

PREVENCIÓ PRIMÀRIA DE LA PREMATURITAT

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Prevenció de la prematuritat

- La prematuritat és la principal causa de morbimortalitat perinatal en els països desenvolupats.
- Representa el 75% de la mortalitat perinatal.
- Té conseqüències adverses per la salut a llarg termini.

The worldwide incidence of preterm birth: a systematic review of maternal mortality and morbidity

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Bull World Health Organ 2010;88:31–38 | doi:10.2471/BLT.08.062554

Table 3. Preterm birth rates, number of preterm births by United Nations geographical region/subregion and percentage of births covered by the estimates in a systematic review of the worldwide incidence of preterm birth

Region/subregion ^a	Preterm births		Preterm birth rate		Percent coverage of estimates ^e
	No. in 1000s	95% CI ^b	%	95% CI ^b	
World total	12 870	12 228–13 511	9.6	9.1–10.1	85.8
More developed countries	1 014	982–1 046	7.5	7.3–7.8	
Less developed countries	7 685	7 109–8 261	8.8	8.1–9.4	
Least developed countries	4 171	3 891–4 452	12.5	11.7–13.3	
Africa	4 047	3 783–4 311	11.9	11.1–12.6	72.7
Eastern	1 686	1 481–1 891	14.3	12.5–16.0	
Middle	602	535–669	11.6	10.3–12.9	
Northern	407	290–523	8.7	6.2–11.2	
Southern	228	191–265	17.5	14.6–20.3	
Western	1 125	1 036–1 215	10.1	9.3–10.9	
Asia	6 907	6 328–7 486	9.1	8.3–9.8	90.9
Eastern	724	650–798	3.8	3.4–4.1	
South-central	4 467	3 944–4 991	11.4	10.0–12.7	
South-eastern	1 271	1 062–1 480	11.1	9.3–13.0	
Western	396	290–501	7.9	5.8–9.9	
Central	49	21–77	3.8	1.6–5.9	
Europe	466	434–498	6.2	5.8–6.7	94.8
LA and the Caribbean	933	858–1 009	8.1	7.5–8.8	79.3
Caribbean	48	33–63	6.7	4.7–8.8	
Central America	295	263–326	9.1	8.2–10.1	
South America	591	524–658	7.9	7.0–8.8	
North America^d	490	479–482	10.6	10.5–10.6	100
Oceania					91.0
Australia/New Zealand	20	20–20	6.4	6.3–6.6	
Rest of Oceania	16	11–20	6.4	4.6–8.2	

CI, confidence interval; PI, prediction interval.

^a Countries categorized according to United Nations classification.

^b Whereas PIs were calculated for country estimates based on the model, CIs were derived for the regional/subregional aggregate estimates that utilized data from studies as well as modelled estimates.

^c Refers to the proportion of live births for which data were available and model-based estimates were not generated.

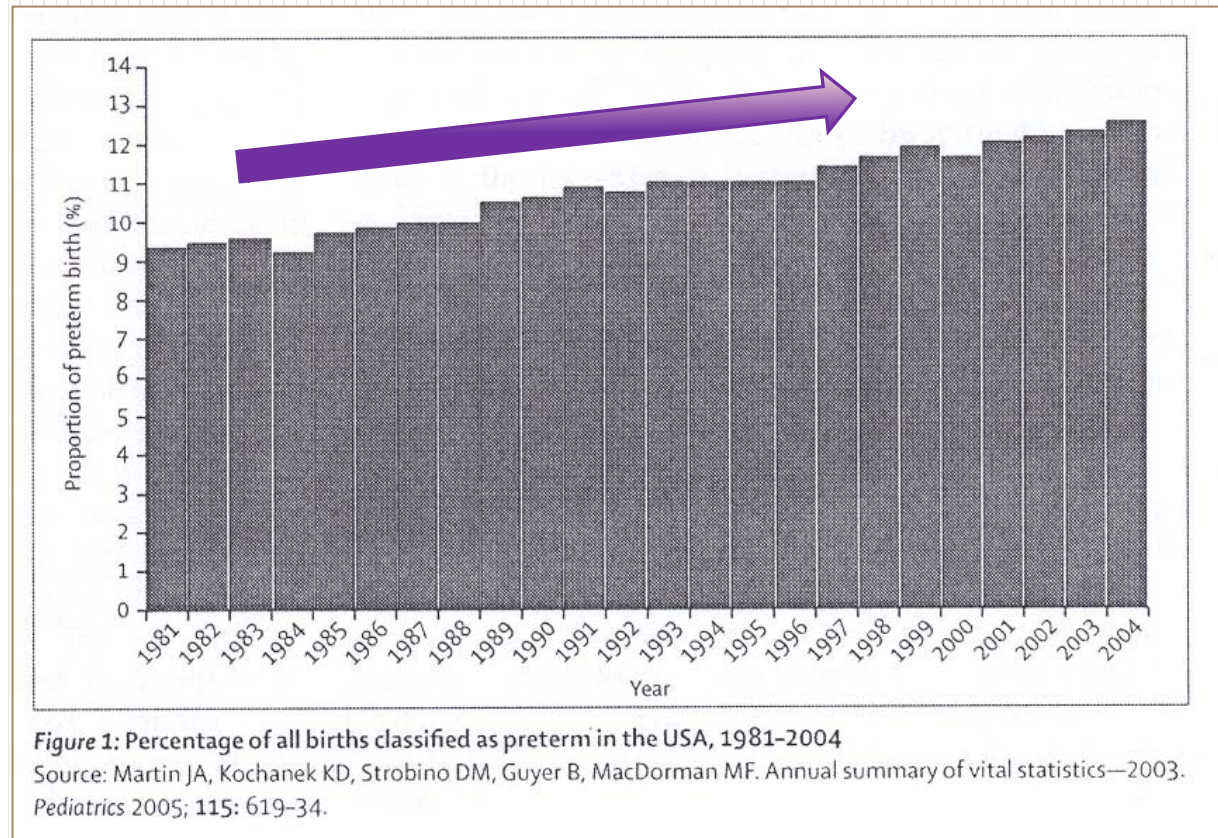
^d Excluding Mexico, which is included under Latin America.

Lancet. 2008 Jan 5;371(9606):75-84.

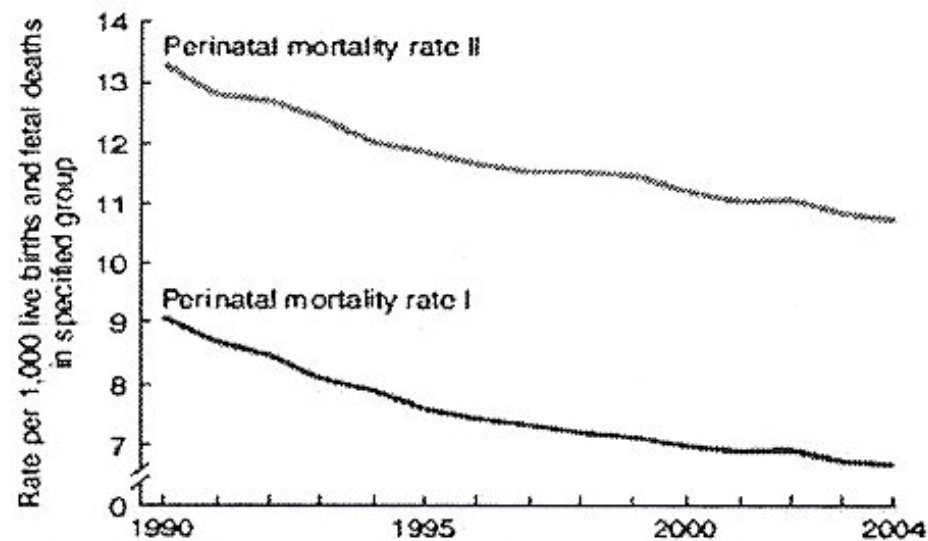
Epidemiology and causes of preterm birth.

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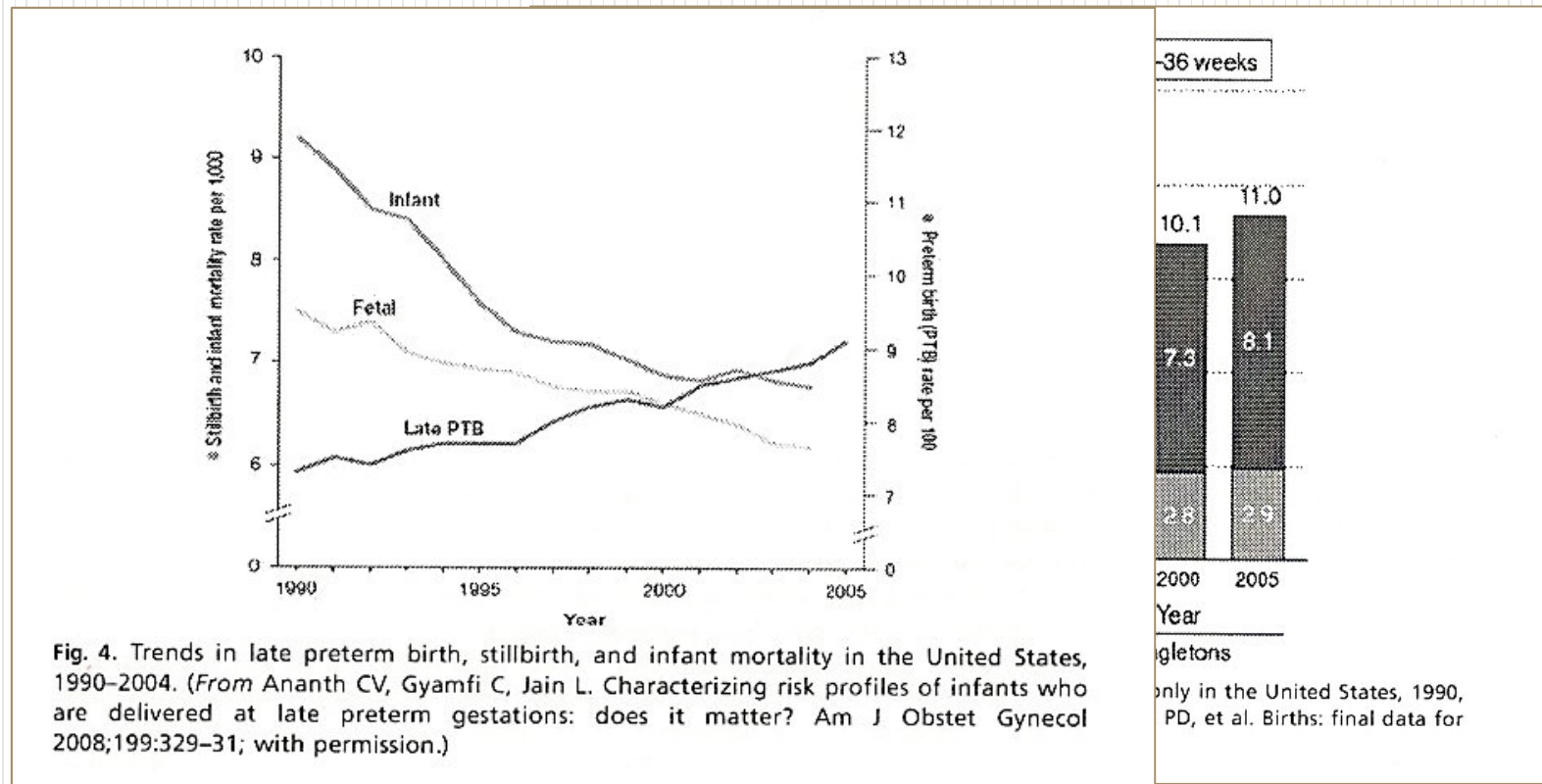
Mortalitat perinatal



NOTE: Perinatal I includes infant deaths less than 7 days of age and fetal deaths 20 weeks or more. Perinatal II includes infants less than 28 days of age and fetal deaths 20 weeks or more.

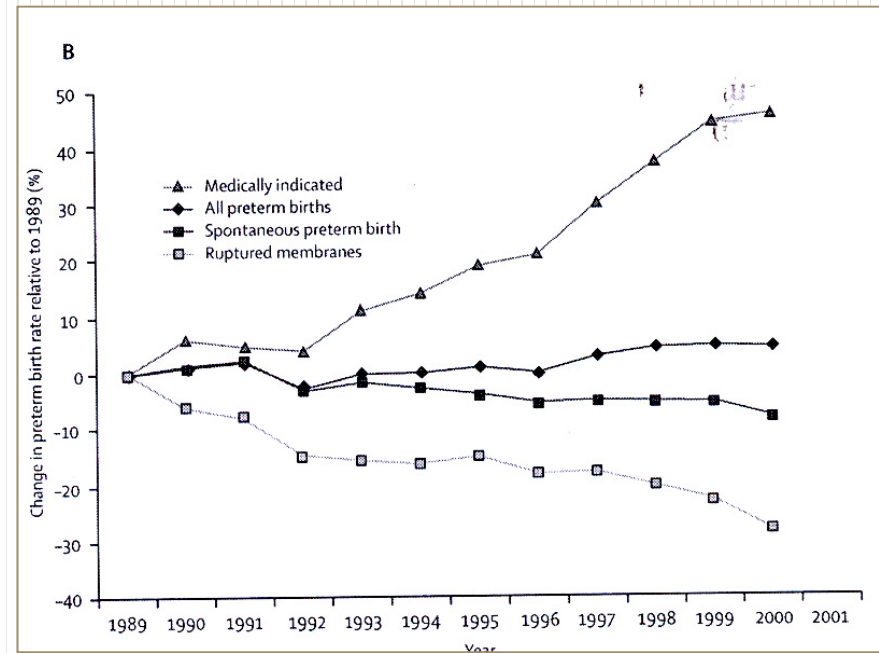
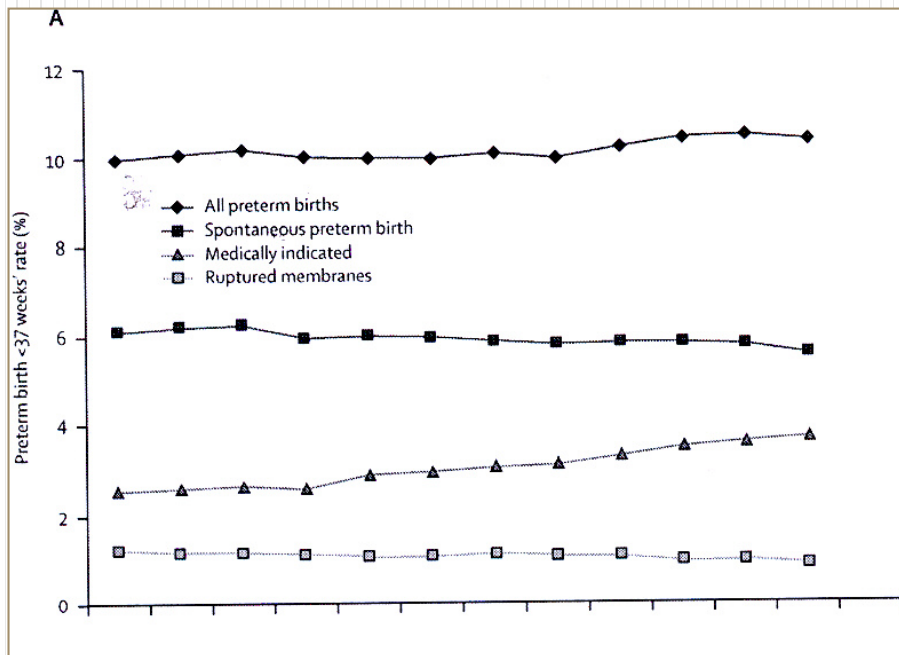
Fig. 2. Perinatal mortality rates in the United States, 1990–2004. (Data from Mathews TJ, MacDorman MF. Infant mortality from the 2005 period linked birth/infant death data set. *Natl Vital Stat Rep* 2008;57:1–32.)

Mortalitat perinatal



Goals and strategies for prevention of preterm birth: an obstetric perspective. *Lang CT, Iams JD. Pediatr Clin North Am.* 2009 Jun; 56(3):537-63

Epidemiologia



Epidemiology and causes of preterm birth. *Goldenberg RL et al. Lancet 2008 Jan 5;371 (9606):75-84*

Prevenció de la prematuritat

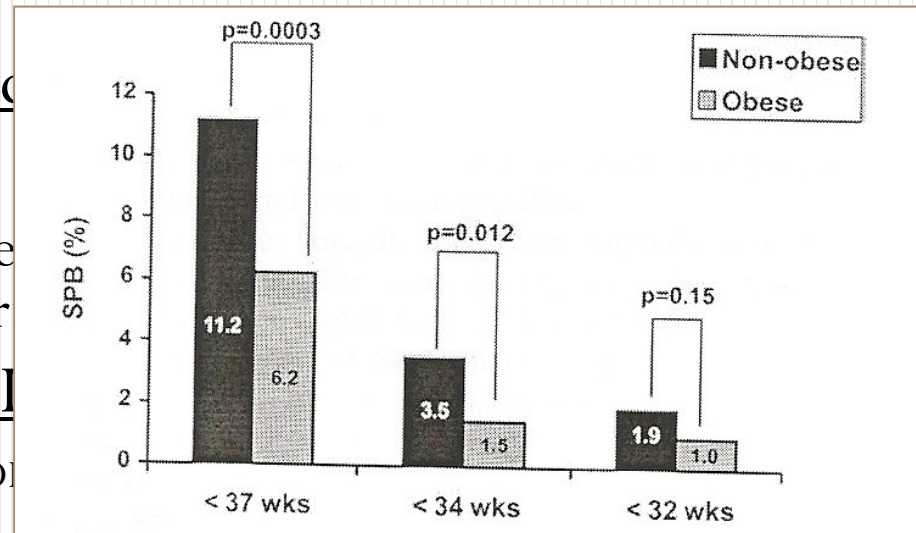
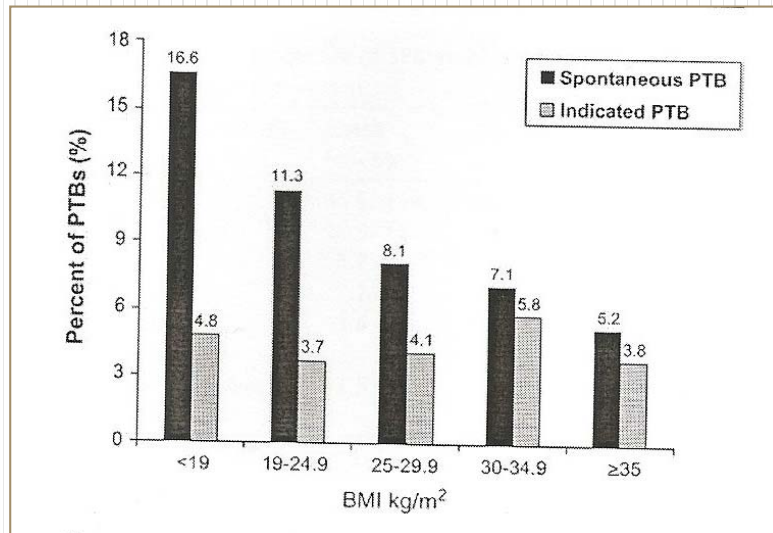
Intervencions destinades a reduir la morbiditat i mortalitat perinatal

- **P. primària**
- **P. secundària**
- **P. terciària**

Prevenció primària

1. Factors de risc clínics
 - Pregestacionals
 - Gestacionals
2. Mesures de prevenció primària

FACTORS DE RISC CLÍNICS: Pregestacionals



- Cirurgia uterina prèvia:

- instrumentacions uterines (legrats, conitzacions).
- Presència de malformacions uterines.

Association between maternal body mass index and spontaneous and indicated preterm birth. Hendler I et al. *Am J Obst Gynecol* 2005 ;192:882-6.

FACTORS DE RISC CLÍNICS:

Pregestacionals

- Tècniques de reproducció assistida (20%)
- Gestació múltiple (15-20%)
- Edat:
 - <20 anys: major taxa de PP
 - dones blanques: menor taxa de PP 20-24 anys pel primer embaràs, 25-29 anys pels següents embarassos
 - dones negres: pel primer i següents embarassos, menors taxes de 25-29 anys.
- Període intergenèsic

Birth spacing and risk of adverse perinatal outcomes: a meta-analysis.

Conde-Agudelo A, Rosas-Bermúdez A, Kafury-Goeta AC.

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Table 5. Meta-analysis of Dose-Response Regression Slopes and Prediction of the Risk of Adverse Perinatal Outcomes for Interpregnancy Intervals <18 Months and >59 Months

Risk Increase	Increase, % (95% CI)		
	Preterm Birth (12 Studies)	LBW (7 Studies)	SGA (12 Studies)
Per month for intervals < 18 mo*	1.92 (1.80-3.04)	3.25 (3.09-3.41)	1.52 (1.40-1.64)
Per month for intervals >59 mo†	0.55 (0.49-0.61)	0.91 (0.83-0.99)	0.76 (0.71-0.81)
Predicted by the model			
Interpregnancy interval, mo			
3	28.8 (27.0-30.6)	48.8 (46.4-51.2)	22.8 (21.0-24.6)
6	23.0 (21.6-24.5)	39.0 (37.1-40.9)	18.2 (16.8-19.7)
9	17.3 (16.2-18.4)	29.3 (27.8-30.7)	13.7 (12.6-14.8)
12	11.5 (10.8-12.2)	19.5 (18.5-20.5)	9.1 (8.4-9.8)
15	5.8 (5.4-6.1)	9.8 (9.3-10.2)	4.6 (4.2-4.9)
18-59‡	1.00	1.00	1.00
72	6.6 (5.9-7.3)	10.9 (10.0-11.9)	9.1 (8.5-9.7)
96	19.8 (17.6-22.0)	32.8 (29.9-35.6)	27.4 (25.6-29.2)
120	33.0 (29.4-36.6)	54.6 (49.8-59.4)	45.6 (42.6-48.6)
144	46.2 (41.2-51.2)	76.4 (69.7-83.2)	63.8 (59.6-68.0)

Abbreviations: CI, confidence interval; LBW, low birth weight; SGA, small for gestational age.
 *Risk increase per each month that interpregnancy interval is shortened from 18 months.
 †Risk increase per each month that interpregnancy interval is lengthened from 59 months.
 ‡Reference category.

Table 4. Odds Ratios for the Association Between Interpregnancy Interval and Adverse Perinatal Outcomes in Cohort and Cross-sectional Studies

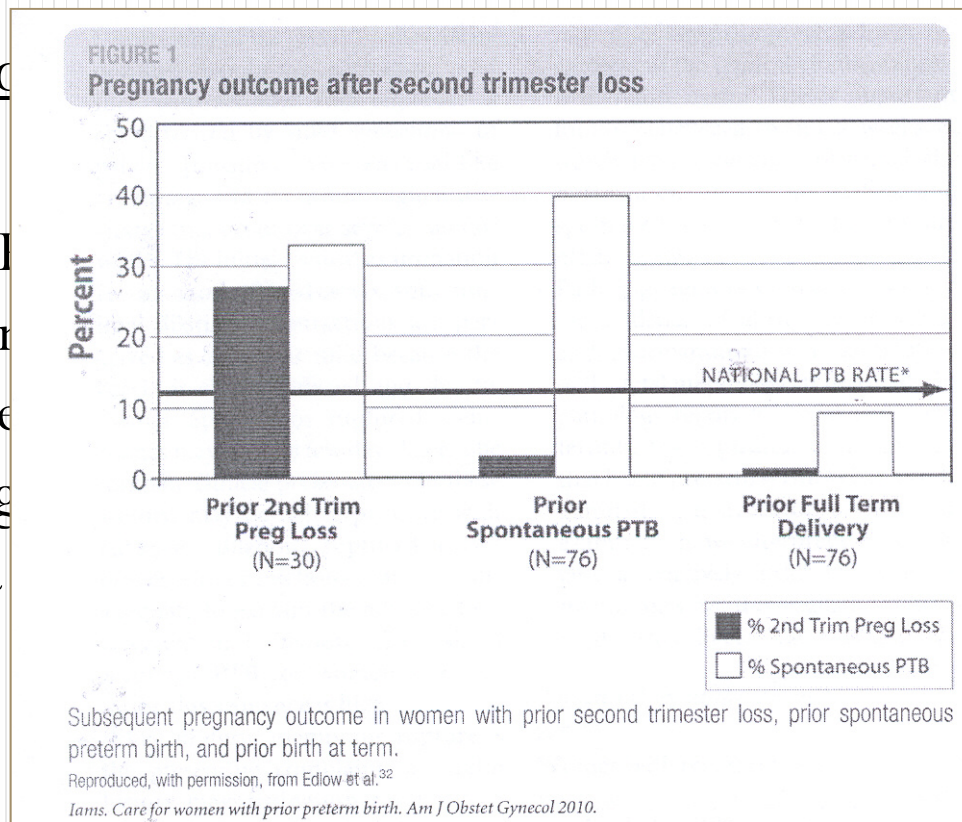
Interpregnancy Interval, mo	Preterm Birth	Low Birth Weight	Small for Gestational Age
Pooled Unadjusted Results			
<6	No. of studies: 8 ^{25,33,40,49,50,52,55,64} OR (95% CI): 1.77 (1.54-2.04) I ² , %*: 95	6 ^{21,33,40,49,56,64} 2.12 (1.98-2.26)	7 ^{21,22,33,49,52,55,64} 1.39 (1.20-1.61)
6-11	No. of studies: 9 ^{25,27,33,40,49,50,52,55,64} OR (95% CI): 1.23 (1.15-1.31) I ² , %*: 85	6 ^{21,33,40,49,56,64} 1.23 (1.15-1.32)	8 ^{21,22,24,33,49,52,55,64} 1.18 (1.14-1.23)
12-17	No. of studies: 9 ^{25,27,33,40,49,50,52,55,64} OR (95% CI): 1.11 (1.03-1.20) I ² , %*: 56	7 ^{21,27,33,40,49,56,64} 1.08 (1.02-1.14)	8 ^{21,22,24,33,49,52,55,64} 1.08 (1.06-1.11)
18-23†	No. of studies: 9 ^{25,27,33,40,49,50,52,55,64} OR: 1.00	7 ^{21,27,33,40,49,56,64} 1.00	8 ^{21,22,24,33,49,52,55,64} 1.00
24-59	No. of studies: 6 ^{27,49,50,52,55,64} OR (95% CI): 1.03 (1.00-1.07) I ² , %*: 28	6 ^{27,33,40,49,56,64} 1.07 (0.99-1.15)	7 ^{22,24,33,49,52,55,64} 1.07 (0.98-1.18)
≥60	No. of studies: 5 ^{27,49,50,52,64} OR (95% CI): 1.27 (1.17-1.39) I ² , %*: 93	4 ^{27,49,56,64} 1.49 (1.17-1.89)	5 ^{22,24,49,52,64} 1.36 (1.20-1.54)
Pooled Adjusted Results			
<6	No. of studies: 8 ^{25,39,40,49,50,52,55,64} OR (95% CI): 1.40 (1.24-1.58) I ² , %*: 69	4 ^{40,49,52,64} 1.61 (1.39-1.86)	6 ^{22,39,49,52,55,64} 1.26 (1.18-1.33)
6-11	No. of studies: 9 ^{25,39,40,49,50,52,55,64} OR (95% CI): 1.14 (1.10-1.17) I ² , %*: 87	4 ^{40,49,52,64} 1.14 (1.10-1.18)	7 ^{22,24,39,49,52,55,64} 1.11 (1.04-1.19)
12-17	No. of studies: 9 ^{25,39,40,49,50,52,55,64} OR (95% CI): 1.07 (1.03-1.11) I ² , %*: 26	4 ^{40,49,52,64} 1.05 (1.01-1.09)	7 ^{22,24,39,49,52,55,64} 1.06 (1.01-1.10)
18-23†	No. of studies: 8 ^{25,39,40,49,50,52,55,64} OR: 1.00	4 ^{40,49,52,64} 1.00	7 ^{22,24,39,49,52,55,64} 1.00
24-59	No. of studies: 8 ^{25,39,40,49,50,52,55,64} OR (95% CI): 0.99 (0.97-1.02) I ² , %*: 0	4 ^{40,49,52,64} 1.01 (0.98-1.03)	7 ^{22,24,39,49,52,55,64} 1.02 (0.99-1.05)
≥60	No. of studies: 7 ^{25,39,40,49,50,52,64} OR (95% CI): 1.20 (1.17-1.24) I ² , %*: 95	4 ^{40,49,52,64} 1.43 (1.27-1.62)	6 ^{22,24,39,49,52,64} 1.29 (1.20-1.39)

Abbreviations: CI, confidence interval; OR, odds ratio.
 *Heterogeneity test (see "Methods" section).
 †Reference category.

FACTORS DE RISC CLÍNICS: Pregestacionals

- Història clínica

- FACTORS DE RISC CLÍNICS
- Risc de recidiva
- Risc invencible
- Pèrdua gestacional
- Història clínica



time

8.1% pel tercer)

Induced termination of pregnancy and low birthweight and preterm birth: a systematic review and meta-analyses.

Shah PS, Zao J; Knowledge Synthesis Group of Determinants of preterm/LBW births.

Collaborators (11)

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Table 3. Results of association of induced abortion and LBW/PT/SGA births

Infant status	Results	History of one induced abortion versus no history of induced abortion	History of >1 induced abortions versus no history of induced abortions
LBW	Number of studies	18	5
	Participants	280 529	49 347
	Risk in exposed (%)	6.4	7.9
	Risk in non-exposed (%)	4.9	5.0
	UAOR (95% CI)	1.35 (1.20, 1.52)	1.72 (1.45, 2.04)
	PAR (%)	3.8	N/A
PT	Number of studies	22	7
	Participants	268 379	158 421
	Risk in exposed (%)	8.7	21.8
	Risk in non-exposed (%)	6.8	7.8
	UAOR (95% CI)	1.36 (1.24, 1.50)	1.93 (1.38, 2.71)
	PAR (%)	3.2	N/A
SGA	Number of studies	3	2
	Participants	38 835	35 422
	Risk in exposed (%)	9.8	5.3
	Risk in non-exposed (%)	8.8	8.8
	UAOR (95% CI)	0.87 (0.69, 1.09)	1.06 (0.84, 1.33)

UAOR, unadjusted odds ratio.

FACTORS DE RISC CLÍNICS:

Gestacionals

- Tabac
- Infecció:
 - Infeccions severes (pielonefritis, neumònia, apendicitis)
 - Vaginosi bacteriana: Augment 1.5-3 vegades del risc de PP.
 - Altres infeccions genitals
 - Bacteriúria asimptomàtica (risc de part preterme de 1.9)
 - Reducció del risc de pielonefritis (OR 0.23, 0.13-0.41)
 - Reducció del risc de LBW (OR 0.66, 0.49-0.89)
 - Reducció del part preterme (OR 0.37, 0.10-1.36)

Mesures de prevenció primària

- Preconcepcionals
- Postconcepcionals

Prevenció primària preconcepcional

- Intervencions d'educació pública
 - Percepció errònia de seguretat per la milloria de la medicina neonatal
 - Conscienciar sobre la prematuritat com a causa de mortalitat perinatal
 - Informar sobre els factors de risc evitables (instrumentacions uterines repetides, tabac,...)
- Polítiques públiques i professionals
 - Efecte més immediat (limitació n° embrions transferits)
 - Enfoc social
- Suplements nutricionals
- Tabac

Prevençió primària postconcepcional

- Profilaxi mèdica dels parts pretermes indicats
 - AAS baixa dosi, calci, Vit C i E: no efecte sobre la preeclàmpsia ni el part preterme.
- Atenció prenatal i suport social
 - Atenció prenatal precoç
 - Adolescents
 - Atenció prenatal, suport social, visites a domicili, educació maternal
- Modificació de l'activitat materna
- Suplements nutricionals (calci, Vit E i C, àc. grassos omega-3 poliinsaturats)
- Tabac: Consell de 5-15 minuts (RR 1.7, 95% CI 1.3-2.2)
- Atenció periodontal
- Tractament antibiòtic

Prevençió primària durant la gestació

- Intervencions que han demostrat ser inefectives:
 - Suplements nutricionals
 - Atenció periodontològica
 - Screening de la vaginosis bacteriana
 - Cerclatge cervical
- Intervencions que han demostrat ser efectives:
 - Programes de deshabitució tabàquica
 - Screening i tractament de la bacteriúria asimptomàtica
 - Administració de progesterona si LC < 15mm

Prevention of Preterm Birth Based on Short Cervix: Progesterone

Eduardo B. da Fonseca, MD,^{*,†} Rievani Damião, MD,^{*} and Kypros Nicolaides, MD^{*}

Preterm delivery, which occurs in about 5%-13% of pregnancies in most countries, is the main cause of neonatal morbidity and mortality. Symptomatic treatment of pregnancies presenting in preterm labor with corticosteroids has improved perinatal outcome but has not reduced the incidence of preterm delivery. Recent evidence suggests that the rate of preterm delivery may be reduced by the prophylactic use of progesterone in women with a history of preterm delivery and in those with a short cervical length identified by routine transvaginal sonography. This review summarizes the evidence (level A evidence) of the effectiveness of progesterone on the rate of preterm birth.

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KEYWORDS preterm birth, progesterone, short cervical length, transvaginal ultrasound

Screening en dones de baix risc

- ❖ Mesura de Longitud cervical (LC)
- ❖ Mesures de prevenció: Cerclatge / Progesterona

Prevention of Preterm Birth Based on Short Cervix: Progesterone

Valor de la mesura de la LC

❖ Gestacions úniques:

❖ Risc de part preterme inversament relacionat amb la LC

LC	Població general	Taxa de detecció PPT <32 SG	Taxa de detecció PPT <34 SG
LC ≤ 25 mm	10%	55%	20.4%
LC ≤ 20 mm	5%	48%	
LC ≤ 15 mm	1%	35%	25.8%

❖ Gestacions múltiples:

❖ LC ≤ 15 mm en 5% de les dones

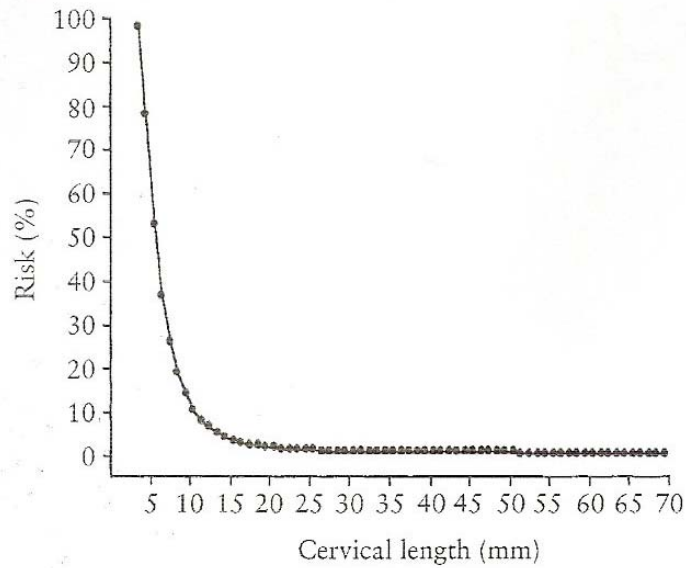


Figure 5 Risk for spontaneous delivery at ≤ 32 weeks according to cervical length at 23 weeks of gestation

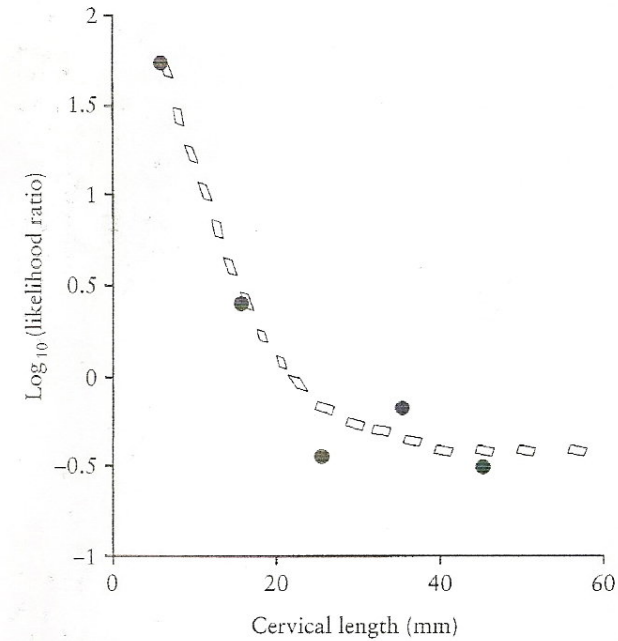


Figure 4 Likelihood ratios for spontaneous delivery at ≤ 32 weeks according to cervical length at 23 weeks of gestation ($\log_{10}(\text{likelihood ratio}) = 0.00005 \times \text{cervical length}^3 + 0.0058 \times \text{cervical length}^2 - 0.2284 \times \text{cervical length} + 2.7151$)

Table 2 Frequency distribution of cervical lengths in the women delivering at > 32 and ≤ 32 weeks and the likelihood ratio (LR) (observed and regressed) and risk for delivery at ≤ 32 weeks

Cervical length (mm)	Delivery > 32 weeks		Delivery ≤ 32 weeks		Observed LR	Regressed LR	Risk %
	n	%	n	%			
0-10	10	0.81	8	42.11	51.92	51.51	78.2
11-20	77	6.24	3	15.79	2.53	2.66	4.0
21-30	371	30.09	2	10.53	0.35	0.71	1.1
31-40	494	40.06	5	26.32	0.66	0.48	0.7
41-50	213	17.27	1	5.26	0.30	0.42	0.6
51-60	59	4.79	0	0.00	—	0.24	0.4
61-70	9	0.73	0	0.00	—	0.04	0.1

Prevention of Preterm Birth Based on Short Cervix: Progesterone

Progesterona en pacients amb cèrvix curt

❖ Pacients asimptomàtiques

Prevention of preterm birth based on short cervix: progesterone

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Table 1 Outcome For Progesterone vs Placebo Among Pregnant Women With a Short Cervix

Authors	PTB Wk: RR (95% CI)	Perinatal Death	Neonatal Death	RDS
Fonseca et al ¹³	<34: 0.56 (0.36-0.86)	0.38 (0.10-1.38)	0.29 (0.06-1.42)	0.59 (0.26-1.29)
DeFranco et al ¹⁴	≤32: 0% vs 29.6%	NA	0% vs 3.7%	0.18 (0.02-1.31)
Dodd et al ³⁶	<34: 0.58 (0.38-0.87)	0.38 (0.10-1.40)	0.29 (0.06-1.37)	0.59 (0.29-1.19)

Abbreviations: PTB, preterm birth; wk, week; NA, not available; RDS, respiratory distress syndrome; RR, relative risk; CI, confidence interval.

Table 2 Selected Ongoing Trials of Progesterone and Short Cervical Length

Registry	Title	Sponsors	Chief Investigator	Aim	Enrolment
NCT00615550	Pregnant Short Cervix Trial	Columbia Laboratory	George W. Creasy, Roberto Romero, Sonia Hassan	Reduction in the birth ≤ 326/7 wk	450
NCT00439374	RCT of Progesterone to Prevent Preterm Birth in Nulliparous Women With a Short Cervix	Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD)	Catherine Y. Spong	Reduction in the birth ≤ 37 wk	1000
NCT00694967	A Randomized Trial of Cerclage Versus 17 α -Hydroxyprogesterone Caproate for Treatment of a Short Cervix	Lehigh Valley Hospital	Orion Rust, MD	Reduction in the birth ≤ 35 wk	92

Abbreviation: wk, week.

Prevention of Preterm Birth
Based on Short Cervix: Progesterone

Progesterona en pacients amb cèrvix curt

❖ L'administració profilàctica de progesterona en dones amb cèrvix curt **disminueix la incidència de part preterme.**

❖ Podria ser útil el screening de la LC de rutina i l'administració profilàctica de progesterona en els casos de cèrvix curt. (ACOG, 2008: *no recomana el screening de la LC de rutina*)

❖ Podríem oferir l'administració profilàctica de **progesterona:**

- ❖ G. úniques i H^a prèvia de part preterme
- ❖ LC ≤ 15 mm

GUIDELINES

Guidelines for the management of spontaneous preterm labor: identification of spontaneous preterm labor, diagnosis of preterm premature rupture of membranes, and preventive tools for preterm birth

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NEBOJSA RADUNOVIC¹², MIKE ROBSON¹³, STEPHEN C. ROBSON¹⁴, CIHAT SEN¹⁵,
ANDREW SHENNAN¹⁶, FLORIN STAMATIAN¹⁷, & YVES VILLE¹⁸

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EINES PREVENTIVES

- Cerclatge cervical
- Pesari cervical
- Progesterona

Guidelines for the management of spontaneous preterm labor: identification of spontaneous preterm labor, diagnosis of preterm premature rupture of membranes, and preventive tools for preterm birth

CERCLATGE CERVICAL

❑ Indicacions:

- **≥ 3 avortaments tardans o ≥ 3 parts prematurs previs : \downarrow PP 32 al 15%**
 - Antecedent de conització o malformacions uterines: No evidència suficient
 - Gestació múltiple: efecte deleteri
 - Dilatació cervical i contraccions uterines: efecte controvertit
-
- ✓ **No evidència de la seva utilitat a població general quan $LC \leq 25$ mm**
 - ✓ Sí que pot ser útil a gestacions úniques amb antecedent de part prematur (< 36 SG) i
LC < 25 mm

Guidelines for the management of spontaneous preterm labor: identification of spontaneous preterm labor, diagnosis of preterm premature rupture of membranes, and preventive tools for preterm birth

PESARI CERVICAL

❑ Indicacions:

- Possible efecte preventiu en:
 - **Dones asimptomàtiques**
 - **Cèrvix curt (LC ≤ 25 mm) a les 20-24 SG**
 - **G. úniques**
- ✓ No resultats concloents en g. múltiples
- ✓ Calen més assajos randomitzats
- ✓ Recomana el seu ús en el marc de protocols de recerca

Guidelines for the management of spontaneous preterm labor: identification of spontaneous preterm labor, diagnosis of preterm premature rupture of membranes, and preventive tools for preterm birth

PROGESTERONA

□ Indicacions:

- Gestants asimptomàtiques amb antecedent de part prematur
 - **A gestants nul.líparees amb gestació única i amb LC < 15 mm** (es necessiten més estudis)
 - Després de tractar un episodi de APP a gestants nulíparees amb gestacions úniques (es necessiten més estudis)
- ✓ No útil en g. múltiples

GRÀCIES

