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Prevention of Prematurity in Twins

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Disclosure

- ▶ No conflicts of interest to declare

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Objectives

- ▶ Preterm birth – Introduction
- ▶ Cervical length & prediction of PTB in twins
- ▶ Progesterone
- ▶ Cerclage
- ▶ Pessary

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Preterm Birth – Introduction

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Preterm Birth

- ▶ Preterm birth 8% Canada
- ▶ Twin births account for 17-20% of all PTB
- ▶ Greater than 50% twins deliver preterm
- ▶ Prematurity leading causing of neonatal morbidity and mortality
- ▶ Multiple pregnancy increasing – ART, LMA



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Sonographic Cervical Length - Twins

Transvaginal sonographic cervical length for the prediction of spontaneous preterm birth in twin pregnancies: a systematic review and metaanalysis

Agustin Conde-Agudelo, MD, MPH; Roberto Romero, MD; Sonia S. Hassan, MD; Lami Yeo, MD

2010

Cervical length measurement for the prediction of preterm birth in multiple pregnancies: a systematic review and bivariate meta-analysis

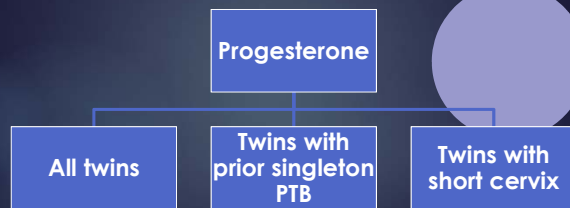
A. C. LIM*, M. A. HEGEMAN†, M. A. HUIS IN 'T VELD*, B. C. OPMEER‡, H. W. BRUNSE§ and B. W. J. MOL*

2011

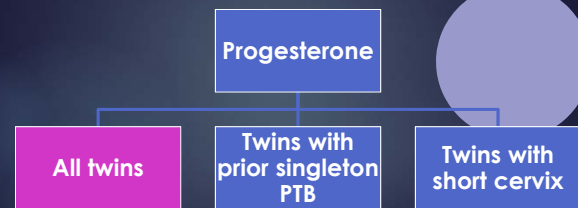
- ▶ TVUS cervical length is a predictor of PTB in twins

Progesterone

Progesterone



Progesterone



Progesterone – Unselected twins

Prenatal administration of progestogens for preventing spontaneous preterm birth in women with a multiple pregnancy (Review)

Dodd JM, Grivell RM, OBrien CM, Downswell T, Deussen AR

- ▶ Cochrane Review, 2017
- ▶ 17 studies, 4773 women

Progesterone – Unselected twins

	Vaginal Progesterone	IM Progesterone
Outcome	RR (95% CI)	
PTB < 37 weeks	0.97 (0.89 – 1.06)	1.05 (0.98 – 1.13)
PTB < 34 weeks	0.83 (0.63 – 1.09)	1.54 (1.06 – 2.26)
PTB < 28 weeks	1.22 (0.68 – 2.21)	1.08 (0.75 – 1.55)
PPROM	0.61 (0.23 – 1.60)	1.17 (0.84 – 1.63)

Progesterone compared to placebo or no intervention

Progesterone – Unselected twins

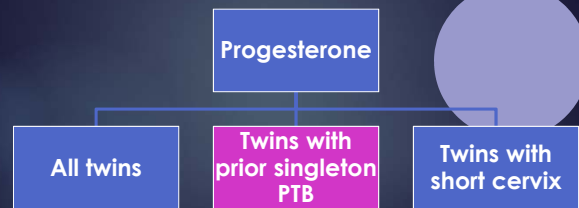
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	Vaginal Progesterone	IM Progesterone
Outcome	RR (95% CI)	
Birthweight <2500g	0.95 (0.88-1.03)	0.99 (0.9-1.08)
Neonatal mortality	1.53 (0.75-3.15)	0.92 (0.44-1.91)

Progesterone compared to placebo or no intervention

Progesterone

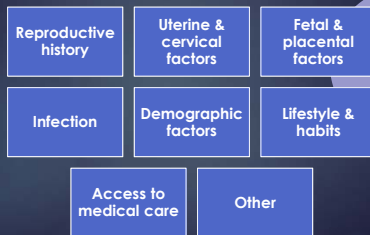
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Progesterone – Prior PTB

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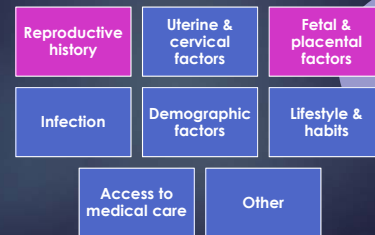
PTB Risk Factors



Progesterone – Prior PTB

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PTB Risk Factors



Recurrence of Spontaneous PTB

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- ▶ Singleton – Singleton
- ▶ Singleton – Twin
- ▶ Twin – Singleton

Recurrence of Spontaneous PTB

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- ▶ Singleton – Singleton (OR 2 – 7 if one prior PTB)
- ▶ Singleton – Twin
- ▶ Twin – Singleton

Recurrence of Spontaneous PTB

- ▶ Singleton – Singleton (OR 2 – 7 if one prior PTB)
- ▶ Singleton – Twin
- ▶ Twin - Singleton

[illegible]

Schaaf et al. 2012 (BJOG)

Recurrence of Spontaneous PTB

- ### ► Singleton - Twin

Gestational Age (weeks) Index Singleton Birth	Subsequent Twin Delivery OR (95% CI)
Term >37	Reference
<37	7.8 (5.5-11.2)
34 – 36 ^a	7.3 (5.0-10.6)
30 – 33 ^a	14.0 (3.9 – 50.5)
22-29 ^a	9.5 (1.8-48.9)

Schaaf et al. 2012 (BJOG)

Recurrence of Spontaneous PTB

- ▶ Singleton – Singleton (OR 2 – 7 if one prior PTB)
- ▶ Singleton – Twin
- ▶ Twin – Singleton

[illegible]

Menzies et al. 2018

Data presented at SMFM 2018, submitted for publication

Recurrence of Spontaneous PTB

- ▶ **Twin – Singleton**

Study or Subgroup	Pretest Test		Test Results		Odds Ratio		Odds Ratio	
	Events	Total	Events	Total	Weight	M-H, Total, 95% CI	M-H, Total, 95% CI	
Benoudia et al. 2012	4	168	4	168	16.06%	3.372 [0.56, 13.42]		
Facile et al. 2012	13	99	8	68	6.6%	4.993 [0.00, 22.87]		
Elattaf et al. 2012	16	144	2	111	4.8%	0.871 [0.30, 2.02]		
Elouadi et al. 2012	39	192	39	192	100%	1.0 [0.11, 9.12]		
Memoud et al. 2014	44	252	8	126	26.7%	3.122 [0.62, 9.78]		
Total (95% CI)	146	252	8	126	100.0%	2.76 [1.64, 4.71]		
Test for heterogeneity: $\chi^2 = 2.54$, df = 4, $P = 10\%$								
Test for overall effect: $Z = 4.65$ ($P = 0.00021$)								

GRADE

 Moderate

Data presented at SMFM 2018, submitted for publication

Effectiveness of progestogens to improve perinatal outcome in twin pregnancies: an individual participant data meta-analysis

E Schuit,^{1,2} S Stock,¹ L Rode,¹ DJ Rouse,¹ AC Lim,¹ JE Norman,¹ AH Nassar,¹ V Serra,¹ CA Combs,¹ C Vayssières,¹ MM Aboulghar,¹ S Wood,¹ E Çetinoğlu,¹ CM Briery,¹ EB Fonseca,¹ K Worda,¹ A Tabor,¹ EA Thom,¹ SN Caritis,¹ J Ajwad,¹ IM Uhta,¹ A Perales,¹ J Messegue,¹ K Meurel,¹ T Garite,¹ MA Aboulghar,¹ YM Amin,¹ S Ross,¹ C Cam,¹ A Karateke,¹ JC Morrison,¹ EF Magann,¹ KH Nicolaides,¹ NPA Zulfattoh,¹ RHH Groenewold,¹ KGM Moons,¹ A Kwee,¹ BWJ Mol,¹ a Global Obstetrics Network (GoNet) collaboration

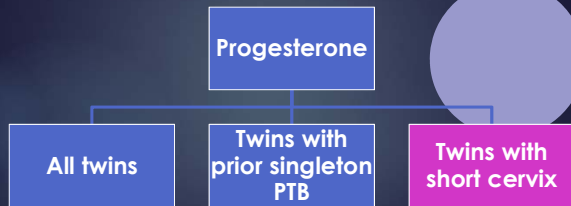
- ▶ Systematic review & meta-analysis
- ▶ 13 studies, 3768 women
- ▶ Primary composite outcome
- ▶ Sub-group analysis of twins with prior singleton PTB

Schuit et al. (2012)

- ▶ Subgroup analysis of women with prior singleton PTB
 - ▶ Total 90 women
 - ▶ Vaginal progesterone vs. controls
 - ▶ RR 2.0 (95% CI 0.93 – 4.2)

Progesterone

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Vaginal progesterone decreases preterm birth and neonatal morbidity and mortality in women with a twin gestation and a short cervix: an updated meta-analysis of individual patient data

R. ROMERO^{1,2,3,4}, A. CONDE-AGUILO^{1,2}, W. EL-REFAIE⁵, L. RODE^{2,3}, M. L. BRIZOT^{1,2}, E. CETINGOZ^{1,2}, V. SERRA^{1,2,3}, L. DA FONSECA^{1,2}, M. S. ABDELHATEZ², A. TABOR^{1,2}, A. PERALES^{1,2,3}, S. S. HASSAN^{1,2} and K. H. NICOLAIDES⁶ 2017

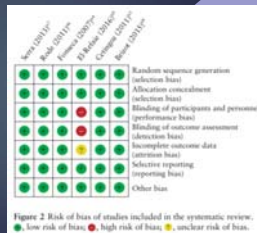
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- ▶ Systematic review & meta-analysis
 - ▶ Updated from a 2012 study (52 women in 3 RCTs)
 - ▶ 6 studies included
- ▶ Primary outcome – PTB < 33 weeks
- ▶ Included twin gestations with midtrimester asymptomatic CL ≤25mm

Romero et al., 2017

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- ▶ 5 of 6 studies - vaginal progesterone vs. placebo
- ▶ El-Rafaie study vaginal progesterone vs. no treatment



Romero et al., 2017

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PTB < 33 weeks

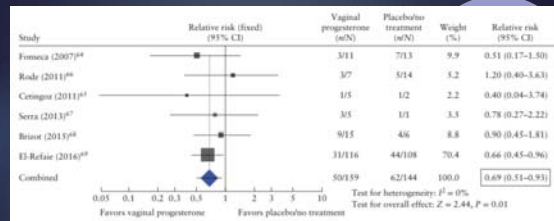


Figure 3 Forest plot of the effect of vaginal progesterone on the risk of preterm birth < 33 weeks' gestation. CI, confidence interval.

Romero et al., 2017

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Table 3 Effect of vaginal progesterone on the risk of preterm birth

Outcome	Trials (n ⁶⁰)	Events (n/Total (N))		Pooled RR (95% CI)	I ² (%)	NNT (95% CI)
		Vaginal progesterone	Placebo/no treatment			
Preterm birth < 37 weeks	6 ¹⁴⁻¹⁹	137/159	131/144	0.94 (0.86-1.02)	0	—
Preterm birth < 36 weeks	6 ¹⁴⁻¹⁹	112/159	110/144	0.92 (0.80-1.05)	0	—
Preterm birth < 35 weeks	6 ¹⁴⁻¹⁹	90/159	89/144	0.83 (0.69-0.99)	0	9 (5-147)
Preterm birth < 34 weeks	6 ¹⁴⁻¹⁹	63/159	78/144	0.71 (0.56-0.91)	0	6 (4-21)
Preterm birth < 32 weeks	6 ¹⁴⁻¹⁹	29/159	46/144	0.51 (0.34-0.77)	0	6 (5-14)
Preterm birth < 30 weeks	6 ¹⁴⁻¹⁹	14/159	22/144	0.47 (0.25-0.86)	0	12 (9-47)
Preterm birth < 28 weeks	6 ¹⁴⁻¹⁹	9/159	12/144	0.51 (0.24-1.08)	0	—
Spontaneous preterm birth < 33 weeks	6 ¹⁴⁻¹⁹	42/159	54/144	0.67 (0.48-0.93)	0	8 (5-38)
Spontaneous preterm birth < 34 weeks	6 ¹⁴⁻¹⁹	55/159	69/144	0.71 (0.54-0.93)	0	7 (5-30)

CI, confidence interval; NNT, number needed to treat; refs, reference numbers; RR, relative risk.

Romero et al., 2017

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Vaginal progesterone vs. placebo/no treatment	
Gestational age at delivery (weeks)	Pooled RR (95% CI)
< 37	0.94 (0.86 - 1.02)
< 36	0.92 (0.8 - 1.05)
< 34	0.71 (0.56 - 0.91)
< 32	0.51 (0.34 - 0.77)
< 30	0.47 (0.25 - 0.86)
< 28	0.51 (0.24 - 1.08)

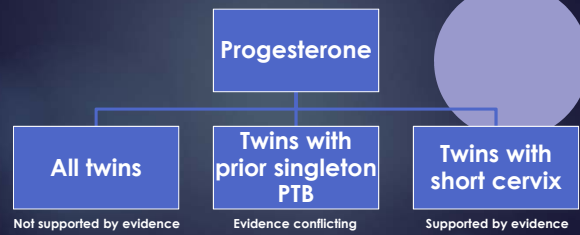
Romero et al., 2017

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Vaginal progesterone vs. placebo/no treatment	
Gestational age at delivery (weeks)	Pooled RR (95% CI)
< 37	0.94 (0.86 – 1.02)
< 36	0.92 (0.8 – 1.05)
< 34	0.71 (0.56 – 0.91)
< 32	0.51 (0.34 – 0.77)
< 30	0.47 (0.25 – 0.86)
<28	0.51 (0.24 – 1.08)

Progesterone

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Cerclage

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Cerclage for Short Cervix on Ultrasonography

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Meta-Analysis of Trials Using Individual Patient-Level Data
 Vincenza Berghella, MD, Anthony O. Odibo, MD, Meekai S. To, MD, Orion A. Rust, MD, and Sietse M. Althuisius, MD 2005

- ▶ Meta-analysis
- ▶ 4 studies included
 - ▶ 3 studies included twin data
- ▶ Primary outcome – preterm birth
- ▶ Secondary outcomes – perinatal mortality

Berghella et al. 2005

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Table 1. Descriptive Data for Each Trial

Study	Hospitals (n)	Population Screened	Singletons With Prior PTB (%) ^a	GA at Screening (wk)	Cervical Length (mm)	Funnelling (%)	Declined Randomization (%)
Rust ^b	1	All singletons, twins and triplets	102/207 (49)	16–24	< 25	≥ 25	38/229 (14)
Althuisius ^c	2	Singletons with suspected cervical incompetence; twins	26/35 (74)	14–27	< 25	...	NA
To ^d	12	All singletons	44/253 (17)	22–24	≤ 15	...	217/470 (46)
Berghella ^e	2	Singletons with risk factors for PTB and twins	36/57 (63)	14–24	< 25	> 25	67/128 (52)

PTB, preterm birth; GA, gestational age; NA, not available.
^a For total singletons.

Berghella et al. 2005

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Table 2. Selected Outcomes

Population	Outcome	Cerclage (%)	No Cerclage (%)	RR (95% CI)
Total				
PTB < 37 wk	127/301 (42.3)	127/301 (42.3)	127/301 (42.3)	0.94 (0.86–1.02)
PTB < 36 wk	80/201 (40.0)	80/201 (40.0)	80/201 (40.0)	0.92 (0.8–1.05)
PTB < 34 wk	40/101 (39.6)	40/101 (39.6)	40/101 (39.6)	0.71 (0.56–0.91)
PTB < 32 wk	20/101 (19.8)	20/101 (19.8)	20/101 (19.8)	0.51 (0.34–0.77)
PTB < 30 wk	10/101 (9.9)	10/101 (9.9)	10/101 (9.9)	0.47 (0.25–0.86)
PTB < 28 wk	5/101 (5.0)	5/101 (5.0)	5/101 (5.0)	0.51 (0.24–1.08)
Singletons				
Rust ^b	102/207 (49)	102/207 (49)	102/207 (49)	0.94 (0.86–1.02)
Althuisius ^c	26/35 (74)	26/35 (74)	26/35 (74)	0.92 (0.8–1.05)
To ^d	44/253 (17)	44/253 (17)	44/253 (17)	0.71 (0.56–0.91)
Berghella ^e	36/57 (63)	36/57 (63)	36/57 (63)	0.51 (0.34–0.77)
Twins				
PTB < 37 wk	10/101 (9.9)	10/101 (9.9)	10/101 (9.9)	0.94 (0.86–1.02)
PTB < 36 wk	5/101 (5.0)	5/101 (5.0)	5/101 (5.0)	0.92 (0.8–1.05)
PTB < 34 wk	2/101 (2.0)	2/101 (2.0)	2/101 (2.0)	0.71 (0.56–0.91)
PTB < 32 wk	1/101 (1.0)	1/101 (1.0)	1/101 (1.0)	0.51 (0.34–0.77)
PTB < 30 wk	0/101 (0.0)	0/101 (0.0)	0/101 (0.0)	0.47 (0.25–0.86)
PTB < 28 wk	0/101 (0.0)	0/101 (0.0)	0/101 (0.0)	0.51 (0.24–1.08)
Triplet				
PTB < 37 wk	0/101 (0.0)	0/101 (0.0)	0/101 (0.0)	0.94 (0.86–1.02)
PTB < 36 wk	0/101 (0.0)	0/101 (0.0)	0/101 (0.0)	0.92 (0.8–1.05)
PTB < 34 wk	0/101 (0.0)	0/101 (0.0)	0/101 (0.0)	0.71 (0.56–0.91)
PTB < 32 wk	0/101 (0.0)	0/101 (0.0)	0/101 (0.0)	0.51 (0.34–0.77)
PTB < 30 wk	0/101 (0.0)	0/101 (0.0)	0/101 (0.0)	0.47 (0.25–0.86)
PTB < 28 wk	0/101 (0.0)	0/101 (0.0)	0/101 (0.0)	0.51 (0.24–1.08)
Declined Randomization				
PTB < 37 wk	38/229 (16.6)	38/229 (16.6)	38/229 (16.6)	0.94 (0.86–1.02)
PTB < 36 wk	21/174 (12.0)	21/174 (12.0)	21/174 (12.0)	0.92 (0.8–1.05)
PTB < 34 wk	10/101 (9.9)	10/101 (9.9)	10/101 (9.9)	0.71 (0.56–0.91)
PTB < 32 wk	5/101 (5.0)	5/101 (5.0)	5/101 (5.0)	0.51 (0.34–0.77)
PTB < 30 wk	2/101 (2.0)	2/101 (2.0)	2/101 (2.0)	0.47 (0.25–0.86)
PTB < 28 wk	1/101 (1.0)	1/101 (1.0)	1/101 (1.0)	0.51 (0.24–1.08)
Perinatal Mortality				
PTB < 37 wk	10/101 (9.9)	10/101 (9.9)	10/101 (9.9)	0.94 (0.86–1.02)
PTB < 36 wk	5/101 (5.0)	5/101 (5.0)	5/101 (5.0)	0.92 (0.8–1.05)
PTB < 34 wk	2/101 (2.0)	2/101 (2.0)	2/101 (2.0)	0.71 (0.56–0.91)
PTB < 32 wk	1/101 (1.0)	1/101 (1.0)	1/101 (1.0)	0.51 (0.34–0.77)
PTB < 30 wk	0/101 (0.0)	0/101 (0.0)	0/101 (0.0)	0.47 (0.25–0.86)
PTB < 28 wk	0/101 (0.0)	0/101 (0.0)	0/101 (0.0)	0.51 (0.24–1.08)
Stillbirth				
PTB < 37 wk	10/101 (9.9)	10/101 (9.9)	10/101 (9.9)	0.94 (0.86–1.02)
PTB < 36 wk	5/101 (5.0)	5/101 (5.0)	5/101 (5.0)	0.92 (0.8–1.05)
PTB < 34 wk	2/101 (2.0)	2/101 (2.0)	2/101 (2.0)	0.71 (0.56–0.91)
PTB < 32 wk	1/101 (1.0)	1/101 (1.0)	1/101 (1.0)	0.51 (0.34–0.77)
PTB < 30 wk	0/101 (0.0)	0/101 (0.0)	0/101 (0.0)	0.47 (0.25–0.86)
PTB < 28 wk	0/101 (0.0)	0/101 (0.0)	0/101 (0.0)	0.51 (0.24–1.08)
Neonatal Mortality				
PTB < 37 wk	10/101 (9.9)	10/101 (9.9)	10/101 (9.9)	0.94 (0.86–1.02)
PTB < 36 wk	5/101 (5.0)	5/101 (5.0)	5/101 (5.0)	0.92 (0.8–1.05)
PTB < 34 wk	2/101 (2.0)	2/101 (2.0)	2/101 (2.0)	0.71 (0.56–0.91)
PTB < 32 wk	1/101 (1.0)	1/101 (1.0)	1/101 (1.0)	0.51 (0.34–0.77)
PTB < 30 wk	0/101 (0.0)	0/101 (0.0)	0/101 (0.0)	0.47 (0.25–0.86)
PTB < 28 wk	0/101 (0.0)	0/101 (0.0)	0/101 (0.0)	0.51 (0.24–1.08)

Berghella et al. 2005

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Outcome	Cerclage n/N (%)	No cerclage n/N (%)	RR (95% CI)
PTB < 35 weeks	18/24 (75%)	9/25 (36%)	2.15 (1.15-4.01)
Perinatal mortality	11/48 (23%)	3/50 (6%)	2.66 (0.83-8.54)

Berghella et al. 2005

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- ▶ Cerclage increases risk of PTB in twins
- ▶ 49 women included in study (24 in cerclage group, 25 in no cerclage group)
- ▶ Authors noted limitation due to small sample size

Cerclage for short cervix in twin pregnancies: systematic review and meta-analysis of randomized trials using individual patient-level data

GABRIELE SACCONE¹, ORION RUST², SIETSKIE ALTHUISIUS¹, AMANDA ROMAN³ & VINCENZO BERGHELLA⁴ 2015

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- ▶ New analysis 10 years after previous study
- ▶ Same studies included in analysis
- ▶ Results were adjusted for confounders
 - ▶ Gestational age at randomization
 - ▶ Previous PTB

Saccone et al. 2015

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Table 2. Primary and secondary outcomes in all twin pregnancies.

Outcome	Cerclage (n = 24)		Control (n = 25)		RR (95% CI)	aOR (95% CI)
	n	%	n	%		
PTB < 37 weeks	22	91.7	19	76.0	1.18 (0.91-1.53)	1.13 (0.17-8.66)
PTB < 35 weeks	18	75.0	9	36.0	1.63 (0.88-3.02)	1.44 (0.66-7.11)
PTB < 34 weeks	15	62.5	6	24.0	2.19 (0.72-6.63)	1.17 (0.23-3.79)
PTB < 32 weeks	11	45.8	4	16.0	2.48 (0.96-6.37)	1.77 (0.88-3.39)
PTB < 28 weeks	7	29.2	2	8.0	2.62 (0.72-9.51)	1.66 (0.62-4.01)
PTB < 24 weeks	5	20.8	0	0	N/A	N/A
Perinatal deaths	11/48	22.9	3/50	6.0	2.66 (0.83-8.54)	2.04 (0.55-8.32)
Low birthweight	42/48	87.5	29/50	58	1.39 (1.06-1.83)	1.23 (0.85-2.55)
Very low birthweight	25/48	52.1	7/50	14.0	3.31 (1.58-6.91)	2.22 (1.07-5.73)
Respiratory distress syndrome	15/48	31.3	3/50	6.0	5.07 (1.75-14.70)	3.88 (1.09-21.03)
Intraventricular hemorrhage	3/48	6.3	3/50	6.0	1.13 (0.27-4.74)	1.09 (0.21-4.98)
Sepsis	0/48	0	2/50	4.0	0.23 (0.01-4.58)	0.18 (0.01-5.68)
NICU	5/22	22.7	11/20	55.0	0.35 (0.06-2.12)	0.45 (0.12-2.49)

- ▶ Logistic regression performed to correct data for confounders

Saccone et al. 2015

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Table 2. Primary and secondary outcomes in all twin pregnancies.

Outcome	Cerclage (n = 24)		Control (n = 25)		RR (95% CI)	aOR (95% CI)
	n	%	n	%		
PTB < 37 weeks	22	91.7	19	76.0	1.18 (0.91-1.53)	1.13 (0.17-8.66)
PTB < 35 weeks	18	75.0	9	36.0	1.63 (0.88-3.02)	1.44 (0.66-7.11)
PTB < 34 weeks	15	62.5	6	24.0	2.19 (0.72-6.63)	1.17 (0.23-3.79)
PTB < 32 weeks	11	45.8	4	16.0	2.48 (0.96-6.37)	1.77 (0.88-3.39)
PTB < 28 weeks	7	29.2	2	8.0	2.62 (0.72-9.51)	1.66 (0.62-4.01)
PTB < 24 weeks	5	20.8	0	0	N/A	N/A
Perinatal deaths	11/48	22.9	3/50	6.0	2.66 (0.83-8.54)	2.04 (0.55-8.32)
Low birthweight	42/48	87.5	29/50	58	1.39 (1.06-1.83)	1.23 (0.85-2.55)
Very low birthweight	25/48	52.1	7/50	14.0	3.31 (1.58-6.91)	2.22 (1.07-5.73)
Respiratory distress syndrome	15/48	31.3	3/50	6.0	5.07 (1.75-14.70)	3.88 (1.09-21.03)
Intraventricular hemorrhage	3/48	6.3	3/50	6.0	1.13 (0.27-4.74)	1.09 (0.21-4.98)
Sepsis	0/48	0	2/50	4.0	0.23 (0.01-4.58)	0.18 (0.01-5.68)
NICU	5/22	22.7	11/20	55.0	0.35 (0.06-2.12)	0.45 (0.12-2.49)

- ▶ Cerclage does not increase risk PTB (but also does not decrease risk)

Efficacy of ultrasound-indicated cerclage in twin pregnancies

Amanda Roman, MD; Burton Rochelson, MD; Nathan S. Fox, MD; Matthew Hoffman, MD, MPH; Vincenzo Berghella, MD; Vrunda Patel, MD; Ilia Calluzzo, MD; Gabriele Saccone, MD; Adiel Fleischer, MD 2015

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- ▶ Retrospective cohort (1995 – 2012, 4 institutions)
- ▶ Asymptomatic women, twin gestations
- ▶ TVUS CL ≤ 25mm (subgroup analysis of ≤ 15mm)
- ▶ Primary outcome – PTB < 34 weeks

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TABLE 2
Perinatal outcomes of twin pregnancies with cervical length ≤ 25 mm

Variable	UIC n = 57	Control n = 83	P value
GA at delivery, wk	32.05 \pm 5.1	32.58 \pm 4.63	.82
Birthweight, g ^a	1739 \pm 767	1714 \pm 737	.7
Birthweight <1500 g ^a	37/114 (32.4)	64/166 (38.5)	.26
Apgar <7 at 5 min ^b	14/114 (8.7)	21/166 (12.6)	1.0
PPROM	9 (15.7)	12 (14.5)	.81
Admission to NICU (born alive only)	68/102 (66.6)	111/156 (71.1)	.5
Perinatal mortality	20/114 (17.5)	19/166 (11.4)	1.0

Variables described as mean \pm SD or frequencies (percentage).

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Perinatal outcomes by cervical length subgroups

Outcome	UIC	Control	aOR (95% CI) ^a	P value
Diagnosis to delivery interval, wk				
CL ≤ 25 mm	12.58 \pm 4.83	10.53 \pm 4.97	—	.02
CL 16–25 mm	12.66 \pm 5.3	11.3 \pm 5.1	—	.32
CL ≤ 15 mm	12.52 \pm 4.5	8.76 \pm 4.65	—	<.001

- Cerclage prolonged pregnancy by 3.75 weeks in subgroup of women with CL ≤ 15 mm ($p < 0.001$)

Roman et al. 2015

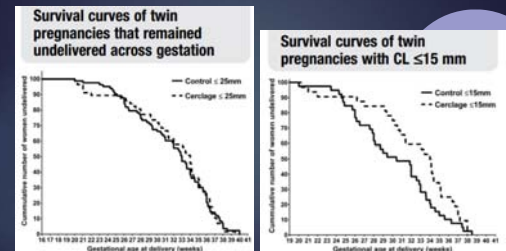
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PTB < 34 weeks	Cerclage	Control	aOR (95% CI)
CL ≤ 25 mm	29	53	0.37 (0.16–1.1)
CL 16–25 mm	13	22	1.05 (0.56–1.9)
CL ≤ 15 mm	16	31	0.51 (0.31–0.83)

- Decreased odds of PTB < 34 weeks in cerclage group if CL ≤ 15 mm (aOR 0.51)

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- Limitations of study
 - Retrospective methodology
 - Relatively small sample size
 - CL ≤ 25 mm: 57 women in cerclage group, 83 in control
 - CL ≤ 15 mm: 32 women in cerclage group, 34 in control

Pessary

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PTB Prevention - Pessary

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- ▶ Pessaries may prevent PTB by:
 - ▶ Altering the angle of the cervix, thus shifting weight of gravid uterus on the cervix
 - ▶ Obstruction of internal cervical os, thus acting as a barrier for ascending infection

Arabin Pessary

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Cervical pessary to prevent preterm birth in women with twin gestation and sonographic short cervix: a multicenter randomized controlled trial (PECEP-Twins)

2016

Maria Goya, MD, PhD; Maria de la Calle, MD, PhD; Laia Pratcorona, MD; Carme Mercadé, MD; Carlota Rodó, MD; Begoña Muñoz, MD, PhD; Miquel Juan, MD; Ariana Serrano, MD; Elisa Lúria, MD, PhD; Teresa Higuera, MD, PhD; Elena Camarero, MD, PhD; Luis Cabero, MD, PhD, on behalf of the PECEP-Twins Trial Group

- ▶ RCT, 5 centres in Spain
- ▶ Randomized to pessary (68 women) vs. expectant (66 women) at 22 weeks
- ▶ CL ≤ 25 mm
- ▶ Significant reduction in PTB < 34 weeks in pessary group
 - ▶ 16.2% women delivered < 34 weeks in pessary group vs. 39.4% controls

Prevention of preterm birth with pessary in twins (PoPPT): a randomized controlled trial

2017

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- ▶ RCT, 23 women in each arm (intention to treat analysis)
- ▶ Women with twin gestation randomized to Bioteque pessary or no pessary
- ▶ CL ≤ 30 mm
- ▶ No reduction in PTB in pessary group



Progesterone, cerclage or pessary?

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Preterm birth prevention in twin pregnancies with progesterone, pessary, or cerclage: a systematic review and meta-analysis

2017

A. Jarde,^a O. Lutsiv,^a CK Park,^b J. Barrett,^c J. Beyene,^b S. Saito,^a JM Dodd,^a PS Shah,^d JL Cook,^a AB Biringer,^e L. Giglia,^f Z. Han,^g K. Staub,^h W. Mundie,ⁱ C. Vera,^h L. Sabatino,^h SK Liyanage,^a SD McDonald^a

- ▶ 23 trials, 6626 women
- ▶ Primary outcomes – PTB < 37 weeks, < 34 weeks
- ▶ Secondary outcomes – neonatal and maternal

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Table 2. Primary outcomes of systematic review and meta-analysis of prevention of preterm birth in twin pregnancies with progesterone, pessary, and cerclage, compared with placebo or treatment as usual

Outcome	Intervention	Studies	n	χ^2	P	RR (95% CI)	P ^a
Preterm birth < 34 weeks of gestation	Progesterone	10	2180	0.09	55%	0.91 (0.70-1.18)	0.26
	Vaginal	7	1751	0.04	38%	0.82 (0.64-1.05)	
	Intramuscular	3	429	0.16	60%	1.18 (0.66-2.12)	
	Cerclage	3	43	0.53	39%	1.21 (0.34-4.31)	
	Pessary	2	1311	0.36	87%	0.71 (0.29-1.71)	
Preterm birth < 37 weeks of gestation	Progesterone	13	3686	0.00	30%	1.01 (0.95-1.08)	0.15
	Vaginal	6	1584	0.01	41%	0.94 (0.83-1.07)	
	Intramuscular	7	2102	0.00	8%	1.04 (0.98-1.12)	
	Cerclage	3	78	0.00	0%	1.11 (0.75-1.85)	
	Pessary	2	929	0.00	0%	0.98 (0.86-1.07)	
Neonatal death	Progesterone	12	8006	0.12	21%	1.16 (0.76-1.79)	0.53
	Vaginal	5	3847	0.00	0%	1.38 (0.78-2.43)	
	Intramuscular	7	4159	0.34	43%	1.03 (0.51-2.11)	
	Cerclage	1	8	—	—	5.57 (0.44-70.55)	
	Pessary	3	4210	0.00	2%	0.89 (0.57-1.38)	

- ▶ No significant difference in primary outcome for each of the interventions

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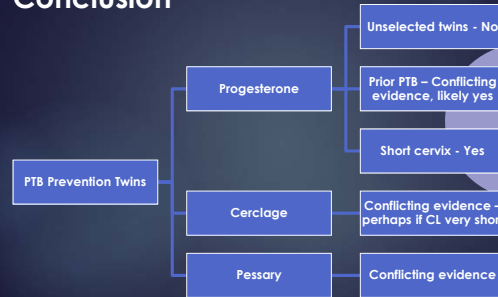
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Secondary Outcomes	RR (95% CI)
Neonatal mechanical ventilation	0.68 (0.53 – 0.88)
Early neonatal death	0.49 (0.33 – 0.73)

- Significant reduction in selected secondary outcomes in women taking vaginal progesterone

Conclusion

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Questions

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References

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