Practice Patterns in Cervical Cancer Screening and Human Papillomavirus Testing

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Abstract

The use of human papillomavirus DNA testing plus Papanicolaou (Pap) testing (cotesting) for cervical cancer screening in women 30 years and older has been recommended since 2006. However, few studies have detailed the adoption of such cotesting in clinical practice. We examined the trends in monthly percentage of Pap tests ordered as cotests in our laboratory over a 2.5-year period and used joinpoint regression to identify periods in which there was a change in the average monthly proportion of cotests. Cotesting of patients 30 years and older increased from 15.9% in January 2008 to 39.4% in June 2010. In patients aged 18 to 29 years, cotesting initially increased, but showed a downward trend in the last 14 months of the study, ending at 7.7% in June 2010. Our study highlights increased adoption of age-appropriate cotesting as well as the persistence of age-inappropriate cotesting.

Clinical practice guidelines are established by professional organizations to aid clinical decision making by recommending management that maximizes patient benefit while minimizing harm and providing the most cost-effective care. In the United States, several such sets of clinical practice guidelines exist for cervical cancer screening with Papanicolaou (Pap) testing and high-risk human papillomavirus (HPV) DNA testing, as well as for clinical management of uterine cervical abnormalities. One of these is a set of consensus guidelines developed by The American Society for Colposcopy and Cervical Pathology (ASCCP) in 2001,[1] and updated in 2006.[2] Interim guidelines were issued by the ASCCP in 2004[3] endorsing the use of HPV testing in conjunction with cervical cytologic tests in women aged 30 years or older, referred to as "cotesting," after the Food and Drug Administration (FDA) approved this use of the HPV test. Routine HPV testing of negative cytologic specimens in women younger than age 30 years is of low clinical usefulness given the high prevalence of HPV infections, most of which will spontaneously resolve, in the adolescent and young adult population in the United States.[4] Thus HPV cotesting with a normal Pap test result among patients aged less than 30 years is not an FDA-approved use of the HPV test, nor is it endorsed by the ASCCP guidelines.

In addition, the 2006 ASCCP guidance recommends that women who are cotested and have negative findings on both the Pap and HPV tests should not be rescreened before 3 years, because the combined negative predictive value for the 2 tests is higher than 99%.[3,5] The American Congress of Obstetricians and Gynecologists (ACOG) endorsed the 2006 ASCCP recommendations in a practice bulletin in December 2009.[6] The American Cancer Society (ACS) issued

provisional recommendations in 2002, with FDA approval, that support the use of cotesting as an option for cervical cancer screening.[7]

Most assessments of provider ordering practices in gynecologic cytology and HPV testing reported to date are based on self-reported data from provider surveys, many using case vignettes,[8-11] rather than on actual testing patterns observed from the laboratory perspective. A few studies have used laboratory data to evaluate cervical cancer screening practices, including an earlier study from our institution which reported that the overall proportion of HPV cotesting in women over age 30 years (from February 2004-December 2007) was 7.8% and that the proportion of Pap tests ordered as a cotest reached a plateau of approximately 13% by the end of the study period.[12] Another study that used laboratory data to evaluate HPV ordering practices found that 23% of HPV tests ordered in the course of 1 year were inappropriate and unnecessary according to the ASCCP guidelines.[13]

The objective of this study was to extend our observation of trends in ordering practices for Pap tests and associated HPV tests and to further assess temporal changes in the cervical cancer screening practices based on specimens submitted to our laboratory. We used 2.5 years of specimen data from the Johns Hopkins Hospital Division of Cytopathology in Baltimore, MD.

Materials and Methods

Data were retrieved from the Pathology Data System (PDS), which is an internally developed laboratory information system administrated by the Johns Hopkins Hospital (JHH) Department of Pathology. In this study, we extracted PDS data that included Pap specimens processed by the JHH Division of Cytopathology and HPV tests processed by the JHH Division of Microbiology. The Johns Hopkins Bloomberg School of Public Health Institutional Review Board determined the study to be "exempt human subjects research" and the requirement to obtain informed consent was waived.

A statistical programmer deidentified the PDS data to create a limited dataset for the analysis. The limited dataset contained all liquid-based Pap specimens processed by the JHH Division of Cytopathology from January 1, 2008, to June 30, 2010 (n = 75,396). All Pap specimens were processed using SurePath (Becton Dickinson, Franklin Lakes, NJ), and for each Pap specimen, the dataset included a unique specimen identifier, a unique patient identifier, date the Pap specimen was taken, Pap diagnosis, HPV test result if ordered, and clinic from which the specimen originated. In addition, for each specimen, the patient's age, race, sex, home ZIP code, and health insurance type were collected. Pap diagnoses were categorized as "negative for intraepithelial lesion or malignancy (negative)," "atypical squamous cells of undetermined significance (ASCUS)," "atypical squamous cells, cannot exclude high-grade squamous intraepithelial lesion (ASC-H)," "low-grade squamous intraepithelial lesion (LSIL)," high-grade squamous intraepithelial lesion (HSIL)," "low-grade squamous intraepithelial lesion, cannot exclude high grade (LSIL-H)," "atypical glandular cells of undetermined significance (AGUS)," "squamous cell carcinoma (SCC)," "adenocarcinoma (ADCA)", and "specimen unsatisfactory/discarded." HPV testing was performed using the digene HC2 HPV test (Qiagen, Gaithersburg, MD) and results were categorized as "negative," "positive," and "equivocal," based on the following cut-offs determined by the JHH Division of Microbiology: negative HPV, less than 0.85 relative light units (RLU); equivocal HPV, 0.85 to 3.0 RLU; and positive HPV, more than 3.0 RLU. Pap test specimen records were categorized based on 2 Pap test ordering codes developed internally in our laboratory indicating either "Pap test with reflex HPV only" or "Pap test with HPV (cotest)."

For the present analysis, we excluded specimens that were unsatisfactory for evaluation or discarded because of collection or labeling errors (n = 442). We excluded records with unknown patient age, those from patients younger than 18 years, and those from patients older than 89 years (n = 1,766). Records with unknown or male sex listed were eliminated (n = 314). In addition, we excluded specimens from subspecialty referral clinics (colposcopy, human immunodeficiency virus, adolescent, gynecologic oncology, n = 3,262) to reflect screening practices among healthy adult women. We also eliminated records from clinics that submitted only 1 Pap specimen during the entire study period (n = 35). Specimens that were not ordered by the clinician as either reflex or cotest were excluded from analysis (n = 7).

Patient results were categorized into the following age groups for analysis: 18 to 20 years (ie, adolescents), 21 to 29 years, and 30 years or older. These age groupings were based on the ASCCP recommendations that women younger than 21 years should not be screened with the Pap test, and if they are, and are diagnosed with an ASCUS result, they should not be tested for HPV. The ASCCP also recommends that women in the 21- to 29-year-old age group receive cytologic screening with reflex HPV testing for a Pap diagnosis of ASCUS. Cotesting is only recommended in women aged 30 years or older, because of the high prevalence of HPV infection in the younger population.

We calculated the monthly proportion of cotests for 2 age groups (18-29 and ≥30 years) by dividing the total number of Pap tests ordered as cotests by the total number of Pap tests ordered in the same age group in a given month.

To establish whether the screening interval was extended in patients having dual negative cotest findings, we tracked all patients who received a dual negative cotest result in the

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first year of our study (2008), and recorded all repeat Pap and HPV testing results during the remainder of the study period.

We used the Joinpoint Regression Program (Version 3.5.1, National Cancer Institute, Rockville, MD) to identify points at which the changes in the monthly rate of cotesting among the 2 age groups were significant. Joinpoint analysis identifies time points when a significant change in the slope of the trend is detected. Briefly, the analysis starts with 0 joinpoints (a straight line), then tests whether additional joinpoints (up to 3) are significantly different. The best-fitting model was chosen based on the Monte Carlo permutation method, which maintained an overall 2-sided *P* value of less than .05. All data management and analyses were conducted using Excel 2010 spreadsheets (Microsoft, Redmond, WA).

Results

The final analytic dataset contained 69,570 Pap specimen records (92.3% of total data) from 50,392 unique patients submitted from 723 unique providers among 115 unique clinics in the Baltimore, MD, metropolitan area. The mean number of Pap test specimens submitted per patient was 1.38 (range 1-8). A total of 17,518 HPV test specimens were included in the analytic dataset. Patient demographics are highlighted in **Table 1**. Most of the patients were either white (41.5%) or black (43.2%), and had a home ZIP code of either Baltimore city (41.5%) or a surrounding Maryland county (43.0%).

HPV reflex testing in patients 21 years of age or older was performed on a mean of 97.2% of Pap test specimens diagnosed as ASCUS over the entire study period. HPV testing was positive in 53.9% of all ASCUS Pap tests, comparable to rates reported in other laboratories.[14,15]

Among patients aged 30 years and older, the mean monthly proportion of HPV cotesting was 27.7% during the entire study period. The monthly proportion of cotesting among all Pap tests in this age group was 15.9% in January 2008, and increased to 39.4% by the end of the study period, June 2010 **Figure 1**. The monthly proportion of cotesting peaked in February 2010, at 45.2%, and remained above 38% for the first 6 months of 2010.

Among patients in the 18- to 29-year-old age group, the mean monthly proportion of HPV cotests was 7.6% during the study period. The monthly proportion of cotesting in this age group rose from 5.3% in January 2008 to 7.7% in June 2010. This nonrecommended use of cotesting peaked in May 2009 at 11.2% but remained above 7% for the first 6 months of 2010.

For both age groups, 3 periods of monthly percent change in cotesting were identified using joinpoint regression. For patients aged 18 to 29 years, they were January 2008 to September 2008, October 2008 to April 2009, and May 2009 to June 2010. The latter 2 of these periods showed statistically significant trends. For patients aged 30 to 89 years, the 3 periods were January 2008 to January 2009, February 2009 to August 2009, and September 2009 to June 2010. One of these trends (February 2009-August 2009) was statistically significant **Table 2**.

For adolescent patients (18-20 years) screening with Pap and HPV testing is not recommended; a total of 4,057 Pap test specimens were submitted for this age group during the study

Table 1
Patient Characteristics (n = 50,392)

Characteristic	No. (%)
Age group	
18 to 20	3,277 (6.5)
21 to 29	13,130 (26.1)
30 to 39	11,012 (21.8)
40 to 49	9,108 (18.1)
50 to 59	7,252 (14.4)
60 to 69	4,481 (8.9)
70 to 89	2,132 (4.2)
Race	
White	20,922 (41.5)
Black	17,217 (34.2)
Asian	1,714 (3.4)
Hispanic	1,561 (3.1)
Indian	122 (0.2)
Other	1,365 (2.7)
Unknown	7,491 (14.9)
Home ZIP code	
Baltimore city	23,867 (41.5)
Other Maryland	21,669 (43.0)
Out of state	1,976 (3.9)
Unknown	2,880 (5.7)

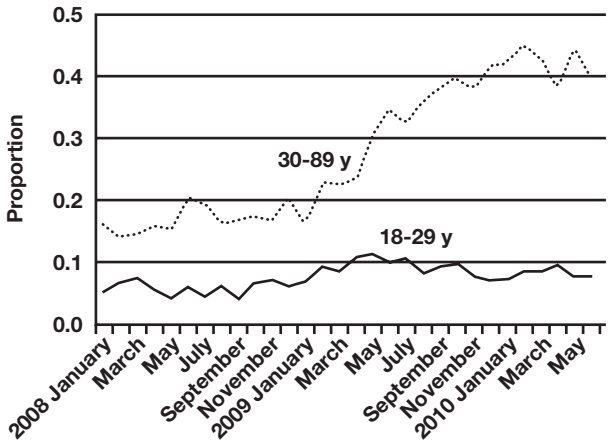

Figure 1 The monthly proportions of cotests from January 2008 to June 2010 are shown for 2 age groups. The proportion of cotests in women aged 30 years and older (appropriate use) grew to approximately 40% at the end of the study period. The proportion of cotesting for women aged 18 to 29 (inappropriate use) reached a plateau at less than 10%.

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Table 2
Cotesting by Age Group With Associated Time Trends, Including MPC Estimates*

	Time Trend 1		Time Trend 2		Time Trend 3	
Age Group	**Period**	**MPC**	**Period**	**MPC**	**Period**	**MPC**
≥30 y	January 2008 to January 2009	1.84 (–0.1 to 3.8)	February 2009 to August 2009	10.7† (6.0 to 15.6)	September 2009 to June 2010	1.0 (–0.6 to 2.7)
18-29 y	January 2008 to September 2008	–2.65 (–7.5 to 2.5)	October 2008 to April 2009	10.6† (3.2 to 18.5)	May 2009 to June 2010	–2.2† (–3.8 to –0.4)

MPC, Monthly percent change.
* Data shown are percentages (95% confidence interval).
† MPC is statistically significant from 0.

period. Of these, 280 (6.9%) were ordered as cotests. Reflex HPV testing was performed in 387 (93.2%) of the 415 Pap test results diagnosed as ASCUS, and in 23 (82.1%) of the 28 Pap test results diagnosed as ASC-H.

To evaluate whether patients with a dual negative cotest result were being screened at a longer interval, we looked at all women who underwent cotesting in the first year of our study (2008). Of the 3,081 patients who had a dual negative cotest in the first year of the study, 785 (25.5%) underwent repeat testing during the remaining portion of the total 2.5-year study period. Of those 785 patients, the repeat Pap and HPV results remained negative in 730 patients (93.0%). Of those patients with abnormal Pap results on repeat testing, the diagnoses rendered were ASCUS (n = 18), atypical glandular cells (n = 2), and ASC-H (n = 1). No cases of LSIL, HSIL, or carcinoma were detected on repeat Pap testing.

We compared the ordering practices at the 2 clinics that submitted the 2 highest volumes of Pap test results in patients aged 30 years or older (7,188 and 4,086 Pap tests, respectively; a combined total of 23.8% of submitted Pap tests in patients aged 30 years or older). The difference in trends of ordering practices is highlighted in **Figure 2**. At "clinic 1," the monthly proportion of cotests ranged from 2.5% to 13.6% in women aged 30 years or older during the study period. In contrast, for "clinic 2," the monthly cotesting rate ranged from 0% to 100% during the study period, but remained above 94% from June 2009 through June 2010.

Of the 14,714 Pap tests ordered as cotests, 13,701 (93.1%) were diagnosed as negative on Pap testing, and HPV testing was positive in 6.0% of those specimens. Among women 30 years or older with negative Pap test results, the HPV positivity rate was 4.7%, comparable to previously reported rates.[16,17] In women aged 18 to 29 years with negative Pap test findings, the HPV positivity rate was 18.1% **Table 3**.

HPV testing was performed on 402 (19.5%) of 2,065 specimens diagnosed as LSIL, LSIL-H, and HSIL, and was positive in 85.0%, 92.3%, and 84.2% of those cases, respectively. HPV testing was performed in 2 of 5 cases diagnosed as SCC and was positive in 1 of those 2 cases (Table 3).

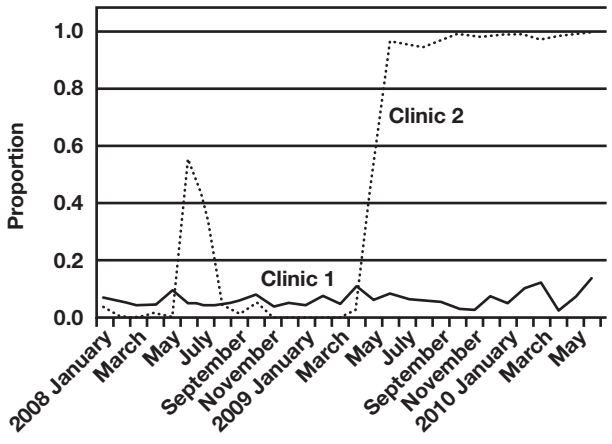

Figure 2 The 2 clinics with the largest volumes of submitted Papanicolaou tests in women aged 30 years and older showed a marked difference in the proportion of cotesting. Clinic 1 showed little adoption of cotesting over the study period while clinic 2 achieved 100% cotesting at the end of the study period. An increase in cotesting in clinic 1 in June and July 2008 followed by near absence of cotesting was the result of a first attempt to implement clinic-wide cotesting which was suspended until management and billing implications were resolved.

Discussion

Our study assessed cervical cancer screening practices from the laboratory perspective using records from over 69,500 Pap specimens among more than 50,000 unique patients, 115 unique clinics, and 723 unique providers. Our results show a rise in the overall proportion of cotesting in our laboratory during a course of 2.5 years, corresponding with a gradual adoption of the ASCCP practice guidelines for cervical cancer screening. However, the overall monthly proportion of age-appropriate cotesting still remained less than 45% at the conclusion of the study. Cotesting in patients aged 18 to 29 years decreased significantly during the last 14 months

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Table 3
HPV Results by Papanicolaou Diagnosis in All Patients*

HPV Test	NEG	ASCUS	ASC-H	LSIL	LSIL-H	HSIL	SCC	ADCA	AGUS	Total
Not performed	50,267 (78.5)	101 (3.3)	35 (11.7)	1,347 (81.5)	114 (74.5)	202 (78.0)	3 (60.0)	6 (50.0)	50 (53.2)	52,125
Performed	13,781 (21.5)	2,945 (96.7)	265 (88.3)	306 (18.5)	39 (25.5)	57 (22.0)	2 (40.0)	6 (50.0)	44 (46.8)	17,445
Positive	842 (6.1)	1,588 (53.9)	182 (68.7)	260 (85.0)	36 (92.3)	48 (84.2)	1 (50)	0 (0)	6 (13.6)	2,963
Negative	12,567 (91.2)	1,176 (39.9)	68 (25.7)	35 (11.4)	3 (7.7)	4 (7.0)	0 (0)	6 (100)	36 (81.8)	13,895
Equivocal	372 (2.7)	181 (6.1)	15 (5.7)	11 (3.6)	0 (0)	5 (8.8)	1 (50)	0 (0)	2 (4.5)	587
Total	64,048	3,046	300	1,653	153	259	5	12	94	69,570

ADCA, adenocarcinoma; AGUS, atypical glandular cells of undetermined significance; ASC-H, atypical squamous cells cannot exclude high grade squamous intraepithelial lesion; ASCUS, atypical squamous cells of undetermined significance; HPV, human papillomavirus; HSIL, high-grade squamous intraepithelial lesion; LSIL, low-grade squamous intraepithelial lesion; LSIL-H, low-grade squamous intraepithelial lesion, cannot exclude high grade; NEG, negative for squamous intraepithelial lesion; SCC, squamous cell carcinoma.
* Data shown are number (%) of patients.

of our study, showing an average monthly decrease of 2.2%.

Despite the fact that cotesting in women younger than 30 years is neither FDA approved nor recommended by the ASCCP, a mean of 7.6% of all Pap tests ordered in the 18- to 29-year-old population were ordered as cotests in our study. Although the monthly proportion of this nonrecommended testing stayed below 10% for the last 12 months of our study, all of these tests are considered unnecessary and waste resources that could be better used in cervical neoplasia screening and management.

Our data show increased use of the cotest in cervical cancer screening in our laboratory, but detailed analysis indicates that practice patterns varied widely by clinic. The comparison of our 2 highest-volume clinics for women aged 30 years or older was striking. "Clinic 1" had no clinic-wide policy in place to encourage cotesting and monthly proportions of cotests ranged from 2.5% to 13.6% of Pap tests during the study period. In contrast, "clinic 2" established a policy in May 2009 recommending that all practitioners order routine Pap tests as cotests. There was no change in physicians or other providers, or any significant change in administrative personnel in "clinic 2" during this time, rather the policy change reflected a consensus decision to standardize Pap test ordering. The monthly proportion of cotesting in "clinic 2" ranged from 0% to 100% during the study period, but remained above 94% from June 2009 through June 2010. A 2-month increase in cotesting in June and July of 2008 was attributed to a first attempt to implement widespread cotesting in "clinic 2," which was deferred while the management and billing implications of cotesting were evaluated by the practice. This highlights the importance of clinic-level factors in how testing is ordered. Clinics must use mechanisms to not only facilitate ordering of HPV tests and enable appropriate billing but also ensure proper follow-up and treatment of patients with abnormal test results.

We examined all patients who received a dual negative cotest during the first year of our study (2008), and found that 785 (25.5%) of 3,081 underwent repeat cotesting during the remainder of the study period, with the cotest remaining dual-negative in 730 patients (93%). Although the possibility of a prior abnormal Pap test result or positive HPV test result may have precipitated more frequent surveillance, the ASCCP guidelines advocate a return to a 3-year screening interval after a negative cotest result, regardless of prior history. Though this subset of patients was a small component of our total study population (1.6% of total patients), over one quarter of those with dual negative test results underwent repeat testing at an interval less than 3 years. Thrall et al[16] also found that follow-up was inconsistent with published guidelines in approximately half of the cotested patients. As the overall proportion of cotesting increases in our population, the number of women being tested at inappropriately short intervals has the potential to grow proportionately and the purported cost benefits of lengthened screening intervals may not be fully realized.

Multiple factors are likely to be driving this practice, including patient demand for the most complete workup available and provider desire to maintain yearly gynecologic examination of patients. At present in many settings there is no economic disincentive for performing the repeated tests; however, reimbursement may change as payors change their payment schedules to reflect widely endorsed guidelines.

Numerous factors influence Pap and HPV test ordering and adoption of clinical practice guidelines in many different clinical settings. These include provider characteristics; practice setting; legal, financial, and regulatory factors; laboratory factors; and patient-level factors[18] We considered changes in these multiple factors influencing Pap and HPV test ordering to explain the changes in ordering practices. No changes were made to the laboratory requisition during our study period, and no laboratory-driven provider education was provided during the study timeframe. No changes in the FDA-approved uses of the HPV test were made during the study period. We were unable to obtain specific information regarding reimbursement for the HPV test by various health insurance carriers, and thus are unable to link reimbursement with any change in test ordering practice.

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While changes in cotesting practices cannot be directly linked to a particular event, a marketing campaign by Qiagen aimed at the general public as well as at clinicians occurred in the Baltimore area in late 2008. Direct-to-consumer advertising for pharmaceutical and other medical devices has been shown to influence patient and provider behavior.[19] Specifically in the realm of HPV testing, direct-to-consumer advertising has been shown to increase overall HPV test use, both appropriate and inappropriate.[20] The Qiagen marketing campaign preceded the increase in HPV cotesting by several months, but the delay may be related to a lag time for practitioners to implement changes in their practice and/or direct-to-consumer advertising–influenced demand for testing by patients.

Finally, it is also important to acknowledge that the laboratory plays a role in providing a more cost-effective service to patients and to the system as a whole. To improve turnaround time in our laboratory, HPV testing on cotests is initiated before the cytologic diagnosis is rendered; thus HPV testing was performed on 402 cases of dysplasia and 2 cases of SCC. This testing is unnecessary and redundant but illustrates the difficult balance that laboratories face in the current healthcare environment where rapid turnaround time is expected by the laboratory's customers. Despite the recognition of this unnecessary testing, our laboratory has been unable to develop a solution to avoid this practice because clinicians expect to receive HPV test results concurrent to the results of the Pap test. This problem is expected to grow as the overall number of cotests increases. A survey of laboratory practices in the year 2006 indicated that 58% of laboratories offered nonrecommended combinations of HPV testing, including reflex testing on ASC-H, LSIL, HSIL, and atypical glandular cells, and 45% of laboratories offered low-risk HPV testing, which has been shown to have no usefulness in triaging abnormal cervical cytology results.[14] The continued use of low-risk HPV testing was also noted in a survey of clinicians, and one suggestion to end this unnecessary practice was for laboratories to stop offering the test regardless of demand.[21] It is unclear why these practices continue despite evidence that they are of no use, but education of laboratory leaders is also essential to allow for the most efficient and meaningful testing for patients.

A recent review article by Colgan[22] summarizes many of the barriers and challenges to compliance with the ASCCP guidelines, particularly among generalists, as the algorithms become more complex. Colgan emphasizes the role that the laboratory can play in guiding appropriate test ordering and even making management recommendations based on risk assessment tools that incorporate clinical and laboratory data, such as one proposed by Austin et al.[23]

Our study provides a better understanding of cervical cancer screening practices in the many clinics that submit specimens to our laboratory, and highlights opportunities for improvement in the ordering practices for Pap and HPV tests. It also provides benchmark data that clinicians and laboratories can use to assess their test-ordering practices.

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References

1. Wright TC Jr, Cox JT, Massad LS, et al. 2001 Consensus Guidelines for the management of women with cervical cytological abnormalities. *JAMA*. 2002;287:2120-2129.
2. Wright TC Jr, Massad LS, Dunton CJ, et al. 2006 consensus guidelines for the management of women with abnormal cervical cancer screening tests. *Am J Obstet Gynecol*. 2007;197:346-355.
3. Wright TC Jr, Schiffman M, Solomon D, et al. Interim guidance for the use of human papillomavirus DNA testing as an adjunct to cervical cytology for screening. *Obstet Gynecol*. 2004;103:304-309.
4. Dunne EF, Unger ER, Sternberg M, et al. Prevalence of HPV infection among females in the United States. *JAMA*. 2007;297:813-819.
5. Mayrand MH, Duarte-Franco E, Rodrigues I, et al. Human papillomavirus DNA versus Papanicolaou screening tests for cervical cancer. *N Engl J Med*. 2007;357:1579-1588.
6. AGOG Committee on Practice Bulletins–Gynecology. ACOG Practice Bulletin no. 109: Cervical cytology screening. *Obstet Gynecol*. 2009;114:1409-1420.
7. Saslow D, Runowicz CD, Solomon D, et al. American Cancer Society guideline for the early detection of cervical neoplasia and cancer. *CA Cancer J Clin*. 2002;52:342-362.
8. Holland-Barkis P, Forjuoh SN, Couchman GR, et al. Primary care physicians' awareness and adherence to cervical cancer screening guidelines in Texas. *Prev Med*. 2006;42:140-145.
9. Saraiya M, Irwin KL, Carlin L, et al. Cervical cancer screening and management practices among providers in the National Breast and Cervical Cancer Early Detection Program (NBCCEDP). *Cancer*. 2007;110:1024-1032.
10. Saraiya M, Berkowitz Z, Yabroff KR, et al. Cervical cancer screening with both human papillomavirus and Papanicolaou testing vs Papanicolaou testing alone: what screening intervals are physicians recommending? *Arch Intern Med*. 2010;170:977-985.
11. Yabroff KR, Saraiya M, Meissner HI, et al. Specialty differences in primary care physician reports of Papanicolaou test screening practices: a national survey, 2006 to 2007. *Ann Intern Med*. 2009;151:602-611.

DOI: 10.1309/AJCPPVX91HQMNYZZ

12. Phelan DF, Boitnott JK, Clark DP, et al. Trends of human papillomavirus testing in cervical cancer screening at a large academic cytology laboratory. *Obstet Gynecol.* 2011;118(2 Pt 1):289-295.
13. Shirts BH, Jackson BR. Informatics methods for laboratory evaluation of HPV ordering patterns with an example from a nationwide sample in the United States, 2003-2009. *J Pathol Inform.* 2010;1:26.
14. Moriarty AT, Schwartz MR, Eversole G, et al. Human papillomavirus testing and reporting rates: practices of participants in the College of American Pathologists Interlaboratory Comparison Program in Gynecologic Cytology in 2006. *Arch Pathol Lab Med.* 2008;132:1290-1294.
15. Tworek JA, Jones BA, Raab S, et al. The value of monitoring human papillomavirus DNA results for Papanicolaou tests diagnosed as atypical squamous cells of undetermined significance: a College of American Pathologists Q-Probes study of 68 institutions. *Arch Pathol Lab Med.* 2007;131:1525-1531.
16. Thrall MJ, Russell DK, Facik MS, et al. High-risk HPV testing in women 30 years or older with negative Papanicolaou tests: initial clinical experience with 18-month follow-up. *Am J Clin Pathol.* 2010;133:894-898.
17. Castle PE, Fetterman B, Poitras N, et al. Five-year experience of human papillomavirus DNA and Papanicolaou test cotesting. *Obstet Gynecol.* 2009;113:595-600.
18. Davis DA, Taylor-Vaisey A. Translating guidelines into practice: a systematic review of theoretic concepts, practical experience and research evidence in the adoption of clinical practice guidelines. *CMAJ.* 1997;157:408-416.
19. Donohue JM, Cevasco M, Rosenthal MB. A decade of direct-to-consumer advertising of prescription drugs. *N Engl J Med.* 2007;357:673-681.
20. Price RA, Frank RG, Cleary PD, et al. Effects of direct-to-consumer advertising and clinical guidelines on appropriate use of human papillomavirus DNA tests. *Med Care.* 2011;49:132-138.
21. Lee JW, Berkowitz Z, Saraiya M. Low-risk human papillomavirus testing and other nonrecommended human papillomavirus testing practices among U.S. health care providers. *Obstet Gynecol.* 2011;118:4-13.
22. Colgan TJ. The 2006 consensus guidelines for the management of women with abnormal cervical screening tests: challenges remain. *Cancer Cytopathol.* 2010;118:233-237.
23. Austin RM, Onisko A, Druzdzel MJ. The Pittsburgh Cervical Cancer Screening Model: a risk assessment tool. *Arch Pathol Lab Med.* 2010;134:744-750.

DOI: 10.1309/AJCPPVX91HQMNYZZ