Progesteron'un düşük ve preterm doğumları önlemedeki yeri (Lehine)

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Progesteron

Kolesterol

Pregnenolon

Progesteron

17-α- Hidroksi pregnenolon

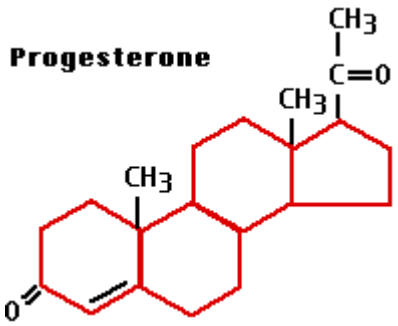
17- Hidroksi progesteron

Dehidro-epi androsteron

Andro-stenedion

Östriol

Östron



- Corpus luteum
- Plasenta

- Desidualizasyon
- İmplantasyon- gest. devamı
- Myometriyal kontraktilite inh.
- Meme gelişimi

Progesteron

- İlk olarak corpus luteum tarafından salınır.
- 7.- 9. haftada plasenta üretimi devralır.
- Embryonun sağlıklı bir şekilde implantasyonunu sağlar.
- Gebeliğin devamı için gerekli

Gebelikte progesteron kullanımı

- Luteal faz desteği
- Düşük tehdidi

- Preterm doğumu önleme

- Vaginal (günlük)
  - Jel 90 mg progesteron
- Oral/Vaginal (günlük)
  - Kapsül 100 mg mikronize progesteron
- İM (haftalık)
  - Amp 250 mg Hidroksiprogesteron kaproat

TABLE 3

Progesterone: pharmacologic types and protocols

Type	Route	Dose (mg)	Timing	References
Synthetic 17P	IM	250	Weekly from 16-20 wk	7,12,15,19
	IM	341	Twice weekly	11,19
	IM	250	Thrice weekly	19
	IM	500	Weekly	15
	IM	250	Every 3 days from 28 wk	15
	IM	1000	Weekly from 16 wk	15
	IM	25	Every 5 days	14
Natural progesterone	Vaginal	200	Nightly, 24-33 wk	8,19
	Vaginal	400	Daily, 18 wk to delivery	6,19
	Vaginal	100	Daily capsules to 34 wk	13
	Vaginal	90	Daily, 18 wk to delivery	9
	Oral	900-1600	Daily, from onset of PTL	18

IM, intramuscular; *PTL*, preterm labor; *17P*, 17-alpha-hydroxyprogesterone.

Tita. Progesterone for preterm birth prevention: an evolving intervention. Am J Obstet Gynecol 2009.

1. Trimester Kanamaları

- **Korpus luteumun yeterli progesteron üretmemesi sonucu implantasyon için uygun endometrium gelişimi olmaması.**
- **Luteal fazda endometriumun progesterona yetersiz yanıtı.**
- **Lh aşırı salınımı ,hiperandrojenemik durumlar veya foliküler fazda kalitesiz oosit gelişiminin estrojen sekresyonu ve progesteron korpus luteum fonksiyonuna kötü etkisi**

- **Günümüzde 1. trimesterde subkoriyonik hematom ve vaginal kanama ile ilişkili komplikasyonların önlenmesi için bilimsel temelli tedaviler yoktur.**
- **Birçok hekim ilk trimester kanamalı gebelerde progesteronu yaygın olarak tedavide kullanmaktadır.**

Progesteron

İmmünolojik faktörler

Myometriyal hiperkontraktilite

Nöroendokrin eksiklikler

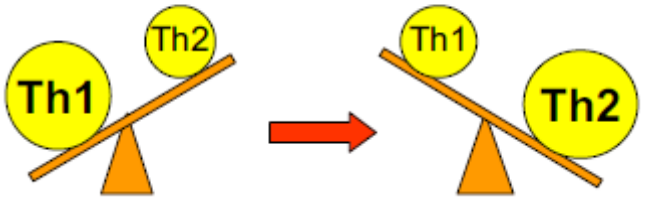
Progesterone

↓

Progesterone-induced blocking factor

Th 1	→ **Th2**
TNF-α IFN-γ IL-2 IL-12 IL-18	**IL-3** **IL-4** **IL-5** **IL-6** **IL-10** **IL-13**

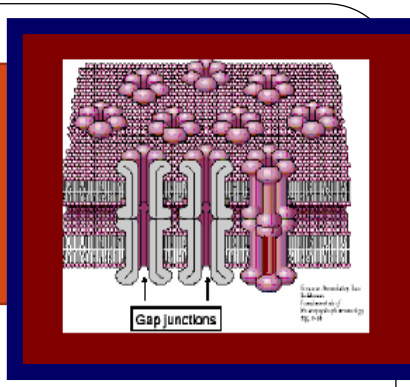
Shift to Th2 dominance



Decidual NK activity ↓

Walch K. Best Practice and Research Clin Obstet Gynecol 2008

2. Myometriyal kontraktilite



Myometriyal hücre kontraktilitesini etkileyen genlerin ekspresyonunun regülasyonu

GENOMİK

- Membran reseptörlerine bağlanarak hücresel aktiviteyi regüle eder.

NON GENOMİK

3. Nöroendokrin eksiklikler

Apoptozis önler.

Ekstravillöz trofoblastların desiduaya invazyonunu arttırır.

Daya S. Maturitas 2009

Progesteron desteği-1.trimester

Abortus imminens

Tekrarlayan gebelik kayıpları

IVF

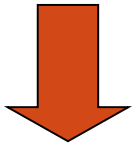
Abortus imminens

THE COCHRANE COLLABORATION®

Progestogen for treating threatened miscarriage

Hayfaa A Wahabi[1], Amel A Fayed[2], Samia A Esmaeil[1], Rasmieh A Al Zeidan[1]

[1]Chair of Evidence-Based Healthcare and Knowledge Translation, King Saud University, Riyadh, Saudi Arabia. [2]King Saud bin Abdul Aziz University for Health Sciences, Riyadh, Saudi Arabia; Alexandria University, Alexandria, Egypt



❖**Düşük tehdidi olan gebelerde progesteron faydalı olabilir.**
Çalışma sayısı az ! Hasta sayısı az!

Tekrarlayan düşükler

Progestogen for preventing miscarriage

David M Haas[1], Patrick S Ramsey[2]

[1]Department of Obstetrics and Gynecology, Indiana University School of Medicine, Indianapolis, Indiana, USA. [2]Division of Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, Uniformed Services University of Health Sciences, Bethesda, MD, USA

Cochrane Database of Systematic Reviews 2013, Issue 10.

- **Gebelikte rutin progesteron kullanımına gerek yoktur**
- **Tekrarlayan düşükleri olan hastalarda yararlı olabilir.**

- Erken doğum ve düşük doğum ağırlığının önlenmesinde profilaktik progesteron kullanımı anlamlıdır.
- Progesteronun etkisi, risk grubuna, uygulama yolu ve dozuna bağlı değişebilmektedir.
- Erken doğum eylemi durmuş olgularda günlük 400 mg vaginal progesteron kullanımı düşünülebilir.

Doğal Progesteron

- Doğal progesteron, 18-25. haftada başlayıp, günlük 90-400 mg dozlarda ve genellikle vaginal yolla uygulanmaktadır.
- Oral mikronize progesteron kullanımı başka bir alternatiftir.
- Vaginal uygulama ile karaciğerden first-pass etki olmaz ve biotolerabilite daha iyidir.
- Vaginal uygulama ile İ.M. uygulamaya kıyasla endometrial etki daha fazladır. Uterin first-pass etki söz konusudur.

Sentetik Progesteron (17-α-hidroksiprogesteron)

- Sentetik progesteron İ.M. yolla verilir.
- Doz haftada 1-3 kez , 25-1000 mg arasında değişir.
- %50'den fazla olguda yan etki görülür.
- Doğan çocukların 4 yıldan fazla takiplerinde, uzun süreli yan etki, genital anomali yada cinsiyet rollerinde farklılık izlenmemiştir.

TABLE 1

Individual clinical trials of progesterone for preventing preterm birth since 2000

Study	Design	Sample Size	Progesterone intervention	Population (indication)	Primary outcome(s)
Borna and Sahabi[6]	RCT (no placebo)	70	400 mg vaginal suppository daily	Arrested (threatened) PTL	(1) Latency (days) (2) Recurrence of PTL
O'Brien et al[9]	RCT (placebo controlled)	659	90 mg vaginal gel	Prior SPTB, 18-22 wk	PTB ≤ 32 wk
Fonseca et al[8]	RCT (placebo controlled)	250	200 mg vaginal capsule daily until 34 wk	Short cervix ≤ 15 mm at 20-25 wk	Spontaneous PTB < 34 wk
Rouse et al[7]	RCT (placebo controlled	661	250 mg 17P IM until 35 wk	Twins at 16-20 wk	(1) PTB < 35 wk or IUFD < 35 wk
Facchinetti et al[11]	RCT (no placebo)	60	341 mg 17P IM twice weekly	Arrested PTL	Change in cervical length
Meis et al[12]	RCT (placebo controlled)	463	250 mg 17P IM weekly	Prior SPTB, 16 wk	PTB < 37 wk
da Fonseca et al[13]	RCT (placebo controlled)	142	100 mg daily vaginal suppository until 34 wk	Prior SPTB, 24 wk onward	PTB < 37 wk

IM, intramuscular; *IUFD*, intrauterine fetal demise; *PTB*, preterm birth; *PTL*, preterm labor; *RCT*, randomized clinical trial; *SPTB*, spontaneous preterm birth; *17P*, 17-alpha-hydroxyprogesterone.

Tita. Progesterone for preterm birth prevention: an evolving intervention. Am J Obstet Gynecol 2009.

TABLE 2

Metaanalyses of clinical trials of progesterone for preterm birth prevention since 2000

Study	No. of trials	No. of women (infants)	Progesterone intervention	Population (indication)	Primary outcome(s)
Dodd et al[19]	11	2425 (3187)	Any antenatal use to prevent PTB	(1) Prior SPTB (2) Multiples (twins) (3) Short cervix (4) Threatened PTL	(1) Perinatal death (2) PTB < 34 wk (3) Neurodevelopmental handicap
Coomarasamy et al[18]	9 (cumulative metaanalysis)	> 1062	Any antenatal use	(1) Risk factors for PTB excluding multiples	(1) PTB < 37 wk (2) PTB < 34 wk (3) RDS
Mackenzie et al[17]	3	648	Second-trimester use	(1) Increased risk for SPTB	PTB < 37 wk
Dodd et al[16]	6	988	Any antenatal use	Any pregnancy	(1) Perinatal death (2) PTB < 34 wk (3) Neurodevelopmental handicap
Dodd et al[15]	7	1020	Any antenatal use	Singletons	Multiple adverse infant and maternal outcomes
Sanchez-Ramos et al[14]	10	1339	Any antenatal use (placebo controlled)	Women at risk for PTB	(1) PTB < 37 wk (2) Perinatal mortality

PTB, preterm birth; *PTL*, preterm labor; *RDS*, respiratory distress syndrome; *SPTB*, spontaneous preterm birth.

Tita. Progesterone for preterm birth prevention: an evolving intervention. Am J Obstet Gynecol 2009.

Progestational agents for treating threatened or established preterm labour (Review)

Su LL, Samuel M, Chong YS

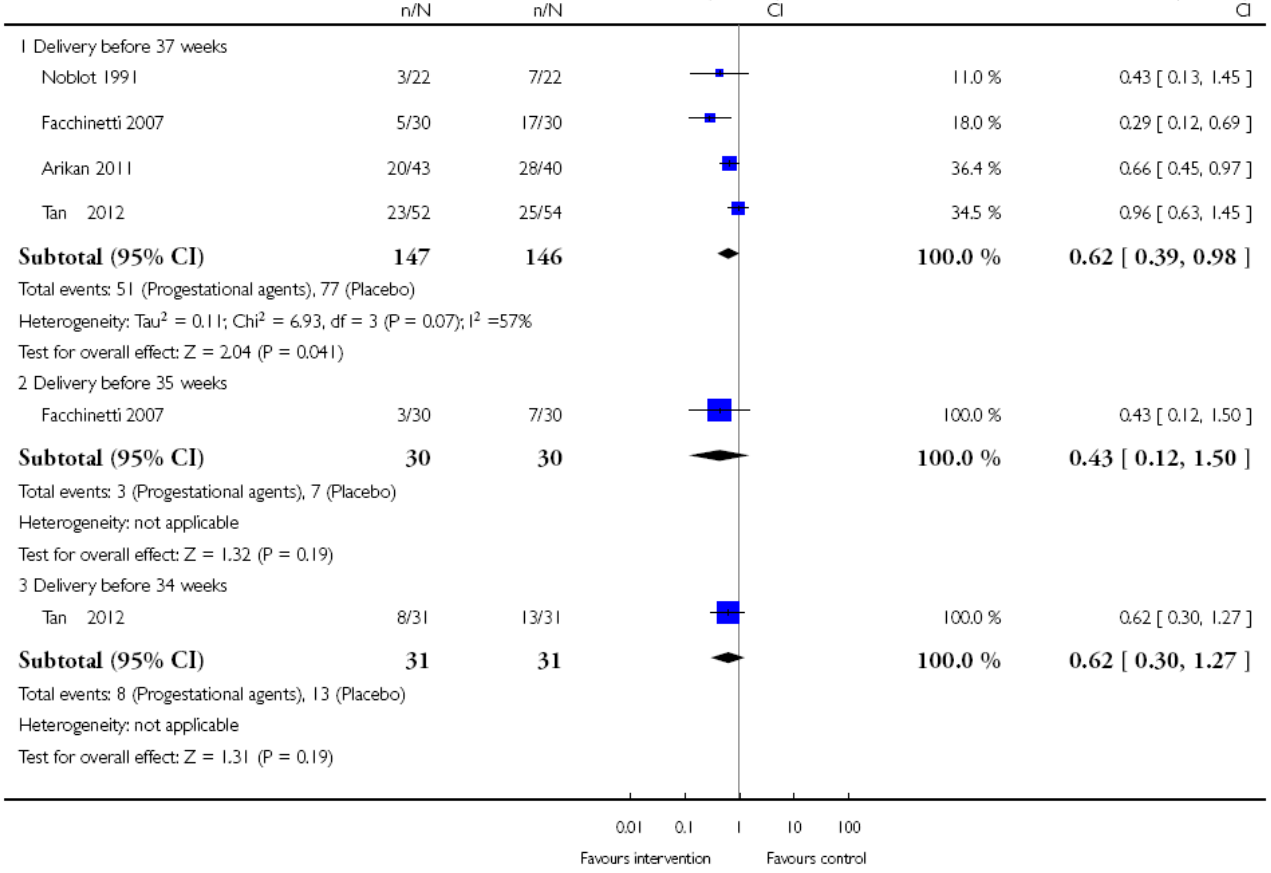
Analysis 1.1. Comparison 1 Progestational agents versus placebo, Outcome 1 Preterm delivery.

Review: Progestational agents for treating threatened or established preterm labour

Comparison: 1 Progestational agents versus placebo

Outcome: 1 Preterm delivery

Study or subgroup	Progestational agents n/N	Placebo n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 Delivery before 37 weeks					
Noblot 1991	3/22	7/22		11.0 %	0.43 [0.13, 1.45]
Facchinetti 2007	5/30	17/30		18.0 %	0.29 [0.12, 0.69]
Arikan 2011	20/43	28/40		36.4 %	0.66 [0.45, 0.97]
Tan 2012	23/52	25/54		34.5 %	0.96 [0.63, 1.45]
Subtotal (95% CI)	**147**	**146**		**100.0 %**	**0.62 [0.39, 0.98]**
Total events: 51 (Progestational agents), 77 (Placebo)					
Heterogeneity: $Tau^2 = 0.11$; $Chi^2 = 6.93$, df = 3 (P = 0.07); $I^2 = 57\%$					
Test for overall effect: Z = 2.04 (P = 0.041)					
2 Delivery before 35 weeks					
Facchinetti 2007	3/30	7/30		100.0 %	0.43 [0.12, 1.50]
Subtotal (95% CI)	**30**	**30**		**100.0 %**	**0.43 [0.12, 1.50]**
Total events: 3 (Progestational agents), 7 (Placebo)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.32 (P = 0.19)					
3 Delivery before 34 weeks					
Tan 2012	8/31	13/31		100.0 %	0.62 [0.30, 1.27]
Subtotal (95% CI)	**31**	**31**		**100.0 %**	**0.62 [0.30, 1.27]**
Total events: 8 (Progestational agents), 13 (Placebo)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.31 (P = 0.19)					



Erken Doğum Öyküsü

- Öyküsünde erken doğum olan olgularda, %30-50 oranında erken doğumda azalma bildirilmiştir.
- 2500 gram altı yenidoğanlarda % 3-40 azalma bildirilmiştir.
- Progesteron grubunda ortalama doğum ağırlığı 475 gram daha fazladır.

TABLE 4

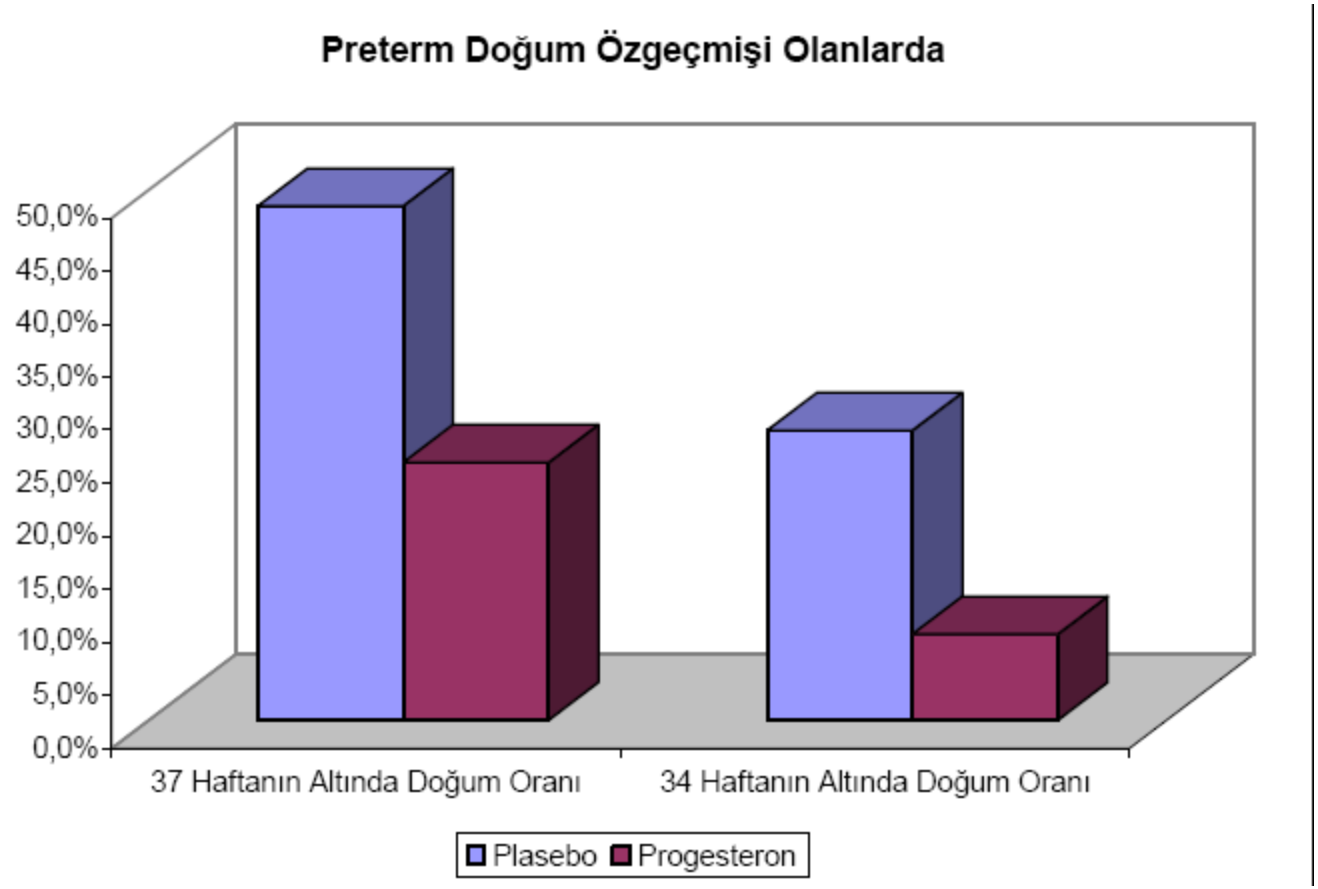
Selected perinatal outcomes among women with a history of spontaneous preterm birth: progesterone vs placebo

Study	PTB[a] wk: RR (95% CI)	Perinatal death RR (95% CI)	Neonatal death wk: RR (95% CI)	Mean GA (wk)[b]	RDS wk: RR (95% CI)
Dodd et al[19]	< 34: 0.15 (0.04-0.64)[c] < 37: 0.68 (0.45-1.02)	0.65 (0.38-1.11)	0.44 (0.16-1.18)	n/a	0.79 (0.57-1.10)
O'Brien et al[9]	≤ 32: 0.9 (0.52-1.56) < 37: 1.08 (0.76-1.52)	n/a	0.87 (0.29-2.60)	36.6 vs 36.6	0.91 (0.56-1.50)
Mackenzie et al[17]	< 37: 0.57 (0.36-0.90)[c]	0.39 (0.07-2.24)	n/a	+1.92 (0.37-4.21)[c]	0.64 (0.39-1.07)
Meis et al[12]	< 37: 0.66 (0.54-0.81)[c] < 32: 0.58 (0.37-0.94)[c]	0.64 (0.30-1.37)	0.44 (0.17-1.13)	n/a	0.63 (0.38-1.05)
da Fonseca et al[13]	< 37: 0.49 (0.25-0.96)[c]	n/a	n/a	n/a	n/a

CI, confidence interval; *GA*, gestational age; *n/a*, not available; *PTB*, preterm birth; *RDS*, respiratory distress syndrome.
Except where indicated, all data represent relative risks (95% CI) that, when < 1, favor progesterone.

[a] GA cut-off given; [b] Actual mean GA or difference in mean GA (95% confidence interval [CI]) for progesterone use compared with placebo or no treatment; [c] Results indicate statistical significance.

Tita. Progesterone for preterm birth prevention: an evolving intervention. Am J Obstet Gynecol 2009.



Dr.Elçin Erçetingöz Yüksek Riskli gebelerde Preterm Eylem ve Doğumun Önlenmesinde Mikronize Progesteronun İntravajinal Kullanımı Umzanlık Tezi Zeynep Kamil Hastanesi, 2007

Kısa Serviks

- ≤ 15 mm, servikal uzunluğu olan olgularda 200 mg vaginal progesteron kullanımı < 34 hafta erken doğumları %45-50 azaltmıştır.

Table 2. Progesterone Versus Placebo in Women With a Short Cervix Identified on Ultrasound

Outcome	No. Studies	Participants	Relative Risk	95% CI
Primary				
Perinatal death	1	274	0.38	0.10–1.40
Preterm birth at less than 34 wk	**1**	**250**	**0.58**	**0.38–0.87**
Secondary infant				
Birth weight less than 2,500 g	1	274	0.96	0.73–1.27
Respiratory distress syndrome	1	274	0.59	0.29–1.19
Need for assisted ventilation	1	274	0.65	0.36–1.16
Intraventricular hemorrhage, all grades	1	274	0.51	0.05–5.53
Retinopathy of prematurity	1	274	5.07	0.25–104.70
Necrotizing enterocolitis	1	274	0.34	0.01–8.23
Neonatal sepsis	**1**	**274**	**0.28**	**0.08–0.97**
Fetal death	1	274	1.01	0.06–16.06
Neonatal Death	1	274	0.29	0.06–1.37

CI, confidence interval.
Bold indicates statistically significant results.

Dodd JM.Progestererone for the Prevention of Preterm Birth Obstetrics &Gynecology,2008,112,129-134

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

Sensitivity analysis of direct and indirect comparison metaanalyses

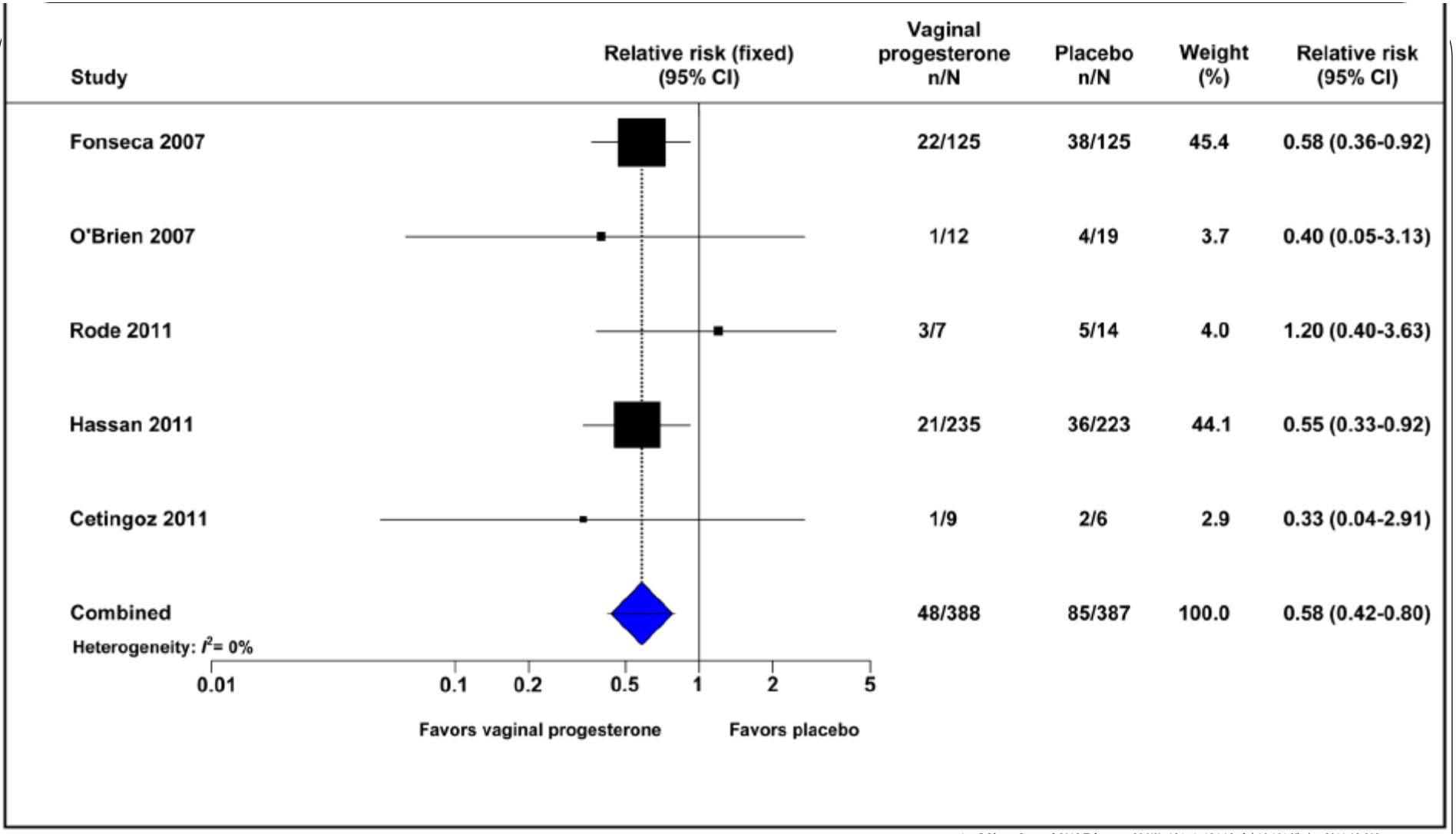
	Direct comparisons						Indirect comparison: vaginal progesterone vs cerclage	
	Vaginal progesterone vs placebo			Cerclage vs no cerclage				
Outcome	Intervention, n/N (%)	Control, n/N (%)	Relative risk (95% CI)	Intervention, n/N (%)	Control, n/N (%)	Relative risk (95% CI)	Relative risk (95% CI)	*P* value[a]
Preterm birth								
<32 wk	8/71 (11.3)	24/82 (29.3)	0.44 (0.22–0.87)	40/203 (19.7)	64/201 (31.8)	0.63 (0.45–0.88)	0.70 (0.33–1.50)	.88
<28 wk	5/71 (7.0)	14/82 (17.1)	0.46 (0.19–1.11)	28/203 (13.8)	43/201 (21.4)	0.65 (0.43–1.00)	0.71 (0.27–1.88)	.88
<35 wk	17/71 (23.9)	35/82 (42.7)	0.59 (0.37–0.95)	57/203 (28.1)	85/201 (42.3)	0.67 (0.51–0.88)	0.88 (0.51–1.52)	.96
<37 wk	31/71 (43.7)	46/82 (56.1)	0.80 (0.58–1.10)	82/203 (40.4)	123/201 (61.2)	0.67 (0.55–0.82)	1.19 (0.82–1.74)	.94
Perinatal mortality	4/71 (5.6)	7/82 (8.5)	0.61 (0.20–1.91)	19/203 (9.4)	33/201 (16.4)	0.58 (0.35–0.98)	1.05 (0.30–3.64)	.98

[a] For the test of association.

Conde-Agudelo. Vaginal progesterone vs cervical cerclage. Am J Obstet Gynecol 2013.

Study (year) / Study type	Progesterone / Dosage	Treatment GA / Inclusion criteria	Cases / Controls	Result		p / RR / OR (95% CI)
				Cases	Controls	
Fonseca[25] (2007) / RCT	Micronized progesterone 200 mg vagina daily	GA 24 to 34 wk / - Cervical length ≤ 15 mm at 20 – 25 wk	250 / 163	Delivery GA < 34 wk: 19.2%	Delivery GA < 34 wk: 34.4%	RR = 0.56 (0.36, 0.86)
DeFranco[28] (2007) / RCT	Micronized progesterone gel 90 mg vagina daily	GA 16-22 to 37 wk / - Previous preterm birth - Cervical length < 28 mm in the mid-trimester	19 / 27	Delivery GA < 32 wk: 0%	Delivery GA ≤ 32 wk: 29.6%	p = 0.014
Hassan[29] (2011) / MC-RCT	Micronized progesterone gel 90 mg vagina daily	GA 20-24 to 37 wk / - Cervical length 10-20 mm at 19+0 - 23+6 wk	235 / 223	Delivery GA < 28 wk: 5.1%	Delivery GA < 28 wk: 10.3%	RR = 0.50 (0.25, 0.97) p = 0.04
				Delivery GA < 33 wk: 8.9%	Delivery GA < 33 wk: 16.1%	RR = 0.52 (0.31, 0.91) p = 0.02
				Delivery GA < 35 wk: 14.5%	Delivery GA < 35 wk: 23.3%	RR = 0.62 (0.42, 0.92) p = 0.02
Romero[30] (2012) / Meta-analysis	Progesterone vagina daily	- Cervical length < 25 mm in the mid-trimester	388 / 387	Delivery GA < 28 wk		RR = 0.50 (0.30, 0.81)
				Delivery GA < 33 wk		RR = 0.58 (0.42, 0.80)
				Delivery GA < 35 wk		RR = 0.69 (0.55, 0.88)
				Respiratory distress syndrome		RR = 0.48 (0.30, 0.76)
				Neonatal morbidity and mortality		RR = 0.57 (0.40, 0.81)
				Birthweight < 1,500 gm		RR = 0.55 (0.38, 0.80)

RCT: Randomized, placebo-controlled, double-blind study, MC-RCT: Multi-center, randomized, placebo-controlled, double-blind study, GA: Gestational age



Am J Obstet Gynecol. 2012 February ; 206(2): 124.e1–124.19. doi:10.1016/j.ajog.2011.12.003.

Figure 3.
Effect of vaginal progesterone on preterm birth before 33 weeks

VAGINAL PROGESTERONE IN WOMEN WITH AN ASYMPTOMATIC SONOGRAPHIC SHORT CERVIX IN THE MIDTRIMESTER DECREASES PRETERM DELIVERY AND NEONATAL MORBIDITY: A SYSTEMATIC REVIEW AND META-ANALYSIS OF INDIVIDUAL PATIENT DATA

Roberto ROMERO, MD[1], Kypros NICOLAIDES, MD[2], Agustin CONDE-AGUDELO, MD, MPH[1], Ann TABOR, MD[3,4], John M. O'BRIEN[5], Elcin CETINGOZ, MD[6], Eduardo DA FONSECA, MD[7], George CREASY, MD[8], Katharina KLEIN, MD[9], Line RODE, MD[3], Priya SOMA-PILLAY, MD[10], Shalini FUSEY, MD[11], Cetin CAM, MD[6], Zarko ALFIREVIC, MD[12], and

Çoğul Gebelikler

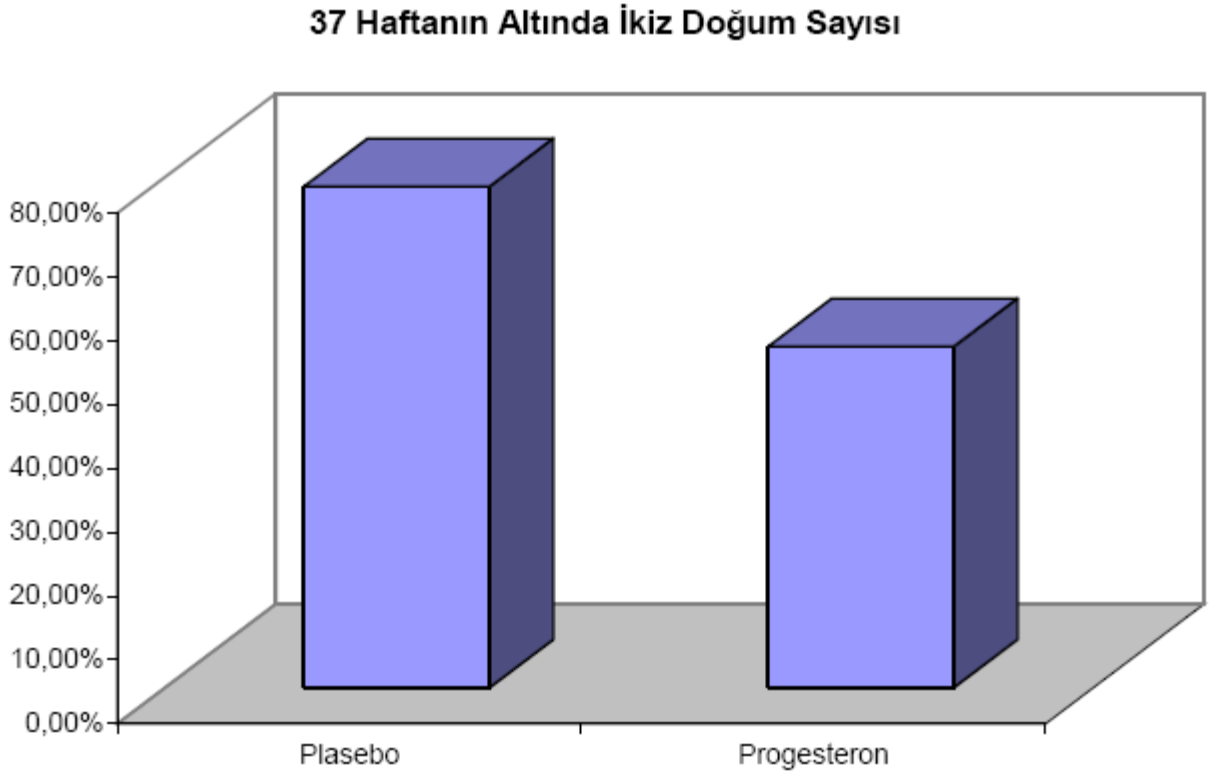
- Seçilmemiş ikiz gebeliklerde İ.M. 17P kullanımının <35 hafta doğumlara etkisinin olmadığı görülmüştür.
- 200 mg vaginal progesteronun çoğul gebeliği olup, kısalmış serviksi olanlarda etkili olmadığı görülmüştür.

Table 3. Progesterone Versus Placebo in Women With a Multiple Pregnancy

Outcome	No. Studies	Participants	Relative Risk	95% CI
Primary				
Perinatal death	1	154	1.95	0.37–10.33
Secondary maternal				
Cesarean section	1	652	0.99	0.88–1.12
Antenatal corticosteroids	1	654	0.91	0.70–1.17
Antenatal tocolysis	**1**	**654**	**0.75**	**0.57–0.97**
Secondary infant				
Preterm birth at less than 37 wk	2	732	1.01	0.92–1.12
Birth weight less than 2,500 g	1	1,276	0.94	0.86–1.02
Respiratory distress syndrome	1	1,280	1.13	0.86–1.48
Need for assisted ventilation	1	1,280	0.93	0.69–1.26
Intraventricular hemorrhage, grades 3 or 4	1	1,280	1.20	0.40–3.54
Retinopathy of prematurity	1	1,280	NE*	NE*
Necrotizing enterocolitis	1	1,280	0.77	0.17–3.42
Neonatal sepsis	1	1,280	0.95	0.55–1.63
Patent ductus arteriosus	1	1,280	0.60	0.34–1.05

CI, confidence interval; NE, not estimable.
Bold indicates statistically significant results.

Dodd JM.Progestererone for the Prevention of Preterm Birth Obstetrics &Gynecology,2008,112,129-134



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Durmuş Erken Doğum

- Erken doğumu durdurulmuş 70 kadına 400mg/gün vaginal progesteron verilmiş.
- Doğum ortalama 12 gün uzatılmış,
- Düşük doğum ağırlığı RR 0.52,
- RDS riski 0.30 bulunmuş.
- YDYBÜ yatışı % 39' dan % 24'e düşmüş.
- Neonatal sepsis oranı % 18 'den %5'e düşmüş.

Vaginal progesterone for maintenance tocolysis: a systematic review and metaanalysis of randomized trials

Anju Suhag, MD; Gabriele Saccone, MD; Vincenzo Berghella, MD

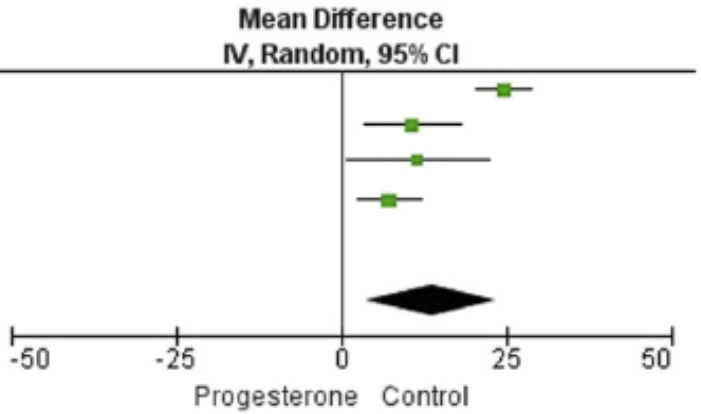
FIGURE 5

Forest plot for latency

Study or Subgroup	Progesterone Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Areia 2013	63.46	10.1	26	38.8	4.95	26	27.2%	24.66 [20.34, 28.98]
Arikan 2011	32.1	17.8	43	21.2	16.3	40	24.8%	10.90 [3.56, 18.24]
Borna 2008	36.1	17.9	37	24.5	27.2	33	21.2%	11.60 [0.67, 22.53]
Sharami 2010	23.88	18.01	80	16.67	12.9	83	26.9%	7.21 [2.39, 12.03]
Total (95% CI)			**186**			**182**	**100.0%**	**13.80 [3.97, 23.63]**

Heterogeneity: $Tau^2 = 87.65$; $Chi^2 = 30.58$, df = 3 ($P < 0.00001$); $I^2 = 90\%$

Test for overall effect: $Z = 2.75$ ($P = 0.006$)



CI, confidence interval.

Suhag. Vaginal progesterone for maintenance tocolysis. Am J Obstet Gynecol 2015.

TABLE 5

Outcomes for progesterone vs placebo among other groups at risk for preterm birth

Study/indication	PTB[a] wk: RR (95% CI)	Mean GA (wk)[b]	Perinatal death wk: RR (95% CI)	Neonatal death wk: RR (95% CI)	RDS wk: RR (95% CI)
SHORT CERVIX					
Fonseca et al[8]	< 34: 0.56 (0.36-0.86)[c]		0.38 (0.10-1.38)	0.29 (0.06-1.42)	0.59 (0.26-1.29)
DeFranco et al[10] (< 28 mm)	≤ 32: 0 vs 29.6%[c]	+1.7 (36.3 vs 34.6)	n/a	0 vs 3.7%	0.18 (0.02-1.31)
Dodd et al[19]	< 34: 0.58 (0.38-0.87)[c]	n/a	0.38 (0.10-1.40)	0.29 (0.06-1.37)	0.59 (0.29-1.19)
MULTIPLE					
Rouse et al[7]	< 35: 1.1 (0.9-1.4)	-0.3 (34.6 vs 34.9)	n/a	n/a	1.2 (0.8-1.6)
Dodd et al[16]	< 37: 1.62 (0.81-3.25)	n/a	1.95 (0.37-10.33)	n/a	n/a
Dodd et al[19]	< 37: 1.01 (0.92-1.12)		1.95 (0.37-10.33)	n/a	1.13 (0.86-1.47)
THREATENED PTB					
Borna and Sahabi[6]	n/a	+2 (36.7 vs 34.5)[c]	n/a	n/a	0.30 (0.11-0.83)[c]
Facchinetti et al[11]	< 37: 0.29 (0.12-0.69)[c]	n/a	n/a	n/a	n/a
Dodd et al[19]	< 37: 0.29 (0.12-0.69[c]	n/a	n/a	n/a	0.30 (0.11-0.83)[c]

CI, confidence interval; *GA*, gestational age; *n/a*, not available; *PTB*, preterm birth; *RDS*, respiratory distress syndrome; *RR*, relative risk.
Except where indicated, all data represent relative risks (95% confidence interval) that, when < 1, favor progesterone.

[a] GA cut-off given; [b] Difference in mean GA (respective mean GA) for progesterone use compared with placebo or no treatment; [c] Results indicate statistical significance.

Tita. Progesterone for preterm birth prevention: an evolving intervention. Am J Obstet Gynecol 2009.

Risk faktörleri Olmadan Kombine Sonuçlar

- Erken doğumlar önlenmiş ve erken doğumlara bağlı düşük doğum ağırlığı %40-50 azalmıştır.
- IVH %75 azalmış ve NEC azalmıştır.
- Progesteron dozu etkide anlamlı bulunmamıştır.

TABLE 6

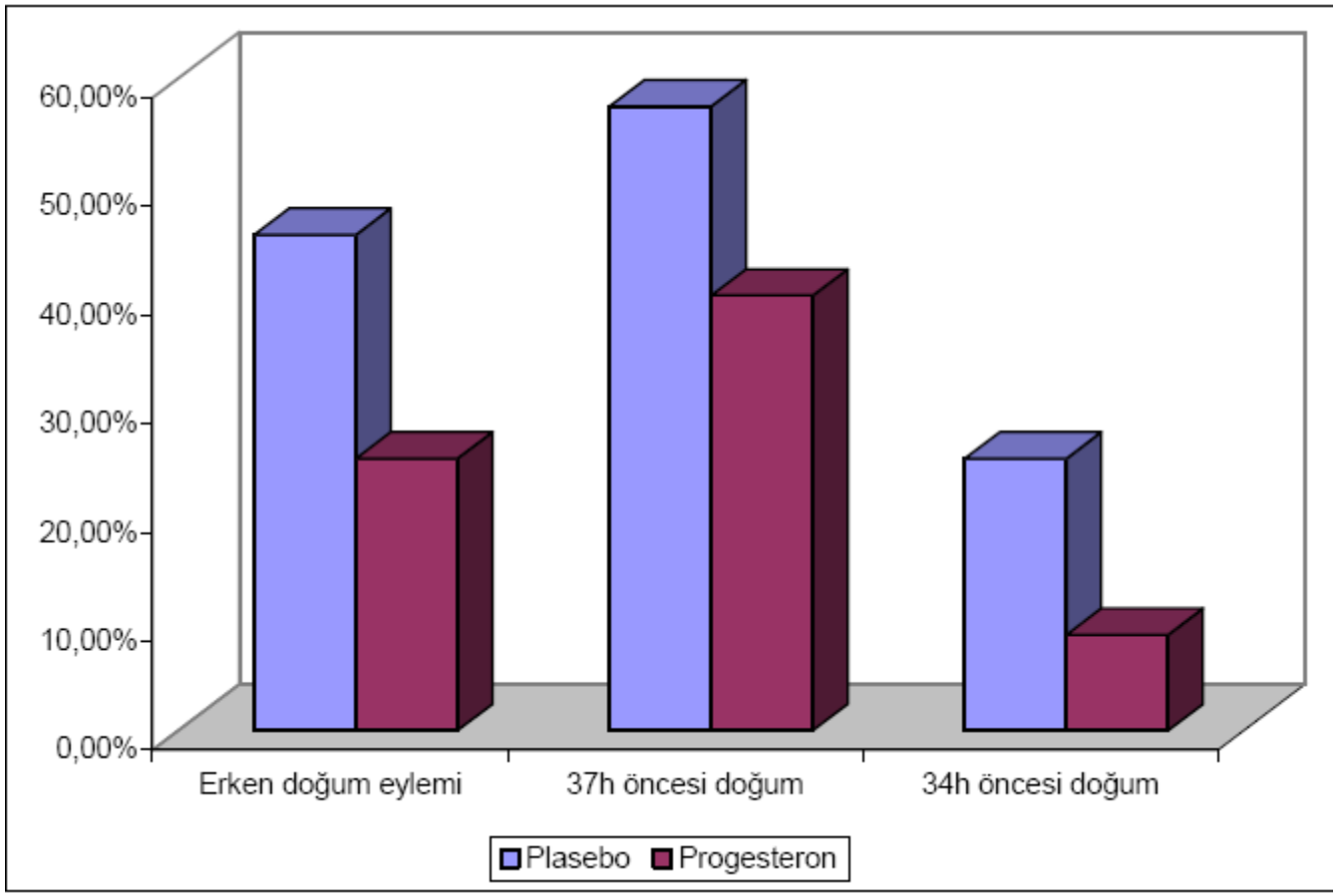
Outcomes for progesterone vs placebo for metaanalyses without stratification by risk factors for preterm birth

Study/indication	PTB[a] wk: RR (95% CI)	Perinatal death RR (95% CI)	Neonatal death wk: RR (95% CI)	Mean GA (wk)	RDS wk: RR (95% CI)
Coomarasamy et al[18]	< 37: 0.42 (0.31-0.57)[b] < 34: 0.51 (0.34-0.77)[b]	n/a	n/a	n/a	0.55 (0.31-0.96)[b]
Dodd et al[16]	< 37: 0.65 (0.54-0.79)[b] < 34: 0.15 (0.04-0.64)[b]	0.66 (0.37-1.19)	0.59 (0.27-1.30)	n/a	0.63 (0.38-1.05)
Dodd et al[15]	< 37: 0.59 (0.49-0.72)[b]	0.60 (0.32-1.12)	0.44 (0.14-1.13)	n/a	0.63 (0.38-1.05)
Sanchez-Ramos et al[14]	< 37: 0.45 (0.25-0.80)[b]	0.69 (0.38-1.26)	n/a	n/a	0.83 (0.25-2.76)

CI, confidence interval; *GA*, gestational age; *n/a*, not available; *PTB*, preterm birth; *RDS*, respiratory distress syndrome; *RR*, relative risk.
Except where indicated, all data represent relative risks (95% confidence interval) that, when < 1, favor progesterone.

[a] GA cut-off given for progesterone use compared with placebo or no treatment; [b] Results indicate statistical significance.

Tita. Progesterone for preterm birth prevention: an evolving intervention. Am J Obstet Gynecol 2009.



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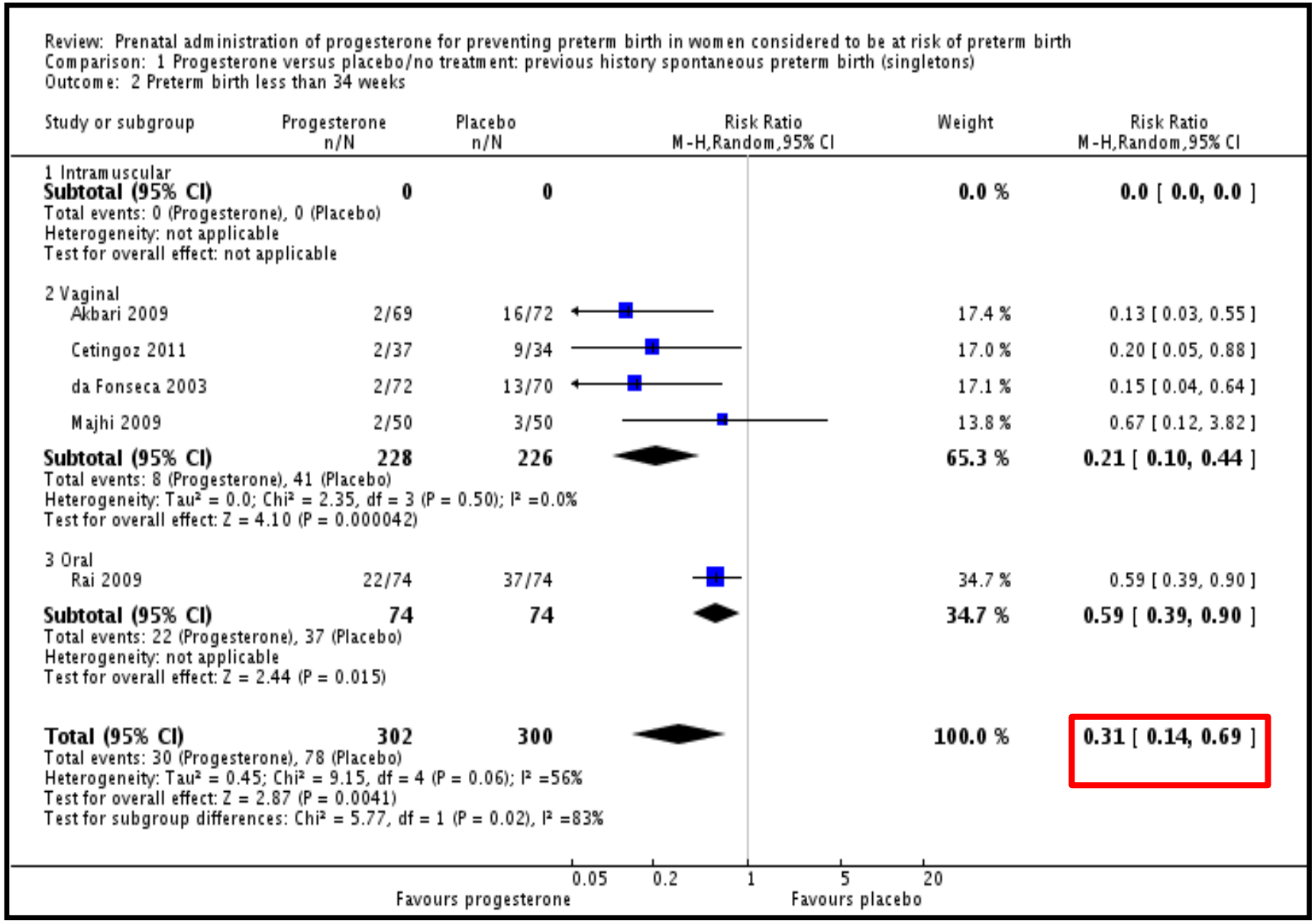
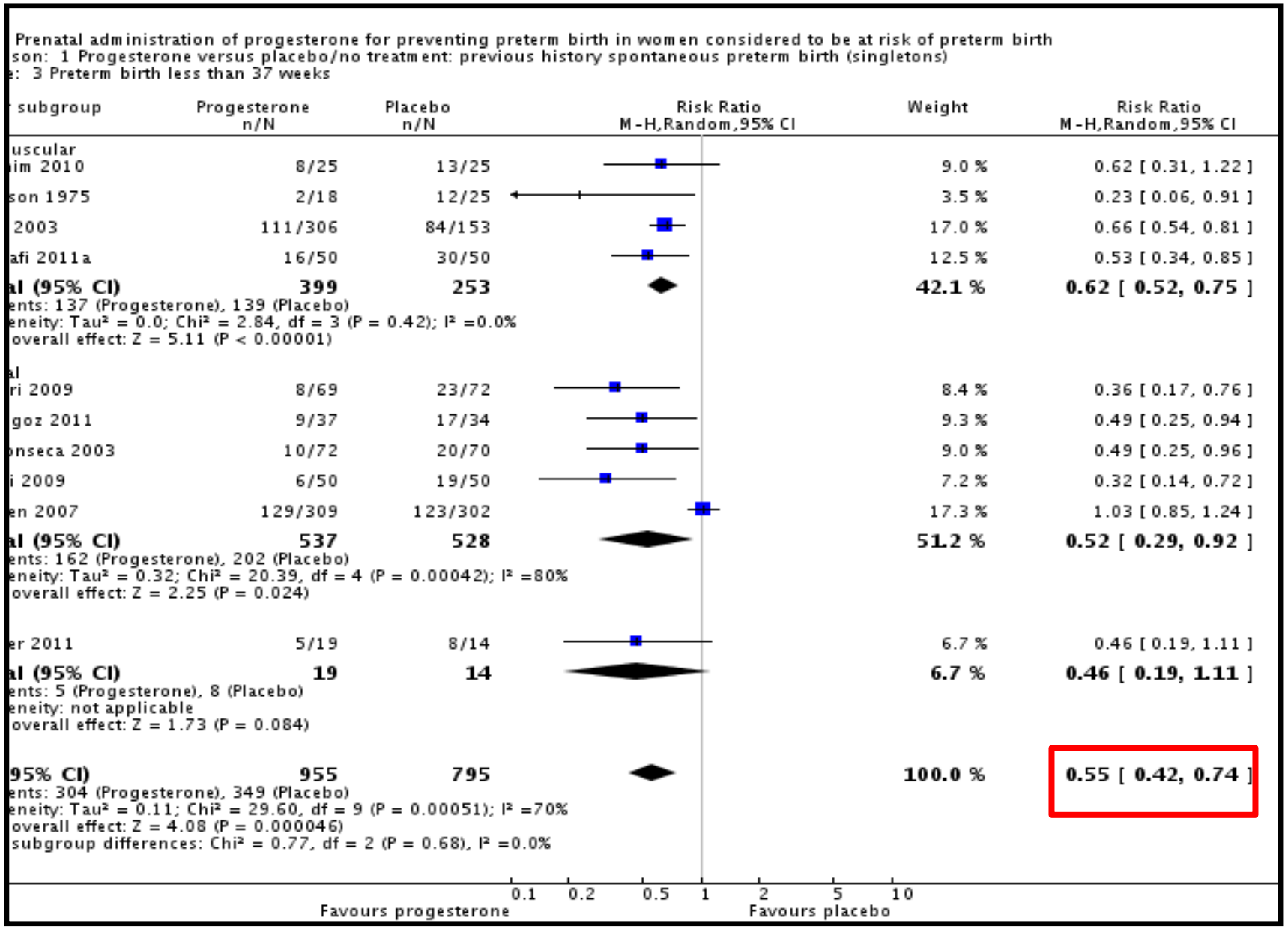


Dodd JM, Jones L, Flenady V, Cincotta R, Crowther CA. Prenatal administration of progesterone for preventing preterm birth in women considered to be at risk of preterm birth. Cochrane Database Syst Rev. 2013 Jul 31;7:CD004947.



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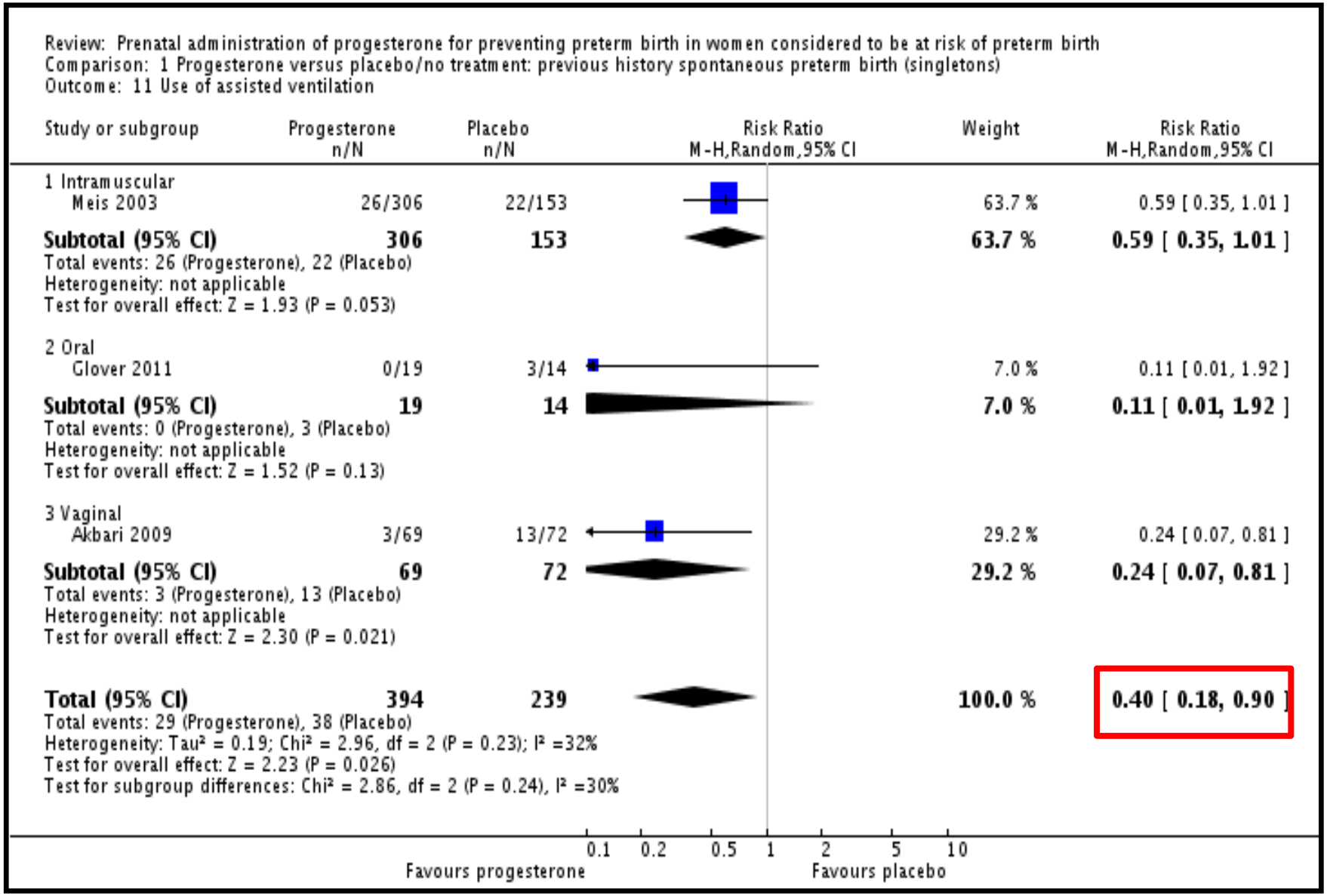

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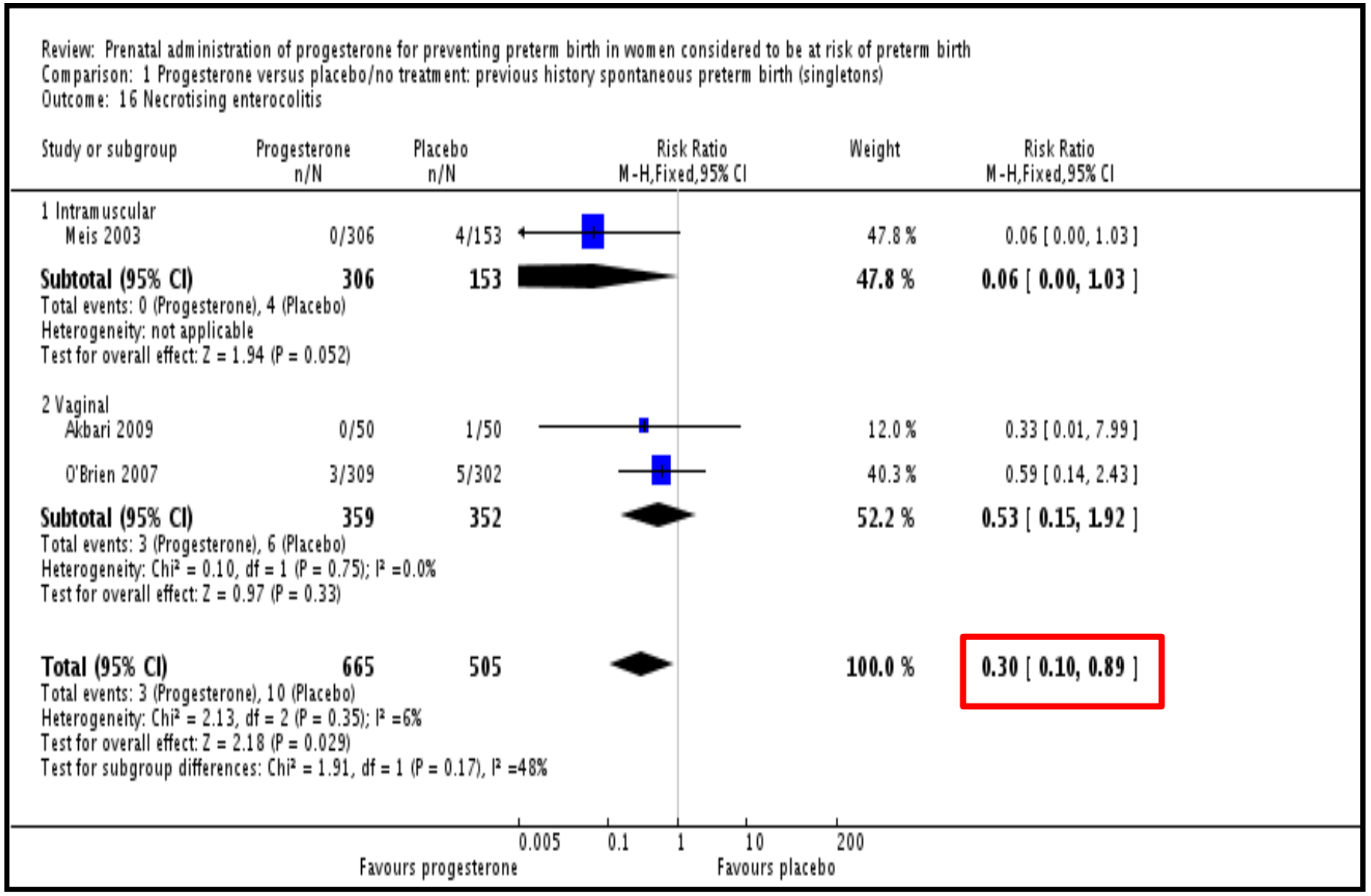

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- ACOG daha önceden erken doğumu olan olgulara, erken doğum önlenmesi için progesteron kullanımını önermektedir.
- Tek gebeliği olan ve serviksi < 15 mm olan olgulara önerilmektedir.

- Erken doğum ve düşük doğum ağırlığının önlenmesinde profilaktik progesteron kullanımı anlamlıdır.
- Progesteronun etkisi, risk grubuna, uygulama yolu ve dozuna bağlı değişebilmektedir.

- 1.Önceden Erken doğum öyküsü olan olgularda 24. haftadan önce başlayarak günlük 100 mg'dan fazla olmak üzere vaginal progesteron kullanımı, erken doğumun önlenmesinde etkilidir.

- 2.Kısa serviksi olan olgularda (≤ 15 mm) 200 mg vaginal progesteron etkili bulunmuştur.
- 3.İkiz gebeliklerde progesteron rutin olarak endike değildir ama önceden erken doğum öyküsü ya da kısa serviks durumlarında uygulanabilir.
- 4.Erken doğum eylemi durmuş olgularda günlük 400 mg vaginal progesteron kullanımı düşünülebilir.