Cytology and Human Papillomavirus Screening Test Results Associated With 2827 Histopathologic Diagnoses of Cervical Intraepithelial Neoplasia 2/3

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Context.—Cervical screening in the United States increasingly involves newer US Food and Drug Administration–approved cytologic methods and adjunctive high-risk human papillomavirus (hrHPV) DNA testing.

Objective.—To document cervical screening test performance preceding histopathologic cervical intraepithelial neoplasia (CIN) 2/3 diagnoses.

Design.—Preceding screening test results with computer-imaged, liquid-based cytology (LBC) and hrHPV results were analyzed for 2827 patients with histopathologic CIN 2/3 diagnoses.

Results.—Of 2827 patients with CIN 2/3 diagnoses, 2074 (73.4%) had system LBC findings within 4 months of CIN 2/3 diagnoses: high-grade squamous intraepithelial lesion (n = 862; 41.6%), low-grade squamous intraepithelial lesion (n = 464; 22.4%), atypical squamous cells of undetermined significance (n = 445; 21.5%), atypical squamous cells, cannot exclude high-grade squamous intraepithelial lesion (n = 288; 13.9%), and atypical glandular cells/adenocarcinoma in situ (n = 15; 0.7%). Of the 2827 patients, 1488 (52.6%) also had earlier system LBC results at more than 4 months to 3 years before CIN 2/3 diagnoses. Of 454 patients who also had earlier hrHPV results within 4 months of CIN 2/3 diagnoses, 786 (97.4%) had hrHPV+ results. Of 454 patients who also had earlier hrHPV results at more than 4 months to 3 years before CIN 2/3 diagnoses: 377 (83.0%) had one or more abnormal LBC results; 786 (97.4%) had hrHPV+ results. Of 454 patients who also had earlier hrHPV results, 110 (24.2%) had one or more hrHPV+ result, and 33 (7.3%) had both positive and negative HPV results.

Conclusion.—Patients with histopathologic CIN 2/3 had recent abnormal LBC results, most often, high-grade squamous intraepithelial lesions. Among cotested patients, 97.4% (786 of 807) tested hrHPV+. However, a significant number of patients tested during an extended period of several years had earlier negative Papanicolaou or negative HPV test results, suggesting the recent development of some CIN 2/3 lesions and supporting the value of cotesting for enhanced detection of other developing, small, inaccessible, or nondiagnostic precursor lesions.


The primary goal of cervical screening is the identification and removal of intraepithelial precancerous lesions, which, if left untreated, would, at some future time, become invasive cervical cancer. The desired result is a decrease in the incidence of invasive cervical cancer in the screened population. Histopathologic results remain a key foundation of cervical screening efforts in the United States, and biopsy diagnoses of cervical intraepithelial neoplasia (CIN) 2 or worse represent the clinical threshold leading to ablative or excisional therapy. Despite evidence that intraepithelial lesions classified as CIN 3 are more likely to progress to invasive cancer and less likely to regress than intraepithelial lesions classified as CIN 2, a CIN 2/3 threshold for excision is still generally retained because the distinction between CIN 2 and CIN 3 is not always clear. Furthermore, colposcopic evaluation and biopsy of patients with abnormal cytologic screening test results that are less severe than high-grade squamous intraepithelial lesion (HSIL) have been recommended to maximize histopathologic identification of CIN 2/3 lesions commonly associated with cytologic abnormalities less severe than HSIL. In fact, the largest available US studies reflecting the use of the conventional Papanicolaou (Pap) test have repeatedly shown that more histopathologic CIN 2/3 lesions are identified in patients with a preceding abnormal Pap test interpretation of atypical squamous cells of undetermined significance (ASC-US) than are identified in patients with a preceding abnormal Pap test interpretation of HSIL or any other specific abnormal cytologic result. In contrast, large US
series documenting prior cytologic screening test results in patients with histopathologic CIN 2/3 lesions diagnosed after screening with newer prevalent methods of liquid-based cytology (LBC), computer-assisted screening, and adjunctive high-risk human papillomavirus (hrHPV) testing remain surprisingly limited. Accordingly, we conducted a retrospective study and evaluated screening test histories of patients with histopathologic CIN 2/3 lesions diagnosed during a 65-month period between July 2005 and November 2010. The results of surgical pathology reports, preceding Pap tests, and preceding hrHPV DNA tests were collected from the laboratory information system. The UPMC system database at Magee-Womens Hospital (MWH) of the UPMC (Cerner Corporation, Kansas City, Missouri) laboratory information system was used, employing the ThinPrep Imaging System 10 (Hologic Inc, Marlborough, Massachusetts). Staining of slides was performed on a Sakura Tissue-Tek Automated Slide Stainer (Sakura Finteck USA Inc, Torrance, California). Beginning in December 2004, location-guided, computer-assisted screening of ThinPrep Pap tests slides was used, employing the ThinPrep Imaging System 40 (Hologic Inc, Marlborough, Massachusetts). The ThinPrep Imaging System performed analyses on batches of up to 250 ThinPrep Pap tests slides with specialized imaging software. All specimens were processed and evaluated in the pathology laboratory at MWH and reported using current Bethesda System 2001 terminology.41 In this report, all low-grade squamous intraepithelial lesion (LSIL) and HSIL results and other current Bethesda System result terminology refer to cytologic interpretations. The MWH cytopathology laboratory is a large, subspecialized academic hospital laboratory that usually reports more than 100 000 Pap tests per year from a large, integrated hospital health system that serves a metropolitan area with significantly older-age population profile than that of the national average.12 The reporting profile of the laboratory is documented in numerous recent publications.13–28

### MATERIALS AND METHODS

#### Patient Accrual

After obtaining institutional review board approval at the University of Pittsburgh Medical Center (UPMC), a retrospective study was initiated. A computer-based search of the CoPath (Cerner Corporation, Kansas City, Missouri) laboratory information system database at Magee-Womens Hospital (MWH) of the UPMC was carried out to retrieve cases with histopathologic diagnoses of CIN 2 or CIN 3 (CIN 2/3) diagnosed during a 65-month period between July 2005 and November 2010. The results of surgical pathology reports, preceding Pap tests, and preceding hrHPV DNA tests were collected from the laboratory information system. The UPMC is a large, integrated private health system in which Pap tests are collected by a highly diverse group of clinical providers that includes gynecologists, family physicians, internists, nurse practitioners, physician assistants, and house-staff trainees.

#### Cytologic Methods

Cytologic testing used ThinPrep Pap tests4 prepared according to manufacturer’s specifications from PreservCyt samples using an automated processor (ThinPrep 3000, Hologic Inc, Marlborough, Massachusetts). Staining of slides was performed on a Sakura Tissue-Tek Automated Slide Stainer (Sakura Finteck USA Inc, Torrance, California). Beginning in December 2004, location-guided, computer-assisted screening of ThinPrep Pap tests slides was used, employing the ThinPrep Imaging System40 (Hologic Inc, Marlborough, Massachusetts). The ThinPrep Imaging System performed analyses on batches of up to 250 ThinPrep Pap tests slides with specialized imaging software. All specimens were processed and evaluated in the pathology laboratory at MWH and reported using current Bethesda System 2001 terminology.41 In this report, all low-grade squamous intraepithelial lesion (LSIL) and HSIL results and other current Bethesda System result terminology refer to cytologic interpretations. The MWH cytopathology laboratory is a large, subspecialized academic hospital laboratory that usually reports more than 100 000 Pap tests per year from a large, integrated hospital health system that serves a metropolitan area with a significantly older-age population profile than that of the national average.12 The reporting profile of the laboratory is documented in numerous recent publications.13–28

#### hrHPV DNA Screening Testing

The hrHPV DNA testing was ordered by UPMC system clinical providers according to several ordering options as follows: reflex HPV testing following atypical squamous cell (ASC) Pap test interpretations, routine HPV cotesting with Pap tests from women 30 years and older, and HPV cotesting regardless of either age or Pap test results. The hrHPV DNA detection in ThinPrep Pap test PreservCyt vial fluid was performed using the US Food and Drug Administration (FDA)–approved Hybrid Capture 2 (HC2) assay method (Qiagen Corp, Minden, Germany)42 that tests for hrHPV and intermediate-risk HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 68. The results of hrHPV DNA testing were either positive or negative, based on a threshold of 1 pg/mL HPV DNA.

#### Histopathologic Diagnosis

All diagnoses of CIN 2/3 in this study refer to histopathologic interpretations of surgical pathology specimens, including cervical biopsies, endocervical curettage specimens, and/or diagnostic, excisional procedures using loop electrosurgical excision procedures or cold knife cervical conization. Histopathologic diagnoses were rendered by subspecialized staff pathologists at MWH whose practices are largely limited to examination of gynecologic and breast pathology specimens. Cases initially diagnosed as CIN 2/3 are required to be confirmed by a second reviewing pathologist.43 Immunohistochemical staining with P16 and Ki-67 is also liberally used by staff pathologists to increase the reliability of CIN 2/3 diagnoses.44 Cytology results reported before initial histopathologic diagnoses of CIN 2/3 are usually recorded in the surgical pathology report. Prior negative Pap tests are rescreened and evaluated as part of departmental quality improvement procedures. Prior abnormal Pap tests are also routinely reviewed and correlated with follow-up histopathology. For this study, if an abnormal cytology result occurred within 4 months before the surgical procedure establishing the initial histopathologic diagnosis of CIN 2/3, the immediately preceding abnormal Pap test result was regarded as the trigger for the surgical procedure and histopathologic diagnosis of CIN 2/3.

#### RESULTS

A total of 2827 patients with histopathologic CIN 2/3 diagnoses were identified during the study period. Diagnostic excisional procedures were documented in 1638 patients (57.9%), and 118 patients (4.2%) had subsequent hysterectomies. The average patient age was 30.7 years, with a range from 16 to 91 years.

#### Triggers of Diagnostic Surgical Procedures

Papanicolaou test findings within 4 months of CIN 2/3 diagnoses preceded diagnostic surgical procedures in 2074 of 2827 patients (73.4%) identified in our database. Papanicolaou test findings leading to diagnostic procedures and CIN 2/3 diagnoses included a wide spectrum of abnormal Pap test findings within 4 months of CIN 2/3 diagnosis. High-grade squamous intraepithelial lesion was the most common abnormal cytologic result (41.6%; 862 of 2074), whereas LSIL and ASC-US results preceded 22.4% (464 of 2074) and 21.5% (445 of 2074) of CIN 2/3 diagnoses, respectively. Atypical squamous cells, cannot exclude HSIL (ASC-H) results preceded 13.9% (288 of 2074) of CIN 2/3 diagnoses, and atypical glandular cells/adenocarcinoma in situ preceded less than 1% (15 of 2074).

#### Other Cytology Results

Of the 2827 patients with CIN 2/3 diagnoses, 1488 (52.6%) were found to have other, earlier, UPMC system cytology results at more than 4 months to 3 years before histopathologic CIN 2/3 diagnoses (Table 2). These less-
proximate Pap test results were in addition to the abnormal Pap tests obtained during the 4 months immediately preceding CIN 2/3 diagnoses. Of those 1488 patients with CIN 2/3 diagnoses, 978 (65.7%) had at least one earlier, abnormal cytology result, whereas 911 of 1488 (61.2%) had at least one earlier, negative cytology result during the more-extended, preceding period; 401 of 1488 (26.9%) had both abnormal and normal Pap test results, and 510 of 1488 (34.3%) had an earlier, negative Pap test result only. The range of cytologic abnormalities among 978 patients with earlier, abnormal cytology results are shown in Table 3. For patients with multiple earlier, abnormal Pap test results involving squamous cells, the most-abnormal result was recorded using the following hierarchical order: HSIL > ASC-H > LSIL > ASC-US. Patients with either prior atypical glandular cells results or both LSIL and ASC-H results were listed separately. Low-grade squamous intraepithelial lesion and ASC-US were the most-common earlier, abnormal Pap test results: 166 of 978 patients (17.0%) with earlier abnormal cytology findings had prior HSIL results.

**HPV Test Results**

Of 2827 patients with CIN 2/3 diagnoses, 807 (28.6%) had HC2 hrHPV test results within 4 months of initial diagnostic biopsies; 786 of 807 (97.4%) had HPV\(^+\) results. Papanicolaou and accompanying HPV test results preceding the 807 follow-up CIN 2/3 diagnoses are shown in Table 4. Atypical squamous cells of undetermined significance in the Pap test results were the most-common abnormal cytology result with adjunctive HPV testing, accounting for roughly half of the cases. High-grade squamous intraepithelial lesion was the third most-common Pap test result, following ASC-US and ASC-H. The HPV\(^+\) rates associated with CIN 2/3 diagnoses were similar in the various abnormal Pap test categories. In addition to HPV results from tests within 4 months before the CIN 2/3 diagnoses, 454 of 807 patients (56.3%) had earlier UPMC system HPV results more than 4 months and up to 3 years before the CIN 2/3 diagnoses (Table 5). Of the 454 patients, 377 (83.0%) had at least one HPV\(^+\) result during the more-extended preceding period.

**COMMENT**

Among 2074 patients with CIN 2/3 diagnoses and abnormal UPMC system, computer-imaged, LBC Pap test results within the previous 4 months, HSIL was the most common abnormal cytology result, documented in 862 patients (41.6%). Low-grade squamous intraepithelial lesion was the next most-common abnormal, prior Pap test result in 22.4% (464 of 2074), followed by ASC-US in 21.5% (445 of 2074), ASC-H in 13.9% (288 of 2074), and atypical glandular cells/adenocarcinoma in situ in less than 1% (15 of 2074) (Table 1). The largest comparable reported US data set is from Kaiser Permanente in Northern California, which reported screening-test data associated with 3649 histopathologic CIN 2/3 diagnoses rendered between January 1, 2003, and June 30, 2009, on patients 30 years and older screened with conventional Pap smears and HC2 hrHPV cotesting.\(^a\) Among the 3649 patients with CIN 2/3 diagnoses and preceding, abnormal, Kaiser conventional Pap test results, ASC-US was the most common abnormal cytology

### Table 2. Earlier Papanicolaou Test Results in 1488 Patients

<table>
<thead>
<tr>
<th>Papanicolaou Test Results</th>
<th>Patients, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>At least one abnormal test result</td>
<td>978 (65.7)</td>
</tr>
<tr>
<td>At least one normal test result</td>
<td>911 (61.2)</td>
</tr>
<tr>
<td>Both normal and abnormal test results</td>
<td>401 (26.9)</td>
</tr>
<tr>
<td>Total</td>
<td>1488 (100)</td>
</tr>
</tbody>
</table>

\(^a\) Patients with earlier cytology results do not include those whose abnormal Papanicolaou tests were performed ≤4 mo before histopathologic cervical intraepithelial neoplasia 2 or 3 diagnoses. Earlier tests were performed more than 4 mo up to 3 y before cervical intraepithelial neoplasia 2 or 3 diagnoses.

### Table 3. Abnormal Papanicolaou (Pap) Test Results From Patients With Earlier Abnormal Pap Results\(^b\)

<table>
<thead>
<tr>
<th>Abnormal Pap</th>
<th>Patients, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HSIL</td>
<td>166 (17.0)</td>
</tr>
<tr>
<td>LSIL</td>
<td>363 (37.1)</td>
</tr>
<tr>
<td>ASC-H</td>
<td>108 (11.0)</td>
</tr>
<tr>
<td>ASC-US</td>
<td>310 (31.7)</td>
</tr>
<tr>
<td>LSI/ASC-H(^a)</td>
<td>26 (2.7)</td>
</tr>
<tr>
<td>AGC</td>
<td>5 (0.5)</td>
</tr>
<tr>
<td>Total</td>
<td>978 (100.0)</td>
</tr>
</tbody>
</table>

\(^a\) Patients’ earlier tests were performed more than 4 mo up to 3 y before cervical intraepithelial neoplasia 2 or 3 diagnoses. The abnormal Pap tests that triggered the surgical procedures are not included.

### Table 4. Liquid-Based Cytology Results in 807 Patients With Adjunctive High-Risk Human Papillomavirus (hrHPV) Test Results\(^a\)

<table>
<thead>
<tr>
<th>Accompanying Abnormal Papanicolaou</th>
<th>Cases With hrHPV Test Results, No. (%)</th>
<th>Cases With Positive hrHPV Test Results, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASC-US</td>
<td>410 (50.8)</td>
<td>404 (98.5)</td>
</tr>
<tr>
<td>ASC-H</td>
<td>180 (22.3)</td>
<td>172 (95.6)</td>
</tr>
<tr>
<td>LSIL</td>
<td>51 (6.3)</td>
<td>50 (98.0)</td>
</tr>
<tr>
<td>HSIL</td>
<td>137 (17.0)</td>
<td>136 (99.3)</td>
</tr>
<tr>
<td>AGC</td>
<td>4 (0.5)</td>
<td>4 (100)</td>
</tr>
<tr>
<td>Papanicolaou N/A</td>
<td>25 (3.1)</td>
<td>20 (80.0)</td>
</tr>
<tr>
<td>Total</td>
<td>807 (100)</td>
<td>786 (97.4)</td>
</tr>
</tbody>
</table>

\(^a\) Both Papanicolaou tests and HPV testing were performed ≤ 4 months before cervical intraepithelial neoplasia 2 or 3 diagnoses.

### Table 5. High-Risk Human Papillomavirus (hrHPV) Test Results in 454 Patients With Earlier Test Results\(^b\)

<table>
<thead>
<tr>
<th>Earlier hrHPV Test Results</th>
<th>Cases, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>At least one negative test result</td>
<td>110 (24.2)</td>
</tr>
<tr>
<td>At least one positive test result</td>
<td>377 (83.0)</td>
</tr>
<tr>
<td>Both positive and negative test results</td>
<td>33 (7.3)</td>
</tr>
<tr>
<td>Total</td>
<td>454 (100)</td>
</tr>
</tbody>
</table>

\(^b\) Patients’ earlier tests were performed more than 4 mo up to 3 y before cervical intraepithelial neoplasia 2 or 3 diagnoses. The abnormal Papanicolaou tests that triggered the surgical procedures are not included.

**Papanicolaou and HPV Tests for Women With CIN 2/3—Zhao et al**
result, documented in 1323 patients (36.3%). High-grade squamous intraepithelial lesion was the second most-common, abnormal Pap test result in 917 of 3649 patients (25.1%), followed by LSIL in 751 of 3649 patients (20.6%), ASC-H in 481 of 3649 patients (13.2%), and atypical glandular cells in 177 of 3649 patients (4.9%). Similar results were reported earlier from the same Kaiser Permanente facility in a 1998 report, which documented “ASCUS” as the leading abnormal, conventional Pap test result, preceding high-grade cervical neoplasia in 38.8% (17 851 of 46 009) of cases. Preservation of cytologic nuclear detail with immediate wet fixation in the LBC vial, harvesting in the LBC vial of most collected cells otherwise routinely discarded on conventional test collection devices, computer-assisted screening, and conservative MWH cytotecnologist workload policies, are all likely contributing factors for the increased likelihood of an HSIL result preceding a histopathologic CIN 2/3 diagnosis in our report. Although the advantages of LBC have been questioned in Italian and Dutch clinical trials using laboratories relatively inexperienced with the LBC method and lacking clearly documented LBC proficiency, clinical trials in the more tightly quality-assured UK National Health System have documented significantly enhanced performance with LBC compared with conventional cytology. Most (65.7%; 978 of 1488) patients with CIN 2/3 diagnoses and additional earlier UPMC system Pap test results at 4 months to 3 years before the CIN 2/3 diagnoses had at least one abnormal Pap test result. That finding reflects observations that CIN 2/3 lesions often develop and enlarge slowly during a period of years in a manner allowing detection during routine periodic screening, even when a relatively insensitive screening method is employed. Indeed, studies adjusted for verification bias have estimated the average sensitivity of the conventional Pap test at about 50%, but modeling still estimates that periodic screening every 3 years with the conventional Pap test can prevent about 85% of all (mostly slowly-growing) cervical cancers. On the other hand, 61.2% of the same 1488 patients (n = 911) had at least one earlier negative Pap test result during a period of several years. During the study period between July 2002 and November 2010, less than 1.5% of all cervical cytology samples were conventional Pap tests. Prior negative Pap results likely reflect both some newly developing incident CIN 2/3 lesions as well as other CIN 2/3 lesions, which were either initially too small to be reliably sampled or were located in more difficult-to-sample locations in the cervix. Internal quality assurance reviews at MWH generally confirm negative findings in negative Pap test results obtained within 5 years of CIN 2/3 diagnoses; quality assurance reviews less-commonly document questionable cellular changes identifiable at least partially because of hindsight or outcome bias. Available data now indicate that the interval between incident HPV 16 or HPV 18 infection and biopsy-confirmed CIN 2/3 can be as short as a few months. Only 17% (166 of 978) of earlier, available, abnormal Pap tests were interpreted as HSIL, documenting a predominance of less-proximate, low-grade or indeterminate, abnormal Pap test findings. The range of earlier Pap abnormalities likely reflect both the effects of multiple HPV infections unrelated to later diagnosed CIN 2/3 lesions as well as progression of some less-advanced lesions to CIN 2/3. Along these lines, intraepithelial lesions associated with HPV 18–induced cervical neoplasias are more likely to be associated with nondiagnostic or indeterminate intraepithelial changes than they are with intraepithelial lesions associated with HPV 16–induced cervical neoplasias. Positive HPV test results were reported within 4 months of histopathologic CIN 2/3 diagnoses in 786 of 807 patients (97.4%), findings similar to the observation that carcinogenic HPV genotypes were detectible in 95.4% (580 of 608) of women with confirmed CIN 3 in the Atypical Squamous Cells of Undetermined Significance and Low Grade Squamous Intraepithelial Lesion Triage Study (ALTS). Available HPV test results in our study were ordered most often as reflex HPV tests after ASC Pap test results and less commonly as routine cotests. Reflex HPV testing has been common at MWH for many years, reflecting our center’s participation as 1 of 4 clinical trial sites in ALTS, which helped establish reflex HPV testing of ASC-US Pap tests as a standard US practice. In recent years, the percentage of MWH clinicians ordering routine HPV cotesting in women 30 years and older has been increasing. Routine cotesting has been formally advocated by 2 of the authors as an approach judged most likely to minimize false-negative screening test results and cervical cancer diagnoses in screened women. Earlier additional HPV test results at more than 4 months to 3 years before the CIN 2/3 diagnoses were also available in 454 patients; 83% (n = 377) had at least one prior positive result, likely reflecting the current consensus that persistent hrHPV infection is a prerequisite for development of CIN 2/3. On the other hand, 24.2% (110 of 454) of patients with earlier HPV test results had at least one negative result. Some of these earlier negative HPV results could reflect subsequent HPV infections causing CIN 2/3 after earlier negative HPV results. In other patients, however, fluctuating positive and negative HPV test results may reflect a number of factors: multiple HPV infections with clearance of earlier infections, failure to sample lesional cells, unrecognized technical testing problems, variable host immunologic responses, and changes over time in the viral load of developing cervical neoplasias. Nationwide monitoring data from Australia reports fewer negative HPV results (11%) concurrent with high-grade cervical histology diagnoses and much more-frequent negative HPV results (29%) when HPV tests precede high-grade histology findings by 24 to 30 months. Kaiser Permanente has documented that, in the setting of routine conventional Pap test and FDA-approved HC2 HPV cotesting, 27 of 87 patients (31%) who develop invasive cervical cancers had negative baseline HPV test results within 5 years of cancer diagnoses. In the UK, in the ARTISTIC trial, 3 of 12 women (25%) diagnosed with invasive cervical carcinomas had negative baseline HPV test results in the first round of screening during several years had baseline, negative HC2 hrHPV test results. At MWH, negative HC2 HPV test results were documented in 3 of 31 cervical squamous cell carcinomas (9.7%) where HC2 hrHPV testing occurred in the previous 12 months; carcinogenic HPV DNA was detected by polymerase chain reaction in squamous cell carcinoma tumor tissues of all 3 patients with earlier, negative hrHC2 results. Additional studies are needed to better understand factors associated with negative hrHPV DNA test results in women developing both histopathologic CIN 2/3 lesions and invasive cervical carcinomas. This study documents that patients with histopathologic CIN 2/3 diagnoses had recent, abnormal Pap results, with HSIL the most-common, recent, abnormal cytology result in 41.6% (862 of 2074) of patients. This finding differs from...
large, conventional test series in which ASC-US test results have been the most-common, abnormal Pap result (36%–39%) preceding CIN 2/3 diagnoses. Among patients cotested for hrHPV within 4 months of CIN 2/3 diagnoses, 97% also tested hrHPV+.

However, significantly few patients with CIN 2/3 had negative Pap or negative HPV test results over a more-extended period of several years, consistent with recent onset of some CIN 2/3 lesions, as well as reflecting the challenges inherent in detecting other developing, small, inaccessible, or nondiagnostic intraepithelial CIN 2/3 precursor lesions. Because this was a retrospective rather than a prospective study, patients may have had additional tests or procedures not reflected in the laboratory information system records or provided clinical histories.

References


