Table 1: Biopsy results for LSIL, LSIL-H, ASC-H, and HSIL

	Cytopathologic interpretation in SurePath™	Positive predictive value (PPV) for			
		Group A Negative result on biopsy	**Group B** Low grade (HPV & CIN-1) result on biopsy	**Group C** High grade (CIN-2 & CIN-3) result on biopsy	**Total (792)**
1	**LSIL***	32% (179/557)	58% (323/557)	**10% [b](55/557)**	100% (557)
2	**LSIL-H***	**24%[a] (21/88)**	*43%*[c] (38/88)	33%[b] (29/88)	100% (88)
3	**ASC-H***	32%[a] (12/38)	*37%* [c] (14/38)	31%[b] (12/38)	100% (38)
4	**HSIL**	5% (6/109)	26% (28/109)	69% (75/109)	100% (109)

* Positive predictive values between groups 1,2,&3 were compared by performing separate 2 × 3 Chi-square tests for rows 1 & 2 and for rows 2 & 3. Applying the Bonferroni correction for multiple testing the significance level was adjusted to 0.025. The statistical comparison between LSIL and LSIL-H shows Chi-square value of 35.7 with p value less than 0.001, consistent with statistically significant difference between these two groups indicating they represent two separate entities. However, for LSIL-H and ASC-H the Chi-square is 0.87 with p value nearly equal to 1, consistent with lack of any significant difference between these two groups.

LSIL-H[b] and ASC-H[b] showed higher PPV for high grade dysplasia on biopsy, but prevalence of negative results was lower for LSIL-H, as compared to ASC-H[a]. In summary, LSIL-H overlapped on one side with ASC-H for high grade risk, and with LSIL on other side for higher risk for low grade lesion[c]. The possibility of negative result with LSIL-H[a] was intermediate between HSIL and LSIL or ASC-H.

ASC-H patterns may represent hyperchromatic crowded groups which should be scrutinized carefully for proper interpretation as reported previously [21,22].

The management of LSIL-H cases has not been addressed currently by the ASCCP guidelines [6,22-25]. Based on the biopsy pattern in this study and review of the literature, the initial management may be similar to that of LSIL with referral to colposcopy [6,7], but the subsequent approach may be comparable to HSIL (and ASC-H) (Figure 5). Or, the management may be entirely similar to ASC-H. Some of the issues to be considered while planning management guidelines include: A. How to manage patients with negative or unsatisfactory colposcopy results? B. Would a conservative approach similar to LSIL or ASC-H cases be optimum? C. Should endocervical sampling be obtained if the colposcopic examination is satisfactory? D. Would a cone biopsy similar to HSIL cases ever be indicated in evaluation of LSIL-H category?

As the risk of high grade dysplasia associated with LSIL-H is comparable with ASC-H, (Table 1, Figure 4) and the association with lower incidence of negative results is similar to LSIL, it is reasonable to apply some combination of ASC-H and LSIL management guidelines. Possible application of the HSIL approach at later stages of the algorithm may be needed (Figure 5). For ASC-H and LSIL, ASCCP recommends initial colposcopy [6,26]. If the colposcopic evaluation in the LSIL-H management algorithm suggested in Figure 4 is negative, the cytology and biopsy material should be reviewed. If the review leads to a change in the interpretation, one should follow the appropriate ASCCP algorithm [6,26]. As compared to the choice of following either the LSIL or ASC-H algorithm, the application of the suggested guidelines will require a relatively small proportion (approximately 1 out of four cases) of already rare LSIL-H cases to go through slightly increased number of clinical encounters (Figure 5). These guidelines may be evaluated comparatively with other possible alternative combinations to refine it further as indicated by follow up studies in the future.

Another alternative to LSIL-H as a distinct category is to continue with current approach of communicating two distinct interpretations, LSIL and ASC-H, for a given single cervical specimen. Although this approach accommodates 2001 Bethesda System terminology, it has several disadvantages, including difficulties in organizing quality assurance statistics. This, however, may interfere with the management approach based on current ASCCP guidelines [6,22-25]. The current recommendation is to refer both LSIL and ASC-H cases to colposcopy, but LSIL-H cases have a significantly lower chance of negative results (Table 1), and so relatively aggressive follow up steps may be indicated at later stages of management. Another challenge is difficulty in verifying the risk of progression to high grade dysplasia for two separate interpretations.

HPV DNA testing has been suggested to be a simple alternative with sensitivity and negative predictive value approaching 100% for detecting HSIL [26-29]. The role of HPV testing in primary screening of cervical cancer currently has been effective in the ASCUS category. Its role in other categories is evolving. It has also been reported to be helpful in ASC-H cases [27]. However, in LSIL-H, most of the cases are expected to be positive for HPV testing and so its role may be limited. In the current study, coincidental observation of HPV test results were available in 34 out of total 88 LSIL-H cases. HPV testing was positive for high risk HPV in 94% (32 out of 34). Cervical biopsy in two