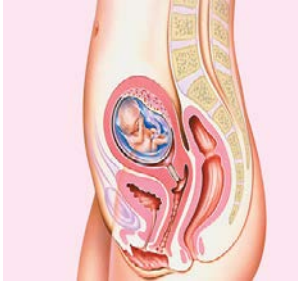
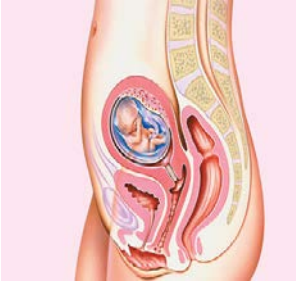


POCT testen
Ikv preterme bevalling

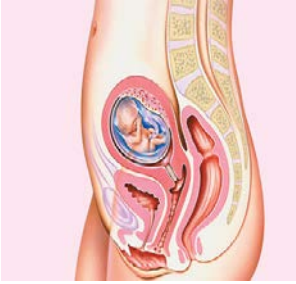
Dr. Bram Ngo
ASO klinische biologie

Inhoud



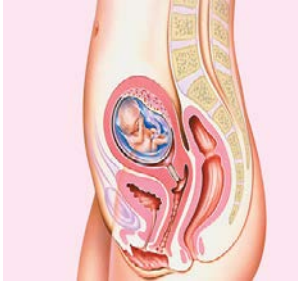
- Vraagstelling
- Definities
- Potentiële merkers
- Prestatiekenmerken/literatuur
- Besluiten

Inhoud



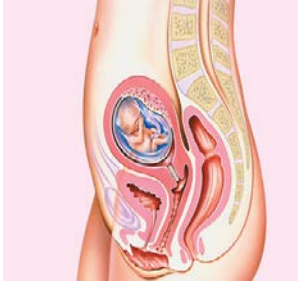
- Vraagstelling
- Definities
- Potentiële merkers
- Prestatiekenmerken/literatuur
- Besluiten

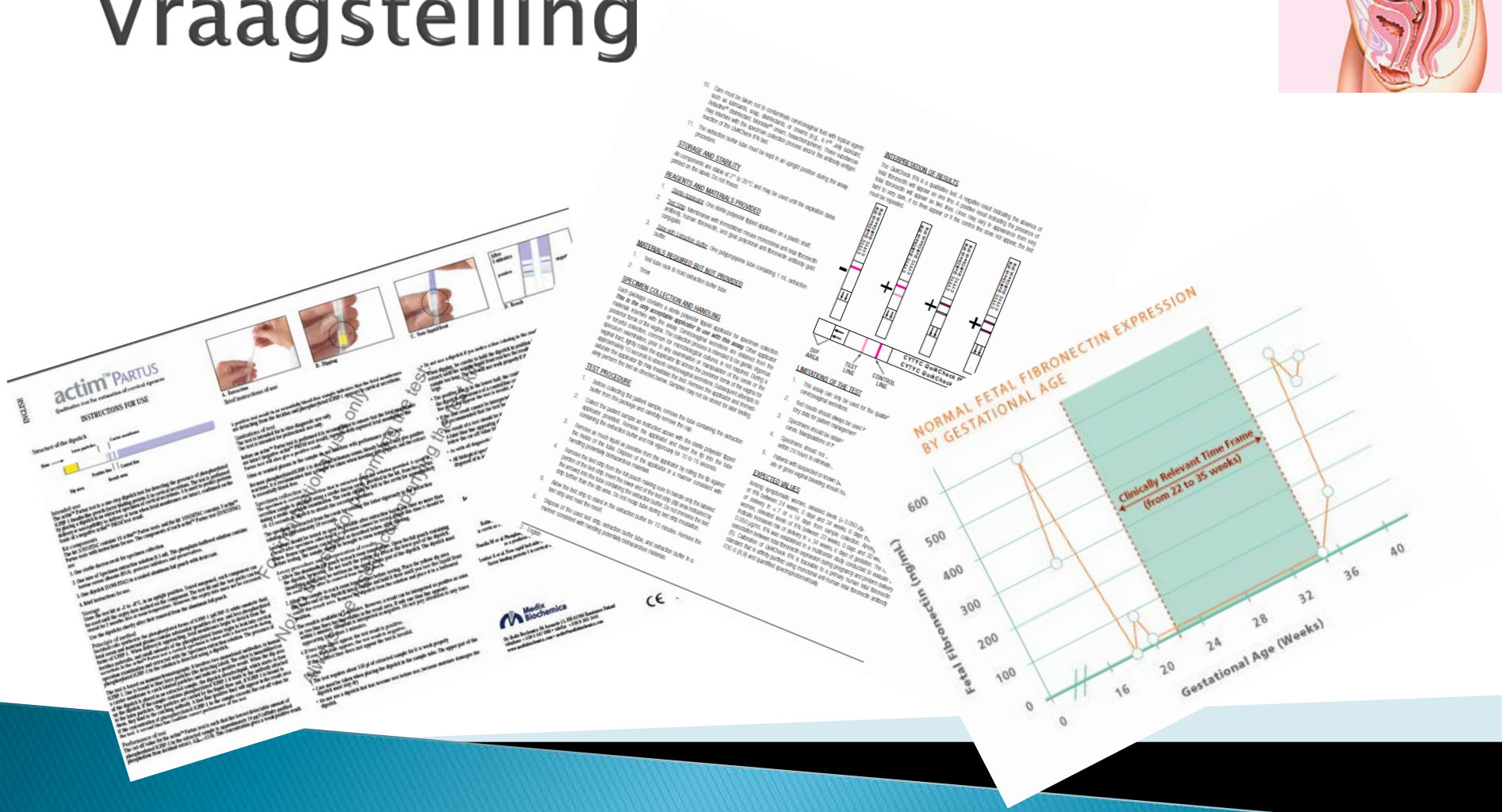
Vraagstelling



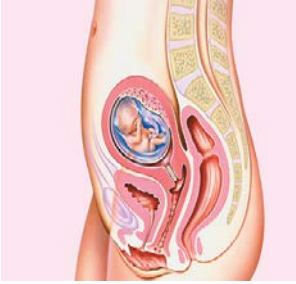
- Bepaling van een biochemische merker voor de voorspelling van een preterme geboorte

Vraagstelling



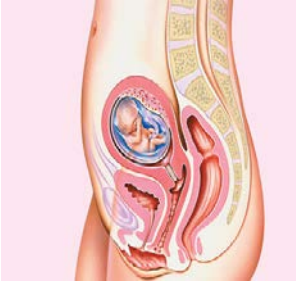


Vraagstelling



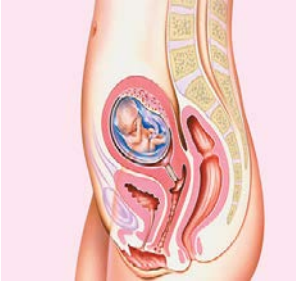
- Bepaling van een biochemische merker voor de voorspelling van een preterme geboorte

Inhoud



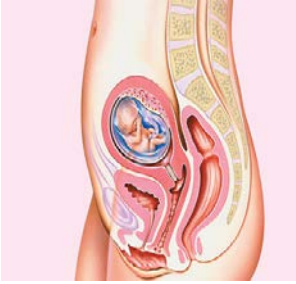
- Vraagstelling
- Definities
- Potentiële merkers
- Prestatiekenmerken/literatuur
- Besluiten

Preterme geboorte



- Geboorte voor 37 weken zwangerschap
- +/- 10% van alle zwangerschappen
- (ernstige) complicaties
  - !!! < 34 weken
- Uitstellen van bevalling

Nood aan merker ???



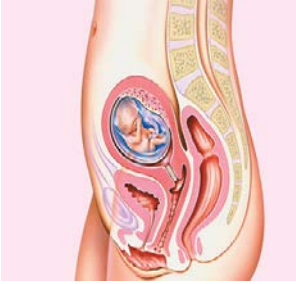
- Symptomen
  - Regelmatige, aanhoudende premature contracties

    ! Slechts ¼ zal binnen 48h bevallen

- Biofysische gegevens
  - Kans op preterme bevalling ~ 1/cervixlengte

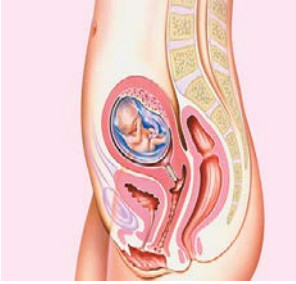
- R/ bedrust, opname, corticosteroïden, tocolytica

Inhoud



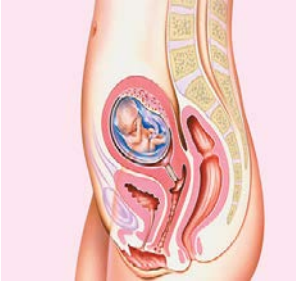
- Vraagstelling
- Definities
- Potentiële merkers
- Prestatiekenmerken/literatuur
- Besluiten

Potentiële merkers

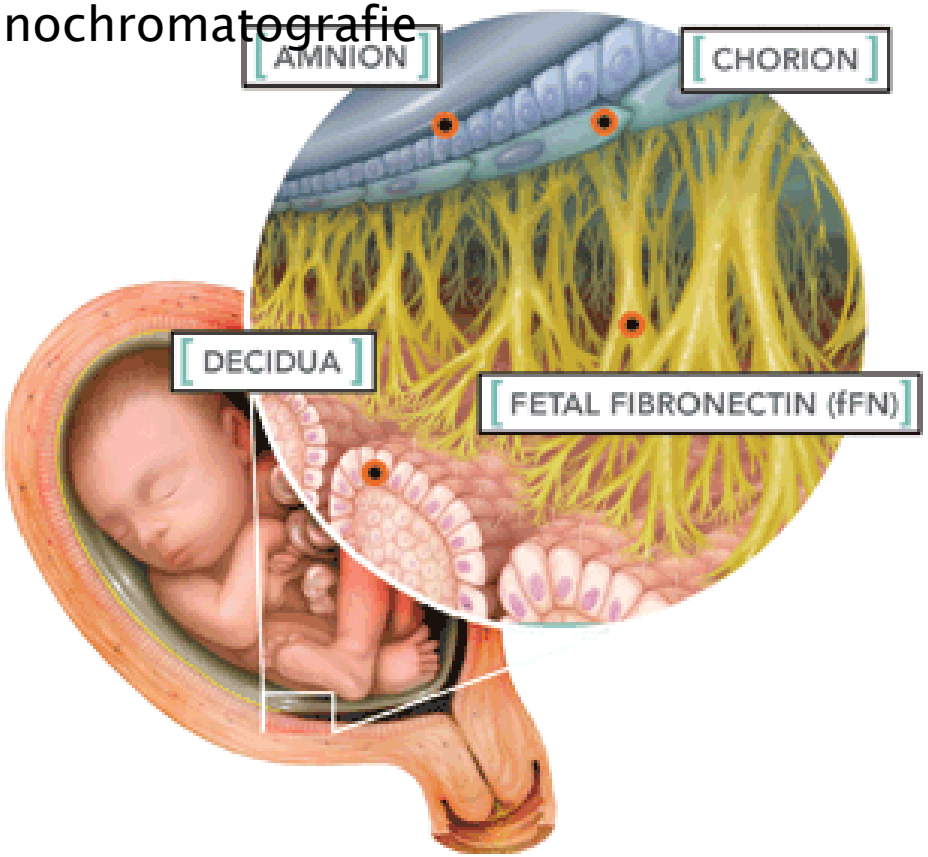


- Biofysisch
  - Contracties
  - Cervixlengte
- Biochemisch
  - Prolactine (cervicovaginaal)
  - fFN (cervicovaginaal)
  - hCG (cervicovanginaal)
  - phIGFBP-1 (cervicovaginaal)
  - IL-6 (amnionvocht)
  - CRP (serum)
  - Matrix metalloprotease-9 (serum)

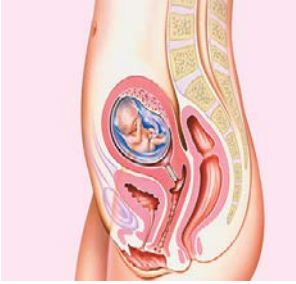
Potentiële merkers

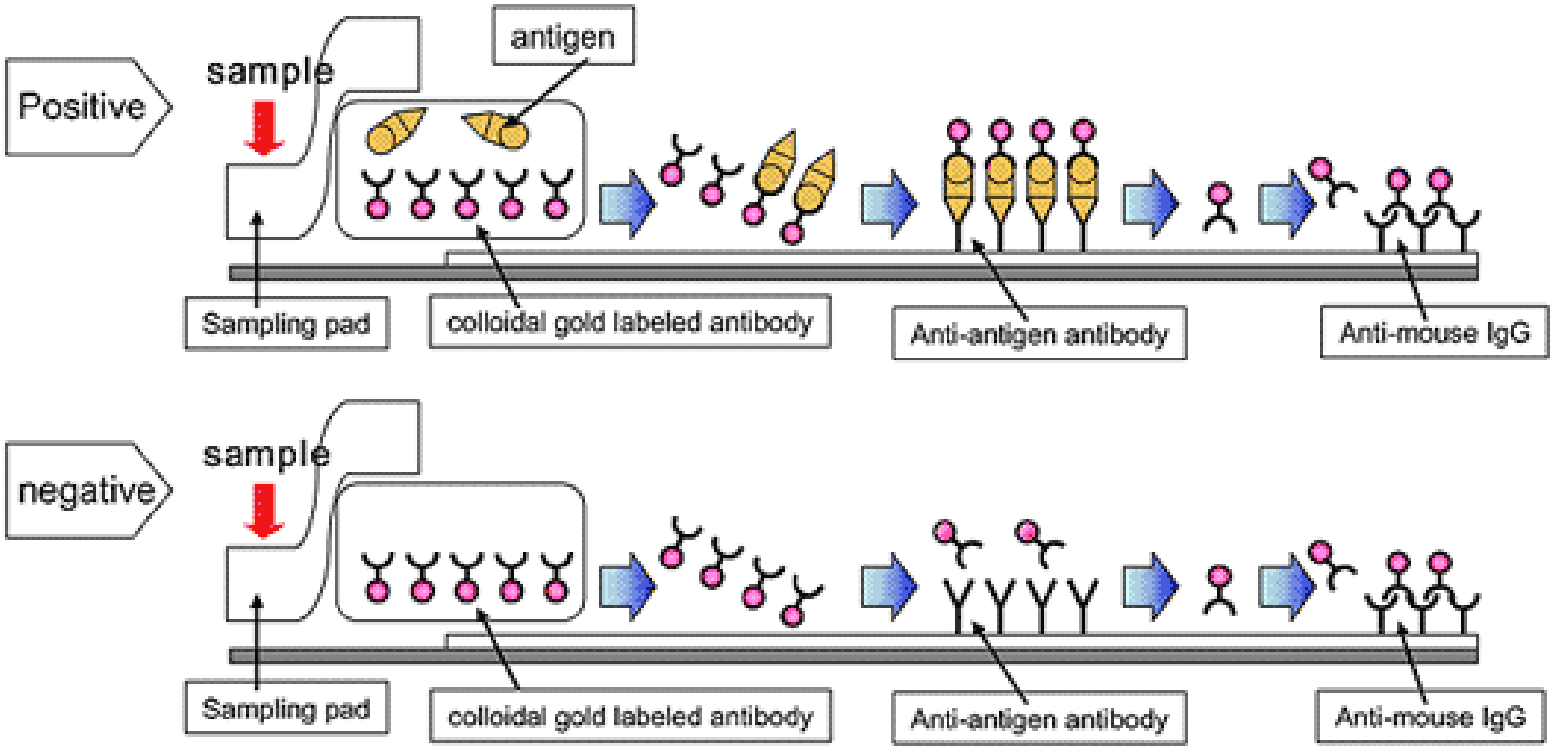


- fFN
  - Amnionvocht, placentale weefsel, decidua basalis
  - Lijm: rol implantatie + placenta-uteriene hechting
  - Detectie: vaste-fase immunochromatografie

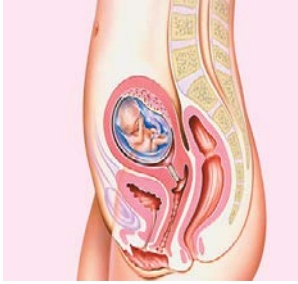


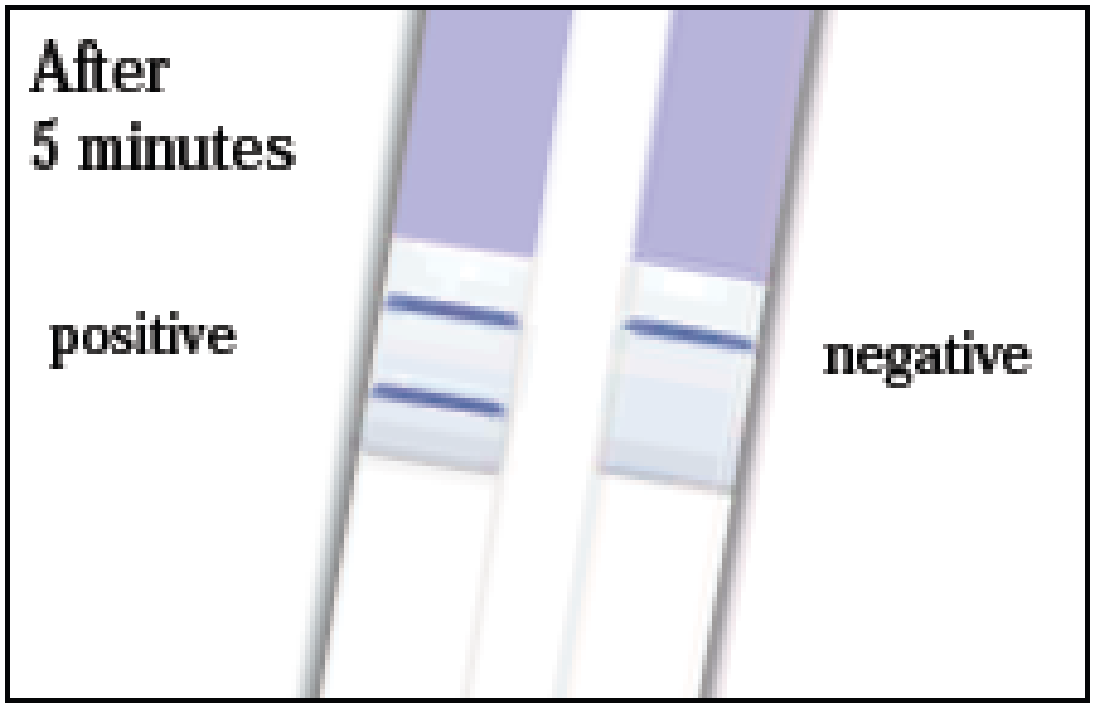
Potentiële merkers



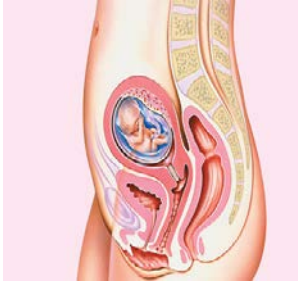


Potentiële merkers

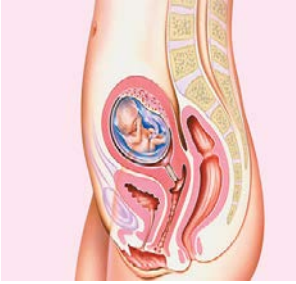




Potentiële merkers

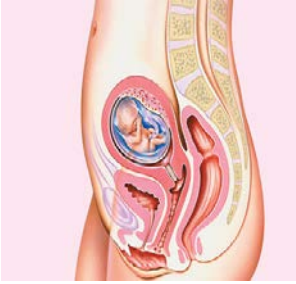


Potentiële merkers



- phIGFBP-1
  - Amnionvocht, decidua basalis
  - Rol in foetale + placentale groei
  - Graad van fosforylatie afhankelijk van herkomst
  - Detectie: vaste-fase immunochromatografie

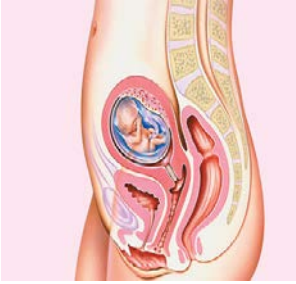
Potentiële merkers



HYPOTHESE:

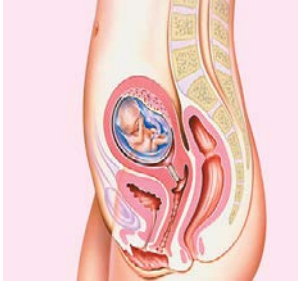
Vrijkomen van de merker in cervicovaginaal secreet door mechanische of inflammatoir gemediëerde schade

Inhoud

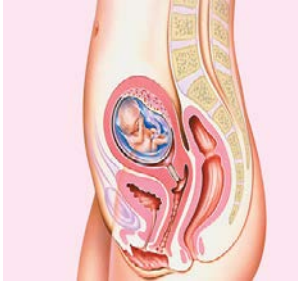


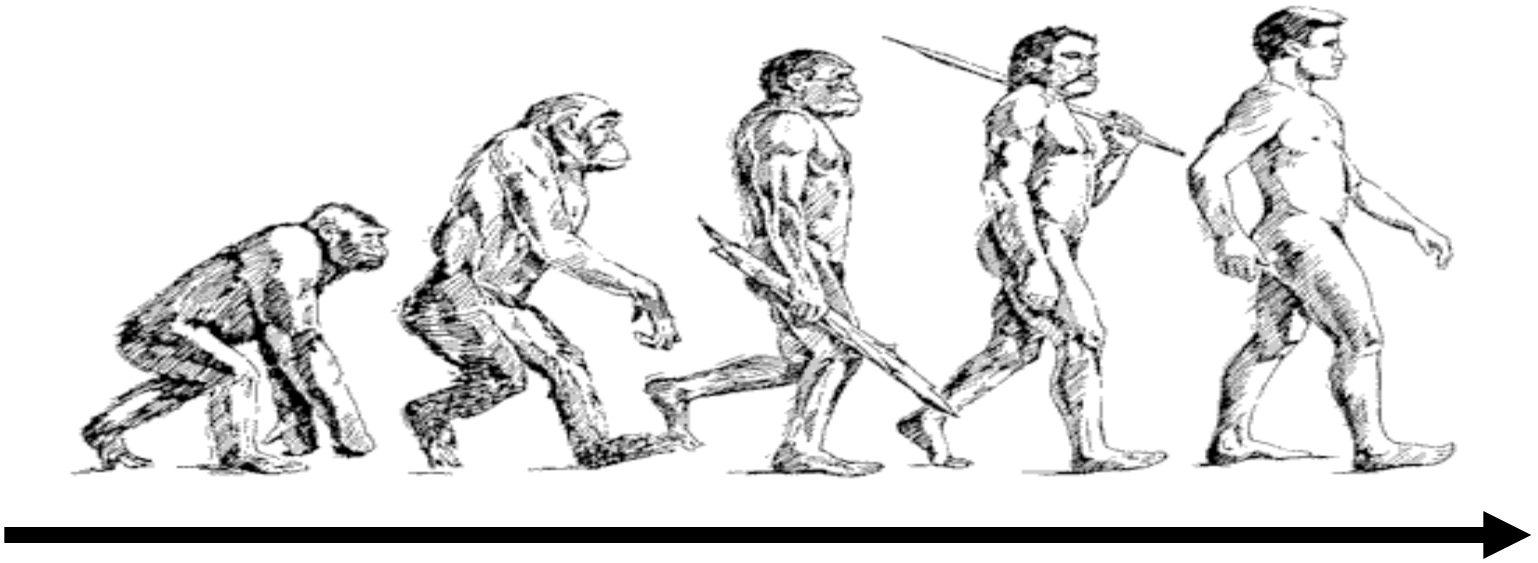
- Vraagstelling
- Definities
- Potentiële merkers
- Prestatiekenmerken/literatuur
- Besluiten

Prestatiekenmerken/literatuur

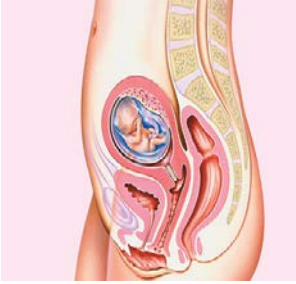


Prestatiekenmerken/literatuur





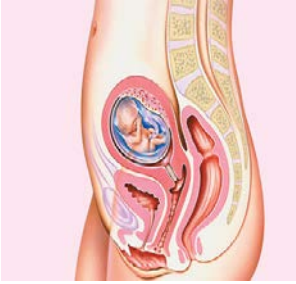
Prestatiekenmerken/literatuur



fFN

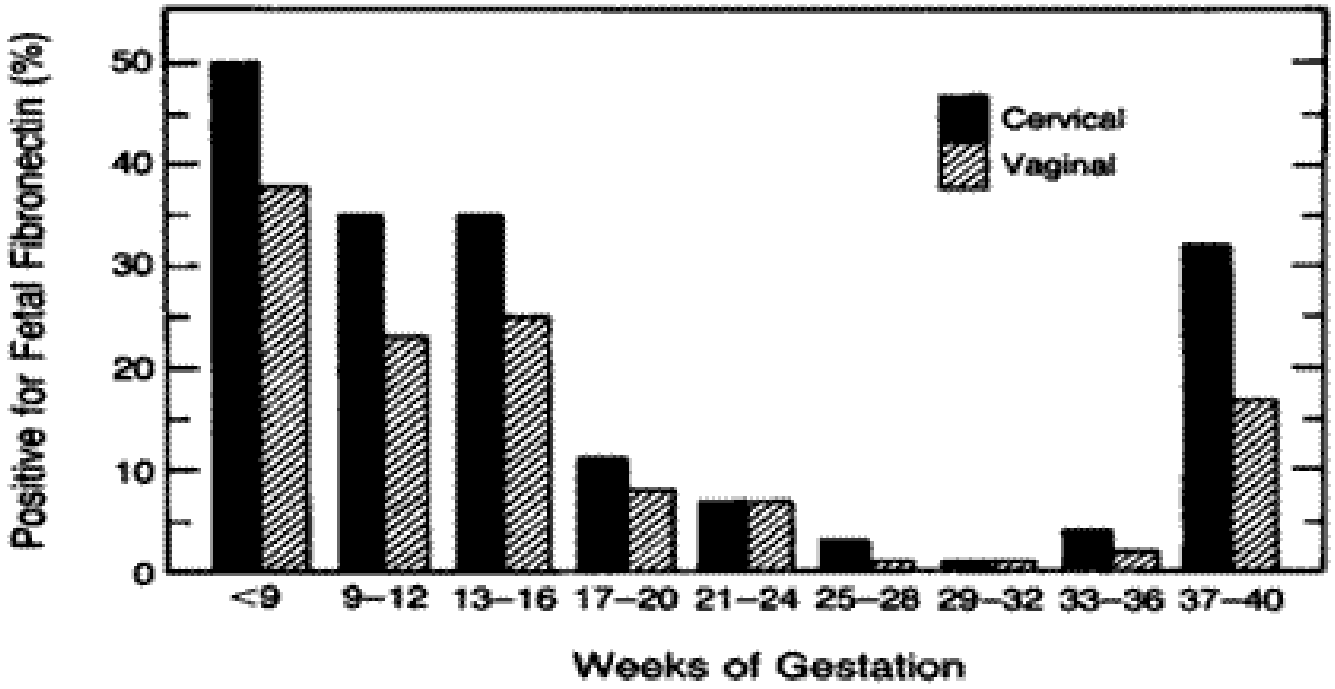
phIGFBP-1

Prestatiekenmerken/literatuur

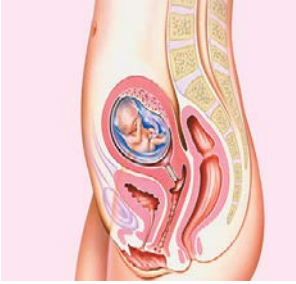


Lockwood et al.

Fetal fibronectin in cervical and vaginal secretions as a predictor of preterm delivery. N Engl J Med 1991; 325:669-674.



Prestatiekenmerken/literatuur

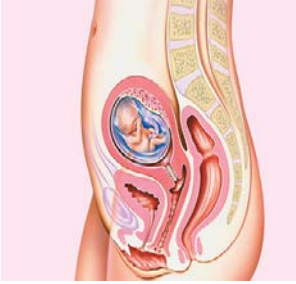


Lockwood et al.

Fetal fibronectin in cervical and vaginal secretions as a predictor of preterm delivery. N Engl J Med 1991; 325:669-674.

Variable	Positive for Fetal Fibronectin		Negative for Fetal Fibronectin		P Value†
	Preterm Delivery (N = 49)	Delivery at Term (N = 10)	Preterm Delivery (N = 11)	Delivery at Term (N = 47)	
Gestational age at sampling (wk)	29.9±4.0	30.8±3.7	29.5±3.3	31.7±3.1	0.05
Gestational age at delivery (wk)	31.3±4.2	38.4±1.1	32.7±3.1	38.7±1.4	0.0001
Days between sampling and delivery	11±17	54±30	23±26	49±24	0.0001
Birth weight (g)	1980±795	3266±610	2195±872	3220±554	0.0001
Cervical dilatation on admission (cm)	2.6±1.9	1.4±1.1	1.3±1.3	0.9±0.9	0.001
Uterine contractions/hr on admission	10.2±9.8	4.4±5.8	9.2±9.7	7.6±12.3	NS

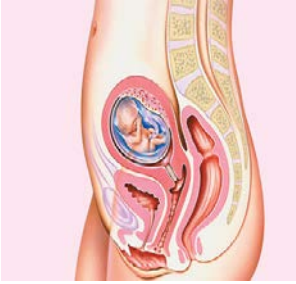
Prestatiekenmerken/literatuur



fFN

phIGFBP-1

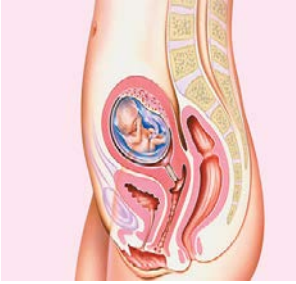
Prestatiekenmerken/literatuur



Performantiekarakteristieken in literatuur

- Agustin Conde-Agudelo, Cervicovaginal fetal fibronectin for the prediction of spontaneous preterm birth in multiple pregnancies: a systematic review and meta-analysis. *The Journal of Maternal-Fetal and Neonatal Medicine*.December 2010; 23(12): 1365-1376
- Honest H, Bachmann LM, Gupta JK, Kleijnen J, Khan KS. Accuracy of cervicovaginal fetal fibronectin test in predicting risk of spontaneous preterm birth: systematic review. Br Med J;325:301.
- Leitich H, Egarter C, Kaider A, Hohlagschwandtner M, Berghammer P, Husslein P. Cervicovaginal fetal fibronectin as a marker for preterm delivery: a meta-analysis. Am J Obstet Gynecol;180:1169-1176
- Faron G, Boulvain M, Irion O, Bernard PM, Fraser WD. Prediction of preterm delivery by fetal fibronectin: a metaanalysis. Obstet Gynecol;92:153-158.
- Chien PF, Khan KS, Ogston S, Owen P. The diagnostic accuracy of cervico-vaginal fetal fibronectin in predicting preterm delivery: an overview. Br J Obstet Gynaecol;104:436-444.
- DELIA MARIA PATERNOSTER. Cervical phIGFBP-1 in the evaluation of the risk of preterm delivery. Acta Obstetricia et Gynecologica.; 86: 151_155.
- Shai E. Elizur. Insulin-like Growth Factor Binding Protein-1 Detection in Preterm Labor: Evaluation of a *Bedside Test. Am. J. of Perinatology* ; 22/6: 305-309.
- K Kwek, Evaluation of a Bedside Test for Phosphorylated Insulin-like Growth Factor Binding Protein-1 in Preterm Labour Ann Acad Med Singapore;33:780-3.
- Lembet A. New rapid bed-side test to predict preterm delivery: phIGFBP-1 in cervical secretions. *Acta obstet gynaecol scand* ; 81: 706-712.
- FUAT AKERCAN. Value of cervical ph IGFBP-1 in the prediction of preterm labor. The journal of reproductive medicine 2004; 49: 368-372.
- Kekki M. IGFBP-1 in cervical secretion as a predictor of preterm delivery. *Acta Obst Gynecol Scand* : 80: 546-551.
- Bong K. S. IGFBP-1 in cevical secretion as a predictor of preterm delivery. ???? 2001. 44/12
- R. E. BITTAR. Predicting preterm delivery in asymptomatic patients with prior preterm delivery by measurement of cervical length and phosphorylated insulin-like growth factor-binding protein-1. *Ultrasound Obstet Gynecol*; 29: 562-567
- R. E. BITTAR. Cervival IGFBP (phIGFBP-1) in patients at increased risk for preterm delivery: Prelimanry results.
- Devleta Balic. Insulin-like growth factor-binding protein-1 (IGFBP-1) in cervical secretions as a predictor of preterm delivery. The Journal of Maternal-Fetal and Neonatal Medicine, May; 21(5): 297-300
- Derya Eroglu. Prediction of Preterm Delivery among Women with Threatened Preterm Labor Gynecol Obstet Invest;64:109-116.
- Hua-Sieng Ting, Comparison of Bedside Test Kits for Prediction of Preterm Delivery: Phosphorylated Insulin-like Growth Factor Binding Protein-1
- (pIGFBP-1) Test and Fetal Fibronectin Test. Ann Acad Med Singapore;36:399-402.
- ….

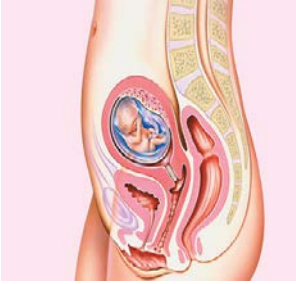
Prestatiekenmerken/literatuur



fFN

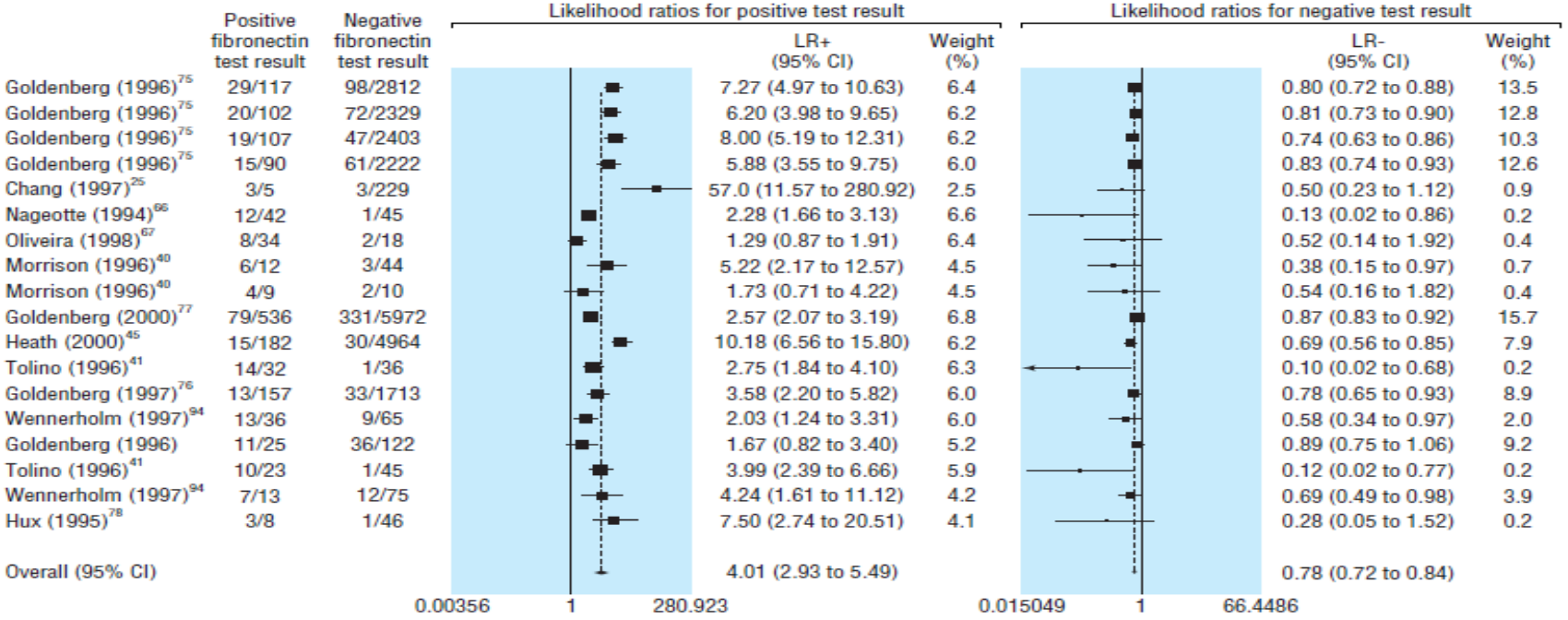
phIGFBP-1

Prestatiekenmerken/literatuur

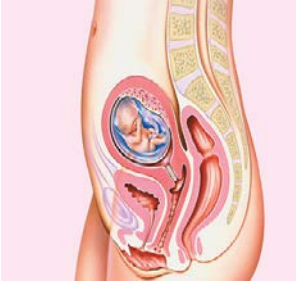


Honest et al.

Accuracy of cervicovaginal fetal fibronectin test in predicting risk of spontaneous preterm birth: systematic review. BMJ 2002; 325:301.



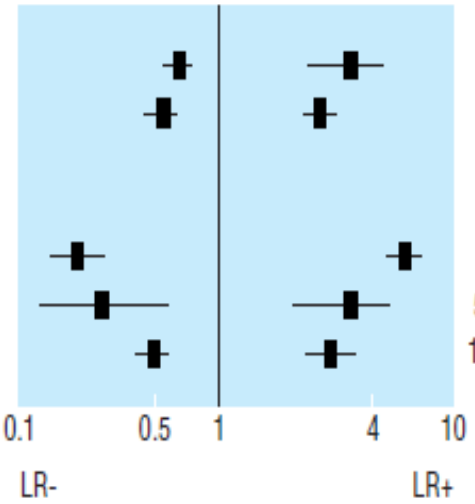
Prestatiekenmerken/literatuur



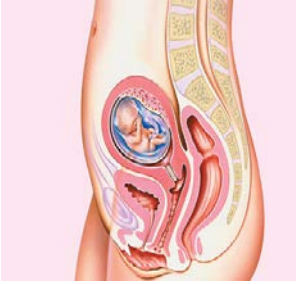
Honest et al.

Accuracy of cervicovaginal fetal fibronectin test in predicting risk of spontaneous preterm birth: systematic review. BMJ 2002; 325:301.

Population/ birth outcome (No of studies)	Weighted pretest probability Median (%)	Summary likelihood ratios (95% CI)		Post-test probabilities (95% CI)	
		Negative test result	Positive test result	Negative test result	Positive test result
Asymptomatic					
<34 weeks (n=12)	4.2	0.78 (0.72 to 0.84)	4.01 (2.93 to 5.49)	3.0 (2.8 to 3.2)	13.7 (10.4 to 17.8)
<37 weeks (n=23)	12.2	0.52 (0.44 to 0.62)	2.94 (2.47 to 3.50)	6.7 (5.8 to 7.9)	29.0 (25.6 to 32.7)
Symptomatic					
7-10 days (n=14)	3.0	0.25 (0.20 to 0.31)	5.42 (4.36 to 6.74)	0.8 (0.6 to 0.9)	14.4 (11.9 to 17.2)
<34 weeks (n=8)	15.7	0.32 (0.16 to 0.66)	3.64 (2.32 to 5.73)	5.6 (2.9 to 10.9)	40.4 (30.2 to 51.6)
<37 weeks (n=27)	21.2	0.48 (0.41 to 0.56)	3.27 (2.74 to 3.92)	11.4 (9.9 to 13.1)	46.8 (42.4 to 51.3)



Prestatiekenmerken/literatuur

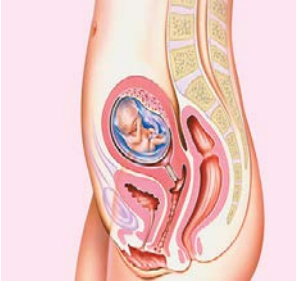


Cervicovaginal fetal fibronectin testing among symptomatic women and number of women needed to be treated (NNT) at 31 weeks' gestation with antenatal steroids to prevent one case of neonatal respiratory distress syndrome (RDS) associated with spontaneous preterm birth within 7-10 days of testing

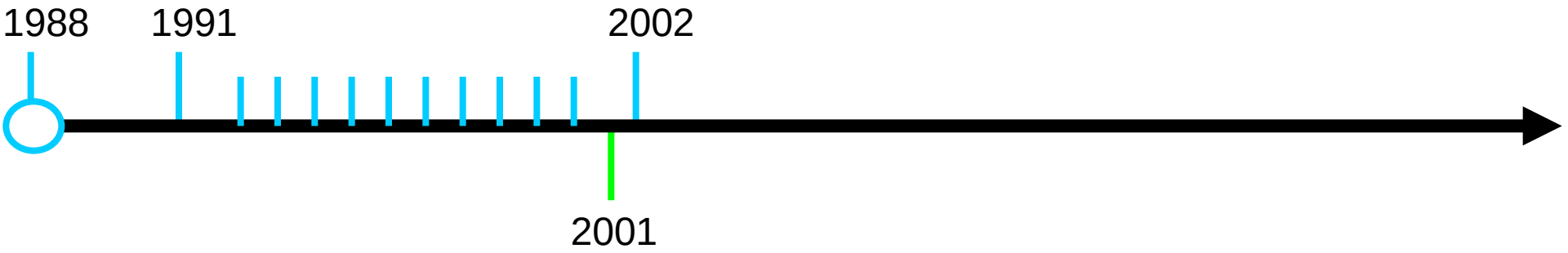
Test result	Probability of spontaneous preterm birth within 7-10 days of testing (%)	Risk of RDS at 32 weeks' gestation[56 57]	Rate of RDS* at 32 weeks' gestation (%)	NNT†
No testing	4.5‡	0.53	2.0	109
Test positive	20.6§	0.53	11.0	17
Test negative	1.0§	0.53	0.4	509

*Calculated as probability of spontaneous preterm birth for positive test result at 32 weeks (31 weeks+7-10 days)=20.6%. Risk of RDS at this gestation=0.53[56;57], therefore, probability of RDS in neonate of woman with positive result=20.6 x 0.53=11% (similar calculation may be carried out for negative result).
† For example, rate of RDS at 32 weeks' gestation=11%, converted to odds of RDS without treatment=11/(100–11)=0.12. Odds of treatment benefit=0.12×0.53=0.064 (where 0.53 is odds ratio for treatment benefit of antenatal steroids, obtained from Cochrane review,[6] which coincidentally, is the same figure as the risk for RDS at 32 weeks' gestation), converted to rate of RDS after antenatal steroid treatment=0.064/(1+0.064)=0.059. Rate difference of RDS between treatment and without antenatal steroid treatment=0.12–0.059=0.061 and number need to treat is 1/0.061=17. This means that with positive test results, 17 symptomatic women who presented at 31 weeks' gestation need to be treated with antenatal steroids to prevent one case of RDS (similar calculation may be carried out for negative test result).
‡Pretest probability of spontaneous preterm birth within 7-10 days of testing for symptomatic women presenting at 31 weeks' gestation.[21;22;46;50;51;58-65] (see webextra table).
§Calculation of probabilities with likelihood ratios shown in figure 6: pretest probability (4.5%) converted to pretest odds=4.5/(100–4.5)=0.047; post-test odds for spontaneous preterm birth among women with a positive test=pretest odds×LR+=0.047×5.45= 0.26 (LR+ indicates likelihood ratio for positive result). This is then converted to post-test probability=0.26/(0.26+1)=0.206=20.6% (a similar calculation may be carried out for negative test result using LR- found in figure 6).

Prestatiekenmerken/literatuur

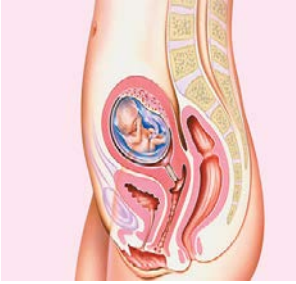


fFN



phIGFBP-1

Prestatiekenmerken/literatuur

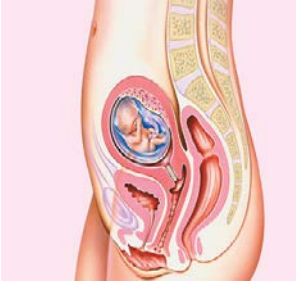


Kekki et al.

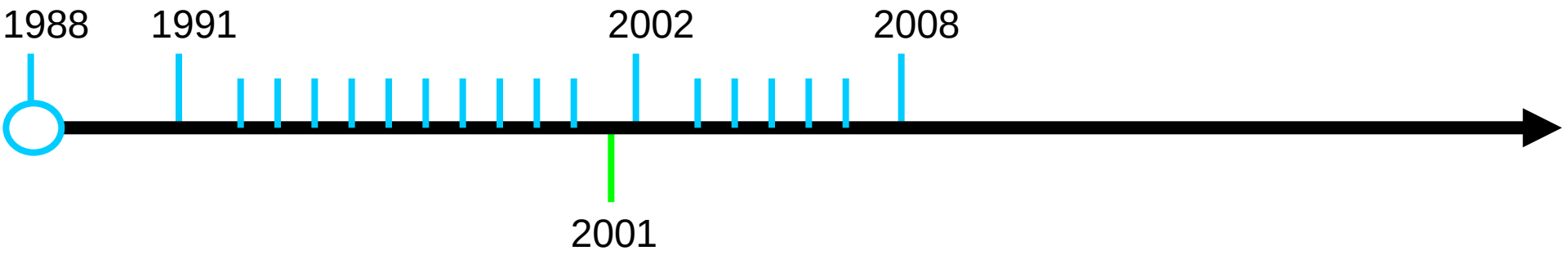
Insulin-like growth factor-binding protein-1 in cervical secretion as a predictor of preterm delivery. Acta Obstet Gynecol Scand 2001; 80: 546–551.

Variable	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	*p*
Age ≥35 years	2.1 (0.4–9.7)	39 (1.1–1340)	0.04
Nulliparity	2.1 (0.5–8.3)	0.3 (0.0–4.8)	0.4
phIGFBP-1 ≥10μg/L	10 (2.2–47)	24 (1.2–487)	0.04
Infection	26 (3.9–167)	5.4 (0.3–111)	0.3
Admission	1.8 (0.4–8.4)	34 (1.1–1067)	0.04
Twins	13 (1.1–161)	224 (1.0–52689)	0.05
Previous preterm delivery	1.4 (0.1–14)	0.9 (0.0–162)	1.0

Prestatiekenmerken/literatuur

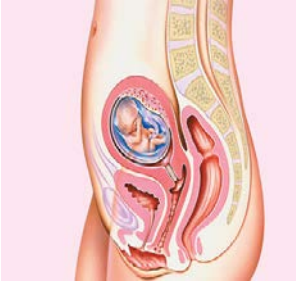


fFN



phIGFBP-1

Prestatiekenmerken/literatuur



Analysis 2.1. Comparison 2 Comparison 01 FFN knowledge versus no knowledge, Outcome 02 Preterm birth < 34 week, Outcome 1 Outcome 02 Preterm birth < 34 week.

Review: Fetal fibronectin testing for reducing the risk of preterm birth

Comparison: 2 Comparison 01 FFN knowledge versus no knowledge, Outcome 02 Preterm birth < 34 week

Outcome: 1 Outcome 02 Preterm birth < 34 week

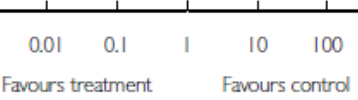
Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Grobman 2004	5/50	3/50		33.5 %	1.67 [0.42, 6.60]
Ness 2007	2/46	4/45		45.2 %	0.49 [0.09, 2.54]
Plaut 2003	2/43	2/47		21.3 %	1.09 [0.16, 7.42]
Total (95% CI)	**139**	**142**		**100.0 %**	**1.01 [0.41, 2.47]**

Total events: 9 (Treatment), 9 (Control)

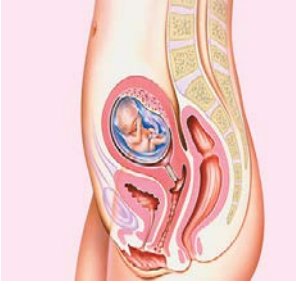
Heterogeneity: $Chi^2 = 1.26$, $df = 2$ ($P = 0.53$); $I^2 = 0.0\%$

Test for overall effect: $Z = 0.03$ ($P = 0.98$)

Test for subgroup differences: Not applicable



Prestatiekenmerken/literatuur



Analysis 6.1. Comparison 6 Comparison 01 FFN knowledge versus no knowledge, Outcome 06 Birthweight 2500 grams, Outcome 1 Outcome 06 Birthweight < 2500 g.

Review: Fetal fibronectin testing for reducing the risk of preterm birth

Comparison: 6 Comparison 01 FFN knowledge versus no knowledge, Outcome 06 Birthweight 2500 grams

Outcome: 1 Outcome 06 Birthweight < 2500 g

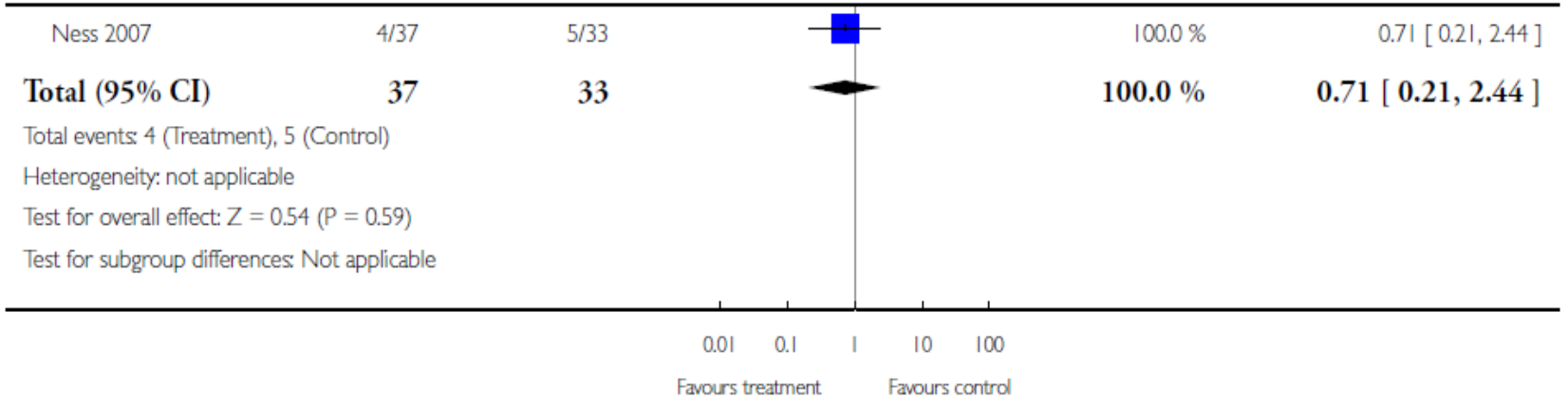
Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Ness 2007	4/37	5/33		100.0 %	0.71 [0.21, 2.44]
Total (95% CI)	**37**	**33**		**100.0 %**	**0.71 [0.21, 2.44]**

Total events: 4 (Treatment), 5 (Control)

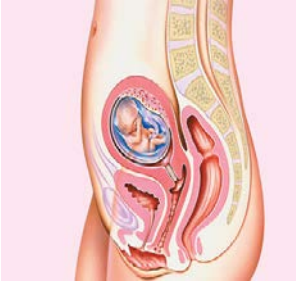
Heterogeneity: not applicable

Test for overall effect: Z = 0.54 (P = 0.59)

Test for subgroup differences: Not applicable



Prestatiekenmerken/literatuur



Analysis 8.1. Comparison 8 Comparison 01 FFN knowledge versus no knowledge, Outcome 08 Maternal hospitalization, Outcome 1 Outcome 08 Maternal hospitalization.

Review: Fetal fibronectin testing for reducing the risk of preterm birth

Comparison: 8 Comparison 01 FFN knowledge versus no knowledge, Outcome 08 Maternal hospitalization

Outcome: 1 Outcome 08 Maternal hospitalization

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Grobman 2004	13/50	14/50		49.3 %	0.93 [0.49, 1.77]
Lowe 2004	16/46	12/51		40.1 %	1.48 [0.78, 2.79]
Ness 2007	9/47	3/46		10.7 %	2.94 [0.85, 10.16]
Total (95% CI)	**143**	**147**		**100.0 %**	**1.36 [0.90, 2.07]**

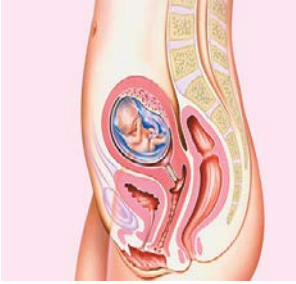
Total events: 38 (Treatment), 29 (Control)

Heterogeneity: $Chi^2 = 2.89$, $df = 2$ ($P = 0.24$); $I^2 = 31\%$

Test for overall effect: $Z = 1.44$ ($P = 0.15$)

Test for subgroup differences: Not applicable

Prestatiekenmerken/literatuur



Analysis 9.1. Comparison 9 Comparison 01 FFN knowledge versus no knowledge, Outcome 09 Tocolysis, Outcome 1 Outcome 09 Tocolysis.

Review: Fetal fibronectin testing for reducing the risk of preterm birth

Comparison: 9 Comparison 01 FFN knowledge versus no knowledge, Outcome 09 Tocolysis

Outcome: 1 Outcome 09 Tocolysis

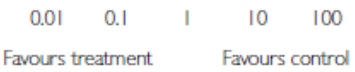
Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Grobman 2004	8/50	9/50		14.0 %	0.89 [0.37, 2.12]
Lowe 2004	22/46	23/51		33.9 %	1.06 [0.69, 1.63]
Ness 2007	9/36	6/27		10.6 %	1.13 [0.46, 2.78]
Plaut 2003	25/43	28/47		41.5 %	0.98 [0.69, 1.38]
Total (95% CI)	**175**	**175**		**100.0 %**	**1.01 [0.78, 1.30]**

Total events: 64 (Treatment), 66 (Control)

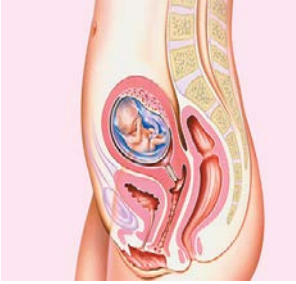
Heterogeneity: $Chi^2 = 0.23$, df = 3 (P = 0.97); $I^2 = 0.0\%$

Test for overall effect: Z = 0.06 (P = 0.95)

Test for subgroup differences: Not applicable



Prestatiekenmerken/literatuur



Analysis 10.1. Comparison 10 Comparison 01 FFN knowledge versus no knowledge, Outcome 10 Steroids for fetal lung maturity, Outcome 1 Outcome 10 Steroids for Fetal Lung Maturity.

Review: Fetal fibronectin testing for reducing the risk of preterm birth

Comparison: 10 Comparison 01 FFN knowledge versus no knowledge, Outcome 10 Steroids for fetal lung maturity

Outcome: 1 Outcome 10 Steroids for Fetal Lung Maturity

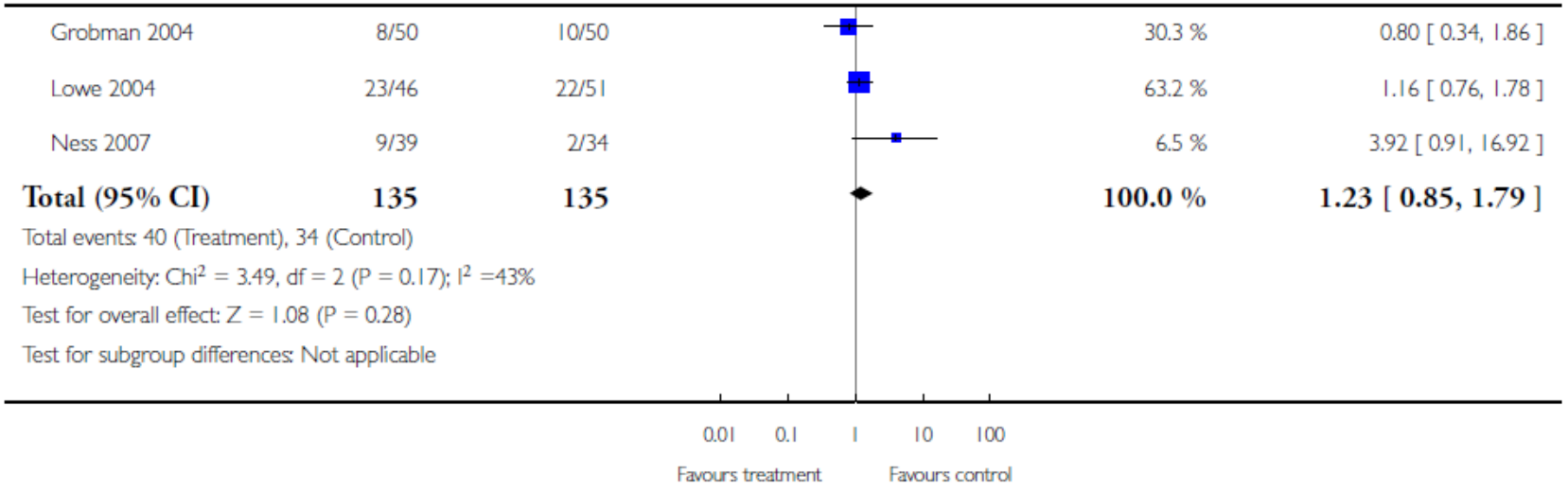
Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Grobman 2004	8/50	10/50		30.3 %	0.80 [0.34, 1.86]
Lowe 2004	23/46	22/51		63.2 %	1.16 [0.76, 1.78]
Ness 2007	9/39	2/34		6.5 %	3.92 [0.91, 16.92]
Total (95% CI)	**135**	**135**		**100.0 %**	**1.23 [0.85, 1.79]**

Total events: 40 (Treatment), 34 (Control)

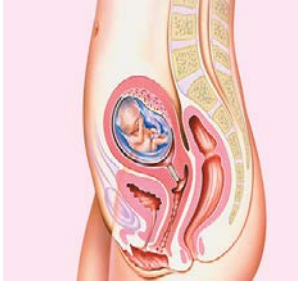
Heterogeneity: $Chi^2 = 3.49$, $df = 2$ ($P = 0.17$); $I^2 = 43\%$

Test for overall effect: $Z = 1.08$ ($P = 0.28$)

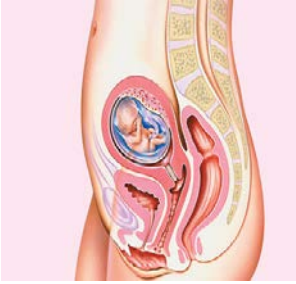
Test for subgroup differences: Not applicable



Test nuttig ????



Prestatiekenmerken/literatuur

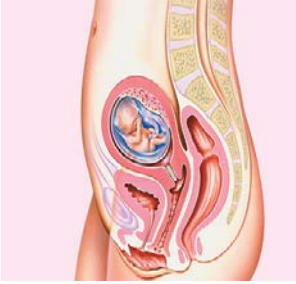


Vis et al.

Why were the results of randomized trials on the clinical utility of fetal fibronectin negative? A systematic review of their study designs. Am J of perinatology 2011; 28:145-150.

Criteria	Explanation
Randomization of discordant test results (discordancy design)[14,17,18]	Randomization of the therapy decision if the test result indicates a different treatment than standard care
Fixed management protocol based on test result[14,17,18]	Therapy decisions strictly based on the test result
Description of interventions in relation to the test result[15–17]	Details of which patients got what treatment in relation to their test result, or description of cases when protocol was not followed
Evaluation of learning curve	Evaluation for temporal change in treatment decisions
Sample size calculations in agreement with the prevalence of the test results	Power calculation takes into account that the test may affect the primary outcome only of the subgroup of patients with shifted risk assessments due to that test

Prestatiekenmerken/literatuur

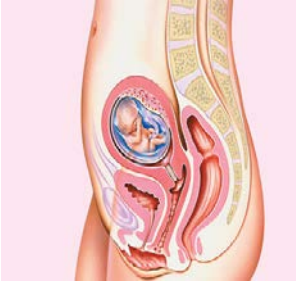


Vis et al.

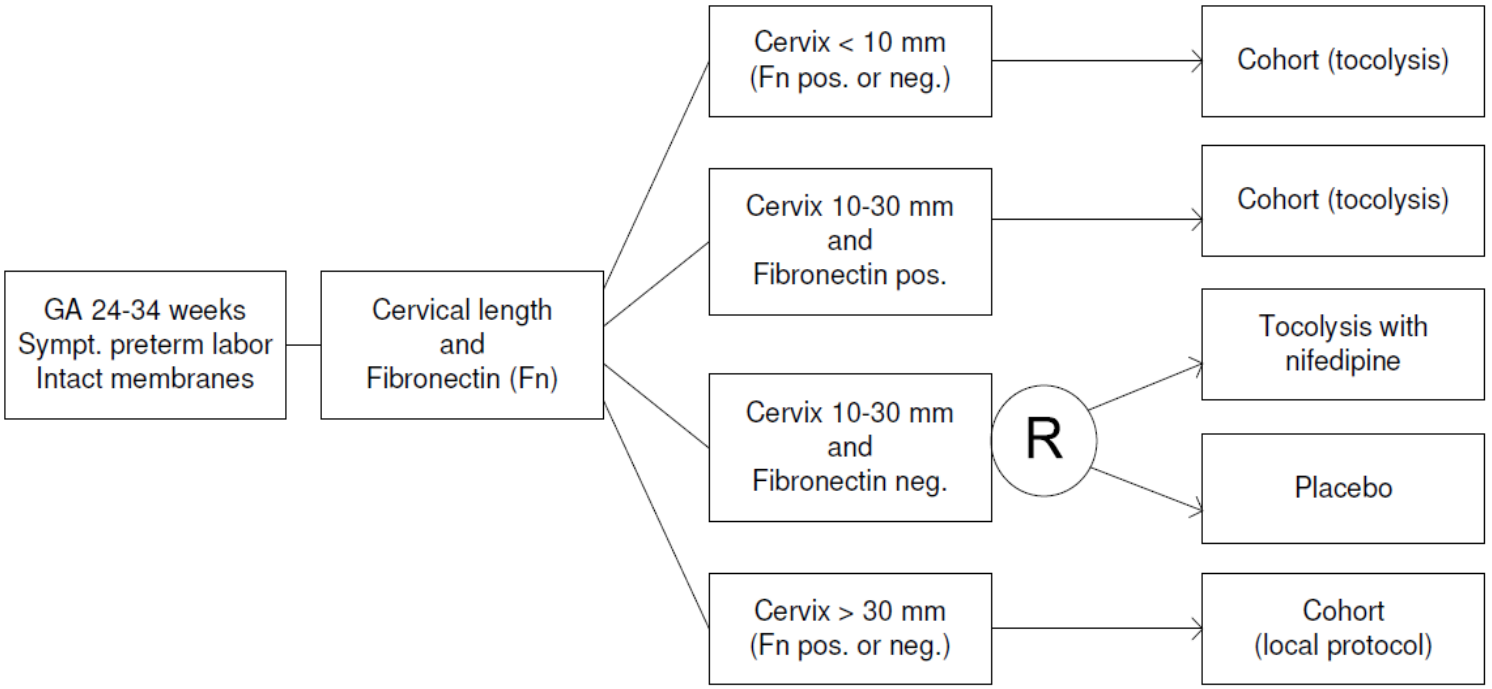
Why were the results of randomized trials on the clinical utility of fetal fibronectin negative? A systematic review of their study designs. Am J of perinatology 2011; 28:145-150.

Methodology	Grobman et al[20]	Lowe et al[21]	Ness et al[22]	Plaut et al[23]
Discordancy design	No	No	No	No
Fixed management protocol	No	No	No	No
Description of given therapy in relation to test result	No	No	No	Yes
Learning curve evaluated	Yes	No	No	No
Sample size calculations in agreement with the prevalence of the relevant test results	Yes	Yes	Unclear	Terminated prematurely

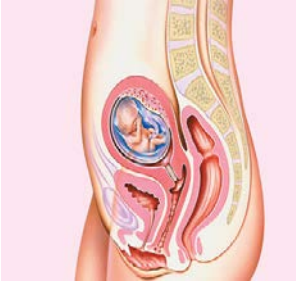
Prestatiekenmerken/literatuur



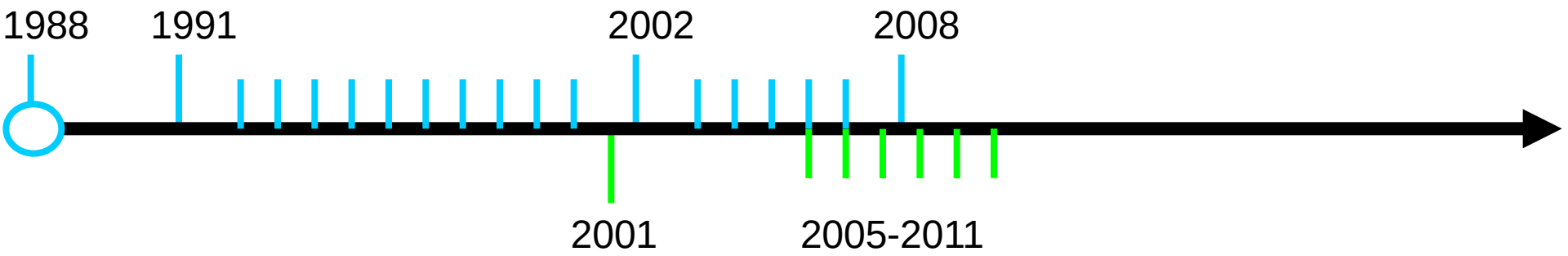
APOSTEL-I trial



Prestatiekenmerken/literatuur

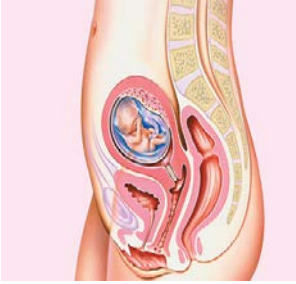


fFN



phIGFBP-1

Prestatiekenmerken/literatuur

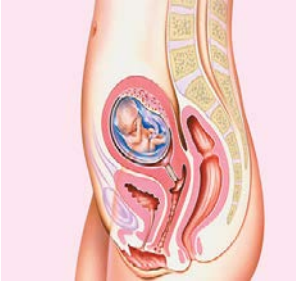


Danti et al.

The combination of short cervical length and phIGFBP-1 in the prediction of preterm delivery in symptomatic women. J Matern Fetal Neonatal Med *2011; 24:1262-6.*

	Cervical length ≤30 mm	Cervical length 20–30 mm	Cervical length <20 mm
Delivery within 7 days (*n*)	4/60	1/41	3/19
Positive phIGFBP/delivery within 7 days (*n*)	2/4	1/1	1/3
phIGFBP-1 LR+	1.65 (0.57–4.74)	3.64 (2.20–6.01)	0.89 (0.16–4.97)
phIGFBP-1 LR−	0.72 (0.27–1.94)	0	1.07 (0.44–2.59)
Sensitivity	50% (7–93%)	100% (2–100%)	33% (1–91%)
Specificity	70% (56–81%)	73% (56–85%)	63% (35–85%)
Positive predictive value	11% (1–33%)	8% (0–38%)	14% (0–58%)
Negative predictive value	95% (83–99%)	100% (91–100%)	83% (52–98%)

Prestatiekenmerken/literatuur

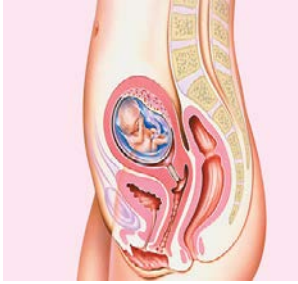


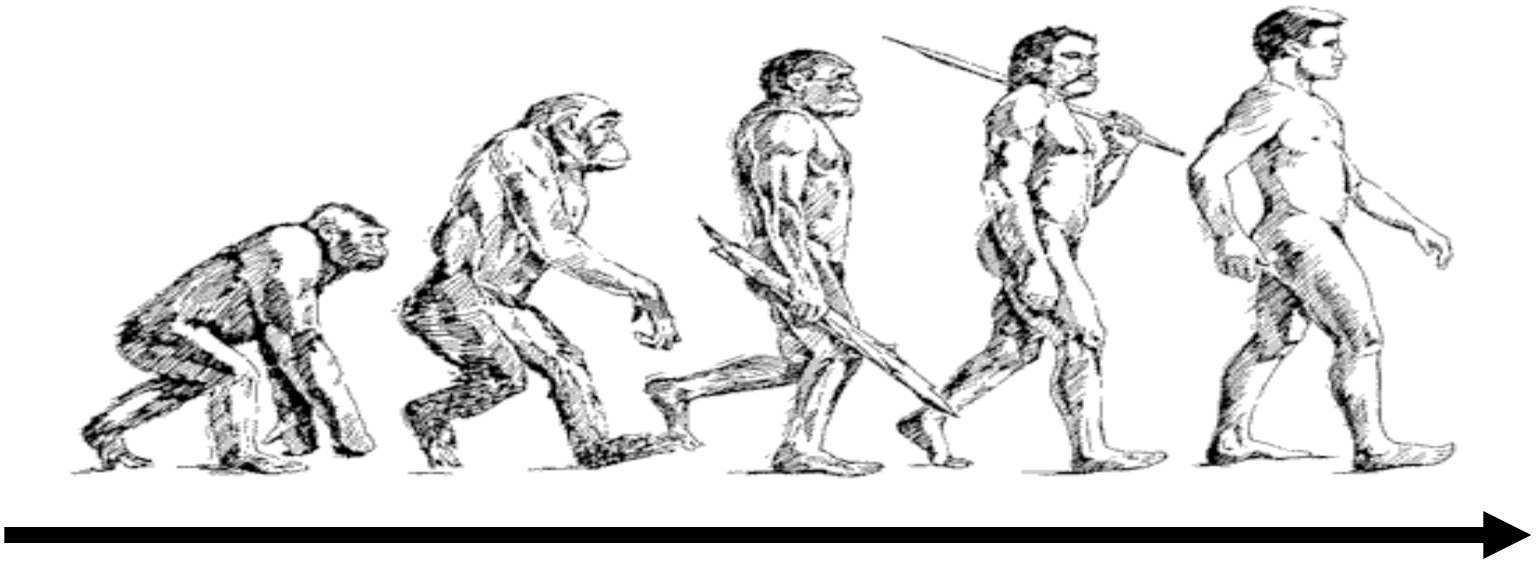
Riboni et al.

Biochemical markers predicting pre-term delivery in symptomatic patients: phosphorylated insulin-like growth factor binding protein-1 and fetal fibronectin. Arch Gynecol Obstet *2011;284:1325-9.*

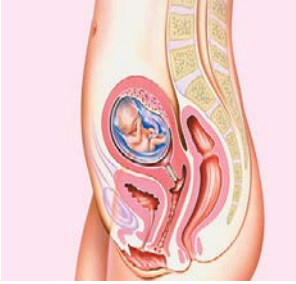
Parameter	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
phIGFBP-1 test				
7 days	50	83.7	10.8	97.7
<34 g. w.	64.3	85.7	24.3	97.1
<37 g. w.	52.9	89.2	48.7	90.8
fFN test				
7 days	50	80.2	9.1	97.6
<34 g. w.	62.5	82.5	22.7	96.4
<37 g. w.	50	85.9	45.5	88

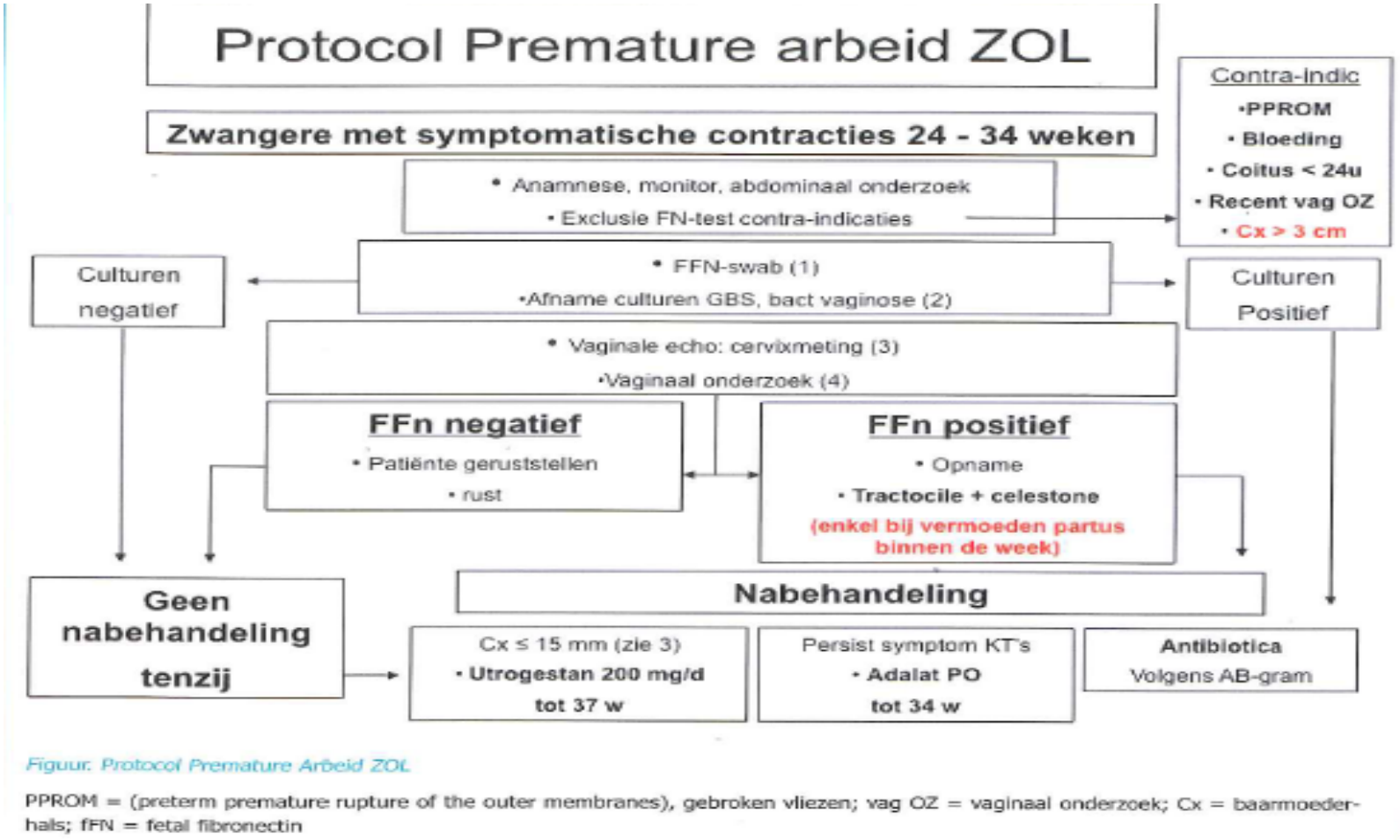
Besluiten





Praktisch voorbeeld

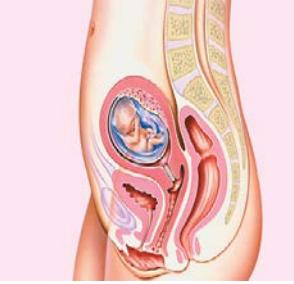


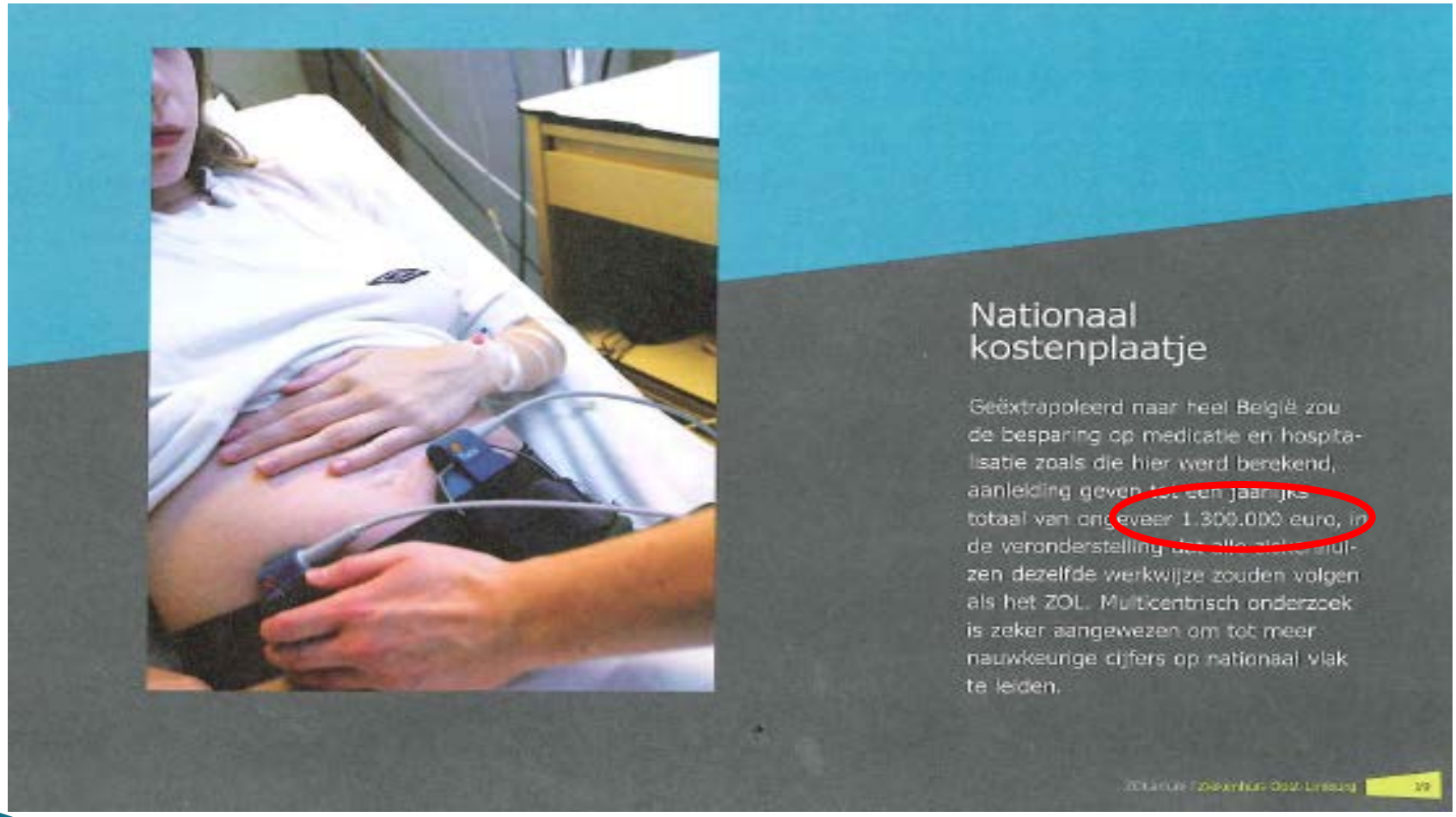


Figuur. Protocol Premature Arbeid ZOL

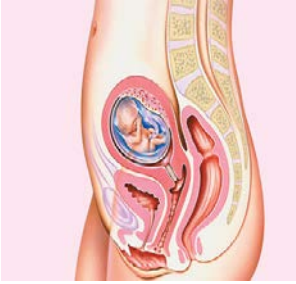
PPROM = (preterm premature rupture of the outer membranes), gebroken vliezen; vag OZ = vaginaal onderzoek; Cx = baarmoederhals; fFN = fetal fibronectin

Praktisch voorbeeld





Praktisch voorbeeld

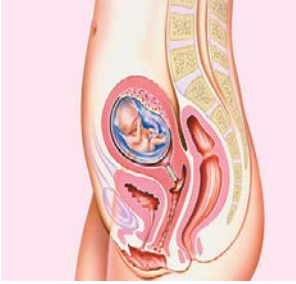


- 20 kuren uitgespaard (€550/kuur)
- € 18.000 aan opnames uitgespaard

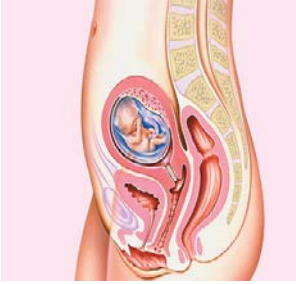
- TOTAAL: € 29.000

ADVERSE CLINICAL OUTCOME???

Besluiten



- Gebruiken bij symptomatische zwangeren
- Uitsluiten van bevalling binnen de 7 dagen
- Resultaten APOSTEL-I studie afwachten?



Bedankt voor de aandacht
VRAGEN???