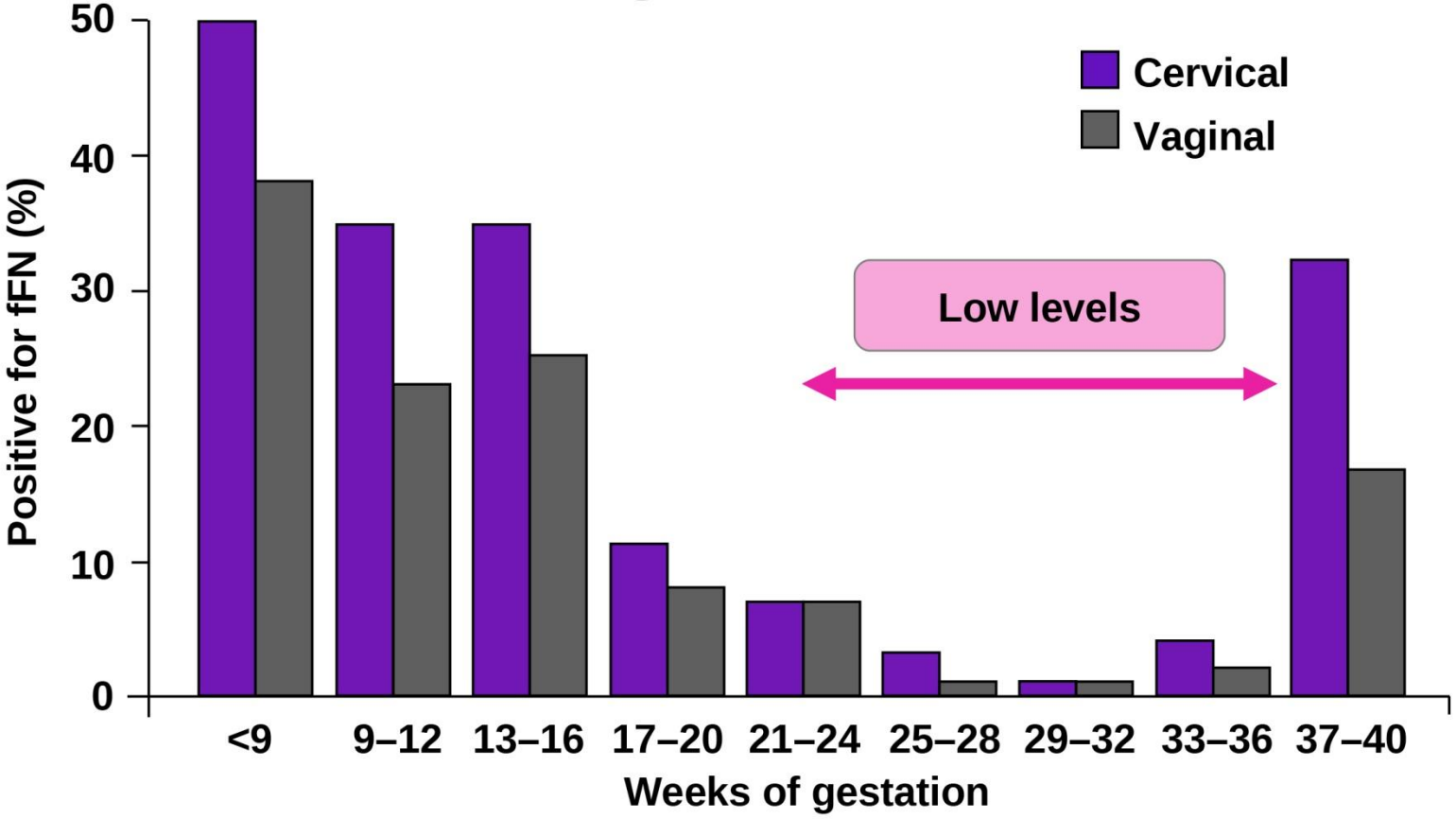


<u>Amniotic fluid</u>
calgranulins
defensins
IL-6
IL-8

<u>Saliva</u>
oestriol

<u>Serum</u>
G-CSF
ferritin
defensins
calgranulins
IGF BP-1 fragment
relaxin
Vitamins and micronutrients
CRP, CD163

Cervicovaginal fFN levels are normally low between 22–37 weeks of gestation



Positive samples were defined as containing >0.05 µg of fibronectin

Lockwood CJ, et al. N Engl J Med 1991;325:669–674 (Link).

Fetal Fibronectin

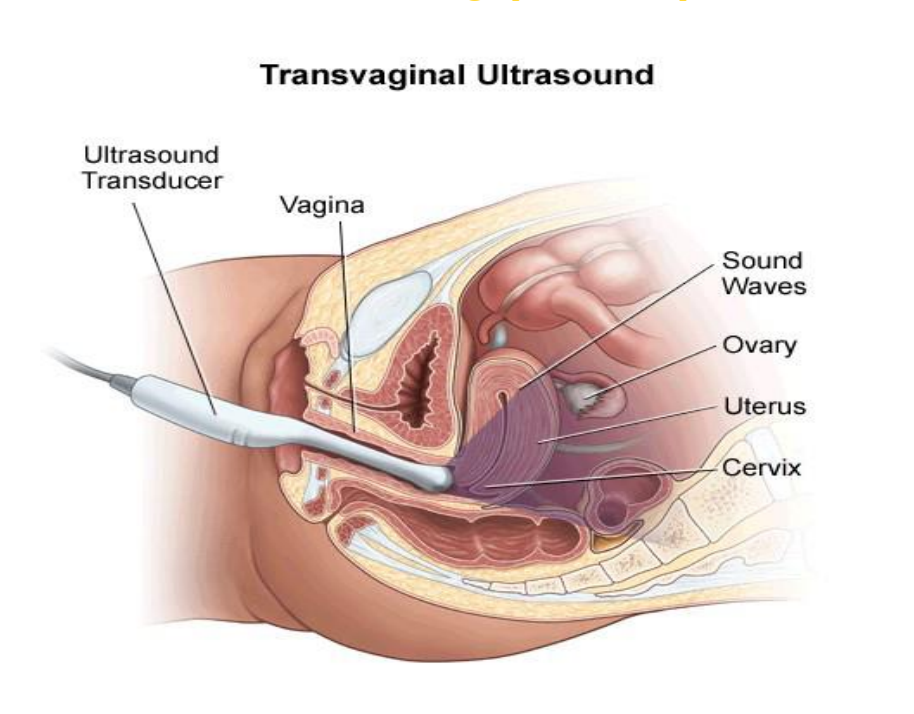
- Disruption of the chorio-decidual interface-------preterm labour
  Infection
  Stress &haemorrhage.
- +ve test-----increase the risk of PL.
- Help in ---- In-patient admission
  In-utero transfer
  Administration of steroids.

Cervical Sonographic Assessmrnt

- High sensitivity and positive predictive value---especialy in symptomatic pts.
- Routine measurement at 22-24 wks----- can be used to identify a group at high risk of early preterm birth.
- Cx length of ≤ 1.5 cm----26% deliver preterm < 34 wks.
- Management of short cx is controversial.

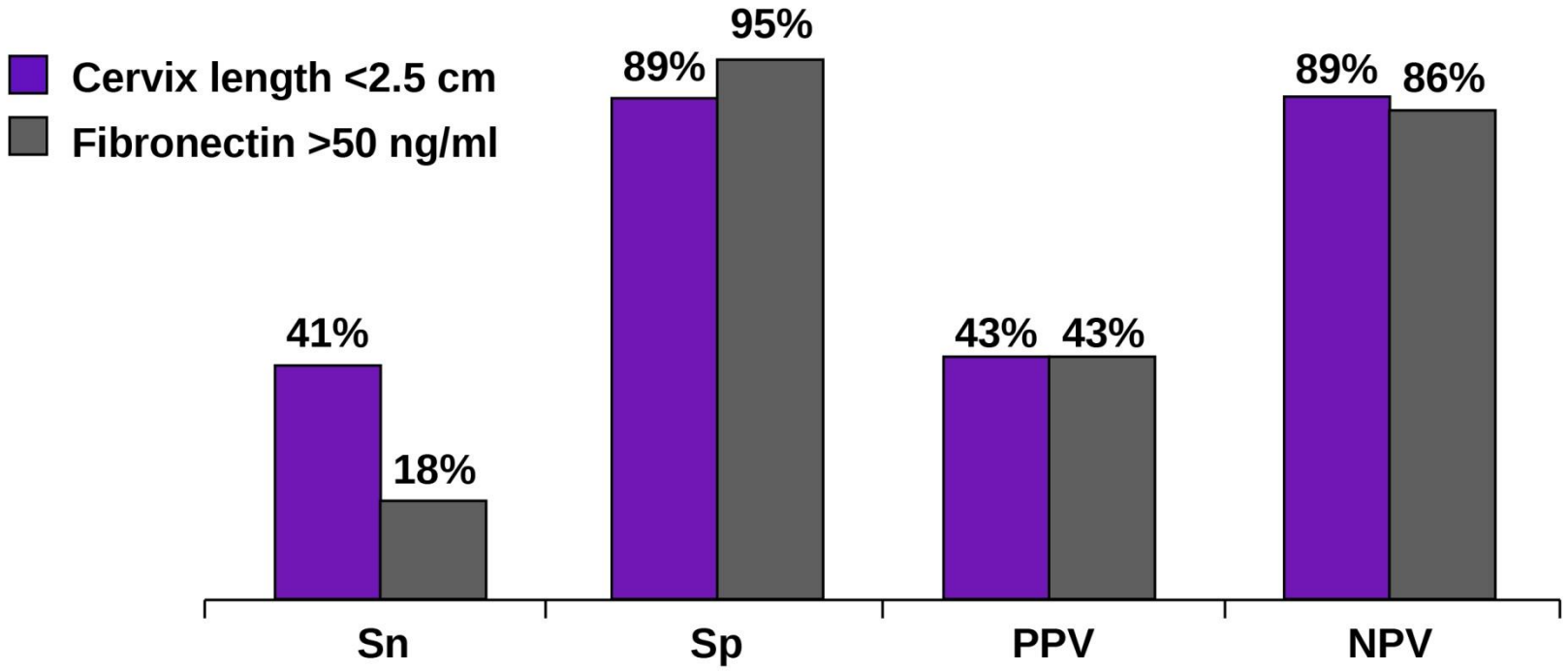
Diagnostic tests available to predict preterm labor

Cervical length can be measured by transvaginal ultrasound scanning (TVUSS)



Cervicovaginal fFN levels can be determined using a test

Cervical length and fFN measurement provide similar value as predictors of preterm birth



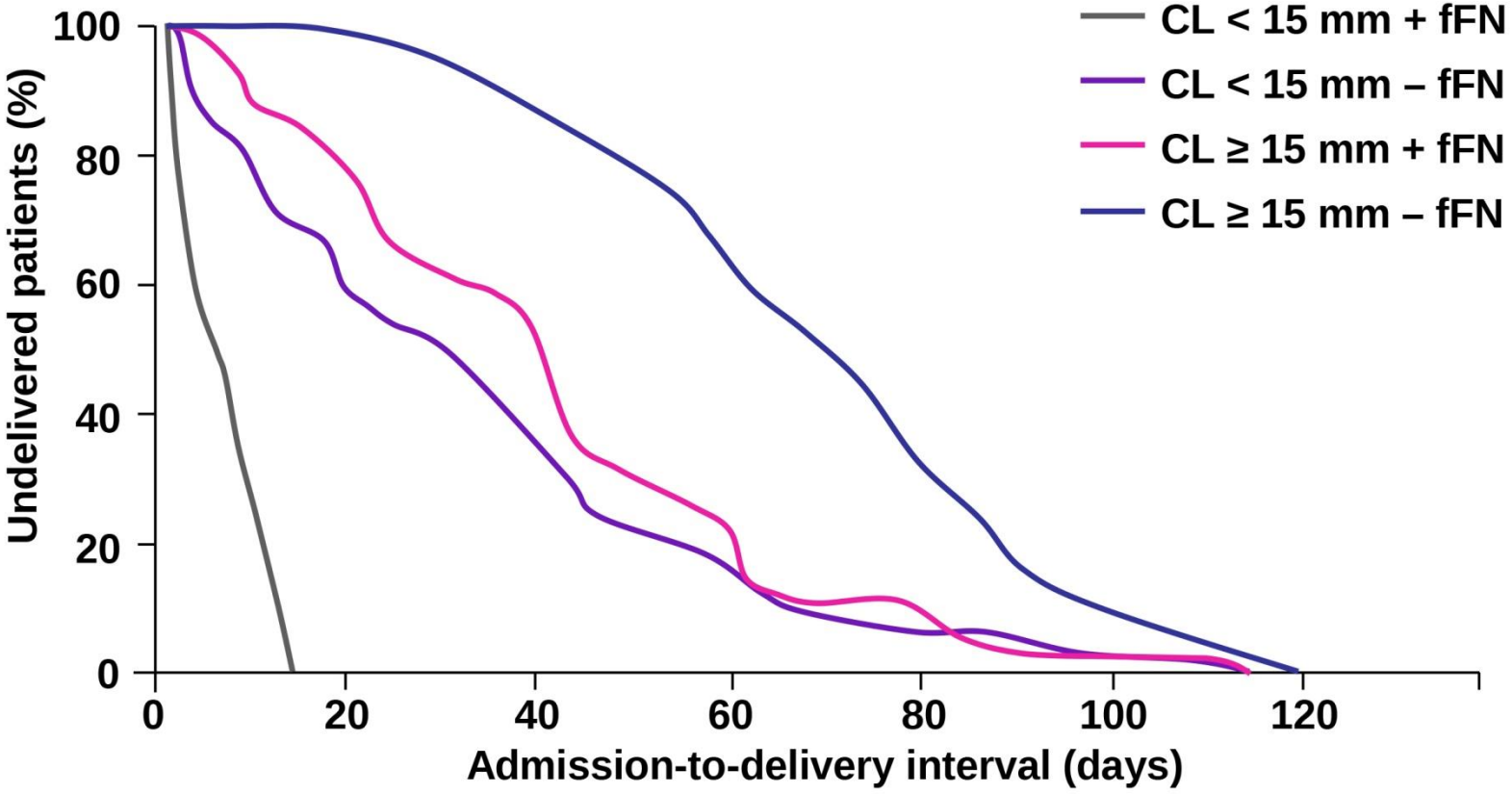
Cervical imaging and fFN measurements at 22–24 weeks;
preterm birth defined as <35 weeks

Sn=sensitivity; Sp=specificity; PPV=positive predictive value; NPV=negative predictive value

Ables AZ. J Fam Pract 2005;54:245–252; (Pubmed)
(Adapted from Iams JD, et al. NEJM 2002;364:250–255.)

Cervical length and fFN measurement used together provide the most accurate prediction

Kaplan-Meier survival curve of the admission-to-delivery interval according to cervical length and fFN results



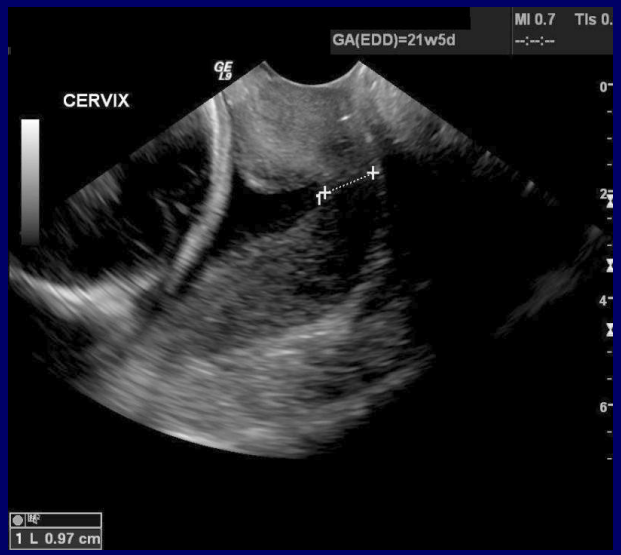
Adapted from Gomez R, et al. Am J Obstet Gynecol. 2005;192:350–359. (Pubmed)

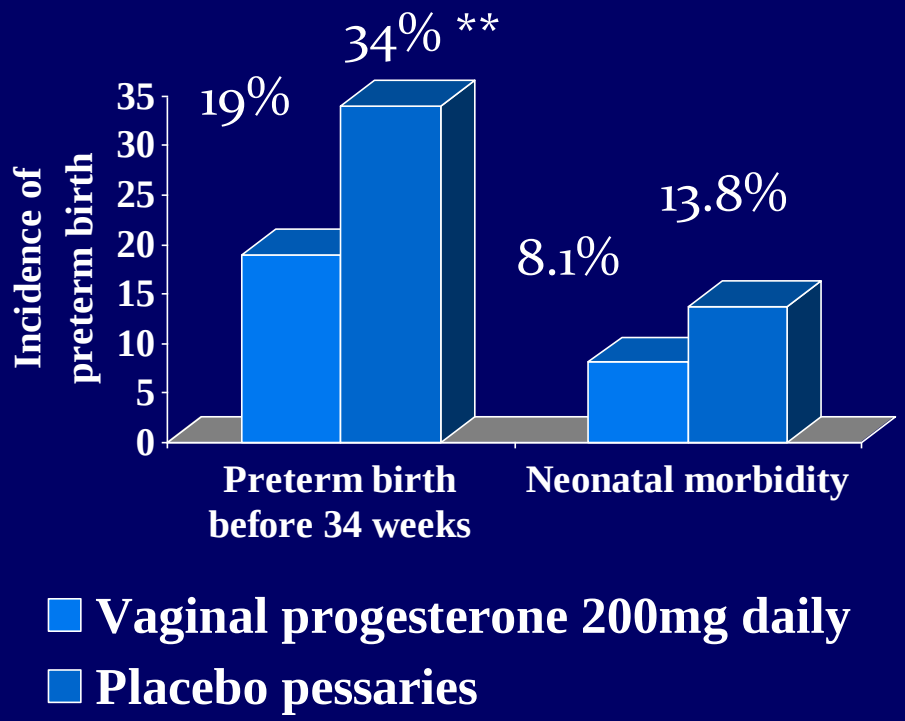
Prevention

- Cervical cerclage
- Progestrone
- Detection and treatment of vaginal and intrauterine infection.
- Non-steroidal anti-inflammatory.

Which groups of women may benefit?

2. Those with a short cervix – e.g. < 15mm?





Fonseca et al 2007 N Engl J Med 357: 462

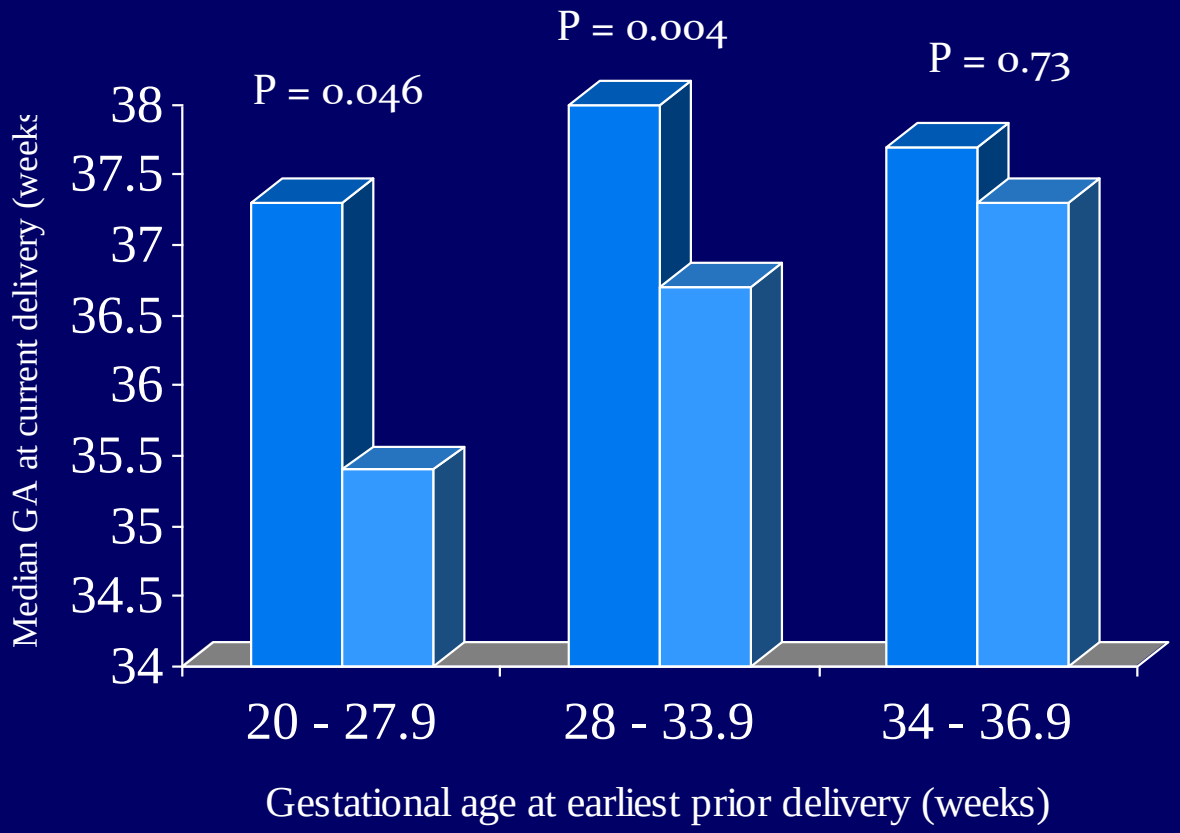
Scanning at around 22 weeks gestation
413 women with cervical length < 15mm
250 of these randomised to pro or placebo 200mg nocte

Relative risk 0.56 (95% 0.36 – 0.86) for reduction in preterm birth
Relative risk 0.59 (0.26 – 1.25) for neonatal morbidity

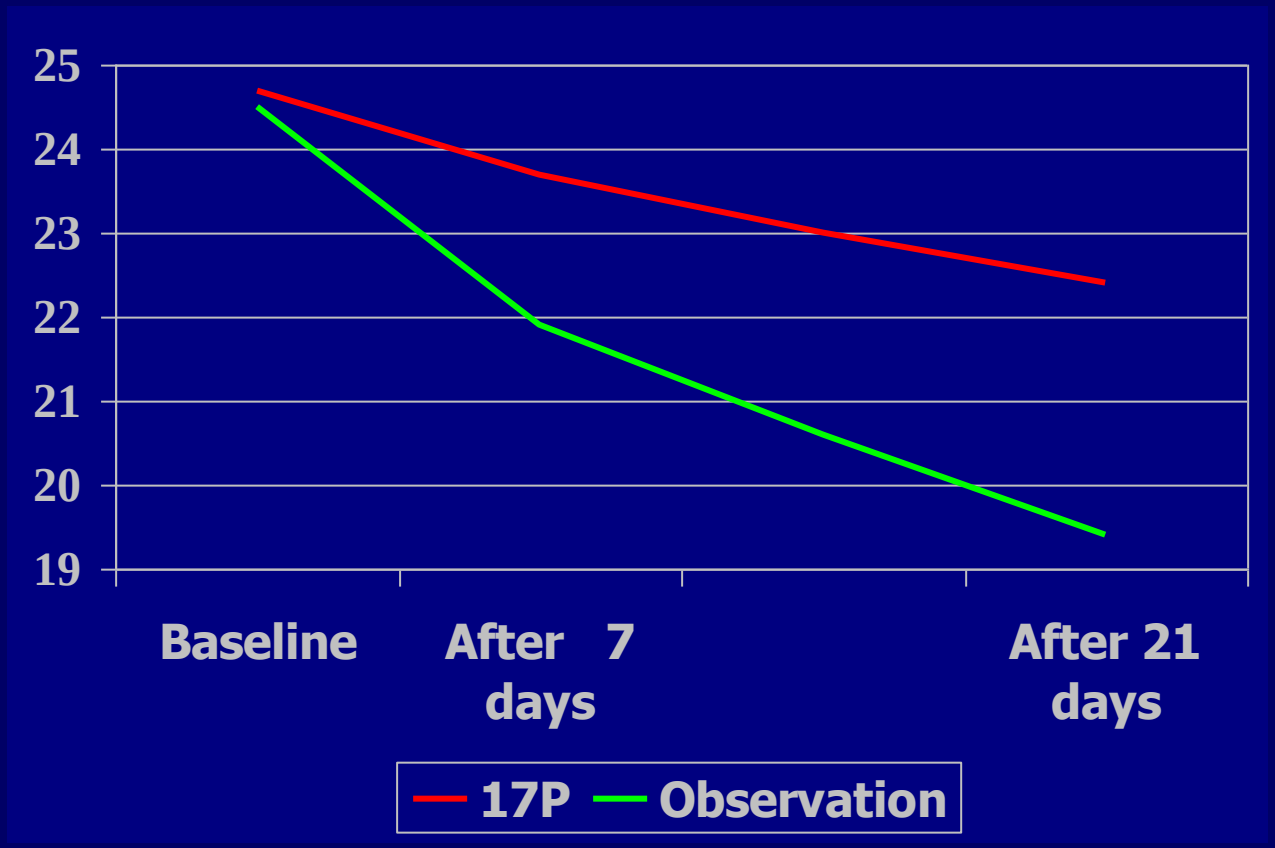
used
Primary outcome delivery before 34 weeks
PTB < 34 weeks was 19% in progesterone group
PTB < 34 weeks was 34% in placebo group
Decreased perinatal mortality also noted 2.4% vs 5.6%

Which groups of women may benefit?

1. Women with previous preterm birth ?



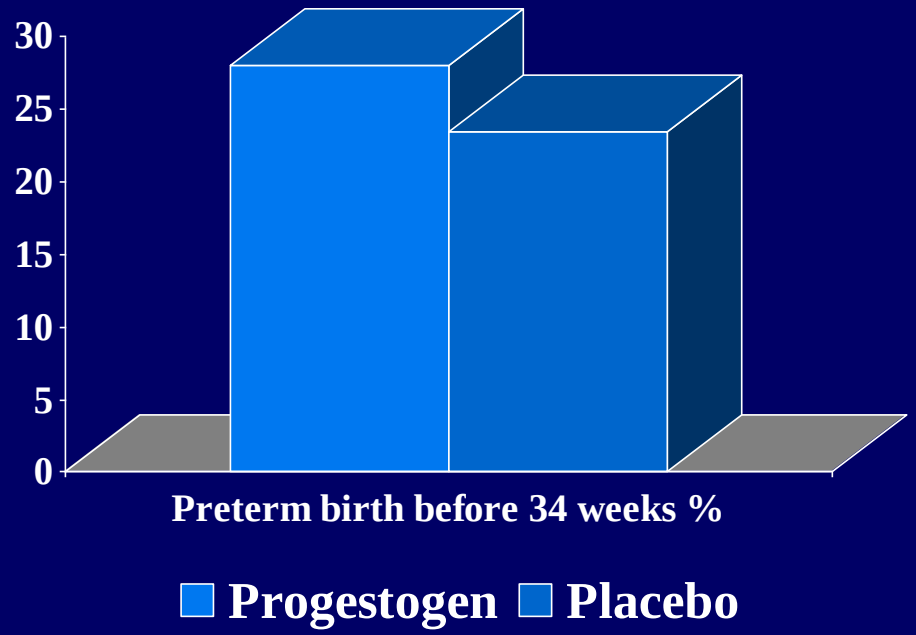
Spong et al (2005) Am J Obstet Gynecol 193: 1127


25
24
23
22
21
20
19
Baseline
After 7 days
After 21 days
17P
Observation

Which groups of women may benefit?

Those with twin pregnancy?

Two large RCTs and meta-analysis of > 1200 women



Norman et al (2009) Lancet 2009 373: 2034

No difference in spont or indicated preterm births between two groups 0 around 10% indicated, rest spontaneous

Numbers 42% vs 37% overall
17% vs 14% before 32 weeks

Harms?

Increased embryolethality noted in animal studies with 10x the human dose (progesterone) and 1x the human dose (17 OHP caproate)

Trend to more antepartum and intrapartum fetal deaths in the 17 OHP caproate group, in the Meis study although not significant

2% v. 1.3% RR 1.5 (0.31 – 7.34)

Trend to increased risk of miscarriage before 20 weeks in the 17OHP group 1.5% v 0

Increase incidence of gestational diabetes in women received 17 OH progesterone coproate.

Progesterone used as a treatment for miscarriage - 14 trials of sufficient quality for meta-analysis including 11 controlled trials

Of six fetal deaths, 5 before 2 weeks

PTL----Diagnosis

- Regular Uterine contractions

  (4/20 minutes)

- Cervical changes

  Dilatation ≥ 2 cm

  Effacement > 80%

Management

- Initial evaluation: Hx, Exam, MSU.
- Contraindications to inhibit labour:

Absolute

-Fetal death

-Cong anomalies incomp.with life.

-Chorioamnionitis

-Fetal indication for immediate delivery

-Maternal indication for immediate del.

Management----cont

Relative

-Intrauterine growth restriction.

-Pre-eclampsia.

-Vaginal bleeding

-Cervical dilatation > 4 cm

Tocolytic agents

- B-Adrenergic agonists
- Prostaglandin synthetase inhibitors.
- Mgso4
- Calcium channel blockers
- Oxytocine antagonists---Atosiban

B- Adrenergic agonists

- Absolute contraindications:

  -Cardiac disease. –Anaemia

  -Hyperthyroidism -MAO inhibitors

- Fetal and neonatal effects:

  -Fetal tachycardia

  -Neonatal hypoglycemia

  -? Neonatal intraventricular haemorrhage.

B-Adrenergics---Side Effects

-Palpitation -Myocardial ischaemia

-arrhythmias –Pulmonary edema

-Dilutional anaemia

-Decrease mean arterial pressure

-glucose intolerance

-Hypokalemia

-Paralytic ilius.

Magnesium Sulphate

- 5-8mg/dl blood level----inhibit uterine cont.
- Preferable in---- cardiac, hyperthyroid, DM
- Side effect: Flushes&dizziness
  Decrease temperature
  Respiratory depression
- Contraindicatios: Myasthenia G, renal fail.
- Antidote: Ca gluconate.

Magnesium sulphate neuroprotection

- Reduces cerebral palsy, including moderate and severe cases
- • Does not increase death

PG synthetase Inhibitor

- Indomethacin.
- Side effects:
  - G.I complications
  - Premature closure of ductus arteriosus
  - Oligohydramnios

PTL----Glucocorticoids

- Synthesis of phosphatidyl choline.
- Promotes the release of surfactant from type 2 pneumocytes.
- Beneficial----- < 34 wks
- Recommended 24-36 wks
- Effect lasts for one wk.
- Multiple courses.
- Beta methasone 12 mg IM repeated in 24 hrs.

ORACLE 2 Antibiotics or placebo for PTL int. membs.

	Eryth	Plac	RR
Cerebral palsy	53	27	1.93

	Co-amox	Plac	RR
Cerebral palsy	50	30	1.69

Preterm Rupture of Membrane

- Before 37 completed wks.
- Premature ROM, prolonged ROM
- Etiology:

-Focal thinning.

-Reduced elasticity.

-Alteration in the supportive connective tissue.

-Nutritional and dietary factors

Decrease vit C, Cupper, Zinc -Smoking

PROM--Etiology

- Sexual activity
- Pregnancy related conditions:
  - -Multiple pregnancy.
  - -Polyhydramnios.
  - -Marginal insertion of the cord.
- Infection
- History of PROM---- Recurrence 20%

PROM Management

- History---Gush of fluid from the vagina
- Speculam:
  -Diagnosis -Cord prolapse –dilatation
  -HVS
- Nitrazine paper test:
  Ph 7-7.5 yellow-----blue
- Arborization or ferning
- U/S-----decrease AF index---Supportive.
- Alpha feto protein.

PROM----Management

- Search for any evidence of chorioaniomitis:
  - -Fever –Maternal and fetal tachycardia
  - -Uterine tenderness
  - -Uterine contration
  - -Foul smelling vag discharge
  - -Increase WBC.

PROM Manag---cont

- Infection:

  -Membranes no longer act as abarrier.

  -Loss of antibacterial activity of AF.

  -Fetal mortality increase with a latent period of 24 hrs.

- Prematurity:

  Majority of perinatal death are due to prematurity not sepsis.

PROM Mang----cont

- Hospitalisation
- Vital signs
- Fetal heart and NST
- WBC, C-reactive protein
- Antibiotics
- Corticosteroids.
- Tocolytic agents.
- < 34 wks----Expectant
- > 34 wks----Delivery