

Preterm labour/ birth

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ANNE GEORGE



Introduction

- Preterm birth is a leading cause of perinatal morbidity and mortality
 - About 15 million births per year are preterm
 - Prevention is an important healthcare priority
 - Early identification of risk factors provides an opportunity for intervention
 - However, many preterm births occur among women without risk factors
 - IATROGENIC CONTRIBUTION
- 

Early Prediction of small babies:

- Small fetuses:
- -20 % starved
- 75 % normal
- 5 % abnormal
- Pyramid of care: If all normal
- 12 w
- 20-24 w
- 32 w or 36 w
- 41 w

BORN TOO SOON:

- PRETERM DELIVERY:
- GLOBAL ACTION REPORT ON PRETERM BIRTH
- 15 MILLION per annum (10 % of births)
- RATE IS INCREASING!!!!
- > 1 MILLION NEWBORN DEATHS per annum

PREDICTION OF PRETERM BIRTH:

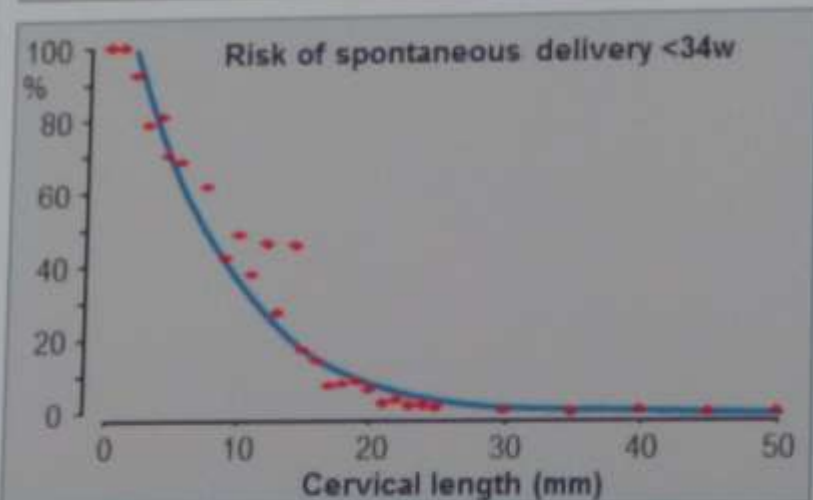
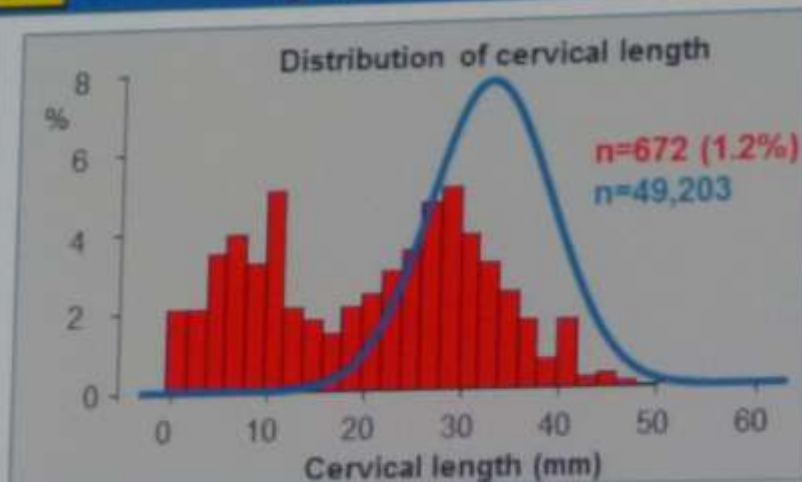
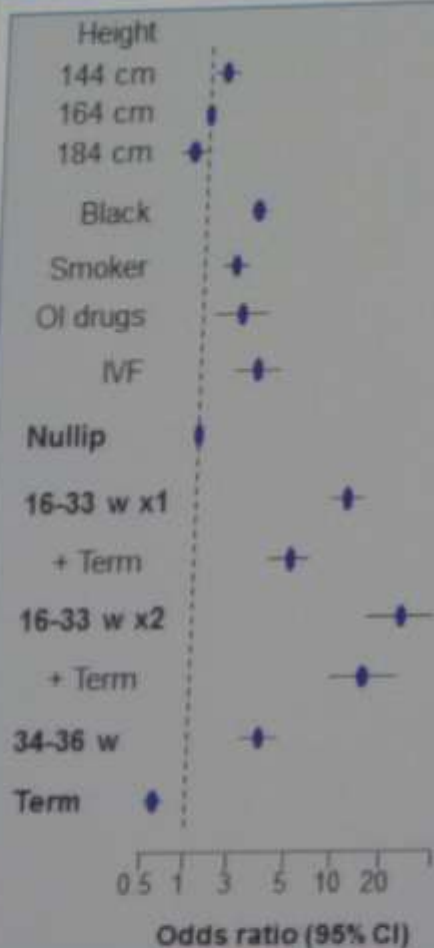
- DELIVERY < 34 WEEKS 1,8 %
- IATROGENIC 1/3
- SPONTANEOUS 2/3
- SINGLETONS 2 %
- TWINS 15 %



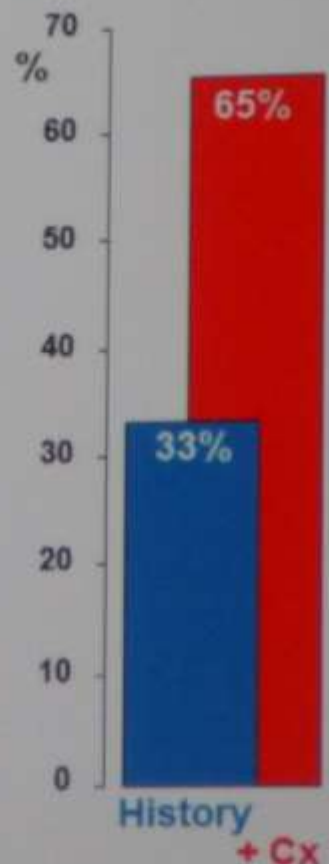
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Prediction of **spontaneous** preterm birth <34w

Singletons 22 w: History plus cervical length



DR for FPR 1



PREVENTION OF PRETERM BIRTH IN TWINS:

- BEDREST: NO, ACTUALLY WORSENS OUTCOME SLIGHTLY
- PROGESTERONE:
 - 31 to 26 %
 - 25 to 20 %
 - 15 to 19 %
- ARABIN PESSARY:
 - DOES NOT WORK FOR TWINS!



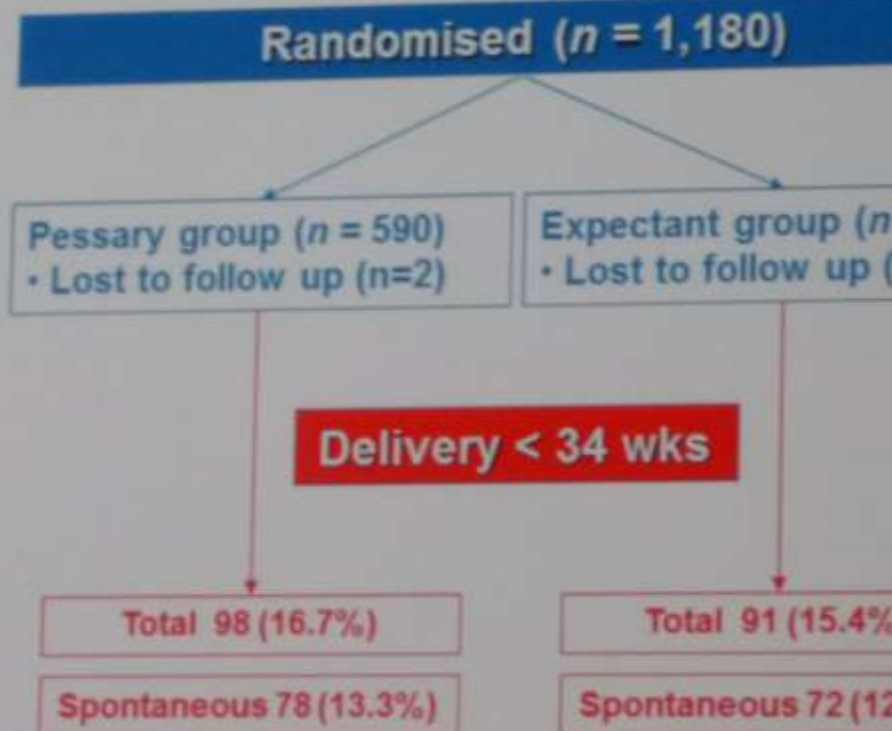
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Prevention of preterm birth in tw



Spain: Canary, Granada, Murcia
Albania, Austria, Brazil, Chile, England, Germany,
Hong Kong, Italy, Portugal, Slovenia

FMF study in twins



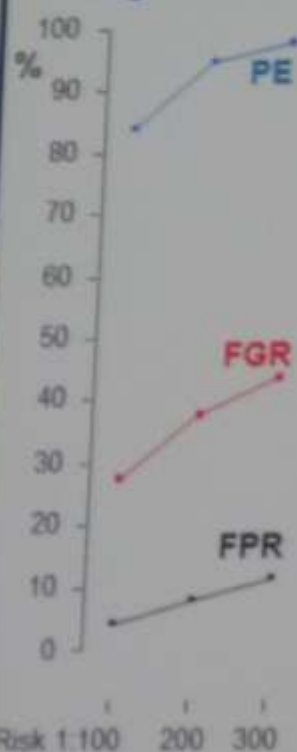


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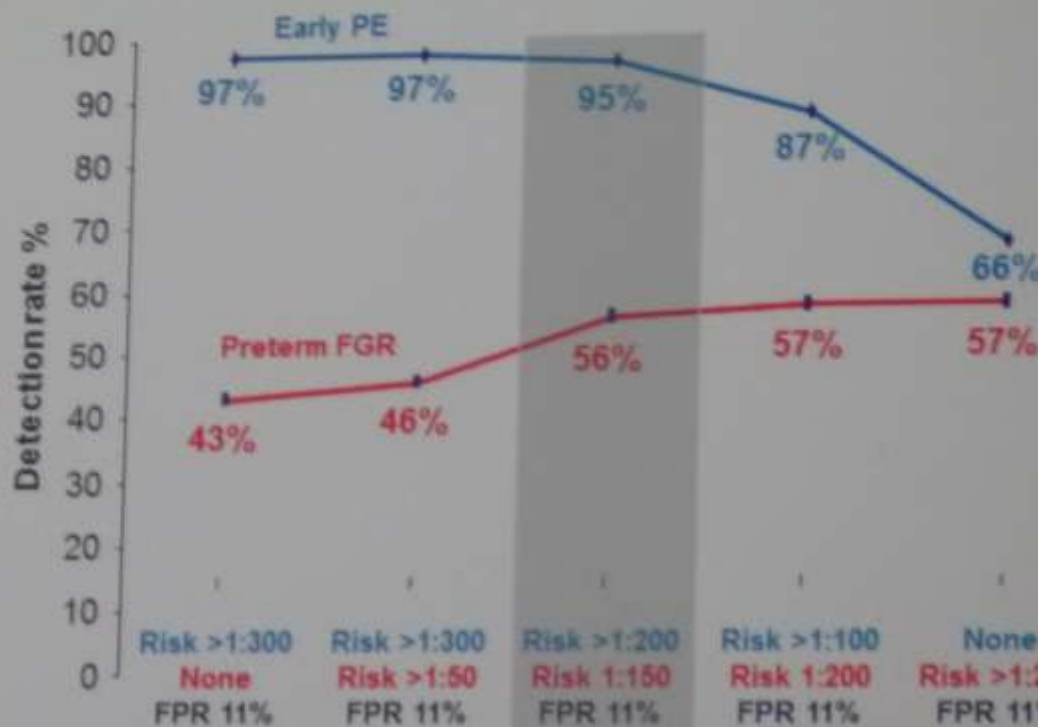
Early prediction of FGR and PE

History, uterine PI, MAP, PAPP-A, PLGF at 11-13wks

Algorithm for PE



Algorithm for FGR





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FGR: Management



**Singleton pregnancies
n=75,394**

**FGR <32 wks
164 (0.2%)**

**Preeclampsia
75 (46%)**

**No preeclampsia
89 (54%)**

Potentially effective interventions

- **Progesterone**
- Treat infections, eg. asymptomatic bacteruria, GBHS
- Smoking: reduce / stop if possible
- Vaginal pessary: Arabin “ring & funnel”
- ART: ↓ twinning + higher order multiples
- **Cervical cerclage**
- Fatigue + physical exertion
- Nutrition, eg. L-carnitine



Progesterone

- Natural
 - Synthetic
- 

Preparations


Natural

- Administration PV or oral (micronised)
- Vaginal route – high uterine bio-availability and systemic side effect profile benign; doses: 90 mg to 400 mg
- Oral preparations – sleepiness, fatigue, headache; dose: 900 mg to 1600 mg; first pass through liver, poorer bio-availability



Preparations

Synthetic

- 17 –alphahydroxyprogesterone
 - Intramuscular administration
 - Doses of 25mg every 5 days to 100mg weekly
 - Begin from 16 weeks
- 

Progesterone - history of PTB

Interest in progesterone supplementation re-kindled in 2003:

- **Meis, NEJM – 459 patients**
- **da Fonseca, Am J Obstet Gynecol – 142 patients**

Statistically significant reduction in PTB < 34w

Progesterone – history of PTB


Ultrasound Obstet Gynecol 2007; **30**: 687–696

Progesterone vaginal gel for the reduction of recurrent preterm birth: primary results from a randomized, double-blind, placebo-controlled trial

J. M. O'BRIEN¹, C. D. ADAIR², D. F. LEWIS³, D. R. HALL⁴, E. A. DEFRANCO⁵, S. FUSEY⁶,
P. SOMA-PILLAY⁷, K. PORTER⁸, H. HOW⁹, R. SCHACKIS¹⁰, D. ELLER¹¹, Y. TRIVEDI¹²,
G. VANBUREN¹³, M. KHANDELWAL¹⁴, K. TROFATTER¹⁵, D. VIDYADHARI¹⁶,
J. VIJAYARAGHAVAN¹⁷, J. WEEKS¹⁸, B. DATTEL¹⁹, E. NEWTON²⁰, C. CHAZOTTE²¹,
G. VALENZUELA²², P. CALDA²³, M. BSHARAT²⁴ and G. W. CREASY²⁵

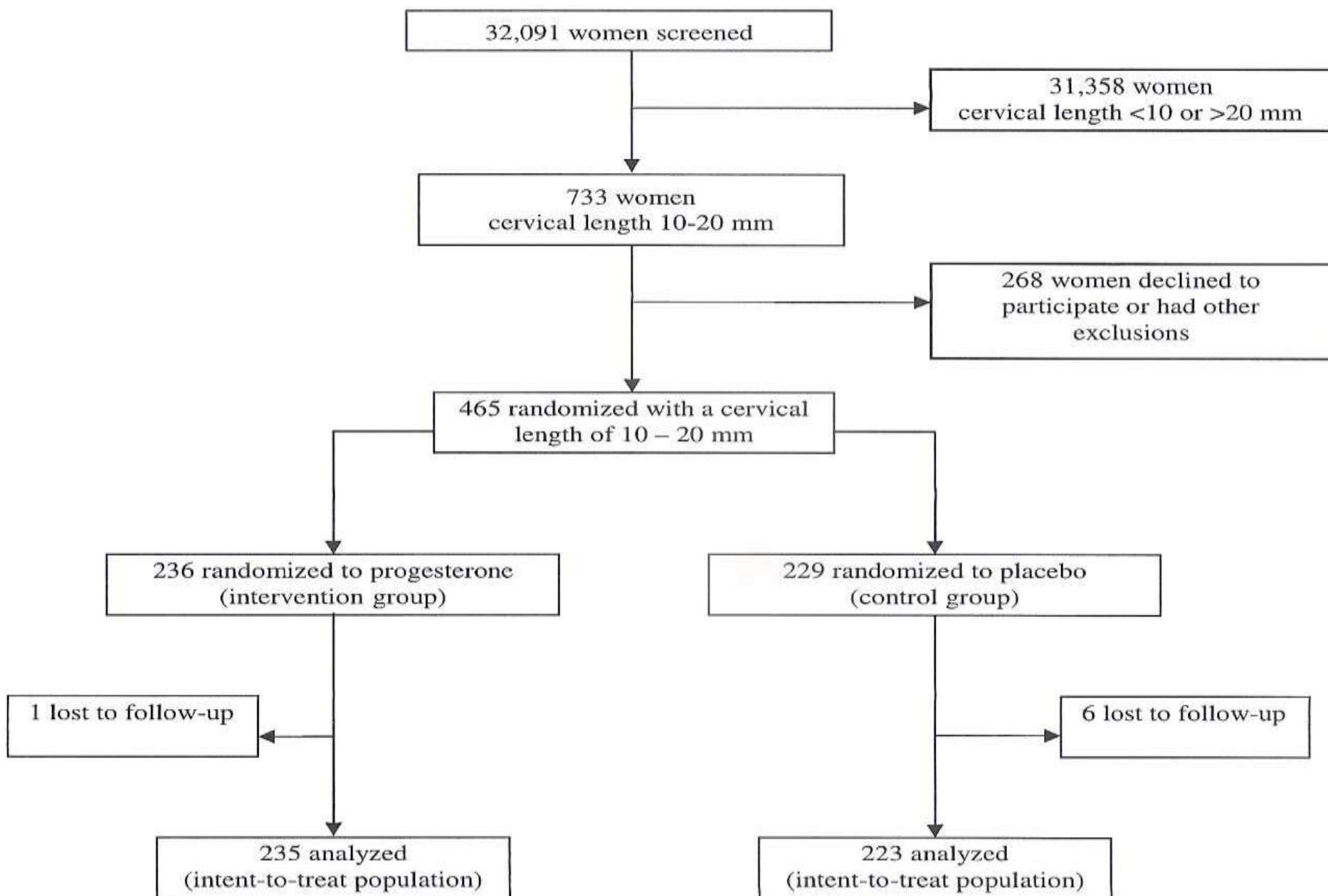


Progesterone - history of PTB

- 659 with prior history of PTB
 - Randomised to progesterone or placebo
 - Progesterone supplementation did not reduce frequency PTB compared to placebo
 - No difference in maternal or neonatal outcome
- 

Progesterone - short cervix

- Fonseca et al, NEJM 2007
- Screened 24 620 pregnant women
- 413 (1.7%) women had short cervix (15mm or less)
- Randomised to progesterone or placebo
- Reduction in PTD < 34 weeks (19% vs 34%, 95% CI 0.36-0.86)
- Non significant reduction in neonatal morbidity



Short cervix

Ultrasound Obstet Gynecol 2011

Vaginal progesterone reduces the rate of preterm birth in women with a sonographic short cervix: a multicenter, randomized, double-blind, placebocontrolledtrial

Sonia S. Hassan, MD^{1,2}; Roberto Romero, MD^{1,3}; Dommeti Vidyadhari, MD, DGO, MBBS⁴; Shalini Fusey, MD, DGO, MBBS⁵; Jason Baxter, MD, MSCP⁶; Meena Khandelwal, MD⁷; Jaya Vijayaraghavan, MD, DGO, MBBS⁸; Yamini Trivedi, MD, DGO, MBBS⁹; Priya Soma-Pillay, MBChB, FCOG¹⁰; Pradip Sambarey, PhD, MD, MBBS¹¹; Ashlesha Dayal, MD¹²; Valentin Potapov, MD, PhD¹³; John O'Brien, MD¹⁴; Vladimir Astakhov, MD, PhD¹⁵; Oleksandr Yuzko, MD, PhD¹⁶; Wendy Kinzler, MD¹⁷; Bonnie Dattel, MD¹⁸; Harish Sehdev, MD¹⁹; Liudmila Mazheika, MD, PhD²⁰; Dmitriy Manchulenko, MD²¹; Maria Teresa Gervasi, MD²²; Lisa Sullivan, PhD²³; Agustin Conde-Agudelo, MD, MPH¹; James A. Phillips, DrPH²⁴; and George W. Creasy, MD²⁵, for the PREGNANT Trial

Cervical length technique

- Empty bladder
- Prepare condom covered vaginal probe
- Guide probe into anterior fornix of vagina
- Sagittal long-axis view of endocervical canal
- Withdraw probe until image is blurred then reapply just enough pressure to restore image
- Measure cervical length (3 measurements)
- Fundal pressure for 15 seconds, re-measure

Progesterone - short cervix

- **45% reduction in PTB before 33 weeks**
(8.9% vs 16%; $p=0.02$; CI 0.33-0.92)
- **PTB < 35 weeks**
(14% vs 23%; $p=0.02$; CI 0.42-0.92)


Progesterone - short cervix

- **Respiratory distress syndrome**
3% vs 7.6%; $p=0.03$; CI 0.17-0.92
- **Any neonatal morbidity or mortality event**
7.7% vs 13.5%; $p=0.04$; CI 0.33-0.99
- **Birth weight <1500g**
6.4% vs 13.6%; $p=0.01$; CI 0.26-0.85



Progesterone - short cervix


Numbers needed to treat

- 14 patients to prevent 1 preterm birth
 - 22 patients to prevent 1 case of RDS
- 



Implications

Universal screening of women with a short cervix identifies patients at risk and can now be coupled with intervention




Progesterone – acute PTL

Progesterone supplementation associated with:

- less shortening of the cervix
- reduced rate of preterm delivery
- fewer complications of prematurity
- higher birth weight



Progesterone – not beneficial

- Twin gestations
 - Triplet pregnancies
 - Fetal fibronectin positive pregnancy
 - Preterm premature rupture of membranes
- 



Cerc1age



Cerclage – history of PTB

- Elective cerclage based only history may be justified in women with 3 or more 2nd trimester losses. (MRC/RCOG RCT of cervical cerclage; BJOG 1993)
- In such a population cerclage will reduce risk of PTB <33 weeks from 32 to 15%



Prior cerclage

- Once a cerclage, not always a cerclage. (Fejgin 1994)
- Prior cerclage: to repeat or not to repeat? That is the question. (Pelham 2008)



Prior cerclage not an indication for repeat cerclage

Cerclage – short cervix

- Meta-analysis (4 trials); Berghella 2005
- Cerclage beneficial in women with cervical length <25mm before 24 weeks only if they had a prior PTB
- Birth <35 weeks reduced from 39% without cerclage to 23% with cerclage (RR 0.61; CI 0.40 – 0.92)
- No difference in perinatal mortality

Cerclage – short cervix

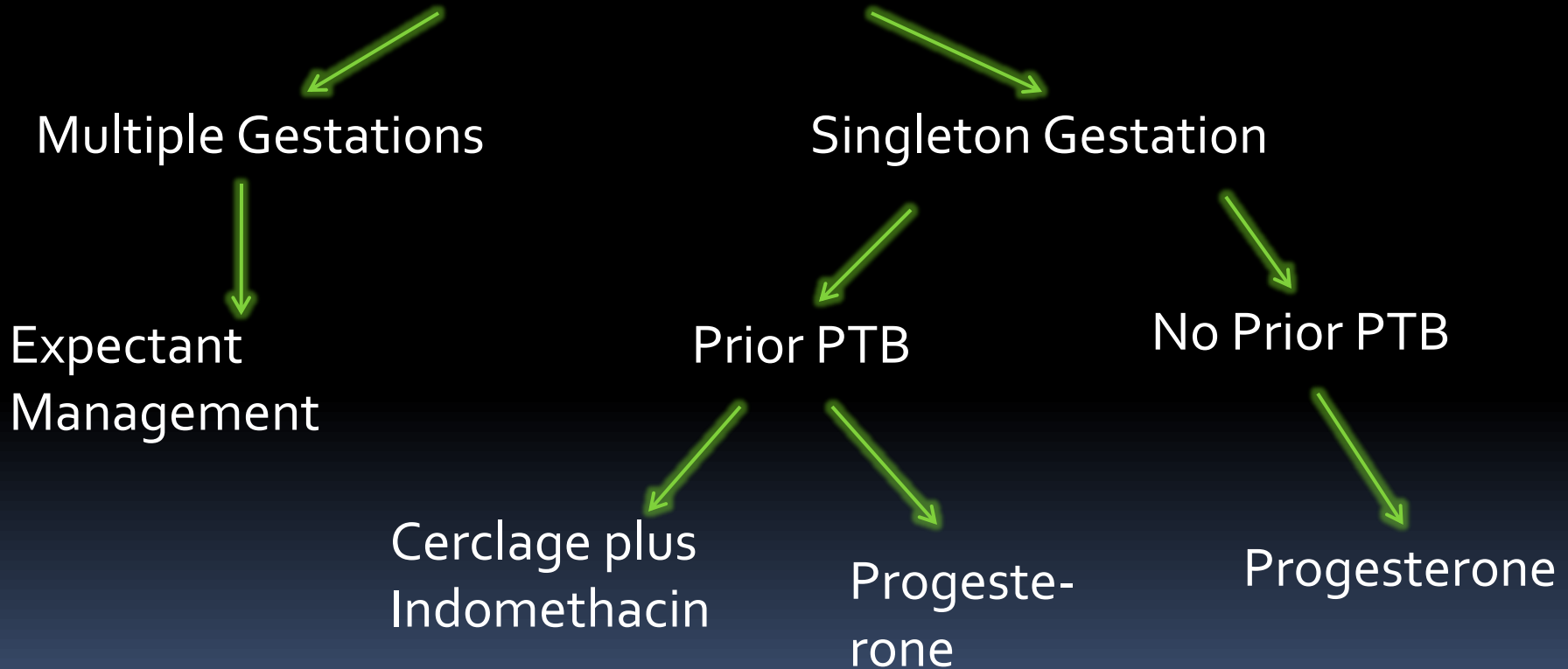
- Vaginal Ultrasound Trial Consortium
- 302 patients
- Short cervix and history of preterm birth
- Significant benefit only in women with cervical length $<15\text{mm}$ (RR 0.23; CI 0.08-0.66)

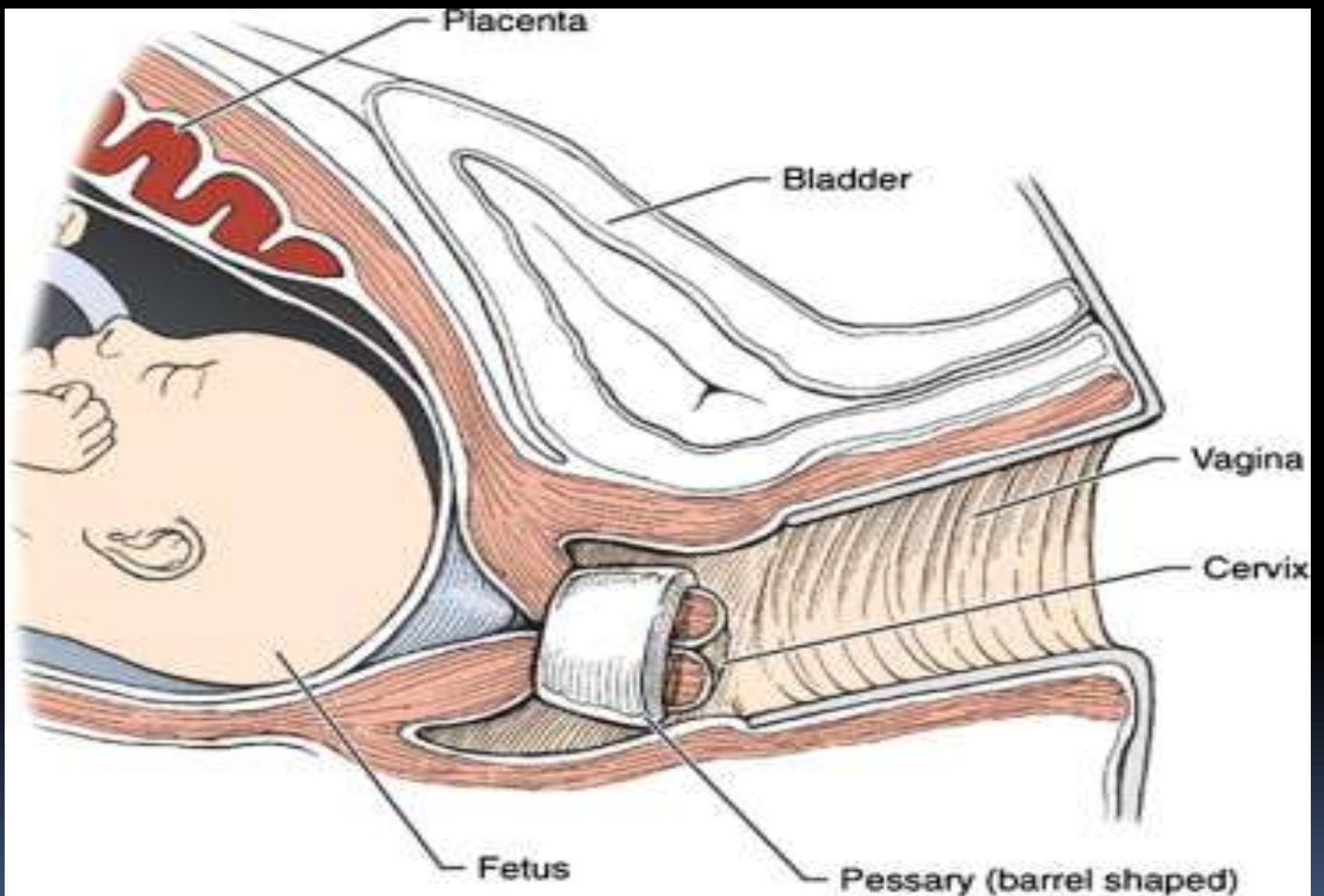
Cerclage or progesterone

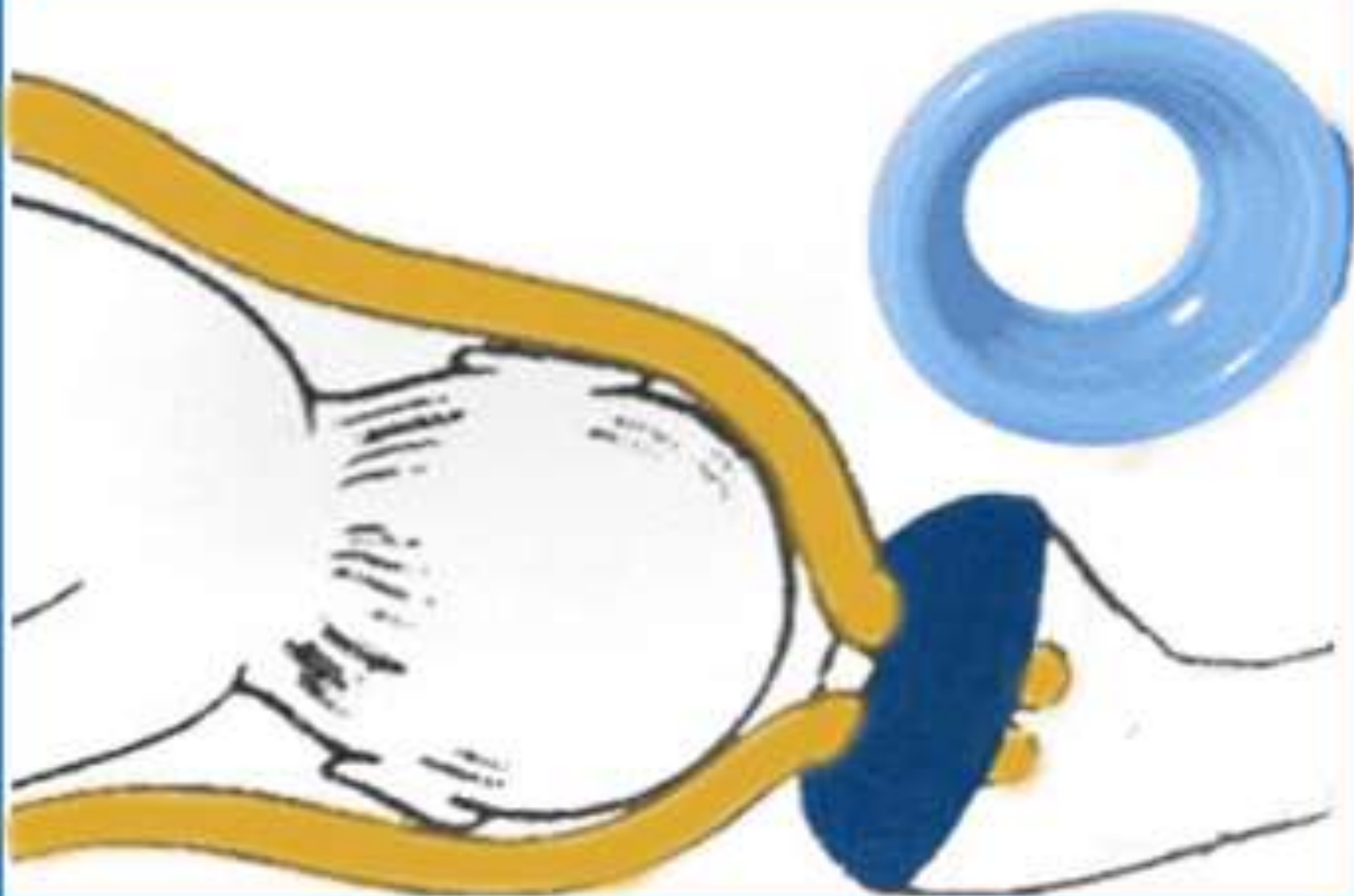
- Not enough evidence comparing the 2 treatment modalities
- Small study of 79 patients cerclage superior to 17-alpha hydroxyprogesterone if cervical length <15mm
- No difference if cervical length <25mm

Algorithm for short cervical length

Cervical length < 25mm







A



B



C





Conclusion

- A short cervix on TVU is the best predictor of imminent preterm labour. ?Universal screening in the midtrimester.
 - Successful management of these patients depends on the understanding that short CL is the final pathway of various causes of preterm labour
 - There probably isn't one management technique that could be used across the board in all patients
 - Therapy tailored to each unique clinical situation
 - TLC also plays an important role in preventing PTB
- 