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**Obstetric outcomes after excisional
procedures: Universal cerclage or close
follow-up**

Tevfik GUVENAL, M.D

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Overview

- The majority of women diagnosed with cervical dysplasia are of childbearing age.
- The average age of women with CIN is between 25 and 30 years of old.
- The impact of excisional treatment of CIN on the outcomes of subsequent pregnancies has been an area of active research for the past decade.

Excisional Procedures

- Loop electrosurgical excisional procedure (LEEP, LLETZ)
- Cold Knife Conisation (CKC)
- Laser conization

- LEEP is the most commonly used treatment technique for CIN.

Adverse obstetric outcomes

- Preterm birth
- Premature rupture of the membranes
- Low birth weight
- Admission to neonatal intensive care
- Perinatal mortality

Randomised Control Trials

**Systematic Reviews and Meta-analyses
Cohort trials
(Retrospective)**

Conisation, LEEP

No treatment

Preterm delivery rates

Preterm delivery rates

Obstetric outcomes after conservative treatment for intraepithelial or early invasive cervical lesions: systematic review and meta-analysis

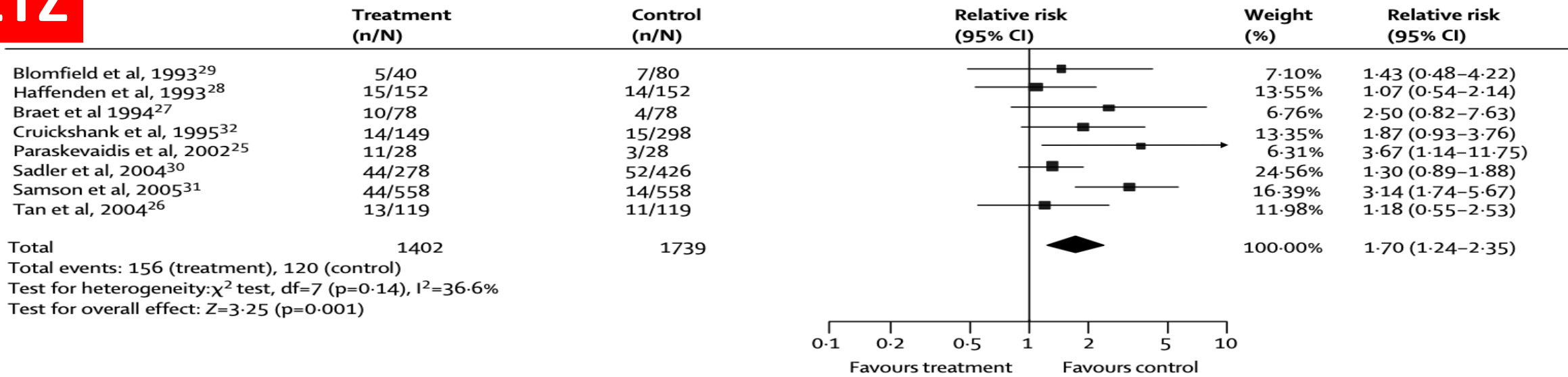


Lancet 2006; 367: 489–98

M Kyrgiou, G Koliopoulos, P Martin-Hirsch, M Arbyn, W Prendiville, E Paraskevaidis

Data from 27 studies

- ✓ CKC and LEEP were associated with a significant increase in the risk of preterm delivery, low birthweight, and pPROM
- ✓ It was concluded that all excisional treatment procedures might be associated with adverse pregnancy outcomes



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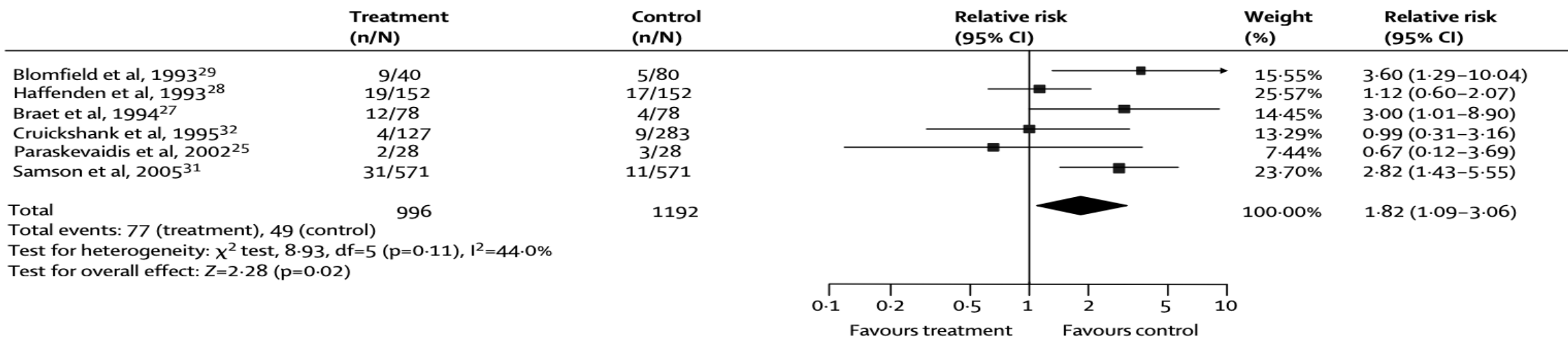


Figure 1: Forest plot showing association between LLETZ and (A) preterm delivery and (B) low birthweight

Figure 4: Forest plot showing association between cold knife conisation and (A) preterm delivery and (B) low birthweight

BMJ 2008

Perinatal mortality and other severe adverse pregnancy outcomes associated with treatment of cervical intraepithelial neoplasia: meta-analysis

M Arbyn, head of unit of cancer epidemiology¹, leader, working package HPV screening,²
 M Kyrgiou, assistant,³ C Simoens, assistant,¹ A O Raifu, assistant,¹ G Koliopoulos, senior lecturer,⁴
 P Martin-Hirsch, consultant gynaecological oncologist,³ W Prendiville, associated professor,⁵
 E Paraskevaidis, head of department⁴

	CKC	> LC	> LLETZ	> LA
Excised Cx Volume:				
PD (<37/40)	✓	✓	✓	X
Severe PD (<32/40)	✓	-	X	X
Extreme PD (<28/40)	✓	-	X	X
PM	✓	✓	X	X

Pregnancy outcome after cervical conisation: a retrospective cohort study in the Leuven University Hospital

BJOG 2009

A van de Vijver,^a W Poppe,^b J Verguts,^b M Arbyn^c

599 women
(LLETZ, laser or cold knife)
55 pregnancy after postcon. vs
55 control

Leuven-1 study

Table 4. Pregnancy outcome (dichotomic variables)

Variable	Study group		Control group		P-value
	Number	%	Number	%	
Preterm delivery (<37 weeks)	14/55	25.5	2/55	3.6	0.002
Severe preterm delivery (<34 weeks)	6/55	10.9	0/55	0	0.031
Complications during pregnancy	22/55	40	14/55	25.5	0.15
PPROM	5/55	9.1	1/55	1.8	0.20
Preterm contractions	5/55	9.1	0/55	0	0.057
Use of oxytocin	16/44	36.4	17/55	30.9	0.67



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journal homepage: www.elsevier.com/locate/ejogrb



Full length article

Pregnancy outcome after cervical conisation: A 2nd retrospective cohort study in the Leuven University Hospital

Kim van Velthoven^{a,*}, Willy Poppe^a, Hannah Verschuere^a, Marc Arbyn^b

97 women with excisional treatment (mostly LLETZ)

No increase in preterm birth rate after conisation

No relationship between volume or depth of the cone and preterm birth could be found.

A significant decrease in all dimensions was observed with time



2017

Leuven-2 study

Loop Electrosurgical Excision Procedure and Risk of Preterm Birth: A Systematic Review and Meta-analysis

Shayna N. Conner, MD^{*,1}, Heather A. Frey, MD¹, Alison G. Cahill, MD, MSCI¹, George A. Macones, MD, MSCE¹, Graham A. Colditz, MD, DrPH², and Methodius G. Tuuli, MD, MPH¹

¹Department of Obstetrics and Gynecology, Washington University in St. Louis

²Department of Surgery, Washington University in St. Louis

- 1. women with a history of LEEP**
- 2. women with unknown or no history of cervical dysplasia**
- 3. women with history of cervical dysplasia, but no cervical excision**

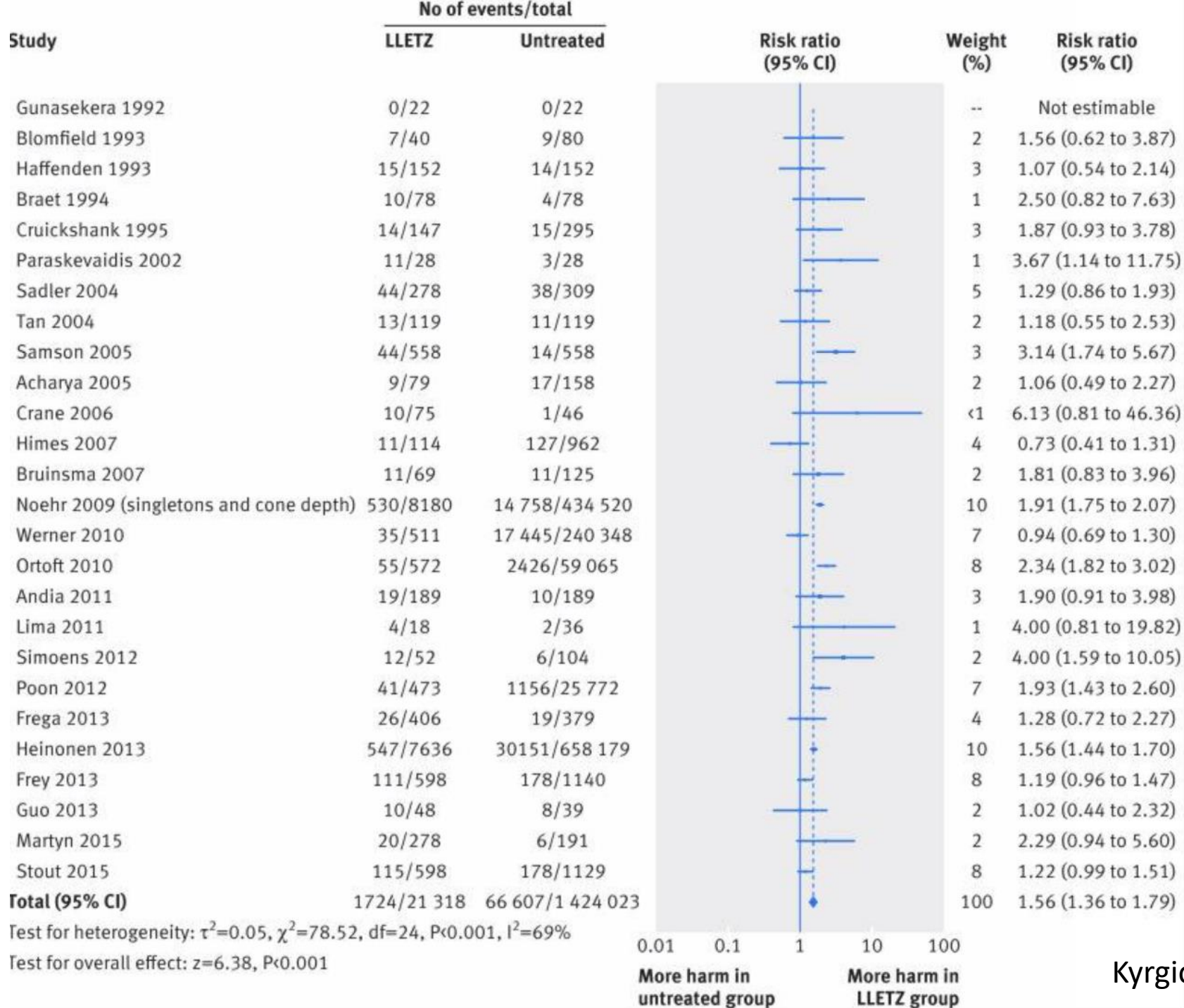
Conclusion—Women with history of LEEP have similar risk of preterm birth when compared to women with prior dysplasia, but no cervical excision. Common risk factors for both preterm birth and dysplasia likely explain findings of association between LEEP and preterm birth, but LEEP itself may not be an independent risk factor for preterm birth.

Adverse obstetric outcomes after local treatment for cervical preinvasive and early invasive disease according to cone depth: systematic review and meta-analysis

Kyrgiou, M. et al.

71 studies (6 338 982 participants; 65 082 treated/6 292 563 untreated).

Conclusions Women with CIN have a higher baseline risk for prematurity. Excisional and ablative treatment further increases that risk. The frequency and severity of adverse sequelae increases with increasing cone depth and is higher for excision than for ablation.





Obstetric outcomes after conservative treatment for cervical intraepithelial lesions and early invasive disease (Review)

Kyrgiou M, Athanasiou A, Kalliala IEJ, Paraskevaidi M, Mitra A, Martin-Hirsch PPL, Arbyn M,

(Authors listed in order of contribution)

Authors' conclusions

Women with CIN have a higher baseline risk for prematurity. Excisional and ablative treatment appears to further increase that risk.

The frequency and severity of adverse sequelae increases with increasing cone depth and is higher for excision than it is for ablation.

However, the results should be interpreted with caution as they were based on low or very low quality (GRADE assessment) observational studies, most of which were retrospective.

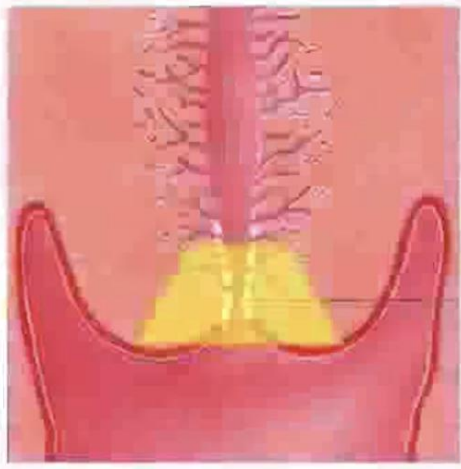
Deeper Excision, Greater Risk

- The risk of preterm birth increases with increasing cone depth (“dose effect”).
 - Risk was higher after CKC
- The risk was increased
 - twofold for excisions of more than 10 mm,
 - threefold for more than 15-17 mm, and
 - fivefold for excisions exceeding 20 mm in depth.
- LEEP removed an average 11.2 ± 3.8 mm (a mean cervical length of 29.5 ± 4.0 mm)

The treatment effect increased with increasing Tx cone length/volume...

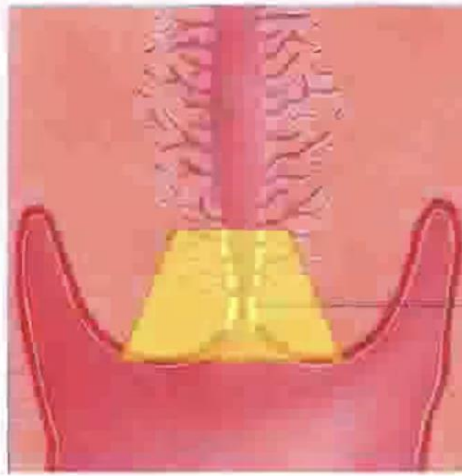
<10/12mm

1.54 [1.09, 2.18]



>10/12mm

1.93 [1.62, 2.31]



>15/17mm

2.77 [1.95, 3.93]



>20mm

4.91 [2.06, 11.68]



Risk ratio
(95% CI)



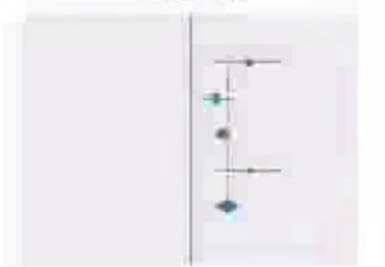
0.01 0.1 1 10 100
More harm in untreated group More harm in treated group

Risk ratio
(95% CI)



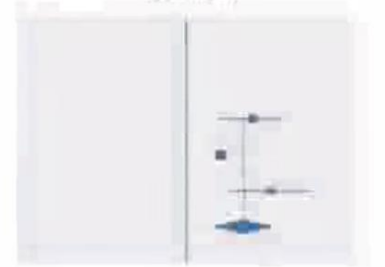
0.01 0.1 1 10 100
More harm in untreated group More harm in treated group

Risk ratio
(95% CI)



0.01 0.1 1 10 100
More harm in untreated group More harm in treated group

Risk ratio
(95% CI)



0.01 0.1 1 10 100
More harm in untreated group More harm in treated group

Pregnancy outcome following loop electrosurgical excision procedure (LEEP) a systematic review and meta-analysis

**Gong Jin · Zhang LanLan · Chen Li ·
Zhang Dan**

Conclusions: LEEP is associated with an increased risk of subsequent preterm delivery ($\leq 32/34$, ≤ 28 weeks) and other serious pregnancy outcomes. But increasing LEEP volume or depth is not associated with an increased rate of preterm birth.

Cervical length after LEEP treatment

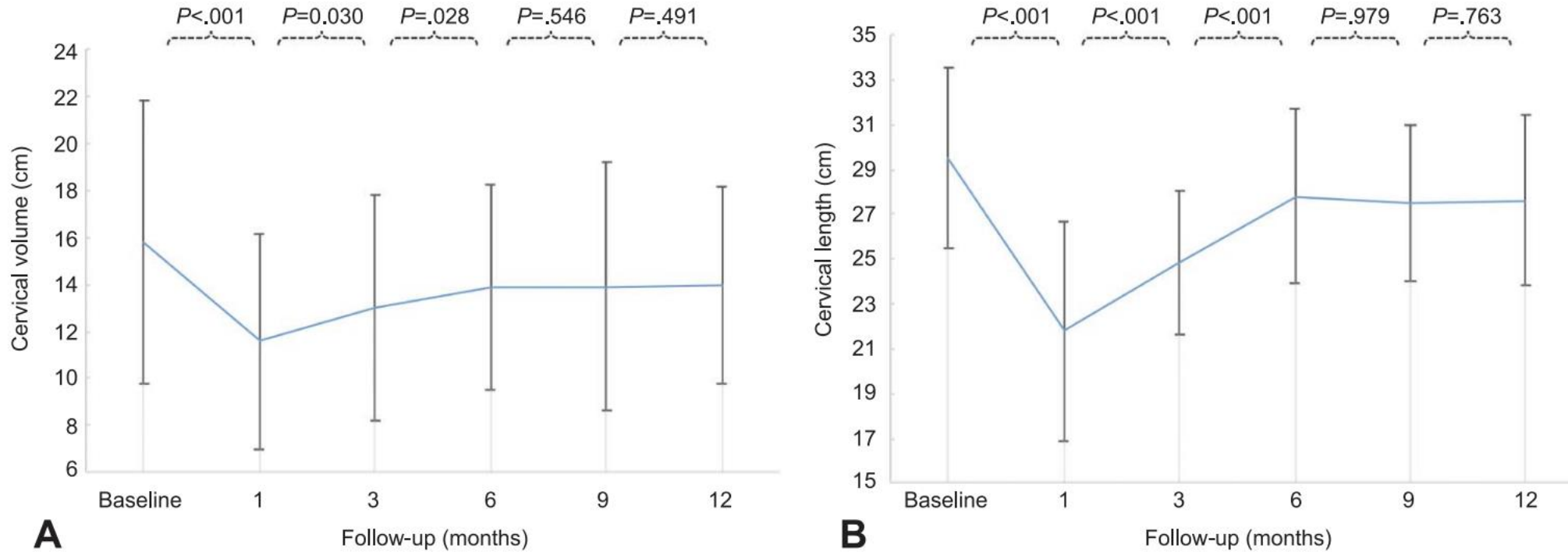


Fig. 3. Serial changes in cervical volume (**A**) and length (**B**) during 1-year follow-up after loop electrosurgical excision procedure.

What causes of preterm birth after CIN treatment?

- The mechanical weakness secondary to loss of cervical tissue (shortened cervix)
- Immunomodulation relating to HPV infection affecting parturition pathways
- Altering cervicovaginal bacterial flora (cervicovaginal microbiota)

What are the strategies to prevent of preterm delivery after exicional treatments?

Strategies to prevent preterm delivery...

- Cervical cerclage
- Progesterone treatment
- Pessary

Cervical Cerclage

- Many obstetricians believe that preterm birth following cervical excision is a result of 'cervical weakness', which can be corrected by cerclage.
- The rate of cervical cerclage insertion was higher for treated for CIN than non-treated women 4.0% v 0.7%.
- To date, there is no randomized trial to evaluate the effect of prophylactic cervical cerclage after conization.

The role of prophylactic cerclage in preventing preterm delivery after electrosurgical conization

Mi-Young Shin, Eun-Sung Seo, Suk-Joo Choi, Soo-Young Oh,
Byoung-Gie Kim, Duk-Soo Bae, Jong-Hwa Kim, Cheong-Rae Roh

Department of Obstetrics and Gynecology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

Retrospective study,
56 pregnant (postconisation)
25 women with cerclage
31 were managed expectantly

Preterm Birth rates

CL \leq 25 mm (cerclage): 12/25 (48%)

CL \leq 25 mm (no cerclage): 7/31 (23%)

CL \leq 20 mm (cerclage): 7/25 (28%)

CL \leq 20 mm (no cerclage): 4/31 (13%)

NS

Conclusion: The rate of preterm delivery was significantly higher in women with a history of electrosurgical conization before pregnancy. However, prophylactic cervical cerclage did not prevent preterm delivery in these patients.

Table 1. Comparison of demographic characteristics and antenatal parameters between the expectant group and cerclage group

	Expectant (n=31)	Cerclage (n=25)	p-value
Age (yr)	32 (28-40)	30 (24-41)	0.136
Height (cm)	162.0 (153.0-172.0)	162.0 (147.0-172.0)	0.535
Weight (kg)	67.0 (51.8-87.2)	62.0 (49.4-81.0)	0.052
Nulliparity	8 (25.8)	13 (52.0)	0.044
History of preterm delivery*	2 (6.5)	2 (8.0)	1.000
Abortion history*	4 (12.9)	3 (12.0)	1.000
IVF-ET pregnancy*	0 (0.0)	2 (8.0)	0.195
Smoking*	1 (3.2)	1 (4.0)	1.000
Indication for conization			
CIN I*	7 (22.6)	3 (12.0)	0.485
CIN II*	5 (16.1)	6 (24.0)	0.514
CIN III	10 (32.3)	7 (28.0)	0.730
CIS	9 (29.0)	9 (36.0)	0.579
Cone depth (cm)	2.0 (1.0-3.0)	2.0 (1.3-3.2)	0.635
Cervical length (cm)	3.0 (1.5-5.8)	2.6 (1.1-3.4)	0.008
≤2.5	7 (22.6)	12 (48.0)	0.055
≤2.0	4 (12.9)	7 (28.0)	0.176
Funneling	1 (3.3)	2 (8.0)	0.585
Interval between conization and pregnancy (mo)	19 (1-55)	19 (3-96)	0.471

Table 2. Comparison of obstetric outcomes between the expectant group and the cerclage group

	Expectant (n=31)	Cerclage (n=25)	p-value
Antepartum bleeding episode*	0 (0.0)	3 (12.0)	0.083
Admission due to preterm labor	11 (35.5)	10 (40.0)	0.729
Frequency of admission due to preterm labor per patient	0 (0-2)	0 (0-2)	0.575
Admission duration for preterm labor per patient [†] (day)	11 (1-33)	8 (1-38)	0.750
Tocolytics use	8 (25.8)	7 (28.0)	0.854
Antenatal corticosteroid use	6 (19.4)	6 (24.0)	0.674
Gestational age at delivery (wk)	38.0 (27.3-40.4)	38.2 (25.0-40.6)	0.788
Preterm delivery* (wk)			
Before 28	2 (6.5)	2 (8.0)	1.000
Before 34	6 (19.4)	5 (20.0)	1.000
Before 37	9 (29.0)	9 (36.0)	0.579
Preterm premature rupture of membranes (wk)			
Before 28*	2 (6.5)	2 (8.0)	1.000
Before 32*	5 (16.1)	4 (16.0)	1.000
Before 34	7 (22.6)	5 (20.0)	0.815
Before 37	13 (41.9)	10 (40.0)	0.884
Delivery mode			
Vaginal delivery	18 (58.1)	9 (36.0)	0.100
Cesarean delivery	13 (41.9)	16 (64.0)	0.100
Emergency cesarean delivery*	9/13 (69.2)	11/16 (68.8)	1.000
Cesarean delivery indication			

Pregnancy outcome after cervical conization: risk factors for preterm delivery and the efficacy of prophylactic cerclage

Ka Hyun Nam, Ja Young Kwon, Young-Han Kim, Yong-Won Park

Department of Obstetrics and Gynecology, Yonsei University College of Medicine, Seoul, Korea

Retrospective study

65 cases who had received cervical conization,

Only 6 patients had cerclage

CL \leq 25 mm (cerclage): 3/6 (50%) CL \leq 25 mm (no cerclage): 16/59 (27%)

Conclusion: The type of conization, the volume of specimen, and second trimester cervical length may be the risk factors for preterm birth in patients who have a prior history of cervical conization. Prophylactic cerclage may not be helpful in preventing preterm birth, therefore more careful consideration should be paid in deciding cerclage after conization during prenatal counseling.

Cervical Cerclage

- The cerclage may itself be a risk factor for preterm delivery.
- Sutures can act as a foreign body which may cause uterine irritability and lead to contractions after a cerclage procedure.
- A significant increase of pathogenic flora in the vagina and cervix after cerclage

Cervical Cerclage

- Multifilament/braided sutures such as Mersilene tape have been traditionally used for cervical cerclage.
- These sutures favours bacterial colonisation over monofilament suture and is associated with poorer wound healing.

Henry-Stanley MJ, Surg Infect 2010
Fowler JR, Clin Orthop Relat Res. 2013
Kindinger LM, . Sci Transl Med. 2016
Mehta P, . Br J Ophthalmol. 2004
Slack M, Int Urogynecol J Pelvic Floor Dysfunct. 2006
Van Winkle W, Surg Gynecol Obstet. 1975

Interventions to Try to Prevent Preterm Birth in Women With a History of Conization: A Systematic Review and Meta-analyses

Marinela Grabovac, MD;¹ Anne Mary Lewis-Mikhael, MD; PhD;¹ Sarah D. McDonald, MD, MSc^{1,2,3}

¹Department of Obstetrics & Gynecology, McMaster University, Hamilton, ON

²Department of Health Research Methods, Evidence, and Impact, McMaster University, Hamilton, ON

³Department of Radiology, McMaster University, Hamilton, ON

To determine the role of cerclage, progesterone, and pessary,
To compare the effectiveness of these treatments

Table 3. Summary of secondary research question outcomes in systematic review/meta-analyses of preterm birth prevention after conization

Interventions vs. Number of Intervention Comparison

CONCLUSION

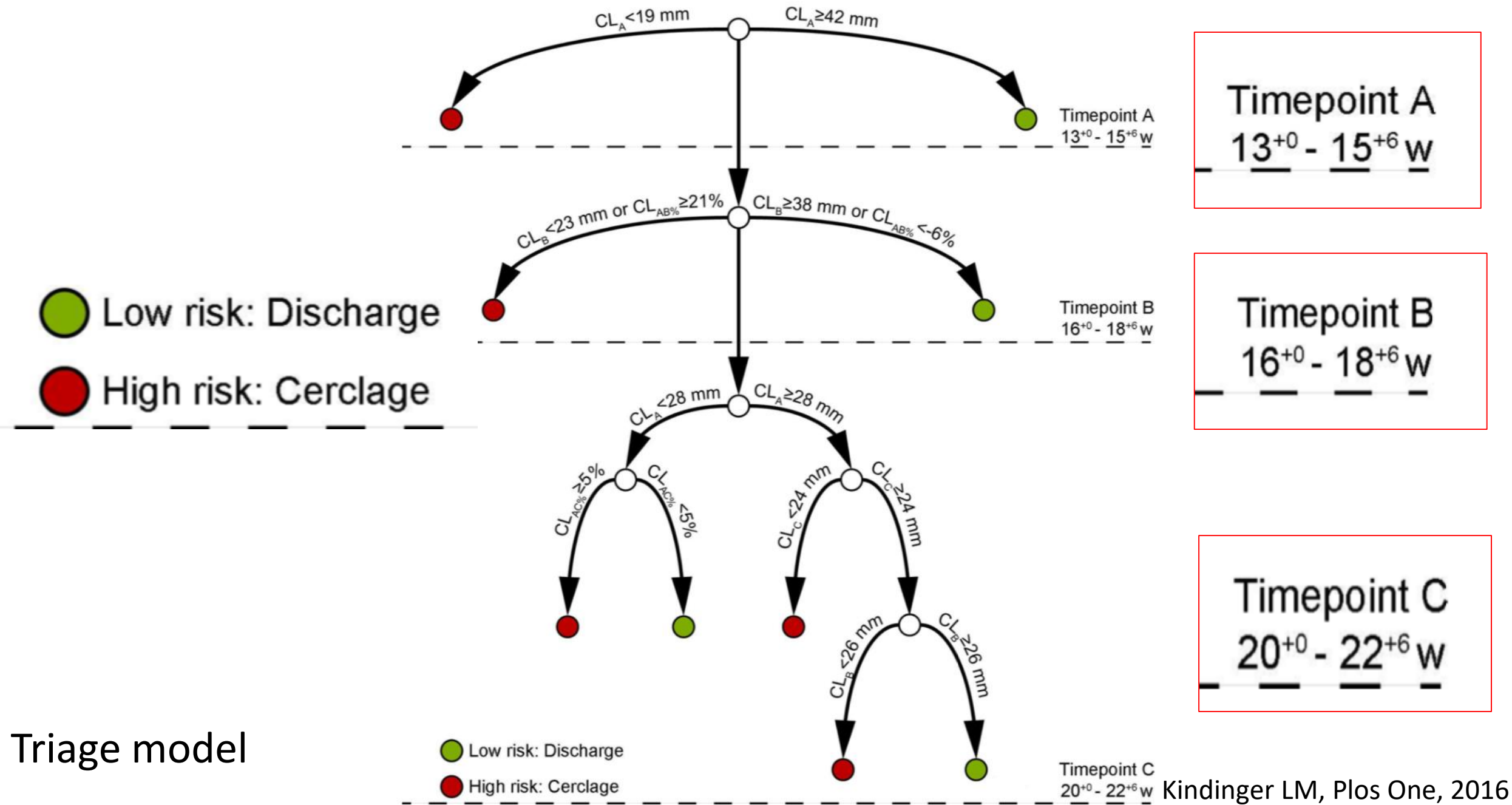
In women with a previous conization and a current singleton gestation, the existing evidence, which is likely limited due to confounding by indication, does not support cerclage or other interventions used to try to decrease preterm birth. Evidence from RCTs in this population is necessary.

Preterm Birth Prevention Post-Conization: A Model of Cervical Length Screening with Targeted Cerclage

Lindsay M. Kindinger^{1,2}, Maria Kyrgiou^{1,3*}, David A. MacIntyre¹, Stefano Cacciatore¹, Angela Yulia^{1,4}, Joanna Cook¹, Vasso Terzidou^{1,4}, T. G. Teoh^{1,2}, Phillip R. Bennett^{1,3}

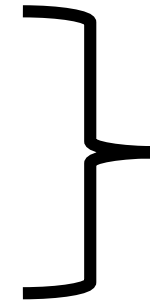
- to develop a triage prediction model to differentiate high-risk women for PD
- to evaluate the impact of suture material on the efficacy of ultrasound indicated cervical cerclage.

CONC: The rate of PD in women post-conization may be reduced by targeted cervical cerclage



A Triage screening model

- CL is <19 mm between 13 and 16 week
- CL is <23 mm between 16 and 19 week,
- CL is <26 mm between 20 and 23 weeks

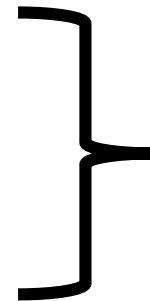


High Risk



Cerclage

- CL is ≥ 42 mm between 13 and 16 week,
- CL is ≥ 38 mm between 16 and 19 week
- CL is ≥ 26 mm between 20 and 23 weeks



Low Risk

CL is between 23-38 mm at 16-18 weeks, intermediate risk
(CL should re-evaluated at 20-23 week)

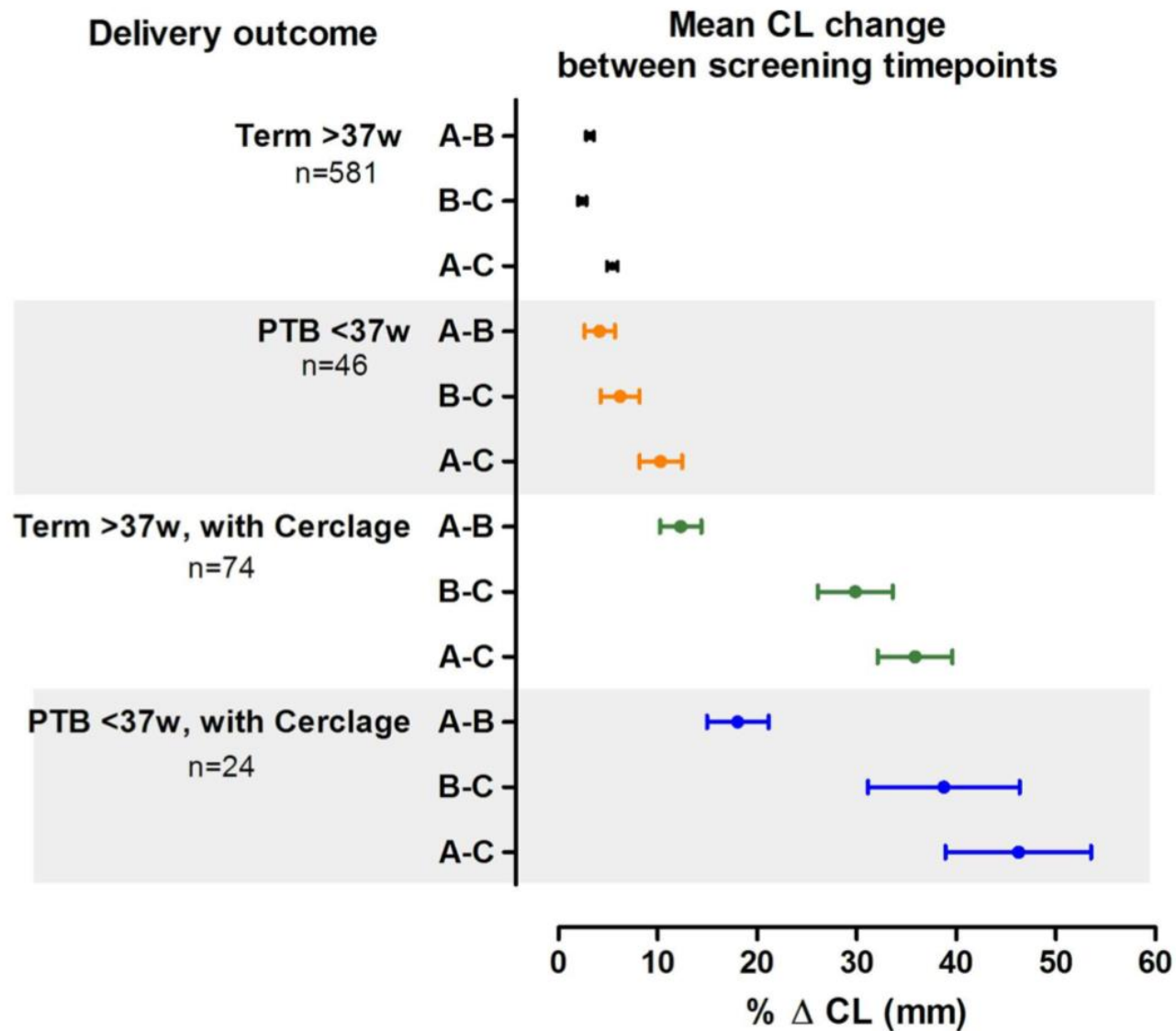


Fig 2. Mean difference in CL (mean % Δ CL) between time-points A: 13+0–15+6 weeks, B: 16+0–18+6 weeks, C: 20+0–22+6 weeks (A-B, B-C, and A-C) according to delivery outcome and cerclage insertion. In women receiving a cerclage, mean CL started above 25mm at timepoint A, and went on to shorten, most significantly at timepoint C. The greatest difference in CL is observed between timepoints B-C and A-C in those that received a cerclage and went on to deliver preterm <37weeks, followed by term delivery with a cerclage. (% Δ CL = percentage change in CL (mm) between screening time points; PTB = preterm birth <37 weeks; Screening time points = A: 13+0–15+6 weeks, B: 16+0–18+6 weeks, C: 20+0–22+6 weeks; SD = standard deviation; Term = birth >37 weeks; W = weeks).

Cervical cerclage

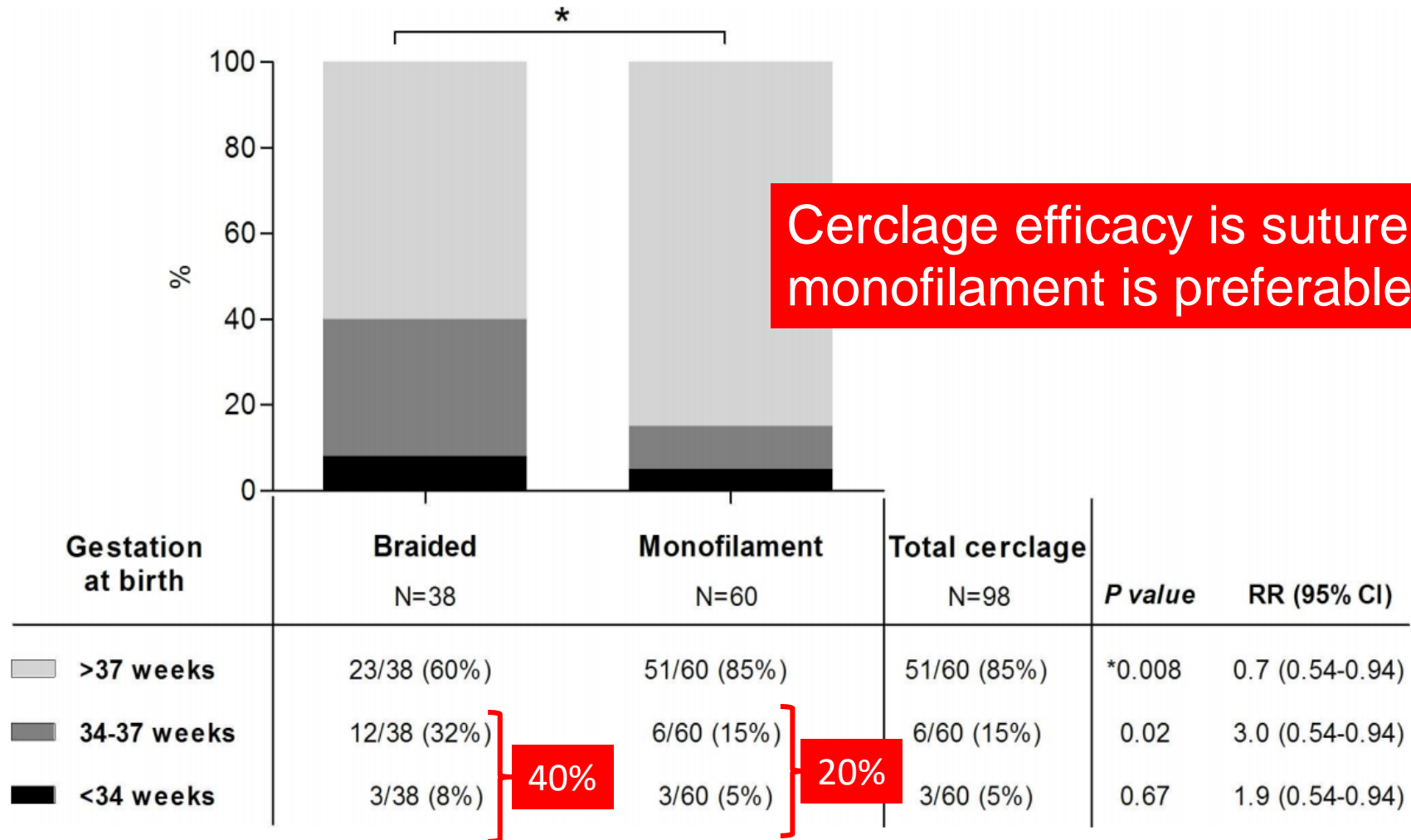


Fig 1. Gestation at delivery in women with an ultrasound-indicated cerclage for CL <25mm before 24weeks: a comparison of suture material braided versus monofilament. Preterm birth <37weeks was significantly higher ($P = 0.08$) in women with braided cerclages, compared to monofilament cerclages. This difference is most notable among those delivering late preterm birth (34-37weeks).

Conclusions

- Women with CIN have a higher baseline risk of preterm birth than women from the general population.
- Excisional treatment has been associated with an increased risk of preterm birth, perinatal morbidity, and mortality in a subsequent pregnancy.
- The risk of preterm delivery appears to be directly related to the depth of conization and the amount of cervical tissue removed.
- Unnecessary interventions, especially deep excisions in a woman of childbearing age, may do more harm than good.

Conclusions

- The efficacy and safety of the prophylactic cervical cerclage is still controversial.
- In pregnancy after postconisation, close observation, especially with the mid-trimester cervical length measurement is needed
- Cervical cerclage can be performed by using monofilament sutures in cases with short cervix (<25 mm) in the second trimester.
- Interventions such as progesterone treatment to prevent preterm birth after excisional treatment should investigate in future studies.

Thank you for your attention