

Cervical Shortening = Preterm Parturition.*

and

The Rx for Short Cervix is Progesterone.

What Does This Mean for Patient Care ?

- **Cerclage Reduces Preterm Birth, But How ?**
- **If Cerclage Helps, Maybe Pessary Could Too ?**

**** In Singleton Pregnancy***

Cervical Cerclage

- Increased Risk of PTB Women with Twins
- Beneficial in Women w/ Prior SPTB + Short Cx
 - Berghella Meta-Analyses
 - Conde-Agudelo Meta-Analysis
 - Owen Vaginal Ultrasound Cerclage Trial
- Progesterone & Cerclage Equally Effective
 - Conde-Agudelo
 - Neither Affect Rate of Cervical Shortening
 - Durnwald AJOG 2009, Pessel AJOG 2013, Drassinower UOG 2015
- Most Effective for Cervix ≤ 15 mm
 - Owen Vaginal Ultrasound Cerclage Trial

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 Chalworapongsa, MD; John M. O'Brien, MD; Elcin Cetingoz, MD; Eduardo da Fonseca, MD; George Creasy, MD; Priya Soma-Pillay, MD; Shallni Fusey, MD; Cetin Cam, MD; Zarko Alfirevic, MD; Sonia S. Hassan, MD

Cerclage vs. Vaginal Progesterone

Preterm Birth - No Difference

- < 28 Weeks - No Difference
- < 32 Weeks - No Difference
- < 35 Weeks - No Difference
- < 37 Weeks - No Difference

Perinatal Mortality - No Difference



Cerclage for Hx PTB + Short Cervix

The NICHD Vaginal Ultrasound Cerclage Trial

Owen et al AJOG 2009

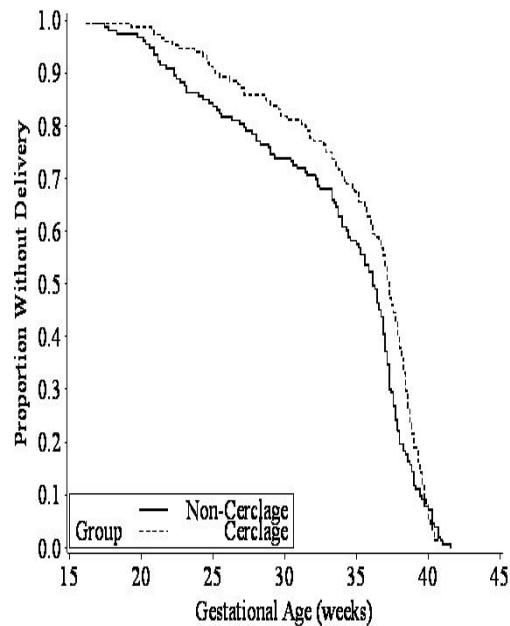
- Entry: Prior PTB between 17 and 34 weeks
- 1016 followed with transvaginal sonography
- 798 w/ Cervix ≥ 25 mm \rightarrow Routine care
 - 69% maintained Cx ≥ 25 mm past 23 weeks
 - **16% delivered < 35 weeks**
- 302 w/ Cervix < 25 mm
 - Randomized to Cerclage vs. Routine Care
- Births < 35 Wks: **42%** Routine vs. **32%** Cerclage
- RR = 0.67, 95% CI, 0.42 to 1.07; p = 0.09



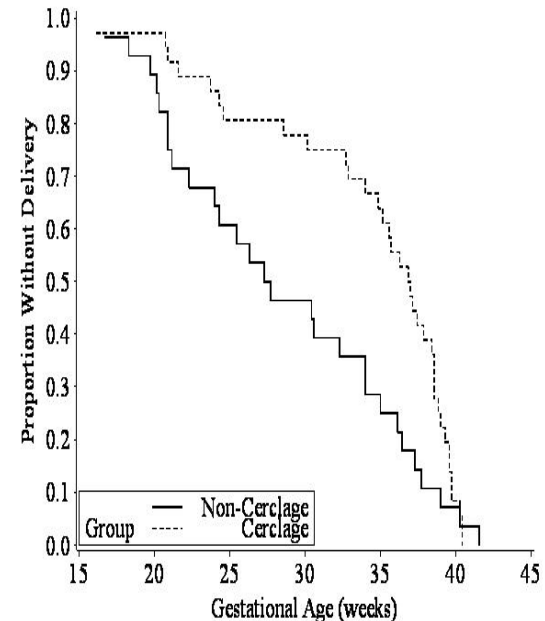
NICHD Vaginal Ultrasound Cerclage Trial

Survival Curves

Cerclage Helps Cx < 15 mm or Visible Membranes



Cervix < 25 mm



Cervix < 15 mm



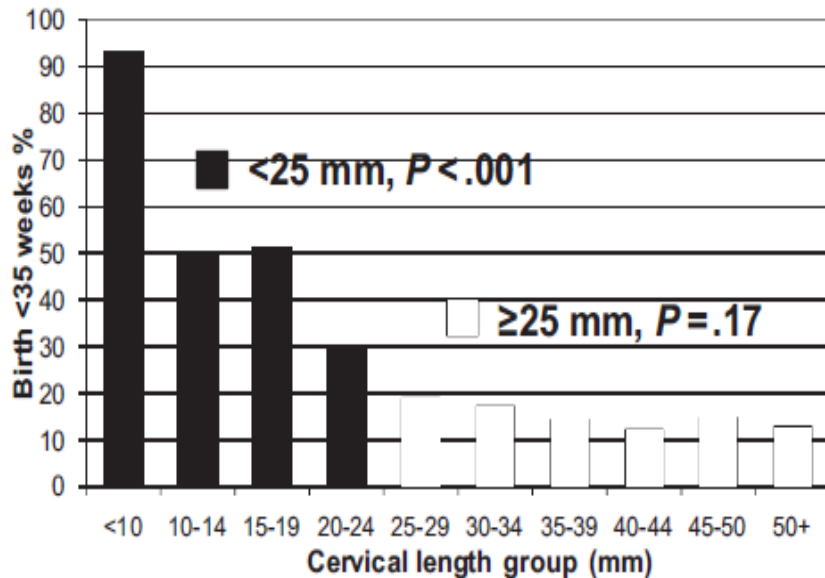
The Vaginal Ultrasound Cerclage Trial

Risk of Recurrent Preterm Birth in Women With Prior PTB and Cervical Length > 25 mm

No Evidence of a Cervical Length Gradient

FIGURE 2

Relationship between CL groups and birth <35 weeks



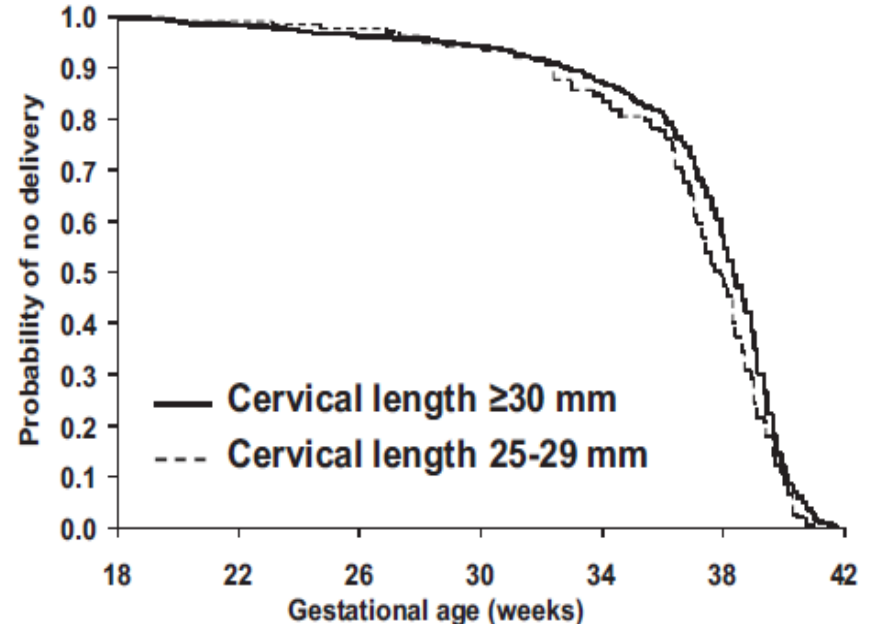
Rates of preterm birth <35 weeks by CL group in both <25 mm, no-cerclage, internal comparison cohort and ≥25 mm, failed-to-shorten cohort.

CL, cervical length.

Owen. Cervical lengths ≥25 mm and preterm birth. Am J Obstet Gynecol 2010.

FIGURE 3

Kaplan-Meier survival curves of CL groups





Probability of delivery across gestation in ≥25 mm cohort, comparing women with CLs 25-29 mm and those with CLs ≥30 mm.

CL, cervical length.

Owen. Cervical lengths ≥25 mm and preterm birth. Am J Obstet Gynecol 2010.

Cerclage for Short Cervix

What Do The Studies Mean?

- Stitch  PTB risk in women w/ twins
 - Twin Short Cervix \neq Singleton Short Cervix
- Stitch  PTB in women w/ Hx sPTB, but ...
- Reduced risk mostly in women with **very short cervix** or visible membranes, so
- What Does Cerclage Do ?
 - **Protect Exposed Membranes?** Maintain Cervical Mucous?
 - Alter the Force Vector? **Prevent Prolapse?**
 - **Correct a structural defect ?**

Comparison of **Vaginal Progesterone**, **Cerclage** and **Cervical Pessary** for Women with Hx PTB + Short Cervix

Alfirevic Z, Owen J, Carreras Moratonas E, Sharp AN, Szychowski JM, Goya M.
Ultrasound Obstet Gynecol. 2013 Feb;41(2):146-51

Comparison of Data from 3 Studies

- 142 Cerclage in USA
 - 59 Vaginal Progesterone in UK
 - 42 Pessary in Spain
- No Differences in Outcome for Cx < 25 mm

No Studies of **Progestogens** AND **Cerclage** Versus Either One Alone (Owen 2ndry QNS)

Arabin Cervical Pessary

- Flexible ring-like silicone device
- Varying sizes
 - Outer diameter ranging from 65-70 mm
 - Inner diameter ranging from 32-35 mm
 - Height curvature ranging from 21-30 mm



Image: Goya M, Pratcorona L, Merced C, et al. Cervical pessary in pregnant women with a short cervix (PECEP): An open-label randomised controlled trial. Lancet 2012

Arabin Cervical Pessary

- Small inner diameter fits around the cervix
 - Mechanically prevents exposure of the fetal membranes
- Changes the inclination of the cervical canal posteriorly
 - Centers the weight of the pregnancy on the anterior lower uterine segment

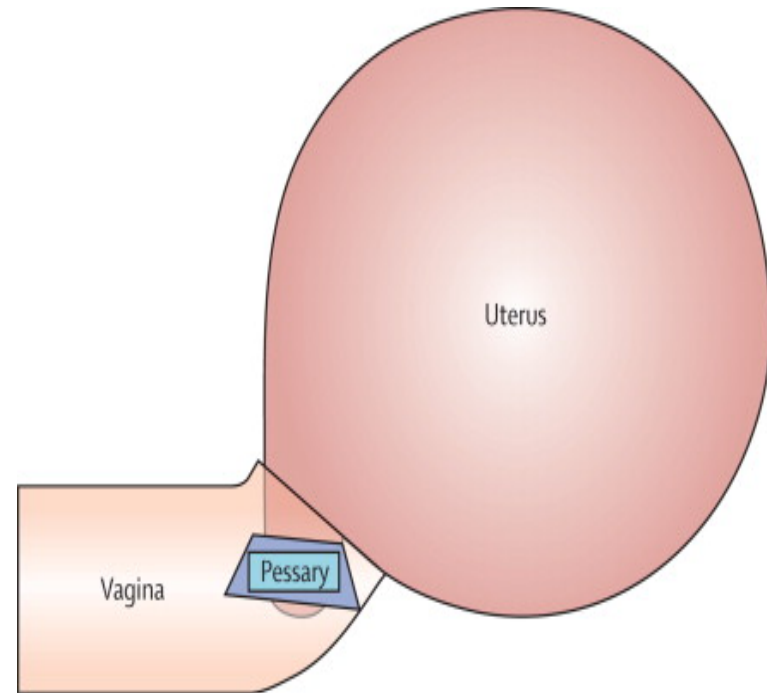


Image: Goya M, Pratcorona L, Merced C, et al. Cervical pessary in pregnant women with a short cervix (PECEP): An open-label randomised controlled trial. Lancet 2012

Studies of Cervical Pessary to Prevent Preterm Birth

- Most are observational or case-controlled
- 4 Randomized Trials in Singletons
 - **Forster** 1986
 - Entry = Dx Cervical Incompetence
 - Pessary (130) vs. Cerclage (120)
 - Type of pessary not specified
 - Outcome = Gest Age at delivery → **No Δ**
 - **Goya** - Lancet 2012- **PECEP** Trial
 - **Hui** – Am J Perinatol 2013
 - **Nicolaides** – **FMF** – 2015

Cervical pessary in pregnant women with a short cervix (PECEP): an open-label randomised controlled trial

Maria Goya, Laia Pratcorona, Carme Merced, Carlota Rodó, Leonor Valle, Azahar Romero, Miquel Juan, Alberto Rodríguez, Begoña Muñoz, Belén Santacruz, Juan Carlos Bello-Muñoz, Elisa Llurba. Teresa Hiaueras. Luis Cabero, Elena Carreras*, on behalf of the Pesario Cervical para Evitar Prematuridad (PECEP) Trial Group* *Lancet 2012; 379: 1800–06*

Cervical Sonography in General OB \approx 12,000 ♀

- 726 w/ Cervix \leq 25 mm @ 20 – 23 weeks
- 385 Consented – RCT Arabin Pessary or Expectant
- Primary Outcome Birth < 34 Weeks

Cervical Sonography in A General Obstetrical Population $\approx 12,000$ ♀

Goya et al Lancet 2012

726 w/ Cervix ≤ 25 mm



385 Consented



192

Pessary



190

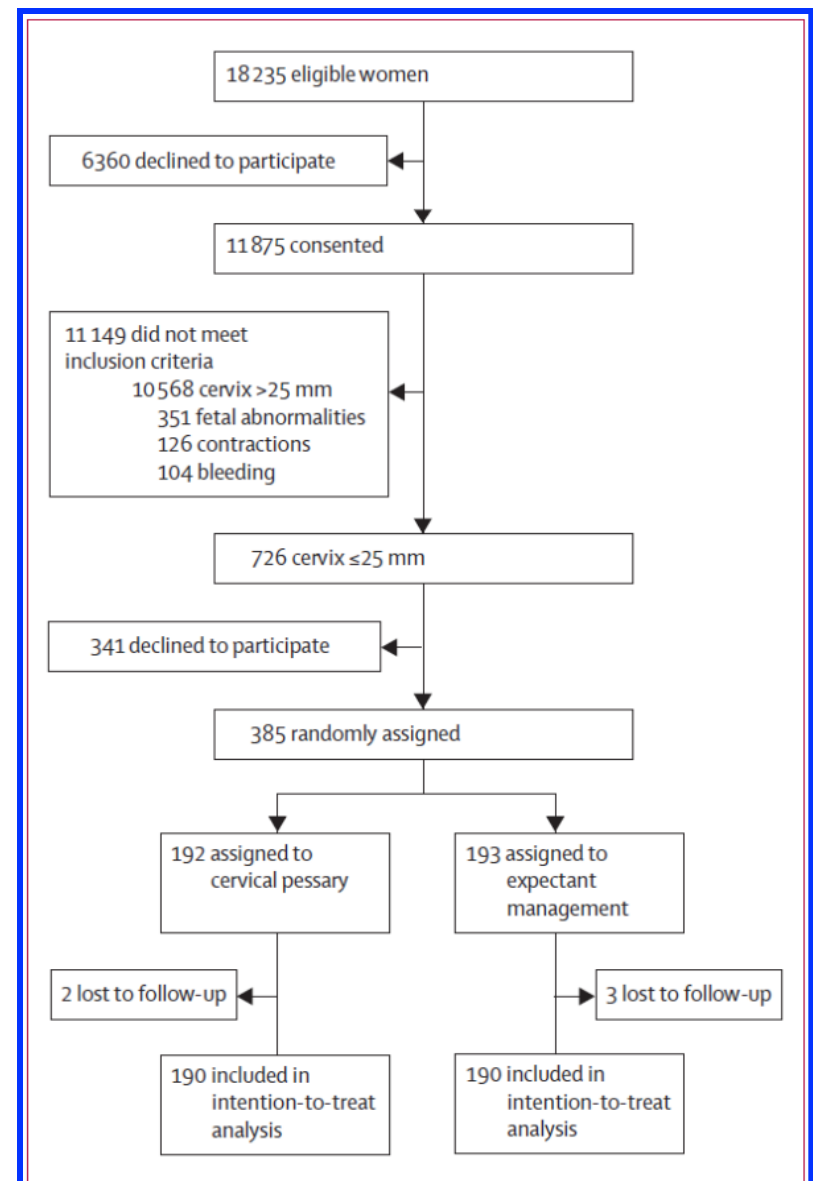


193

Expectant



190



Cervical pessary in pregnant women with a short cervix (PECEP): an open-label randomised controlled trial

Primary Outcome = Spontaneous PTB <34 weeks

6% in Pessary vs. 27% in Expectant

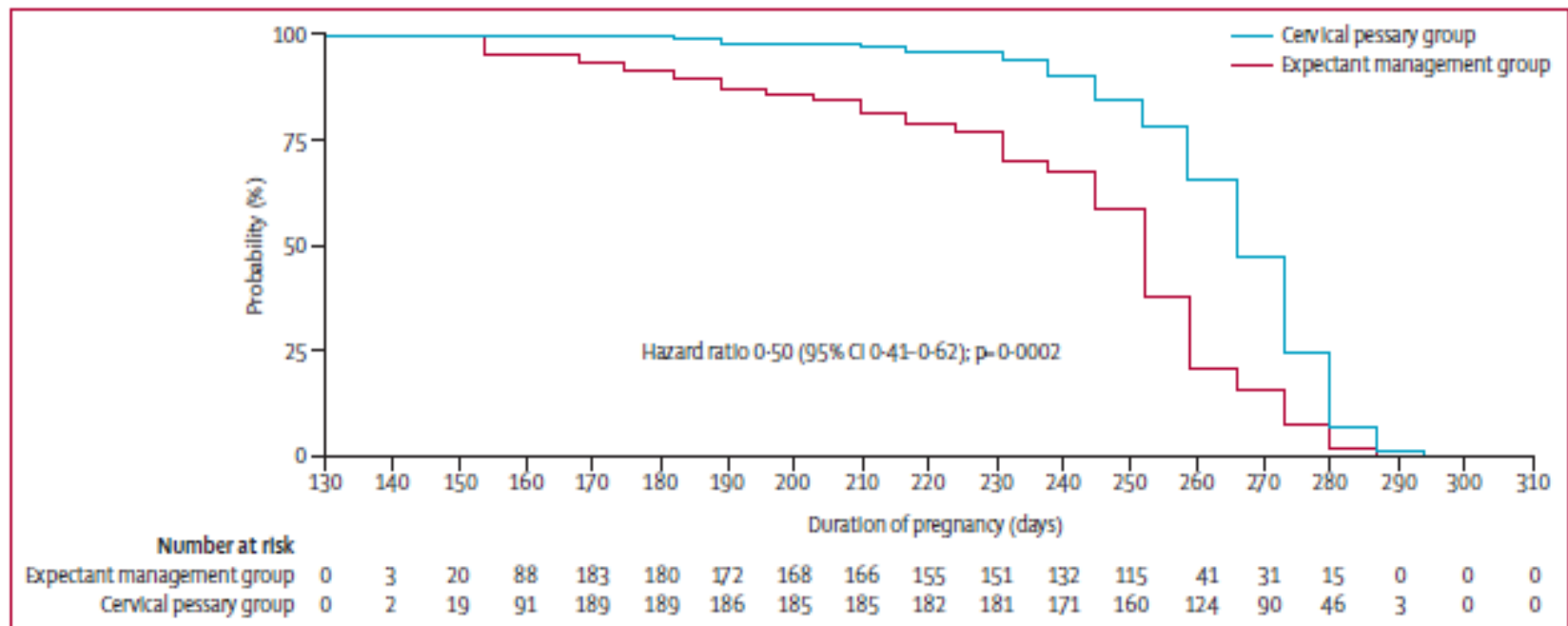


Figure 5: Kaplan-Meier plot of the probability of continued pregnancy without delivery in the cervical pessary and expectant management groups

Cervical pessary in pregnant women with a short cervix (PECEP): an open-label randomised controlled trial

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% PTB > Than Others Expectantly Managed

- **27%** PTB < 34 weeks in Goya control arm
- PTB rate in unselected untreated women
 - **18 %** < 35 weeks in **Preterm Prediction** in women w/ Cx ≤ 25 mm at 22 - 24 weeks
 - **15%** < 35 wks in **Taipale & Hiilesmaa** ≤ 25 mm
 - **16%** < 33 weeks in **Hassan** Placebo 10-20 mm

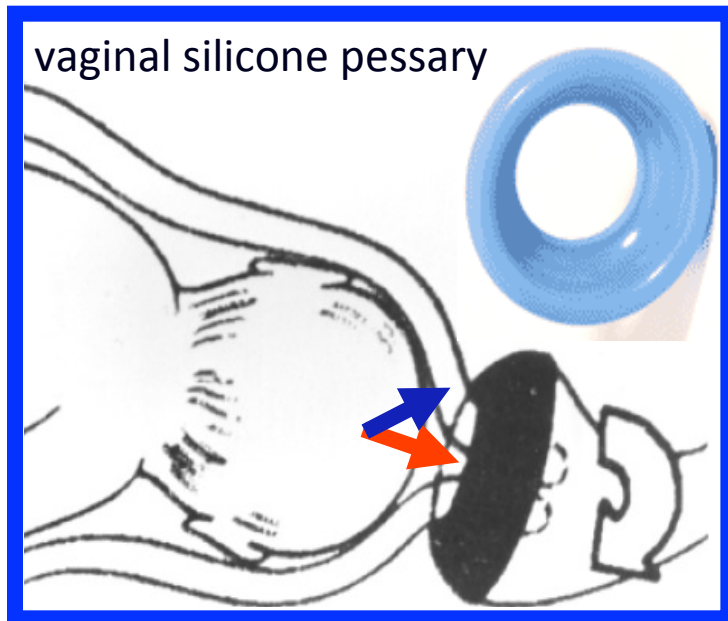
Cerclage Pessary for Preventing Preterm Birth in Women with a Singleton Pregnancy and a Short Cervix at 20 to 24 Weeks: A Randomized Controlled Trial

Hui et al – Chinese University of Hong Kong - *Am J Perinatol* 2013

- 4438 Cx Sono at 20-24 Wks → 206 (4.6%) < 25 mm
 - Excluded cervical insufficiency, cerclage, Cx dilation
- 108 Consented → Arabin Pessary or Expectant Rx
 - 53 Pessary Cx 19 mm vs. 58 Expectant Cx 20 mm
- Primary Outcome Delivery < 34 Weeks
 - Pessary Arm – 9.4% < 34 Weeks
 - Expectant Arm – 5.5 % < 34 Weeks

Preterm Birth Prevention

Pessary for Short Cx at 18-24w



FMF Study to be Presented at the
14th World Congress in Fetal Medicine
21st to 25th June 2015 in Crete, Greece

Slide Courtesy of Professor Nicolaides

Randomized study: Pessary vs Expectant Cervical length ≤ 25 mm at 20-24 wks

(n = 935)

**Pessary group
(n = 466)**

**Expectant group
(n = 469)**

Birth < 34 wks

Total 60 (12.9%)

Total 53 (11.3%)

**Spontaneous 52
(11.2%)**

**Spontaneous 49
(10.5%)**

Care for Singleton Pregnancy in Women with a History of PTB

- Detailed History of Gest Age & Labor Course
- Spontaneous PTB → Rx w/ Progestogen 16 wk
 - 17-OHPC 250 / Week, **or** Vaginal P 200 / Day
 - Cervical Length 16 – 24 Weeks → Cerclage if $< 25\text{mm}$
 - Continue Progestogen if Cerclage Placed
- Uncertain Presentation in Prior PTB
 - Review Labor Course & Pain, Placental Pathology
 - Rx Progestogen, **or** Rx Only If Cervix $\leq 25\text{ mm}$
- Indicated PTB → No Progesterone

Any Role for Pessary? No.

Care for Singleton Pregnancy in Low Risk Women

- Detailed History of All Pregnancies
 - Gestational Age & Labor Course
- Social &/or Medical Risks → Cervix Scan 18-22
 - Cervical Length ≤ 20 mm – Rx Vaginal P **or** 17P
 - Role for Cerclage?
- Prior Birth at Term – Review Symptoms
- Symptoms 16 – 32 Weeks
 - Premenstrual Δ , Pressure, Change Vaginal Mucus
 - Use Cervical Sonography

Care For Women with Past or Current Multiple Gestation

- **Detailed History of OB Hx & Conception**
- **Prior Singleton Preterm Birth, Now Twins**
 - Spontaneous PTB → Progestogen – 17P or Vag P
 - Cervical Ultrasound 16 – 24 Weeks → Cerclage
- **Prior Twin Preterm Birth, Now Singleton**
 - Twins < 34 Weeks → ↑ Risk of Singleton PTB
 - Treat as Hx SPTB – 5 studies show increased risk
 - Twins ≥ 34 Weeks – No Increased Risk
 - Treat as Normal

Any Role for Pessary?



Prevention of Preterm Birth in Twins RCT Pessary vs. Expectant

Randomised ($n = 1,180$)

Pessary group ($n = 588$)

Expectant group ($n = 589$)

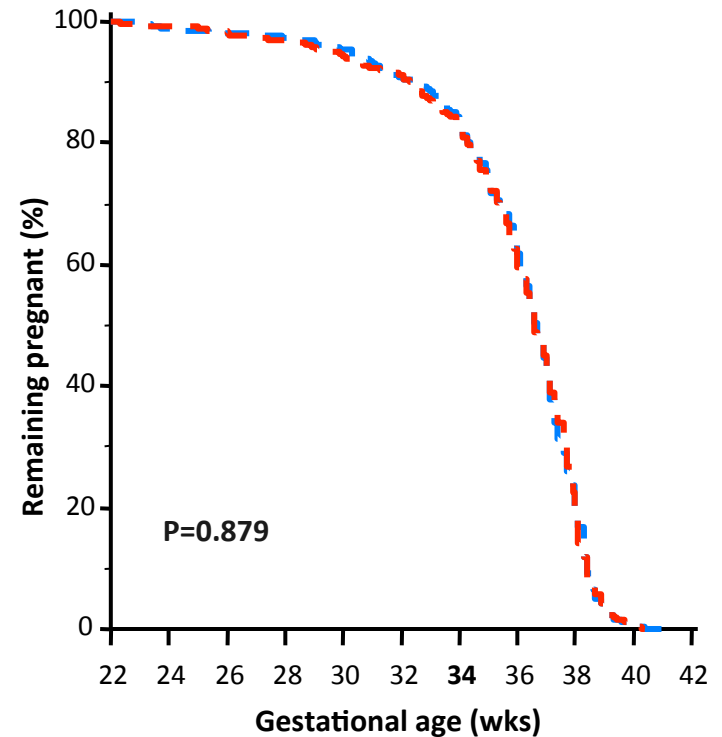
**Delivery < 34
wks**

Total 98 (16.7%)

**Spontaneous 80
(13.6%)**

Total 92 (15.6%)

**Spontaneous 76
(12.9%)**



Group: Expectant

588 583 578 574 562 535 487 365 118 3 1

Group: Pessary

588 584 576 569 555 536 484 351 111 3 0

FMF Study to be Presented at the 14th World Congress in Fetal Medicine

Slide Courtesy of Professor Nicolaides

Summary

- *Cervical Sonography Has Destroyed the Old Phenotypic Categories of Preterm Birth*
- **Some Preterm Births Are Preceded By Short Cx**
 - Many But Not All Are Progestogen-Responsive
 - Cerclage Helps When Cervix Is Very Short – How?
 - Pessary Probably Does Not Help
 - Hx PTB w/o Short Cervix → No Progestogen Effect
- **Short Cervix in Multiple Gestation is Not Helped By Either Progesterone or Cerclage**
 - The Mechanism of Cervical Shortening is Different