

Repeat Pap Testing and Colposcopic Biopsies in the Underserved

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OBJECTIVE: To quantify repeat Pap testing and colposcopic biopsies among women in the National Breast and Cervical Cancer Early Detection Program between 2003 and 2006 (N=955,494).

METHODS: Rates of repeat Pap testing (two tests within 9 months) and colposcopic biopsies were estimated along with 95% confidence intervals (CIs). Odds ratios and 95% CIs for receipt of colposcopic biopsy compared with repeat Pap testing were estimated from multivariable logistic regression models. Finally, we estimated positive predictive values and 95% CIs of cervical intraepithelial neoplasia (CIN) 2 or worse (CIN 3, carcinoma in situ, invasive cancer) for two strategies: 1) repeat Pap testing followed by colposcopic biopsy and 2) colposcopic biopsy alone.

RESULTS: There were 39,583 and 53,880 women with repeat Pap testing and colposcopic biopsy, respectively, from 2003 to 2006. Overall, age-standardized rates of repeat Pap testing and colposcopic biopsies were 37.2 per 1,000 women and 39.3 per 1,000 women, respectively. Younger women, Hispanic women, and African-American women were more likely to receive colposcopic biopsies compared with repeat Pap tests. Positive predictive values of colposcopic biopsy were highest after abnormal Pap test results

(27% after a result of atypical squamous cells, cannot exclude high-grade squamous intraepithelial lesion, 70% after a result of high-grade squamous intraepithelial lesion/squamous cell cancer).

CONCLUSION: Colposcopic biopsies are common among young women after being screened for cervical cancer and, except among those with the most severe Pap test results, may not be efficient in detecting serious disease. These results conflict with current recommendations for less aggressive follow-up for most young women.

(*Obstet Gynecol* 2009;114:1049–56)

LEVEL OF EVIDENCE: II

The Centers for Disease Control and Prevention's (CDC) National Breast and Cervical Cancer Early Detection Program (NBCCEDP) provides screening and early detection for underserved women in the United States.¹ Although follow-up for mammography in the NBCCEDP has been studied,^{2,3} less attention has been focused on rescreening and diagnostic procedures associated with cervical cancer screening. Follow-up after cervical cancer screening depends on the original screening results, previous screening history and results, and factors such as human papillomavirus (HPV) status when known. Women living in low-socioeconomic areas have higher rates of cervical cancer,⁴ and this may influence the treatment preferences of local providers. Prior reports using NBCCEDP data^{5–9} have not estimated the rate of colposcopic biopsies in the NBCCEDP and the positive predictive value of those biopsies.

The American Society for Colposcopy and Cervical Pathology guidelines for the treatment of women with cervical cytological abnormalities¹⁰ are summarized in Table 1. Each treatment algorithm has trade-offs in terms of ability to detect disease, economic costs, inconvenience to patients, and potential loss to follow-up.^{10–15} In particular, low-grade lesions among young women may not require colposcopic biopsy as suggested in older age groups.¹⁴ Creating a balance

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Dr. Trivers was supported in part by the Research Participation Program at the Centers for Disease Control and Prevention (CDC), administered by the Oak Ridge Institute for Science and Education through an interagency agreement between the U.S. Department of Energy and CDC.

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.

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Financial Disclosure

The authors did not report any potential conflicts of interest.

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ISSN: 0029-7844/09



Table 1. American Society for Colposcopy and Cervical Pathology Consensus Guidelines for Initial Treatment of Women With Cervical Cytological Abnormalities,¹⁰ 2003–2006

| Pap Test Result | Possible Follow-Up Schemes | | |
|---|----------------------------|----------------------|---------------------------|
| | Repeat Pap Test at 4–6 mo | Immediate Colposcopy | High-Risk HPV DNA Testing |
| Atypical squamous cells of undetermined significance | X | X | X |
| Atypical squamous cells, cannot exclude high-grade squamous intraepithelial lesion | | X | |
| Low-grade squamous intraepithelial lesions, high-grade squamous intraepithelial lesions, atypical glandular cells | | X | |

HPV, human papillomavirus.

between adequate diagnostic follow-up to rule out severe disease without overtreatment of potentially benign conditions is a critical challenge, particularly in a setting of limited resources. Overtreatment could lead to unexpected harms and increased costs; however, undetected lesions could lead to cancer.¹⁶ Our study aims were to quantify diagnostic and follow-up procedures performed after cervical cancer screening in the NBCCEDP during 2003–2006, to estimate how rates of these procedures differed by age and race, and to calculate positive predictive values as a measure of their clinical efficiency in detecting serious disease.

MATERIALS AND METHODS

The NBCCEDP collects a series of standardized minimal data elements on women enrolled in the program, including basic demographic information (eg, age, race). Also collected is information on breast and cervical cancer screening and diagnostic and follow-up tests paid for by the NBCCEDP. The study population for this report was all women receiving at least one NBCCEDP-supported Pap test between January 1, 2003, and June 30, 2006. The screening cutoff of June 30, 2006, allowed for complete screening and diagnostic follow-up data to be available for our analysis. The study timeframe (2003–2006) also allowed time for physicians to implement the new 2001 American Society for Colposcopy and Cervical Pathology Consensus Guidelines on the management of cervical cytological abnormalities¹⁰ and the updated 2001 Bethesda classification system, which includes the following categories: normal; atypical squamous cells of undetermined significance (ASC-US); low-grade squamous intraepithelial lesions (LSIL); atypical squamous cells, cannot exclude high-grade squamous intraepithelial lesions; atypical glandular cells; high-grade squamous intraepithelial lesions (HSIL); and squamous cell cancer.¹⁷

Race/ethnicity was self-reported. If a woman considered herself to be of Hispanic ethnicity, she was

classified as such, regardless of her race, resulting in mutually exclusive race/ethnicity groups (Hispanic, white, African American, Asian or Pacific Islander, American Indian/Alaska Native, or multiracial). Women reporting neither Hispanic ethnicity nor racial classification were classified as unknown. Age in years at first program Pap test between 2003 and 2006 was categorized (18–29, 30–39, 40–49, 50–64, and 65 or older for rate standardization and 18–20, 21–29, 30–39, 40–49, 50–64, and 65 or older for modeling). The proportion of women 65 years of age or older is small because the NBCCEDP serves only those women not covered by Medicare Part B.¹ The CDC's institutional review board has approved secondary analyses of minimal data elements data by CDC scientists to address specific research questions concerning breast and cervical cancer screening.

Rates of short-interval repeat Pap testing were calculated as the number of women with two Pap tests within a 9-month period in the NBCCEDP per 1,000 women. A maximum interval of 9 months was chosen, rather than 4–6 months as the clinical guidelines recommend, to allow lag time for follow-up Pap tests to be completed. A time period of less than 1 year was necessary to differentiate between rescreening and regular, annual Pap screening. The colposcopic biopsy rate was calculated as the number of women with at least one colposcopic biopsy per 1,000 women. Women who received both repeat Pap testing and colposcopic biopsy were included in the numerators for calculating both the repeat Pap testing and colposcopic biopsy rates (n=11,783). Rates were age-standardized to the age distribution of the NBCCEDP population in 2000 using the five age groups stated previously. Age standardization is a way to age adjust estimates using the age distribution of a “standard” population, in this case the entire NBCCEDP population in 2000.

To investigate predictors of the procedure used (colposcopic biopsy or repeat Pap), we constructed a



multivariable model for receipt of colposcopic biopsy only compared with repeat Pap testing only. Logistic regression was used to estimate odds ratios (ORs) and 95% confidence intervals (CIs) adjusted for age, race and ethnicity, and Pap test result (preceding the biopsy or the repeat Pap test).

The positive predictive value of colposcopic biopsy only was calculated as the number of women with a diagnosis of cervical intraepithelial neoplasia (CIN) 2 or worse (CIN 3, carcinoma in situ, or invasive cancer) divided by the number of women receiving only a colposcopic biopsy. The positive predictive value of repeat Pap testing followed by colposcopic biopsy was calculated as the number of women diagnosed with CIN 2 or worse divided by the number of women receiving repeat a Pap test followed by colposcopic biopsy. For this calculation, the colposcopic biopsy had to occur more than 2 weeks after the second Pap test was done to exclude Pap tests done in conjunction with a colposcopic biopsy and had to be part of the management for the second Pap test result. Positive predictive values were age standardized to the 2000 NBCCEDP population. The positive predictive values were not calculated to compare each strategy with each other but merely to quantify the degree to which each strategy detects serious disease.

RESULTS

During the study period, 955,494 women had at least one valid Pap test. About 45% of the population was white, 13% was African American, and 29% was Hispanic; 80% was 40 years of age or older. African-American and Asian or Pacific Islander women were older than white women in the program, whereas American Indian/Alaska Native women were younger (Table 2). Missing data were minimal; race had the

greatest amount of missing data (those classified as unknown) at approximately 2%.

Of the 955,494 women, 39,583 (4%) had a repeat Pap test and 53,880 (6%) had a colposcopic biopsy. Ninety-one percent of the population (n=873,814) received neither procedure, 3% (n=27,800) received a repeat Pap test but not a colposcopic biopsy, 4% (n=42,097) received a colposcopic biopsy but not a repeat Pap test, and 1% received both (n=11,783). Table 3 details age-specific and age-adjusted rates of repeat Pap tests and colposcopic biopsy by race and ethnicity. The overall age-adjusted rates of repeat Pap tests and colposcopic biopsies were 37.2 per 1,000 women and 39.3 per 1,000 women, respectively. When stratified by race and ethnicity, the highest rate of repeat Pap testing was observed among multiracial and American Indian/Alaska Native women. The highest colposcopic biopsy rate was among white women. For all races, the rates of both types of procedure were highest among women 18–29 years and decreased with increasing age.

To better elucidate the factors that might influence a provider's choice of a repeat Pap test compared with a colposcopic biopsy, the initial Pap test results of those receiving repeat Pap testing only or colposcopic biopsy only were examined (data not shown). Among women with repeat Pap test only, 50% had a test result of normal on the initial and repeat Pap tests. Among women with colposcopic biopsy only, 22% of women had a preceding Pap test result of ASC-US and 68% had a Pap test result of LSIL or worse (LSIL 44%, atypical squamous cells, cannot exclude high-grade squamous intraepithelial lesions 5%, or HSIL/squamous cell cancer 19%). After the colposcopic biopsy, 26% of women had no abnormality found, 42% had CIN 1, and 31% had CIN 2 or worse.

Table 2. Age-by-Race Distribution of Women Who Received At Least One Pap Test in the National Breast and Cervical Cancer Early Detection Program, 2003–2006*

| | All | White | African American | Asian/Pacific Islander | American Indian/Alaska Native | Hispanic | Multiracial | Unknown |
|-------------|----------------|----------------|------------------|------------------------|-------------------------------|----------------|--------------|--------------|
| Age (y) | 955,494 (100) | 432,434 (45.3) | 124,768 (13.1) | 52,349 (5.5) | 50,397 (5.3) | 272,062 (28.5) | 4,994 (0.5) | 18,490 (1.9) |
| 18–29 | 90,171 (9.4) | 40,471 (9.4) | 8,361 (6.7) | 2,277 (4.4) | 12,190 (24.2) | 24,149 (8.9) | 1,084 (21.7) | 1,639 (8.9) |
| 30–39 | 98,170 (10.3) | 35,191 (8.1) | 8,262 (6.6) | 4,052 (7.7) | 8,570 (17.0) | 39,505 (14.5) | 527 (10.6) | 2,063 (11.2) |
| 40–49 | 347,036 (36.3) | 160,550 (37.1) | 45,108 (36.2) | 17,106 (32.7) | 15,364 (30.5) | 100,565 (37.0) | 1,693 (33.9) | 6,650 (36.0) |
| 50–64 | 405,543 (42.4) | 193,825 (44.8) | 61,150 (49.0) | 26,902 (51.4) | 13,734 (27.3) | 100,611 (36.7) | 1,658 (33.2) | 7,663 (41.4) |
| 65 or older | 14,574 (1.5) | 2,397 (0.6) | 1,887 (1.5) | 2,012 (3.8) | 539 (1.1) | 7,232 (2.7) | 32 (0.6) | 475 (2.6) |

Data are n (%).

* Complete screening data available through 6/30/06.



Table 3. Age-Specific and Age-Adjusted Rates (95% Confidence Intervals) of Short-Interval Repeat Pap Testing* and Colposcopic Biopsies,† by Race and Ethnicity, National Breast and Cervical Cancer Early Detection Program, 2003–2006‡

| | All | White | African American | Asian/Pacific Islander | American Indian/Alaska Native | Hispanic | Multiracial | Unknown |
|--------------------------------------|------------------------|------------------------|------------------------|------------------------|-------------------------------|------------------------|------------------------|------------------------|
| Short-interval repeat Pap test rate* | | | | | | | | |
| N | 39,583 | 19,190 | 3,943 | 1,661 | 4,312 | 9,459 | 506 | 512 |
| Age (y) [§] | | | | | | | | |
| 18–29 | 87.2 (85.4–89.1) | 81.7 (79.1–84.4) | 47.0 (42.5–51.5) | 60.2 (50.4–69.9) | 171.0 (164.3–177.6) | 64.8 (61.7–67.9) | 254.6 (228.7–280.5) | 64.1 (52.2–75.9) |
| 30–39 | 52.9 (51.5–54.3) | 58.9 (56.5–61.4) | 32.8 (29.0–36.6) | 44.2 (37.8–50.5) | 102.7 (96.3–109.1) | 41.4 (39.4–43.4) | 163.2 (131.6–194.7) | 34.4 (26.5–42.3) |
| 40–49 | 41.1 (40.4–41.7) | 46.2 (45.2–47.3) | 33.9 (32.2–35.5) | 37.0 (34.2–39.8) | 54.9 (51.3–58.5) | 35.3 (34.1–36.4) | 47.3 (37.1–57.4) | 29.5 (25.4–33.5) |
| 50–64 | 29.7 (29.2–30.2) | 32.7 (31.9–33.5) | 28.2 (26.9–29.5) | 25.2 (23.3–27.0) | 35.6 (32.5–38.7) | 25.8 (24.8–26.8) | 38.6 (29.3–47.9) | 17.7 (14.8–20.7) |
| 65 or older | 16.2 (14.1–18.2) | 16.3 (11.2–21.3) | 13.8 (8.5–19.0) | 17.4 (11.7–23.1) | 29.7 (15.4–44.0) | 16.0 (13.1–18.9) | 0 (0.2–16.6) | 8.4 (0.2–16.6) |
| Age-adjusted rate | 37.2 (36.9–37.6) | 40.9 (40.3–41.5) | 30.9 (30.0–31.9) | 31.9 (30.4–33.4) | 52.3 (50.2–54.4) | 31.5 (30.8–32.2) | 58.5 (51.9–65.0) | 24.6 (22.4–26.8) |
| Colposcopic biopsy rate [†] | | | | | | | | |
| N | 53,880 | 29,636 | 5,521 | 1,351 | 1,849 | 14,293 | 310 | 920 |
| Age (y) [§] | | | | | | | | |
| 18–29 | 279.1 (276.2–282.0) | 366.4 (361.7–371.1) | 292.9 (283.2–302.7) | 155.0 (140.2–169.9) | 79.2 (74.4–84.0) | 245.6 (240.2–251.1) | 170.7 (148.3–193.1) | 278.2 (256.5–299.9) |
| 30–39 | 85.9 (84.2–87.7) | 115.1 (111.8–118.4) | 79.8 (73.9–85.6) | 35.5 (29.8–41.2) | 39.8 (35.7–43.9) | 77.0 (74.4–79.7) | 60.7 (40.3–81.1) | 80.5 (68.7–92.2) |
| 40–49 | 34.9 (34.3–35.5) | 41.1 (40.1–42.0) | 26.4 (24.9–27.9) | 26.8 (24.4–29.2) | 23.2 (20.9–25.6) | 32.7 (31.6–33.8) | 28.9 (21.0–36.9) | 26.2 (22.3–30.0) |
| 50–64 | 19.6 (19.2–20.0) | 21.4 (20.7–22.0) | 19.4 (18.3–20.5) | 14.1 (12.6–15.5) | 13.0 (11.1–14.9) | 18.9 (18.0–19.7) | 26.5 (18.8–34.3) | 15.7 (12.9–18.4) |
| 65 or older | 14.8 (12.8–16.7) | 7.5 (4.1–11.0) | 19.1 (12.9–25.3) | 8.9 (4.8–13.1) | 13.0 (3.4–22.5) | 18.3 (15.2–21.3) | 0 (0.2–16.6) | 8.4 (0.2–16.6) |
| Age-adjusted rate | 39.3 (38.9–39.6) | 47.6 (47.0–48.2) | 36.3 (35.3–37.3) | 25.0 (23.7–26.3) | 21.0 (19.7–22.4) | 36.3 (35.6–36.9) | 34.7 (29.5–39.9) | 33.6 (31.3–35.9) |

* Rates calculated as number of women with at least two valid Pap tests within 9 months per 1,000 women.

† Rates calculated as number of women with at least one colposcopic biopsy per 1,000 women.

‡ Complete screening data available through June 30, 2006.

§ Age at first program Pap test between 2003 and 2006.

|| Age-standardized to the 2000 National Breast and Cervical Cancer Early Detection Program population.



Table 4. Predictors of Type of Procedure (Colposcopic Biopsy Compared With Short-Interval Repeat Pap Testing), National Breast and Cervical Cancer Early Detection Program, 2003–2006*

| Characteristic | Women With Colposcopic Biopsy (n) | Women With Repeat Pap Testing (n) | Adjusted OR [†] (95% CI) |
|---|-----------------------------------|-----------------------------------|-----------------------------------|
| Age (y) | | | |
| 18–20 | 6,293 | 999 | 10.96 (9.90–12.15) |
| 21–29 | 15,363 | 3,356 | 7.92 (7.38–8.49) |
| 30–39 | 6,641 | 3,402 | 3.51 (3.26–3.78) |
| 40–49 | 8,265 | 10,406 | 1.37 (1.29–1.46) |
| 50–64 | 5,357 | 9,438 | 1.0 (reference) |
| 65 or older | 178 | 199 | 1.34 (0.99–1.81) |
| Race/ethnicity | | | |
| African American | 4,552 | 2,974 | 1.14 (1.06–1.23) |
| Asian/Pacific Islander | 967 | 1,277 | 0.72 (0.64–0.82) |
| American Indian/Alaska Native | 1,071 | 3,534 | 0.15 (0.13–0.17) |
| Hispanic | 11,235 | 6,401 | 1.24 (1.17–1.31) |
| Other [‡] | 976 | 764 | 0.69 (0.60–0.80) |
| White | 23,296 | 12,850 | 1.0 (reference) |
| First Pap test result [§] | | | |
| Atypical squamous cells of undetermined significance | 10,146 | 9,799 | 6.46 (6.10–6.83) |
| Low-grade squamous intraepithelial lesion | 17,963 | 1,395 | 60.20 (55.89–64.84) |
| Atypical squamous cells, cannot exclude high-grade intraepithelial lesion | 2,187 | 117 | 142.65 (117.03–173.88) |
| High-grade squamous intraepithelial lesion/squamous cell cancer | 7,319 | 100 | 506.90 (412.84–622.38) |
| Atypical glandular cells | 2,278 | 186 | 124.53 (106.0–146.29) |
| Normal | 2,204 | 16,203 | 1.0 (reference) |

OR, odds ratio; CI, confidence interval.

* Complete screening data available through June 30, 2006.

[†] Comparing odds of colposcopic biopsy only compared with repeat Pap testing only; ORs are adjusted for all other variables in the column.

[‡] Includes multiracial and unknown.

[§] From the first test of the repeat Pap testing sequence or from the test preceding the biopsy.

After adjusting for race and ethnicity and prior Pap test result, women aged 18–20 and 21–29 years were substantially more likely than women aged 50–64 years to receive colposcopic biopsy instead of repeat Pap test (OR 10.96, 95% CI 9.90, 12.15 and OR 7.92, 95% CI 7.38, 8.49, respectively) (Table 4). The likelihood of receiving colposcopic biopsy rather than repeat Pap test decreased with age until age 50. Compared with white women, Asian or Pacific Islander and American Indian/Alaska Native women were less likely to receive biopsy than repeat Pap testing, whereas Hispanic and African-American women were more likely to receive biopsy.

The positive predictive value of repeat Pap testing followed by colposcopic biopsy was lower than that of colposcopic biopsy alone in detecting CIN 2 or worse (Table 5). The more severe the Pap test result, the higher the positive predictive value for CIN 2. For colposcopic biopsy alone, the positive predictive value was about 70% for HSIL/squamous cell cancer compared with 12–13% for ASC-US or LSIL Pap results, respectively. Similar results were observed for the positive predictive value of repeat Pap testing

followed by colposcopic biopsy. Within each Pap-test-result category, positive predictive value decreased with age. Age-adjusted positive predictive values did not differ substantially by race and ethnicity for either procedure.

DISCUSSION

Similar to previous NBCCEDP results,⁷ younger women (younger than 39 years) in this analysis were most likely to receive colposcopic biopsy. These results are, in part, inconsistent with updated guidelines that follow-up should be less aggressive for adolescent women (younger than 21 years) with abnormal tests.¹⁴ The exact reasons that young women were more likely to receive colposcopic biopsies are unknown. One explanation might be that younger women in our study population could have been referred into the NBCCEDP after obtaining an abnormal screening result elsewhere, representing a group at higher risk of HPV exposure and abnormal Pap results than that in the general population. Therefore, our findings among younger women may not reflect those in the general population.



Table 5. Positive Predictive Values With 95% Confidence Intervals of Short-Interval Repeat Pap Testing Followed by a Colposcopic Biopsy* and Colposcopic Biopsy Alone† in Determining CIN 2 or Worse Disease National Breast and Cervical Cancer Early Detection Program, 2003–2006‡

| | Pap Test Result [§] | | | | HSIL/Squamous Cell Cancer |
|--|------------------------------|------------------|------------------|------------------|---------------------------|
| | Normal | ASC-US | LSIL | ASC-H | |
| Short-interval repeat Pap testing followed by a colposcopic biopsy | | | | | |
| N | 229 | 1,697 | 1,720 | 214 | 526 |
| All | 4.8 (2.0–7.6) | 11.5 (10.0–13.1) | 11.9 (10.3–13.4) | 23.4 (17.6–29.1) | 54.2 (49.9–58.5) |
| Age (y) [¶] | | | | | |
| 18–29 | 2.8 (–2.9–8.4) | 16.9 (13.1–20.7) | 14.8 (12.1–17.6) | 28.8 (16.1–41.6) | 54.7 (47.4–62.1) |
| 30–39 | 2.6 (–2.6–7.8) | 14.7 (10.1–19.2) | 15.8 (11.2–20.4) | 39.3 (20.0–58.6) | 54.2 (43.3–65.2) |
| 40–49 | 5.1 (0.7–9.4) | 10.6 (8.1–13.1) | 9.4 (6.8–11.9) | 16.2 (7.6–24.8) | 57.7 (49.9–65.5) |
| 50–64 | 7.3 (0.2–14.4) | 7.3 (5.0–9.5) | 7.0 (4.2–9.8) | 20.0 (9.6–30.4) | 48.6 (38.9–58.3) |
| Age-adjusted PPV [#] | 5.8 (1.9–9.7) | 9.2 (7.7–10.7) | 8.7 (6.9–10.4) | 20.2 (14.0–26.4) | 52.1 (46.3–57.9) |
| Colposcopic biopsy alone | | | | | |
| N | 2,187 | 10,059 | 17,859 | 2,160 | 7,225 |
| All | 8.1 (6.9–9.2) | 16.9 (16.1–17.6) | 19.6 (19.0–20.2) | 31.3 (29.3–33.2) | 70.4 (69.3–71.4) |
| Age (y) [¶] | | | | | |
| 18–29 | 12.6 (9.8–15.4) | 20.1 (19.0–21.2) | 21.5 (20.8–22.3) | 34.7 (31.5–37.8) | 68.2 (66.6–69.9) |
| 30–39 | 10.8 (7.4–14.3) | 17.4 (15.5–19.2) | 20.9 (19.3–22.5) | 37.6 (32.5–42.8) | 75.8 (73.5–78.0) |
| 40–49 | 5.1 (3.5–6.8) | 12.4 (10.9–13.8) | 14.3 (13.0–15.7) | 26.9 (22.9–30.8) | 71.2 (69.0–73.3) |
| 50–64 | 6.0 (4.1–7.9) | 9.8 (8.2–11.5) | 10.2 (8.5–11.9) | 23.2 (19.2–27.2) | 68.2 (65.4–71.1) |
| Age-adjusted PPV [#] | 6.3 (5.1–7.5) | 11.8 (10.7–12.8) | 12.8 (11.8–13.9) | 26.7 (24.1–29.2) | 69.9 (68.2–71.6) |

ASC-US, atypical squamous cells of undetermined significance; LSIL, low-grade squamous intraepithelial lesions; ASC-H, atypical squamous cell, cannot exclude high-grade squamous intraepithelial lesion; HSIL, high-grade squamous intraepithelial lesion; PPV, positive predictive value.

* PPV calculated as proportion of women with a diagnosis of CIN 2 or worse among those getting a repeat Pap test followed by a colposcopic biopsy in same cycle as second Pap test and occurring more than 2 weeks after the second Pap test.

† PPV calculated as proportion of women with a diagnosis of CIN 2 or worse among those getting a colposcopic biopsy only.

‡ Complete screening data available through 6/30/06.

§ Result of Pap test before biopsy.

|| Women 65 years or older are included in the “All” category, but estimates are not shown separately for that group.

¶ Age at first program Pap test between 2003 and 2006.

Age-standardized to the 2000 National Breast and Cervical Cancer Early Detection Program population.

To investigate whether a woman’s Pap test history before the start of the study may have influenced what type of procedure she received, we classified women on the basis of their program Pap test history in the 2 years before the study (January 1, 2001–December 31, 2002). Approximately 80% of women did not have a Pap test that was provided through the NBCCEDP in the 2 years before the study, and, as such, data on these women are unavailable for that time period. This lack of information may have lead clinicians to do the more definitive procedure to rule out severe disease. However, additionally adjusting for Pap test history in the 2 years before the start of the study did not change the findings, suggesting that this did not explain fully why some groups of women were more likely to receive colposcopic biopsies than repeat Pap tests. Therefore, to the extent possible, we have ruled out prior Pap-test history as the reason younger women were more likely to

receive colposcopic biopsies than repeat Pap tests. This suggests some of the medical practices reported in this article may not be indicated and that findings of both low-grade and high-grade disease in the younger age groups are amenable to more conservative management for up to 2 years of follow-up as is recommended.

Compared with other race/ethnicities, Asian or Pacific Islander and American Indian/Alaska Native women were more likely to receive repeat Pap tests than colposcopic biopsy, whereas Hispanic and African-American women were more likely to receive colposcopic biopsy. The reasons for this are unknown, and further investigation is needed. However, because the entire study population is of similar socioeconomic status, differences in race are probably not entirely caused by differences in socioeconomic status. There is variation across programs (eg, some reach more women than others); thus, some of the



observed differences by race may reflect program-level differences. Given the number of programs, it is not feasible to present program-specific results, and data-sharing restrictions prevent the presentation of such data. The minimal data elements data undergo extensive quality assurance, monitored at the national level, including comparing minimal data elements data with clinical and service standards.¹

Positive predictive values were less than 13% for test results that were LSIL or less severe. Coupled with the observation that 71% of women who underwent biopsy had a preceding Pap test result of LSIL or worse, this suggests that there may be little clinical advantage to biopsies in this group. The positive predictive values reported here are similar to those from other programs,^{18,19} including the NBCCEDP.^{3,6}

This analysis has limitations. First, our minimal data elements data set may not capture fully all elements used for clinical decision making. Data on clinician's impression at colposcopy, receipt and results of screening and diagnostic tests received outside of the program, and results of HPV testing were not available. Positive HPV test may explain the type of follow-up procedure. However, immediate colposcopy for cytologically normal, HPV-positive women younger than 35 years of age may lead to overtreatment and should be avoided,²⁰ although retesting is necessary.²¹ Finally, the NBCCEDP is not population-based and covers a small percentage of eligible women.²²

Strengths of the analysis are that the NBCCEDP is the only nationwide cervical cancer screening program in the United States. Data quality is high; variables for Pap test results, final diagnosis and receipt of colposcopy with biopsy from the minimal data elements data have more than 90% concordance with data abstracted from medical records (unpublished results). The availability of data from a wide variety of providers and clinical settings provides a unique picture of clinical practices in this country. Providers who serve women enrolled in the NBCCEDP are more often mid-level providers but provide medical care comparable with that of nonprogram providers,⁹ suggesting that variations in provider care may reflect individual differences in clinical decision making and not necessarily reflect program-level differences. Minimal data elements data often are used to monitor public health practice and can provide data on the timeliness, adequacy, and appropriateness of follow-up of clinical care.¹

Our findings may have important cost implications for the NBCCEDP, given the estimated \$3.6 billion spent on direct costs related to abnormal test

results and low-grade lesions.²³ We estimate additional direct costs (95% CI) of \$1.94 (\$0.96–\$2.95) and \$10.53 (\$3.95–\$16.10) to the NBCCEDP for repeat Pap testing or colposcopic biopsy.^{24,25} These additional costs are substantial when extrapolated to the more than 300,000 women who receive screening annually in the NBCCEDP (http://www.cdc.gov/cancer/nbccedp/data/summaries/national_aggregate.htm).

In conclusion, colposcopic biopsies were common among young women in the NBCCEDP, in whom serious disease was not most common. Such results have not been published previously for a large, screened population in the United States, particularly for the vulnerable population served by the NBCCEDP. The observed strategies had low positive predictive values for test results of LSIL or less severe, suggesting these common strategies might not be efficient in detecting serious disease.

REFERENCES

1. Ryerson AB, Benard VB, Major AC. The National Breast and Cervical Cancer Early Detection Program 1991–2002 national report. Atlanta (GA): Department of Health and Human Services; 2005.
2. Smith-Bindman R, Chu PW, Miglioretti DL, Sickles EA, Blanks R, Ballard-Barbash R, et al. Comparison of screening mammography in the United States and the United Kingdom [published erratum appears in JAMA 2004;291:824]. JAMA 2003;290:2129–37.
3. Ehemann CR, Benard VB, Blackman D, Lawson HW, Anderson C, Helsel W, et al. Breast cancer screening among low-income or uninsured women: results from the National Breast and Cervical Cancer Early Detection Program, July 1995 to March 2002 (United States). Cancer Causes Control 2006 Feb;17:29–38.
4. Benard VB, Coughlin SS, Thompson T, Richardson LC. Cervical cancer incidence in the United States by area of residence, 1998–2001. Obstet Gynecol 2007;110:681–6.
5. Sawaya GF, McConnell KJ, Kulasingam SL, Lawson HW, Kerlikowske K, Melnikow J, et al. Risk of cervical cancer associated with extending the interval between cervical-cancer screenings. N Engl J Med 2003;349:1501–9.
6. Benard VB, Ehemann CR, Lawson HW, Blackman DK, Anderson C, Helsel W, et al. Cervical screening in the National Breast and Cervical Cancer Early Detection Program, 1995–2001. Obstet Gynecol 2004;103:564–71.
7. Benard VB, Lawson HW, Ehemann CR, Anderson C, Helsel W. Adherence to guidelines for follow-up of low-grade cytologic abnormalities among medically underserved women. Obstet Gynecol 2005;105:1323–8.
8. Cooper CP, Saraiya M, McLean TA, Hannan J, Liesmann JM, Rose SW, et al. Report from the CDC. Pap test intervals used by physicians serving low-income women through the National Breast and Cervical Cancer Early Detection Program. J Womens Health (Larchmt) 2005;14:670–8.
9. Saraiya M, Irwin KL, Carlin L, Chen X, Jain N, Benard V, et al. Cervical cancer screening and management practices among providers in the National Breast and Cervical Cancer Early Detection Program (NBCCEDP). Cancer 2007;110:1024–32.



10. Wright TC Jr, Cox JT, Massad LS, Twigg LB, Wilkinson EJ. ASCCP-Sponsored Consensus Conference. 2001 Consensus Guidelines for the management of women with cervical cytological abnormalities. *JAMA* 2002;287:2120-9.
11. Rogstad KE. The psychological impact of abnormal cytology and colposcopy. *BJOG* 2002;109:364-8.
12. Marteau TM, Walker P, Giles J, Smail M. Anxieties in women undergoing colposcopy. *Br J Obstet Gynaecol* 1990;97:859-61.
13. Kim JJ, Wright TC, Goldie SJ. Cost-effectiveness of alternative triage strategies for atypical squamous cells of undetermined significance. *JAMA* 2002;287:2382-90.
14. Wright TC, Massad LS, Dunton CJ, Spitzer M, Wilkinson EJ, Solomon D, et al. 2006 consensus guidelines for the management of women with abnormal cervical cancer screening tests. *Am J Obstet Gynecol* 2007;197:346-55.
15. Ferris DG, Wright TC, Litaker MS, Richart RM, Lorincz AT, Sun XW, et al. Triage of women with ASCUS and LSIL on Pap smear reports: management by repeat Pap smear, HPV DNA testing, or colposcopy? *J Fam Pract* 1998;46:125-34.
16. Solomon D. Chapter 14: role of triage testing in cervical cancer screening. *J Natl Cancer Inst Monogr* 2003;31:97-101.
17. Solomon D, Davey D, Kurman R, Moriarty A, O'Connor D, Prey M, et al. The 2001 Bethesda System: terminology for reporting results of cervical cytology. *JAMA* 2002;287:2114-9.
18. Ronco G, Giubilato P, Naldoni C, Zorzi M, Anghinoni E, Scalisi A, et al. Activity level and process indicators of organized programmes for cervical cancer screening in Italy. *Epidemiol Prev* 2006;30(1 Suppl 3):27-40.
19. Dalla Palma P, Giorgi Rossi P, Collina G, Buccoliero AM, Ghiringhello B, Lestani M, et al. The risk of false-positive histology according to the reason for colposcopy referral in cervical cancer screening: a blind revision of all histologic lesions found in the NTCC trial. *Am J Clin Pathol* 2008;129:75-80.
20. Ronco G, Giorgi-Rossi P, Carozzi F, Confortini M, Dalla Palma P, Del Mistro A, et al. Results at recruitment from a randomized controlled trial comparing human papillomavirus testing alone with conventional cytology as the primary cervical cancer screening test. *J Natl Cancer Inst* 2008;100:492-501.
21. Ronco G, Giorgi-Rossi P, Carozzi F, Dalla Palma P, Del Mistro A, De Marco L, et al. Human papillomavirus testing and liquid-based cytology in primary screening of women younger than 35 years: results at recruitment for a randomised controlled trial. *Lancet Oncol* 2006;7:547-55.
22. Tangka FK, Dalaker J, Chattopadhyay SK, Gardner JG, Royalty J, Hall IJ, et al. Meeting the mammography screening needs of underserved women: the performance of the National Breast and Cervical Cancer Early Detection Program in 2002-2003 (United States). *Cancer Causes Control* 2006;17:1145-54.
23. Chesson HW, Blandford JM, Gift TL, Tao G, Irwin KL. The estimated direct medical cost of sexually transmitted diseases among American youth, 2000. *Perspect Sex Reprod Health* 2004;36:11-9.
24. Ekwueme DU, Gardner JG, Subramanian S, Tangka FK, Bapat B, Richardson LC. Cost analysis of the National Breast and Cervical Cancer Early Detection Program: selected states, 2003 to 2004. *Cancer* 2008;112:626-35.
25. Kulasingam SL, Kim JJ, Lawrence WF, Mandelblatt JS, Myers ER, Schiffman M, et al. Cost-effectiveness analysis based on the atypical squamous cells of undetermined significance/low-grade squamous intraepithelial lesion Triage Study (ALTS). *J Natl Cancer Inst* 2006;98:92-100.

