Question 1:

Given that the primary risk to excisional procedures used in the management of precancerous cervical lesions seems to be related to future reproductive outcomes, do your young patients’ future fertility plans (e.g., a 28-year-old sterilized woman with three children and no plans for more compared with the same woman if unsterilized with no children) affect your recommendations for ablative compared with excisional techniques? What data do you provide women in your counseling on the risks and benefits of excisional compared with ablative techniques relative to their reproductive plans?

Response from Drs. Sawaya and Smith-McCune:

Evidence from randomized trials indicates that excisional and ablative therapies have similar efficacies, but ablative therapies have the advantages of a lower risk of hemorrhage, lower procedural costs, and no concurrent charges for the pathological specimen. Thus, we believe that ablation is a high-value option and we offer it as a first-line therapy to young women who meet criteria, regardless of their reproductive capabilities. When loop excision is recommended, we discuss the possibility of preterm delivery in a future pregnancy and provide the information in absolute terms. For example: “About 10 out of 100 births in the U.S. are preterm. After loop excision, the risk may be as high as 17 out of 100.”

Question 2:

In ablative procedures, the margins of the treatment area are not evaluated, but one could safely assume that some patients have incomplete coverage of the lesions. Why, then, do you recommend that all women with ablative treatment be followed in the same way as women after an excisional procedure with negative margins?
A recent systematic review did not identify randomized trials directly comparing cure rates between excisional procedures with negative margins and cryotherapy, in which margin status is unknown (see Cochrane Database Syst Rev. 2013;12:CD001318). Observational studies, however, suggest that cure rates are similar: 93% with loop excision with negative margins (see Lancet Oncol 2007;8:985–93) and 89% for cryotherapy, especially if a double freeze technique is used (see Int J Gynaecol Obstet 2013;120:218–23). Using the risk-based approach outlined in current guidelines, these women would be followed similarly.

Question 3:

Is there a role for the human papillomavirus (HPV) vaccine in the management of women at any age with persistently abnormal cervical screening?

Response from Drs. Sawaya and Smith-McCune:

The vaccine is approved for use in girls and women aged 9–25 years (bivalent) or 26 years (quadrivalent and nonavalent), and is most effective when administered before the onset of sexual activity. There is no role for the vaccine in the indicated scenario for hastening clearance of HPV or reversing HPV-related disease. Data from vaccine trials, specifically in women with abnormal cytology at the time of vaccination, showed that the vaccine was not effective at preventing HPV-related disease outcomes (see Am J Obstet Gynecol 2008;198:261 e1–11). Further, U.S. Food and Drug Administration (FDA) labeling specifically states: “Gardasil is not intended to be used for treatment of active external genital lesions; cervical, vulvar, vaginal, and anal cancers; CIN; VIN; VaIN, or AIN” (see http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM111263.pdf). Similar language is included in the labeling for the nonavalent HPV vaccine. The bivalent vaccine labeling states: “CERVARIX has not been demonstrated to provide protection against disease from vaccine and non-vaccine HPV types to which a woman has previously been exposed through sexual activity” (see http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM186981.pdf). Data about vaccine efficacy in women over the age of 25–26 years is either not available (bivalent or nonavalent) or show lack of overall efficacy for averting cervical intraepithelial neoplasia (CIN) 2+ (quadrivalent) (see Br J Cancer 2011;105:28–37). FDA labeling specifically states: “Gardasil has not been demonstrated to prevent HPV-related CIN 2/3 or worse in women older than 26 years of age” (see http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM111263.pdf).

Question 4:

What do you recommend for screening of women who present for care at or beyond the age of 65 years and report that they have not had prior cervical screening?

Response from Drs. Sawaya and Smith-McCune:

We recommend screening for women aged 65 years and older who have never been screened because never-screened, older women are at the highest risk for cervical cancer. Decision analytic modeling suggests that these women can benefit from a few screening rounds while incurring relatively few harms (see http://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0068198/). An upper age limit for never-screened women has not been established. Clinicians should use clinical judgment, taking into account co-morbidities, to determine if the projected benefits of screening outweigh the harms in individual women.
Question 5:

Do you recommend excisional procedures for patients who have undergone ablative procedures and continue to have persistently abnormal cytology? Would you recommend multiple ablative procedures prior to an excisional procedure? If so, how many?

Response from Drs. Sawaya and Smith-McCune:

Limited evidence suggests that repeat ablation has a higher failure rate than primary treatment (see http://www.path.org/publications/files/RH_cryo_white_paper.pdf). Thus, we generally do not recommend repeat ablation to our patients.

Question 6:

What is the evidence that women aged at least 25 years with cytologic interpretations of HSIL (high-grade squamous intraepithelial lesion) or ASC-H (atypical squamous cells cannot rule out HSIL) but with no CIN2+ and adequate initial colposcopy benefit from colposcopy and cytology at 6 months rather than the American Society of Colposcopy and Cervical Pathology’s (ASCCP) and the American College of Obstetricians and Gynecologists’ recommended cytology and high-risk HPV testing at 12 months?

Response from Drs. Sawaya and Smith-McCune:

Women in this scenario are at a relatively high risk of having CIN2+ that was missed on initial colposcopy. Current guidelines recommend colposcopy and cytology at 6 months for women aged 21–24 years. We do not believe that a less aggressive approach (co-testing in 12 months) is warranted in women over the age of 25 years given that the expected prevalence of underlying CIN2+ is at least as high, if not higher, among older women with similar cytologic findings (see Health Technol Assess 2009;13:1–150, iii–iv). In addition, cancer incidence increases with age, supporting a vigilant surveillance strategy in older women with HSIL or ASC-H.