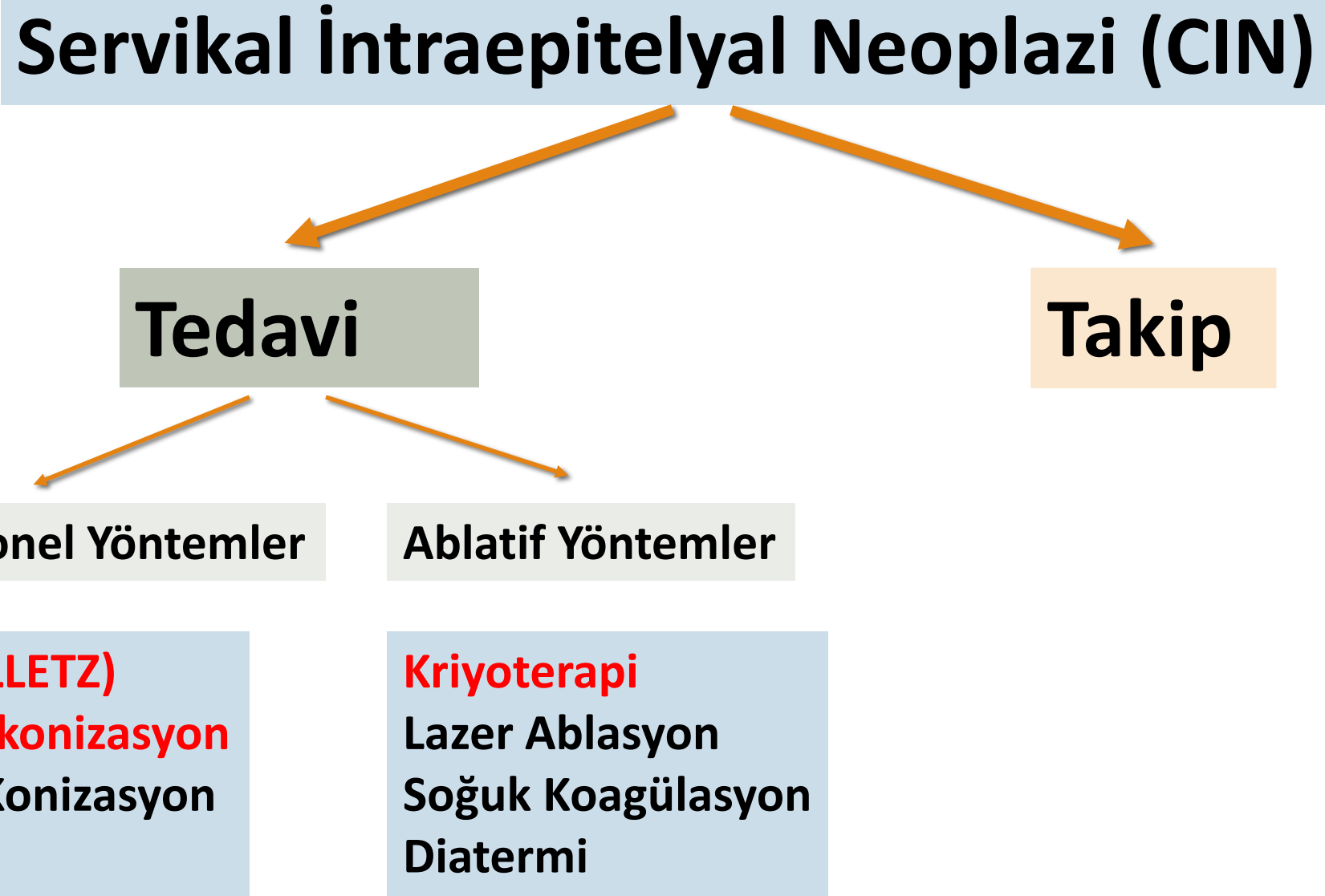


Kriyoterapinin Kolposkopi Uygulamasında Yeri Vardır/Yoktur

Dr. Doğan Vatansever

Koç Üniversitesi Hastanesi

Servikal İntıraepitelyal Neoplazi (CIN)



```
graph TD; A[Servikal İntıraepitelyal Neoplazi (CIN)] --> B[Tedavi]; A --> C[Takip]; B --> D[Eksizyonel Yöntemler]; B --> E[Ablatif Yöntemler]; D --> F["LEEP (LLETZ)  
Soğuk konizasyon  
Lazer Konizasyon"]; E --> G["Kriyoterapi  
Lazer Ablasyon  
Soğuk Koagülasyon  
Diatermi"]
```

Tedavi

Takip

Eksizyonel Yöntemler

LEEP (LLETZ)
Soğuk konizasyon
Lazer Konizasyon

Ablatif Yöntemler

Kriyoterapi
Lazer Ablasyon
Soğuk Koagülasyon
Diatermi

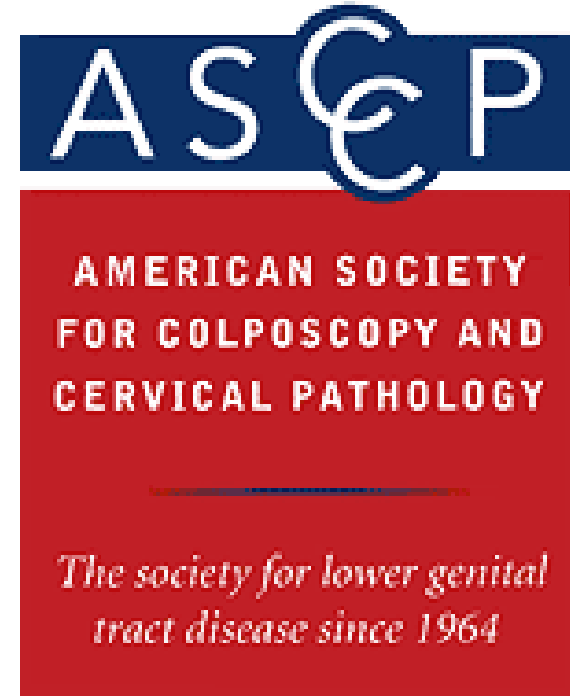
Kriyoterapi Endikasyonlar

1. 2 yıl ya da daha fazla süredir persiste eden CIN 1

- Kolposkopi yetersiz ise,
- ECC CIN 2 ya da 3 geldi ise,
- Daha önce CIN için tedavi olmuş ise,

Eksizyon tercih edilir.

2. CIN 2, 3 (Kolposkopi yeterli ise)



Kriyoterapi Endikasyonlar

- Yeterli Kolposkopi (TZ tam olarak görülmeli)
- CIN tanısı biyopsi ile konmuş olmalı, tek başına sitoloji yetersiz
- Sitoloji ve histoloji uyumlu olmalı
- ECC negatif olmalı
- İnvaziv kanser şüphesi olmamalı

	KRİYOTERAPİ	LEEP
OFİSTE UYGULAMA KOLAYLIĞI	+	+
MALİYET	+	+
TANISAL P/S ELDE ETME	-	+
ETKİNLİK	?/-	+
FERTİLİTEYE ETKİ	+	-
OBSTETRİK SONUÇLAR	+	-
MORBİDİTE	+	-

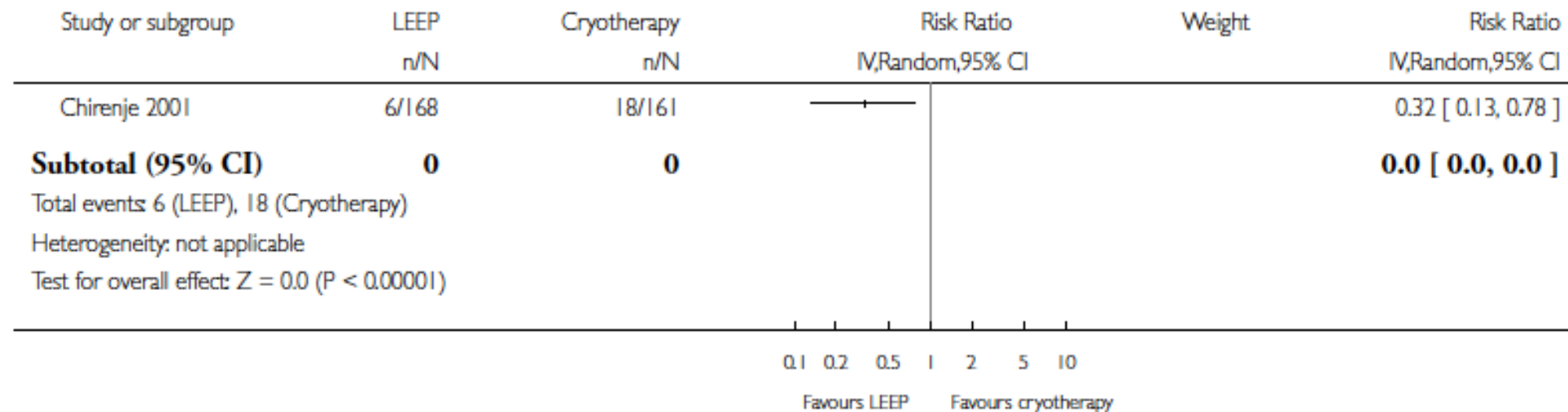
Etkinlik

Analysis 11.2. Comparison 11 LEEP versus cryotherapy, Outcome 2 Residual disease at 12 months.

Review: Surgery for cervical intraepithelial neoplasia

Comparison: 11 LEEP versus cryotherapy

Outcome: 2 Residual disease at 12 months



[procedure
aepithelial](#)



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International Journal of Gynecology and Obstetrics

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



REVIEW ARTICLE

Systematic reviews and meta-analyses of benefits and harms of cryotherapy, LEEP, and cold knife conization to treat cervical intraepithelial neoplasia



Nancy Santesso^a, Reem A. Mustafa^{a,b}, Wojtek Wiercioch^a, Rohan Kehar^a, Shreyas Gandhi^a, Yaolong Chen^c, Adrienne Cheung^d, Jessica Hopkins^a, Rasha Khatib^{a,e}, Bin Ma^c, Ahmad A. Mustafa^f, Nancy Lloyd^a, Darong Wu^g, Nathalie Broutet^h, Holger J. Schünemann^{a,i,*}

Table 1

Effects of cryotherapy, LEEP, and cold knife conization at 12 months.^a

Outcomes	Percentage/RR (95% CI) ^b	Number of studies	Number of events/number of participants
Cryotherapy			
Recurrence of CIN 2–3	5.342 (3.879 to 6.805)	12	562/13 907
Major bleeding	0.034 (– 0.030 to 0.098)	17	39/11 570
Major infection	0.014 (– 0.038 to 0.065)	18	7/11 938
PID	0.006 (– 0.48 to 0.060)	13	3/10 995
Damage to organs	0.022 (– 0.056 to 0.100)	7	3/4974
Minor bleeding	0.006 (– 0.051 to 0.064)	17	12/8757
Premature delivery	2.25 (0.14 to 34.98) ^c	1	2/117
HPV clearance	–	–	–
LEEP			
Recurrence of CIN 2–3	5.312 (3.702 to 6.922)	19	391/8269
Major bleeding	0.226 (0.131 to 0.320)	40	121/16 423
Major infection	0.128 (0.011 to 0.245)	19	37/7796
PID	0.139 (0.005 to 0.273)	12	33/5913
Damage to organs	0.221 (0.070 to 0.371)	12	21/5727
Minor bleeding	0.363 (0.281 to 0.444)	53	308/19 861
Premature delivery	1.85 (1.59 to 2.15) ^c	8	26 352/656 581
HPV clearance	64.706 (56.242 to 73.169)	1	77/119
Cold knife conization			
Recurrence of CIN 2–3	1.431 (0.8323 to 2.030)	11	228/17 616
Major bleeding	0.859 (0.651 to 1.066)	26	216/9311
Major infection	0.089 (– 0.082 to 0.260)	11	12/3443
PID	0.138 (– 0.032 to 0.309)	6	9/3003
Damage to organs	0.276 (0.057 to 0.494)	8	17/3180
Minor bleeding	2.450 (2.084 to 2.816)	27	324/7638
Premature delivery	3.41 (2.38 to 4.88) ^c	3	2009/30 216
HPV clearance	72.269 (64.322 to 80.216)	1	86/119

Abbreviations: LEEP, loop electrosurgical excision procedure including large loop excision of the transformation zone; RR, risk ratio; CIN, cervical intraepithelial neoplasia; PID, pelvic inflammatory disease.

Etkinlik

International Journal of Gynecology and Obstetrics 120 (2013) 218–223



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



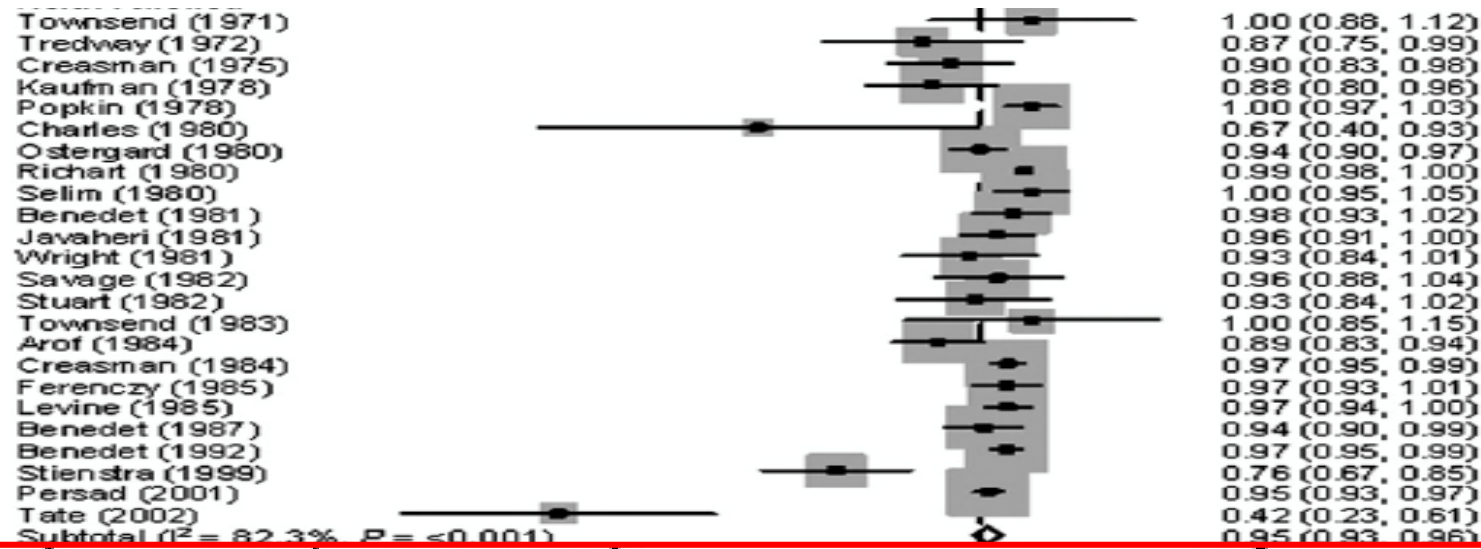
REVIEW ARTICLE

Meta-analysis of the effectiveness of cryotherapy in the treatment of cervical intraepithelial neoplasia

Catherine Sauvaget*, Richard Muwonge, Rengaswamy Sankaranarayanan

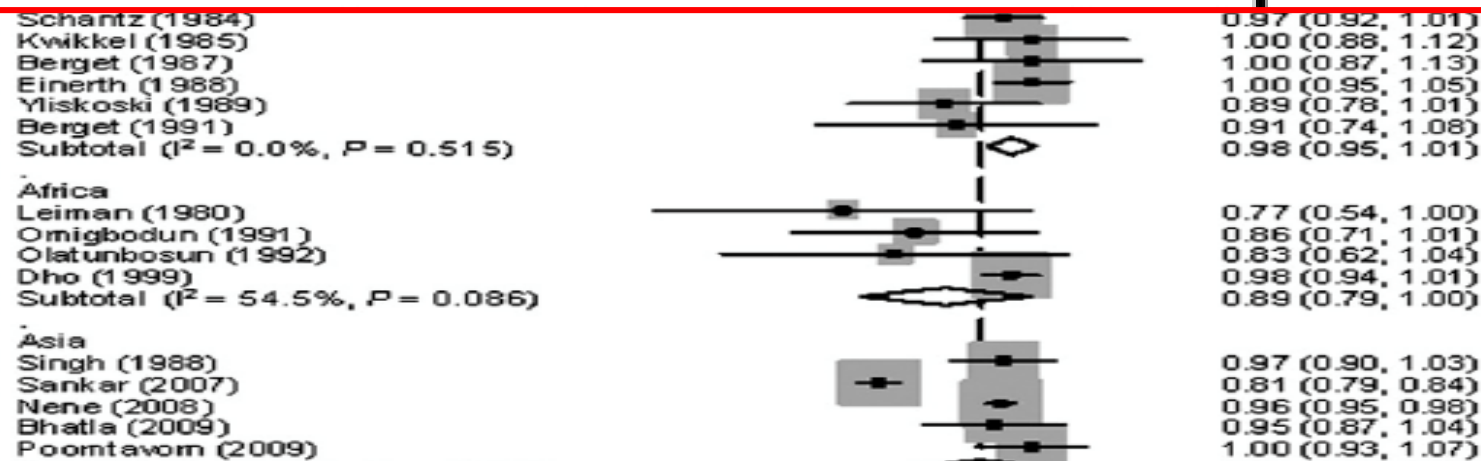
Screening Group, Early Detection and Prevention Section, International Agency for Research on Cancer, Lyon, France

Cryotherapy cure rates of cervical intraepithelial neoplasia 1 lesions according to geographic region.



Overall ($I^2 = 87.3\%$, $P = <0.001$)

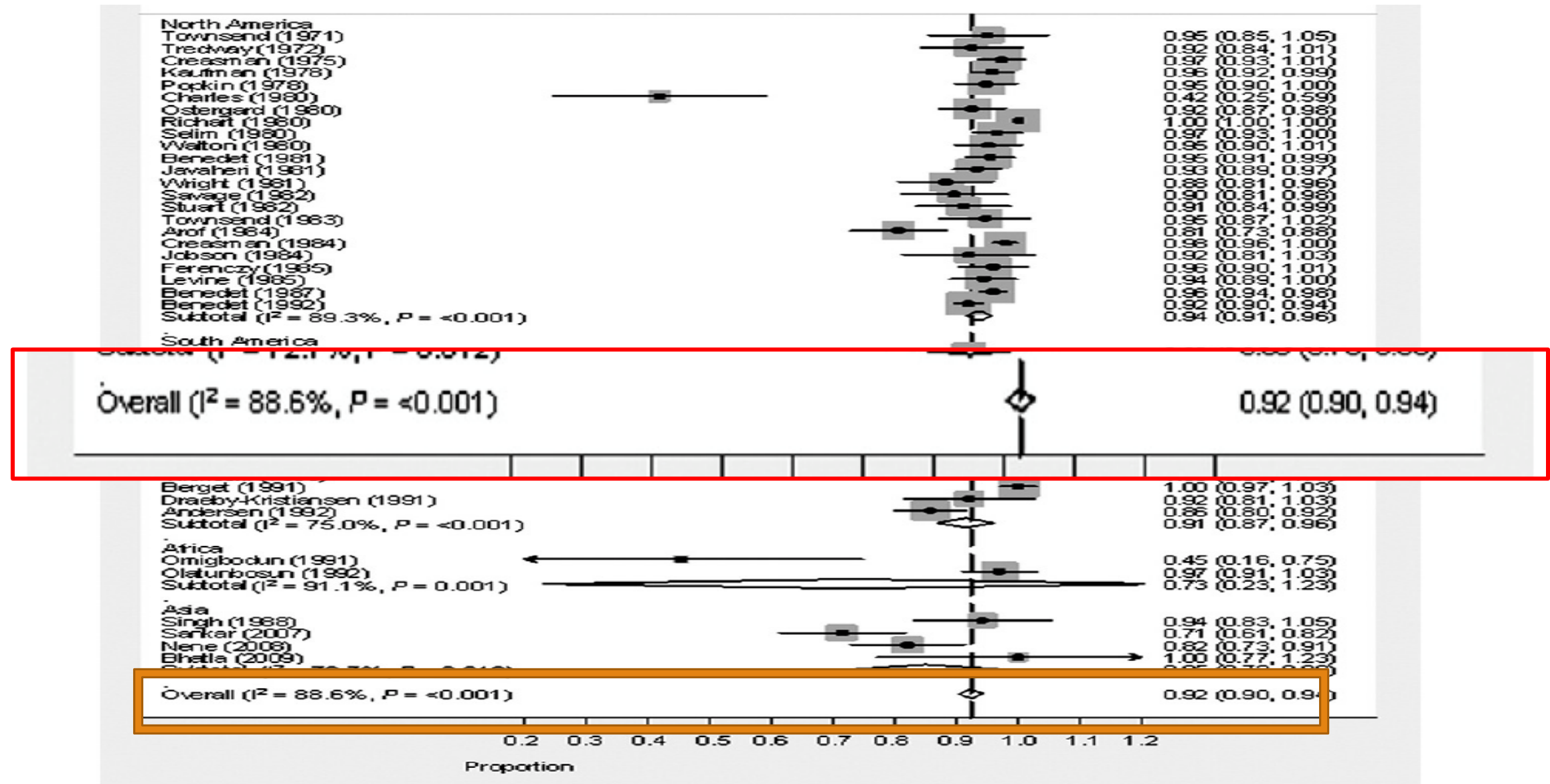
0.94 (0.92, 0.96)



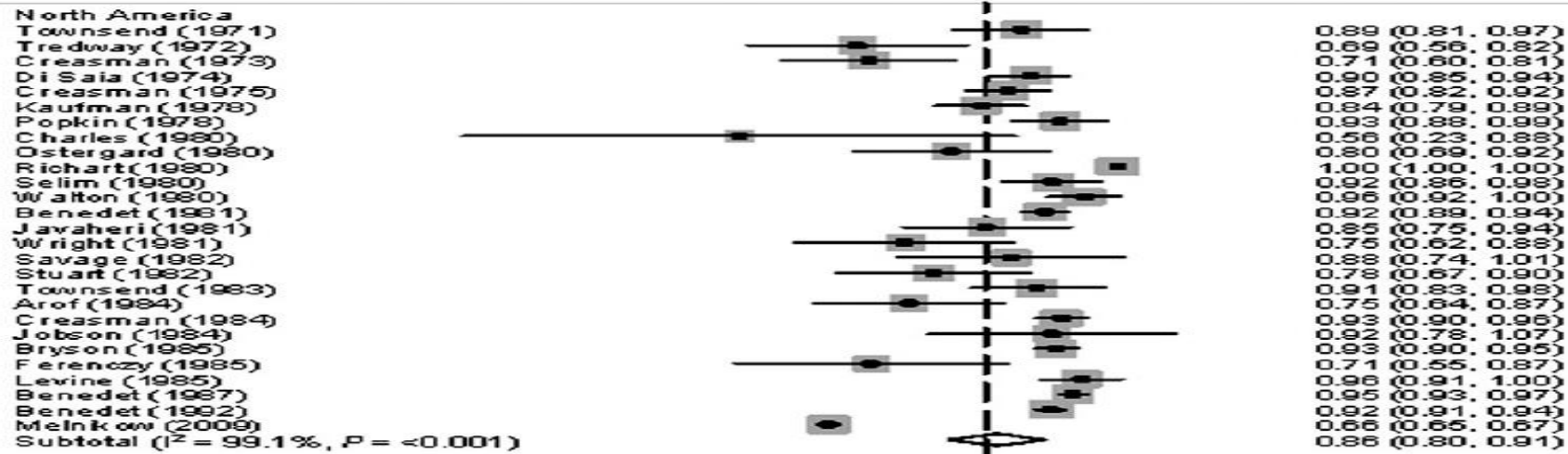
Overall ($I^2 = 87.3\%$, $P = <0.001$)

0.94 (0.92, 0.96)

Cryotherapy cure rates of cervical intraepithelial neoplasia 2 lesions according to geographic region.

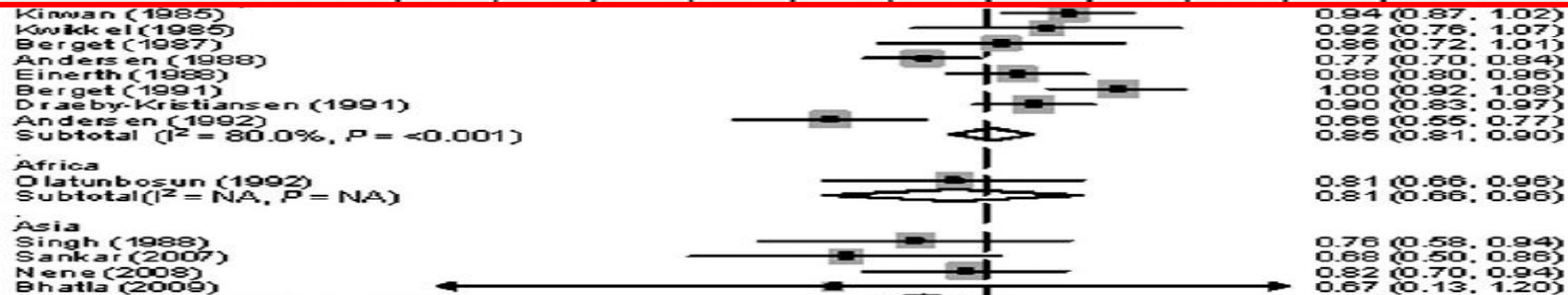


Cryotherapy cure rates of cervical intraepithelial neoplasia 3 lesions according to geographic region.



Overall ($I^2 = 98.6\%$, $P = <0.001$)

0.85 (0.80, 0.89)



Proportion

GYNECOLOGY

A randomized clinical trial comparing cervical dysplasia treatment with cryotherapy vs loop electrosurgical excision procedure in HIV-seropositive women from Johannesburg, South Africa



Jennifer S. Smith, PhD; Busola Sanusi, MA; Avril Swarts, MSc; Mark Faesen, FCOG; Simon Levin, FRCOG; Bridgette Goeieman, MBBCh; Sibongile Ramotshela, PN; Ntombiyenkosi Rakhombe, PN; Anna L. Williamson, PhD; Pam Michelow, MD; Tanvier Omar, FCPATH (SA); Michael G. Hudgens, PhD; Cynthia Fimhaber, MD

RCT, 166 pts, 86 LEEP vs 80 Kriyoterapi

6. Ayda CIN2, 3 10.8 vs. 24.3

12. Ayda CIN2, 3 27.2 vs. 18.5 p =0.21

Fark Yok

TANISAL P/S ELDE ETME

- Ablatif metodlarda P/S yok.
- Tanısal bir veri yok –Okkült kanser ?
- Tedavi edilen bölgenin sınırlarında hastalık var mı? Bilmiyoruz.

1. Tanısal veri:

Okkült SCC ve Glandüler hastalık;

1189 hasta LEEP,
6 hasta (%0.5) mikroinvaziv SCC,
15 (%1.3) AİS.

Yalnızca 2 mikroinvaziv SCC (% 0.16) smear ve kolposkopide yakalanamamış.

Ferenczy A et al. Obstet Gynecol 1996

TANISAL P/S ELDE ETME

- Ablatif metodlarda P/S yok.
- Tanısal bir veri yok
- Tedavi edilen bölgenin sınırlarında hastalık var mı? Bilmiyoruz.

2. Tanısal veri:

3738 CIN tanılı hasta

Laser ablasyon yapılıyor.

Takipte 9 serviks kanseri gelişiyor (% 0.24)

Pearson SE et al. Br J Obstet Gynecol 1989

TANISAL P/S ELDE ETME

- Ablatif metodlarda P/S yok.
- Tanısal bir veri yok
- Tedavi edilen bölgenin sınırlarında hastalık var mı? Bilmiyoruz.

Cerrahi Sınır:

66 çalışma 35,000 hasta
Cerrahi sınır + olan hastalarda

Tedavi sonrası CIN 2,3

% 18 vs 3; RR 6.09, 95% CI 3.87-9.60

Ghaem Maghami S et al. Lancet Oncol 2007



Incomplete excision of cervical precancer as a predictor of treatment failure: a systematic review and meta-analysis

Marc Arbyn, Charles W E Redman, Freija Verdoodt, Maria Kyrgiou, Menelaos Tzafetas, Sadaf Ghaem-Maghami, Karl-Ulrich Petry, Simon Leeson, Christine Bergeron, Pekka Nieminen, Jean Gondry, Olaf Reich, Esther L Moss

Rezidüel hastalık ya da
nüks oranı 6.6

Cerrahi sınır (+)
RR 4.8, %95 CI 3.2–7.2

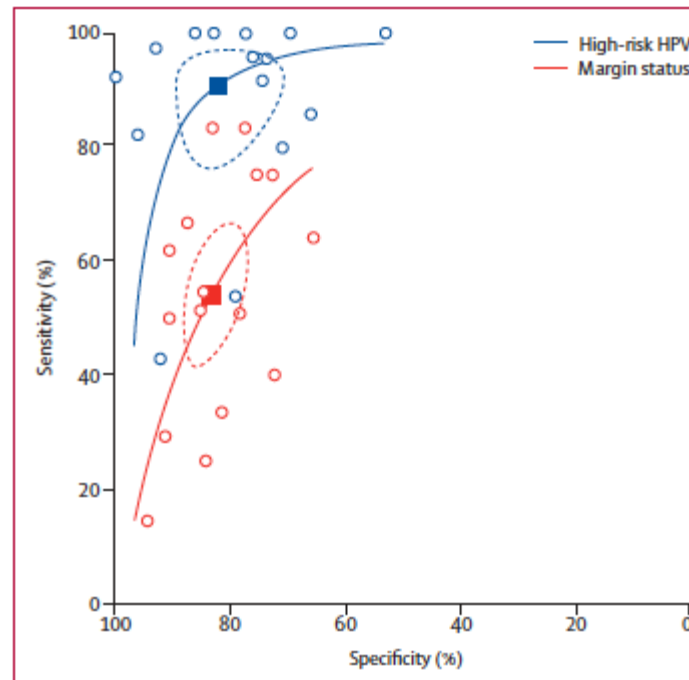
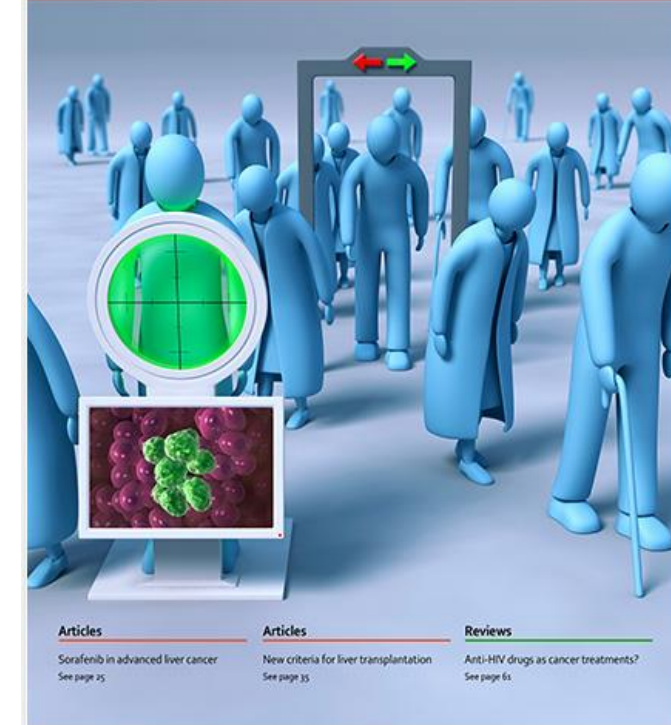


Figure 4: Summary receiver operation characteristic plot of the sensitivity as a function of the specificity for residual or recurrent CIN2+ of margin status and high-risk DNA testing in women treated for CIN2+. CIN2+=cervical intraepithelial neoplasia of grade 2 or worse. HPV=human papillomavirus.



2012 Updated Consensus

Guidelines for the Management of

If CIN 2, CIN 3, or CIN 2,3 is identified at the margins of a diagnostic excisional procedure or in an endocervical sample obtained immediately after the procedure, reassessment using cytology with endocervical sampling at 4–6 months after treatment is preferred (BII). Performing a repeat diagnostic excisional procedure is acceptable (CIII). Hysterectomy is acceptable if a repeat diagnostic procedure is not feasible (CIII).

A repeat diagnostic excisional procedure or hysterectomy is acceptable for women with a histologic diagnosis of recurrent or persistent CIN 2, CIN 3, or CIN 2,3 (BII).

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ID,
MD,
on, MD,
College of
ngham,

Alabama; Division of Cancer Epidemiology and Genetics and Division of Cancer Prevention, National Cancer Institute, Bethesda, Maryland; The Permanente Medical Group, Sacramento, California; and Emory University School of Medicine, Atlanta, Georgia

Fertilite ve Obstetrik Sonuçlar

Servikal Stenoz

- Eksizyonel tedavilerde % 8' e varan oranlarda bildirilmiş.
- İnsizyon derinliği ile doğru orantılı
- Kriyoterapi sonrası < %1

İnfertilite

- CIN tedavisi fertiliteyi etkilemiyor gibi gözükmemektedir.
- 15 çalışmalık bir metaanalizde CIN tedavisi olan vs olmayan; % 88 vs. 95
- Gebelik için 12 aydan fazla süreye ihtiyaç duyan; % 15 vs. 9

Kyrgiou M., BMJ 2014 Metaanaliz

Fertilite ve Obstetrik Sonuçlar

İkinci Trimester Gebelik Kaybı

15,108 Eksizyonel tedavi vs **2,164,000**
Tedavi olmamış, gebelik sonrası tedavi
olan **57,136** CIN hastası

%1.5 vs 0.4

Bjørge T, Obstet Gynecol. 2016

15 çalışma metaanaliz

%1.6 vs 0.4, RR 2.60

Kyrgiou M., BMJ 2014 Metaanaliz

Preterm Prematür Membran Rüptürü(PPROM)

27 çalışma metaanaliz

LEEP vs tedavi olmamış

% 5 vs 2

Ablasyonda artış yok.

Kyrgiou M., Lancet 2006 Metaanaliz



Cochrane
Library

Cochrane Database of Systematic Reviews

Cochrane Database of Systematic Reviews 2017, Issue 11.

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, Bennett P, Paraskevaidis E

1 PTB (<37w)	59	5.242917E6	Risk Ratio (IV, Random, 95% CI)	1.75 [1.57, 1.96]
1.1 Excisional Treatment vs No Treatment	53	4.599416E6	Risk Ratio (IV, Random, 95% CI)	1.87 [1.64, 2.12]
1.2 Ablative Treatment vs No Treatment	14	602370	Risk Ratio (IV, Random, 95% CI)	1.35 [1.20, 1.52]
1.3 Treatment NOS vs No Treatment	2	41131	Risk Ratio (IV, Random, 95% CI)	2.57 [1.39, 4.77]
5 PTB (<28-30w)	8	3.910629E6	Risk Ratio (IV, Random, 95% CI)	2.23 [1.55, 3.22]
5.1 Excisional Treatment vs No Treatment	7	3.337003E6	Risk Ratio (IV, Random, 95% CI)	2.81 [1.91, 4.15]
5.2 Ablative Treatment vs No Treatment	3	568217	Risk Ratio (IV, Random, 95% CI)	1.38 [0.81, 2.36]
5.3 Treatment NOS vs No Treatment	1	5409	Risk Ratio (IV, Random, 95% CI)	1.75 [1.05, 2.91]

6 Perinatal Mortality	23	1.659433E6	Risk Ratio (IV, Random, 95% CI)	1.51 [1.13, 2.03]
6.1 CKC vs No Treatment	7	50588	Risk Ratio (IV, Random, 95% CI)	1.46 [0.83, 2.57]
6.2 LC vs No Treatment	3	906	Risk Ratio (IV, Random, 95% CI)	1.89 [0.26, 13.87]
6.3 NETZ vs No Treatment	1	7399	Risk Ratio (IV, Random, 95% CI)	9.99 [3.13, 31.92]
6.4 LLETZ vs No Treatment	7	302271	Risk Ratio (IV, Random, 95% CI)	1.53 [0.88, 2.67]
6.5 LA vs No Treatment	2	258	Risk Ratio (IV, Random, 95% CI)	3.0 [0.12, 72.74]
6.6 CT vs No Treatment	2	238	Risk Ratio (IV, Random, 95% CI)	0.19 [0.01, 4.59]
6.7 Excisional Treatment	5	820028	Risk Ratio (IV, Random, 95% CI)	1.85 [1.02, 3.36]
NOS vs No Treatment				
6.8 Ablative Treatment NOS	2	472197	Risk Ratio (IV, Random, 95% CI)	0.69 [0.42, 1.13]
vs No Treatment				
6.9 Treatment NOS vs No	1	5548	Risk Ratio (IV, Random, 95% CI)	1.00 [0.63, 1.58]
Treatment				

3 LBW (<1500g)	5	76836	Risk Ratio (IV, Random, 95% CI)	3.00 [1.54, 5.85]
3.1 LC vs No Treatment	1	181	Risk Ratio (IV, Random, 95% CI)	12.75 [1.53, 106.44]
3.2 LLETZ vs No Treatment	1	378	Risk Ratio (IV, Random, 95% CI)	7.0 [0.36, 134.59]
3.3 LA vs No Treatment	2	772	Risk Ratio (IV, Random, 95% CI)	0.68 [0.16, 2.80]
3.4 Excisional Treatment	2	75505	Risk Ratio (IV, Random, 95% CI)	3.34 [2.02, 5.54]
NOS vs No Treatment				
4 LBW (<1000g)	2	2185	Risk Ratio (IV, Random, 95% CI)	2.09 [0.06, 74.71]
4.1 LA vs No Treatment	1	708	Risk Ratio (IV, Random, 95% CI)	0.29 [0.01, 5.50]
4.2 Excisional Treatment	1	1477	Risk Ratio (IV, Random, 95% CI)	11.10 [1.44, 85.79]
NOS vs No Treatment				

Morbidite

International Journal of Gynecology and Obstetrics 132 (2016) 266–271



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Table 1Effects of cryotherapy, LEEP, and cold knife conization at 12 months.^a

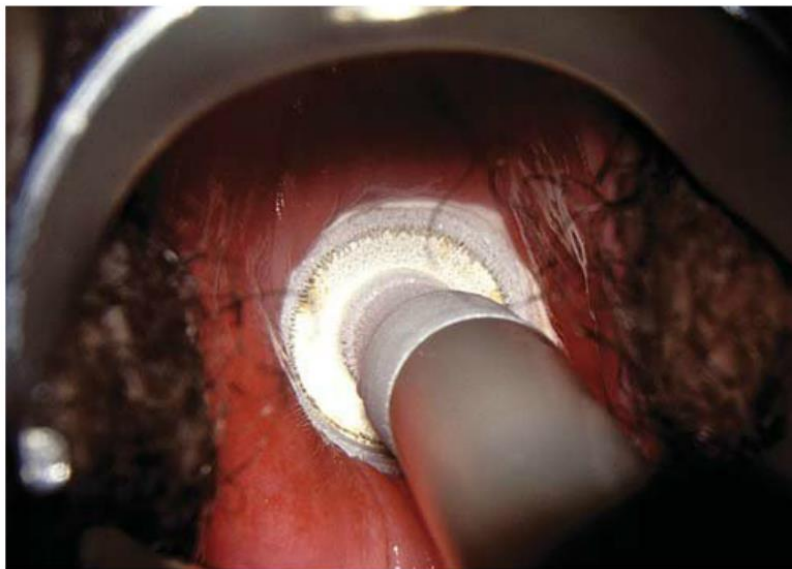
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Abbreviations: LEEP, loop electrosurgical excision procedure including large loop excision of the transformation zone; RR, risk ratio; CIN, cervical intraepithelial neoplasia; PID, pelvic inflammatory disease.

	KRİYOTERAPİ	LEEP
OFİSTE UYGULAMA KOLAYLIĞI	+	+
MALİYET	+	+
TANISAL P/S ELDE ETME	-	+
ETKİNLİK	+	+
FERTİLİTEYE ETKİ	- ?	-
OBSTETRİK SONUÇLAR	+	-
MORBİDİTE	+	-

TEŞEKKÜR EDERİM





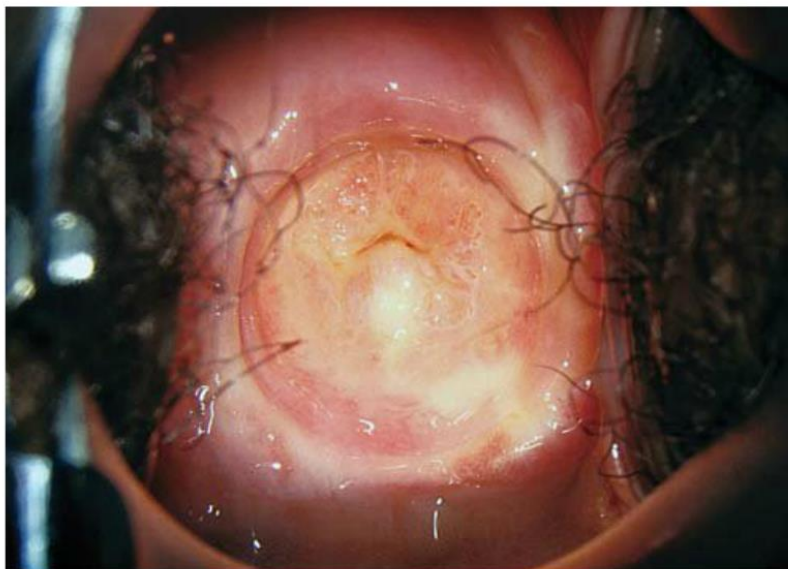
A



B



C



D

Kriyoterapi – Hasta Hazırlığı

- Aydınlatılmış onam
- Gebelik testi
- Mens bitimi yapılmalı
- İşlemden 60 dk. önce NSAİD kullanımı
- Paraservikal blok kullanımı (LH)

TANISAL P/S ELDE ETME

- Ablatif metodlarda P/S yok.
- Tanısal bir veri yok
- Tedavi edilen bölgenin sınırlarında hastalık var mı? Bilmiyoruz.

Cerrahi Sınır:

4417 hasta

**Cerrahi sınır - olan hastalarda;
8.9 (3.3 - 16.8) yıl takip süresi**

Tedavi sonrası CIN 2,3 15 (% 0.35) hastada

4402 (% 99.7) hastada CIN 2,3 yok

Reich et al. Obstet Gynecol 2001

