*LESS IS MORE*

# Cervical Cancer Screening With Both Human Papillomavirus and Papanicolaou Testing vs Papanicolaou Testing Alone

## *What Screening Intervals Are Physicians Recommending?*

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**Background:** Guidelines recommend screening for cervical cancer among women 30 years or older 3 years after a normal Papanicolaou test (hereinafter referred to as Pap test) result or a combined normal screening result (normal Pap/negative human papillomavirus [HPV] test results). We assessed reported recommendations by US primary care physicians (PCPs) on screening intervals that incorporate HPV cotesting compared with Pap testing alone.

**Methods:** From September 1, 2006, through May 31, 2007, we conducted a mailed survey of a representative sample of 1212 PCPs, of whom 950 performed Pap tests and recommended the HPV test for screening or management. The main outcome measure included self-reported data on timing of screening intervals for women with normal results using clinical vignettes.

**Results:** Among Pap test providers who recommend HPV testing, 31.8% reported that they would conduct the next Pap test in 3 years for a 35-year-old woman with 3 normal Pap test results. For a 35-year-old woman with a normal Pap test result and a negative HPV test finding, only 19.0% would conduct the next Pap test in 3 years. Most remaining physicians would conduct the Pap test more frequently. Most PCPs did not recommend a second HPV test or recommended the next HPV test at the same frequency as the Pap test. Physician specialty was strongly associated with guideline-consistent recommendations for the next Pap or HPV test.

**Conclusions:** A lower proportion of PCPs recommend extending screening intervals to 3 years with an HPV cotest than those screening with the Pap test alone. Implementation of effective interventions and strategies that improve physician adherence to recommendations will be important for efficient screening practices.

*Arch Intern Med. 2010;170(11):977-986*

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ANNUAL PAPANICOLAOU (hereinafter referred to as Pap) testing has played a historic role in decreasing the burden of cervical cancer in the United States. For many years, the US Preventive Services Task Force (USPSTF) was the only organization that recommended extending the Pap test screening interval to up to 3 years, as based on evidence that screening annually does not improve outcomes relative to screening every 3 years.[1] Guidelines such as those set by the American Cancer Society (ACS) and American College of Obstetrics and Gynecology (ACOG) traditionally have recommended 3 consecutive normal Pap test findings before switching to screening less often than annually.[2,3]

*See Invited Commentary at end of article*

Improved understanding of human papillomavirus (HPV) infection and the natural history of cervical neoplasia have resulted in the addition of the HPV (DNA) test along with the Pap test (known as HPV cotesting) among women 30 years or older. Although HPV cotesting has further increased the complexity of screening guidelines, it has also resulted in stronger recommendations by the ACOG and ACS to extend screening intervals to 3 years without a requirement of prior normal Pap test results (**Table 1**). The rationale for HPV cotesting is based on greater sensitivity for detection of high-grade cervical precancer and cancer compared with the Pap test and the low risk of developing high-grade precancer and cancer of the cervix for the next 10 years in a woman with negative results from cotesting.[6-8] The USPSTF has not yet recommended HPV cotesting (Table 1). Cost-effectiveness and other studies evaluating HPV cotesting in the United States and

**Table 1. Comparison of Screening Frequency for Cervical Cancer Pap Test (Cytology) Alone vs HPV Cotesting[a]**

| Topic | Recommendation[b] | | | |
|---|---|---|---|---|
| | ACOG (2003)[c] | ACOG (2009) | ACS (2002)[c] | USPSTF (2003)[c] |
| Pap (cytology) test alone | For women aged <30 y, every year<br>For women aged ≥30 y, if 3 consecutive Pap test results are normal, then may change interval to every 2-3 y | For women aged 21-29 y, every 2 y<br>For women aged ≥30 y, if 3 consecutive Pap test results are normal, then may change interval to every 3 y | For women aged <30 y, conventional Pap test every year and liquid-based Pap test every 2 y<br>For women aged ≥30 y, if 3 consecutive Pap test results are normal, then may change interval to every 2-3 y | Regardless of age, at least every 3 y |
| Pap and HPV test at same time (adjunct or cotesting) | For women aged <30 y, HPV cotesting not recommended<br>For women aged ≥30 y, if HPV test result is negative and cytology result is normal, rescreening should occur no more frequently than every 3 y | For women aged 21-29 y, HPV cotesting not recommended<br>For women aged ≥30 y, if HPV test result is negative and cytology result is normal, rescreening should be no sooner than every 3 y | For women aged <30 y, HPV cotesting not recommended<br>For women aged ≥30 y, if HPV test result is negative and cytology result is normal, frequency of combined cytology and HPV DNA testing should not be more often than 3 y | Insufficient evidence[d] |

Abbreviations: ACOG, American College of Obstetrics and Gynecology; ACS, American Cancer Society; HPV, human papillomavirus; Pap, Papanicolaou; USPSTF, US Preventive Services Task Force.

[a] This table refers to frequency of screening only. For more detailed information on other aspects of the guidelines, please see USPSTF,[1] Saslow et al,[2] ACOG Committee on Practice Bulletins,[3] ACOG,[4] and ACOG Committee on Practice Bulletins–Gynecology.[5]

[b] The American College of Physicians and American Academy of Family Physicians accept the USPSTF guidelines as the evidence basis for their recommendations related to cervical cancer screening.

[c] Guidelines available at the time the physician survey was fielded.

[d] The following rationale is provided: "The benefits of HPV testing as an alternative or adjunct to primary Pap screening have not yet been tested in prospective studies. Adding HPV testing to conventional screening is unlikely to be worthwhile, but HPV testing may have a role in primary screening if it can reliably distinguish between women who would benefit from more intensive Pap testing (more frequent, different technologies, or extended over longer periods) and women for whom screening can be less intensive or even discontinued. There are at least 8 studies evaluating HPV testing in large populations underway or recently completed but not yet in the published literature. At the same time, there are few data on the potential harms of HPV testing, which may include anxiety or stigmatization among infected women and affects on relationships with sexual partners."[1]

elsewhere have concluded that lengthening screening intervals is a fundamental assumption and advantage of HPV cotesting.[9-11]

As of 2004, approximately 20% of providers reported ever using HPV cotesting.[12] Extension of screening intervals has encountered concern from patients and health care providers who equate the annual well-woman visit with an annual Pap test. No data have yet been available to document whether this very important corollary to adoption of HPV cotesting—extension of screening intervals—is being adopted by primary care providers (PCPs) in the United States. Using a national survey of PCPs, we assessed current practices by specialty for cervical cancer screening, including physicians' reported recommendations for extending screening intervals with Pap test–based screening only or with the addition of HPV cotesting.

## METHODS

### SURVEY

Using the American Medical Association Physician Masterfile as the sampling frame, we identified a nationally representative sample of PCPs, which included general practitioners (GPs), family practitioners (FPs), general internists (IMs), and obstetrician-gynecologists (Ob-Gyns).[13] The survey was conducted from September 1, 2006, through May 31, 2007, and was considered exempt from the National Institutes of Health institutional review board. A total of 1212 physicians completed the survey with a response rate of 67.5%. We restricted the sample in our main analysis to 950 Pap test providers (representing 112 637 physicians) who ever recommended HPV testing for screening or management. More details about the survey can be found elsewhere.[13]

### MEASURES

We examined reported recommendations for the next screening test for a 35-year-old woman using the following 3 clinical vignettes: (1) no new sexual partners in the past 5 years and 3 consecutive normal Pap test results, (2) no new sexual partners in the past 5 years and 1 normal Pap test result, and (3) a negative HPV test result and a normal Pap test result this year. In each vignette, the Pap tests were performed by the physician, and in vignette 3 no specific mention was made of new sexual partners or previous Pap tests. According to guidelines at the time of the survey,[1-3,14] appropriate responses for the first vignette included a Pap test every 2 to 3 years (ACS and ACOG) or every 3 years (USPSTF). An appropriate response for the second vignette included a Pap test every year (ACS and ACOG) or every 3 years (USPSTF). Because the USPSTF does not base periodicity on previous normal Pap test findings and has consistently recommended that screening intervals be at least every 3 years, we included the response of every 3 years as a conservative but appropriate USPSTF response for vignettes 1 and 2. Vignette 3 included a separate response for the next HPV and Pap tests. Because some guidelines do not specify the optimal next screening test or tests after normal Pap and negative HPV test results, and because HPV testing alone is not approved by the US Food and Drug Administration, the composite

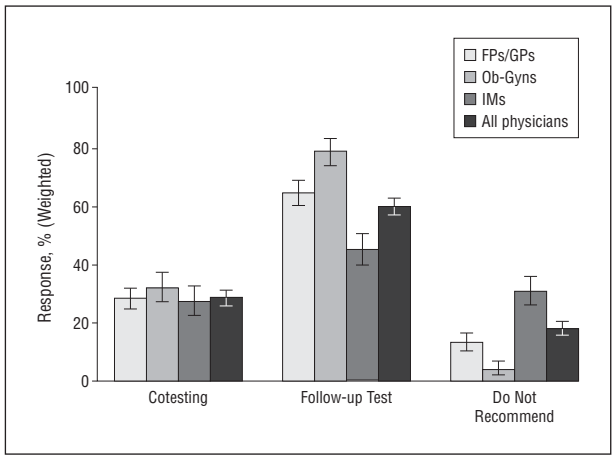


**Figure 1.** Human papillomavirus (HPV) test recommendations by physician specialty (n=1212). Cotesting indicates an HPV and Papanicolaou (Pap) test; follow-up, using an HPV test to follow up after a Pap test with abnormal results. The categories are not mutually exclusive because a physician could respond yes to both follow-up and cotesting. FPs/GPs indicates family physicians/general practitioners; IMs, internists; Ob-Gyns, obstetrician-gynecologists; and error bars, 95% confidence intervals.

measure we considered appropriate includes (1) the next Pap test in 3 years with no HPV test or (2) the next Pap and HPV tests in 3 years. This measure for vignette 3 was used as the outcome in bivariate and multivariate analyses. To prevent loss of information due to missing responses (30 Pap tests and 158 HPV tests), we assumed each missing response to be an unknown when response was given for 1 test only.

In addition to evaluating physician and practice characteristics, we also evaluated the following beliefs: (1) whether a 35-year-old woman with no new sexual partners and whose annual Pap test results during the past 5 years were normal (a woman at low risk of developing cancer) should continue to receive annual pelvic examinations; (2) whether the HPV cotest is more accurate than the Pap test alone; and (3) the effectiveness of conventional cytology, liquid-based cytology, and HPV cotesting. In our formative research, these beliefs were consistently raised as facilitators or barriers to HPV testing or annual screening.

## STATISTICAL ANALYSES

Differences in distributions of physician and practice characteristics and recommendations for Pap and HPV testing frequency were assessed by physician specialty using $\chi^2$ tests. We used the Wald $F$ test to examine the association of physician and practice characteristics and perceptions about screening with guideline-consistent recommendations for the next Pap and/or HPV DNA test in logistic regression analyses. Adjusted variables are presented as predicted marginals,[15] which directly standardizes the covariate distributions of each group to the covariate distribution in the entire population. Standardized results can be compared in the same manner as percentages.

The multivariate model was initially fitted using variables we considered to be clinically relevant to the outcome. After finding very little confounding, we retained in our final model several demographic variables and variables associated with the outcome in a backward regression. A sample weight that accounts for the probability of selection and an adjustment for nonresponse by sample strata was assigned to each survey respondent. We used commercially available statistical software (SUDAAN, version 9.1; RTI International, Research Triangle Park, North Carolina) to apply the sampling weights and to incorporate the stratified survey design in the analysis.

## RESULTS

Among the 1212 clinicians in the sample, 82.0% of PCPs recommended HPV testing. Most clinicians recommended the HPV test to follow up an abnormal Pap test result, with notable specialty differences (IMs, 44.7%; FPs, 64.2%; and Ob-Gyns, 78.2%). Cotesting with HPV was recommended by approximately 28.3% of the 1212 providers with little variation by specialty (**Figure 1**).

### HPV TESTING

Characteristics of the 950 PCPs recommending HPV testing are similar to those of the larger sample of all Pap test providers[13] (**Table 2**). As expected, significant variability was observed for Pap test volume per month. Although 72.9% of IMs ordered or performed at most 20 Pap tests per month, 77.5% of Ob-Gyns ordered or performed more than 40 tests per month. Most physicians used liquid-based Pap tests most commonly, although there was variability across specialty ($P<.001$). Among Ob-Gyns, 86.2% agreed with the statement that a woman at low risk should continue to receive annual pelvic examinations compared with 66.1% of FPs and 63.7% of IMs ($P<.001$).

### REPORTED RECOMMENDATIONS FOR PAP TEST SCREENING INTERVALS WITHOUT HPV TESTING

Only 31.8% of physicians reported recommending the next Pap test in 3 or more years for a 35-year-old woman with no new sexual partners in the past 5 years and 3 consecutive normal Pap test results; this recommendation did not vary by specialty. However, a larger proportion of Ob-Gyns (46.1%) reported that they would conduct another Pap test in 1 year, compared with FPs (30.7%) and IMs (22.4%) (**Figure 2**). When the same vignette was modified to describe only 1 normal Pap test result in the past year, those who would conduct the next Pap test in 1 year rose to 81.0%, with differences by specialty (82.2%, 89.1%, and 72.8% among FPs, Ob-Gyns, and IMs, respectively).

### REPORTED RECOMMENDATIONS FOR PAP TEST INTERVALS WITH HPV COTESTING

For a 35-year-old woman with normal Pap and negative HPV test results, 19.0% would conduct the next Pap test in 3 or more years, as recommended by guidelines. Most of the remaining physicians (78.0%) reported that they would conduct a Pap test more frequently. More Ob-Gyns recommended a 3-year interval than did IMs and FPs (27.7% vs 21.4% and 13.5%, respectively) ($P<.001$) (**Figure 3**A), although the proportion of Ob-Gyns recommending a 3-year interval remained similar to the previous vignette without HPV testing. Few physicians recommended the next HPV test in 3 years, as suggested by ACS and ACOG guidelines (FPs, 10.3%; Ob-Gyns, 22.8%; and IMs, 15.9%). A large percentage (42.8%) recommended not performing an HPV test at all, also an acceptable option per the guidelines (Figure 3B).

**Table 2. Pap and HPV Test Providers and Their Practice Characteristics and Perceptions by Specialty[a]**

| Variable | % of Respondents[b] (N=950) FPs/GPs (n=408) | Ob-Gyns (n=318) | IMs (n=224) |
|---|---|---|---|
| Age group, y[c] | | | |
| <40 | 22.9 | 20.4 | 21.8 |
| 40-49 | 29.3 | 31.4 | 37.1 |
| 50-59 | 29.6 | 31.7 | 30.1 |
| ≥60 | 18.2 | 16.6 | 11.0 |
| Year of medical school graduation[d] | | | |
| 1955-1977 | 23.6 | 24.1 | 15.1 |
| 1978-1985 | 22.0 | 25.1 | 24.0 |
| 1986-1994 | 27.7 | 28.3 | 38.6 |
| 1995-2002 | 26.7 | 22.4 | 22.2 |
| Sex[e] | | | |
| Female | 32.2 | 41.8 | 42.6 |
| Male | 67.8 | 58.2 | 57.4 |
| Race/ethnicity[e] | | | |
| Non-Hispanic white | 75.0 | 66.3 | 58.0 |
| Non-Hispanic black | 2.4 | 9.8 | 6.4 |
| Hispanic | 8.3 | 6.3 | 4.0 |
| Non-Hispanic Asian | 10.4 | 13.3 | 25.4 |
| Other[f] | 3.9 | 4.3 | 6.2 |
| Board certified | | | |
| Yes | 81.0 | 84.8 | 85.0 |
| No | 19.0 | 15.2 | 15.0 |
| Medical school affiliation | | | |
| Yes | 32.9 | 38.9 | 37.3 |
| No | 65.9 | 58.9 | 60.6 |
| Missing | 1.2 | 2.2 | 2.1 |
| CME participation, y[e] | | | |
| ≤3 | 65.6 | 83.3 | 55.6 |
| >3 | 33.4 | 14.2 | 41.0 |
| Missing | 1.0 | 2.5 | 3.4 |
| No. of physicians in practice[g] | | | |
| 1 | 22.1 | 24.5 | 25.7 |
| 2-5 | 48.0 | 39.6 | 33.3 |
| 6-15 | 19.7 | 23.1 | 24.0 |
| ≥16 | 9.3 | 12.3 | 15.9 |
| Missing | 0.9 | 0.5 | 1.1 |
| Specialty setting[d] | | | |
| Single | 73.3 | 75.4 | 60.3 |
| Multiple | 23.2 | 22.8 | 35.8 |
| Missing/other | 3.5 | 1.8 | 3.9 |
| Metropolitan location[e] | | | |
| Urban | 74.9 | 92.1 | 90.7 |
| Rural | 24.2 | 7.9 | 9.3 |
| Missing | 0.9 | 0 | 0 |
| No. of patients seen per week[e] | | | |
| 1-50 | 12.6 | 19.9 | 23.2 |
| 51-75 | 17.3 | 18.1 | 23.1 |
| 76-100 | 29.3 | 28.7 | 30.4 |
| >100 | 38.8 | 31.1 | 22.9 |
| Missing | 2.0 | 2.2 | 0.4 |
| Uninsured patients, %[e] | | | |
| 0-5 | 54.3 | 67.6 | 69.8 |
| 6-25 | 34.3 | 20.4 | 19.8 |
| >25 | 6.7 | 5.3 | 7.0 |
| Don't know/missing | 4.7 | 6.7 | 3.4 |
| Patients insured by Medicaid, %[c] | | | |
| 0-5 | 37.6 | 34.2 | 44.1 |
| 6-25 | 34.9 | 31.1 | 33.0 |
| >25 | 22.3 | 28.2 | 18.1 |
| Don't know/missing | 5.3 | 6.5 | 4.7 |
| Electronic medical record system used in main primary care practice[c] | | | |
| Yes | 46.3 | 39.2 | 42.6 |
| No | 52.2 | 60.0 | 54.8 |
| Missing | 1.5 | 0.8 | 2.6 |

(continued)

**Table 2. Pap and HPV Test Providers and Their Practice Characteristics and Perceptions by Specialty[a] (continued)**

| Variable | % of Respondents[b] (N=950) FPs/GPs (n=408) | Ob-Gyns (n=318) | IMs (n=224) |
|---|---|---|---|
| No. of Pap tests ordered per month[e] | | | |
| 1-10 | 29.8 | 2.3 | 44.5 |
| 11-20 | 27.3 | 3.1 | 28.4 |
| 21-40 | 30.4 | 16.9 | 21.2 |
| ≥41 | 12.5 | 77.5 | 5.5 |
| Missing | 0 | 0.2 | 0.4 |
| Participate in the Breast and Cervical Early Detection Program[d] | | | |
| Yes | 16.3 | 20.0 | 8.2 |
| No | 65.4 | 59.4 | 64.6 |
| Don't know | 16.5 | 17.9 | 24.2 |
| Missing | 1.8 | 2.6 | 3.0 |
| Liquid-based method most often used for cervical cancer screening[e] | | | |
| Yes | 86.8 | 94.1 | 79.3 |
| No | 12.7 | 5.9 | 19.6 |
| Missing | 0.5 | 0.0 | 1.1 |
| Did patients ask for HPV testing in the past 12 mo?[e] | | | |
| Yes | 48.9 | 88.7 | 41.8 |
| No | 50.0 | 10.7 | 57.3 |
| Missing | 1.0 | 0.6 | 0.8 |
| Physician perceptions | | | |
| Strongly/somewhat agree that a 35-year-old woman with no new sexual partners and negative annual Pap test results in the past 5 y should continue receiving annual pelvic examination[e] | | | |
| Yes | 66.1 | 86.2 | 63.7 |
| No/not sure | 32.6 | 12.9 | 34.6 |
| Missing | 1.3 | 0.8 | 1.6 |
| Strongly/somewhat agree that HPV testing with Pap test is more accurate than Pap test alone | | | |
| Yes | 80.3 | 84.4 | 82.8 |
| No/not sure | 18.5 | 14.7 | 14.8 |
| Missing | 1.2 | 0.9 | 2.4 |
| Strongly/somewhat agree that conventional cytology Pap test is effective | | | |
| Yes | 95.4 | 94.1 | 96.4 |
| No | 1.9 | 3.4 | 2.4 |
| Missing | 2.8 | 2.5 | 1.2 |
| Strongly/somewhat agree that liquid-based cytology Pap test is effective[c] | | | |
| Yes | 96.2 | 97.6 | 95.2 |
| No | 1.3 | 0.6 | 4.0 |
| Missing | 2.5 | 1.8 | 0.8 |
| Strongly/somewhat agree that HPV DNA test with Pap test is effective | | | |
| Yes | 91.5 | 92.9 | 91.9 |
| No | 5.9 | 5.3 | 7.7 |
| Missing | 2.6 | 1.8 | 0.4 |

Abbreviations: CME, continuing medical education; FPs/GPs, family physicians/general practitioners; HPV, human papillomavirus; IMs, internists; Ob-Gyns, obstetrician-gynecologists; Pap, Papanicolaou.

[a] Calculations of the $\chi^2$ test for independence for each variable did not include missing responses, except for the percentage of uninsured and percentage of patients insured by Medicaid.

[b] Percentages are weighted to the primary care provider population. Because of rounding, percentages may not total 100.

[c] Differences by specialty, $P<.1$.

[d] Differences by specialty, $P<.01$

[e] Differences by specialty, $P<.001$.

[f] Other includes Native American/Alaska Native, Native Hawaiian/other Pacific Islander, multiple race, other race, and unknown or missing.

[g] Differences by specialty, $P<.05$.

**Table 3** presents the combined response for the timing of the next Pap and HPV tests for a 35-year-old woman who had normal Pap and negative HPV test results. Most providers reported that they would conduct a Pap test every year; only the frequency of HPV testing varied. For example, among physicians who reported that the next Pap test would be performed in a year, the largest percentage reported that they would not conduct an HPV test. Approximately 25% to 37% reported that they would conduct an HPV test every year. Among providers who reported that they would perform a Pap test every 3 years, 50% of IMs and FPs vs 71.6% of Ob-Gyns reported that the next HPV test would also be performed in 3 years. There were no reported recommendations for HPV testing in 3 years without a Pap test.

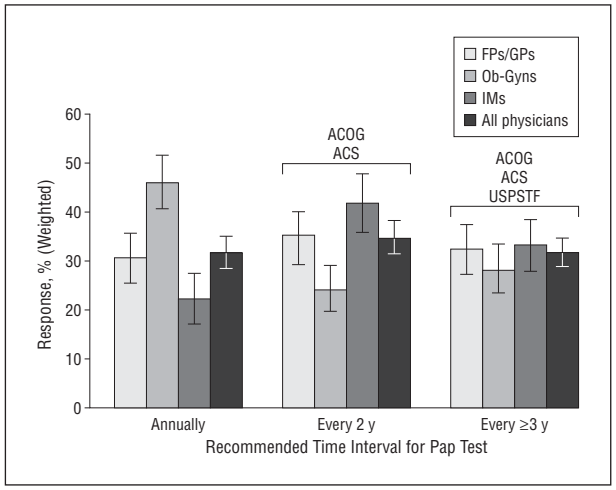


**Figure 2.** Responses by physician specialty concerning the next Papanicolaou (Pap) test. The clinical vignette describes a 35-year-old woman with no new sexual partners in the past 5 years and 3 negative Pap test results. Analysis was limited to 948 providers who were asked about recommendations for Pap testing only (vignette does not include human papillomavirus testing). The US Preventive Services Task Force (USPSTF) says screening at least every 3 years is acceptable (with no mention of need for prior normal test results). Less than 1.3% of physicians reported screening more than every 3 years. Braces indicate adherence to specific guidelines at the time of the survey; error bars, 95% confidence intervals; ACOG, American College of Obstetrics and Gynecology; ACS, American Cancer Society; FPs/GPs, family physicians/general practitioners; IMs, internists; and Ob-Gyns, obstetrician-gynecologists.

**Table 4** shows the relationship of physician and practice characteristics and perceptions with reported recommendations for the next Pap and HPV tests for the vignette of a 35-year-old woman with normal Pap and negative HPV test results. Approximately 17.0% of all physicians recommended a Pap test alone or HPV and Pap tests in 3 years, according to guidelines. After adjusting for all other variables in the model, Ob-Gyns were more likely to recommend extending to triennial screening (27.4%) than FPs (11.9%) or IMs (17.4%). There was a strong association with the outcome for physicians' perceptions about a pelvic examination; physicians who did not agree or were not sure about the statement that a low-risk woman should continue receiving annual pelvic examinations were more likely to follow the guidelines than were physicians who agreed with that statement. The volume of Pap tests ordered per month (albeit with no clear trend), the use of an electronic medical system in the office, and less use of a liquid-based method for cervical cancer screening were also associated with extending intervals.

## COMMENT

Our study using a large, nationally representative survey is, to our knowledge, one of the first to examine whether the addition of HPV testing to routine screening for cervical cancer would prompt PCPs to extend screening intervals among women considered to be at low risk for developing precancer or cancer in the next 3 years. Fewer providers reported recommending extending to triennial screening with HPV cotesting (19.0%) compared with Pap test screening alone (31.8%). Conversely, the percentage who reported that they would recommend annual Pap testing doubled from 31.7% with Pap test alone to 60.1% with

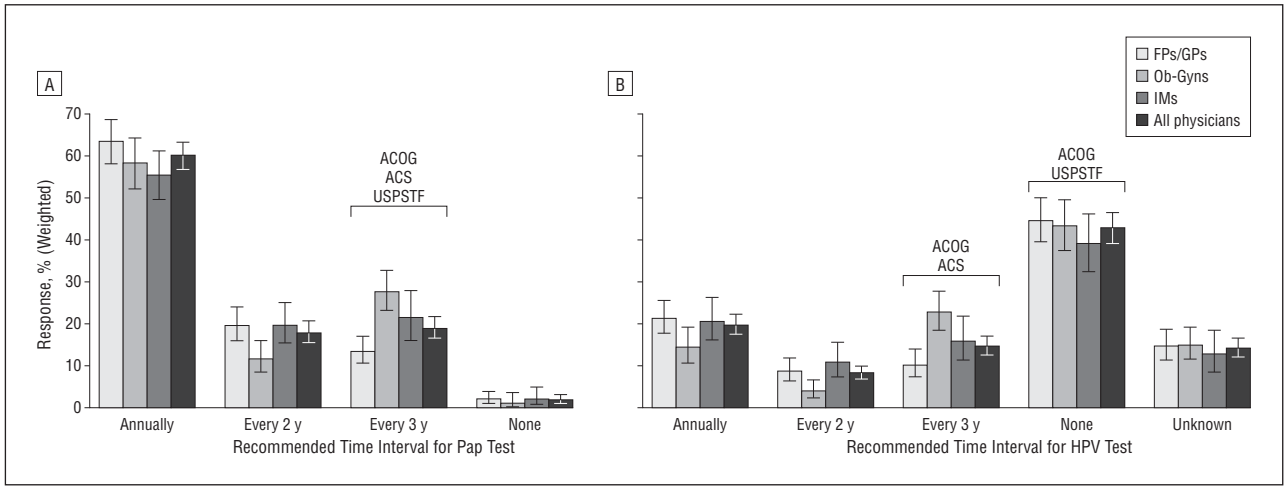


**Figure 3.** Responses by physician specialty concerning the next Papanicolaou (Pap) and human papillomavirus (HPV) tests. A, The clinical vignette asks about the next Pap test for a 35-year-old woman with negative HPV and normal Pap test results this year. Analysis was limited to 928 Pap test providers who also recommended HPV DNA testing. Braces indicate adherence to specific guidelines at the time of the survey. The US Preventive Services Task Force (USPSTF) states that screening at least every 3 years is acceptable (with no mention of need for prior normal tests). B, The clinical vignette asks about the next HPV test for the woman described in part A. Braces indicate adherence to specific guidelines at the time of the survey. ACOG indicates American College of Obstetrics and Gynecology; ACS, American Cancer Society; FPs/GPs, family physicians/general practitioners; IMs, internists; Ob-Gyns, obstetrician-gynecologists; and error bars, 95% confidence intervals.

HPV cotesting. When offered the choice of HPV testing, many physicians deferred to the same pattern they used for Pap testing. That is, recommendations for annual Pap testing were accompanied by HPV testing at the same frequency or, alternatively, HPV testing was not recommended. Clearly, the corollary to HPV cotesting is not being followed.

As expected, there were differences by specialty in screening intervals. Among the Ob-Gyns, the group least likely to extend screening intervals with a Pap test alone in a woman at low risk, the percentage extending to triennial screening with the addition of HPV cotesting did not change markedly. Although Ob-Gyns were more likely than FPs and IMs to report that they would conduct the next HPV test in 3 years, the large majority of all physicians would still conduct the Pap test annually. Among the IMs and FPs, the addition of a negative HPV test result seemed to offer less security in recommending extension to triennial screening than a history of 3 previous normal Pap test results and no new sexual partners. The IMs and FPs reported a decrease in the percentage performing the next Pap test in 3 years. The most likely explanation for the changes by specialty may be lower familiarity with HPV and HPV testing guidelines among IMs and FPs, as found in other studies.[16] In addition, specialty guidelines for FPs and IMs often defer to the USPSTF guidelines, which do not endorse HPV cotesting.[1]

Liquid-based cytology has become the most common type of cytology used, despite recent evidence that liquid-based and conventional cytology have similar test characteristics.[17] One of the most common reasons for its popularity remains that it facilitates HPV cotesting on the same cervical sample. In our study, we found that liquid-based cytology use was associated with a lower likelihood of extending the screening interval, reflecting the contrast between the ease of adoption of emerging technologies and the resistance to screening less frequently. The use of electronic medical record systems was associated with extending the screening interval and serves as an important example of how electronic systems may facilitate reminders to help identify those who are due for screening as well as those who may not need annual screening.

Although PCPs are familiar with assessing the number of sexual partners, the previous number of normal Pap test results, or the history of sexually transmitted infections as traditional risk factors for developing cervical cancer,[18] the concept of HPV status as a risk indicator is relatively new. Castle et al[19] outlined a risk-based approach that takes into account HPV and Pap test results. According to their approach, a combination of negative HPV and normal Pap test results is considered the lowest risk category (<2%) for development of cervical intraepithelial neoplasia 3 in the next 3 years. If providers are using HPV testing, interpretation of traditional risk factors may not matter as much as HPV status. Already, ACOG guidelines state that extending to triennial screening with HPV cotesting can occur, even if a woman has had a new sexual partner in the intervening 3 years.[4]

Other studies have also shown that physicians are resistant to extending Pap screening intervals. Our current findings are surprising given the endorsement of extension of screening intervals with HPV cotesting by 2 major guideline-setting organizations 5 years before our survey was fielded.[2,3] However, numerous studies of physicians' adoption of new guidelines have highlighted the importance of local physician opinion leaders—above and beyond the recommendations of national guidelines—for producing changes in clinical practice.[20,21] The influence of opinion leaders within the local practice community is essential for or against behavior change. Intervention studies have identified mechanisms for this influence[22]; however, our data do not include details necessary to assess the influence of local opinion leaders.

Although current cervical cancer screening guidelines incorporate HPV testing into Pap testing and endorse testing less frequently than the annual screening, there is concern that the recommended triennial screening, especially with HPV cotesting, might result in less frequent visits for other preventive care because cervical cancer screening and annual visits have been so historically linked. Of course, the financial incentive of annual testing (payment per visit) may also play a key role in promoting annual testing. As a direct response to the triennial screening recommendations for HPV testing, in May 2009 the ACOG recently released a statement that reinforced the need for an annual pelvic examination, despite longer intervals between Pap tests. Although many may question the scientific evidence for an annual screening pelvic examination,[23] this is an important statement by ACOG to separate Pap testing from the annual examination. The ACOG quickly followed with a revised

**Table 3. Next Pap and HPV DNA Test Recommendations for 35-Year-Old Women With Negative Results of Both Tests This Year, By Physician Specialty**

| Variable | Respondents[a] FPs/GPs (n=390) | Ob-Gyns (n=307) | IMs (n=202) |
|---|---|---|---|
| Pap test every year, No. of respondents | 255 | 184 | 117 |
| Unknown HPV test | 14.8 | 19.3 | 10.9 |
| No HPV test | 45.1 | 52.1 | 43.1 |
| HPV test every year | 33.4 | 24.8 | 37.4 |
| HPV test every 2 y | 2.2 | 1.0 | 3.2 |
| HPV test every 3 y | 4.4 | 2.6 | 5.3 |
| Pap test every 2 y, No. of respondents | 80 | 36 | 40 |
| Unknown HPV test | 13.8 | 13.6 | 20.0 |
| No HPV test | 46.3 | 48.0 | 29.9 |
| HPV test every year | 0 | 0 | 0 |
| HPV test every 2 y | 36.3 | 29.0 | 45.4 |
| HPV test every 3 y | 3.5 | 9.3 | 4.7 |
| Pap test every 3 y, No. of respondents | 55 | 87 | 45 |
| Unknown HPV test | 14.6 | 6.6 | 10.9 |
| No HPV test | 35.2 | 21.7 | 37.2 |
| HPV test every year | 0 | 0 | 0 |
| HPV test every 2 y | 0 | 0 | 2.0 |
| HPV test every 3 y | 50.2 | 71.6 | 50.0 |

Abbreviations: FPs/GPs, family physicians/general practitioners; HPV, human papillomavirus; IMs, internists; Ob-Gyns, obstetrician-gynecologists; Pap, Papanicolaou.

[a] Percentages are weighted to the primary care provider population in each specialty subgroup category. Because of rounding, percentages may not total 100. Not shown are no Pap test (n=17), unknown Pap test results responses (n=8), other (n=4), and missing (n=22).

**Table 4. Percentage of Physicians Who Recommend the Next Pap and HPV DNA Tests According to Guidelines for a 35-Year-Old Woman With Negative Results of Both Tests This Year[a]**

| Variable | No. of Respondents[b] | Unadjusted Percentage (95% CI) | *P* Value[c] | Adjusted Percentage (95% CI)[d] | *P* Value[e] |
|---|---|---|---|---|---|
| All | 928 | 16.8 (14.6-19.3) | | | |
| Physician specialty | | | | | |
| FPs/GPs | 403 | 11.6 (8.8-15.0) | <.001 | 11.9 (9.2-15.4) | <.001 |
| Ob-Gyns[f] | 314 | 25.8 (21.7-30.4) | | 27.4 (21.3-34.6) | |
| IMs | 211 | 18.7 (13.7-25.0) | | 17.4 (12.6-23.5) | |
| Year of medical school graduation | | | | | |
| 1955-1977[f] | 216 | 15.0 (10.8-18.4) | .77 | 16.2 (11.4-22.4) | .83 |
| 1978-1985 | 211 | 16.4 (11.8-22.2) | | 15.5 (11.0-21.4) | |
| 1986-1994 | 265 | 17.3 (13.0-22.6) | | 17.5 (13.6-22.4) | |
| 1995-2003 | 236 | 18.2 (14.1-23.1) | | 18.2 (14.4-22.8) | |
| Race/ethnicity | | | | | |
| Non-Hispanic white[f] | 640 | 19.8 (16.9-23.0) | <.001 | 19.8 (16.8-23.1) | <.001 |
| Non-Hispanic Asian | 129 | 14.2 (8.9-21.8) | | 13.9 (9.3-20.7) | |
| All other groups | 159 | 7.1 (4.5-11.0) | | 7.8 (4.8-12.4) | |
| Sex | | | | | |
| Female | 335 | 17.2 (13.5-21.8) | .76 | 16.8 (13.1-21.3) | .89 |
| Male[f] | 593 | 16.5 (14.1-19.3) | | 17.1 (14.5-20.0) | |
| No. of physicians in practice | | | | | |
| 1[f] | 221 | 10.5 (7.2-14.9) | <.001 | 14.2 (9.6-20.5) | .12 |
| 2-5 | 390 | 14.1 (11.2-17.8) | | 15.1 (12.0-18.9) | |
| 6-15 | 201 | 20.5 (14.9-27.5) | | 18.7 (13.8-24.9) | |
| ≥16 | 111 | 30.0 (21.7-40.0) | | 22.9 (16.4-30.9) | |
| No. of Pap tests ordered per month | | | | | |
| 1-10[f] | 225 | 15.1 (11.1-20.2) | <.001 | 15.7 (11.2-21.5) | .01 |
| 11-20 | 179 | 18.4 (12.9-25.5) | | 18.7 (13.8-24.9) | |
| 21-40 | 217 | 9.5 (6.4-14.1) | | 10.8 (7.4-15.4) | |
| ≥41 | 306 | 24.6 (20.3-29.5) | | 22.9 (16.2-29.2) | |
| Liquid-based method is the most often used for cervical cancer screening | | | | | |
| Yes | 811 | 16.2 (13.7-19.0) | .12 | 16.0 (13.6-18.8) | .03 |
| No[f] | 113 | 21.7 (15.6-29.4) | | 24.3 (17.5-32.7) | |
| Use of electronic medical record system in office | | | | | |
| Yes | 403 | 22.2 (18.2-26.8) | <.001 | 19.9 (16.1-24.2) | .03 |
| No[f] | 514 | 12.7 (10.2-15.6) | | 14.2 (11.4-17.5) | |
| Strongly/somewhat agree that a low-risk 35-y-old woman (with negative annual Pap test results in past 5 y) should continue receiving annual pelvic examinations | | | | | |
| Yes | 672 | 12.9 (10.8-15.4) | <.001 | 12.8 (10.5-15.5) | <.001 |
| No/not sure | 246 | 26.9 (21.5-33.0) | | 27.5 (22.3-33.3) | |

Abbreviations: CI, confidence interval; FPs/GPs, family physicians/general practitioners; HPV, human papillomavirus; IMs, internists; Ob-Gyns, obstetrician-gynecologists; Pap, Papanicolaou.

[a] Guidelines recommend only a Pap test in 3 years or both HPV and PAP tests in 3 years. Data are weighted to the primary care population design.

[b] Denominators for the percentages. Numbers may not add to 928 because of missing responses.

[c] Based on a Wald *F* test for the association between each variable and the outcome using a logistic regression model.

[d] Based on 899 physicians in the analysis. Percentages are adjusted for all other variables in the model using predictive margins from a logistic regression model.

[e] Based on a global Wald *F* test for the association between each variable and the outcome, adjusted for all other variables in the model, using a logistic regression model.

[f] The referent group in the logistic regression model.

statement in December 2009[5] suggesting more neutral language than a required annual gynecological examination. Many clinicians cite concern from women who want annual Pap testing. Two recent patient preference studies have found that women are receptive to less frequent screening if HPV testing is introduced, especially if accompanied by a provider recommendation.[24,25]

Since the introduction of ACS and ACOG recommendations for HPV cotesting, few studies have highlighted the experiences of managed care organizations that extended their screening intervals. Kaiser Permanente Northern California has had reasonable success in implementing the HPV cotest with conventional Pap tests. During a 5-year period, they reported that greater than 91% of women 30 years or older enrolled in their plan had normal Pap and negative HPV test results. Furthermore, 91.6% of their members 30 years or older who participated in screening elected to have the cotesting option (screening every 3 years if both test results are normal) instead of annual screening.[26] Now, the average interval between negative tests has been extended to 31 months (Walter Kinney, MD, personal communication, December 15, 2009). In many ways, managed care organizations have many of the successful systems to promote evidence-based practices, such as pay-for-performance initiatives that include individual physician accountability, screening guidelines in the practice setting, physician and patient reminder systems, and peer support. The success experienced in a controlled setting such as a managed care organization may not translate into other settings.

The use of HPV cotesting is currently being examined in randomized clinical trials in Europe,[6,11,27,28] and cost-effectiveness studies are also being considered be-

fore adoption of cotesting as part of cervical cancer screening policy. Researchers in Europe are debating whether adoption of HPV cotesting in the national screening programs would result in changes to the recommended start of screening and/or extension of screening intervals among women 30 years or older (beyond the already accepted and practiced 3- to 5-year interval with Pap test–based screening programs alone).[29] Many of the countries are also considering HPV testing as a primary screen followed by triage with Pap test.[6,30,31] In contrast, in the United States, decisions about which screening test to adopt, although taking into account scientific evidence, are largely based on regulatory approval, specialty society recommendations, and cost reimbursement. Direct-to-consumer marketing and legislation may be further influences.[32,33] Further exploration of the relative impact of physician, practice, system, and societal factors associated with physician adherence to screening guidelines will be an important area for future research.

Several cost-effectiveness models for the United States have evaluated the impact of different Pap and HPV cotesting strategies for screening.[34,35] Although these models have not explicitly evaluated the clinical vignette and physician recommendations from our study, as the frequency of Pap and HPV cotesting increases to annual testing, the associated costs increase, with little improvement in life expectancy.[35] Thus, these models suggest that the practice patterns we found in our study are likely to increase costs with little improvement in reducing cervical cancer incidence and increasing survival. Overuse of screening is expensive for the health care system[36,37] and may result in unnecessary follow-up testing,[36] increased risk of colposcopy-associated morbidities and adverse birth outcomes,[38,39] and distress for patients.[40-42] Evaluation of the cost-effectiveness of Pap and HPV cotesting strategies as implemented, along with other considerations, may be useful before resource-limited institutions choose one strategy over the other.

Despite the strengths of using a large national, population-based sample of PCPs with a high response rate, our study has several limitations. We used patient vignettes to elicit physician Pap and HPV test screening recommendations; these vignettes cannot reflect the diversity of women seen in clinical practice or other observable or even unobservable factors that may influence practice. However, clinical vignettes have been shown to be a valid tool for measuring the quality of clinical practice. Physicians may overstate patient receipt of cancer screening and their perceptions of practices that adhere to guidelines,[43] although more recent studies suggest that physician self-report of practice, especially use of clinical vignettes, is reliable.[44,45] Our report shows that approximately 27.0% to 32.0% of PCP specialties recommend HPV cotesting, which is slightly higher than in a 2004 survey, which reported that 20% of PCPs had ever used HPV cotesting. Recent analysis of pathology data systems have reported that approximately 13% of Pap tests among women 30 years or older have HPV cotesting.[46] Any overstatements from self-report would imply that adherence to screening recommendations are lower than reported herein.

In summary, we observed that PCPs' recommended extension of the screening interval to 3 years is actually lower when HPV cotesting is considered. In addition, many physicians reported overscreening women by using both the HPV and Pap tests annually. Until measures are in place to reinforce extended screening intervals among women with negative HPV and normal Pap test results, there is no advantage gained with HPV cotesting, and it is more expensive.

**Accepted for Publication:** January 5, 2010.
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**Financial Disclosure:** None reported.
**Funding/Support:** This study was supported by the National Cancer Institute, Centers for Disease Control and Prevention, and Agency for Healthcare Research and Quality.
**Disclaimer:** The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention or the National Cancer Institute.
**Additional Contributions:** Carrie Klabunde, PhD, of the National Cancer Institute and principal investigator of the National Survey of Primary Care Physicians' Recommendations & Practice for Breast, Cervical, Colorectal, & Lung Cancer Screening, provided coordination and leadership of this effort, and Caroline McLeod, PhD, of WESTAT, provided survey research work.

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**INVITED COMMENTARY**

# Rightsizing Cervical Cancer Screening

Cancer screening strategies must strike a delicate balance between benefits and harms. While the population at large is familiar with cancer screening benefits, screening harms are often not appreciated and generally not discussed. Harms can take many forms, including pain, inconvenience, and morbidity associated with all aspects of screening: testing, follow-up procedures, and treatments. In addition, prolonged surveillance among those with diagnoses of uncertain malignant potential can lead to substantial life disruptions and anxiety. Defining the optimal balance between benefits and harms is often difficult but imperative so that screening benefits are maximized and screening harms minimized.[1]

Screening harms can be mitigated to some degree by setting appropriate lower and upper age limits for screening and avoiding too-frequent testing among average- and low-risk individuals. As a general principle, screening frequency should be driven by 2 major factors: screening test sensitivity and the natural history of disease.[2] Screening strategies for cervical cancer endorsed by ACOG reflect these factors: after 3 or more normal cytology (Pap) test results, screening periodicity may be substantially lengthened in average-risk women aged 30 years or older to every 2 or 3 years[3]; recent updates to the guideline suggest that such women may be screened every 3 years.[4] Requiring a series of normal test results before lengthening screening intervals mini-