



Impact of treatment on fertility



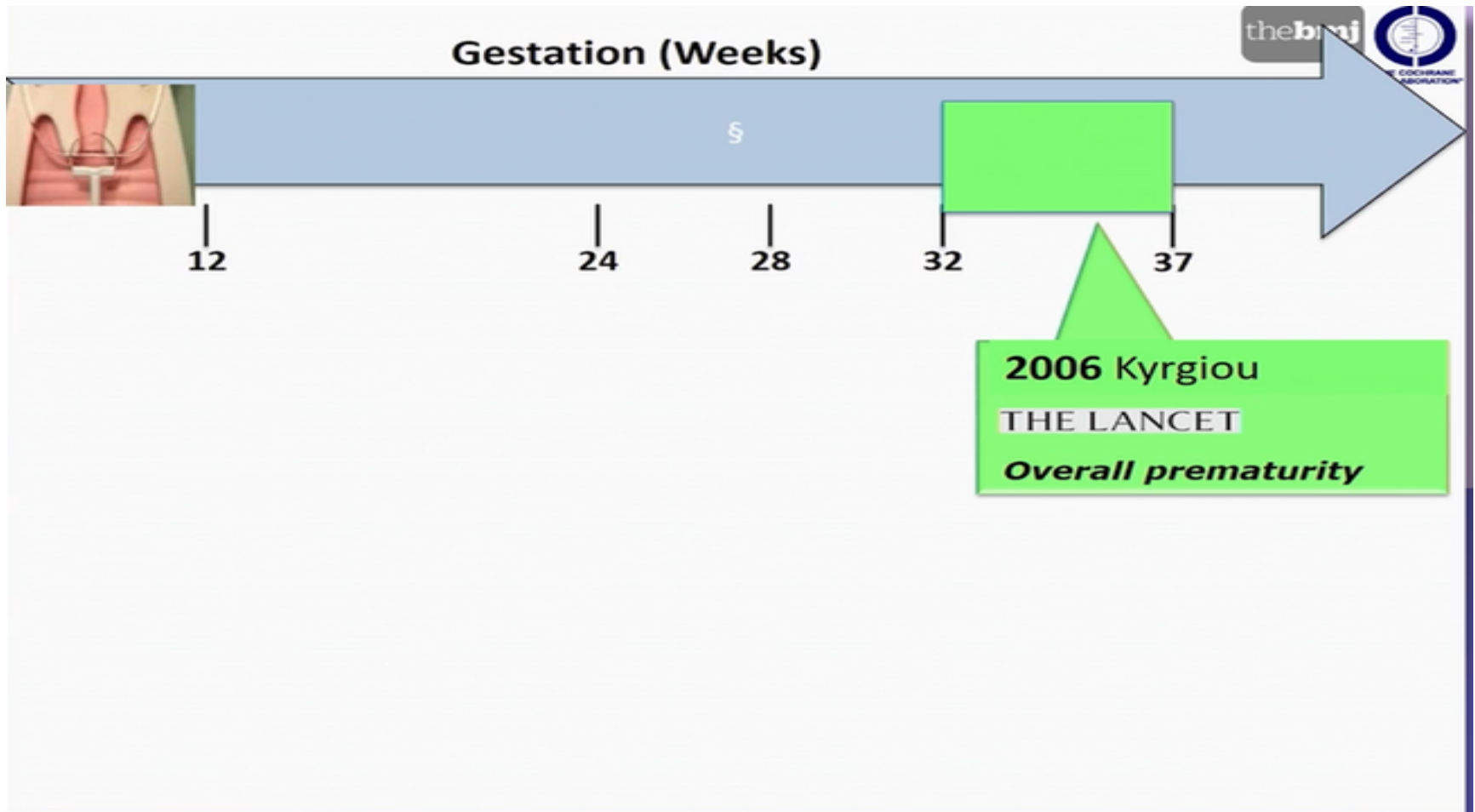
Outline



- Effect on fertility
- Effect on pregnancy
- Treatment considerations



What is the evidence?

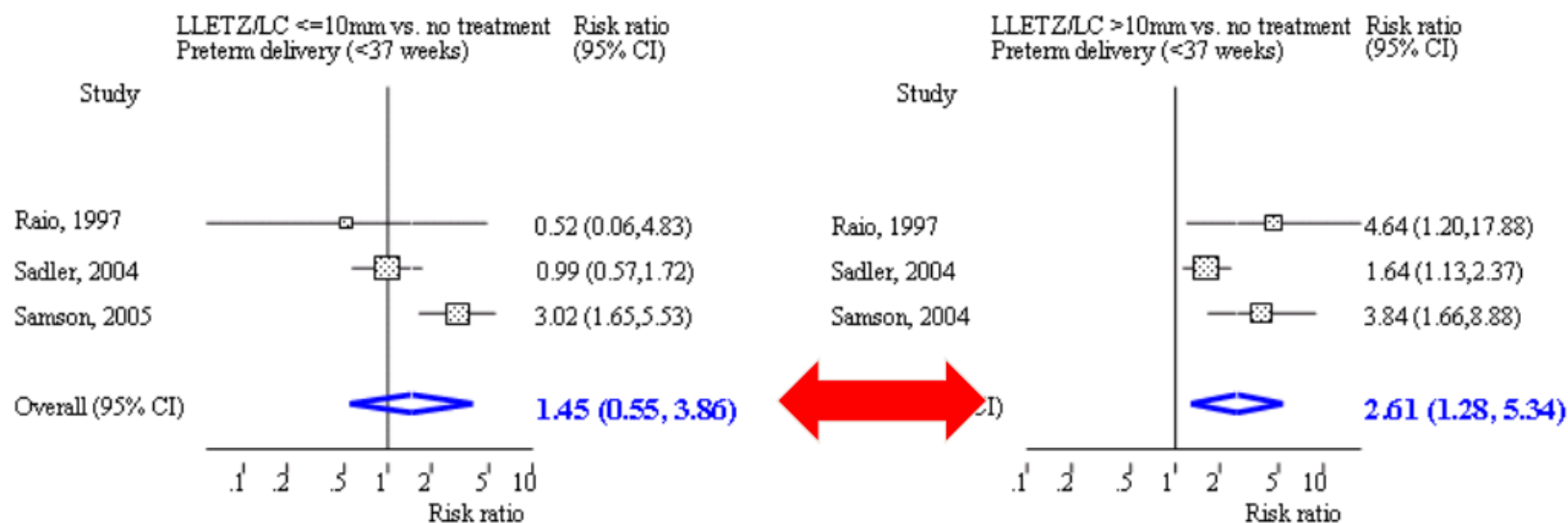


Pre-Term Labour and LLETZ?



< 10 mm

> 10 mm



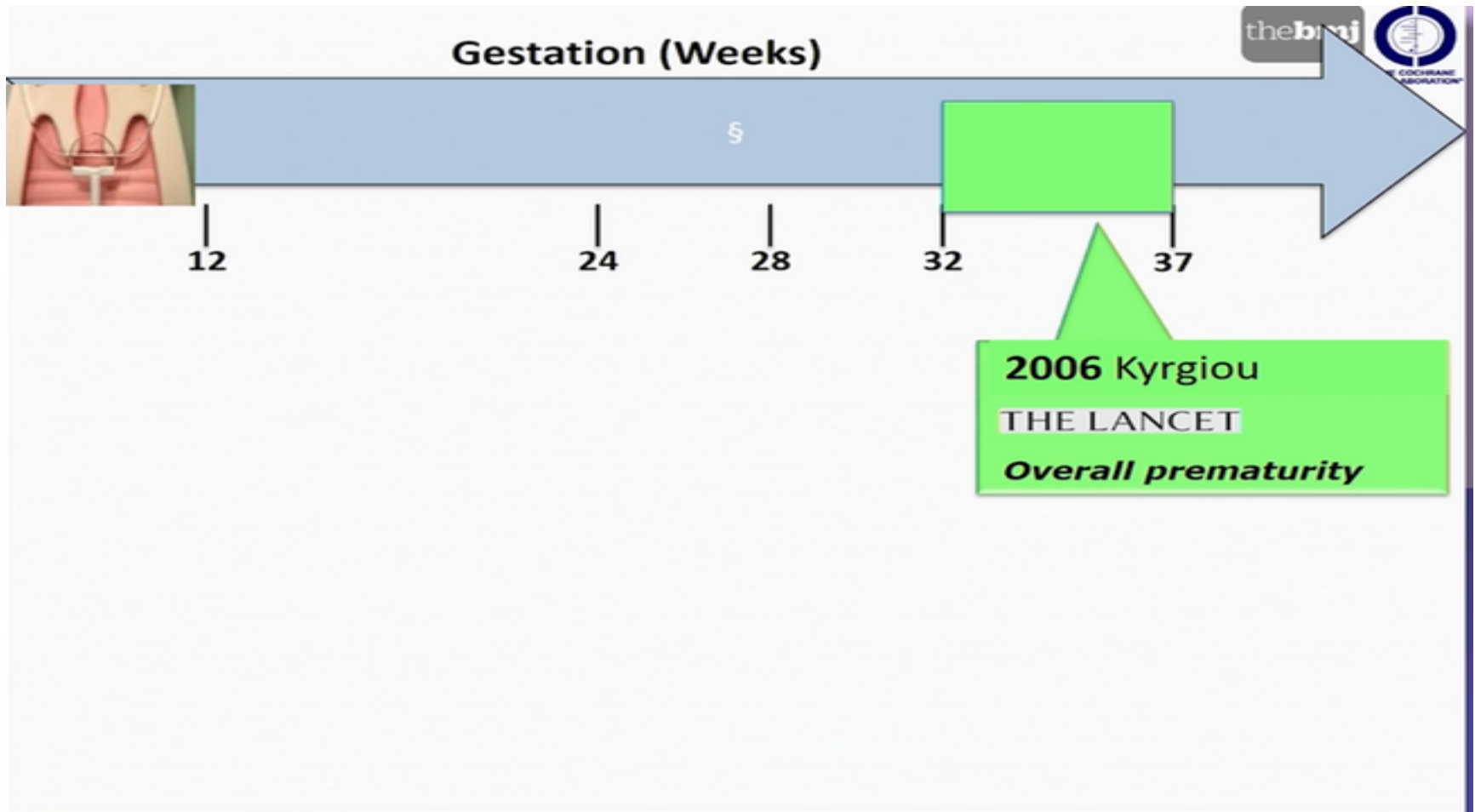
Depth: > 10 mm
< 10 mm

RR: 2.6, 95% CI: 1.3-5.3

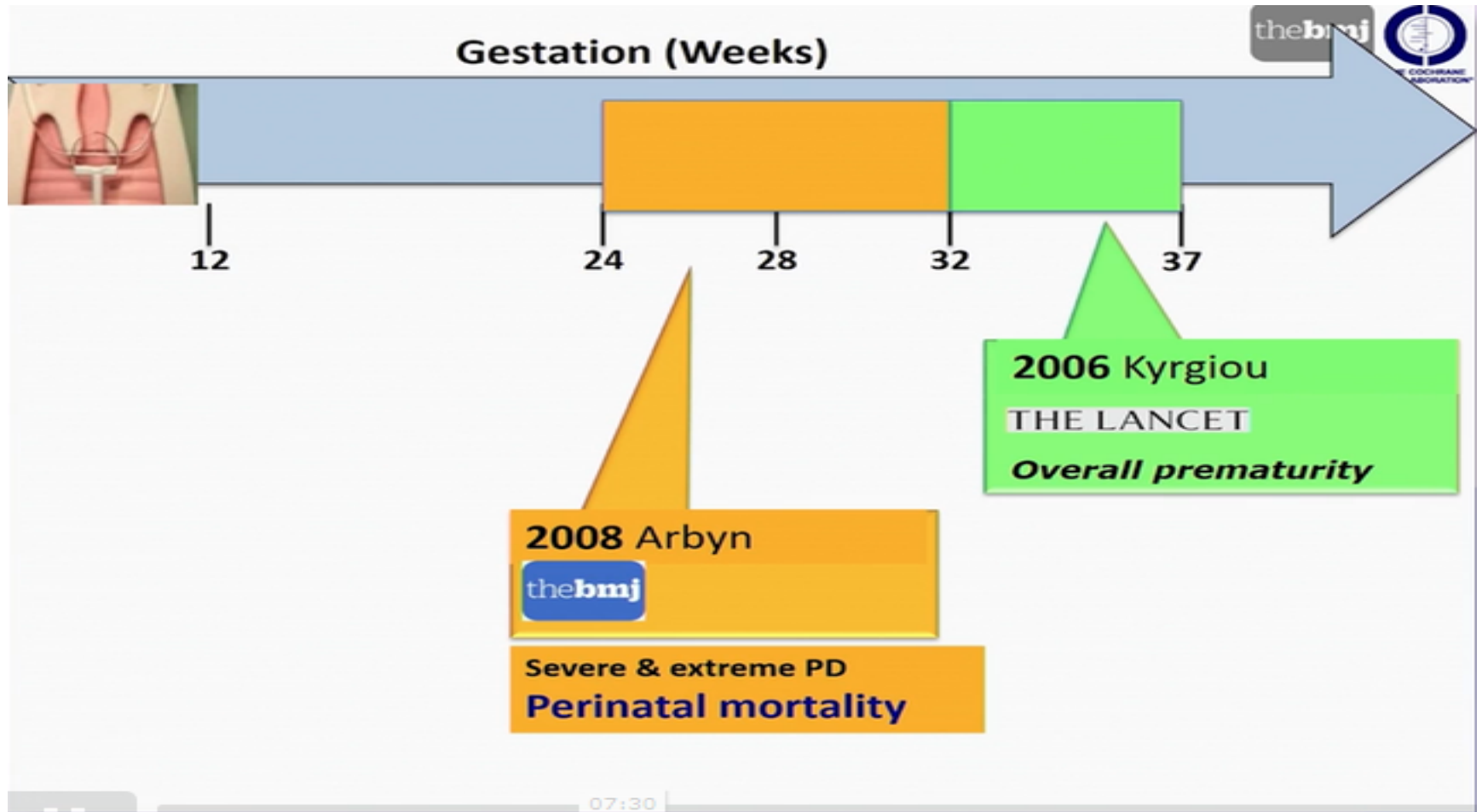
RR: 1.5, 95% CI: 0.6-3.9

Kyrgiou Lancet 2006

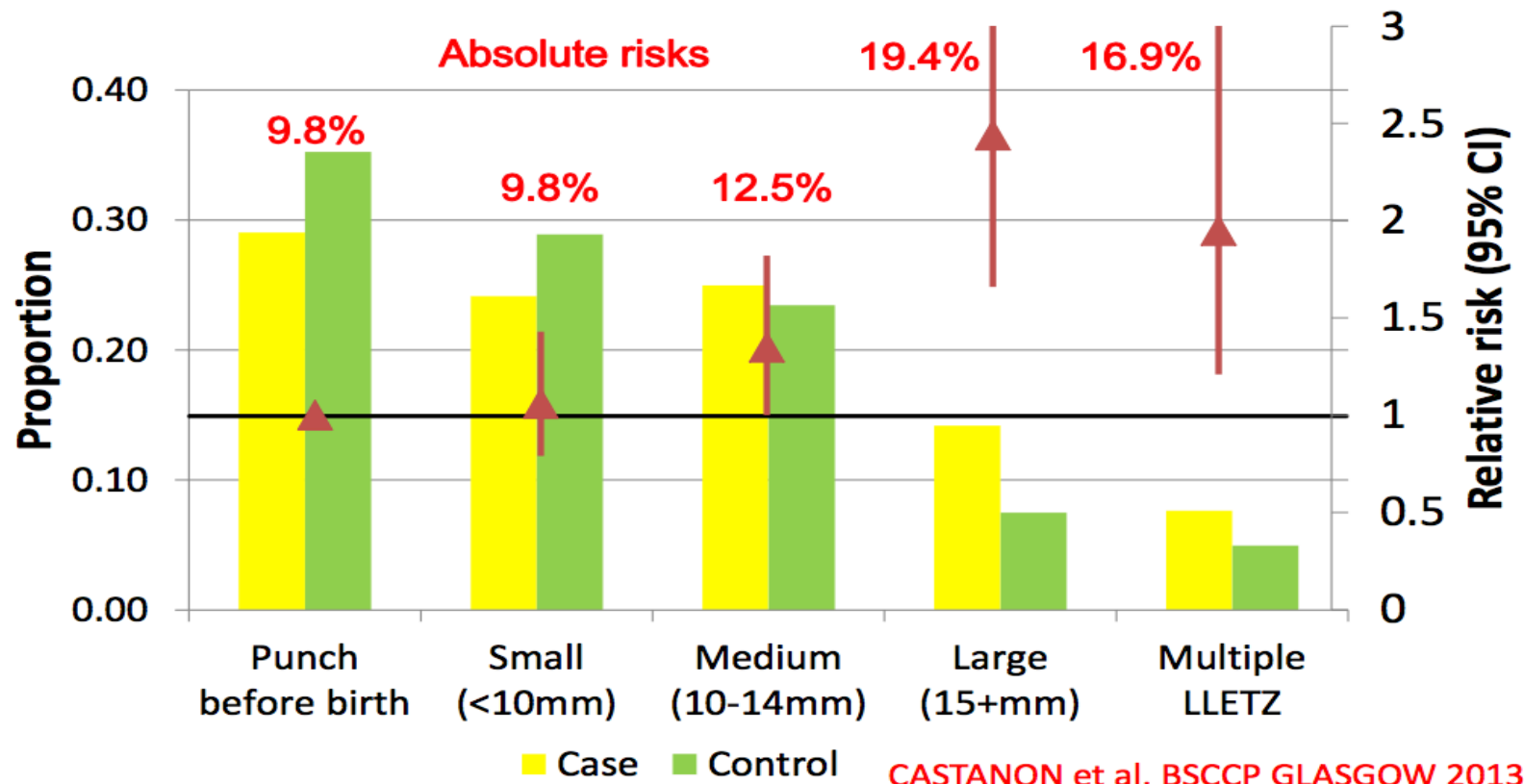
What is the evidence?

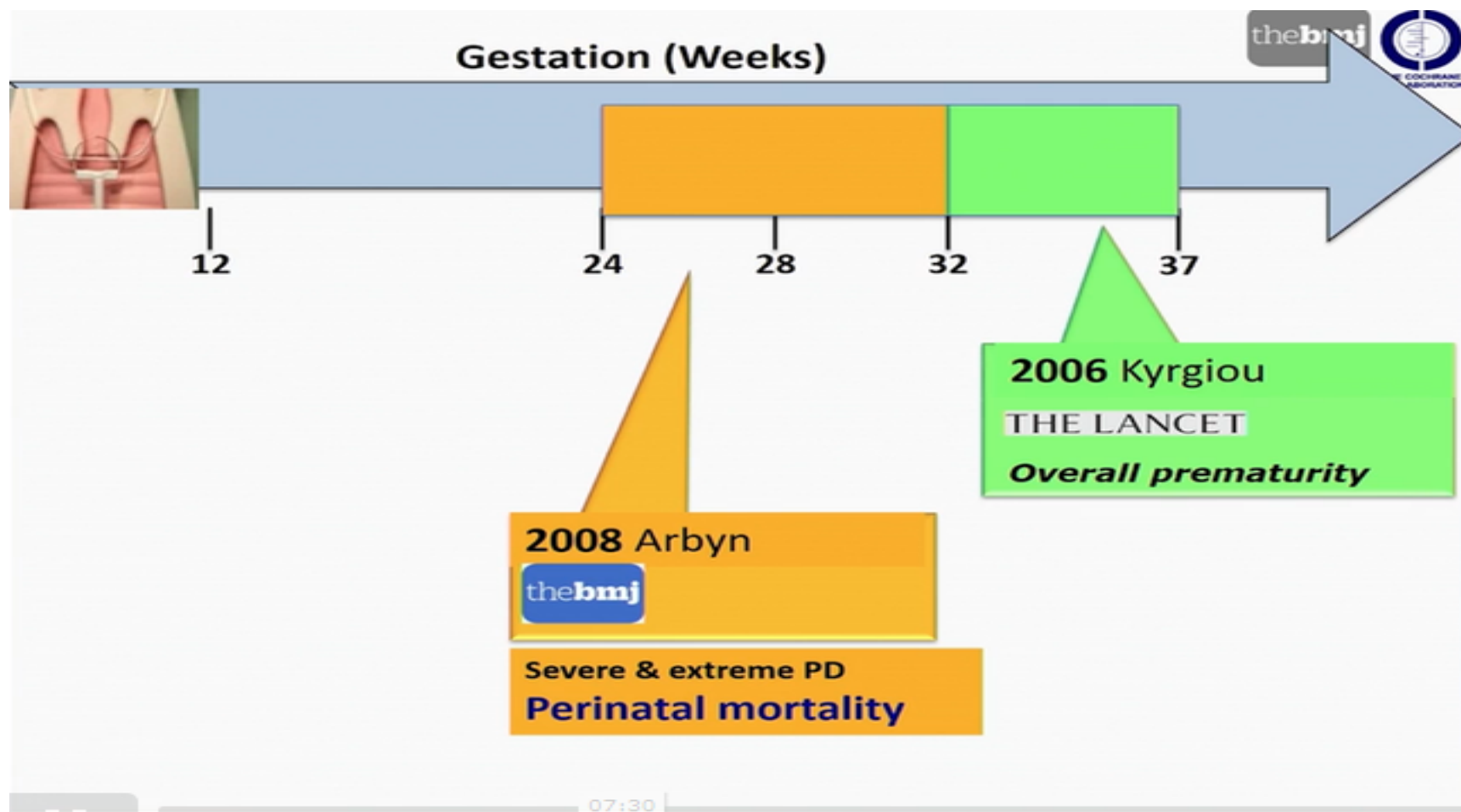


What is the evidence?



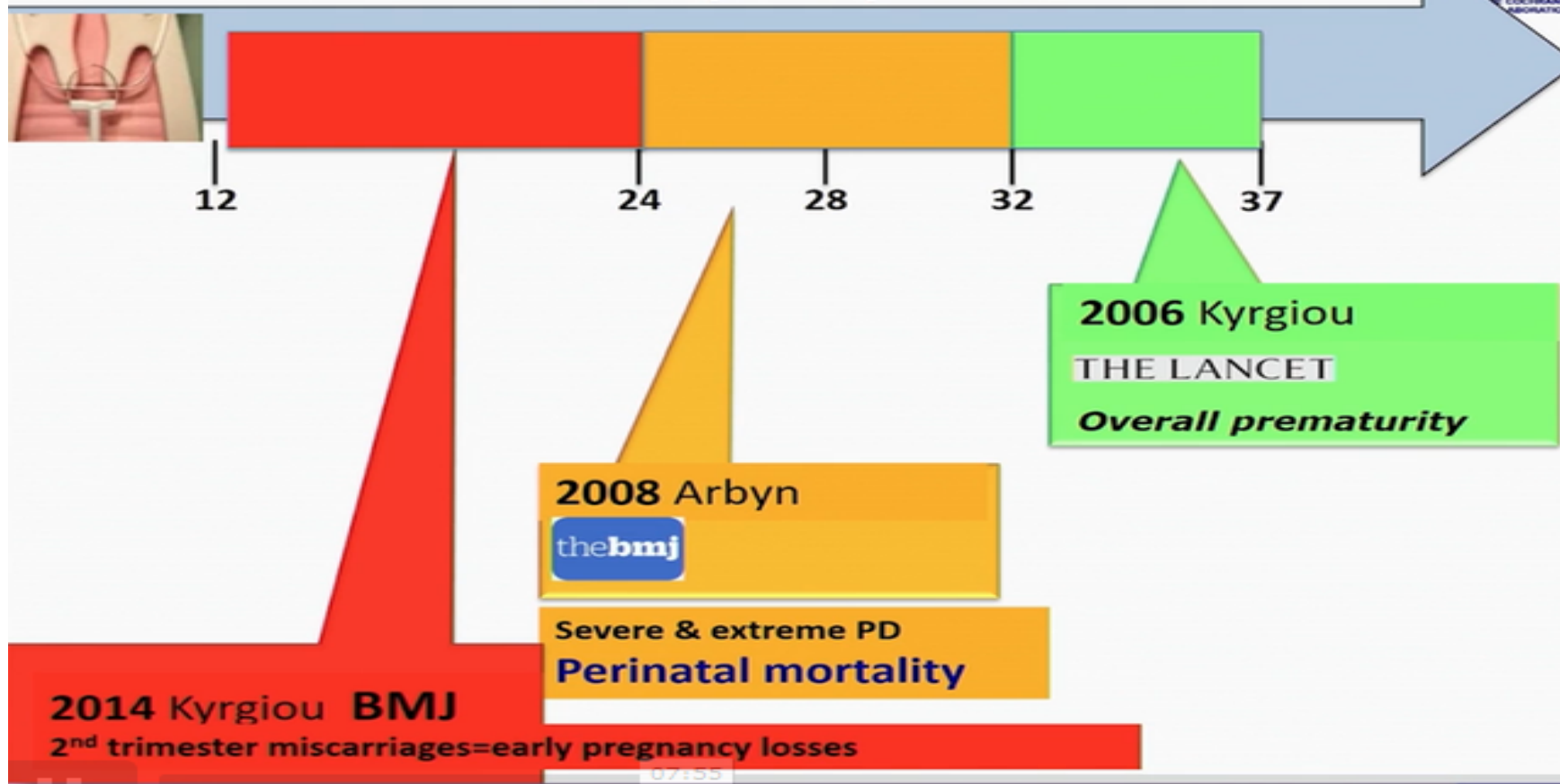
PTL: an association with length







Gestation (Weeks)





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

Maria Kyrgiou, Antonios Athanasiou, Maria Paraskevaidi, Anita Mitra, Ilkka Kalliala, Pierre Martin-Hirsch, Marc Arbyn, Phillip Bennett, Evangelos Paraskevaidis

BMJ August 2016



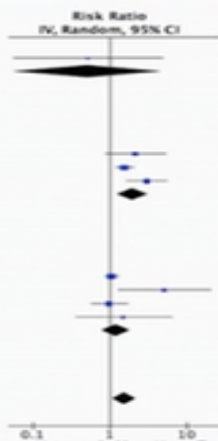
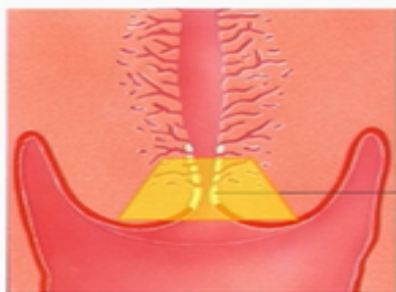
Effect of length



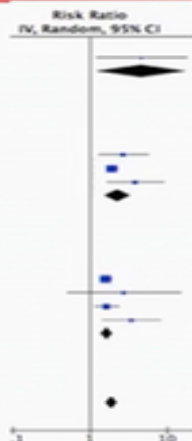
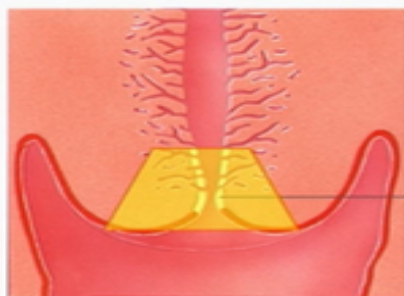
The treatment effect increased with increasing Tx cone length/volume...

JAMA Oncol & BMJ, August 2016

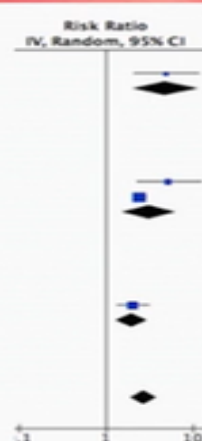
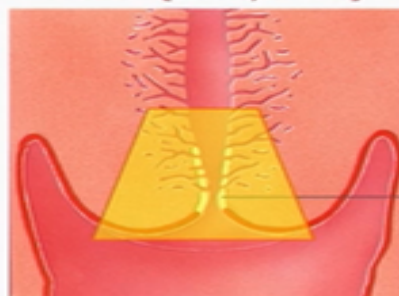
<10/12mm
1.54 [1.09, 2.18]



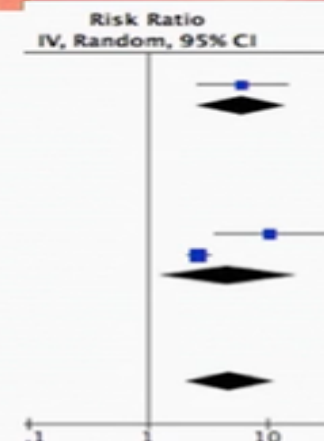
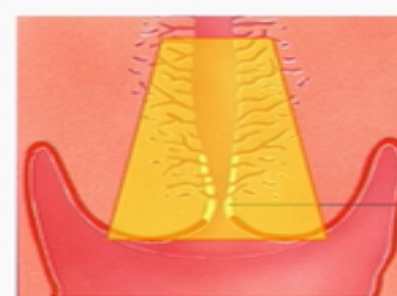
>10/12mm
1.93 [1.62, 2.31]



>15/17mm
2.77 [1.95, 3.93]



>20mm
4.91 [2.06, 11.68]



Summary



- Women with CIN at risk of prematurity
- Treatment increases that risk
- Risk increases with depth
- Risk associated with excision > ablation

Principles of medicine (1)



- First do no harm
- Do not do anything unless you have to

Conservative management



- HG SIL: 30-40 % regress Oster 1993
- CIN2: 50% regression over 12 mo Ho 2011
- Expectant management safe Fuchs 2007
Castel 2009

RESEARCH



OPEN ACCESS

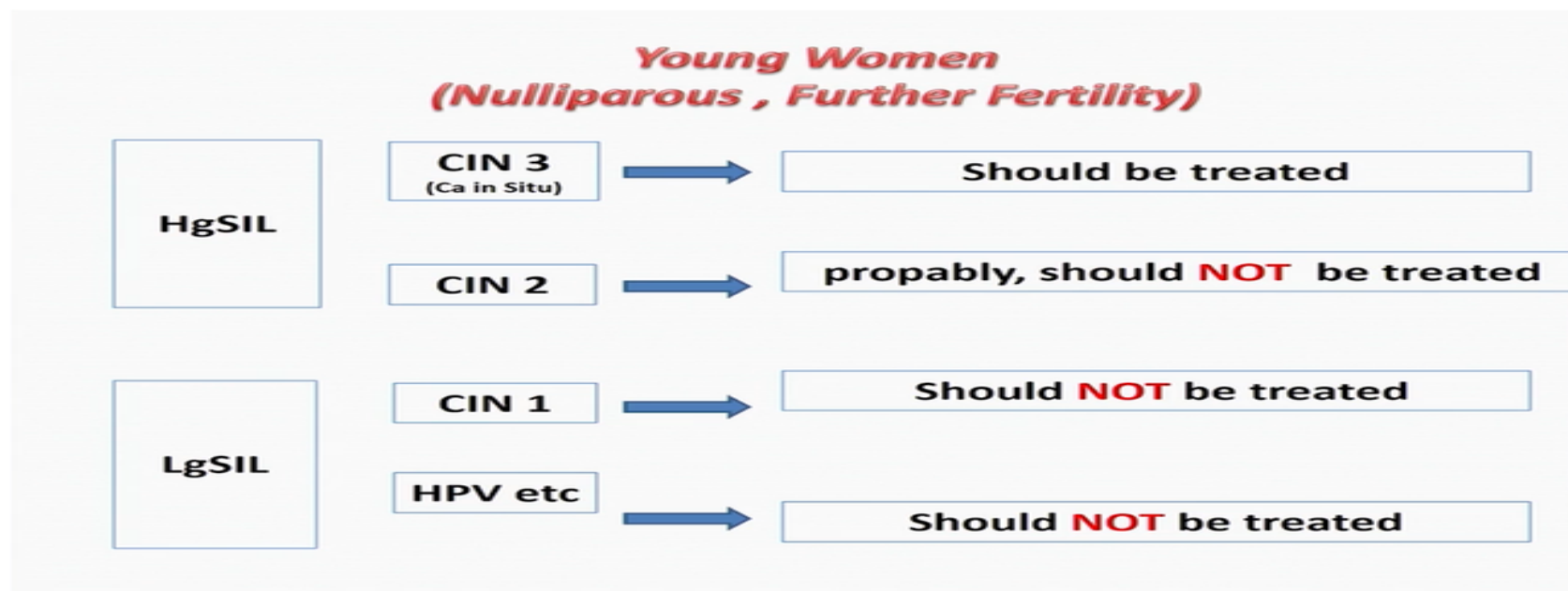
Clinical course of untreated cervical intraepithelial neoplasia grade 2 under active surveillance: systematic review and meta-analysis

Karoliina Tainio,¹ Antonios Athanasiou,² Kari A O Tikkinen,³ Riikka Aaltonen,⁴
Jovita Cárdenas Hernández,⁵ Sivan Glazer-Livson,¹ Maija Jakobsson,¹ Kirsi Joronen,⁴
Mari Kiviharju,¹ Karolina Louvanto,^{1,6} Sanna Oksjoki,⁴ Riikka Tähtinen,⁷ Seppo Virtanen,¹
Pekka Nieminen,¹ Maria Kyrgiou,^{8,9} Ilkka Kalliala^{1,8}

Conservative management summary



- Most CIN2 regresses
- Particularly in young women

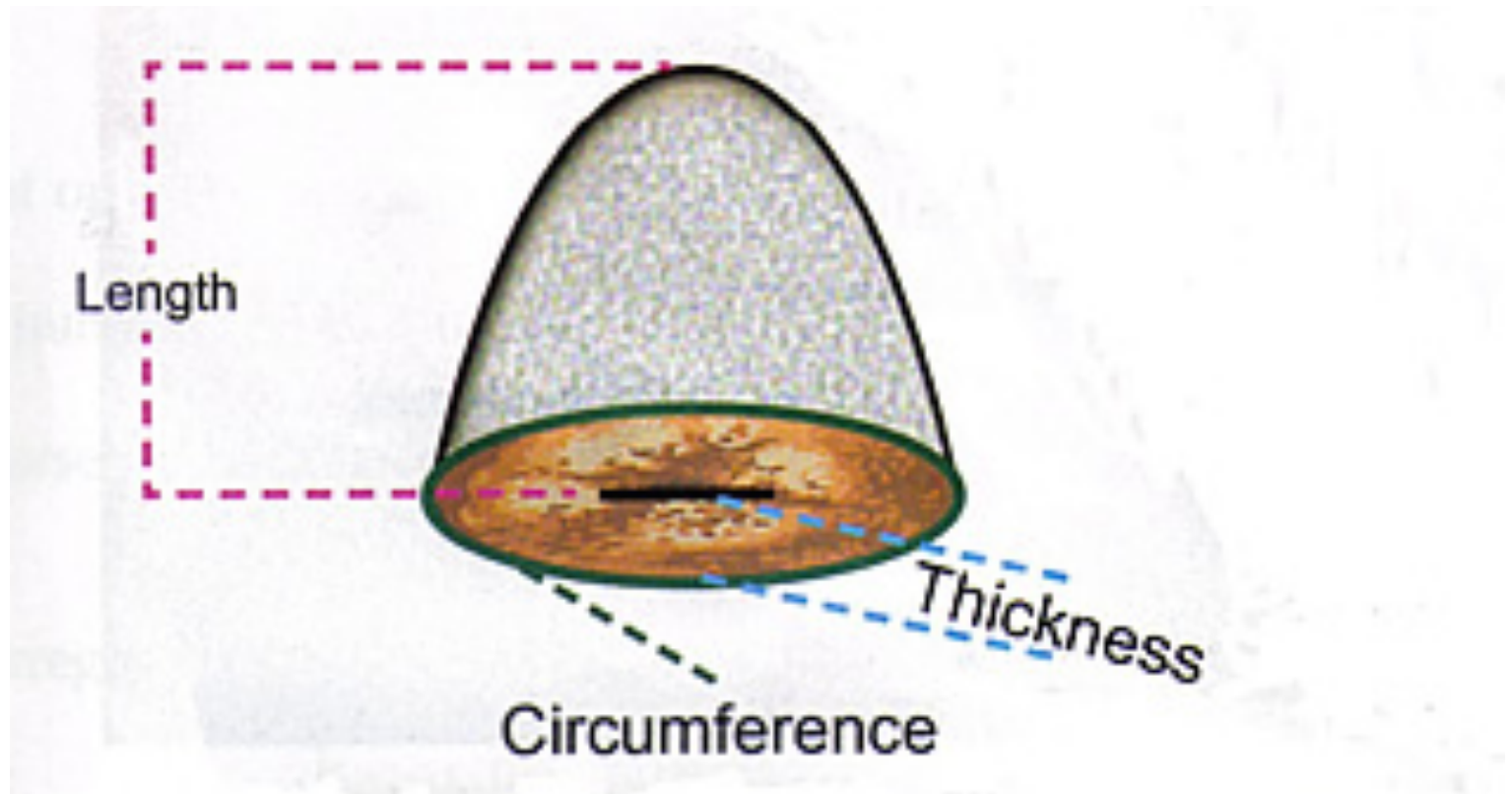


Principles of medicine (2)



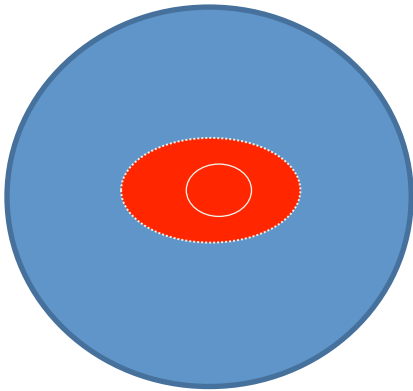
- First do no harm
- Do not do anything unless you have to
- If you have to do it, do it properly

Biopsy length

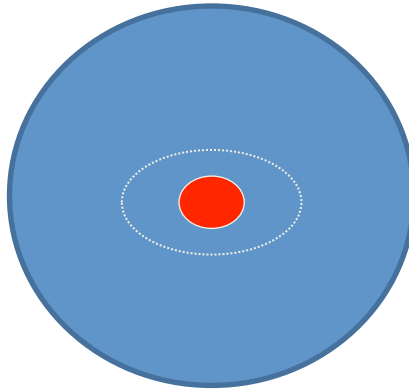


TZ Classification

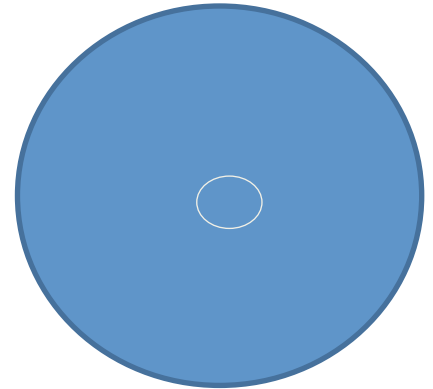
I



II



III



Symposium consensus



DOI: 10.1111/1471-0528.13839
www.bjog.org

Commentary

Risk of preterm birth following surgical treatment for cervical disease: executive summary of a recent symposium

P Sasieni,^a A Castanon,^a R Landy,^a M Kyrgiou,^b H Kitchener,^c M Quigley,^d LCY Poon,^e A Shennan,^f A Hollingworth,^g WP Soutter,^h T Freeman-Wang,^g D Peebles,^h W Prendiville,ⁱ J Patnick^j

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We report on a symposium held in London, UK, on 16 February 2015 to discuss the association between surgical treatment of cervical intraepithelial neoplasia (CIN) and subsequent preterm birth, and to consider appropriate recommendations for the treatment of CIN and management of treated women during pregnancy. The meeting focused on CIN grades 2 and 3 that have been managed surgically. Clinical practice varies internationally: in some countries knife excision is common; in others, laser ablation is the treatment of choice; and in others, treatment predominantly involves outpatient large loop excision of the transformation zone (LLETZ), also called loop electrosurgical excision procedure (LEEP). The meeting was part of the dissemination strategy of the National Institute for Health Research (NIHR)-funded PaCT study (preterm delivery after treatment of the cervical transformation zone). Around 50 people attended, including gynaecologic oncologists, (nurse and medical) colposcopists, obstetricians, and epidemiologists. The authors of this executive summary include the speakers at the symposium, who are also authors of important papers in the subject area, and the symposium chairs, to provide an independent opinion on the views expressed by the audience. Further details on the expertise of the authors can be found in the contribution to authorship.

Meta-analysis suggested that pregnant women previously treated by LLETZ are at approximately twice the risk of a

preterm birth than pregnant women in general.^{1–3} A study from England,⁴ and a recent meta-analysis,⁵ found a much lower relative risk and no association after adjusting for confounding factors. More recent research suggests that the increased risk may be associated with large excisions alone (10–14 mm, and particularly >15 mm), and that the reason for the lack of association in some studies was that the majority of women treated had small excisions.⁵ Assuming the observed associations are causal, how should guidelines be modified to minimise the risk of causing preterm deliveries whilst still effectively preventing progression from CIN to invasive cervical cancer? In thinking about the balance between the harms and benefits of treatment it is important to know about the long-term consequences of late preterm deliveries (34–36 weeks of gestation). Even if the association between LLETZ and preterm birth is not causal, having identified a high-risk group there is a question as to how they should be managed obstetrically.

The first part of the meeting focused on the results of international studies on the association between the treatment of CIN and subsequent risk of preterm delivery.

1 There is strong observational (but no experimental) evidence [level 2a⁶] suggesting a causal link between treatment for CIN and subsequent preterm birth, meeting most of the Bradford Hill criteria for causation.

Type 1 excisions: 80% < 10 mm and 95% < 15 mm

Type 2 excisions: 50% < 10mm and 80 % < 15 mm

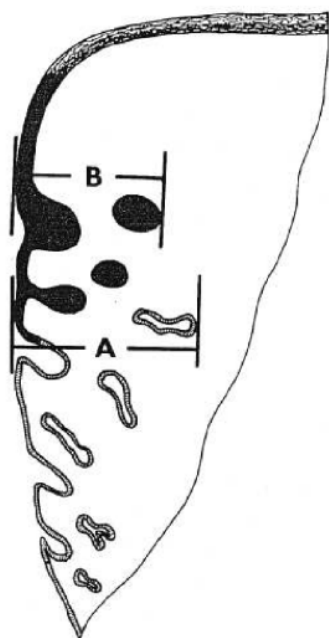
CIN 2 in a young women should not be automatically treated

The Evidence – depth of crypts



Cervical Crypt Involvement by Intraepithelial Neoplasia

M. C. ANDERSON, MB, MRCPATH, AND R. B. HARTLEY, MRCS, LRCP
VOL. 55, NO. 5, MAY 1980 *Obstetrics & Gynecology*



Measurements made on a section from a cervical conization specimen.
A = depth of the deepest crypt; B = depth of the deepest involved crypt.

Depths of Crypts With and Without Involvement by CIN Grade 3

Crypt status	Mean (mm)	Maximum (mm)	Mean +1.96 SD (mm) 95%	Mean +3 SD (mm) 99.7%
Uninvolved	3.38	7.83	5.25	6.30
Involved	1.24	5.22	2.92	3.80



Excision Treatment Guidelines



Type I TZ

Excision length 8mm or greater

Depth of excision and outcome



Histological recurrence and depth of loop treatment of the cervix in women of reproductive age: incomplete excision versus adverse pregnancy outcome

C Ang,^a A Mukhopadhyay,^a C Burnley,^b K Faulkner,^b PA Cross,^c P Martin-Hirsch,^d R Naik^a

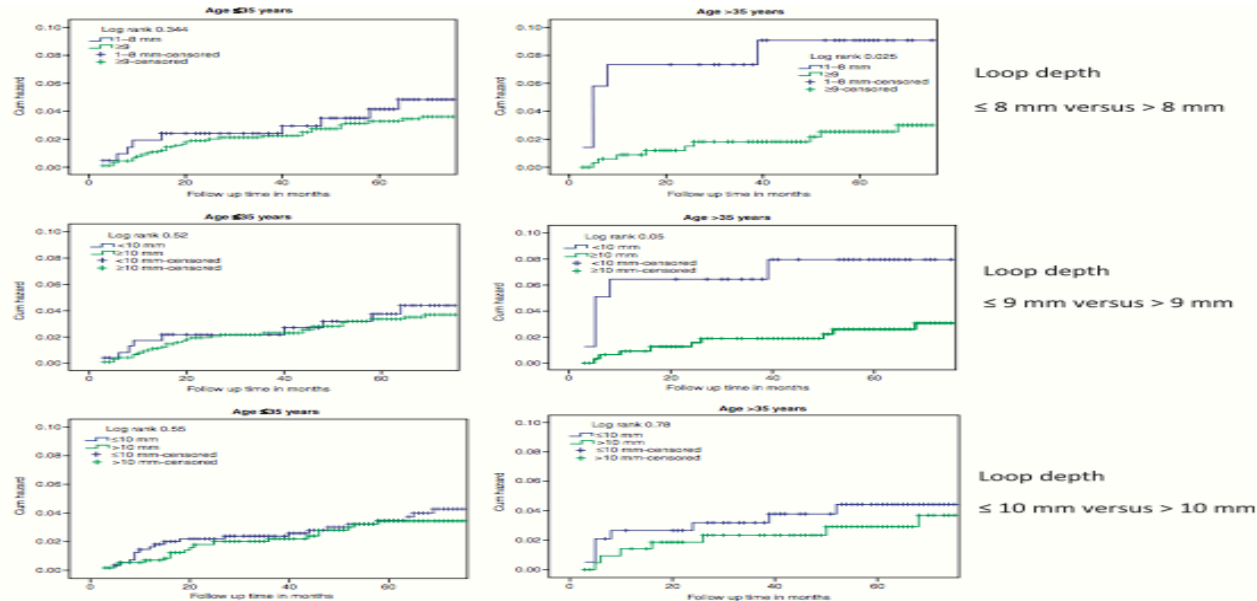
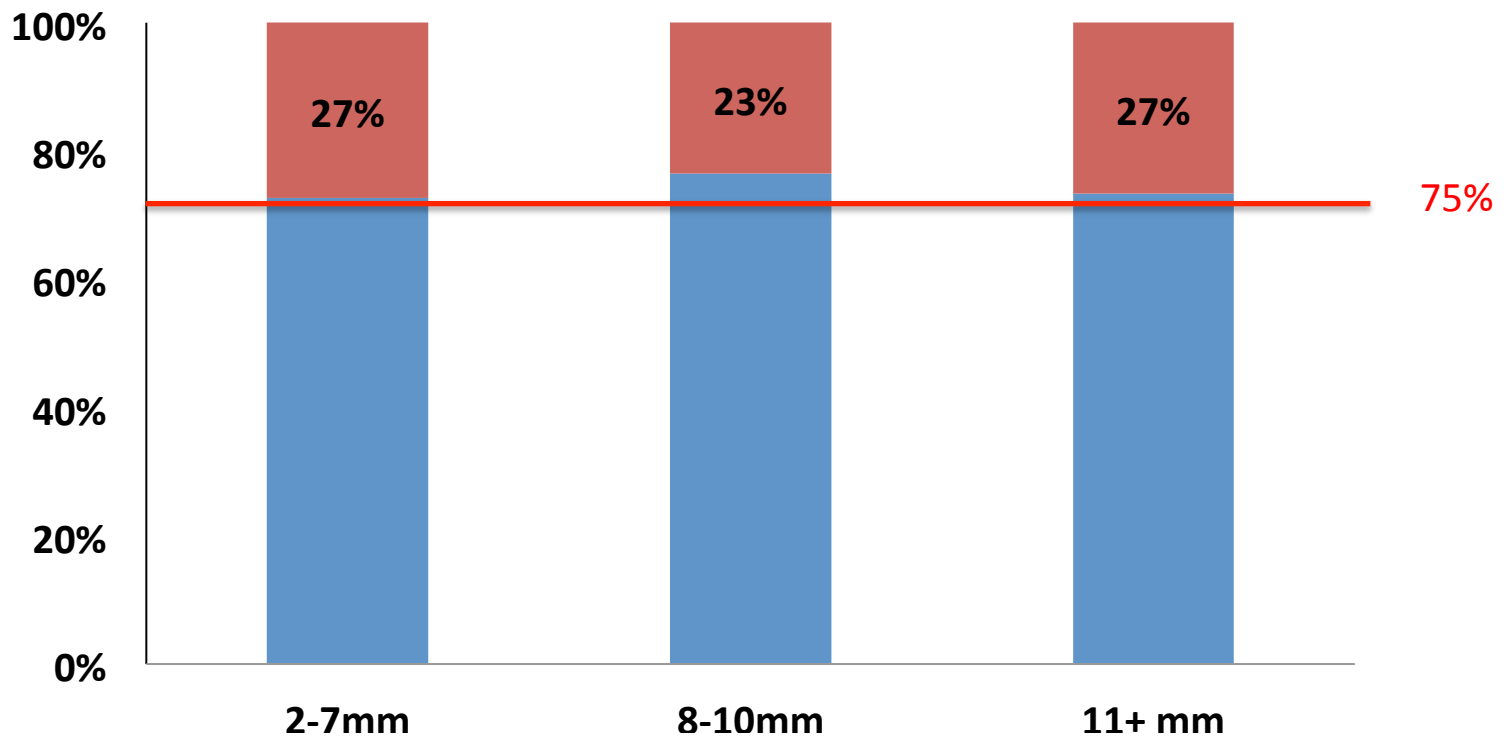


Figure 3. Kaplan-Meier survival curves for histological recurrence at different loop depths in women ≤ 35 years versus > 35 years of age. Higher recurrence seen at lower depths in older women, but no difference in younger women.

No association between depth and outcome in women < 35 yrs

Outcome – Test of Cure at 6 mo



Chi-squared test yielded a p-value of 0.636

Treatment needs to be targeted!



Parting Comments



Is this the best way to treat viral disease?



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6th Satellite Meeting and Training the Trainers

Hotel Pullman Brussels Centre Midi
1st DECEMBER 2018





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