

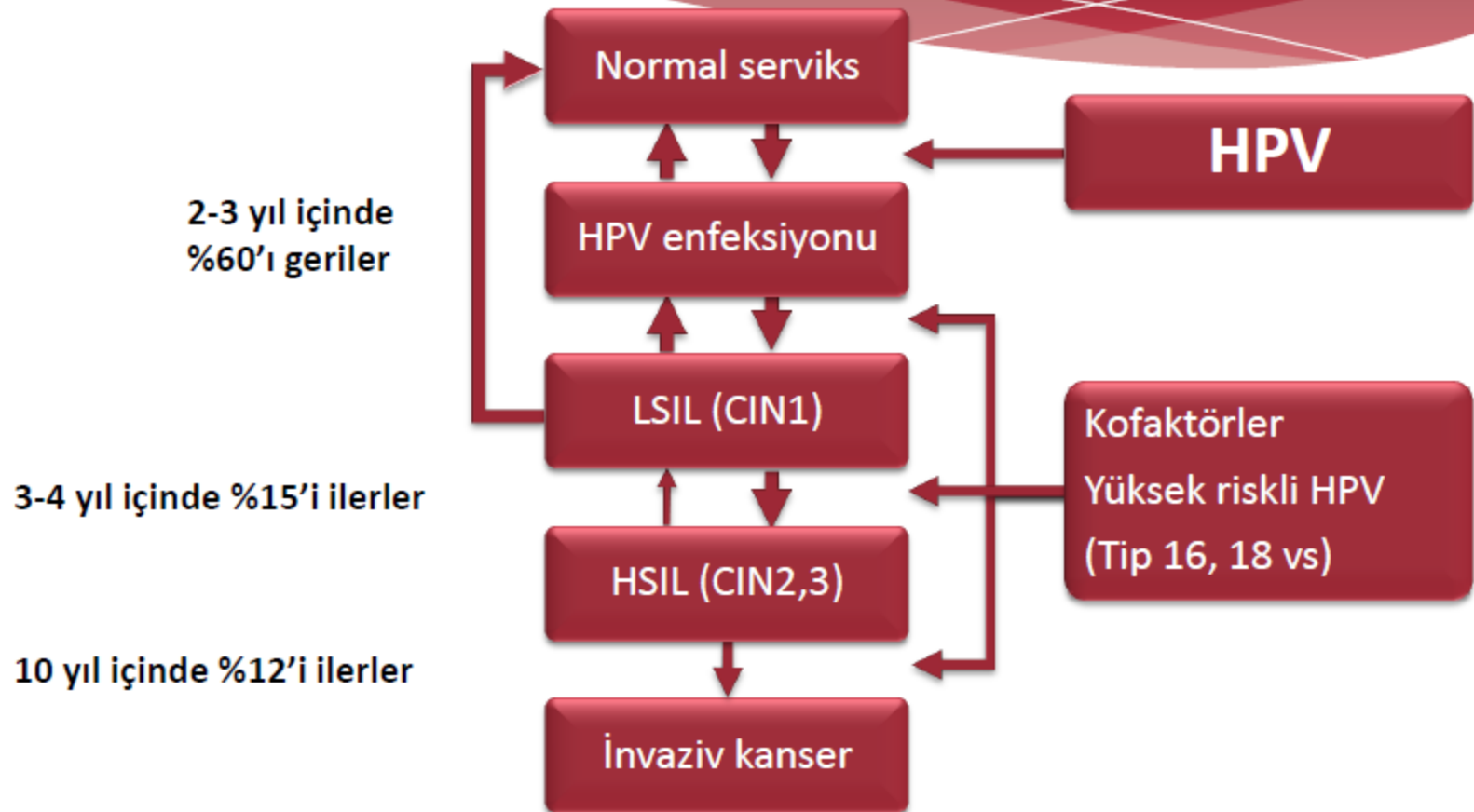


# Random Biopsilerin Kolposkopi Uygulamasında Yeri **Vardır** / Yoktur

Dr. Ahmet Barış GÜZEL

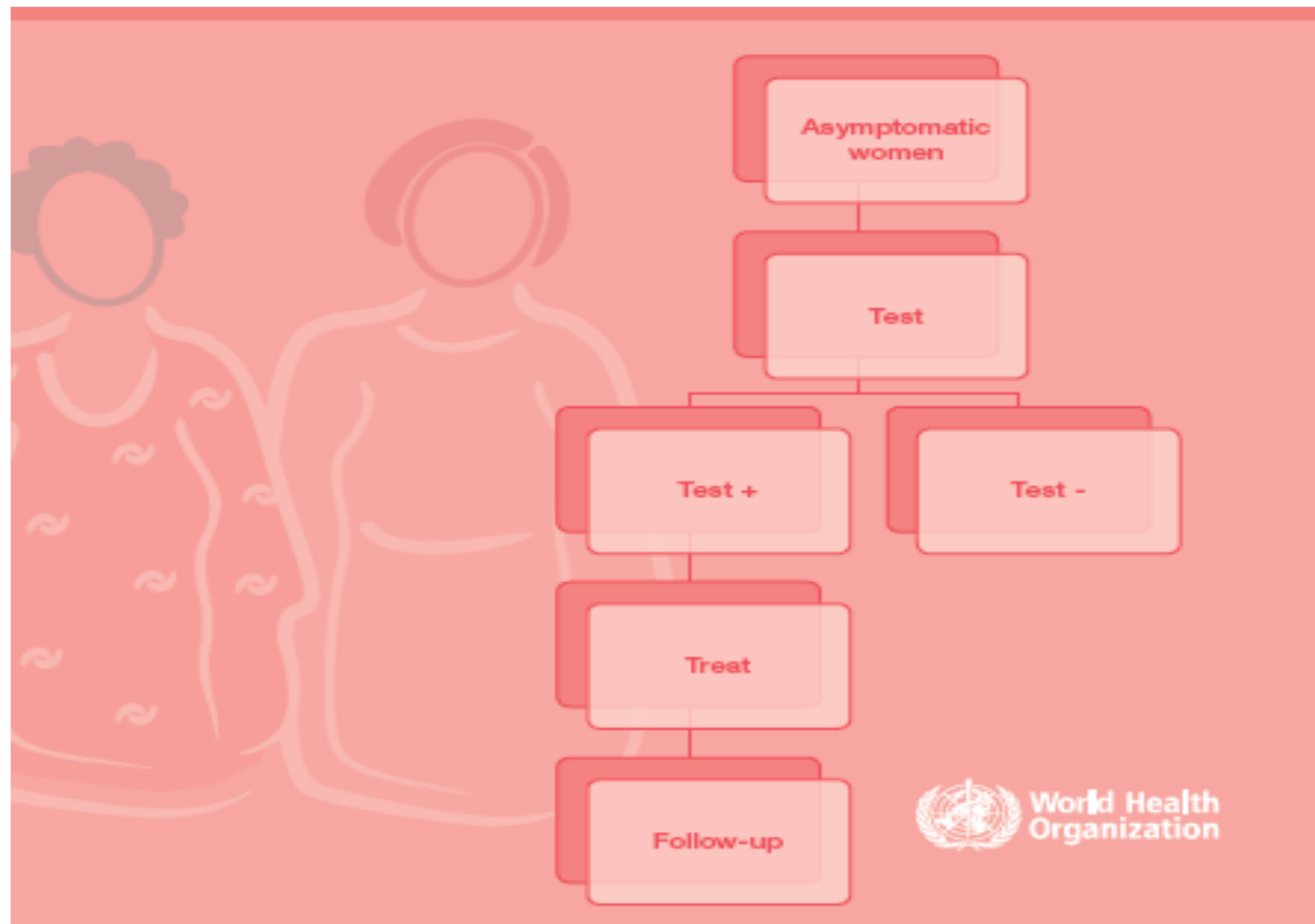
Çukurova Üniversitesi Tıp Fakültesi Kadın  
Hastalıkları ve Doğum AD Jinekolojik  
Onkoloji Cerrahisi Bilim Dalı ADANA

# Serviks Kanseri Gelişimi

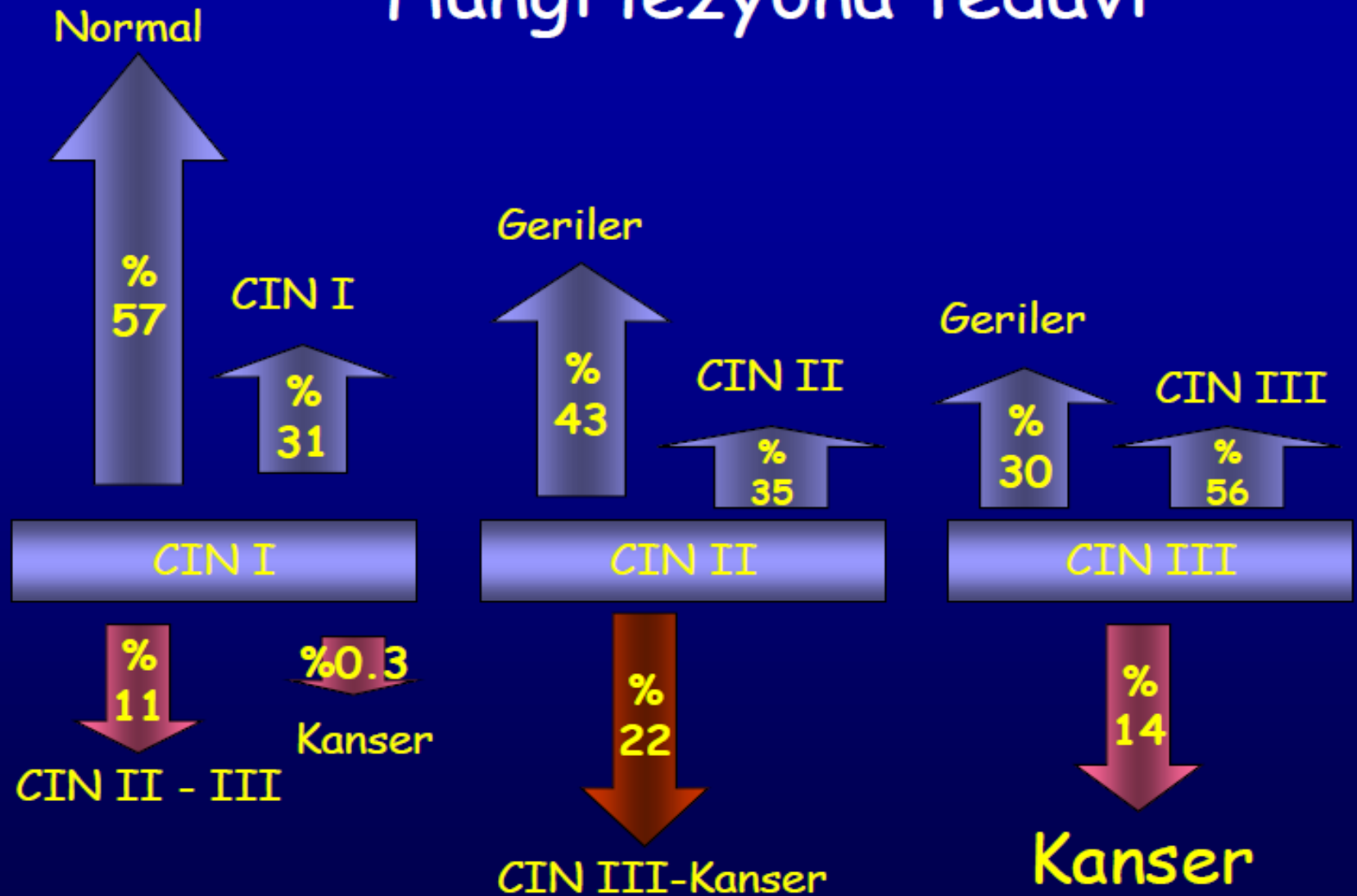


WHO guidelines

## WHO guidelines for screening and treatment of precancerous lesions for cervical cancer prevention



# Hangi lezyona tedavi



# SERVİKSİN PREİNVAZİV LEZYONLARI YÖNETİM

- İzlem
  - Servikal sitoloji
  - HPV testi
  - Kolposkopi ile

# SERVİKSİN PREİNVAZİV LEZYONLARI YÖNETİM

- Tedavi
- Transformasyon zonunun ablasyonu
  - Krioterapi
  - Elektrokoterizasyon
  - Laser ablasyon
- TZ' nun Eksizyonu
  - Loop Electrosurgical Excision Procedure (LEEP)
  - Laser konizasyon
  - Soğuk konizasyon
  - Histerektomi

# Eksizyonel Tedavi Endikasyonları

- Transformasyon zonunun görülmemesi (yetersiz kolposkopi)
- İnvazyon şüphesi varlığı
- Glandüler anormallik şüphesi
- Sitoloji ve histoloji uyumsuzluğu
- Endoservikal kanal tutulumu (ECC+)
- Ablatif tedavi sonrası rekürrens

# SERVİKAL BİOPSİ

- Kolposkopi yeterli, HPV (-), sitoloji normal veya yetersiz.

- Kolposkopi yeterli, anormal bulgular. HPV (+), yüksek gradeli sitolojik anormallik.

Kolposkopi yeterli, normal bulgular. HPV (+), yüksek gradeli sitolojik anormallik.



# Kolposkopi yeterli veya yetersiz

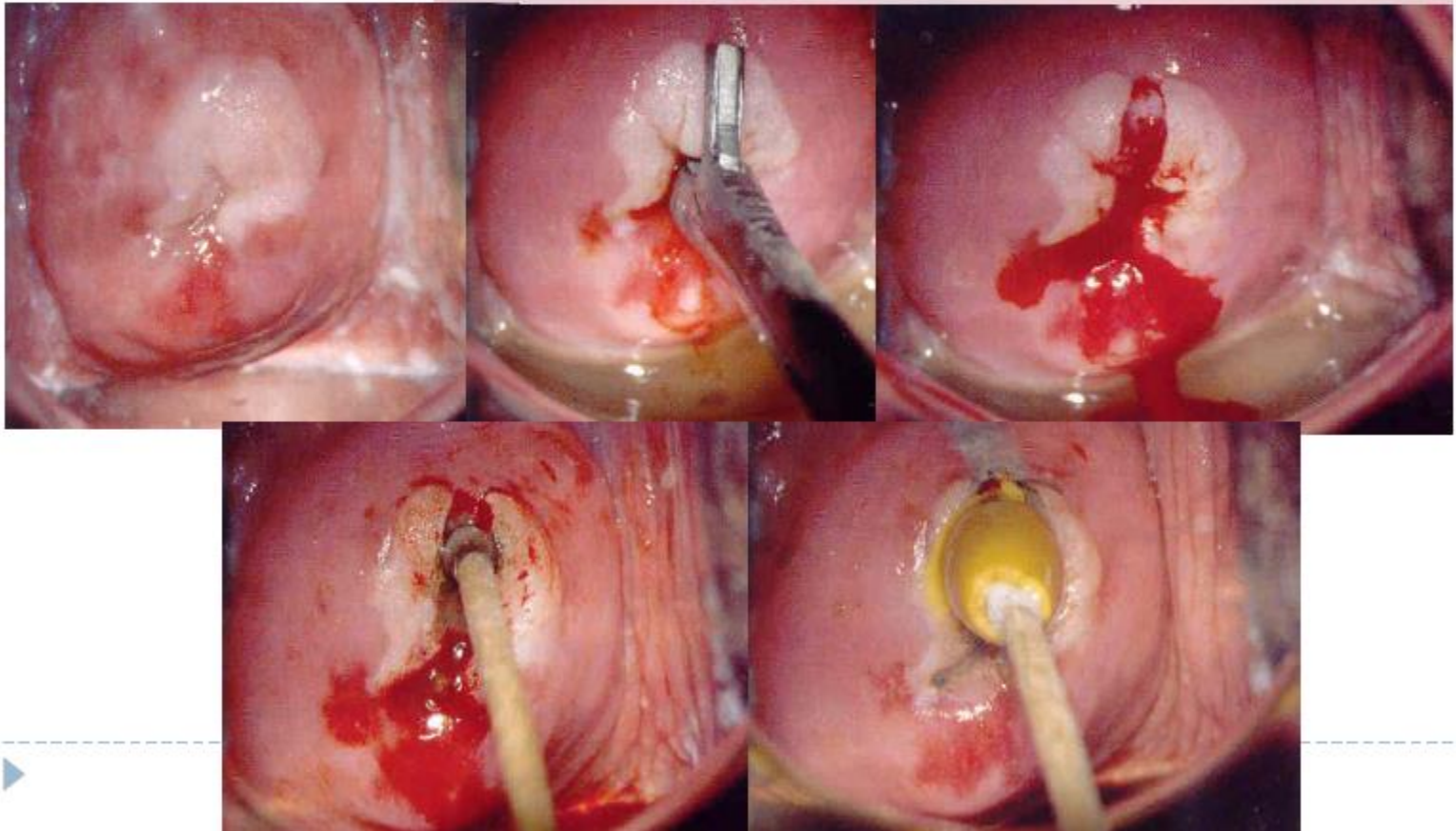
Kolposkopi altında  
Punch HSIL

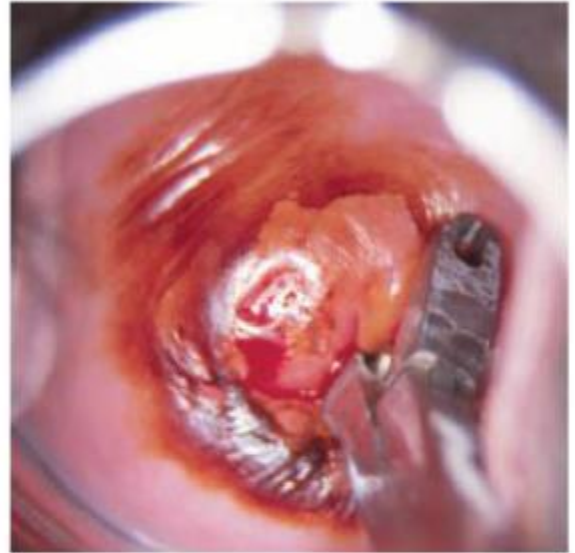
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Gör- Tedavi

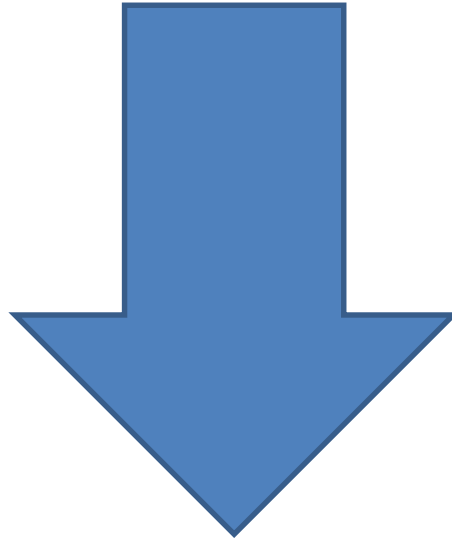
## Eksizyonel Tedaviler

# Biyopsi





# Biyopsilerin Güvenilirliği



- AMAÇ , HEDEF GRUP
- EKSİK TANI VE TEDAVİ
- GEREKSİZ İŞLEM

**SİTOLOJİ NEGATİF, HPV POZİTİF**

- ▶ Negatif sitolojiye rağmen onkojenik HPV(+) kadınlar, HPV(-) olanlara göre, daha sonrası için test tekrarını haklı çıkartacak kadar yüksek CIN3+ riski taşıyorlar ve persiste HPV (+) riski daha da artırıyor.

- ▶ Katki HA, et al. Lancet Oncol. 2011;12:663-72
- ▶ Katki HA, et al. J Low Genit Tract Dis 2013;17:S56-S63
- ▶ Castle PE, et al. BMJ. 2009;339:b2569

- ▶ KPNC kohort, başlangıçtaki her bir sitoloji (-), HPV (+) sonrası yapılan her co-test sonucunda önceki taraması (-) olanlara göre CIN3+ riski artıyor

- ▶ Katki HA, et al. J Low Genit Tract Dis 2013;17:S56-S63

# Klinik pratikte, kolposkopik biopsi kullanımı

## The Use of the Colposcopically Directed Punch Biopsy in Clinical Practice: A Survey of British Society of Colposcopy and Cervical Pathology (BSCCP)-Accredited Colposcopists

*Eva Myriokefalitaki, MD,<sup>1</sup> Charles W.E. Redman, MD, FRCOG,<sup>2</sup> Neelam Potdar, PhD,<sup>1</sup> Philippa Pearmain, MSc,<sup>3</sup> and Esther L. Moss, PhD<sup>1,4</sup>*

**TABLE 5.** Responses on the Question: How Often Would You Perform a Punch Biopsy?

Frequency	%	How often would you perform a punch biopsy in a woman referred with a cytology of:		
		Low-grade (borderline/mild) and low-grade colposcopic features, <i>n</i> (%)	High-grade cytology (moderate/severe) and high-grade colposcopic features, <i>n</i> (%)	Abnormal glandular cells irrespective of colposcopic features, <i>n</i> (%)
Always	100	190 (25.7)	147 (19.9)	136 (18.5)
Most of the time	66–99	336 (45.5)	97 (13.1)	121 (16.5)
Sometimes	33–66	118 (16.0)	123 (16.7)	94 (12.8)
Rarely	1–33	82 (11.1)	281 (38.1)	209 (28.4)
Never	0	13 (1.8)	90 (12.2)	175 (23.8)
Total		739	738	735



# The Use of the Colposcopically Directed Punch Biopsy in Clinical Practice: A Survey of British Society of Colposcopy and Cervical Pathology (BSCCP)-Accredited Colposcopists

**TABLE 2.** Distribution of Number of Punch Biopsies Per Specialty

Specialty	1 biopsy, <i>n</i> (%)	2 biopsies, <i>n</i> (%)	3+ biopsies, <i>n</i> (%)
GOs	37/98 (37.8)	50/98 (51.0)	11/98 (11.2)
Gs	35/127 (27.6)	71/127 (55.9)	21/127 (16.5)
NCs	35/129 (27.1)	78/129 (60.5)	16/129 (12.4)
O&Gs	79/299 (26.4)	167/299 (55.9)	53/299 (17.7)
Others (GPs, GUs)	5/23 (21.7)	12/23 (52.2)	6/23 (26.1)
Overall	191/676 (28.2)	378/676 (56.0)	107/676 (15.8)

**TABLE 3.** Type of Instruments, Anesthetic, and Hemostatic Usages When Obtaining Cervical Punch Biopsy

Frequency	%	Instrument used ( <i>n</i> = 747), <i>n</i> (%)			Local infiltration anesthetic ( <i>n</i> = 746), <i>n</i> (%)	Hemostasis ( <i>n</i> = 747), <i>n</i> (%)		
		Reusable forceps	Single-use forceps	Loop diathermy		Diathermy	Silver nitrate	Monsel solution
Always	100	335 (44.8)	50 (6.7)	3 (0.4)	36 (4.8)			
Most of the time	66–99	299 (40.0)	36 (4.8)	6 (0.8)	21 (2.8)			
Sometimes	33–66	30 (4.0)	50 (6.7)	18 (2.4)	32 (4.3)	35 (4.7)	590 (79)	378 (50.6)
Rarely	1–33	12 (1.6)	75 (10.0)	258 (34.5)	272 (36.5)			
Never	0	8 (1.1)	99 (13.3)	65 (8.7)	385 (51.6)			

## CONCLUSIONS

Colposcopically directed punch biopsy is routinely used by BSCCP-accredited colposcopists; however, the techniques, number of biopsies taken, and rationale for performing a biopsy vary greatly between colposcopists.



Is the Colposcopically Directed  
Punch Biopsy a Reliable Diagnostic  
Test in Women With Minor  
Cytological Lesions?

## The role of the punch biopsy

its use is primarily to confirm the diagnosis before definitive treatment.

This indication is particularly important in the young and nulliparous populations to avoid overtreatment

*Conclusions.* A single colposcopically directed punch biopsy appears to be insufficient to exclude underlying CIN 2 or 3. ■

but a negative punch biopsy result is insufficient to exclude CIN 2 or 3 in this group.

# Accuracy of colposcopy-directed punch biopsies: a systematic review and meta-analysis

M Underwood,<sup>a</sup> M Arbyn,<sup>b</sup> W Parry-Smith,<sup>a</sup> S De Bellis-Ayres,<sup>c</sup> R Todd,<sup>a</sup> CWE Redman,<sup>a</sup> EL Moss<sup>d</sup>

## The number of punch biopsies

- It has been shown that increasing the number of biopsies increases the detection rate of CIN III as does the taking of random biopsies from apparently normal cervical tissue.
- Sensitivity
  - a single punch biopsy is 90%
  - one or more punch biopsies are performed this increases to 93%
  - Multiple biopsies were always performed then the sensitivity would be in the order of 100% (intergroup heterogeneity  $P < 0.001$ )

## ONCOLOGY

# Detection of cervical cancer and its precursors by endocervical curettage in 13,115 colposcopically guided biopsy examinations

Julia C. Gage, PhD, MPH; Máire A. Duggan, MD; Jill G. Nation, MD; Song Gao, MSc; Philip E. Castle, PhD, MPH

**CONCLUSION:** ECC is rarely informative when used routinely in colposcopic practice. Older women referred after high-risk cytology benefit most from ECC.

# Regardless of Skill, Performing More Biopsies Increases the Sensitivity of Colposcopy

For 6 of 7 physicians,  
the yield of CIN 3+ per colposcopy was greater when colposcopically  
directed biopsy was augmented by up to 4  
“random” biopsies plus ECC ( $p = .03$  to  $p < .001$ ).

*Conclusions.* The sensitivity of colposcopy for CIN 3+ varies widely. Performing up to 4 “random” biopsies plus ECC increases the yield of CIN 3+. ■

## Kolposkopik Biyopsilerin $\geq$ CIN II Lezyonlarını Tanıma Oranları (SPOCCS II)

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Kolpo biopsi	208/364	(57.1%)
Kolpo biopsi + saat 2	256/364	(70.3%)
Kolpo biopsi + saat 2, 4	297/364	(81.6%)
Kolpo biopsi + saat 2, 4, 8	329/364	(90.4%)
Kolpo biopsi + saat 2, 4, 8, 10	344/364	(94.5%)
Kolpo biopsi + saat 2, 4, 8, 10 + ECC	364/364	(100%)

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57.1% vs. 70.3% vs. 81.6% vs. 90.9% vs. 94.5% vs. 100%, Chi-Square = 326, df=5,  $p < .001$

## False negative colposcopy is associated with thinner cervical intraepithelial neoplasia 2 and 3<sup>☆</sup>

Bin Yang<sup>a</sup>, Robert G. Pretorius<sup>b,\*</sup>, Jerome L. Belinson<sup>c</sup>, Xun Zhang<sup>d</sup>,  
Raoul Burchette<sup>e</sup>, You-Lin Qiao<sup>d,\*</sup>

To assess whether thinner lesion epithelium or lower nuclear density contribute to false negative colposcopy for dysplasia, we determined epithelial thickness and nuclear density and correlated this with the accuracy of colposcopic impression for cervical quadrants with biopsies of normal, CIN 1, CIN 2 and CIN 3.

*Results.* Mean average epithelial thickness for 33 biopsies of CIN 2/CIN 3 from cervical quadrants with colposcopic impression of normal (184  $\mu\text{m}$ ) was less than that of 111 biopsies of CIN 2/CIN 3 from quadrants with colposcopic impressions of low, high, or cancer (321  $\mu\text{m}$ ,  $p < .001$ ). CIN 2/CIN 3 had higher mean average nuclear density ( $p < .001$ ) and was thinner than normal/CIN 1 ( $p < .001$ ).

*Conclusion.* The inability of expert colposcopists to visualize some CIN 2/CIN 3 is associated with thinner epithelium.

## False negative colposcopy is associated with thinner cervical intraepithelial neoplasia 2 and 3<sup>☆</sup>

Bin Yang<sup>a</sup>, Robert G. Pretorius<sup>b,\*</sup>, Jerome L. Belinson<sup>c</sup>, Xun Zhang<sup>d</sup>,  
Raoul Burchette<sup>e</sup>, You-Lin Qiao<sup>d,\*</sup>

Distribution of 7687 slides from cervical quadrants in Shanxi Province Cervical Cancer Screening Study I and the number of slides in each cell that were chosen for review (in parenthesis)

Histology	Colposcopic impression normal	Colposcopic impression low	Colposcopic impression high	Colposcopic impression cancer	Total
NORMAL	6601 (22)	663 (23)	29 (21)	2 (1)	7295 (67)
CIN 1	149 (25)	61 (23)	14 (14)	0 (0)	224 (62)
CIN 2	22 (22)	32 (32)	25 (25)	4 (4)	83 (83)
CIN 3	9 (9)	12 (12)	21 (21)	17 (17)	59 (59)
CANCER	3 (0)	3 (0)	6 (0)	14 (0)	26 (0)
TOTAL	6784 (78)	771 (90)	95 (81)	37 (22)	7687 (271)

CIN is cervical intraepithelial neoplasia.





## Colposcopically directed biopsy, random cervical biopsy, and endocervical curettage in the diagnosis of cervical intraepithelial neoplasia II or worse

Robert G. Pretorius, MD,<sup>a,\*</sup> Wen-Hua Zhang, MD,<sup>b</sup> Jerome L. Belin: Man-Ni Huang, MD,<sup>b</sup> Ling-Ying Wu, MD,<sup>b</sup> Xun Zhang, MD,<sup>b</sup> You-Lin Qiao, MD, PhD<sup>b,\*\*</sup>

**~21% increased detection rate  
with 'random' biopsy!!!**

## Utility of Random Cervical Biopsy and Endocervical Curettage in a Low-Risk Population

Robert G. Pretorius, MD,<sup>1</sup> Jerome L. Belinson, MD,<sup>2</sup> Faramarz Azizi, MD,<sup>3</sup> Patricia C. Peterson,<sup>1</sup> and Suzanne Belinson, PhD<sup>2</sup>

<sup>1</sup>Department of Obstetrics and Gynecology, Southern California Permanente Medical Group-Fontana, Fontana, CA; <sup>2</sup>Preventive Oncology International, Cleveland, OH; and <sup>3</sup>Department of Pathology, Southern California Permanente Medical Group-Fontana, Fontana, CA

## Regardless of Skill, Performing More Biopsies Increases the Sensitivity of Colposcopy

Robert G. Pretorius, MD,<sup>1</sup> Jerome L. Belinson, MD,<sup>2</sup> Raoul J. Burchette, MS,<sup>3</sup> Shangying Hu, MD,<sup>4</sup> Xun Zhang, MD,<sup>4</sup> and You-Lin Qiao, MD, PhD<sup>4</sup>

<sup>1</sup>Department of Obstetrics and Gynecology, Southern California Permanente Medical Group-Fontana, Fontana, CA; <sup>2</sup>Department of Gynecology, The Cleveland Clinic Foundation, Cleveland, OH; <sup>3</sup>Department of Research and Evaluation, Southern California Permanente Medical Group, Los Robles, CA; and <sup>4</sup>Department of Epidemiology, Cancer Institute/Hospital, Chinese Academy Medical Sciences, Beijing, China

# Are we missing disease and does this need to be revisited?

## Number of Cervical Biopsies and Sensitivity of Colposcopy

*Julia C. Gage, MPH, Vivien W. Hanson, MD, Kim Abbey, BSN, FNP, Susan Dippert, RN, WHCNP, Susi Gardner, BSN, MSN, ARNP, Janet Kubota, BSN, WHCNP, Mark Schiffman, MD, MPH, Diane Solomon, MD, and Jose Jeronimo, MD, for The ASCUS LSIL Triage Study (ALTS) Group\**

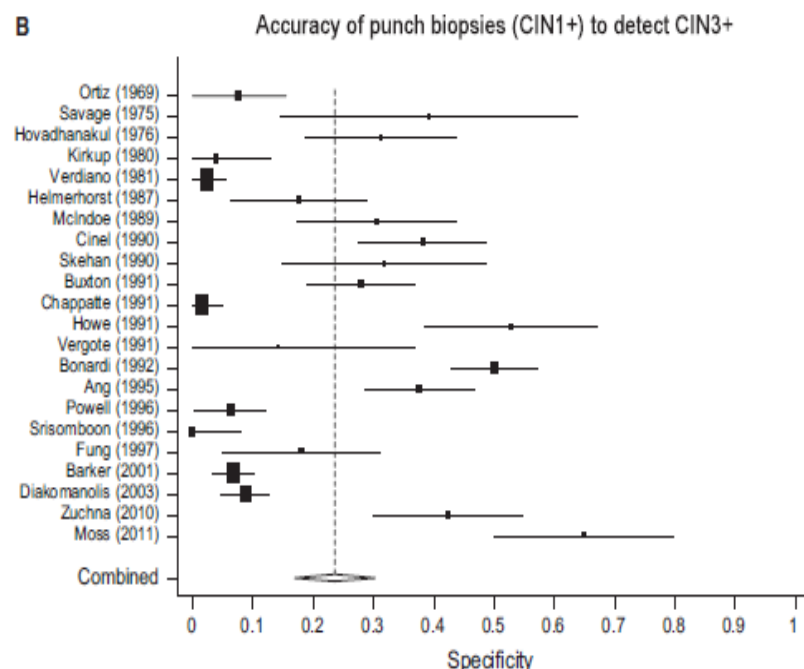
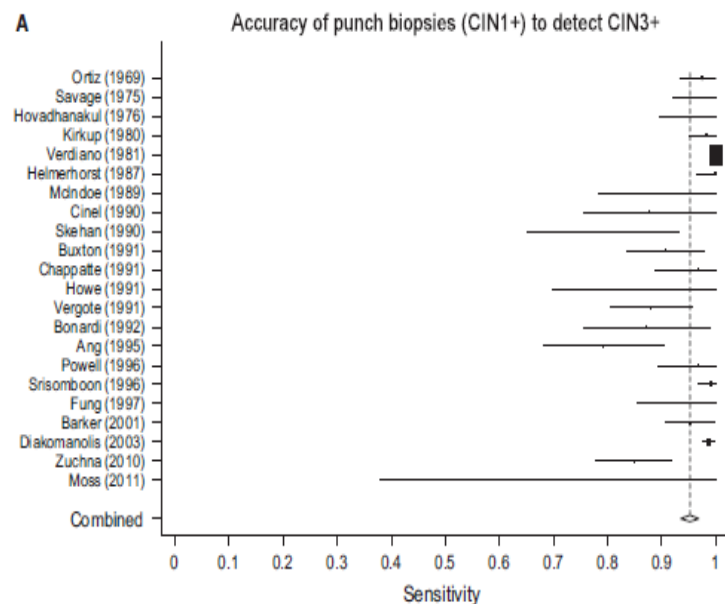
- Sensitivity of colposcopy for detection of CIN2+: 69.9%
- Sensitivity improves when two more biopsies are taken
- Detection does not differ by type of medical training
- ~12-15% detection rate of CIN2+ with random biopsy\*

\* Personal communication

Gage J, et al. *Obstet Gynecol*. 2006; 108: 264–272.  
Pretorius RG et al, *J Low Gent Tract Dis* 2011; Mar 23  
Pretorius RG et al *Am J Obstet Gynecol* 2004; 191:430-4

# Accuracy of colposcopy-directed punch biopsies: a systematic review and meta-analysis

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definitive histology results were identified. The pooled sensitivity for a punch biopsy defined as test cut-off CIN1+ to diagnose CIN2+ disease was 91.3% (95% CI 85.3–94.9%) and the specificity was 24.6% (95% CI 16.0–35.9%). In most of the

# Random biopsy in colposcopy-negative quadrant is not effective in women with positive colposcopy in practice

- Random biopsy is not effective in the negative quadrant in women with positive colposcopy,
- But should be performed in women with cytological HSIL+ but negative colposcopy,
- Or in those with cytological LSIL or HGSL+ and positive HPV but negative colposcopy.
  - Cancer Epidemiology 39 (2015) 237–241

## Colposcopically directed biopsy, random cervical biopsy, and endocervical curettage in the diagnosis of cervical intraepithelial neoplasia II or worse

Even when colposcopy is satisfactory, ECC should be performed.

If cytology is high grade, random biopsies should be considered.

American Journal of Obstetrics and Gynecology (2004) 191, 430–4

**Table II** Yield of CIN II or worse per colposcopically directed biopsy or random biopsy as a function of cytologic smear

Cytologic smear diagnosis	≥CIN II per colposcopic directed biopsy (%) 95% CI	≥CIN II per random biopsy (%) 95% CI	ECC ≥ CIN II per patient biopsied (%) 95% CI
HGSIL or cancer	290/689 (42.1%) 38.4-45.8	97/551 (17.6%) 14.4-20.8	75/196 (38.3%) 31.5-45.1
LGSIL	95/701 (13.6%) 11.0-16.2	50/1389 (3.6%) 2.6-4.6	13/88 (14.8%) 7.4-22.2
ASCUS, high-risk HPV-positive	23/151 (15.2%) 9.5-21.0	19/1117 (1.7%) 0.9-2.5	5/32 (15.6%) 3.0-28.2
AGUS	0/0 (0%) 0-0	4/12 (33.3%) 6.7-60	0/3 (0.0%) 0-0
Total	408/1541 (26.5%) 24.3-28.7	170/3069 (5.5%) 4.7-6.3	93/319 (29.2%) 24.2-34.1

# Abnormal cervical cytology or presence of high-risk human papillomavirus (HPV)

- Clinicians are often faced with absence of visible lesions, raising the question whether a cervical biopsy should be taken.

– Andrew M. Kaunitz, MD reviewing Huh WK et al. Obstet Gynecol 2014 Oct .

# Abnormal cervical cytology or presence of high-risk human papillomavirus (HPV)

- Study designed to assess human papillomavirus (HPV) diagnostics, colposcopy was performed in >8000 nonpregnant participants aged  $\geq 25$
- who had abnormal cytology, high-risk HPV, or both.
- In women with satisfactory colposcopy but no detectable lesions, a single random biopsy of the squamocolumnar junction was performed.

# Abnormal cervical cytology or presence of high-risk human papillomavirus (HPV)

- Among women positive for HPV 16 or 18, the likelihood of random biopsy detecting CIN2 or worse was
  - 24.7% for those with abnormal cytology
  - *and 8.6% for those with normal cytology.*



# Value of Random Cervical Biopsy When Colposcopy Shows No Visible Lesions

- Random biopsy at the squamocolumnar junction substantially increased diagnosis of cervical intraepithelial neoplasia

- Two or more cervical biopsies increases diagnostic yield, these results point to the substantial benefit gained from performing a single random biopsy of the squamocolumnar junction when no colposcopic lesions are identified.
  - Obstet Gynecol 2006; 108:264

# SONUÇ

- Koloposkopide teknik güçlükler
- Kolposkopi yeterli - normal, sitolojik anormallik mevcut olan ve yüksek risk HPV (+) olgularda random biopsilerin yeri vardır.



**Dikkatiniz İçin Teşekkürler!**