



WEBINAR SERIES

**La gestione clinica interattiva della MINACCIA DI PARTO PREMATURO**

Giovedì 4 febbraio 2021  
ore 18.00 -19.00 CET

# La Gestione interattiva della minaccia di parto prematuro

Herbert Valensise & Mariarosaria Di Tommaso



MARIA ha 29 anni

E' alla sua prima gravidanza

Felice e contenta va dal suo ginecologo di fiducia

Il dottore la accoglie, la visita, chiede ecografia ed esami di routine



In realta' il medico e' stato un po' veloce nella anamnesi....

Maria era accompagnata dalla mamma e dal fidanzato  
(contentissimi...)

Maria si vergognava di parlare: non ha detto al dottore che anni prima, con un altro fidanzato, aveva dovuto interrompere la gravidanza indesiderata per ben due volte (con due interruzioni tardive per gravi anomalie)



## Domanda 1

*Questo dato anamnestico:*

1. Non ha alcuna importanza
2. Non è rilevante perché ha cambiato partner
3. Non va ricordato perché potrebbe alterare l'emozione della gravidanza iniziale
4. È importante da tenere in considerazione



## La gestione clinica interattiva della MINACCIA DI PARTO PREMATURO

### PTB: fattori rischio

REVIEW ARTICLE  
Obstetrics Int J Gynecol Obstet 2020; 150: 17-23



### Risk factors for spontaneous preterm delivery

Teresa Cobo<sup>1,2,\*</sup> | Marian Kacerovsky<sup>3,4</sup> | Bo Jacobsson<sup>5,6</sup>

Table III. Univariate analysis of risk factors for indicated preterm birth

Risk factor	Frequency (%)	IPB (%)	Relative risk		Significance
			Value	95% CI	
Age >30 yr	14.7	8.1	2.39	1.65-3.48	$p < 0.001$
Black ethnicity	62.8	4.7	1.57	1.06-2.32	$p = 0.024$
Nulliparity	41.6	4.4	1.11	0.78-1.58	$p = 0.56$
Education <12 yr	35.2	2.7	0.56	0.37-0.85	$p = 0.005$
Previous spontaneous preterm birth	12.4	8.0	2.25	1.51-3.37	$p < 0.001$
Previous IPB	3.6	12.4	3.27	1.90-5.62	$p < 0.001$
Previous stillbirth	3.1	13.3	3.50	2.01-6.12	$p < 0.001$
History medical problems*	15.6	8.5	2.60	1.80-3.76	$p < 0.001$
History of diabetes	3.1	10.8	2.80	1.52-5.17	$p = 0.004$
Chronic hypertension	3.9	17.4	4.89	3.20-7.48	$p < 0.001$
Proteinuria	1.6	21.3	5.57	3.12-9.95	$p < 0.001$
History of lung disease†	4.9	9.1	2.37	1.36-4.10	$p = 0.002$
History of obstetric problems‡	10.4	6.5	1.71	1.08-2.73	$p = 0.023$
Müllerian duct abnormality§	0.4	27.3	6.80	2.55-18.14	$p = 0.009$
Uterine fibroids	3.5	9.8	2.52	1.36-4.67	$p = 0.008$
First-trimester bleeding	19.6	5.8	1.56	1.06-2.30	$p = 0.025$
Hospitalization for preterm labor	0.8	16.7	4.17	1.68-10.39	$p = 0.015$
Any hospitalization	6.9	8.5	2.24	1.37-3.67	$p = 0.001$
Alcohol use in pregnancy	12.1	2.0	0.45	0.21-0.96	$p = 0.032$

IPB, Indicated preterm birth; CI, confidence interval.

\*Including diabetes, hypertension, and cardiac, endocrine, renal, or lung disease.

†Including acute and chronic lung disease.

‡Including müllerian duct abnormality, diethylstilbestrol exposure, cone biopsy, and uterine myomas.

§Including bicornuate uterus, uterine septum, and double uterus.

Fattori materni	Fattori ginecologici e/o ostetrici
Età <18 anni	Pregressa chirurgia del collo dell'utero
Età >40 anni	Pregressa infezione da HPV
Storia familiare di PTT	Pregresse RCU
Razza nera	Fibromatosi uterina
Basso status socio-economico	Endometriosi/adenomiosi
Immigrata	Pregresso PPT
Basso livello di istruzione	Pregresso AS del II trimestre
Limitato accesso alle cure prenatali	Pregresso TC a dilatazione completa
Non coniugata	Pregresso secondo stadio prolungato
Fumo	Concepimento da PMA
Utilizzo sostanze d'abuso	Intervallo tra le gravidanze <6 mesi
Stress	Malattie parodontali
Basso BMI	Sanguinamento nel I o II trimestre
Obesità	Vaginosi batterica
Diabete	Infezioni urinarie

Meis et al., *The preterm prediction study: Risk factors for indicated preterm births*, AJOG, 1998



**Domanda 2**

*Se il rischio anamnestico fosse stato considerato quale sarebbe stata la indicazione corretta?*

1. Non stancarsi molto
2. Effettuare cervicometria a 16 settimane
3. Effettuare cerchiaggio/pessario
4. Prescrivere Progesterone 200 mg/die (e CL ogni 15 gg)





## PROGESTERONE & P. PRETERMINE

# Rischio Anamnestico

36 RCTs included

8523 women  
12515 infants

➤ Progesterone vs placebo for women with a past history of spontaneous PTB

Perinatal mortality	6 studies	N = 1453	<b>RR 0.50</b>	[95% CI 0.33 to 0.75]
Preterm birth < 34 weeks	5 studies	N = 602	<b>RR 0.31</b>	[95% CI 0.14 to 0.69]
Preterm birth < 37 weeks	10 studies	N = 1750	<b>RR 0.55</b>	[95% CI 0.42 to 0.74]
Infant birth weight < 2500 g	4 studies	N = 692	<b>RR 0.58</b>	[95% CI 0.42 to 0.79]
Use of assisted ventilation	3 studies	N = 633	<b>RR 0.40</b>	[95% CI 0.18 to 0.90]
Necrotizing enterocolitis	3 studies	N = 1170	<b>RR 0.30</b>	[95% CI 0.10 to 0.89]
Neonatal death	6 studies	N = 1453	<b>RR 0.45</b>	[95% CI 0.27 to 0.76]
Admission to NICU	3 studies	N = 389	<b>RR 0.24</b>	[95% CI 0.14 to 0.40]
	1 study	N = 148	<b>MD** 4.47</b>	[95% CI 2.15 to 6.79]

Statistically significant reduction  
Statistically significant increase in pregnancy prolongation weeks

No differential effects in terms of route of administration, time of therapy initiation and dose of progesterone for majority of outcomes examined.

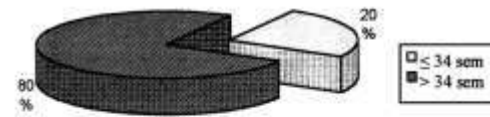


Fig 1. Incidence of preterm delivery before 34th week in natural progesterone group.



Fig 2. Percentage of preterm delivery before 34th week in placebo group.

Table III. Incidence of preterm delivery

	Placebo (n = 70)	Progesterone (n = 72)	P value
<37 wk	20 (28.5%)	10 (13.8%)	.03
34 wk	13 (18.6%)	2 (2.8%)	.002
Admission for threatened preterm labor	22 (31.4%)	14 (19.4%)	NS

Fonseca EB, Crvalho MH, Zugaib M. *Prophylactic administration of progesterone by vaginal suppository to reduce the incidence of spontaneous preterm birth in women at increased risk: a randomized placebo-controlled double-blind study.* Am J Obstet Gynecol 2003; 188:419-24



## Progesterone nel rischio anamnestico: LG



Preterm Labor and Birth Management: Recommendations from the European Association of Perinatal Medicine

2017

G. C. Di Renzo, L. Cabero Rauso, F. Facchinetti, H. Hellmich, C. Halperin, B. Jochims, S. Jergensen, K. F. Lamsas, A. Ritzenthaler, N. Papadimitrakaki, V. Radzinsky, A. Shennan, Y. Yildiz, M. Wiggins & G. H. A. Visser

**Recommendations.** Women with prior history of PTB or late second trimester abortion should be offered 17 OHP-C weekly injection starting early in the 2nd trimester or vaginal progesterone based on individual benefits/risks evaluation with the patient. It should be noted that intramuscular 17 OHP-C has been found to increase by three times the incidence of gestational diabetes in the treated population of pregnant women.



A woman with a singleton gestation and a prior spontaneous preterm singleton birth should be offered progesterone supplementation starting at 16–24 weeks of gestation, regardless of transvaginal ultrasound cervical length, to reduce the risk of recurrent spontaneous preterm birth.



2020

### Raccomandazioni

- **MESSAGGI CHIAVE**  
L'utilizzo dei Progestageni nella prevenzione del parto prematuro in donne a rischio anamnestico o attuale è controverso.
- Nei casi a rischio in cui si opti per la misurazione seriata, sembra ragionevole effettuarla tra 16 e 24 settimane con un intervallo di 1-2 settimane fra le misurazioni (III A)





Il medico non fa nulla di tutto questo

- ✓ Esegue il test della translucenza nucale: negativo
- ✓ Consiglia anche la ricerca del DNA fetale nel sangue materno
- ✓ Aspetta in maschietto evviva!
- ✓ Maria prosegue la gravidanza allegramente



- ✓ Maria continua la sua gravidanza
- ✓ Lavora a "nero" come commessa in un negozio di calzature...fa su e giu' con la scala a prendere i modelli piu' richiesti ma si sente bene
- ✓ Solo ogni tanto qualche doloretto continuo sulla vescica...
- ✓ Il dottore per whatsapp dice che e' tutto normale



- ✓ Questi dolorette sono sempre piu' forti
- ✓ Maria torna dal dottore
- ✓ Il dottore dopo la visita dice che va tutto bene
- ✓ Le da' un po' di magnesio per bocca.....



- ✓ Una sera all'improvviso i dolori sono sempre piu' forti e Maria non e' convinta delle rassicurazioni del suo medico
- ✓ Decide di andare da sola in Pronto Soccorso all'ospedale piu' vicino
- ✓ Alla visita tutto bene
- ✓ Il battito c'e' il bambino si muove...
- ✓ Ma...



### Domanda 3

*Cosa e' indispensabile controllare in una paziente che lamenta algie pelviche?*

1. L'emocromo
2. La PCR
3. La Cervicometria con ecografia
4. Tutte le risposte





Ultrasonographic examination of the uterine cervix is better than cervical digital examination as a predictor of the likelihood of premature delivery in patients with preterm labor and intact membranes

1994  
Volume 171, Number 4  
Am J Obstet Gynecol

Ricardo Gomez, MD,\* Maurizio Galasso, MD,\* Roberto Romero, MD,\*<sup>†</sup> Moshe Mazar, MD,\*  
Yoram Sorokin, MD,\* Luis Gonçalves, MD,\* and Marjorie Treadwell, MD\*

Ultrasonographic examination of the uterine cervix is better than cervical digital examination as a predictor of the likelihood of premature delivery in patients with preterm labor and intact membranes.

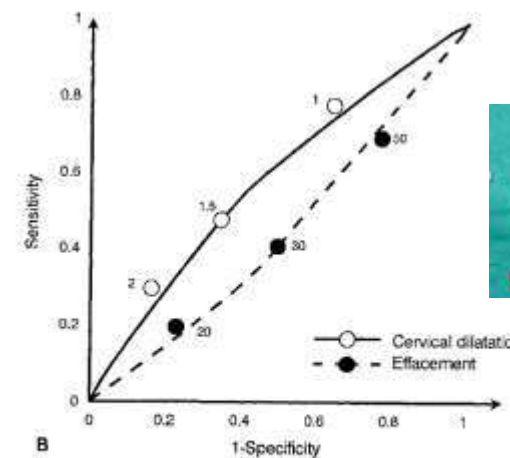
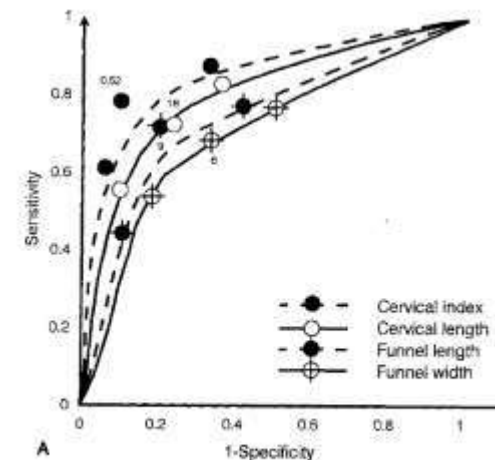


Fig. 3. Receiver-operator characteristic curve analysis of results of clinical and ultrasonographic examination of uterine cervix in diagnosis of preterm delivery. A, Area under curve.



## MESSAGGI CHIAVE

Nelle donne con precedente PPT la cervicometria permette di distinguere differenti profili di rischio che beneficiano del trattamento con progesterone vaginale.

Nelle donne sintomatiche la cervicometria permette di identificare le donne a rischio di parto imminente ed è di ausilio per le conseguenti azioni cliniche e terapeutiche.

Nelle donne a basso rischio di PPT la cervicometria predice il parto pretermine spontaneo ma la sua applicabilità clinica come screening deve essere ancora definita e articolata.

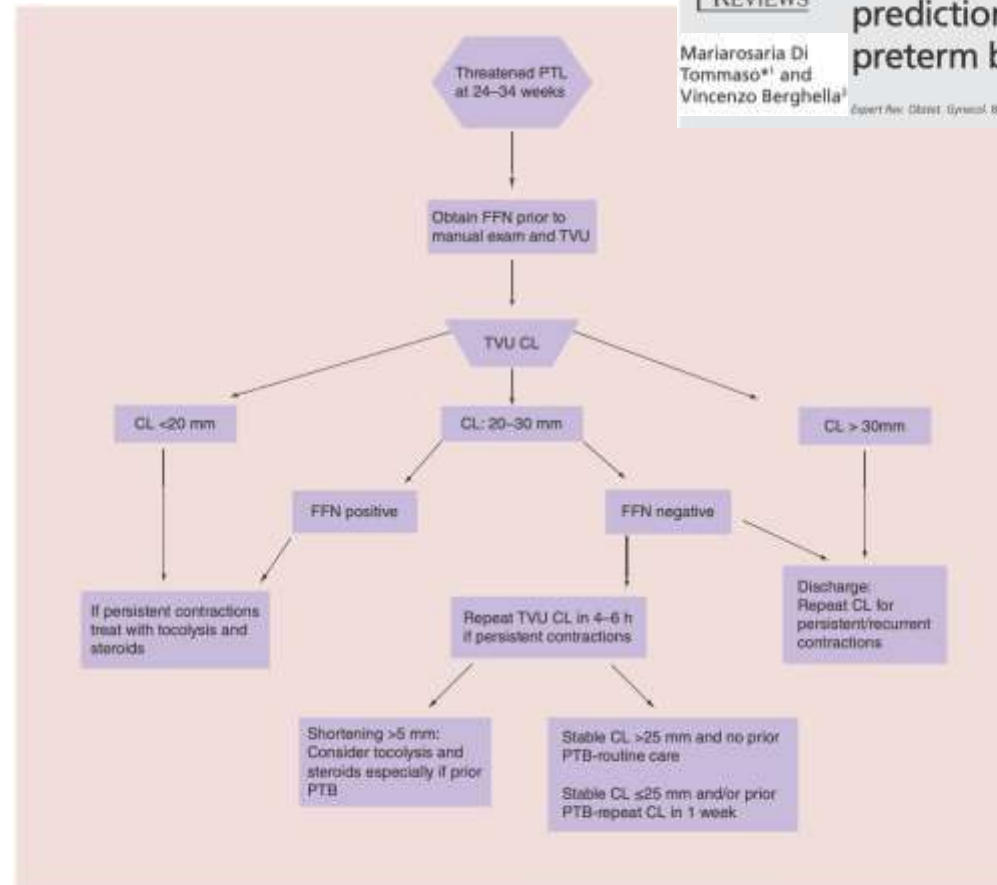
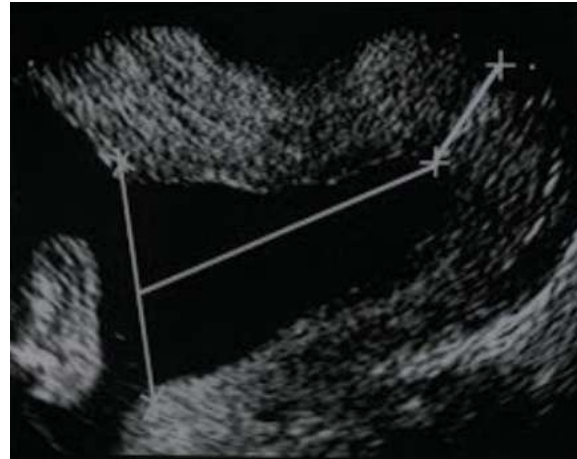


Figure 4. Management protocol using cervical length and fetal fibronectin for symptomatic patients with threatened preterm labor.

CL: Cervical length; FFN: Fetal fibronectin test; PTB: Preterm birth; PTL: Preterm labor; TVU: Transvaginal ultrasonography. Reproduced with permission from [35].



- ✓ Al Pronto Soccorso viene effettuata la cervicometria
- ✓ Ampio funnelling
- ✓ Cervicometria 10
- ✓ Sigh Sigh
- ✓ Che fare?





**Domanda 4**

*Terapia antibiotica?*

1. SI

2. NO





ANTIBIOTICI & PARTO PRETERMINE

Infection and Preterm Labor

Roberto Romero, MD  
Moshe Mazor, MD

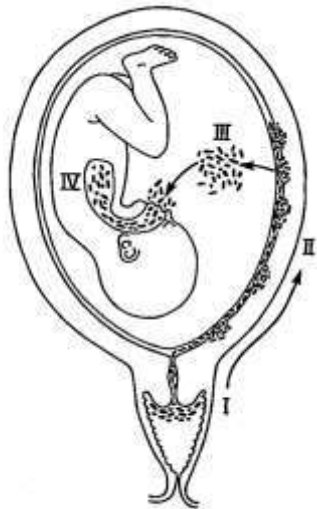


FIG. 1. The stages of ascending infection in preterm labor.

1988

Clinical significance of intra-amniotic inflammation in patients with preterm labor and intact membranes

Bo Hyun Yoon, MD, PhD, Roberto Romero, MD, Jeong Bin Moon, MD, Soonsup Shim, MD, Miha Kim, MD, Gilja Kim, MT, and Jong Kwan Jun, MD, PhD  
Seon L. Kwon

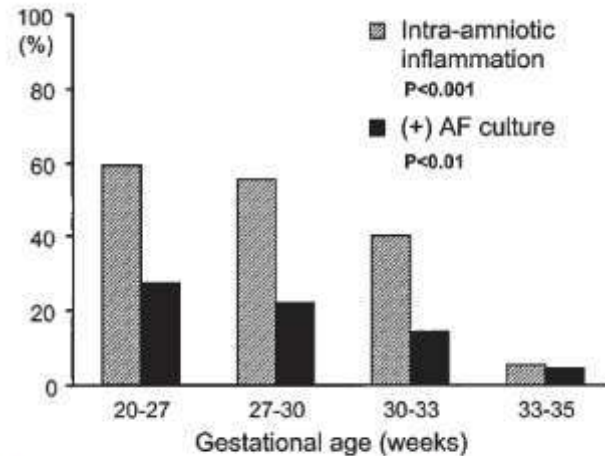


Fig 2. Frequency of a positive amniotic fluid (AF) culture and intra-amniotic inflammation (negative AF culture but with an AF IL-6 of higher than 2.6 ng/mL) as a function of gestational age.

2001

Broad-spectrum antibiotics for spontaneous preterm labour: the ORACLE II randomised trial

ORACLE II

S L Kenyon, D J Taylor, W Tarnow-Mordi, for the ORACLE Collaborative Group\*

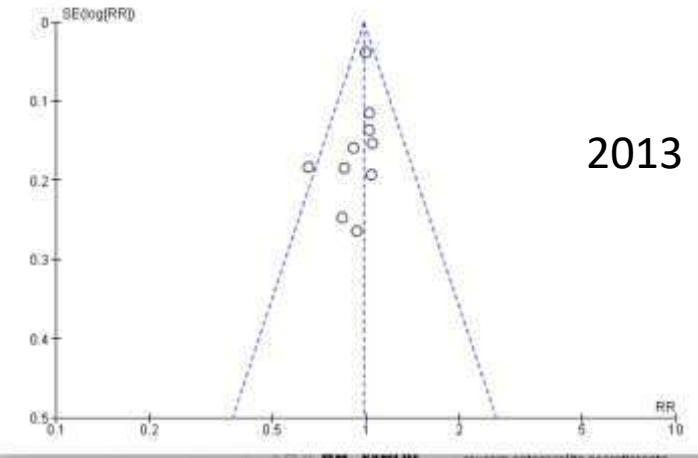
Lancet 2001; 357: 989-94



2001



Figure 4. Funnel plot of comparison: 1 Any antibiotics versus no antibiotics, outcome: 1.12 Preterm birth (< 36 or < 37 weeks).



2013





## ANTIBIOTICI &amp; PARTO PRETERMINE: Linee Guida

## Authors' conclusions

This review did not demonstrate any benefit in important neonatal outcomes with the use of prophylactic antibiotics for women in preterm labour with intact membranes, although maternal infection may be reduced. Of concern, is the finding of short- and longer-term harm for children of mothers exposed to antibiotics. The evidence supports not giving antibiotics routinely to women in preterm labour with intact membranes in the absence of overt signs of infection.

2013

**NICE**  
National Institute for  
Health and Care Excellence

do not offer antenatal prophylactic antibiotics



12  
SETTEMBRE 2013  
Rivista di Ginecologia e Ostetricia del  
GIUGNO 2013

L'antibiotico profilassi non è raccomandata nelle donne con minaccia di parto pretermine a membrane integre in assenza di infezione clinicamente manifesta. (I E)



The American College of  
Obstetricians and Gynecologists  
WOMEN'S HEALTH CARE PHYSICIANS

Thus, antibiotics should not be used to prolong gestation or improve neonatal outcomes in women with preterm labor and intact membranes. This recommendation is distinct from recommendations for antibiotic use for preterm premature rupture of membranes (76) and group B streptococci carrier status (77, 78).



## Domanda 5

*In realtà alla cervicometria è presente sludge, siamo a 20 settimane, quale terapia antibiotica?*

1. Amoxicillina
2. Amoxicillina /Ac Clavulonico
3. Eritromicina
4. Cefalosporine





**Domanda 6**

*Il Progesterone è sempre una terapia protettiva della gravidanza potenzialmente a rischio di parto prematuro?*

1 SI

2. NO



## Short Cervix

Table 3 Gestational age at delivery and neonatal outcome in asymptomatic women with a singleton pregnancy and sonographic short cervix allocated to receive vaginal progesterone gel ( $n = 235$ ) compared with those allocated to receive placebo ( $n = 224$ ): treated patient analysis set

Outcome	Vaginal progesterone (n (%))	Placebo (n (%))	Unadjusted RR (95% CI)*	P*	Adjusted RR (95% CI)†	P†
<b>Primary outcome</b>						
Preterm birth < 33 weeks	21 (8.9)	34 (15.2)	0.59 (0.35–0.98)	0.040	0.56 (0.33–0.93)	0.022
<b>Secondary outcomes</b>						
Preterm birth < 28 weeks	12 (5.1)	21 (9.4)	0.54 (0.27–1.08)	0.077	0.55 (0.28–1.08)	0.075
Preterm birth < 35 weeks	34 (14.5)	50 (22.3)	0.65 (0.44–0.96)	0.030	0.61 (0.41–0.90)	0.012
Preterm birth < 37 weeks	71 (30.2)	74 (33.0)	0.91 (0.70–1.20)	0.516	0.89 (0.68–1.15)	0.377

Hassan SS, Romero R, Vidyadhari D, Fusey S, Baxter JK, Khandelwal M, et al. 2011. *Vaginal progesterone reduces the rate of preterm birth in women with a sonographic short cervix: a multicenter, randomized, double-blind, placebo-controlled trial.* *Ultrasound in Obstetrics & Gynecology* 38:18–31.

«The administration of vaginal progesterone gel to women with a sonographic short cervix in the mid-trimester is associated with a 45% reduction in the rate of preterm birth before 33 weeks of gestation and with improved neonatal outcome».

## PROGESTERONE VAGINALE



✓ Screening universale (19-23 sett)



## FIGO COMMITTEE REPORT

FIGO recommendations regarding the use of transvaginal sonographic cervical length and vaginal progesterone use for the prevention of preterm birth.

Population	All pregnant women with a singleton gestation.
Recommendation	Transvaginal sonographic cervical length measurement at 19–23 6/7 weeks for all pregnant patients. Vaginal progesterone administered to women with a cervical length $\leq 25$ mm. <b><u>200 mg vaginal soft capsules or 90 mg vaginal gel of micronized progesterone can be used for treatment.</u></b>
Time using progesterone	Treatment should begin at the time of the diagnosis of a short cervix until 36 6/7 weeks, labor, or rupture of membranes.
Risk assessment	Transvaginal sonographic cervical length on all patients regardless of obstetrical history.
Other recommendation	When a transvaginal ultrasound is not available other devices may be used as a screening tool to measure objectively and reliably the cervical length.

FIGO Working Group on Best Practice in Maternal-Fetal Medicine. *Int J Gynecol Obstet* 2015; **128**: 80–82

## Updated European Guidelines



THE JOURNAL OF MATERNAL-FETAL & NEONATAL MEDICINE 2017  
<https://doi.org/10.1089/14767058.2017.1323860>



GUIDELINES



**Preterm Labor and Birth Management: Recommendations from the European Association of Perinatal Medicine**

G. C. Di Renzo<sup>a</sup>, L. Cabero Roura<sup>b</sup>, F. Facchinetti<sup>c</sup>, H. Helmer<sup>d</sup>, C. Hubinont<sup>e</sup>, B. Jacobsson<sup>f</sup>, J. S. Jørgensen<sup>g</sup>, R. F. Lamont<sup>h</sup>, A. Mikhailov<sup>i</sup>, N. Papantoniou<sup>j</sup>, V. Radzinsky<sup>k</sup>, A. Shennan<sup>l</sup>, Y. Ville<sup>m</sup>, M. Wielgos<sup>n</sup> and G. H. A. Visser<sup>o</sup>

- ✓ **Asymptomatic women with a sonographically short cervix (25 mm) regardless of their obstetrical history should be offered vaginal progesterone treatment for the prevention of preterm birth and neonatal morbidity.**
- ✓ Two forms of vaginal micronized progesterone can be used daily: **200mg vaginal soft capsules** or 90mg vaginal gel [57].





# Short Cervix after contraction

## Progestogens for Maintenance Tocolysis in Women With a Short Cervix

A Randomized Controlled Trial

Fabio Facchinetti, MD, Patrizia Vergani, MD, Mariarosaria Di Tommaso, MD, PhD, Luca Marozio, MD, PhD, Barbara Acaia, MD, Roberto Vicini, PhD, Lucrezia Pignatti, MD, Anna Locatelli, MD, Marina Spitaleri, MD, Chiara Benedetto, MD, PhD, Barbara Zaina, MD, and Roberto D'Amico, PhD, on behalf of the PROTECT Collaborative Group\*



**CONCLUSION:** The use of progestogens for maintenance tocolysis in women with a short cervix did not reduce the rate of preterm birth.

## Updated European Guidelines

THE JOURNAL OF MATERNAL-FETAL & NEONATAL MEDICINE, 2017  
<https://doi.org/10.1089/1476-7058.2017.1323860>



### Preterm Labor and Birth Management: Recommendations from the European Association of Perinatal Medicine

G. C. Di Renzo<sup>a</sup>, L. Cabero Roura<sup>b</sup>, F. Facchinetti<sup>c</sup>, H. Helmer<sup>d</sup>, C. Hubinont<sup>e</sup>, B. Jacobsson<sup>f</sup>, J. S. Jørgensen<sup>g</sup>, R. F. Lamont<sup>h,i</sup>, A. Mikhailov<sup>j</sup>, N. Papantoniou<sup>k</sup>, V. Radzinsky<sup>l</sup>, A. Shennan<sup>m</sup>, Y. Ville<sup>n</sup>, M. Wielgos<sup>o</sup> and G. H. A. Visser<sup>o</sup>



«In symptomatic women undelivered after an episode of PTL The efficacy of progestogens remain to be clarified».



PROGESTERONE



✓ Donne sintomatiche



## Cosa succede dopo

- ✓ Maria viene ricoverata
- ✓ Terapia, locale di progesterone
- ✓ Situazione locale invariata per 7 giorni
- ✓ Siamo ormai a 21 settimane
- ✓ Rimane il dubbio se fare il cerchiaggio cervicale o meno



**Domanda 7** *Terapia per incontinenza cervicale? Voi cosa fareste?*

1. Cerchiaggio
2. Pessario
3. Nulla



Review

# Physical Examination–Indicated Cerclage

## A Systematic Review and Meta-analysis

Robert M. Ehsanipoor, MD, Neil S. Seligman, MD, Gabriele Saccone, MD, Linda M. Szymanski, MD, PhD, Christina Wissinger, MS, MLIS, Erika F. Werner, MD, MS, and Vincenzo Berghella, MD

Table 3. Bias Assessment for Nonrandomized Studies

Study	Obstetric History	Gestational Age	Dilatation	Evidence of Infection	Tocolysis	Antibiotics
Olatunbosun et al, 1995 <sup>16</sup>	Low	Low	Low	Unable to determine	Low	Low
Morin et al, 1997 <sup>17</sup>	Unable to determine	Unable to determine	High	Unable to determine	Unable to determine	Unable to determine
Novy et al, 2001 <sup>18</sup> (group 2 only)	Low	High	Low	Unable to determine	Unable to determine	Unable to determine
Daskalakis et al, 2006 <sup>19</sup>	Low	Low	Low	Unable to determine	Low	Low
Pereira et al, 2008 <sup>20</sup>	High	High	Low	Unable to determine	Unable to determine	Unable to determine
Stupin et al, 2008 <sup>22</sup>	Low	High	High	Low	Unable to determine	Unable to determine
Ventolini et al, 2009 <sup>21</sup>	Unable to determine	Unable to determine	Unable to determine	Unable to determine	Unable to determine	Unable to determine
Curti et al, 2012 <sup>22</sup>	Low	High	High	High	Low	Unable to determine
Aoki et al, 2013 <sup>23</sup>	Low	High	Unable to determine	Low	Unable to determine	Unable to determine

**CONCLUSION:** Physical examination–indicated cerclage is associated with a significant increase in neonatal survival and prolongation of pregnancy of approximately 1 month when compared with no such cerclage. The strength of this conclusion is limited by the potential for bias in the included studies.



### C-STICH2: Emergency Cervical Cerclage to Prevent Miscarriage and Preterm Birth - a Randomised Controlled Trial

**Main Trial Features**

- A randomised controlled, multicentre trial (RCT) with an internal pilot; a nested qualitative process evaluation and cost-effectiveness analysis.
- Funded by the NIHR HTA (16/151/01)
- Chief Investigator [Dr Katie Morris](#)
- Coordinated by Birmingham Clinical Trials Unit (BCTU)
- Sponsored by Birmingham Women's and Children's NHS Foundation Trust





## La gestione clinica interattiva della MINACCIA DI PARTO PREMATURO

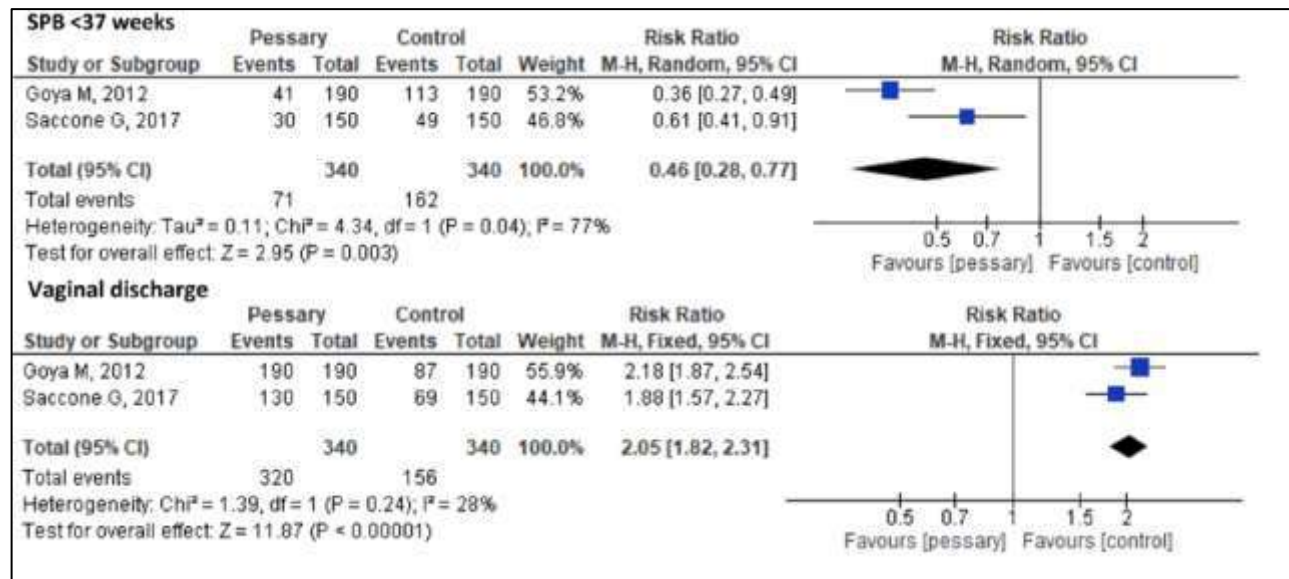
Arch Gynecol Obstet 299, 1215–1231  
2019

**Effectiveness of the cervical pessary for the prevention of preterm birth in singleton pregnancies with a short cervix: a meta-analysis of randomized trials**

Faustino R. Pérez-López<sup>1,2,3</sup> · Peter Chedraui<sup>3,4</sup> · Gonzalo R. Pérez-Roncero<sup>1</sup> · Samuel J. Martínez-Domínguez<sup>1</sup> · The Health Outcomes and Systematic Analyses (HOUSAY) Project

### Assessment of risk of bias in the three RCT

Study	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Goya M, 2012	Low	Low	Low	Low	Low	Low	Low
Nicolaidis KH, 2016	Low	Low	High	Low	Low	Low	Low
Saccone G, 2017	Low	Low	Low	Low	Low	Low	Low



Cervical pessary application was associated with a reduced risk of SPT at < 37 week and higher risk of vaginal discharge





## Cosa e' successo dopo?

- ✓ Maria ha fatto l'intervento di cerchiaggio cervicale
- ✓ Dopo 2 giorni di ospedalizzazione va a casa con terapia protettiva della gravidanza
- ✓ Non va piu' a lavorare...
- ✓ Cambia il dottore di riferimento e si affida ai medici dell'ospedale...



# Ma ahime' a 30 settimane la sera si rompono le membrane

- ✓ Maria si sveglia perdendo liquido caldo....che viene dal canale vaginale
- ✓ In preda al panico corre in ospedale
- ✓ Qui viene visitata
- ✓ Il collo e' chiuso, il cerchiaggio tiene bene, ma il sacco amniotico e' rotto: pPROM



## Domanda 8

Diagnosi: pProm. *Che cosa fareste voi?*

1. Ricovero e rimozione cerchiaggio: parto spontaneo immediato
2. Ricovero e taglio cesareo immediato per la prematurita'
3. Ricovero, rimozione cerchiaggio e terapia di attesa
4. Ricovero senza rimozione cerchiaggio: terapia di attesa



## ACOG PRACTICE BULLETIN

Clinical Management Guidelines for Obstetrician–Gynecologists

NUMBER 217

*(Replaces Practice Bulletin Number 188, January 2018)*

Committee on Practice Bulletins—Obstetrics. This Practice Bulletin was developed by the American College of Obstetricians and Gynecologists' Committee on Practice Bulletins—Obstetrics in collaboration with Robert Ehsanipour, MD and Christian M. Penker, MD.

## Prelabor Rupture of Membranes 2018

nionitis (113, 114). A firm recommendation regarding whether a cerclage should be removed after preterm PROM cannot be made, and either removal or retention is reasonable. Regardless, if a cerclage remains in place with preterm PROM, prolonged antibiotic prophylaxis beyond 7 days is not recommended.



Domanda 9

## Cortisone sì /cortisone no?

*La profilassi della RDS con Betametasone 12mg+12mg*

1. E' indispensabile
2. E' pericolosa perche' aumenta il rischio di infezioni
3. Va fatta soltanto in prossimita' del parto
4. E' inutile





## I medici decidono di ricoverare Maria

- ✓ Non rimuovono il cerchiaggio
- ✓ Iniziano la terapia antibiotica
- ✓ Inducono la maturità polmonare
- ✓ Sorvegliano il benessere fetale con eco e ctg
- ✓ Controllano le condizioni materne con
  - ✓ Emocromo e PCR ogni 48 ore
  - ✓ Temperatura corporea
  - ✓ Tamponi vaginali e rettali



**Domanda 10**

***Il comportamento di attesa e' corretto?***

1. Sì
2. No



## CONDOTTA DI ATTESA



Cochrane Database of Systematic Reviews

2017

Planned early birth versus expectant management for women with preterm prelabour rupture of membranes prior to 37 weeks' gestation for improving pregnancy outcome (Review)

Bond DM, Middleton P, Levett KM, van der Ham DP, Crowther CA, Buchanan SL, Morris J

No differences for:

- Neonatal sepsis
- Proven neonatal infection with positive blood culture
- Perinatal mortality
- Intrauterine deaths

EARLY BIRTH

- ↑  RDS
- ↑  Caesarean Section
- ↑  neonatal death
- ↑  Endometritis
- ↓  Triple-I



## La gestione clinica interattiva della MINACCIA DI PARTO PREMATURO

### CONDOTTA DI ATTESA Linee Guida



Gestione Del Parto Pretermine, SIGO, 2020

- Effettuare un management conservativo < 33.6 settimane in assenza di controindicazioni materno fetali (I A)
- In caso di pPROM > 34 settimane offrire una conduzione d'attesa discussa con i genitori. (I B)



The American College of  
Obstetricians and Gynecologists  
WOMEN'S HEALTH CARE PHYSICIANS

Prelabor Rupture of Membranes, ACOG Practice Bulletin 217 (2020)

- ▶ Patients with preterm PROM before 34 0/7 weeks of gestation should be managed expectantly if no maternal or fetal contraindications exist.



Care of Women Presenting with Suspected  
Preterm Prelabour Rupture of Membranes from  
24+0 Weeks of Gestation  
Green-top Guideline No. 73 June 2019

Recommendation	Evidence Level	Strength	Rationale for the recommendation
Women whose pregnancy is complicated by PPRM after 24 <sup>+0</sup> weeks' gestation and who have no contraindications to continuing the pregnancy should be <u>offered expectant management until 37<sup>+0</sup> weeks</u> ; timing of birth should be discussed with each woman on an individual basis with careful consideration of patient preference and ongoing clinical assessment	1++	A	A Cochrane review found benefits from expectant management, rather than early delivery, following PPRM in women with otherwise uncomplicated pregnancies.



- ✓ Dopo 3 giorni di osservazione le contrazioni cominciano a diventare piu' frequenti
- ✓ La pcr comincia a salire (22, 35)
- ✓ I globuli bianchi sono alti(22.000)
- ✓ Il peso fetale stimato e' di circa 1200/1300 gr (50° centile)
- ✓ Il feto e' cefalico
- ✓ Si decide di espletare il parto



**Domanda 11***Come si deve espletare il parto?*

1. Togliere il cerchiaggio e stimolare il travaglio
2. Togliere il cerchiaggio e aspettare il travaglio spontaneo
3. Togliere il cerchiaggio e fare un taglio cesareo elettivo
4. Somministrare solfato di Mg per neuroprotezione, rimuovere il cerchiaggio ed eventualmente stimolare il travaglio



## Recommendations

Preterm gestational age alone is not a valid indication for CS, unless if there are specific obstetrical indications.

Vaginal delivery appears to be safe and the gold standard for singleton and twins in vertex position.

Caesarean section should be recommended in pre-term labor in the presence of intrauterine growth restriction, breech presentation and in twins with a non-vertex presenting fetus. CS delivery is not recommended but might be an option for pre-viable infants. CS delivery does not prevent the occurrence of neurological sequelae. Short- and long-term maternal risks are clearly increased in case of CS.

## Updated European Guidelines



La prematurità in sé non è indicazione al taglio cesareo

Instrumental delivery is not recommended in pre-term infants. However, if necessary, a low forceps delivery should be preferred to vacuum extraction below 34 weeks.



## La gestione clinica interattiva della MINACCIA DI PARTO PREMATURO

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### Prelabor Rupture of Membranes

#### Preterm (24 0/7–33 6/7 weeks of gestation)

- Expectant management
- Antibiotics recommended to prolong latency if there are no contraindications
- Single-course of corticosteroids; insufficient evidence for or against rescue course
- Treat intraamniotic infection if present (and proceed to delivery)
- A vaginal–rectal swab for GBS culture should be obtained at the time of initial presentation and GBS prophylaxis administered as indicated.
- Magnesium sulfate for neuroprotection before anticipated delivery for pregnancies <32 0/7 weeks of gestation, if there are no contraindications<sup>†</sup>



- ✓ Dopo avere tolto il cerchiaggio ed indotto le contrazioni
- ✓ Si e' avviato un travaglio con l'aiuto della ossitocina
- ✓ Dopo 5 ore di travaglio attivo senza modificazioni della cervice, nonostante le frequenti esplorazioni vaginali e parte presentata alta, sono comparse delle decelerazioni ripetitive
- ✓ I medici hanno deciso di fare un cesareo
- ✓ Maschio 1400 7/9 Indice Apgar
- ✓ Viene affidato ai neonatologi



## Tutti sono felici però...

- ✓ Maria dopo il cesareo ha febbre altissima per 4 giorni
- ✓ Sono tutti preoccupati
- ✓ PCR 120; GB 25000
- ✓ Gli antibiotici tradizionali non funzionano
- ✓ Viene chiesta una consulenza di malattie infettive
- ✓ Lentamente con antibiotici di ultima generazione ad alte dosi Maria si rimette e sta meglio





## Domanda 12

*Ma se non si fosse aspettato si poteva prevenire questa sepsi post parto?*

1. Si
2. No
3. E' imprevedibile
4. Per il feto e' sempre meglio aspettare



Planned early birth versus expectant management for women with preterm prelabour rupture of membranes prior to 37 weeks gestation for improving pregnancy outcome (Review)



2017

## pPROM & rischio di sepsi

**AUTHORS' CONCLUSIONS** we found **no clinically important difference in the incidence of neonatal sepsis.**

**Early planned birth was associated with an increase in the incidence of neonatal RDS, need for ventilation, neonatal mortality, endometritis, admission to neonatal intensive care, and the likelihood of birth by caesarean section, but a decreased incidence of chorioamnionitis.**

Women randomized to **early birth** also had an **increased risk of labor induction,** but a decreased length of hospital stay.

**In women with PPRM before 37 weeks' gestation with no contraindications to continuing the pregnancy, a policy of expectant management with careful monitoring was associated with better outcomes for the mother and baby**



## La gestione clinica interattiva della MINACCIA DI PARTO PREMATURO



**Maternal sepsis**  
Arthur Jason Vaught, MD  
Johns Hopkins School of Medicine, 600 N. Wolfe St, Phipps 228, Baltimore, MD 21287  
2018



### Table 2 – Definition of SIRS.

Temperature > 38.3°C or < 36.0°C  
Heart rate > 90 beats/min  
Respiratory rate > 20 breaths/min or PaCO<sub>2</sub> < 32 mmHg  
White blood cell count > 12,000 cells/mm<sup>3</sup> or  
White blood cell count < 4000 cells/mm<sup>3</sup> or  
Greater than 10% bandemia  
*Must have 2 or more to meet positive criteria for SIRS*



1. Syndrome (SIRS)
2. Sepsis
3. Severe Sepsis
4. Septic Shock

### A!A!A! MEOWS in gravidanza

Normali modificazioni fisiologiche possono essere considerati reperti anormali fuori della gravidanza

SCORE	MET CALL	3	2	1	0	1	2	3	MET CALL
ZONE	PINK	ORANGE	GOLD	YELLOW	WHITE	YELLOW	GOLD	ORANGE	PINK
Respiratory Rate	<5	5-8			9-20		21-30	31-35	>35
Systolic Blood Pressure	<70	70-79	80-89	90-99	100-180		>180		
Heart Rate	<40	40-49			50-100	01-110	111-130	131-140	>140
4 Hour Urine Output		<80	80-120		>120				
Level of Consciousness	Unresponsive	Pain	Agitation/Confusion	Voice	Alert				



Dopo qualche ora dalla nascita Tommaso il bambino non sta benissimo...

- ✓ Presenta instabilità respiratoria per cui viene assistito artificialmente
- ✓ Sviluppa distermia
- ✓ Ha pcr e bianchi alti
- ✓ Deve fare terapia antibiotica
- ✓ Forse l'eco cerebrale mostra qualche segno di iperecogenicità diffusa....



**Domanda 13**

*Ma se fosse nato dopo la rimozione del cerchiaggio sarebbe stato meglio?*

1. Sicuramente
2. Avrebbe avuto altri problemi
3. Non sarebbe cambiato nulla
4. NO. Tuttavia sarebbe stato opportuno evitare esplorazioni vaginali molteplici





## La gestione clinica interattiva della MINACCIA DI PARTO PREMATURO

International Multicentre Term Prelabor Rupture of Membranes Study: Evaluation of predictors of clinical chorioamnionitis and postpartum fever in patients with prelabor rupture of membranes at term

Volume 177, Number 5  
Am J Obstet Gynecol

P. Gareth Seaward, MB, BCh, MMED,<sup>b</sup> Mary E. Hannah, MDCM, MSc,<sup>a, b</sup> Terri L. Myhr, MSc,<sup>a</sup> November 1997  
Dan Farine, MD,<sup>b</sup> Arne Ohlsson, MD, MSc,<sup>a, c</sup> Elaine E. Wang, MDCM, MSc,<sup>a</sup> K. Haque, MD,<sup>a</sup>  
Julie A. Weston, BScN, MSc,<sup>a</sup> Sheila A. Hewson, BA,<sup>a</sup> Gonen Ohel, MD,<sup>a</sup> and Ellen D. Hodnett,  
RN, PhD,<sup>a, d</sup> for the Term Prelabor Rupture of Membranes Study Group

RCT 5041 pz

**Table II.** Significant independent predictors of clinical chorioamnionitis ( $n = 335$ ) with use of multiple logistic regression analysis

Variable	Incidence of chorioamnionitis within each subcategory		Odds ratio	95% Confidence interval	Significance
	No.	%			
No. of digital vaginal examinations before delivery					
<3	14	2			
→ 3-4 (vs <3)	80	4	2.06	1.07-3.97	$p = 0.0307$
5-6 (vs <3)	97	7	2.62	1.35-5.08	$p = 0.0044$
7-8 (vs <3)	79	13	3.80	1.92-7.53	$p = 0.0001$
>8 (vs <3)	65	20	5.07	2.51-10.25	$p = 0.0001$

the iatrogenic risk factor of the number of vaginal examinations was more important than the intrinsic risk factor of duration of membrane rupture in predicting subsequent clinical chorioamnionitis



## La gestione clinica interattiva della MINACCIA DI PARTO PREMATURO

RESEARCH ARTICLE

Open Access

BMC Pregnancy and Childbirth (2020) 20:246



### The correlation between the number of vaginal examinations during active labor and febrile morbidity, a retrospective cohort study

Ohad Gluck\*, Yossi Mizrahi, Hadas Ganer-Herman, Jacob Bar, Michal Kovo and Eran Weiner

**Table 2** Univariate analysis of febrile morbidity complications according to the number of vaginal examinations during labor

Complications	Up to 4 VEs (n = 9716)	5–6 VEs (n = 4624)	7–8 VEs (n = 2999)	9 or more VEs (n = 4844)	p-value
Intrapartum fever	23 (0.23)	36 (0.77)	65 (2.16)	220 (4.54)	<b>&lt; 0.001</b>
Chorioamnionitis	85 (0.87)	72 (1.55)	79 (2.63)	341 (7.03)	<b>&lt; 0.001</b>
Intrapartum febrile morbidity	108 (1.11)	108 (2.32)	144 (4.8)	561 (11.58)	<b>&lt; 0.001</b>
Postpartum fever	56 (0.57)	57 (1.23)	67 (2.23)	139 (2.86)	<b>&lt; 0.001</b>
Endometritis	7 (0.07)	5 (0.11)	5 (0.17)	14 (0.29)	<b>&lt; 0.001</b>
Postpartum febrile morbidity	63 (0.65)	62 (1.37)	72 (2.45)	153 (3.18)	<b>&lt; 0.001</b>
Any febrile morbidity	171 (1.76)	170 (3.67)	216 (7.2)	714 (14.73)	<b>&lt; 0.001</b>

Data are presented as n (%)

Values in bold are statistically significant

Conclusion: The number of VEs performed during labor is directly correlated with febrile morbidity. Performing five or more VEs during labor is independently associated with febrile morbidity; For intrapartum and peripartum febrile morbidity the risk rises as more VEs are performed.



## Epicrisi

- A. Anamnesi completa ed accurata delle pazienti anche apparentemente a basso rischio
- B. Progesterone vaginale è da preferire a quello im
- C. Valutazione della cervicometria nel 2 trimestre indicata anche in assenza di sintomi (screening universale)
- D. Cerchiaggio di emergenza SI/NO vantaggi e svantaggi
- E. pProm un momento insidioso che necessita di un lavoro di equipe in sintonia...