Cervixlängd för prediktion av förtidsbörd

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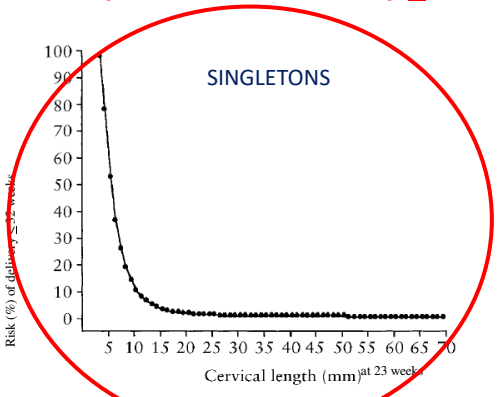
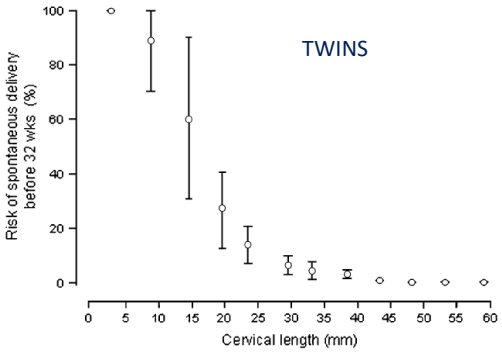
The shorter the cervix (at midgestation) the higher the risk of PTD

Risk of spontaneous delivery ≤ 32 weeks according to cervical length at 23 weeks



Heath et al *UOG 1998;12:312*
n = 2567 (SINGLETONS)



To et al Am J Obstet Gynecol (2006) 194, 1360–5
n =1135 (TWINS)

2

How long is a ”normal cervix” at midgestation?

Patient characteristics	*n* (%)	*Cervical length Mean (SD)* (mm)
Ethnic group		
1 Caucasian	1288 (47.7)	39.5 (9.2)
2 Afro-Caribbean	1285 (47.5)	37.4 (10.7)
3 Other	129 (4.8)	40.1 (9.2)
Age (years)		
1 < 20	193 (7.1)	35.6 (9.0)
2 20–35	2140 (79.2)	38.7 (9.9)
3 > 35	369 (13.7)	39.1 (10.9)

Table 3 Multiple regression analysis to demonstrate significant independent contributions in explaining the variance in cervical length

Patient characteristics	β *(95% CI)*	*p Value*
Obstetric history	−1.97 (−2.95 to −0.98)	< 0.0001
Ethnic group	−2.04 (−2.83 to −1.26)	< 0.0001
Ponderal index	0.15 (0.07 to 0.23)	< 0.0001
Maternal age	0.15 (0.09 to 0.22)	< 0.0001
Cervical surgery	−1.71 (−4.44 to 1.02)	NS

A higher proportion of Afro-Caribbean women (60-100% African DNA) have cervix ≤15 mm: 2.8% vs. 0.5%

Heath et al Ultrasound Obstet Gynecol 1998;12:304–311

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Ultrasound Obstet Gynecol 2011; 38: 1–9
Published online in Wiley Online

Editorial

Prevention of spontaneous preterm birth: universal cervical length assessment and vaginal progesterone in women with a short cervix: time for action!

Stuart Campbell, MD February 2018

Universal cervical-length screening and vaginal progesterone prevents early preterm births, reduces neonatal morbidity and is cost saving: doing nothing is no longer an option

STUART CAMPBELL

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How well can midtrimester sonographic cervical length discrimintae between women who do an do not deliver preterm?

- Sensitivity
- Specificity
- Clinical consequences of screening
  - Number of false positives per one true positive, FP/TP
  - Number needed to screen to detect one spontaneous preterm delivery, NNS
  - Size of high risk group
- NO intervention between test and outcome
- BLINDING

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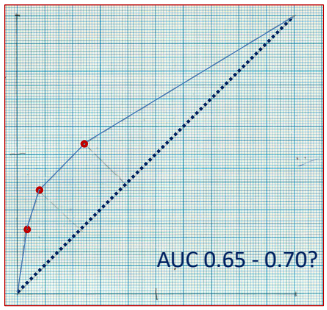
First blinded study: Iams J et al. N Engl J Med 1996;334:567-72

- 2915 women (singleton)
- Ultrasound measurement of cervical length at 22-24 weeks (and 28 weeks)
- 63% black
- Low socioeconomic status
  - 72 % not completed high school
  - 54 % income below $800/month
- Outcome measure: sPTD <35 weeks
- sPTD <35 weeks: 4.3% (n = 126)
- ROC-curve to select cervical length cut-offs

	Cervical length at 22-24 weeks		
	≤20 mm 5th centile	≤25 mm 10th centile	≤ 30 mm 25th centile
Sensitivity	23.0	37.3	54.0
Specificity	97.0	92.2	76.3



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Blinded studies estimating the ability of midtrimester sonographic cervical length to correctly predict preterm delivery

Study	n	Country	Ethnicity	Prevalence sPTD	Measurement week	Outcome sPTD
Iams -96	2915	USA	63% black	4.3%	22-24	<35 weeks
Carvalho -05	1958	Brazil	62% non-white	3.4 %	21-24	<35 weeks
Davies -08	964	Canada	most white?	1.7%	24	<35 weeks
Taipale -98	3694	Finland	99% white	0.8%	18-22 (mean 20)	<35 weeks
Leung -05	2880	Hong Kong	100% Chinese	0.7%	18-22 (mean 20)	<34 weeks

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Blinded studies estimating the ability of midtrimester sonographic cervical length to correctly predict preterm delivery

Study	Outcome sPTD	Measured week	Denom-inator	Sensitivity (%) at cervical length cutoff					AUC
				20mm	25mm	30mm	27mm	29mm	
Iams	<35 weeks	22-24	126	23	37	54	-	-	
Carvalho	<35 weeks	21-24	66	52	58	64	-	-	
Davies	<35 weeks	24	16	6	25	50	-	-	
Taipale	<35 weeks	18-22	31	-	7	-	7	19	
Leung	<34 weeks	18-22	19	11	26	37	37	-	0.68

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Blinded studies estimating the ability of midtrimester sonographic cervical length to correctly predict preterm delivery

Study	Ethnicity	Outcome sPTD	Measured week	Denom-inator	Cervical length cutoff ≤25 mm		
					Size high-risk group	Sensitivity	Specificity
Iams	63% black	<35 weeks	22-24	126	10%	**37%**	**92%**
Carvalho	62% non-white	<35 weeks	21-24	66	11%	**58%**	**91%**
Davies	Most white?	<35 weeks	24	16	3.2%	**25%**	**97%**
Taipale	99% white	<35 weeks	18-22	31	0.3%	**7%**	**100%**
Leung	100% Chinese	<34 weeks	18-22	19	1.8%	**26%**	**98%**

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Second-trimester transvaginal ultrasound measurement of cervical length for prediction of preterm birth: a blinded prospective multicentre diagnostic accuracy study

Swedish CERVIX-study Methods

Vetenskapsrådet

- Prospective blinded multicentre diagnostic accuracy study
- Seven ultrasound units in Sweden (Malmö-Lund, Stockholm, Gothenburg, Falun, Örebro)
- Consecutive asymptomatic women with a singleton pregnancy
- Recruitment at routine second trimester ultrasound examination
- Two measurements of cervical length:
  - 18 to 20 weeks (Cx1), on the day of the routine scan
  - 21 to 23 weeks (Cx2; optional)
- Primary outcome variable: PTD <33 weeks

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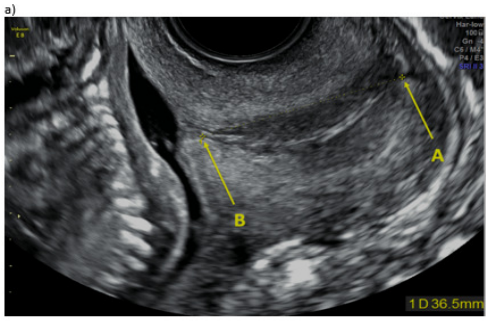
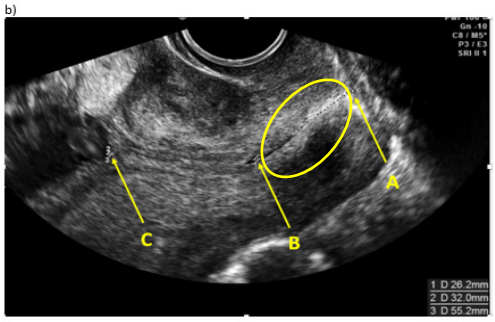


We report results for
the shortest of three measurements
during at least 3 min of
the closed endocervical canal



Measurements performed by
specially trained midwife sonographers
(theoretical education and practical
training, pass of practical test,
quality checks 4 times a year)

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Results

Vetenskapsrådet

- 11 072 women with measurements at 18-20 weeks (Cx 1)
- 6 288 women with measurements at 21-23 weeks (Cx 2)
- About 90% white ethnicity, < 10% low socioeconomic status
- sPTD <33 weeks 0.5% (56/11 072)
- sPTD <33 weeks 0.4% (26/6288)

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Second-trimester transvaginal ultrasound measurement of cervical length for prediction of preterm birth: a blinded prospective multicentre diagnostic accuracy study

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Vetenskapsrådet

1) the ability to correctly predict spontaneous preterm delivery (sPTD) was substantially **better for measurements taken at 21-23 weeks than at 18-20 weeks**

2) the discriminative ability was **better the earlier sPTD occurred**

3) the discriminative ability of a **change in cervical length was not superior** to that of a single measurement at 21-23 weeks

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Vetenskapsrådet

Discriminative ability of endocervical length at 21 to 23 weeks (n=6288) for predicting spontaneous preterm delivery (sPTD) <33 weeks

Cervical length ≤25 mm (n=274; 4.4%)				Cervical length ≤27 mm (n=510; 8.1%)			
Sensitivity, %	Specificity	FP/TP	NNS	Sensitivity, %	Specificity	FP/TP	NNS
38.5%	96%	26	629	54%	92%	35	449

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Blinded studies estimating the ability of midtrimester sonographic cervical length to correctly predict spontaneous preterm delivery

Study	Outcome sPTD	Measured week	Ethnicity	Cervical length cutoff ≤25 mm		
				Size high-risk group	LR+	LR-
Iams	<35 weeks (4.3%)	22-24	63% black	10%	**4.8**	**0.73**
Carvalho	<35 weeks (3.4%)	21-24	62% non-white	11%	**6.4**	**0.46**
Davies	<35 weeks (1.7%)	24	most white?	3.2%	**8.3**	**0.78**
CERVIX	<35 weeks (1.1%)	21-23	90% white	4.4%	**6.3**	**0.78**
Taipale	<35 weeks (0.8%)	18-22	99% white	0.3%	**∞**	**0.93**
Leung	<34 weeks (0.7%)	18-22	100% Chinese	1.8%	**13**	**0.76**
CERVIX	<33 weeks (0.4%)	21-23	26	4.4%	**9.6**	**0.64**

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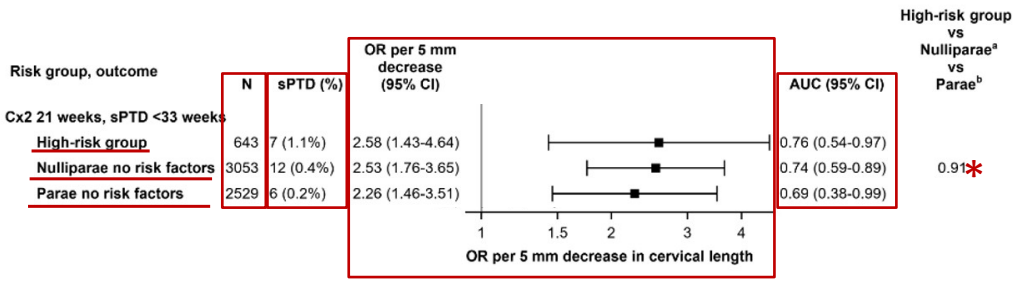
Effect of cervical length on risk of spontaneous preterm delivery <33 weeks in different risk groups

Results from the Swedish CERVIX study



* Interaction P-value

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Swedish CERVIX study

- Reproducibility of cervical length measurements
  - *Acta Obstet Gynecol Scand. 2020 Nov;99(11):1476-1485*
- Health economic analysis (ongoing)
  - Screen all
    - Screen at routine scan (18-20 weeks)
    - Screen at 21-23 weeks
  - Screen high-risk
  - Screen low-risk
  - Screen nuliparae

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General comment on cervical length screening

- The effect of cervical length screening on the total number of preterm deliveries (PTDs) is small
  - only a proportion of PTDs are spontaneous
  - short cervix has a low detection rate of sPTD
  - prophylactic treatment prevents only a small proportion of sPTDs

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General comment on cervical length screening

- Assumptions
  - 50% of PTDs <33 weeks are spontaneous
  - 100% acceptance rate of cervical length screening
  - 50% sensitivity to detect sPTD <33 weeks
  - Prophylaxis reduces number of sPTDs <33 weeks with 30%

Screening could potentially result in a 7.5% reduction in total number of PTDs <33 weeks

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Conclusion

- The shorter the cervix at midgestation the higher the risk of sPTD
- The ability to correctly predict sPTD is better if measurements are performed at 21-23 weeks than at 18-20 weeks
- The discriminative ability of cervical length at 21-23 weeks is better the earlier the sPTD occurs
  - Good for sPTD <29 weeks, intermediate for sPTD <33 weeks, poor for sPTD <37 weeks
- The ability of cervical length at midgestation to discriminate between women who do and do not deliver spontaneously preterm is at most moderate (but the earlier the sPTD the better)

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Conclusion

- The effect of cervical length at 21-23 weeks on the risk of sPTD <33 weeks is similar in high-risk and low-risk women with a singleton pregnancy (in a white population with high socioeconomic status)
- Cervical length screening followed by progesterone prophylaxis in women with a singleton pregnancy has a small effect on the total number of preterm deliveries
- A health economic analysis based on the situation in Sweden is needed (ongoing)

Thank you

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Discriminative ability of cervical length at 21-23 weeks		
sPTD	sPTD n (%)	AUC
<28 GW	3 (0.05)	0.96
<29 GW	5 (0.08)	0.98
<30 GW	10 (0.16)	0.86
<31 GW	15 (0.24)	0.85
<32 GW	18 (0.29)	0.81
<33 GW	26 (0.41)	0.76
<34 GW	41 (0.65)	0.71
<35 GW	69 (1.10)	0.71
<36 GW	114 (1.81)	0.67
<37 GW	225 (3.58)	0.63

Discriminative ability of cervical length at 18-20 weeks		
sPTD	sPTD n (%)	AUC
<28 GW	22 (0.20)	0.83
<29 GW	24 (0.22)	0.84
<30 GW	34 (0.31)	0.77
<31 GW	40 (0.36)	0.76
<32 GW	46 (0.42)	0.71
<33 GW	63 (0.57)	0.68
<34 GW	94 (0.85)	0.65
<35 GW	143 (1.29)	0.62
<36 GW	226 (2.04)	0.61
<37 GW	417 (3.77)	0.60

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Results

- the ability to correctly predict spontaneous delivery <33 weeks was substantially **better for measurements taken at 21-23 weeks than at 18-20 weeks:** AUC 0.76 vs 0.65
- the discriminative ability was **better the earlier the delivery occurred:** AUC for for sPTD <29 weeks <33 weeks and <37 weeks: 0.98 vs 0.76 vs 0.63 (measurements at 21 -23 weeks)
- **change in cervical length** between the two measurements **not superior** to that of a single measurement at 21-23 weeks: one single measurement AUC 0.76, change in mm AUC 0.67 , change in percent AUC 0.68 (measurement at 21-23 weeks)

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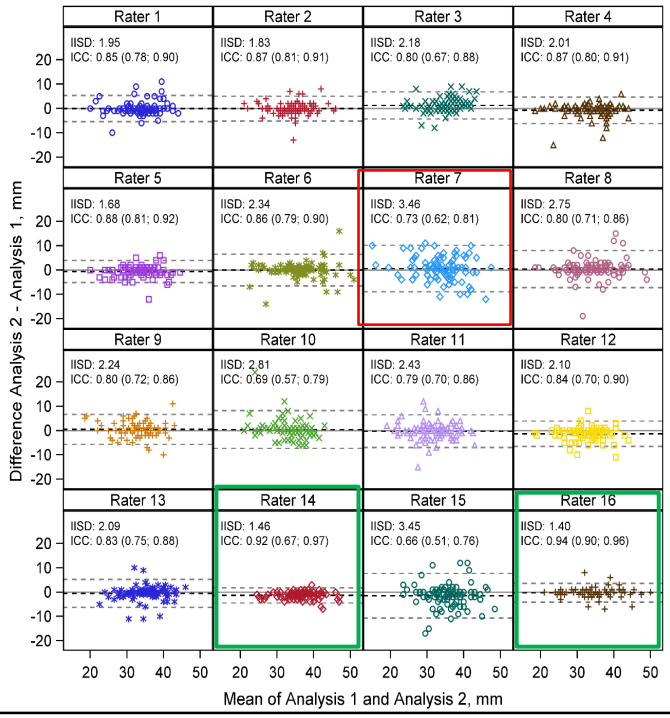

Intra-observer differences (measurements on videoclips)

Acta Obstet Gynecol Scand. 2020 Nov;99(11):1476-1485

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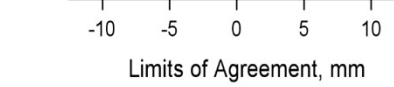
INTER-observer differences, LIVE examinations

	Measurement value Examiner 1 mean(min;max)	Examiner 2 mean(min;max)	Mean diff (LoA)		ICC (95%CI)
Shortest endocervical length (A-B), mm					
Pair A	35.2 (20;44)	34.3 (23;40)	1.0 (-5.4;7.3)		0.76 (0.55; 0.88)
Pair B	36.3 (28;44)	34.9 (27;42)	1.4 (-5.9;8.7)		0.63 (0.36; 0.81)
Pair C	35.4 (23;49)	34.7 (18;52)	0.7 (-11.7;13.2)		0.58 (0.28; 0.78)
Pair D	30.3 (22;40)	30.1 (17;38)	0.1 (-11.1;11.4)		0.31 (-0.08; 0.61)
Pair E	32.7 (23;41)	32.6 (24;40)	0.1 (-7.3;7.6)		0.70 (0.45; 0.85)
Pair F	36.5 (29;49)	36.2 (27;51)	0.3 (-4.1;4.7)		0.91 (0.81; 0.96)
Pair G	40.0 (30;58)	39.2 (28;52)	0.9 (-6.4;8.1)		0.79 (0.59; 0.89)
Shortest endocervical length (A-B), mm (isthmus no for both examiners)					
Pair A	34.8 (20;44)	34.3 (23;40)	0.5 (-5.2;6.2)		0.83 (0.64; 0.92)
Pair B	36.0 (29;44)	34.3 (27;42)	1.7 (-4.2;7.5)	*	0.72 (0.40; 0.88)
Pair C	35.4 (23;49)	34.9 (18;52)	0.5 (-11.3;12.3)		0.64 (0.35; 0.82)
Pair D	33.1 (25;38)	31.1 (26;40)	2.1 (-4.2;8.3)	*	0.57 (0.09; 0.84)
Pair E	34.7 (24;41)	33.2 (24;40)	1.4 (-4.8;7.7)		0.75 (0.44; 0.90)
Pair F	36.9 (29;42)	36.9 (27;43)	0.0 (-3.3;3.3)		0.95 (0.84; 0.98)
Pair G	39.6 (30;58)	39.3 (28;52)	0.3 (-4.1;4.7)		0.92 (0.83; 0.96)



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Results

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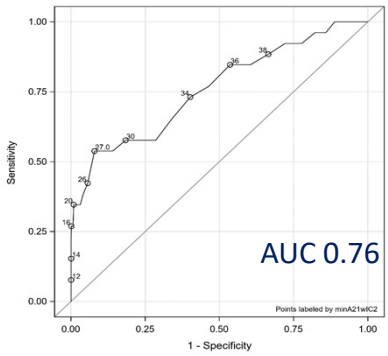
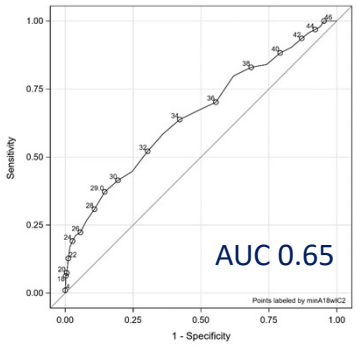
Measurement at **21-23 weeks**



Prediction of sPTD <33 weeks

Measurement at **18-20 weeks**



Prediction of sPTD <33 weeks

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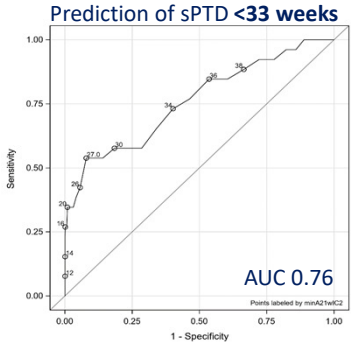
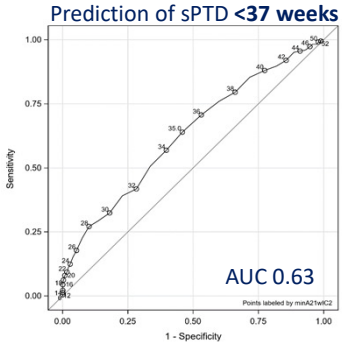
Results

2) the discriminative ability (measurements at 21-23 weeks) was **better the earlier sPTD occurred:** AUC for prediction of sPTD <33 weeks and <37weeks: **0.76 vs 0.63**

Prediction of sPTD **<33 weeks**



Prediction of sPTD **<37 weeks**



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Results

3) the discriminative ability of a **change in cervical length was not superior** to that of a single measurement at 21-23 weeks (prediction of sPTB <33 weeks):

	Prediction of sPTD < 33weeks
	AUC
ONE measurement at 21-23 weeks	0.76
Change in mm	0.67
Change in percent	0.68

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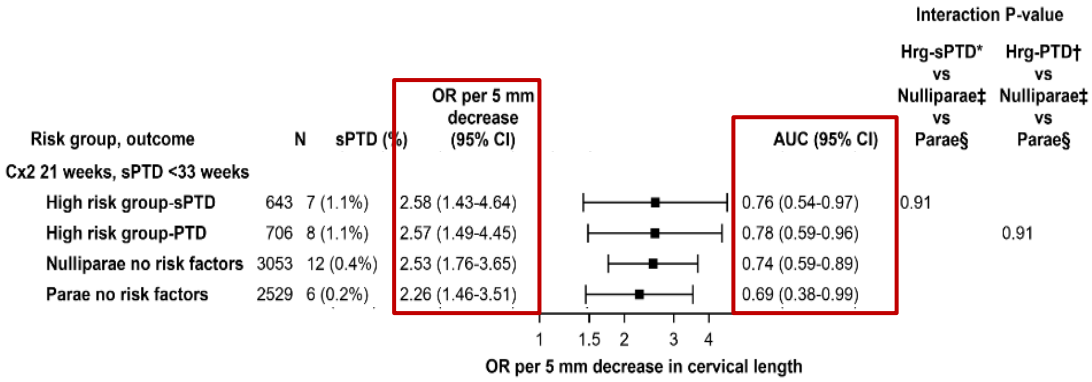
Is the effect of cervical length on the risk of sPTB the same in all asymptomatic women with a singleton pregnancy?

The effect of cervical length at 21-23 weeks on the risk of sPTD <33 weeks expressed as odds ratio per 5 mm decrease in cervical length



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The ability of cervical length measured at 21+0 to 23+6 weeks (Cx2, n=6288) to predict spontaneous preterm delivery <33 weeks

		Cervical length ≤25 mm			
Risk group	**Cervix ≤25 mm %**	**Sensitivity %**	**Specificity %**	**FP/TP**	**NNS**
High risk group-sPTD n=643	11.7	57	88.8	18	161
High risk group-PTD n=706	11.2	50	89.3	19	177
Nulliparae no risk factors n=3053	3.6	25	96.4	36	1018
Parae no risk factors n=2529	3.2	50	96.8	27	843

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