Risk of cervical precancer and cancer among uninsured and underserved women from 2009 to 2017

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Abstract

BACKGROUND: New guidelines for managing cervical precancer among women in the United States use risk directly to guide clinical actions for individuals who are being screened. These risk-

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The authors report no conflict of interest.

based management guidelines have previously only been based on risks from a large integrated healthcare system. We present here data representative of women of low income without continuous insurance coverage to inform the 2019 guidelines and ensure applicability.

OBJECTIVE: We examined the risks of high-grade precancer after human papillomavirus and cytology tests in underserved women and assessed the applicability of the 2019 guidelines to this population.

STUDY DESIGN: We examined cervical cancer screening and follow-up data among 363,546 women enrolled in the Centers for Disease Control and Prevention's National Breast and Cervical Cancer Early Detection Program from 2009 to 2017. We estimated the immediate (prevalent) risks of cervical intraepithelial lesion grade 3 or cancer by using prevalence-incidence mixture models. Risks were estimated for each combination of human papillomavirus and cytology result and were stratified by screening history. We compared these risks with published estimates used in new risk-based management guidelines.

RESULTS: Women who were up-to-date with their screening, defined as being screened with cytology within the past 5 years, had immediate risks of cervical intraepithelial neoplasia grade 3 or higher similar to that of women at Kaiser Permanente Northern California, whose data were used to develop the management guidelines. However, women in the Centers for Disease Control and Prevention's National Breast and Cervical Cancer Early Detection Program had greater immediate risks if they were never screened or not up-to-date with their screening.

CONCLUSION: New cervical risk–based management guidelines are applicable for underinsured and uninsured women with a low income in the United States who are up-to-date with their screening. The increased risk observed here among women who received human papillomavirus–positive, high-grade cytology results, who were never screened, or who were not up-to-date with their cervical cancer screening, led to a recommendation in the management guidelines for immediate treatment among these women.

Introduction

The 2012 and the recent 2019 consensus risk-based guidelines, sponsored by the American Society for Colposcopy and Cervical Pathology (ASCCP), used the principle of equal management for equal risk to determine the management after an abnormal cervical cancer screening result.[1,2] This principle states that if 2 individuals have the same risk of cervical intraepithelial neoplasia (CIN) grade 3 or cancer (CIN3+), irrespective of patient characteristics and test results, their recommended clinical management should be the same. Under the new management guidelines, risk is directly used to determine whether an individual should undergo the following: immediate treatment (immediate CIN3+ risk of 60%); colposcopy with or without biopsy (immediate CIN3+ risk of 4%); or, if no clinical action is needed, whether an individual should return for retesting in 1, 3, or 5 years (5-year CIN3+ risk of 0.5%, 0.15%–0.5%, and <0.15%, respectively). These guidelines were

largely based on calculating the risk of cervical precancer among 1.5 million women in a large integrated healthcare delivery system (Kaiser Permanente Northern California [KPNC]).[3] Our aim was to understand whether these risks, which were estimated from the KPNC data, represent populations at an increased risk of cervical cancer, such as women of low income without continuous insurance coverage.

To ensure applicability to other populations, the 2019 guidelines compared the risks among several groups.[3] Included in their assessment were some of the pre-publication results that we present here for a high-risk population: women served by the Centers for Disease Control and Prevention's (CDC) National Breast and Cervical Cancer Early Detection Program (NBCCEDP). Here, we present the full results of our analysis. Since 1991, NBCCEDP established policies determining eligibility and reimbursement criteria for women with a low income (defined as family income of 250% of the federal poverty level) to gain access to screening and diagnostic exams for breast and cervical cancer.[4] The program currently funds 70 recipients representing health departments in all 50 states, the District of Columbia, 6 US territories, and 13 tribal organizations. Women at the age of 21 to 64 years are eligible for cervical cancer services, prioritizing those who were rarely or never screened (ie, last cervical screening of >5 years ago). The program provides cervical cancer screening services for women at average risk on the basis of the United States Preventive Services Task Force (USPSTF) guidelines[5] and management of abnormal screening results, which are based on the ASCCP guidelines.[1] For women who are diagnosed as having precancers or cancers in the NBCCEDP, treatment is provided through the Centers for Medicare and Medicaid Services (CMS) state Medicaid program or through other means at local or state levels.

The NBCCEDP reimbursement policy evolved over time from USPSTF and ASCCP guidelines.[4] Conventional cytology was used in the NBCCEDP until 2005 when the program also began reimbursing for liquid-based cytology. The NBCCEDP began reimbursing providers for human papillomavirus (HPV) tests to triage atypical squamous cells of undetermined significance (ASC-US) cytology results in 2005 following the 2002 ASCCP consensus guidelines.[6] However, HPV test data were not systematically reported to the CDC until the NBCCEDP data collection was expanded in 2009. Screening with both HPV and cytology (cotesting) was reimbursed and collected as part of the program policy starting in late 2012 following the USPSTF guidelines recommendation update. The program began reimbursing for primary HPV testing in 2019. The program reimbursement rate is based on CMS Medicare fee schedules and American Medical Association current procedural terminology codes.[7]

We estimated the immediate (prevalent at the time of the first visit) risk for diagnosing CIN3+ among women in the CDC's NBCCEDP. We further examined the differences in risk estimates by screening history, age, and race or ethnicity. These risks were compared with risks estimated in the KPNC population to determine whether the 2019 risk-based management guidelines could be applied to underinsured and uninsured women of low income in the United States.

Materials and Methods

Since the NBCCEDP's inception in 1991, the CDC has collected a set of standardized data items called minimum data elements for each service provided by the program. Local providers collect and maintain data on screening, diagnosis, and treatment offered to women. These data are reported to the funded recipients, who then report the data to the CDC as a standardized record on every screening provided. The CDC uses these data to ensure that high-quality screening, diagnostic follow-up, and treatment services are provided. Demographic characteristics and previous history of screening are collected at enrollment. Providers report dates and results of screening tests and any diagnostic procedures, outcomes, and the date of treatment initiation, if applicable. This study used data reported during January 2009 to December 2017 from 50 states, the District of Columbia, 12 tribal organizations, and 5 United States territories. This study was approved by CDC's Institutional Review Board.

We identified women aged 30 to 64 years in the program and eligible for screening, who had an HPV test from January 1, 2009, to December 31, 2017. Until 2019, data were not specifically collected to differentiate among HPV results originating from cotesting or from HPV triage of ASC-US results. Women were excluded from the analysis if they had received a diagnosis for CIN2+ or a hysterectomy before the first HPV-based test.

For women receiving screening services, screening history is determined initially during the patient intake process into the NBCCEDP by either self-report or physician reporting and subsequently updated by using the program's database. The exact wording on the patient intake forms varies from program to program, but generally asks the woman if she has ever been screened for cervical cancer and, if so, what type and when was her last screening test. In this analysis, we stratified women into those who reported being up-to-date with their cervical cancer screening (ie, screened during the past 5 years) and those who were rarely or never screened (ie, not having a screening test during the past 5 years or never having been screened). Of note, our definition of up-to-date screening was screening within the past 5 years rather than strictly adhering to the 3-year retesting interval recommended by current guidelines after a negative cytology result.[5] This allows including as up-to-date individuals who are retested late owing to scheduling difficulties rather than grouping them with women who had previously never been screened. We presented the rarely or never screened category both separately and combined with women having an unknown screening history.

Cytology test results were classified according to the Bethesda terminology as follows: negative for intraepithelial lesion or malignancy (NILM); ASC-US; low-grade squamous intraepithelial lesion (LSIL); atypical glandular cells (AGC); atypical squamous cells, cannot exclude high-grade lesion (ASC-H); high-grade squamous intraepithelial lesion (HSIL); and squamous cell carcinoma (SCC). The designation HSIL+ is used to refer to HSIL and SCC together. Cytology results of ASC-H, AGC, and HSIL+ are also referred to as high-grade cytology. HPV results were classified as positive or negative for any of the 13 high-risk HPV types (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 68). The program did not record the type of HPV test used. Histopathology results were classified in order of severity as normal; CIN grades 1, 2, or 3; or cancer.

Risk assessment

In the NBCCEDP, immediate (prevalent at the initial visit) risks for CIN2+, CIN3+, and cancer were estimated among women and stratified by screening history (screened within 5 years, rarely or never screened, or unknown screening history) and for each combination of cytology (unsatisfactory results were excluded) and HPV results. We further examined differences in absolute risk by age (30–44 and 45–64 years) and race or ethnicity.

In our risk estimates, we use the same definitions and statistical methods used to develop risk estimates for the ASCCP guidelines.[3] These methods and definitions account for differential follow-up with colposcopy or retesting by test results because of disease management recommendations. In brief, we defined precancer or cancer as prevalent at the time of the initial visit if it was detected after a colposcopy referral. We defined incident precancer or cancer as occurring after the initial visit; the exact time of the onset of incident precancer or cancer is known only to occur (eg, interval-censored using statistical terminology) between the last disease-free visit and the time of the precancer or cancer diagnosis. Finally, women without precancer or cancer diagnoses were considered right censored at the time of their last disease-free visit. Women were considered to be CIN2+ and CIN3+ outcome free at a visit only if they had a normal and CIN1 result in colposcopy, a negative cotest, or an HPV-negative with ASC-US follow-up test result. To avoid verification bias (ie, by assuming CIN2+ or CIN3+ outcome free) from positive test results (eg, HPV positive, LSIL, or greater cytology) that were missing colposcopy results, women were considered to have missing disease status at that time. Women whose disease status was never confirmed (eg, positive test results at the initial visit who never underwent colposcopy and never had a subsequent negative cotest or HPV-negative with ASC-US follow-up test result) were considered uninformative for risk estimation.

Prevalence-incidence mixture models were used to estimate risks.[8] These joint models combine a logistic regression model for prevalent disease and a proportional hazard model for interval-censored incident disease, accounting for missing prevalent disease status among those women with positive results at the initial visit who did not undergo immediate colposcopy. The models were stratified by hybrid capture 2 positivity because of nonproportionality of the hazards; cytology results followed the proportionality of hazards. Because most of the women in the cohort only contributed 1 screening cycle to the data, we present only the stable immediate risk estimates and not the incident or cumulative risk estimates. SAS software version 9 (SAS Institute, Cary, NC) was used for data cleaning and processing; R software (The R Foundation, Vienna, Austria) was used for all statistical analyses.

Results

A total of 363,546 women who are at the age of 30-64 years in the NBCCEDP had at least 1 HPV and cytology test since 2009 (Table 1). Most women (75%) were at the age of 40 to 59 years, which is well within the recommended age range for cervical cancer screening.[4] The NBCCEDP population was racially and ethnically diverse with 40.2% Hispanic, 34.7% non-Hispanic White, 13.1% non-Hispanic Black, 5.7% Asian or Pacific Islander, and 4.5% American Indian or Alaskan Native. A large proportion of these women (31.1%) had not

been screened during the past 5 years or had never been screened (unknown history, 11.5%). Results from the initial screening test indicated 13.5% of women were HPV positive; 80.4% of cytology results were normal (7.0% HPV+) followed by 15.8 % ASC-US (33.1% HPV+), 2.4% LSIL (72.4% HPV+), and approximately 0.5% each of ASC-H (66.5% HPV+), HSIL (89.4% HPV+), and AGC (29.7% HPV+). Because our analysis population consists of women with at least 1 HPV and cytology test, without differentiating among the modes of screening (eg, primary cytology with HPV triage vs HPV and cytology cotesting), the proportion of women with ASC-US was higher than would normally be expected in settings conducting cotesting because of the inclusion of women undergoing triage of primary ASC-US cytology.

The distributions of HPV and cytology testing results stratified by screening history are presented in Table 2. For each combination of test result, we reported the number of women who were diagnosed as having CIN2+, CIN3+, or cancer. Compared with women who were up-to-date with screening, women who were rarely or never screened were more likely to have high-grade cytology (1.6% vs 1.2%; $P<.001$), which accounted for 56% of CIN3+ detected in rarely or never screened women compared with 40% of CIN3+ detected in women who were up-to-date with screening. There were slight differences in the proportion that were HPV-positive women (13.0% vs 13.6%). The level of follow-up with colposcopy or retesting differed by test results because of disease management recommendations, but it did not differ by screening history. Most of the women in the cohort were screened only once within the NBCCEDP. Most of those with abnormal results of HPV-positive ASC-US or higher received a colposcopy follow-up, allowing risk estimation of the immediate CIN3+ risks of these results. Women whose test results had a recommended management of a 1-year retesting had lower follow-up with colposcopy or retesting within the program (approximately 50% for HPV negative with LSIL cytology; approximately 25% for HPV positive with normal cytology), although numbers were sufficient for risk estimation. Few women with a combination of test results that recommended retesting in 3 or 5 years (ASC-US/HPV− or NILM/HPV−) returned to the program for their next screening exam, so risk was not presented for these categories.

The immediate CIN3+ risks among NBCCEDP women are stratified by screening history and presented in Table 3. For nearly every combination of HPV and cytology test result, the immediate risk of CIN3+ was higher among women who were rarely or never screened or whose screening history was unknown than among women screened during the past 5 years. Risks were further stratified by age and race or ethnicity and are presented in Supplemental Table 1 and Supplemental Table 2, respectively. Among women with HPV-positive results, older age was associated with lower risk among women screened during the past 5 years (odds ratio [OR], 0.79; 95% confidence interval [CI], 0.69–0.89) but not significantly among women who were rarely or never screened or with unknown screening (OR, 1.09; 95% CI, 0.95–1.24). When stratified by test results and screening history, the risk of CIN3+ did not differ by race or ethnicity. For example, the prevalent risks of HPV-positive and ASC-US results were between 4.4% and 4.7% for non-Hispanic whites, non-Hispanic blacks, and Hispanics who were up-to-date with screening and increased to 5.6% to 7.5% among women who were rarely or never screened. Risk estimates for CIN2+ and cancer are reported in Supplemental Table 3 and Supplemental Table 4, respectively.

Data comparing the risks estimated in KPNC[9] with those in the NBCCEDP are presented in Table 3 and the Figure. Risks estimated among women in the KPNC population were similar to those among women in the NBCCEDP who were screened within the past 5 years but were significantly lower (*P*<.001 for most results) than risks among women in the NBCCEDP who were rarely or never screened or whose screening history was unknown.

Comment

Principal findings

The immediate risk of CIN3+ in underserved women in the NBCCEDP are similar to that of women from KPNC, provided that they are up-to-date on their cervical screening. Women who were rarely or never screened had elevated immediate risks of CIN3+ compared with women who were screened during the past 5 years. The 2019 ASCCP risk-based management consensus guidelines incorporate these data and recommend a different management for women who are not up-to-date with screening. In particular, expedited excisional treatment (ie, proceeding directly to treatment without requiring colposcopic biopsy) is preferred for underscreened women with results of HPV-positive HSIL. This more aggressive management is recommended because the immediate risk of CIN3+ is 64.5%, which exceeds the expedited treatment threshold of 60%. The risk of CIN3+ did not differ by race or ethnicity after accounting for screening history.

Results

The development of risk-based management guidelines for cervical cancer has relied on, as the underlying base population, women from a large integrated health delivery system at KPNC. The KPNC cervical screening program has a uniquely large number of participants (approximately 1.5 million participants) and long-term experience (15 years) with HPV-based screening, permitting precise estimation of precancer risk even for many unusual screening results.[3] However, such a population may not be representative of underinsured and uninsured women of low income. In this study, we report the immediate risks of CIN3+, stratified by HPV and cytology results, in the NBCCEDP, which serves women of low income without continuous insurance coverage.

Clinical implications

Risks among women in the CDC's NBCCEDP screened during the past 5 years were similar to those among women at KPNC, supporting evidence for the applicability of the 2019 ASCCP risk-based management consensus guidelines to diverse settings in the United States.[2,3] Further analysis determined that the increased CIN3+ risk found among rarely or never screened women was not large enough to warrant recommendation of different management guidelines for these women. The exception is for the small but important percentage of rarely or never screened women who had a positive result for HPV with HSIL or SCC cytology results. Citing these results, the 2019 ASCCP guidelines recommend these women undergo expedited treatment because of their uniquely high risk, which exceeds the 60% immediate CIN3+ risk threshold for expedited treatment set by the new guidelines.[2]

The exceptional racial or ethnic diversity of the NBCCEDP allowed for a thorough examination of immediate CIN3+ risks by race and ethnicity. Our analysis found that once stratified by screening history and current test results, risks did not differ by race or ethnicity and should not be a consideration for clinical management. However, the proportions of never or rarely screened differed by race or ethnicity, indicating that risks without adjustment for screening histories could differ.

Research implications

Although our study was able to look at immediate risks, it will be important to conduct long-term follow-up among underserved women to investigate whether women who were rarely or never screened have increased risks in subsequent testing rounds or in postcolposcopy or posttreatment surveillance.

Strengths and limitations

The NBCCEDP is one of the few national programs for underserved women that collects information on cervical cancer screening. In addition, programmatic data were used to inform clinical management guidelines for cervical cancer.

Because the NBCCEDP was not constructed for research purposes, some information on results, such as whether women were undergoing cotesting vs HPV triage for ASC-US cytology, was not collected. As such, we could not infer the distribution of test results under a cotesting scenario.

In this analysis, we were not able to present the risk of the most common low-grade abnormalities, such as HPV-negative results with NILM or ASC-US cytology, because there was insufficient follow-up to estimate the 5-year risk among this cohort of women. Considering the increased risk among women who were never or rarely screened, the lack of follow-up visits among women in the study may need to be further investigated. It is very likely that the follow-up could have been done outside of the program, even with the same provider, yet were not captured in these data. Follow-up of abnormal results remains a current and future focus of the program to ensure that underinsured and uninsured women receive adequate screening and management.

Conclusions

The results from this study indicate that new cervical risk–based management guidelines can be applied to underinsured and uninsured women of low income in the United States who are up-to-date with their screening. These results also highlight the need for clinicians to collect screening history to help ensure that women who are not up-to-date with their screening can receive management appropriate to their increased risks.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Acknowledgments

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AJOG at a Glance

Why was this study conducted?

New risk-based management guidelines for cervical cancer are primarily based on data from a large integrated healthcare delivery system. This study presents the risk from underserved women with a low income in the United States and assess the applicability of the guidelines to such populations.

Key findings

Screening test results in underserved women who were up-to-date with screening imply the same risk as women from a large integrated healthcare delivery system. Not being screened in the past 5 years implies a greater risk for the same test result.

What does this add to what is known?

New management guidelines are largely applicable to underserved populations, but women with human papillomavirus–positive high-grade squamous intraepithelial lesion and who were not screened in the past 5 years should undergo expedited treatment.

A

B
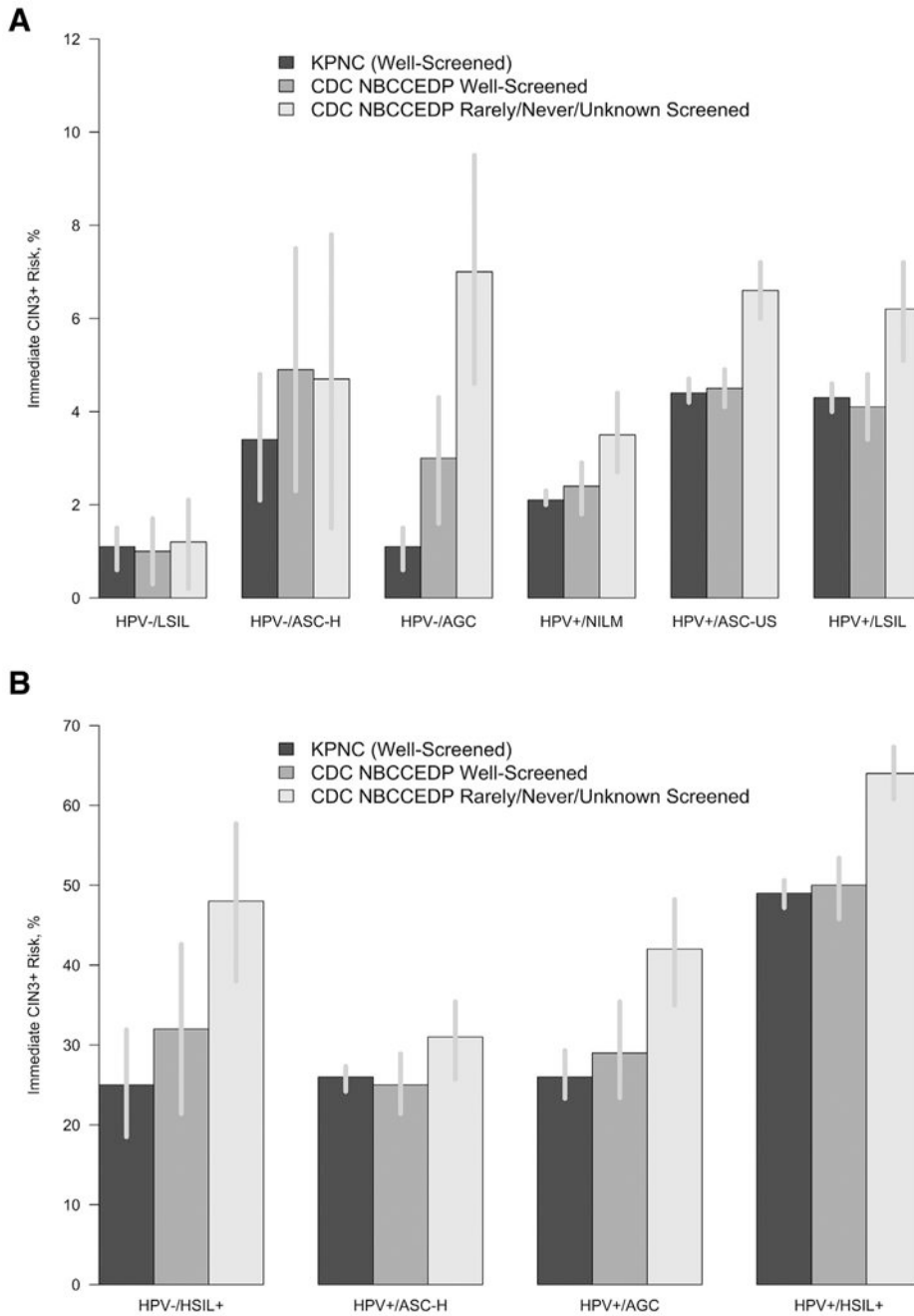
FIGURE. Immediate CIN3+ risk in CDC vs. KPNC by (A) low-risk and (B) high-risk categories
Immediate risk of CIN3 is the percentage of risk of having prevalent CIN3+ at the initial visit.

AGC, atypical glandular cells; *ASC-H,* atypical squamous cells where HSIL cannot be excluded; *ASC-US*, atypical squamous cells of uncertain significance; *CDC*, Centers for Disease Control and Prevention; *CIN3+*, cervical intraepithelial lesion grade 3 or higher; *HPV*, human papillomavirus; *HSIL*, high-grade squamous intraepithelial lesions; *KPNC*, Kaiser Permanente Northern California; *LSIL*, low-grade squamous intraepithelial lesions;

NBCCEDP, National Breast and Cervical Cancer Early Detection Program; *NILM*, negative for intraepithelial lesion or malignancy.

TABLE 1

Demographic characteristics of women in the CDC's NBCCEDP cohort, 2009 to 2017

	n	%
Total	363,546	~
Age, y		
30–39	52,746	14.5
40–49	146,340	40.3
50–59	129,224	35.6
60–64	35,236	9.7
Race and ethnicity		
Non-Hispanic White	125,990	34.7
Non-Hispanic Black	47,482	13.1
Hispanic	146,073	40.2
Asian or Pacific Islander	20,788	5.7
American Indian/Alaskan Native	16,432	4.5
Multiracial	2407	0.7
Unknown	4374	1.2
Screening status		
Screened within 5 y	208,658	57.4
Never or rarely screened	113,126	31.1
Unknown screening history	41,762	11.5
HPV result		
Positive	48,979	13.5
Negative	314,567	86.5
Cytology by HPV result		
NILM	292,296	80.4
HPV negative	271,862	93
HPV positive	20,434	7
ASC-US	57,356	15.8
HPV negative	38,382	66.9

	n	%
HPV positive	18,974	33.1
LSIL	8883	2.4
HPV negative	2455	27.6
HPV positive	6428	72.4
ASC-H	1479	0.4
HPV negative	496	33.5
HPV positive	983	66.5
HSIL+	1863	0.5
HPV negative	198	10.6
HPV positive	1665	89.4
AGC	1667	0.5
HPV negative	1172	70.3
HPV positive	495	29.7
Unsatisfactory	2	0
HPV negative	2	100
HPV positive	0	0

AGC, atypical glandular cell; *ASC-H*, atypical squamous cells; *ASC-US*, atypical squamous cells of uncertain significance; *CDC*, Centers for Disease Control and Prevention; *HPV*, human papillomavirus; *HSIL*, high-grade squamous intraepithelial lesion; cannot exclude HSIL; *LSIL*, low-grade squamous intraepithelial lesion; *NBCCEDP*, National Breast and Cervical Cancer Early Detection Program; *NILM*, negative for intraepithelial lesion or malignancy.

TABLE 2

Distribution of HPV and cytology results of the CDC's NBCCEDP cohort from 2009 to 2017

Test results								Follow-up time, mo		% with colposcopy or follow-up
HPV	Cytology	N	%	CIN2+	CIN3+	Cancer		Median	IQR	
Screened in the past 5 y										
Total		208,656	100.0	2873	1495	236		25	14–42	
HPV Positive	NILM	11,315	5.4	196	115	7		16	13–27	31
	ASC-US	11,754	5.6	1215	545	22		18	13–33	87
	LSIL	3728	1.8	410	159	6		18	13–30	85
	ASC-H	567	0.3	200	138	10		16	12–27	92
	AGC	244	0.1	92	69	15		17	14–29	91
	HSIL+	747	0.4	486	337	37		15	12–26	89
HPV Negative	NILM	152,606	73.1	44	19	4		34	17–50	
	ASC-US	25,186	12.1	104	45	7		26	14–46	57
	LSIL	1461	0.7	31	11	0		15	13–26	90
	ASC-H	293	0.1	29	14	0		17	14–31	91
	AGC	669	0.3	33	19	12		21.5	14–38	87
	HSIL+	86	0.0	33	24	3		11	8–17	87
Rarely or never screened										
Total		113,126	100.0	1827	1124	165		22	14–38	
HPV Positive	NILM	6554	5.8	112	68	11		15	13–25	23
	ASC-US	5130	4.5	636	315	30		16	13–29	84
	LSIL	1862	1.7	215	87	1		16	13–27	81
	ASC-H	293	0.3	121	88	15		14	10–19	85
	AGC	175	0.2	80	67	20		16	10–32	85
	HSIL+	667	0.6	504	402	58		17	13–27	91
HPV Negative	NILM	87,187	77.1	19	13	6		29	16–43.25	
	ASC-US	9926	8.8	31	10	2		27	14–45	
	LSIL	701	0.6	14	3	0		15	13–23	51
	ASC-H	160	0.1	16	7	2		16.5	13–33.25	86

Test results

HPV	Cytology	N	%	CIN2+	CIN3+	Cancer	Follow-up time, mo		% with colposcopy or follow-up
							Median	IQR	
	AGC	386	0.3	31	25	17	15	13–25.75	85
	HSIL+	85	0.1	48	39	3	14	10–26	89
Unknown screening history									
Total		41,762	100.0	721	414	71	28	15–47	
HPV Positive	NILM	2565	6.1	42	21	4	15	13–27	24
	ASC-US	2090	5.0	276	126	15	19	13–30	83
	LSIL	838	2.0	109	59	9	17	13–28	77
	ASC-H	123	0.3	40	23	3	34	19.75–39	79
	AGC	76	0.2	28	22	7	31	13.5–49.75	87
	HSIL+	251	0.6	183	136	22	22	14–36	89
HPV Negative	NILM	32,069	76.8	2	2	1	37	21–58	
	ASC-US	3270	7.8	9	5	2	27	14–47	
	LSIL	293	0.7	9	3	2	15	13–19.5	52
	ASC-H	43	0.1	1	1	0	16	13–6	79
	AGC	117	0.3	7	5	5	17	13–25	84
	HSIL+	27	0.1	15	11	1	13.5	13–20.75	85

AGC, atypical glandular cell; *ASC-H*, atypical squamous cells–cannot exclude HSIL; *ASC-US*, atypical squamous cells of uncertain significance; *CDC*, Centers for Disease Control and Prevention; *CIN2+*, cervical intraepiethial neoplasia grade II or greater; *CIN3*, cervical intraepiethial neoplasia grade III or greater; *HPV*, human papillomavirus; *HSIL*, high-grade squamous intraepithelial lesion; *IQR*, interquartile range; *LSIL*, low-grade squamous intraepithelial lesion; *NBCCEDP*, National Breast and Cervical Cancer Early Detection Program; *NILM*, negative for intraepithelial lesion or malignancy.

TABLE 3

Immediate CIN3+ risk after the first screening with HPV, CDC's NBCCEDP[a] vs KPNC[b]

| Testing results | | CDC's NBCCEDP[a] | | | | | | | | KPNC[b] | |
| | | Screened within the past 5 y | | Rarely, never, or unknown screening (combined) | | Rarely or never screened | | Unknown screening | | | |
HPV	Cytology	Immediate CIN3+ risk (%)	95% CI (%)	Immediate CIN3+ risk (%)	95% CI (%)	Immediate CIN3+ risk (%)	95% CI (%)	Immediate CIN3+ risk (%)	95% CI (%)	Immediate CIN3+ risk (%)	95% CI (%)
Positive	HSIL+	49.6	(45.8–53.4)	64.1	(60.8–67.3)	65.4	(61.6–69.2)	60.4	(54.1–66.8)	48.9	(47.2–50.6)
	AGC	29.4	(23.4–35.4)	41.6	(35.0–48.2)	45.3	(37.3–53.3)	33.3	(22.0–44.7)	26.3	(23.3–29.3)
	ASC-H	25.2	(21.4–28.9)	30.6	(25.7–35.4)	33.8	(28.0–39.7)	22.2	(13.9–30.5)	25.7	(24.2–27.3)
	LSIL	4.1	(3.4–4.8)	6.2	(5.1–7.2)	5.2	(4.1–6.3)	8.4	(6.3–10.6)	4.3	(4.0–4.6)
	ASC-US	4.5	(4.1–4.9)	6.6	(6.0–7.2)	6.7	(5.9–7.4)	6.5	(5.4–7.7)	4.4	(4.2–4.7)
	NILM	2.4	(1.8–2.9)	3.5	(2.7–4.4)	3.6	(2.5–4.6)	3.3	(1.9–4.7)	2.1	(2.0–2.3)
Negative	HSIL+	32.0	(21.4–42.6)	47.8	(38.0–57.7)	50.0	(38.8–61.2)	41.0	(21.0–60.9)	25.2	(18.5–31.9)
	AGC	3.0	(1.6–4.3)	7.0	(4.6–9.5)	7.6	(4.8–10.5)	5.1	(0.8–9.5)	1.1	(0.6–1.5)
	ASC-H	4.9	(2.3–7.5)	4.7	(1.5–7.8)	5.1	(1.4–8.8)	2.9	(0.0–8.6)	3.4	(2.1–4.8)
	LSIL	1.0	(0.3–1.7)	1.2	(0.2–2.1)	0.8	(0.0–1.8)	2.0	(0.0–4.2)	1.1	(0.6–1.5)
	ASC-US	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	0.0	(0.0–0.1)
	NILM	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	0.0	(0.0–0.0)

AGC, atypical glandular cell; *ASC-H*, atypical squamous cells-cannot exclude; *ASC-US*, atypical squamous cells of uncertain significance; *CDC*, Centers for Disease Control and Prevention; *CI*, confidence interval; *CIN3*, cervical intraepiethial neoplasia grade III or greater; *HSIL*, high-grade squamous intraepithelial lesion; *HPV*, human papillomavirus; *LSIL*, low-grade squamous intraepithelial lesion; *KPNC*, Kaiser Permanente Northern California; *LSIL*, low-grade squamous intraepithelial lesion; *N/A*, not available; *NBCCEDP*, National Breast and Cervical Cancer Early Detection Program; *NILM*, negative for intraepithelial lesion or malignancy.

[a] CDC population is at the age of 30 to 64 years who have an HPV test result, which includes primary Papanicolaou test results of ASC-US triaged by HPV

[b] KPNC population is at the age of 25 to 65 years who underwent HPV cotesting. Risk estimates are from Egemen et al.[9]