Random Biopsies have No Place in Colposcopy Practice: *The Con Argument*

Warner K. Huh, MD
Division of Gynecologic Oncology
Department of Obstetrics and Gynecology
Birmingham, AL, USA

Presidential Debate

Disclosures

- WKH: No financial relationships or conflict of interest to disclose

Introduction

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

ELSEVIER

AMERICAN JOURNAL of OBSTETRICS and GYNECOLOGY

www.elsevier.com/locate/ajog

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

Robert G. Pretorius, MD,[a,*] Wen-Hua Zhang, MD,[b] Jerome L. Belins
Man-Ni Huang, MD,[b] Ling-Ying Wu, MD,[b] Xun Zhang, MD,[b]
You-Lin Qiao, MD, PhD[b,**]

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

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

Robert G. Pretorius, MD,[1] Jerome L. Belinson, MD,[2] Faramarz Azizi, MD,[3] Patricia C. Peterson,[1] and Suzanne Belinson, PhD[2]

[1]Department of Obstetrics and Gynecology, Southern California Permanente Medical Group-Fontana, Fontana, CA; [2]Preventive Oncology International, Cleveland, OH; and [3]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,[1] Jerome L. Belinson, MD,[2] Raoul J. Burchette, MS,[3] Shangying Hu, MD,[4] Xun Zhang, MD,[4] and You-Lin Qiao, MD, PhD[4]

[1]Department of Obstetrics and Gynecology, Southern California Permanente Medical Group–Fontana, Fontana, CA; [2]Department of Gynecology, The Cleveland Clinic Foundation, Cleveland, OH; [3]Department of Research and Evaluation, Southern California Permanente Medical Group, Los Robles, CA; and [4]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 Dippery, 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

ATHENA Trial (**A**ddressing **THE** **N**eed for **A**dvanced HPV Diagnostics)

- A prospective study of >47,000 women
- Evaluation of the cobas® HPV Test to identify women with high-grade cervical disease (CIN2+)
  - hrHPV DNA testing and HPV16/18 genotyping
  - Compared to cytology
- Baseline:
  - Investigation in women for whom hrHPV testing is currently recommended in US screening guidelines[1]
    - Women with normal cervical Pap cytology (NILM) ≥30 yrs of age
    - Women with equivocal cervical Pap cytology (ASC-US) ≥21 yrs of age
- Follow-up phase:
  - Safety of test result at baseline over a three year period

Wright TC Jr, *et al. Am J Obstet Gynecol* 2007; 197: 346–355.

ATHENA Trial (**A**ddressing **THE** **N**eed for **A**dvanced HPV Diagnostics)

Colposcopy	**Satisfactory** *(Visualization of cervix & SCJ)*		**Unsatisfactory** *(Partial visualization of SCJ)*		**Unsatisfactory** *(SCJ not visualized)*	
	Lesion(s) visible	No lesion visible	Lesion(s) visible	No lesion visible	Lesion(s) visible	No lesion visible
Biopsy	**All lesions**	**Single biopsy at SCJ**	**All lesions**	**Single biopsy at SCJ**	**All lesions**	**No**
ECC	✗	✗	✗	✓	✓	✓

SCJ, squamoucolumnar junction

Wright TC Jr, *et al. Am J Obstet Gynecol* 2007; 197: 346–355.

ATHENA Trial (**A**ddressing **THE** **N**eed for **A**dvanced HPV Diagnostics)

Original Research

Relevance of Random Biopsy at the Transformation Zone When Colposcopy Is Negative

Warner K. Huh, MD, Mario Sideri, MD, Mark Stoler, MD, Guili Zhang, PhD, Robert Feldman, MD, and Catherine M. Behrens, MD, PhD

ATHENA Trial (**A**ddressing **THE** **N**eed for **A**dvanced HPV Diagnostics)

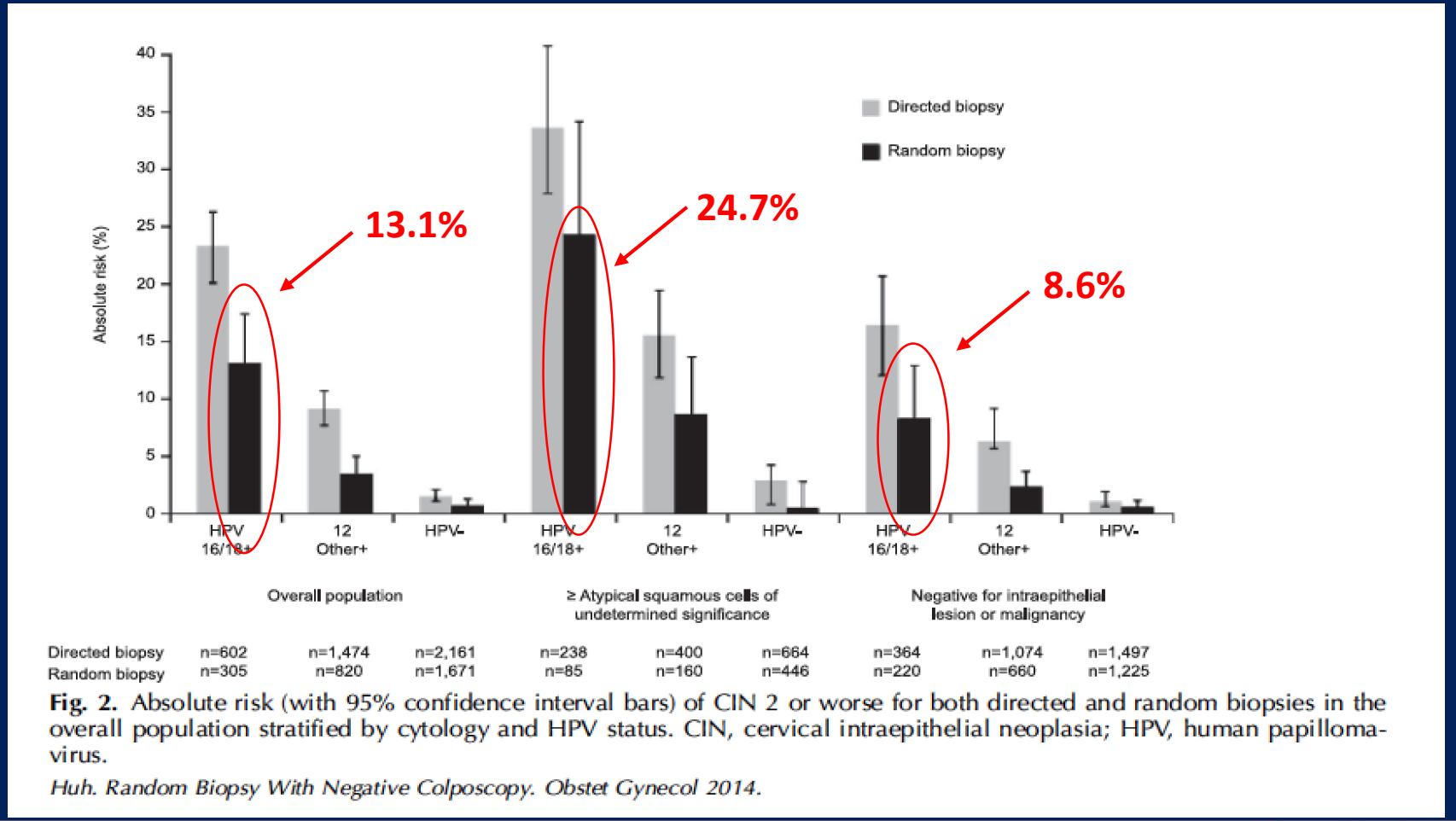

Fig. 2. Absolute risk (with 95% confidence interval bars) of CIN 2 or worse for both directed and random biopsies in the overall population stratified by cytology and HPV status. CIN, cervical intraepithelial neoplasia; HPV, human papillomavirus.

Huh. Random Biopsy With Negative Colposcopy. Obstet Gynecol 2014.

Random Biopsies in Low Risk Women

Low-risk group: <HSIL, HPV 16/18-, normal colposcopy						
Study	Manuscript	N	CIN2+	CIN3+	Proportion CIN2+	Proportion CIN3+
ATHENA	Huh 2014	1225	8	2	0.0065	0.0016
ALTS	in preparation	373	4	2	0.0107	0.0054
BD	in preparation	1572	25	11	0.0159	0.0070
Biopsy	in preparation	19	0	0	0.0000	0.0000
Total		3189	37	15	0.0116	0.0047

- Studies have shown that women with a low prior risk and normal colposcopy impression have a very low risk of prevalent precancer
- **But, what about women who are at higher risk?**

IMPROVE-COLPO Study (Retrospective Arm)

- In the US, most colposcopists perform <2 biopsies per patient
- Recent research indicates that taking more biopsies improves sensitivity and detection of CIN2+; however, this is not being practiced in the US
- Colposcopic impression is typically not documented and has a poor sensitivity to predict CIN2+

So, what do you think?

Its obvious to me….ITS HUGE

- 20-25% increased detection of CIN2+ with random biopsies
  - Improved performance
- In the US, we don’t take enough biopsies
- Is it because we don’t know where (i.e., lesion identification, training)?
- Lesions will only get smaller, as we vaccinate more
- Isn’t ’colposcopy’ about maximally detecting all disease?

The ‘real’ story

- Very little value in random biopsies who are considered low risk
- The yield of CIN2+ with random biopsies in women with ASCUS/HPV+ or LSIL is low (3.6% and 1.7%) (Pretorius, 2004)
- Investigators in the ATHENA trial were blinded to cytology and HPV results (not consistent with clinical practice)
- US colposcopists just need to biopsy more