



fiog – 1° congresso regionale lombardia
dal territorio all'ospedale
lodi, 27-28 marzo 2009

Fattori predittivi di rischio di parto prematuro

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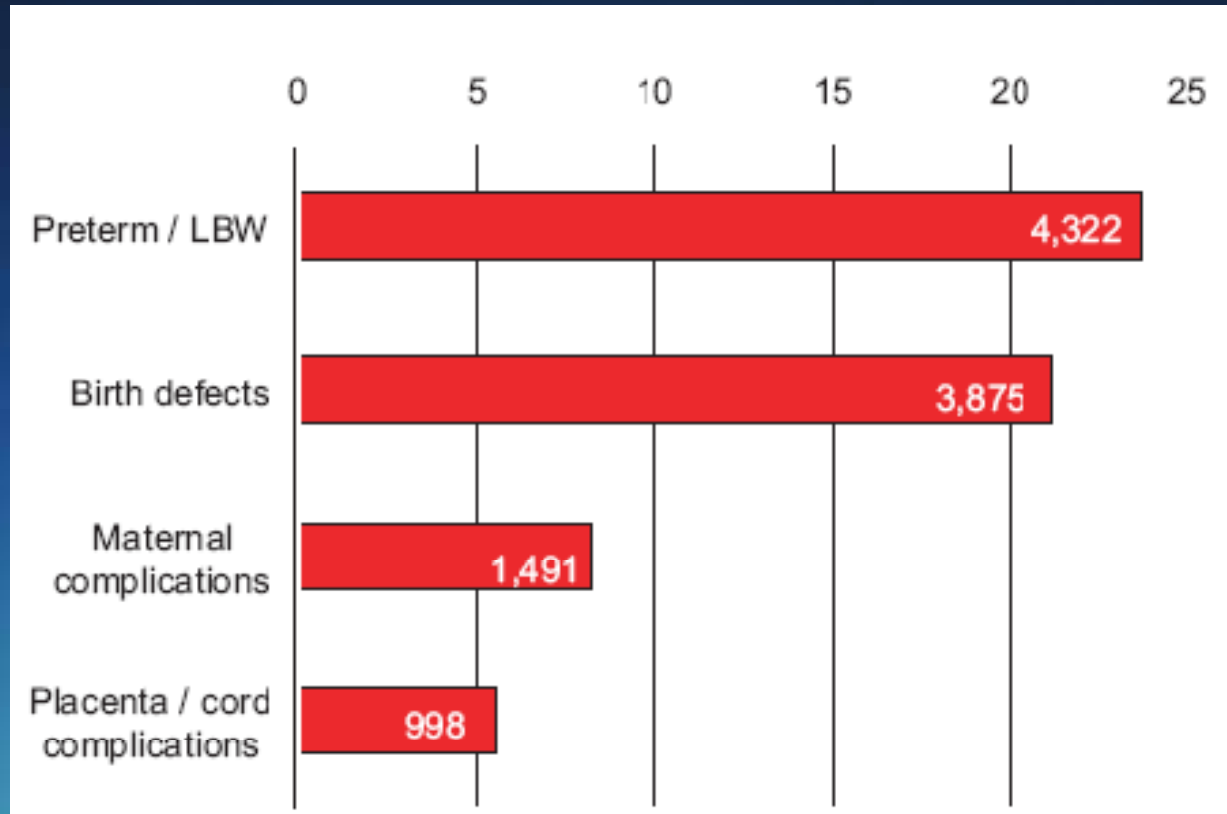
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Medline

	Articoli	Review	Dal...
<u>Preterm delivery</u>	29.968	3.450	1963
<u>Preeclampsia</u>	22.880	2.822	1963
<u>IUGR</u>	13.344	1.905	1966
<u>GDM</u>	7.563	1.129	1970

Parto prematuro

Cause di mortalità neonatale – 2001
[n/100.000 nati vivi]

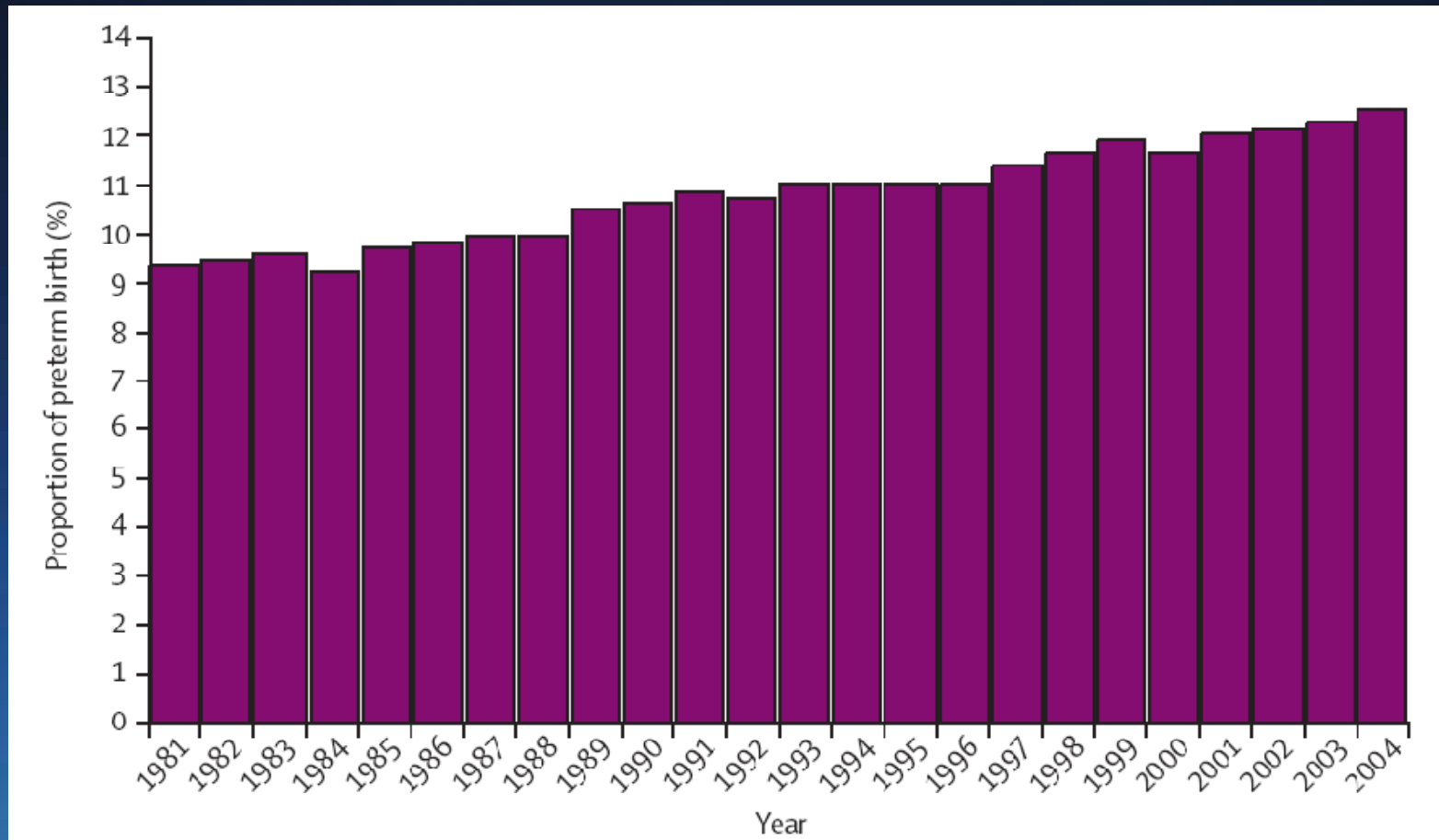


C Spong, Obstet Gynecol 2007

Definizione

- Parto <37 settimana \Leftrightarrow il cut off minimo varia nei vari paesi
- Presso il termine $\Leftrightarrow \geq 34$ settimana [60-70%]
- Media prematurità $\Leftrightarrow 32 - 33^6$ settimane [20%]
- Grave prematurità $\Leftrightarrow 28 - 31^6$ settimane [15%]
- Estrema prematurità $\Leftrightarrow < 28$ settimane [5%]

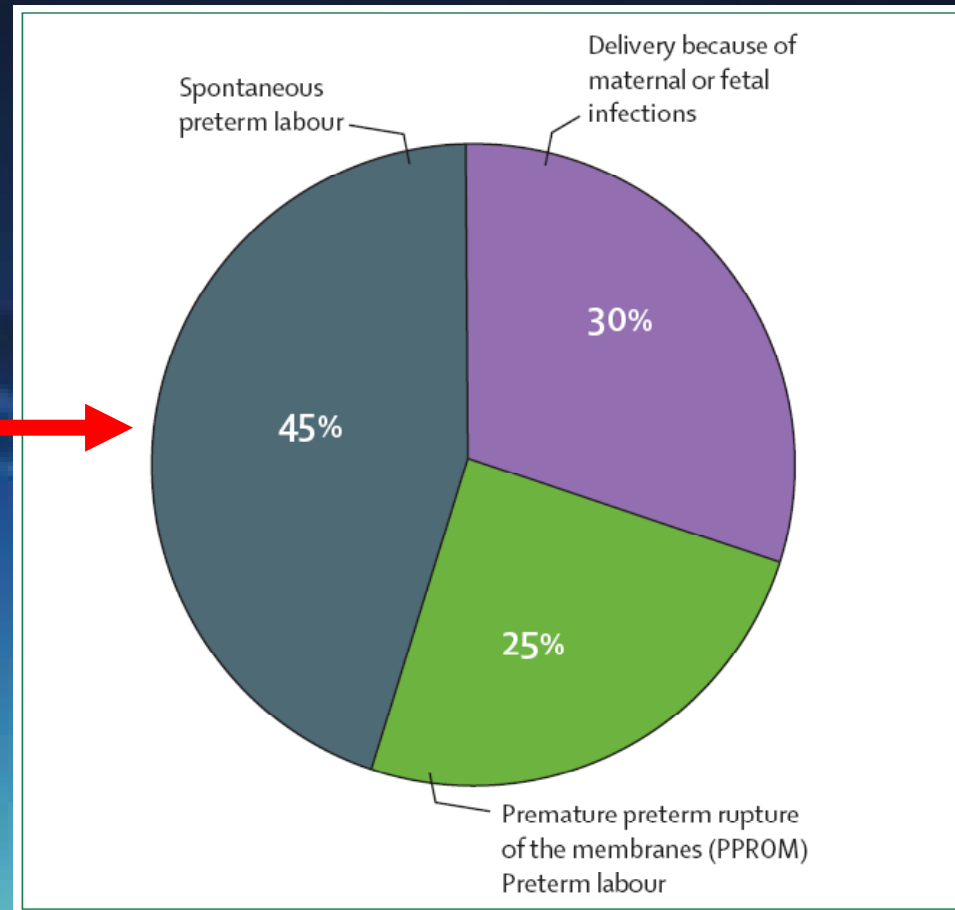
Epidemiologia



JA Martin et al, Pediatrics 2005

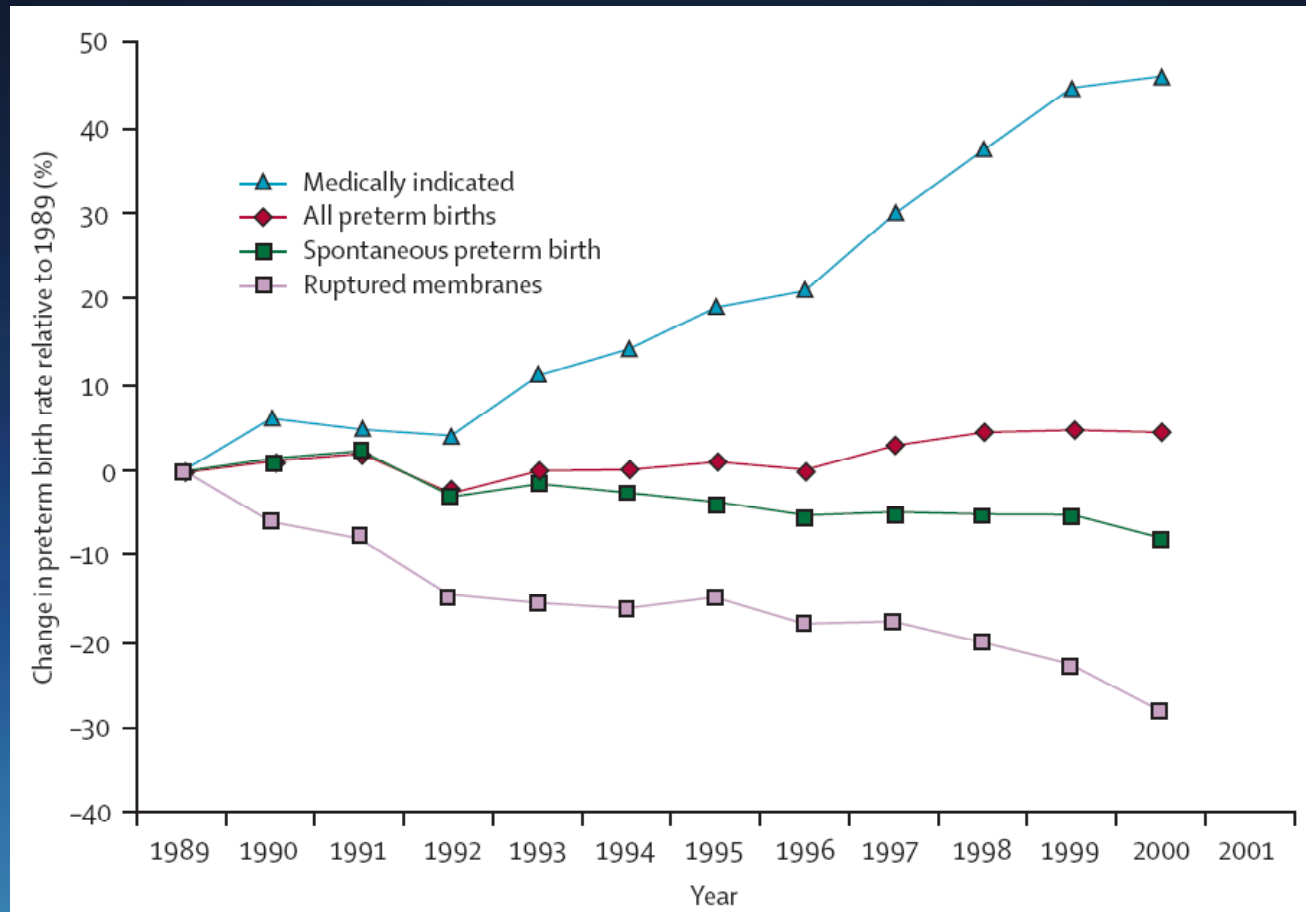
Epidemiologia

Parto
Prematuro
Spontaneo



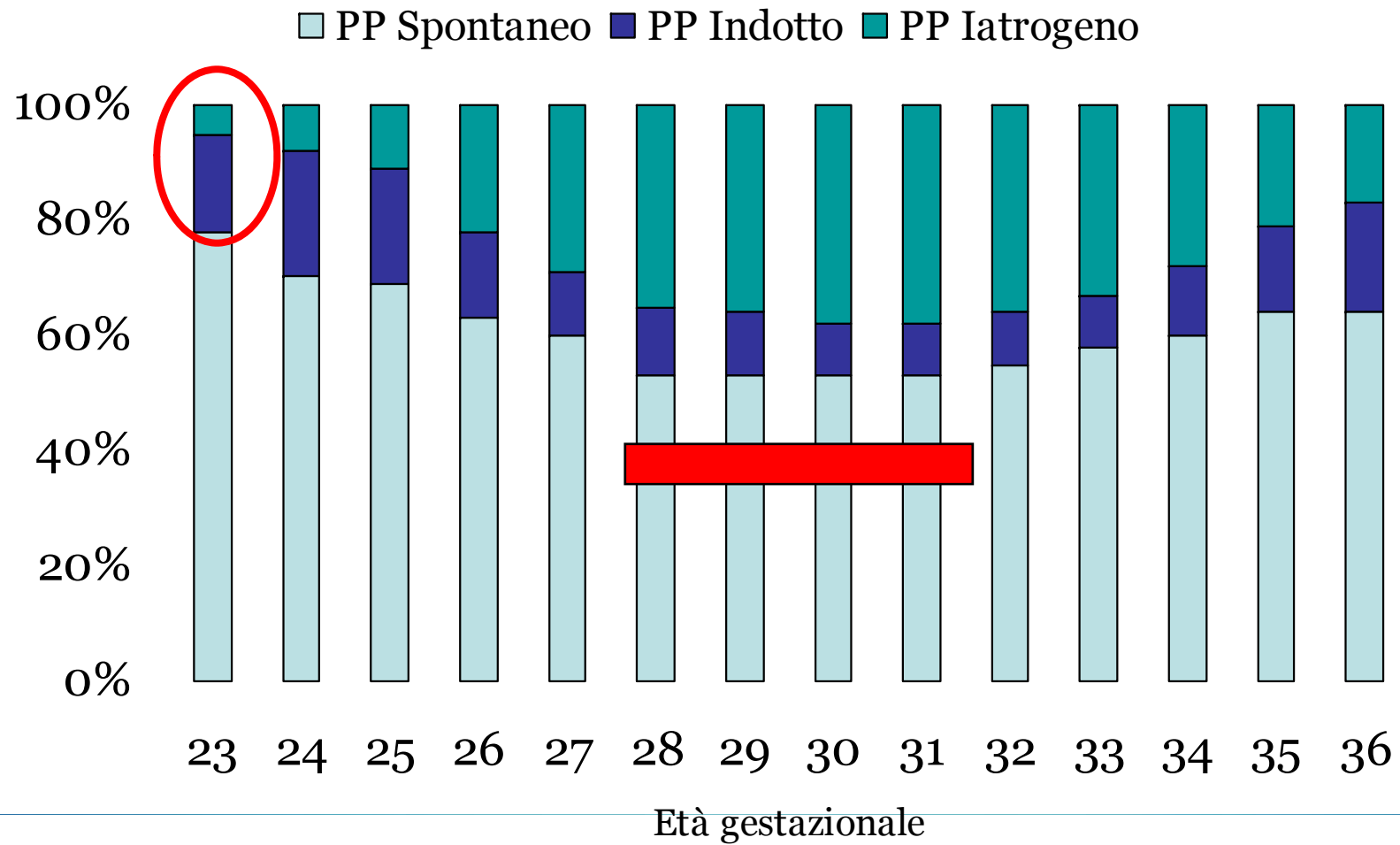
RL Goldenberg et al, Lancet 2008

Epidemiologia



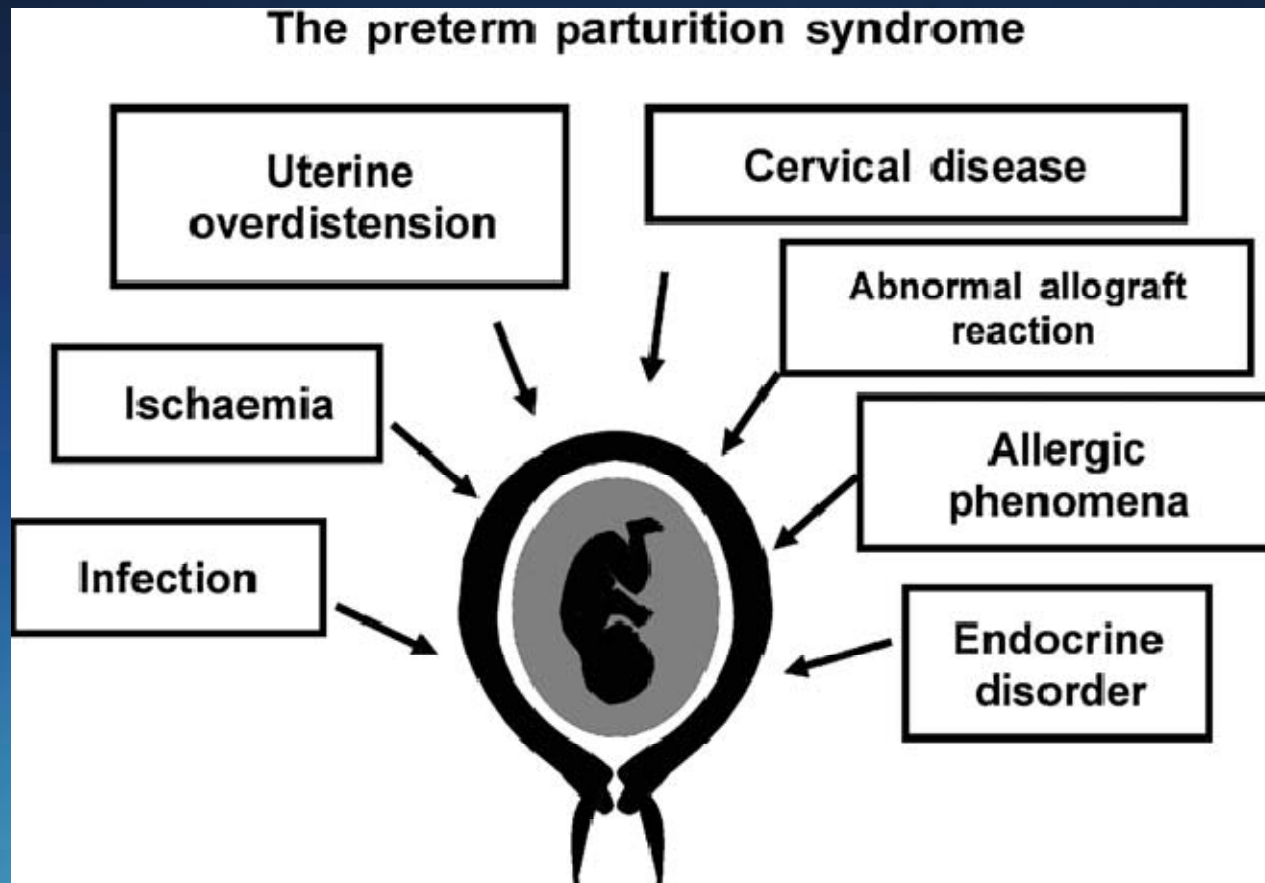
CV Ananth et al, Obstet Gynecol 2005

Epidemiologia



La sindrome del PP

Con **sindrome** si intende, in medicina, un insieme di sintomi e segni clinici [quadro sintomatologico] che può essere dovuto a più malattie o a più eziologie

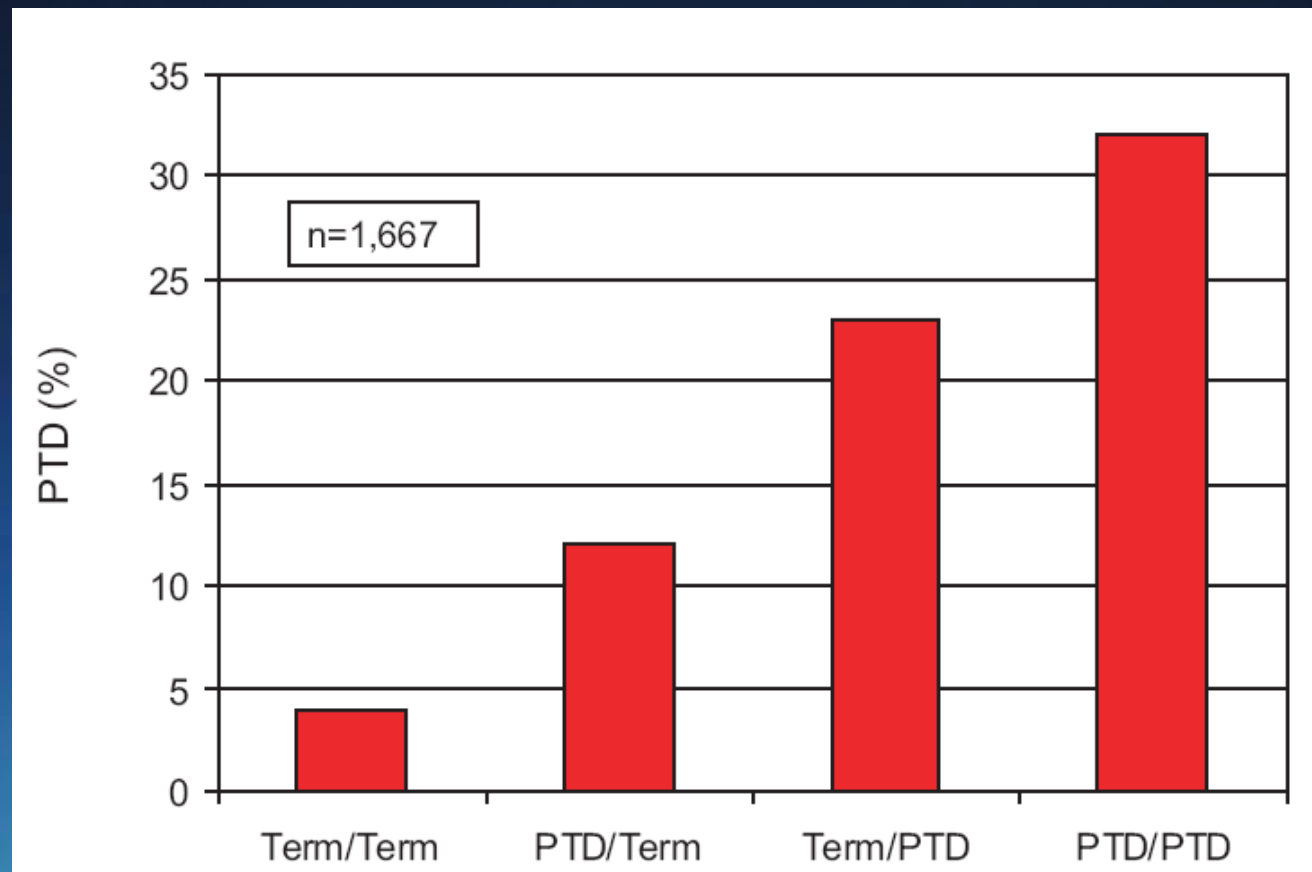


Fattori predittivi: quando?

- Grave – Estrema prematurità $\Leftrightarrow <32$ settimane
 - Elevata mortalità perinatale: inversamente proporzionale all'EG
 - Ogni giorno guadagnato tra 23 e 27 settimane
 - \uparrow sopravvivenza del 3%
 - \downarrow morbilità dal 31% a 23 settimane al 7% a 27

Fattori di Rischio

Precedente Parto Prematuro



C Spong, Obstet Gynecol 2007

Fattori di Rischio

Precedente Parto Prematuro

Gestation at delivery in current pregnancy (wk)	No prior preterm delivery (n = 1301) (%)	Gestation of earliest prior preterm delivery									
		13-22 wk (n = 98)		23-27 wk (n = 59)		28-34 wk (n = 167)		35-36 wk (n = 86)		Any prior preterm delivery (N = 410)	
		%	Relative risk	%	Relative risk	%	Relative risk	%	Relative risk	%	Relative risk
<28	0.23	1.0	4.4	5.1	22.1*	3.0	13.0†	1.2	5.0	2.4	10.6†
<30	0.46	2.0	4.4	5.1	11.0*	3.6	7.8*	1.2	2.5	2.9	6.4†
<32	0.85	3.1	3.6	10.2	12.0†	5.4	6.4†	3.5	4.1	5.1	6.1†
<35	2.5	8.2	3.3*	20.3	8.3†	14.4	5.8†	12.8	5.2†	13.4	5.5†
<37	8.8	15.3	1.7‡	27.1	3.1†	24.0	2.7†	20.9	2.4†	21.7	2.5†

Relative risks are for spontaneous preterm delivery in current gestation compared with risk for gravid women with no prior spontaneous preterm delivery.

* $P < .01$.

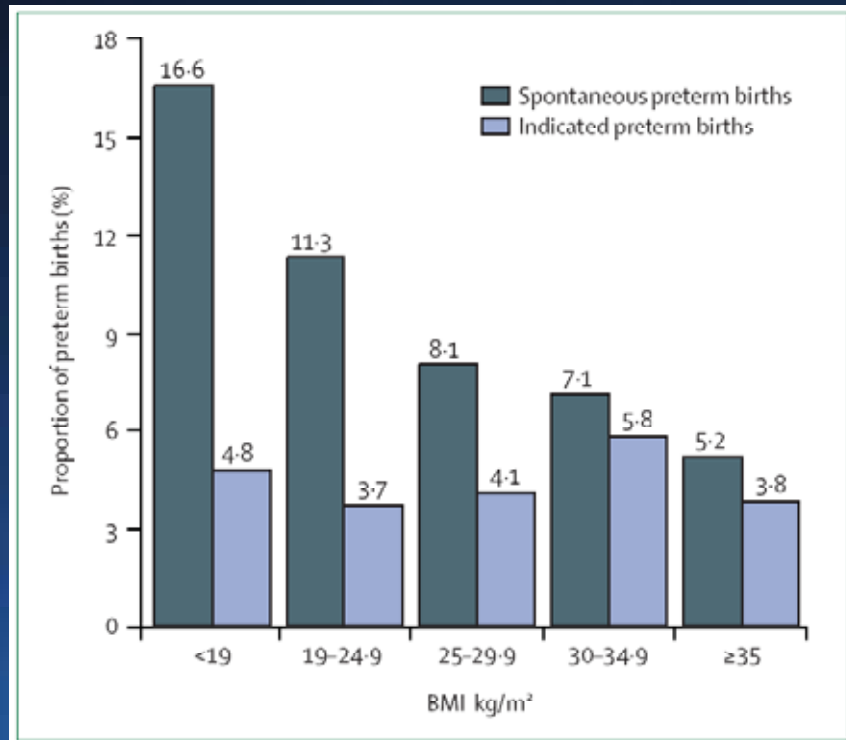
† $P \leq .001$.

‡ $P < .05$.

Fattori di Rischio

Caratteristiche della donna

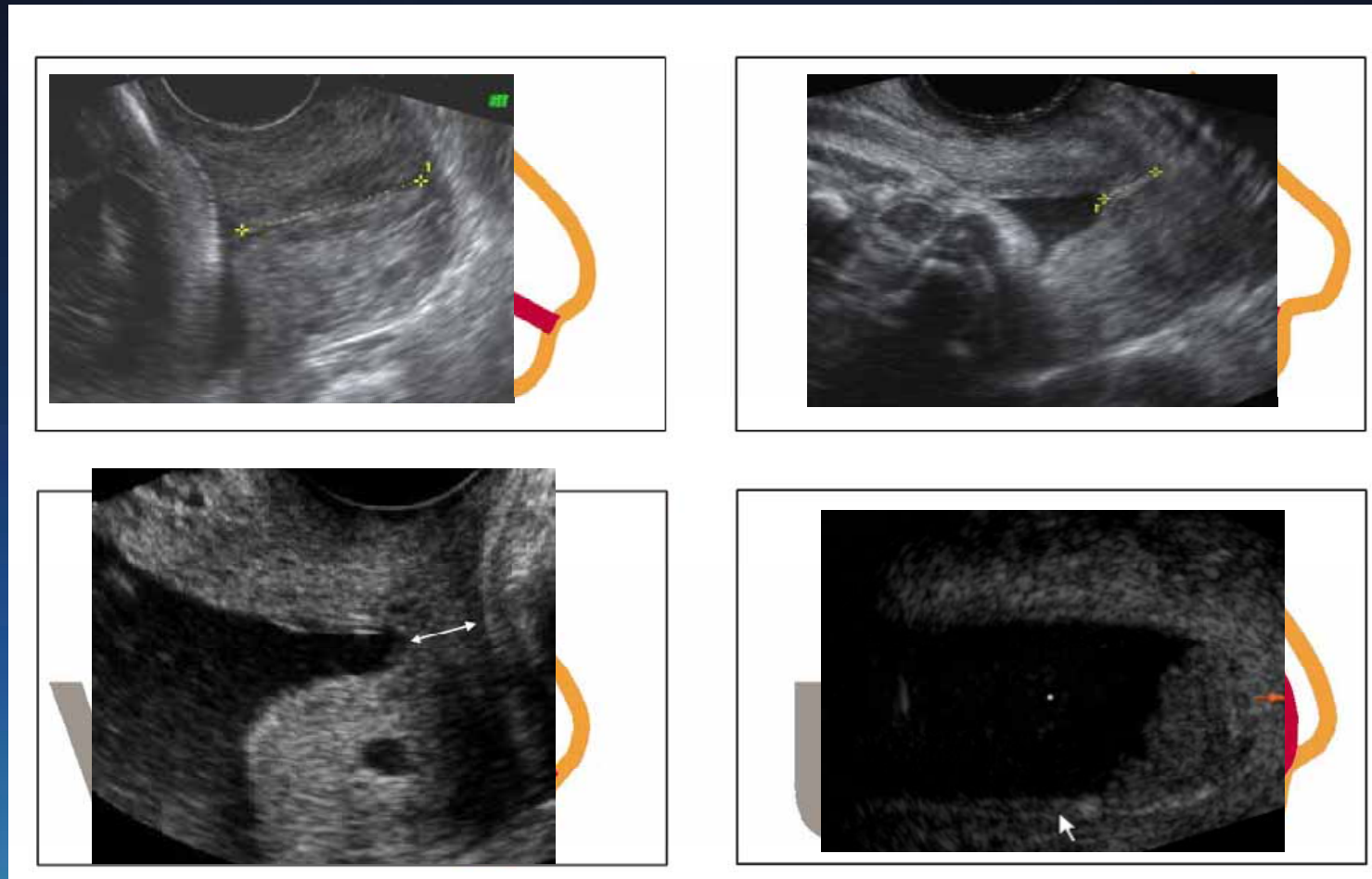
PP & BMI



I Hendler et al, Am J Obstet Gynecol 2005

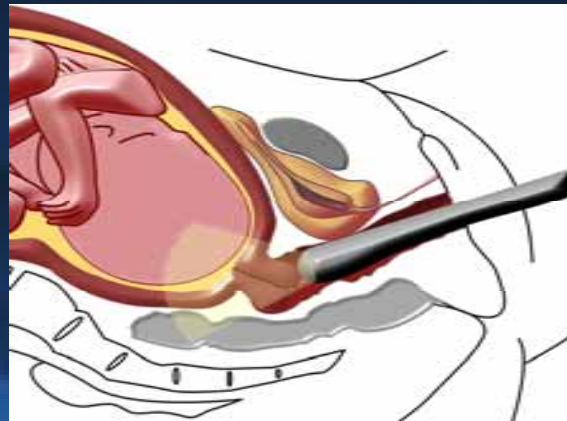
- Età <18>35
- Lavoro faticoso [3.9]
- Stress psico sociale [2.58]
- Stile di vita, fumo, abuso di droga
- Malattia parodontale

Appianamento della cervice

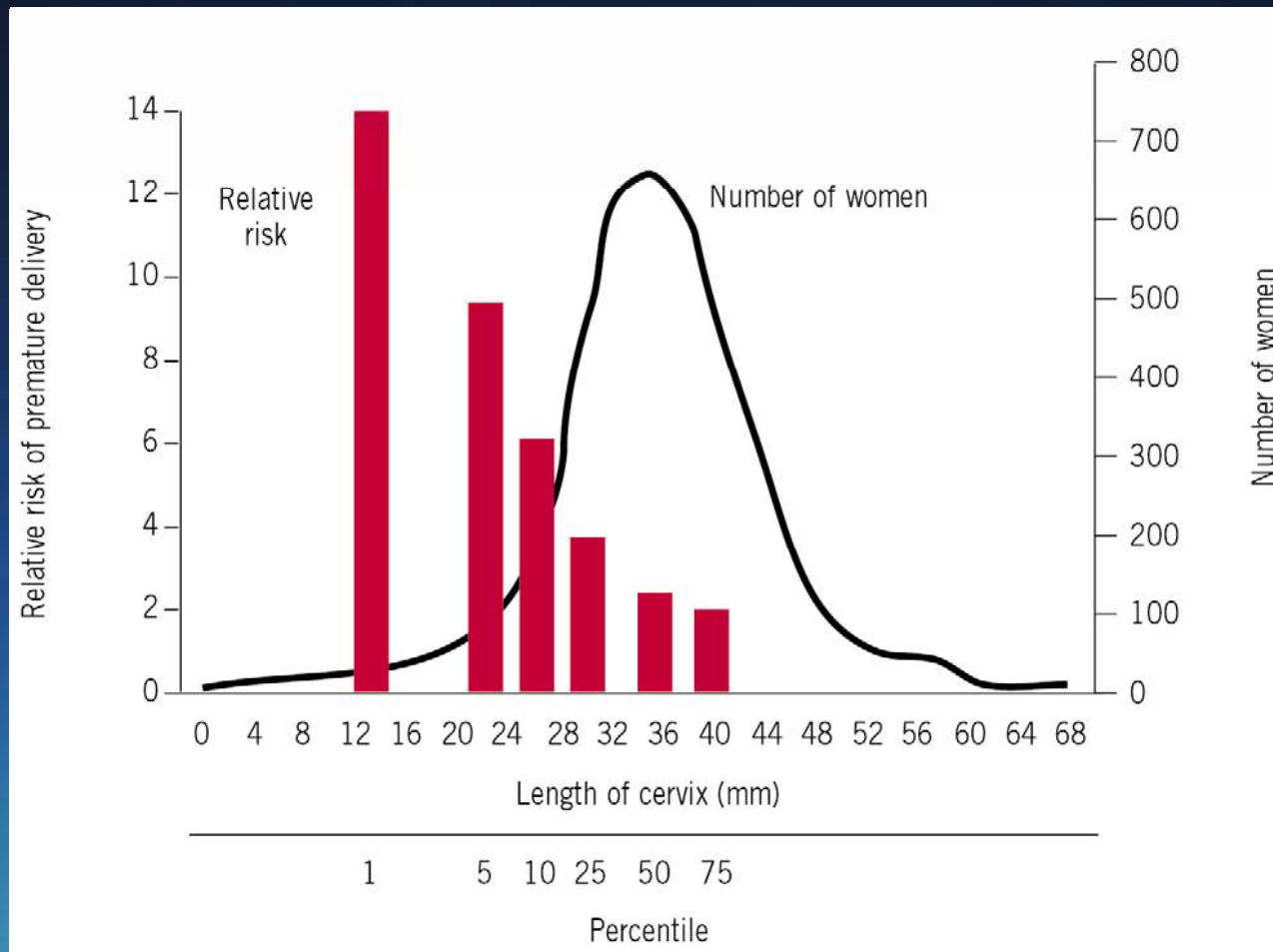


Cervicometria

- Vescica vuota
- Sonda TV nel fornice anteriore
- Sezione sagittale
- NO pressione
- Ingrandimento
- OUI \Rightarrow OUE
- Minore di 3 misure
- Pressione fundica di 15''



Cervicometria 22/24 wks & PP



JD Iams et al, N Engl J Med 1996

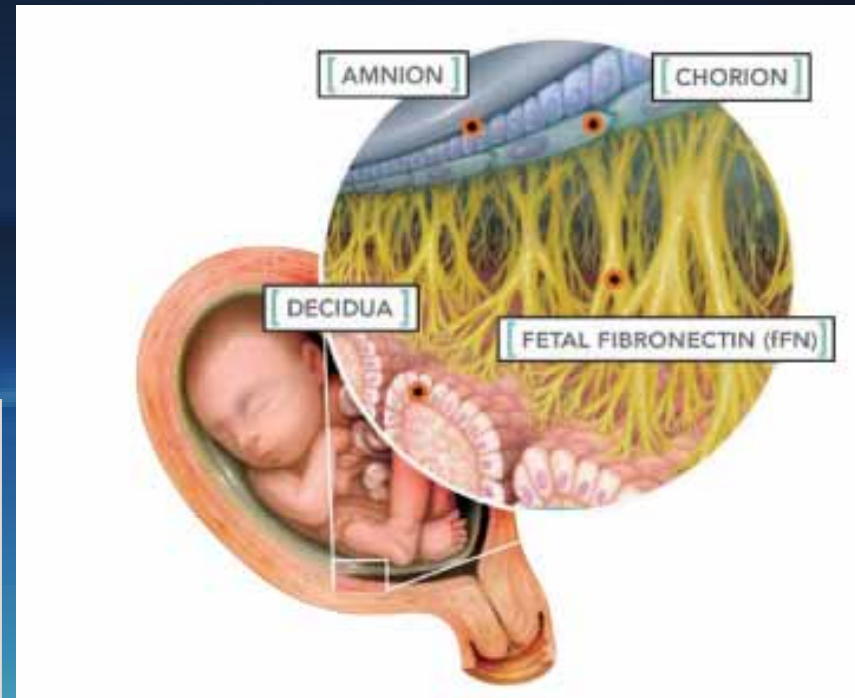
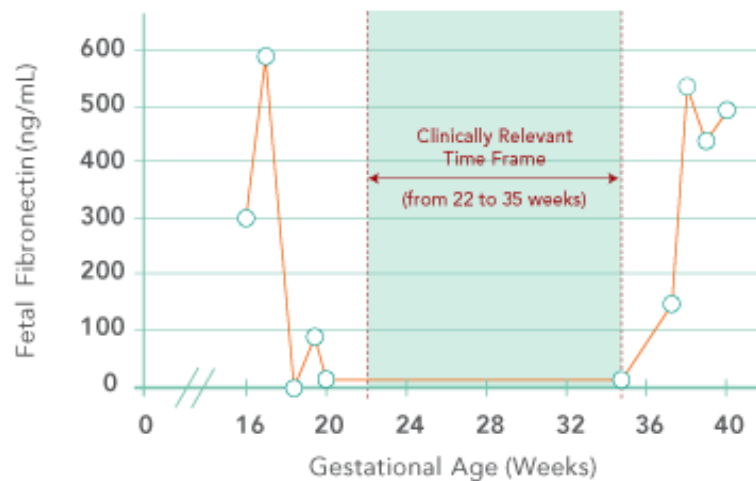
Cervicometria

- Lunghezza cervice
- Lunghezza funnel
- Ampiezza funnel
- % funneling
- Cervical index=
[1+lunghezza funnel]/
lunghezza cervice



Fibronectina

- Glicoproteina
extracellulare ⇒ adesione
tra membrane e parete
uterina

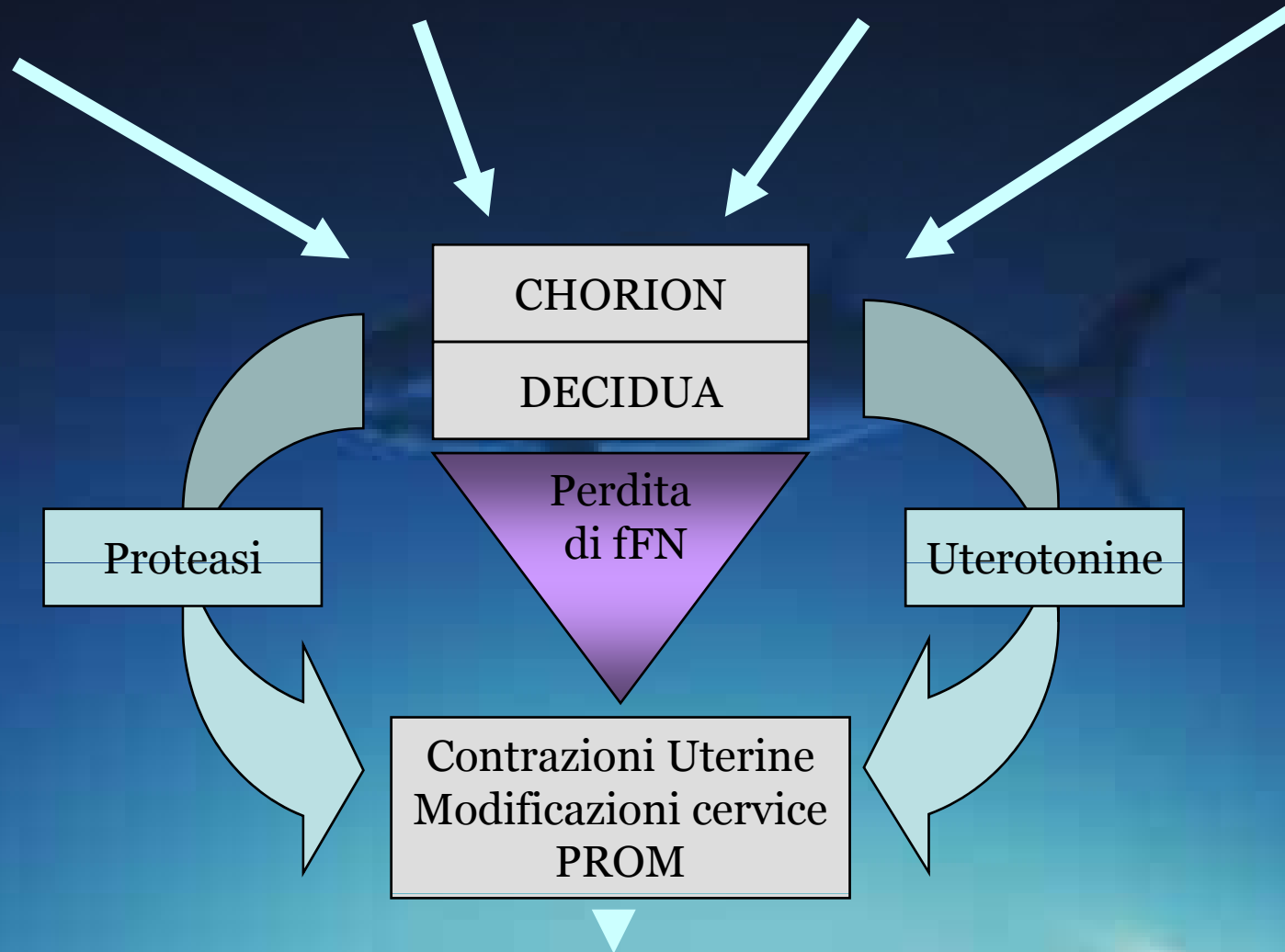


Attivazione asse IIS
Stress MF

Inflammation
Infezione coriondeciduale o
sistemica

Emorragia
deciduale
Distacco

Iperdistensione
uterina
G multifetale
Polidramnios...



PARTO PREMATURO

Fibronectina fetale

Donne asintomatiche

< 34 settimane

< 37 settimane

Donne sintomatiche

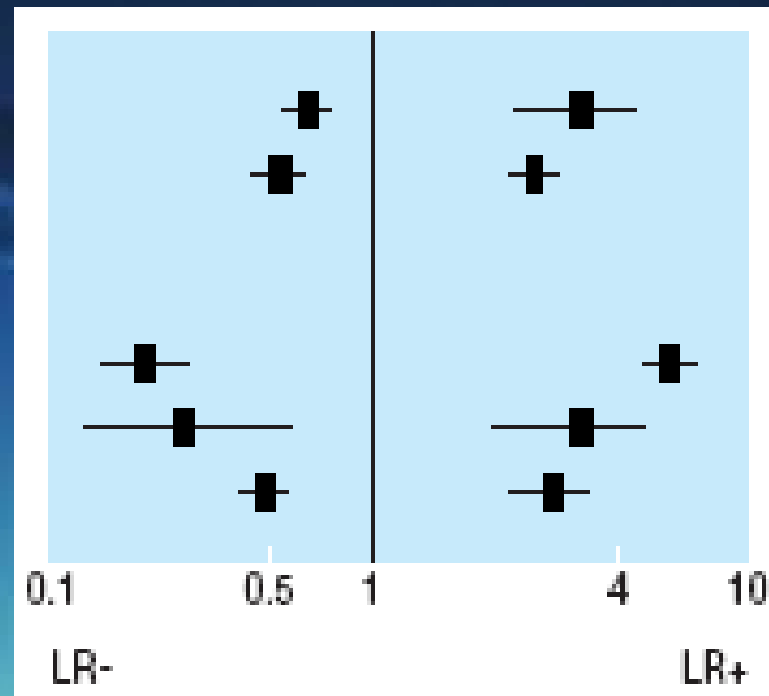
7-10 gg

< 34 settimane

< 37 settimane

Test Negativo

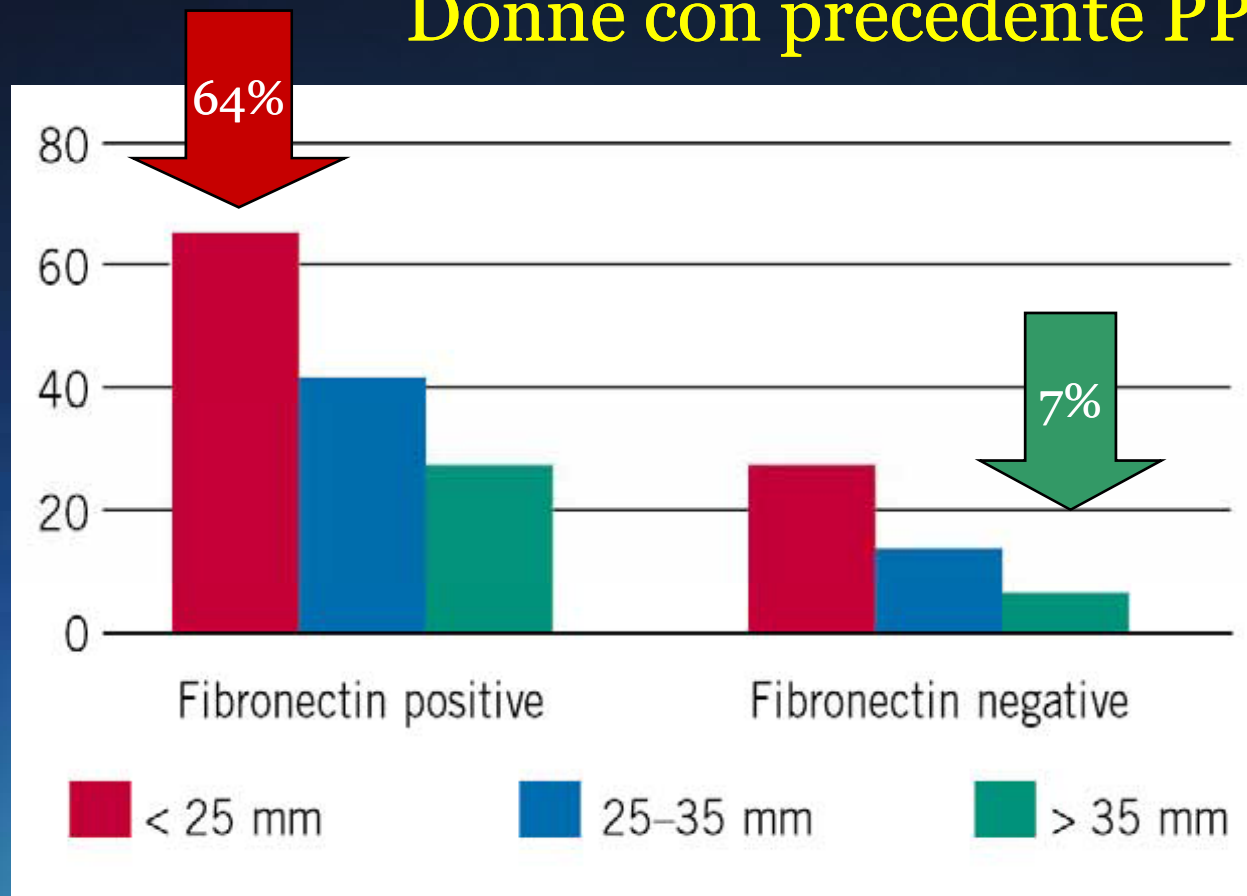
Test Positivo



H Honest et al, BMJ 2002

Cervicometria e Fibronectina

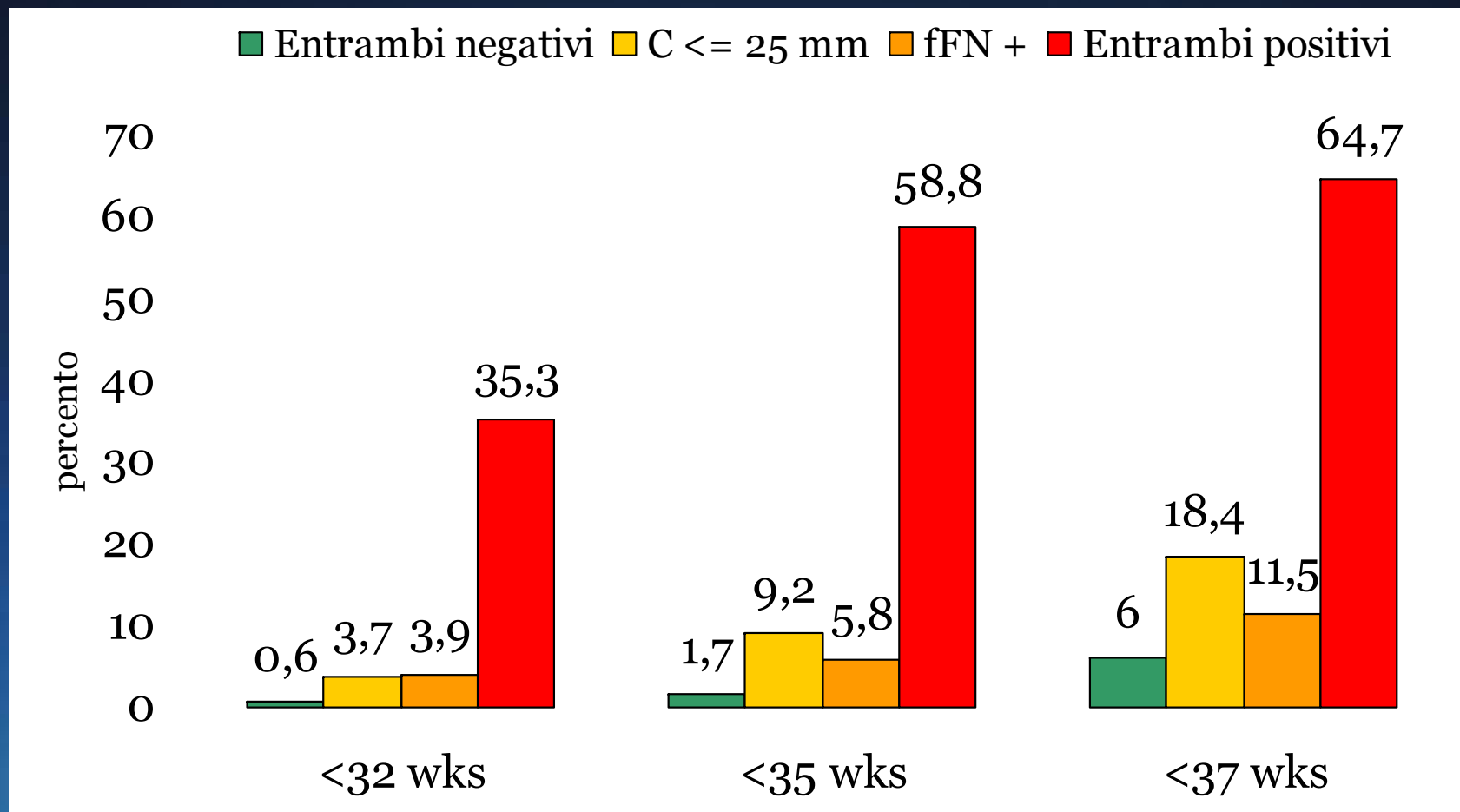
Donne con precedente PP



JD Iams et al, Am J Obstet Gynecol 1998

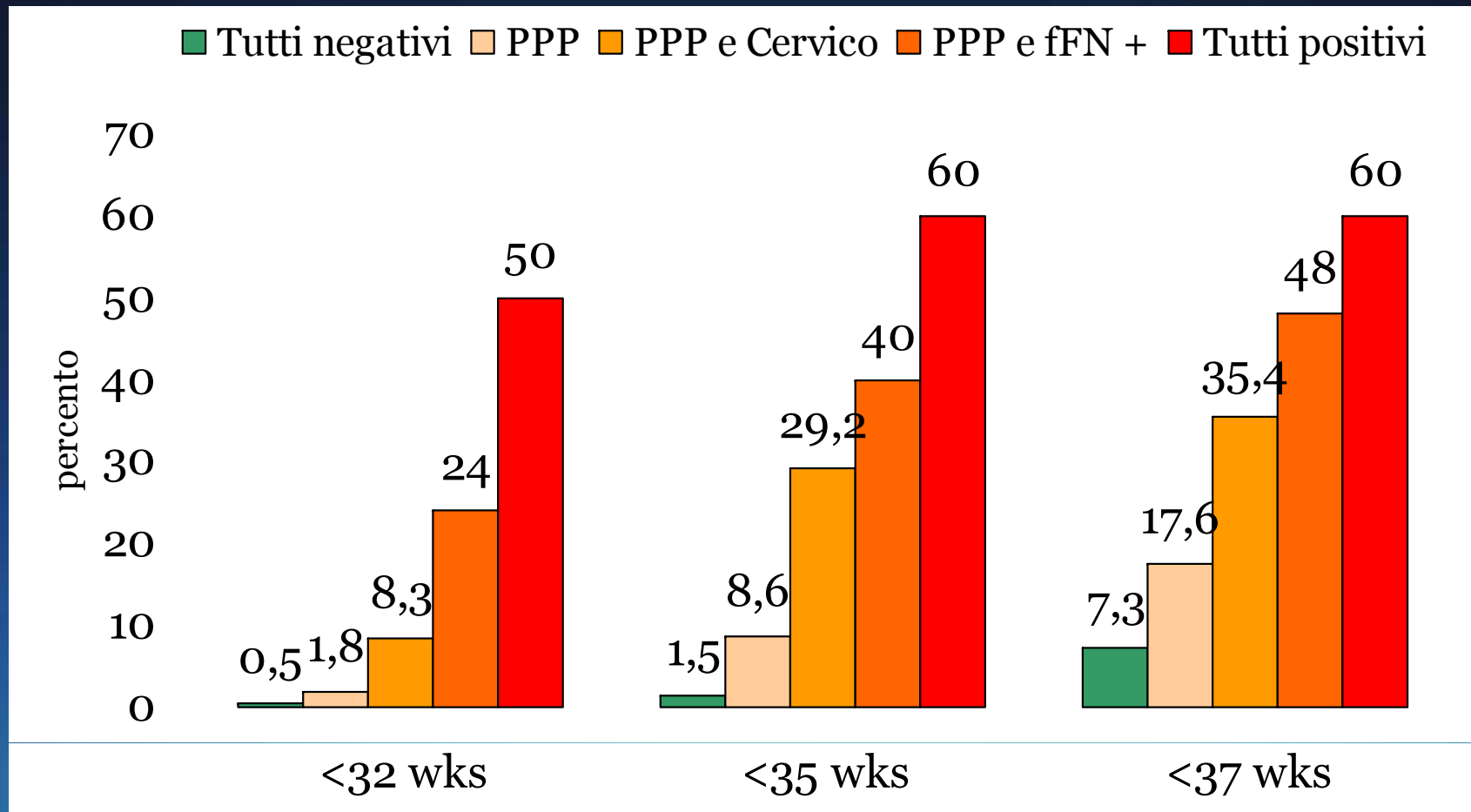
Cervicometria e Fibronectina

Donne nullipare



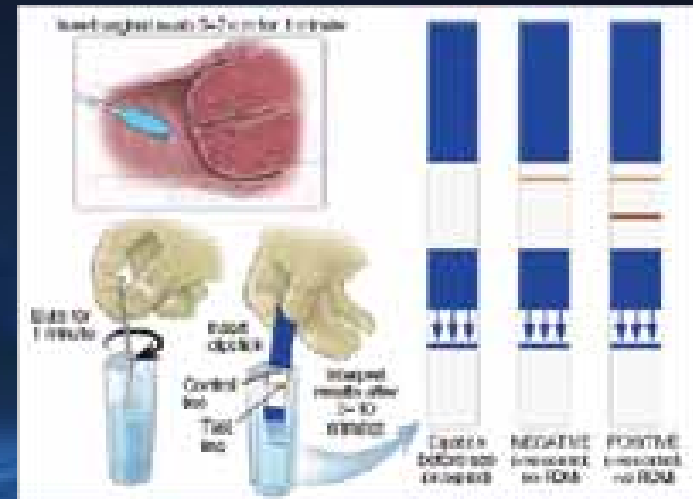
Cervicometria, fFN & PP

Donne multipare



Cervicometria vs fFN

- Costosa
- Non affidabile se:
 - Visita <24 ore
 - Gel, sapone, disinfettanti, creme
 - Rapporto sessuale <24 ore
 - P previa o sanguinamento
- Non costosa
- Semplice
- Non criteri di esclusione
- Migliora la predittività di fFN



Altri predittori

PP <32 settimane

Factor	Source of Data or Fluid	Test Cutoff	n = 48 Cases % Positive	n = 48 Controls % Positive	OR Cases v Controls	Significant (P < .05)
Corticotropin releasing factor	Serum	90 th %ile	10.6	4.3	2.7	No
Alpha fetoprotein	Serum	90 th %ile	36.1	6.4	8.3	Yes
Alkaline Phosphatase	Serum	90 th %ile	22.9	4.2	6.8	Yes
Beta ₂ -macroglobulin	Serum	90 th %ile	6.3	2.1	3.1	No
Ferritin	Serum	90 th %ile	14.6	2.1	8.0	No
Interstitial cell adhesion molecule-1	Serum	90 th %ile	23.4	6.4	4.5	Yes
Interleukin-6	Serum	90 th %ile	10.4	8.3	1.3	No
C-reactive protein	Serum	90 th %ile	10.4	6.3	1.7	No
Cortisol	Serum	90 th %ile	10.4	2.1	5.5	No
Lactoferrin	Serum	90 th %ile	11.6	9.3	1.3	No
Defensins	Serum	90 th %ile	20.9	4.7	5.4	Yes
Relaxin	Serum	90 th %ile	10.9	10.9	1.0	No
Interleukin-10	Serum	90 th %ile	6.4	12.8	0.5	No
Granulocyte colony stimulating factor	Serum	90 th %ile	8.5	10.6	0.8	No
Activan	Serum	Pos	8.5	10.6	0.8	No
Interleukin-6	Cervix	90 th %ile	20.4	6.1	3.9	Yes
Lactoferrin	Cervix	90 th %ile	4.3	0.0	Inf	No
Defensins	Cervix	90 th %ile	10.5	18.4	0.5	No
Sialidase	Cervix	90 th %ile	8.2	6.1	1.4	No
Short cervix	Ultrasound	<25mm	44.9	12.2	5.8	Yes
Fetal fibronectin	Cervix/Vagina	≥50 ng/mL	40.0	2.0	32.7	Yes
Gram stain score	Vagina	≥9	30.0	24.0	1.4	No
PH	Vagina	≥5.0	42.9	18.4	3.3	Yes
Chlamydia	Vagina	Pos	15.2	6.5	2.6	No
Previous SPTB	History	Pos	42.0	14.0	4.5	Yes
Contractions	History	Pos	24.0	32.0	0.7	No
Bleeding	History	Pos	36.0	24.0	1.8	No
Body mass index	Measured	<19.8	29.2	14.6	2.4	No

PP <35 settimane

Factor	Source of Data or Fluid	Test Cutoff	n = 107 % Positive Cases	n = 107 % Positive Controls	OR Cases V Controls	Significant (P < .05)
Corticotropin releasing factor	Serum	90 th %ile	11.7	8.3	1.5	No
Alpha fetoprotein	Serum	90 th %ile	35.3	13.5	3.5	Yes
Alkaline phosphatase	Serum	90 th %ile	14.9	3.3	5.1	Yes
Beta ₂ -macroglobulin	Serum	90 th %ile	5.1	6.8	0.7	No
Ferritin	Serum	90 th %ile	9.9	7.4	1.4	No
Interstitial cell adhesion molecule-1	Serum	90 th %ile	16.4	9.1	2.0	No
Interleukin-6	Serum	90 th %ile	10.0	9.2	1.1	No
C-reactive protein	Serum	90 th %ile	8.3	6.7	1.3	No
Cortisol	Serum	90 th %ile	12.6	7.6	1.8	No
Lactoferrin	Serum	90 th %ile	8.8	11.4	0.8	No
Defensins	Serum	90 th %ile	18.4	10.5	1.9	No
Relaxin	Serum	90 th %ile	13.6	8.2	1.8	No
Interleukin-10	Serum	90 th %ile	4.3	10.3	0.4	No
Granulocyte colony stimulating factor	Serum	90 th %ile	7.7	7.7	1.0	No
Activan	Serum	Pos	14.2	11.7	1.3	No
Interleukin-6	Cervix	90 th %ile	20.0	9.6	2.4	No
Lactoferrin	Cervix	90 th %ile	5.0	0.0	Inf	Yes
Defensins	Cervix	90 th %ile	16.7	10.0	1.8	No
Sialidase	Cervix	90 th %ile	9.6	9.6	1.0	No
Short cervix	Ultrasound	≤25 mm	36.8	9.6	5.5	Yes
Fetal fibronectin	Cervix/vagina	≥50 ng/mL	22.8	3.2	9.1	Yes
Gram stain score	Vagina	≥9	22.8	15.0	1.7	No
PH	Vagina	>5	38.1	21.4	2.3	Yes
Chlamydia	Vagina	Pos	12.8	5.1	2.7	Yes
Previous SPB	History	Pos	43.3	15.0	4.3	Yes
Contractions	History	Pos	31.5	31.5	1.0	No
Bleeding	History	Pos	35.4	20.5	2.1	Yes
Body mass index	Measured	<19.8	30.9	17.9	2.1	Yes

RL Goldenberg et al, Semin Perinatol 2003

Markers biochimici

Infezione endouterina in donne asintomatiche

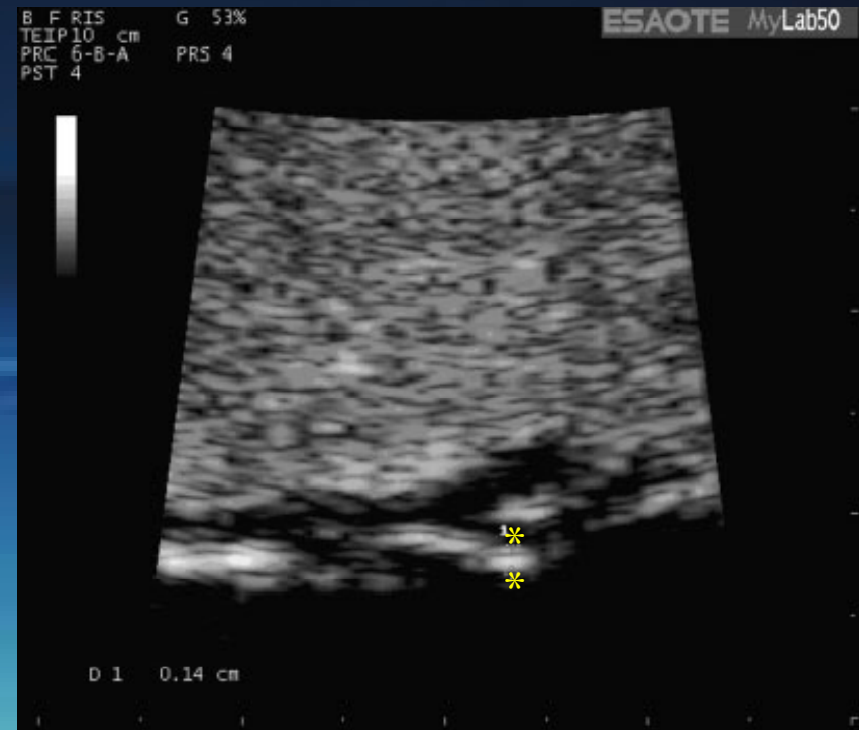
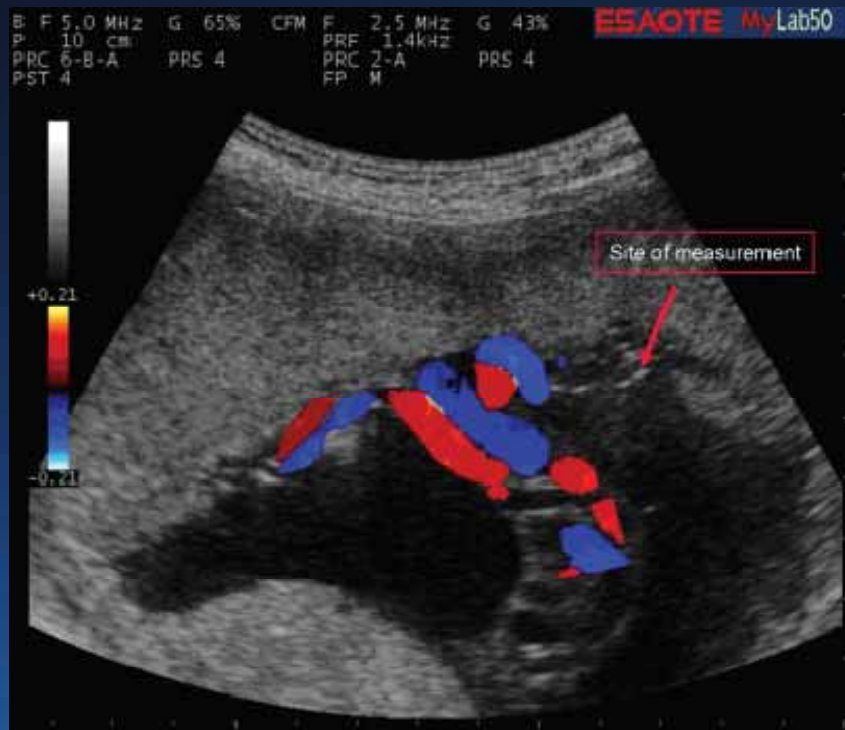
Infection site	Marker
Amniotic fluid	High IL-6 level
Cervix or vagina	Bacterial vaginosis High IL-6 level High ferritin level High fetal fibronectin level High α -fetoprotein level High human chorionic gonadotropin High prolactin level
Serum	High C-terminal propeptide of procollagen High G-CSF High ferritin level Defensins

Infezione endouterina in donne in travaglio

Infection site	Marker
Amniotic fluid	Bacteria Low glucose level High white blood cell count High G-CSF High IL-1 level High IL-6 level
Cervix or vagina	Bacterial vaginosis High G-CSF High tumor necrosis factor- α level High IL-1 level High IL-6 level High IL-8 level High fetal fibronectin level
Serum	High G-CSF High IL-6 level High tumor necrosis factor- α level High C-reactive protein level

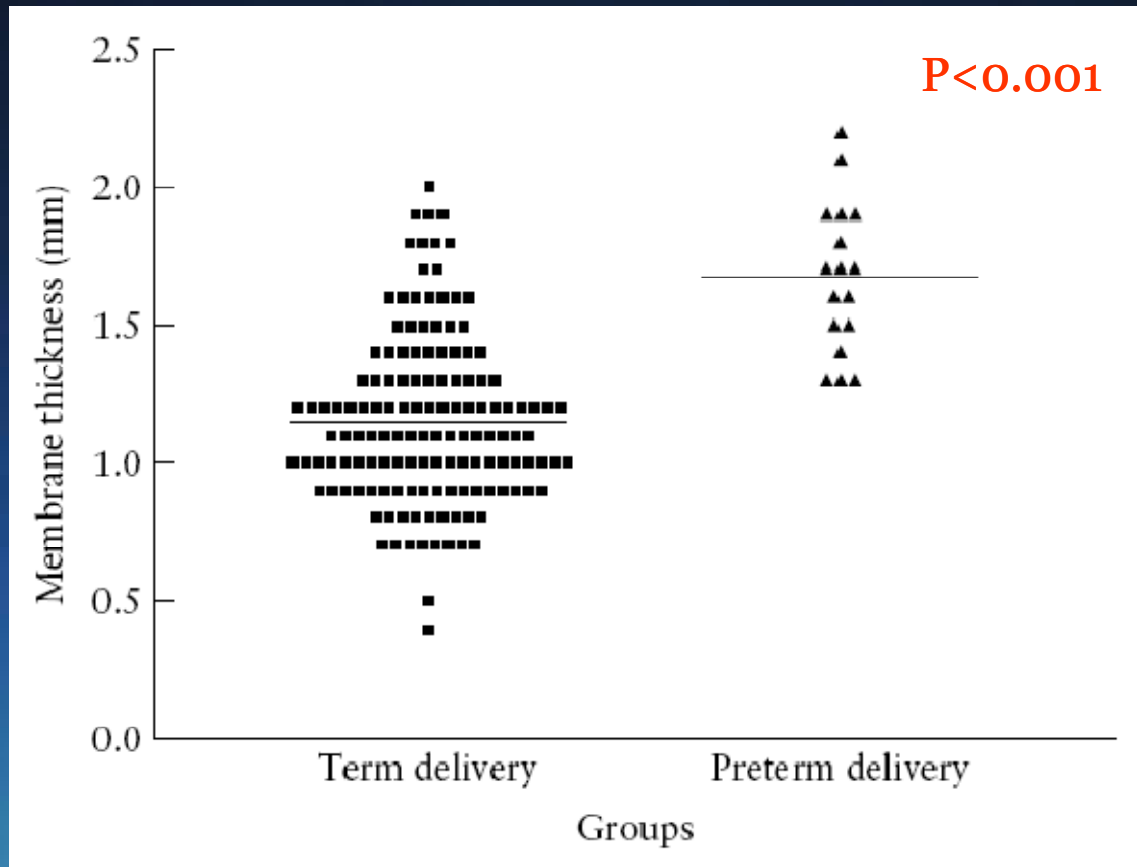
RL Goldenberg et al, Am J Obstet Gynecol 2005

Spessore delle membrane



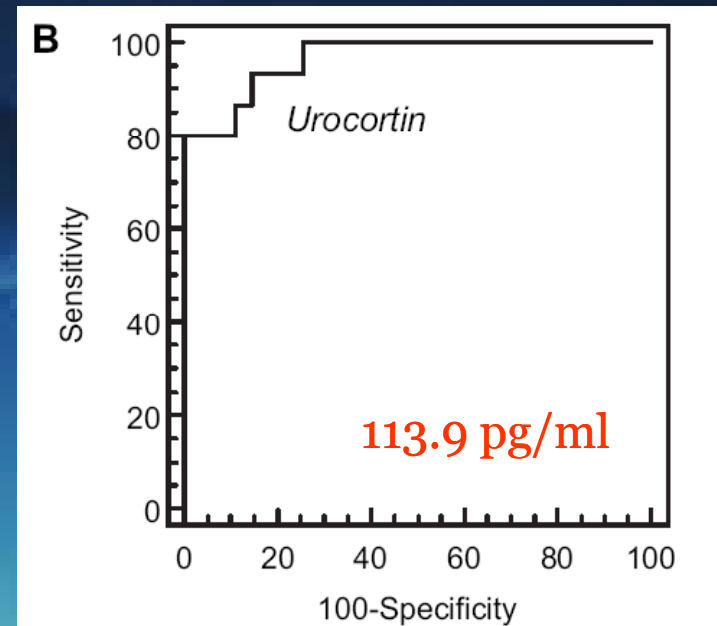
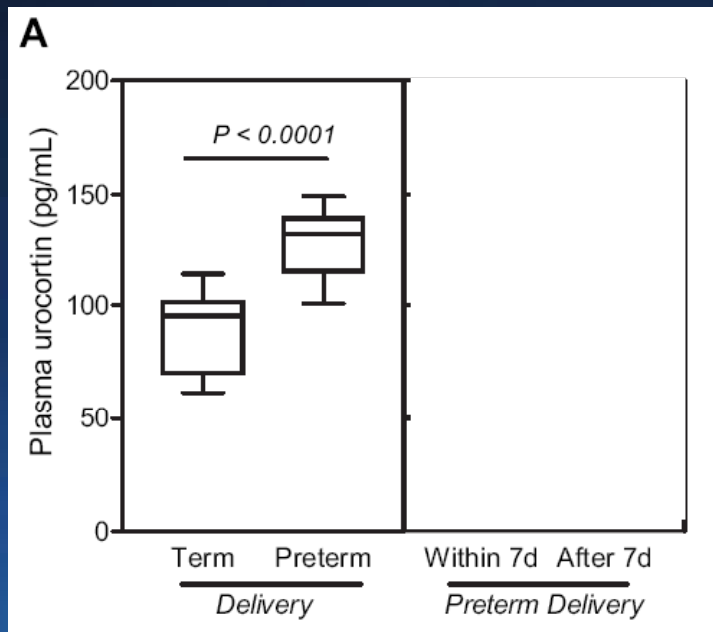
FM Severi et al, Ultrasound Obstet Gynecol 2008

Spessore delle membrane



FM Severi et al, Ultrasound Obstet Gynecol 2008

Urocortina materna



P Florio et al, J Clin Endocrinol Metab 2007

One size fits all?

- Vero vs falso travaglio
- Cervicometria \pm Fibronectina per fare e “graduare” nel tempo la diagnosi
- PP idiopatico? Ma abbiamo cercato ed escluso tutte le possibili cause??
- Il 50% delle diagnosi non sono corrette \Rightarrow il 50% delle diagnosi di travaglio prematuro non finisce con un parto prematuro

Concludendo

- Test biochimici:
 - Per capire il meccanismo fisiopatologico che ha portato al PP?
 - Per identificare la popolazione ad alto rischio per studi di intervento?
 - Per selezionare una popolazione in cui utilizzare uno specifico intervento?
 - Per selezionare una popolazione a basso rischio per evitare un intervento?

A photograph of a sailboat on the water. A woman in a white outfit and cap is sitting on the deck, and a man in a white shirt is at the helm. The boat is moving, creating a wake in the blue water. A large, semi-transparent text box is overlaid on the image, containing a quote in blue font. The quote reads: "We cannot change the wind, but we can adjust our sails" followed by "Anonymous" on a new line.

We cannot change the
wind, but we can
adjust our sails
Anonymous