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Jävsdeklaration

Jag har inga intressekonflikter att deklarera

RESEARCH ARTICLE

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Associations between cervical intraepithelial neoplasia during pregnancy, previous excisional treatment, cone-length and preterm delivery: a register-based study from western Sweden

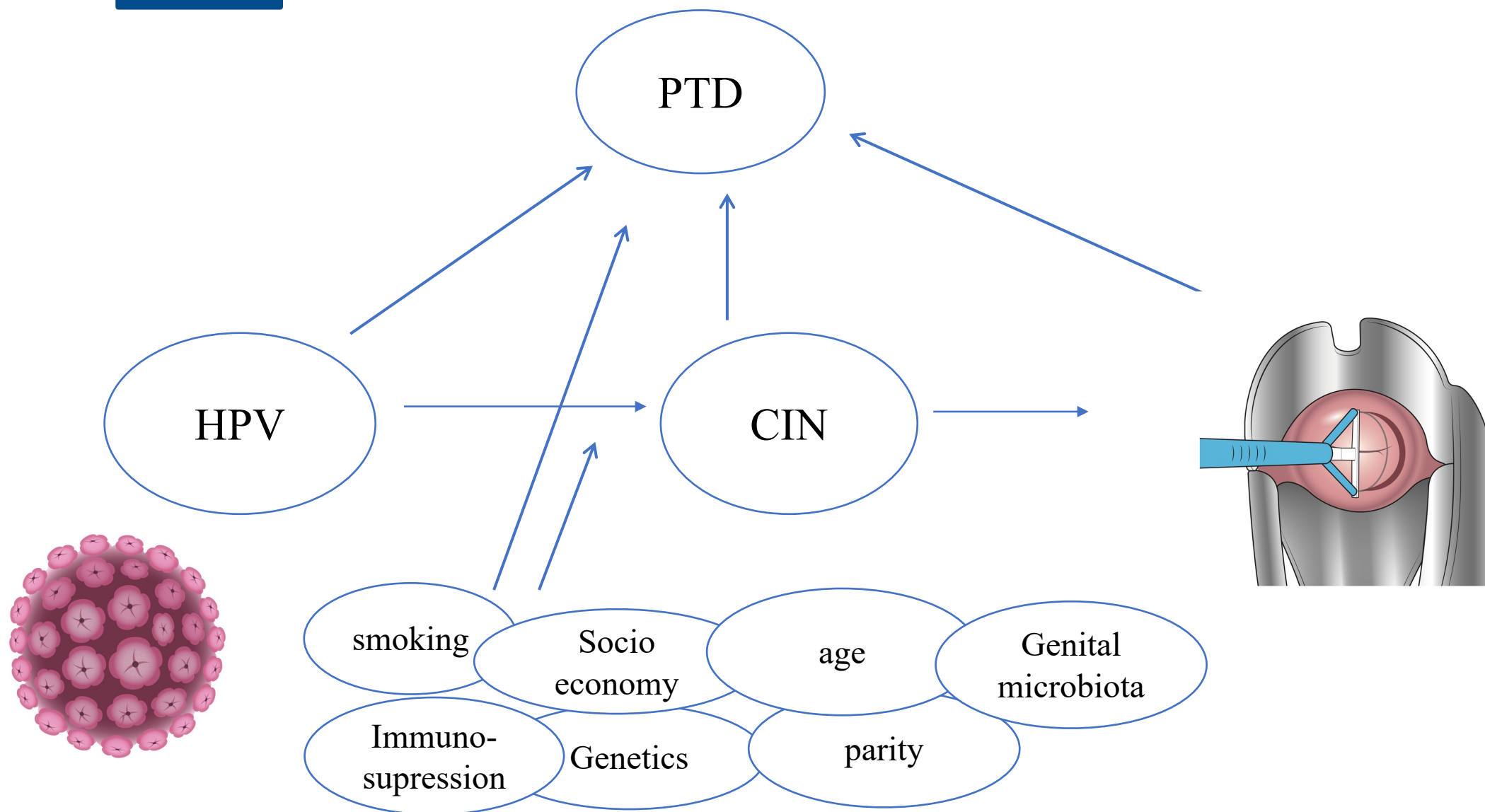


Johanna Wiik^{1,2,3*} , Cecilia Kärrberg^{1,3,4} , Staffan Nilsson^{5,6} , Björn Strander^{1,4} , Bo Jacobsson^{1,3,7}  and Verena Sengpiel^{1,3} 



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Background



Background

Why is excision associated with PTD?

Effect of the treatment

Mechanical weakness?

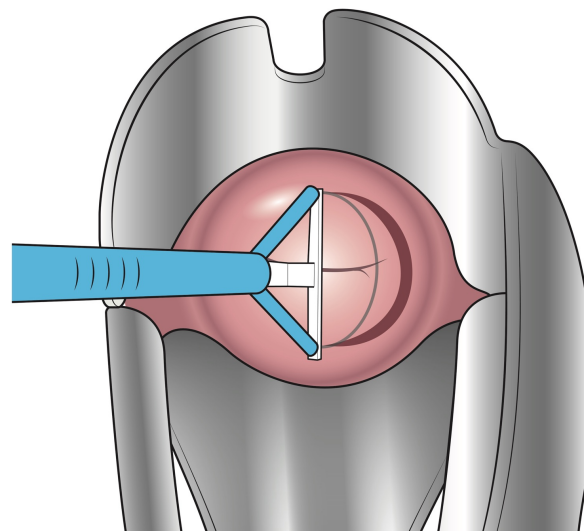
Elasticity?

Inflammation cervix?

Immunomodulation cervix?

Change in cervical microbiota?

Increased risk for ascending bacterial infection?



Other factors

HPV – effect?

Co-variates CIN?

Genetics?

Background

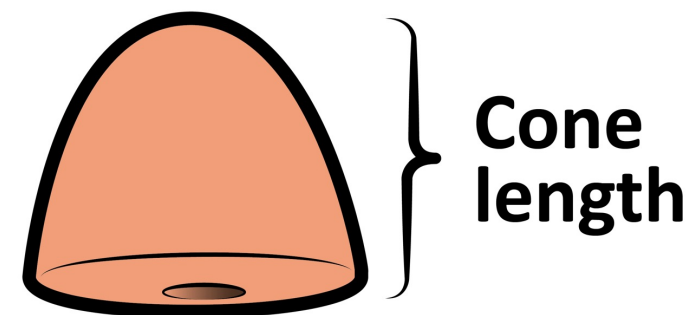
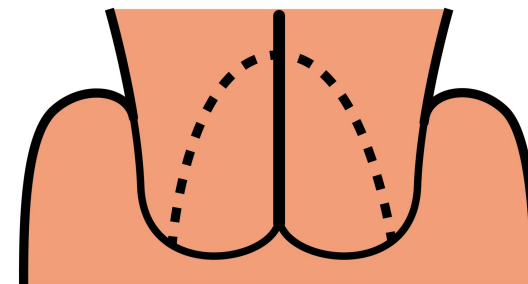
Risk of PTD increase with

- size of excision / cone length

The risk for PTD is uncertain in women with

small treatments ≤ 10 mm

AND compared to women with untreated CIN

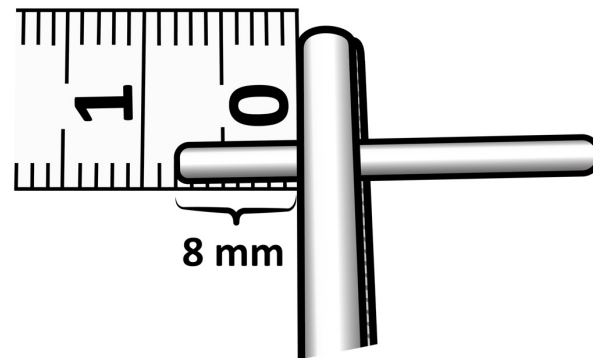
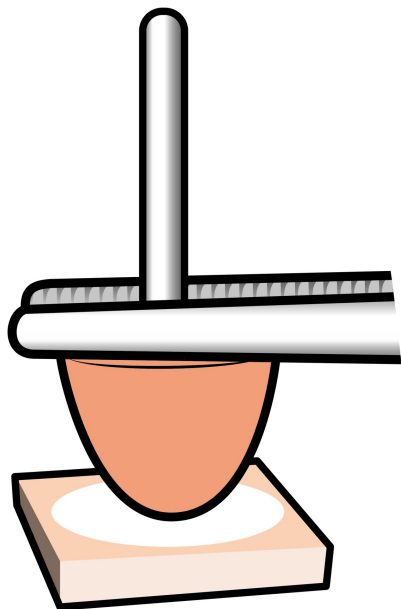


Background

No previous studies on treatment with cone lengths

- measured on fresh samples
- compared to CIN diagnosed during pregnancy

Background / Methods



Measured in fresh tissue since 2008

Aim

- 1) CIN during pregnancy
- 2) Excisional treatment before pregnancy



PTD or
other adverse obstetric and neonatal outcomes

cone length at treatment measured on fresh specimens

Exposure (2008-2016)	Outcome (2008-2016)	Covariates / Confounders
Swedish National Board of Health and Welfare (Socialstyrelsen)		
The Swedish Cancer Register	The Swedish Medical Birth Register (MBR)	The Swedish Medical Birth Register (MBR)
Statistics Sweden		
The Swedish National Cervical Screening Registry (NKCx)		The Swedish Register of Education
		The Total Population Register
		The Income and Tax Assessment Register



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Methods

Study groups

Treated Group

Previous excisional
treatment

N=3,250

Cone lengths
N=2,408

Normal Cervical Cytology Group

Always normal
cytology

N=42,398

CIN during pregnancy Group

Untreated CIN
diagnosed during
pregnancy

N=1,380

Associations between cervical intraepithelial neoplasia during pregnancy, previous excisional treatment, cone-length and preterm delivery: a register-based study from western Sweden

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Results

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	Normal cytology (N=42,398)	CIN during pregnancy (N=1,380)	Unadjusted analyses		Adjusted analyses	
Outcome	%	%	OR	p-value	aOR	p-value
PTD	4.2%	5.4%	1.28	0.041	1.21	0.12
Spontaneous PTD	3.0%	3.6%	1.20	0.22	1.13	0.43
pPROM	1.1%	1.4%	1.29	0.27	1.22	0.39
PROM ≥ 37 weeks	5.1%	5.3%	1.03	0.81	0.95	0.66



Results

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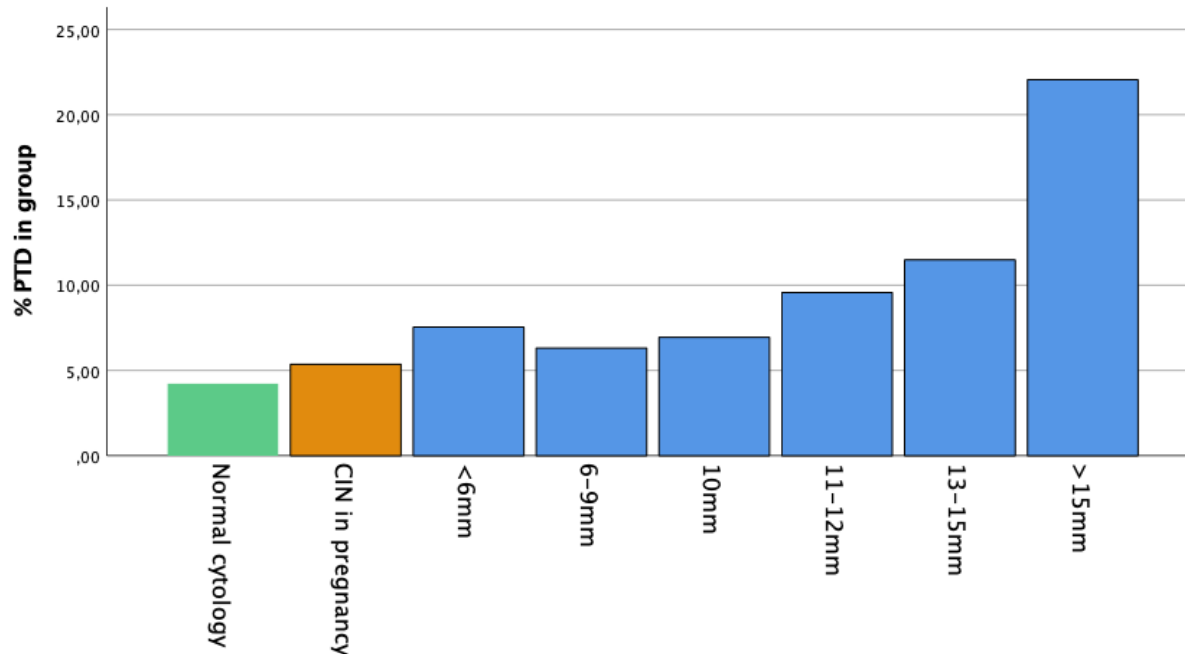
	Treated (N=3,250)	Normal Cytology (N=42,398)	Adjusted analyses		CIN in pregnancy (N=1,380)	Adjusted analyses	
Outcome	%	%	aOR (95% CI)	p-value		aOR (95% CI)	p-value
PTD	7.5%	4.2%	1.75 (1.51-2.01)	<0.001	5.4%	1.60 (1.21-2.12)	0.001
Spontaneous PTD	6.0%	3.0%	2.00 (1.70-2.34)	<0.001	3.6%	1.95 (1.40-2.72)	<0.001
pPROM	3.2%	1.1%	2.63 (2.11-3.28)	<0.001	1.4%	2.74 (1.66-4.51)	<0.001
PROM ≥ 37 weeks	6.9%	5.1%	1.23 (1.06-1.43)	0.008	5.3%	1.38 (1.03-1.85)	0.030



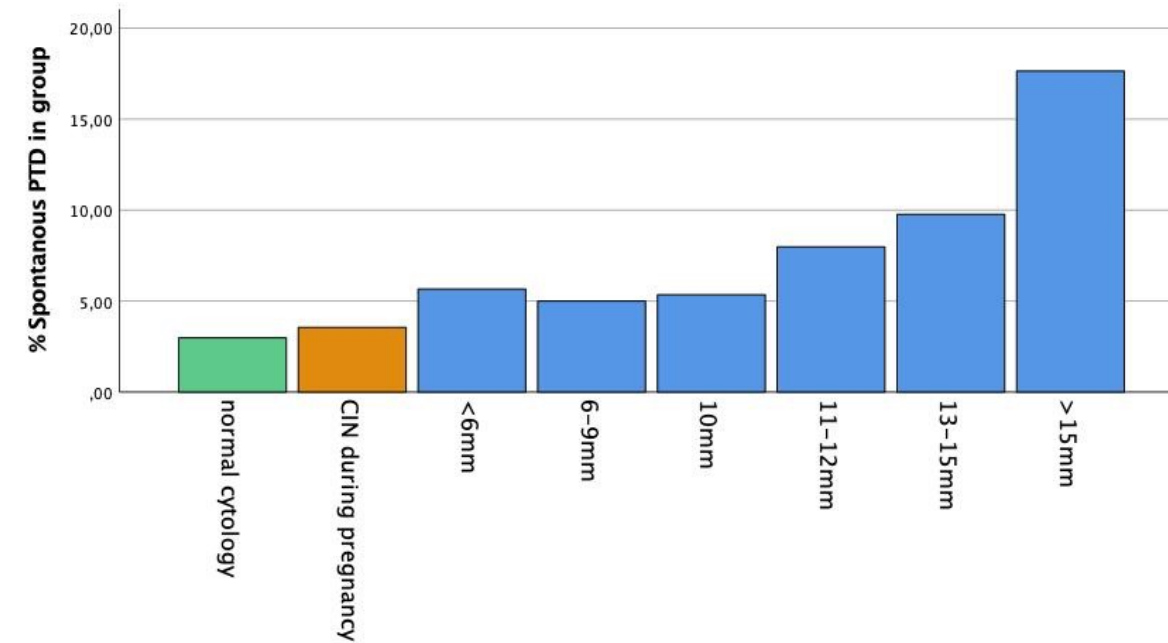
Results

Cone Length 3-31 mm
Mean 9.09 (SD 2.99)

PTD increased with cone length



Normal cytology, CIN in pregnancy and different Cone Length groups



normal cytology, CIN during pregnancy and different cone length groups

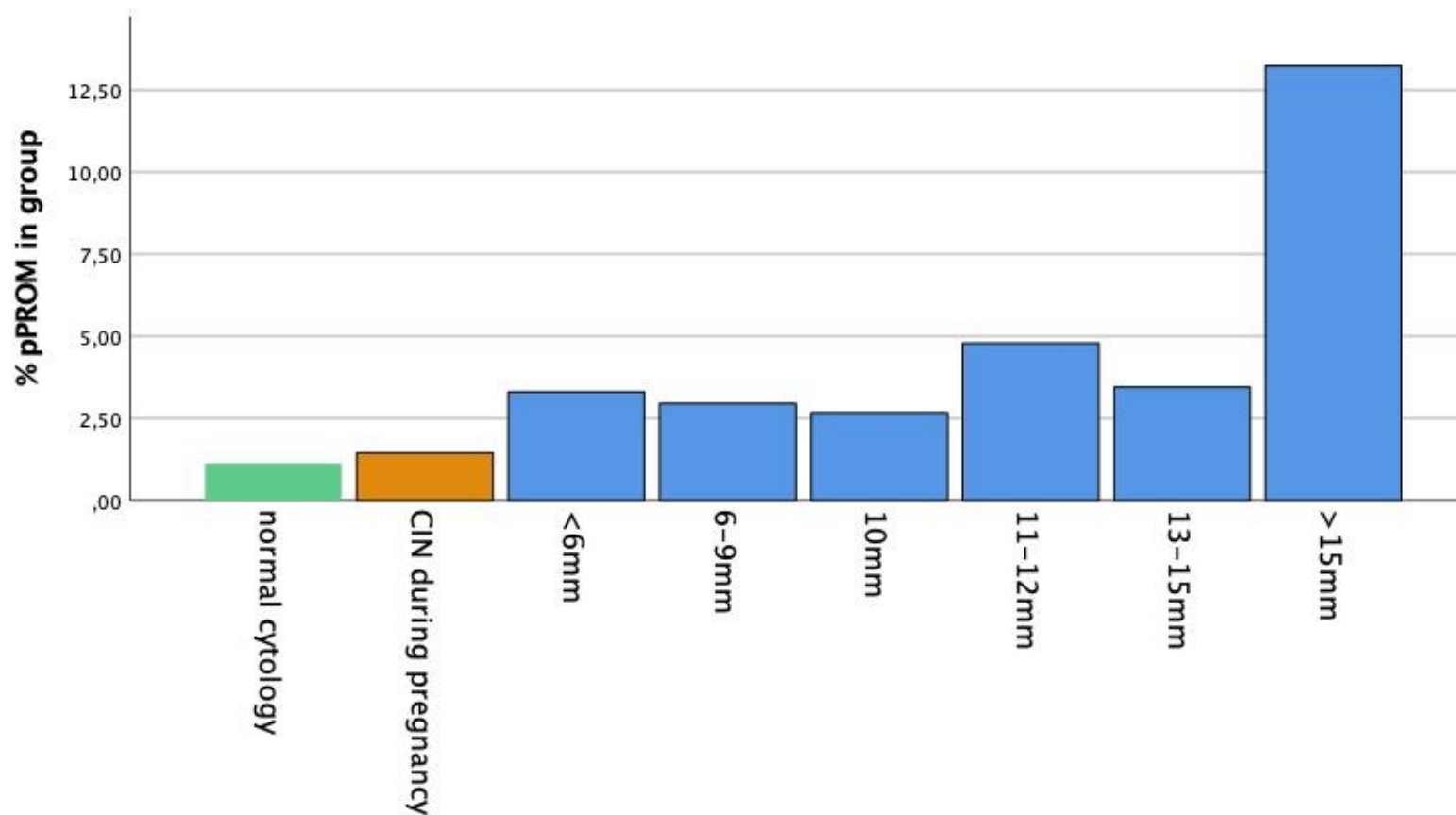
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Results

pPROM increased with cone length



normal cytology, CIN during pregnancy and different cone length groups

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	Normal cytology N=42,398	Treated, ≤10mm N=1,805			Treated, 11-12mm N=361			Treated, 13-15mm N=174			Treated, >15mm N=68		
	n %	n %	aOR ¹	p	n %	aOR	p	n %	aOR ¹	p	n %	aOR	p
PTD	1,794 4.2%	119 6.6%	1.5 (1.3-1.9)	<0.001	33 9.1%	2.2 (1.5-3.2)	<0.001	20 11.5%	2.8 (1.7-4.5)	<0.001	15 22.1%	5.9 (3.3-10.6)	<0.001
Spontaneous PTD	1,264 3.0%	93 5.2%	1.7 (1.4-2.2)	<0.001	27 7.5%	2.6 (1.7-3.9)	<0.001	17 9.8%	3.4 (2.1-5.7)	<0.001	12 17.6%	6.63 (3.5-12.5)	<0.001
pPROM	479 1.1%	53 2.9%	2.3 (1.7-3.1)	<0.001	15 4.2%	3.4 (2.0-5.8)	<0.001	6 3.4%	2.8 (1.2-6.4)	0.014	9 13.2%	11.68 (5.6-24.2)	<0.001
PROM ≥ 37 weeks	2,084 5.1%	113 6.7%	1.2 (1.0-1.4)	0.12	30 9.1%	1.7 (1.1-2.5)	0.009	9 5.8%	1.1 (0.6-2.2)	0.81	10 18.9%	4.1 (2.0-8.3)	<0.001



Results

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	Normal cytology N=42,398	Treated, <6mm N=212			Treated, 6-9 mm N=1,219			Treated, 10mm N=374		
	n %	n %	aOR ¹	p	n %	aOR ¹	p	n %	aOR ¹	p
PTD	1,794 4.2%	16 7.5%	1.7 (1.0-2.9)	0.038	77 6.3%	1.5 (1.2-1.9)	0.002	26 7.0%	1.6 (1.1-2.4)	0.028
Spontaneous PTD	1,264 3.0%	12 5.7%	1.8 (1.0-3.3)	0.044	61 5.0%	1.7 (1.3-2.2)	<0.001	20 5.3%	1.8 (1.1-2.8)	0.017
pPROM	479 1.1%	7 3.3%	2.6 (1.2-5.5)	0.016	36 3.0%	2.4 (1.7-3.3)	<0.001	10 2.7%	2.1 (1.1-3.9)	0.026
PROM ≥ 37 weeks	2,084 5.1%	11 5.6%	0.9 (0.5-1.7)	0.81	79 6.9%	1.2 (0.97-1.6)	0.09	23 6.6%	1.1 (0.7-1.8)	0.55

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Risk for PTD was also increased in treatments ≤ 10 mm

	Treated with cone length ≤ 10 mm N=1,805	CIN in pregnancy group N=1,380	Adjusted analyses	
Outcomes	N (%)	n (%)	aOR (95% CI)	p
PTD <37 weeks	119 (6.6)	74 (5.4)	1.41 (1.02-1.94)	0.038
Spontaneous PTD	93 (5.2)	49 (3.6)	1.73 (1.18-2.54)	0.005
pPROM	53 (2.9)	20 (1.4)	2.44 (1.40-4.28)	0.002



Results

Truncated analyses of $\leq 10\text{mm}$

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	n	aOR (95% CI) ¹	p
PTD	187	1.15 (1.09-1.23)	<0.001
Spontaneous PTD	149	1.18 (1.10-1.25)	<0.001
pPROM	83	1.18 (1.09-1.28)	<0.000
PROM ≥ 37 weeks	162	1.14 (1.05-1.22)	0.001
Chorioamnionitis	9	0.99 (0.74-1.34)	0.97
Neonatal sepsis	45	1.19 (1.07-1.33)	0.002

Risk for PTD increased with 15 % for each millimeter cone length



Conclusion

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- All excisional treatments, **even small ones**, are associated with an increased risk for **PTD**, **spontaneous PTD** and **pPROM**
- Risks increase with increased **cone length**
- Small excisions, **up to 10 mm**, were associated with an increased risk of **PTD**, of about **50%**, and the risk increased further with **cone length** with about **15%** for every extra millimeter cone length



Conclusion

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- Risk for **PROM** \geq 37 weeks and **neonatal sepsis** also increase with **cone length**
- Women with **CIN in pregnancy** also seem to have an increased risk for **PTD**
- Cone length should be measured on fresh samples at treatment in a standardized manner
 - and be available for risk estimation at antenatal surveillance.

Tack!



Medförfattare

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