“Endometrial Intraepithelial Neoplasia Clinical Correlates and Outcomes”  
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1. What was the study design? Why was this design chosen for this study? Are any other designs practical for testing the authors’ hypothesis?

2. Discuss the accuracy of chart review for the exposures analyzed in the tables. Are any of the authors’ conclusions weakened by the inaccuracy of any of the exposures? Are any of the authors’ conclusions weakened by missing data for any of the exposures?

3. Describe the protocol for review and re-review of the index biopsies and subsequent pathology diagnoses. Discuss the purpose of the re-review. What estimate was given for the degree of agreement among the eleven pathologists for pathology interpretation?

4. Tissue samples were obtained with varying procedures (biopsy, curettage, and hysterectomy). Discuss the effect of tissue sampling technique on accuracy of the diagnosis.

5. Review the assumptions underpinning Kaplan-Meier survival analysis. Are any of these assumptions violated in this study? If so, do any of the violations have any significant effect on the analysis?

6. Median follow-up was 74 days and mean follow-up was 269 days. Why was there such a disparity between mean and median? How does this affect Kaplan-Meier analysis, if at all? How does this affect the case-control analysis, if at all? With such short follow-up for most patients, how does one distinguish between concurrent cancer missed in the index biopsy and disease progression?

7. Review the UpToDate section on endometrial hyperplasia. Compare the WHO94 system with the Endometrial Collaborative Group classification criteria. Which method of classification is used by the pathologists in your institution? UpToDate states that the Endometrial Collaborative Group classification is simpler, more reproducible, and more predictive of progression than the WHO94 system; however, it has not caught on. Discuss why the endometrial intraepithelial neoplasia schema has not replaced the WHO94 system.

8. At the end of this questionnaire are photomicrographs of two cases (courtesy of Dr. Richard J. Zaino). Classify the endometrial biopsies with the WHO94 system, then the endometrial intraepithelial neoplasia schema. Was there any disagreement among your group in final classifications? Was there better agreement in one system than the other?

9. Contrast the management of endometrial intraepithelial neoplasia with the management of atypical hyperplasia. Are there any differences?
Case 1. Hematoxylin and eosin [H&E] stained photomicrograph. Upper panel, original magnification x40; lower panel, original magnification x400. Images courtesy of Dr. Richard J. Zaino.
Case 2. Hematoxylin and eosin [H&E] stained photomicrograph. Upper panel, original magnification x40; lower panel, original magnification x400. Images courtesy of Dr. Richard J. Zaino.