State-level progress in reducing cervical cancer incidence among US young women between the pre- and post-human papillomavirus vaccination eras

Chenxi Jiang, MPH[1]; Philip S. Rosenberg, PhD[2]; Jessica Star, MA, MPH[1]; Priti Bandi, PhD[1]; Robert A. Bednarczyk, PhD[3,4]; Ahmedin Jemal, DVM, PhD[1]; Hyuna Sung, PhD[1]

[1]Surveillance, Prevention, & Health Services Research, American Cancer Society, Atlanta, GA, USA

[2]Biostatistics Branch, Division of Cancer Epidemiology and Genetics, Department of Health and Human Services, National Cancer Institute, NIH, Bethesda, MD, USA

[3]Hubert Department of Global Health, Rollins School of Public Health, Emory University, Atlanta, GA, USA

[4]Cancer Prevention and Control Program, Winship Cancer Institute, Emory University, Atlanta, GA, USA

Corresponding Author: Chenxi Jiang, MPH

American Cancer Society, 270 Peachtree Street, Suite 1300, Atlanta, GA 30303, US

Email: chenxi.jiang@cancer.org

Abstract word count: 249/250

Text word count:3197/3000

Table and Figure:3/8

Supplementary Material

Abstract

Background: Despite well-documented national declines in cervical cancer incidence among young women following human papillomavirus (HPV) vaccine implementation, state-level data remain limited.

Methods: Using the US Cancer Statistics Database, differences in cervical cancer incidence rates for women aged 20-31 between the pre-vaccination (2000-2005) and vaccination era (2016-2022) were estimated using rate ratios (RRs) across 47 states and the District of Columbia (DC). Associations between HPV vaccination rates from the National Immunization Survey-Teen and RRs were examined using Spearman's rank test and linear regression models, adjusted for screening rates from the Behavioral Risk Factor Surveillance System.

Results: Nationwide, cervical cancer incidence rates declined by 27% (RR=0.73, 95%CI:0.70 to 0.75) during the vaccination era, from 5.1 to 3.7 per 100,000. Reductions exceeded 50% in DC (RR=0.48, 95%CI:0.15 to 0.81), Rhode Island (RR=0.48, 95%CI:0.21 to 0.76), Michigan (RR=0.48, 95%CI:0.38 to 0.57), and Hawaii (RR=0.49, 95%CI:0.21 to 0.78), with 28 additional states achieving statistically significant reductions of 15-50%. Ten states showed slower decreases (<15%). Notably, progress was lacking in Vermont (RR=1.11; 95%CI:0.21 to 2.00), West Virginia (RR=1.09; 95%CI:0.63 to 1.56), Idaho (RR=0.97; 95%CI:0.42-1.52), Arkansas (RR=0.96; 95%CI:0.64 to 1.29), and Alabama (RR=0.96; 95%CI:0.71 to 1.21). Across states, higher vaccination rates were correlated with lower RRs (i.e., faster decline) (*rho*=-0.42, *P*=0.0027). Every 10% increase in vaccination rates was associated with an 11.5% (95%CI:-17.2% to -5.4%) reduction in RRs, adjusted for screening rates.

Conclusions: Declines in cervical cancer incidence in young women during the HPV vaccination era varied substantially by state, aligning with HPV vaccination rates.

Introduction

Cervical cancer incidence rates in the United States dropped by over 50% since its peak in the 1970s, mainly owing to the widespread uptake of cervical cancer screening. Yet, cervical cancer remains a significant public health concern with an estimated 13,360 new cases and 4,320 deaths each year.[1, 2] To further advance progress, the Advisory Committee on Immunization Practices (ACIP) recommended a three-dose routine human papillomavirus (HPV) vaccination at ages 11-12 years (may commence at age 9) for women through age 26 in 2006, extended to men in 2011, updated to a two-dose schedule in 2016, and introduced shared clinical decision making for women aged 27-45.[3] In 2024, the national HPV vaccination initiation and up-to-date rates among girls were 79.1% and 64.3%, increasing from 17.3% and 13.5% in 2008, respectively.[4, 5]

Consistent with the anticipated vaccination impact, population-based studies have demonstrated declines in infection prevalence of quadrivalent HPV vaccine types and pre-invasive cervical lesions,[6, 7] followed by reductions in invasive cancer incidence and mortality. Between 2001-2006 and 2010-2017, incidence rates dropped by 29-38% in women aged 15-24 and by 13-16% in those aged 25-34 [8, 9], accompanied by a 62% reduction in mortality rates among women under age 25 from 2013-2015 to 2019-2021.[10] However, progress has been assessed primarily at the national level, and the extent of state-level variation remains unclear despite differences in HPV vaccination coverage, screening participation, and health policies affecting access to these preventive services. Using nationwide high-quality population-based data, this study measured the state-level progress in reducing cervical cancer incidence among women aged 20-31 years during the HPV vaccination era.

Methods

Data Sources

State-level cancer incidence data were extracted from the United States Cancer Statistics (USCS) Incidence Analytic Database[11] for women diagnosed with invasive cervical cancer (International Classification of Diseases for Oncology, 3rd edition, C530-C539, excluding histology 9050-9055 [mesotheliomas], 9140 [Kaposi sarcoma], 9590-9993 [hematopoietic and lymphoid neoplasms])[12] from 2000-2021 across 47 states and the District of Columbia (DC). Indiana, Mississippi, and South Dakota were excluded for data quality concerns (Supplementary Methods).[13] Considering the 2006 recommended HPV vaccination age range (9-26 years) and reports on rising cervical cancer incidence among women over 30 years,[14, 15] we restricted analyses to women aged 20-31.

State-level HPV vaccination rates from 2008-2022 were obtained from the National Immunization Survey-Teen (NIS-Teen),[16] a nationally representative survey that collects vaccination data in adolescents aged 13-17 across all U.S. states and territories through telephone interview and follow-up mailed questionnaire for provider verification. Given multiple lines of evidence demonstrating the efficacy and durability of a single-dose regimen,[17-22] we used vaccination rate data for girls who received at least one dose. Cervical cancer screening rates (received cytology-based screening in the past 3 years) were obtained from the Behavioral Risk Factor Surveillance System. The study used de-identified publicly available data, which is considered non-human participants research under the Common Rule (US federal regulation 45 CFR §46); thus, institutional review board approval and informed consent were not needed.

Statistical Analysis

We first visualized trends in age-standardized incidence rates (2000 US standard population) of cervical cancer per 100,000 woman-years from 2000 to 2021 and HPV vaccination rates from 2008 to 2022, nationwide and by state. To smooth year-to-year fluctuations in incidence and HPV vaccination rates, we applied a three-year moving average with Epanechnikov kernel function weights, assigning the greatest weight to the central year and progressively less to adjacent years.[23]

To compare cervical cancer incidence before and after the implementation of HPV vaccination in 2006,[24] we defined 2000-2005 as the pre-vaccination period and designated the most recent six years, 2016-2021, as the vaccination period to capture the latest effect of vaccination. Women diagnosed with cervical cancer from 2016-2021 at ages 20-31 represent individuals who were between ages 5-21 in 2006. We quantified the difference in incidence rates between the two periods in both absolute and relative terms by computing the rate difference (RD) and rate ratio (RR), with corresponding 95% confidence intervals (CIs) calculated using the Delta method.[25] To account for variation in cervical cancer screening rates across states, we adjusted the population denominator by multiplying it by state- and year-specific screening prevalence among women aged 20-31. Incidence rates derived from this adjusted denominator were then used to estimate adjusted RRs and RDs (Supplementary Method).[26]

Ecological associations between smoothed HPV vaccination rates and changes in cancer incidence rates across states (RRs or adjusted RRs) were evaluated using Spearman's rank correlation test, performed for each year from 2008-2015. Similarly, correlations between screening rates (2000-2020) and RRs were evaluated. Additionally, we fitted a linear regression model with log (RR) as the outcome and smoothed HPV vaccination rates as an explanatory variable, with or without adjustment for screening rates. We used SEER*Stat 8.4.3 (National Cancer Institute) to tabulate incidence rates. Statistical analyses were conducted using SAS SUDAAN 9.4 and MATLAB R2025a. A two-sided $P<0.05$ was considered statistically significant.

Results

A total of 22,868 women aged 20-31 years were diagnosed with cervical cancer from 2000-2021, with case counts ranging from 37 in Vermont to 2,677 in California (Table S1). **Figure 1** illustrates trends in cervical cancer incidence rates from 2000-2021 and HPV vaccination rates from 2008-2022, nationwide and by state. Between 2000 and 2021, cervical cancer incidence rates decreased nationally and in most states. However, they remained relatively stable in certain states, including Alabama, Arkansas, Idaho, New Mexico, Vermont, and West Virginia. HPV vaccination rates consistently increased nationwide from 41% in 2008 to 78% in 2022, with state-level rates in 2022 varying from 67% in Wyoming to 92% in Rhode Island.

Figure 2 depicts changes in the cervical cancer incidence rates between 2000-2005 (pre-vaccination era) and 2016-2021 (vaccination era) (case counts, rates, and 95% CIs in Table S2). Nationwide, the incidence rate per 100,000 declined from 5.1 in 2000-2005 to 3.7 in 2016-2021(RD=-1.39; 95%CI:-1.54 to -1.23), reflecting a 27% decrease (RR=0.73; 95%CI:0.70 to 0.75). Across 47 states and DC, the largest absolute declines per 100,000 were observed in Rhode Island (RD=-3.55 ; 95%CI:-6.34 to -0.75), Michigan (RD=-3.41; 95%CI:-4.3 to -2.51), and Louisiana (RD=-3.21; 95%CI:-4.56 to -1.85). The largest, statistically significant relative declines of more than 50% were seen in DC (RR=0.48; 95%CI:0.15 to 0.81), Rhode Island (RR=0.48; 95%CI:0.21 to 0.76), Michigan (RR=0.48; 95%CI:0.38 to 0.57), and Hawaii (RR=0.49; 95%CI:0.21 to 0.78). An additional 28 states achieved significant reductions of 15% to 50%, including the top 10 most populous states. Meanwhile,10 states exhibited smaller changes in trends (<15%). In particular, RRs were relatively higher in Vermont (RR=1.11; 95%CI:0.21 to 2.00), West Virginia (RR=1.09; 95%CI:0.63 to 1.56), Idaho (RR=0.97; 95%CI:0.42 to 1.52), Arkansas (RR=0.96; 95%CI:0.64 to 1.29), and Alabama (RR=0.96; 95%CI:0.71 to 1.21), indicating a lack of progress.

Figure 3 depicts the correlation between cervical cancer incidence rate reduction, represented by RRs, and HPV vaccination rates in 2010, the year with the greatest correlation coefficient (*rho*=-0.42, *P*=0.0027; Table S3 for all years). Using adjusted RRs as the outcome yielded a similar coefficient (*rho*=-0.40, *P*=0.0048). For the corresponding year, the correlation coefficient between screening rates and RRs was -0.15 (*P*=0.3081; Figure S1), with similarly non-statistically significant coefficients estimated for most years (Table S4 for all years). Every 10% increase in HPV vaccination rate was associated with a 11.5% (95%CI:-17.2% to -5.4%) reduction in RRs across states after adjusting for screening rates (Table S5).

Discussion

Based on nationwide, high-quality, population-based cancer registry data, there was a substantial state-level variation in the progress towards reducing cervical cancer incidence in women aged 20-31 years against a backdrop of HPV vaccination. Between 2000-2005 and 2016-2021, incidence rates decreased by more than half in DC, Rhode Island, Michigan, and Hawaii, while remaining largely unchanged in Vermont, West Virginia, Idaho, Arkansas, and Alabama. The marked disparities in state-level progress highlight the pivotal role of state-specific policies, healthcare infrastructure, and social determinants of health in shaping geographically patterned progress in reducing cervical cancer among young women.

Recent modeling studies suggested that if current state variations in vaccination rates persist, the timelines for achieving the WHO's cervical cancer elimination goal (age-standardized incidence rate (all ages) <4 cases per 100,000) could differ by decades.[27, 28] Consistent with this projection, our analysis demonstrates substantial variation in progress—ranging from over 50% reduction to no improvement over the past 20 years—aligned with differences in vaccination rates. Together, these findings underscore the need for targeted policy interventions and public health initiatives, particularly in states with higher cervical cancer burden and low HPV vaccination rates, to advance equitable cancer prevention and support the goal of cervical cancer elimination.

We used HPV vaccine initiation (≥1 dose) rates to measure population-level coverage because up-to-date (completion) rates before 2016, defined as receipt of three doses under the original 2006 guideline,[29] could underestimate population-level protection, considering increasingly robust evidence on the efficacy and durability of single-dose versus multi-dose regimens.[17-22] This evidence was endorsed by the 2022 WHO HPV vaccine position paper[30] and national immunization advisory groups in multiple countries, including the UK.[31, 32] As of 2025, ACIP is reviewing a potential transition to a single-dose schedule for select age groups. Advantages of a single-dose schedule, including simplified logistics, lower costs, and improved uptake,[33] make its potential adoption a critical policy decision. Rigorous evaluation and transparent deliberation are essential to reaching this decision, particularly amid recent ACIP membership and leadership changes that have raised concerns about transparency, independence, and clinical expertise in the committee's review process.[34, 35] If a single-dose regimen is adopted, further studies will be needed to assess its long-term impact on the extent and timing of population-level reductions in cervical cancer incidence.

The substantial variation in HPV vaccination rates across states is likely influenced by a combination of factors, including state policies, the effectiveness of community-based strategies, and cultural, political, or religious circumstances unique to each state. Federally and state-supported initiatives, with active local engagement, such as the Vaccines for Children (VFC) program[36] and Medicaid expansion, played a central role in improving vaccine accessibility and affordability. The VFC program, established in 1994, provides recommended vaccines at no cost for eligible children and adolescents, including those who are American Indian or Alaska Native, Medicaid-eligible, uninsured, or underinsured across all 50 states and the DC. However, the program's reach and integration vary;[36] as of 2021, only 34 states allow pharmacies to participate in the program, and 17 of the 34 states have enrolled pharmacists as VFC providers.[37] Medicaid expansion, as a part of the Affordable Care Act, fully covers the cost of recommended immunizations without cost-sharing and resulted in a doubling of HPV vaccination initiation rates among 13-year-olds in expansion states, compared to an 88% increase in non-expansion states.[38] According to our data, DC and 20 of the 28 states (72%) that adopted Medicaid by 2016 showed significant progress in reducing cervical cancer incidence, compared to 11 of the 19 states (58%) that adopted Medicaid later or did not adopt (Table S6). Continuing to monitor, support, and expand these programs remain crucial to sustaining vaccination rate and reducing disparities across states.

Since 2006, 40 states and DC have proposed HPV vaccine-related legislation, including school-entry requirements (SER), funding administration programs, and education programs.[39, 40] Numerous barriers, such as concerns over parental autonomy, the stigma associated with vaccines against sexually transmitted infections, and the flexibility of opt-out options,[40] made the wide implementation of these policies challenging. Although almost all US jurisdictions have considered adopting a policy that requires HPV vaccination for school attendance, only DC, Hawaii, Puerto Rico, Rhode Island, and Virginia have successfully incorporated SER into law or received an administrative ruling from the health department as early as 2008.[41] Our findings of more than 50% reduction in cervical cancer incidence rates in each of these states align with the observed impact of SERs on HPV vaccination rates.[40] Virginia was an exception, showing a relatively modest reduction (24%), which may partly reflect its lenient exemption policies, permitting HPV-specific philosophical exemptions without supporting documentations.[42, 43] This pattern exemplifies the dual effect of exemption policies—although lenient rules may increase parental acceptance of SER, it also risks undermining vaccination coverage, thereby reducing the intended public health impact. Continuous surveillance of exemption rates and HPV-related disease trends can help states refine policies, ensuring exemptions do not significantly compromise herd immunity. Strengthening education campaigns to counter misinformation, incentivizing vaccination, and requiring additional counseling for those seeking exemptions could also be effective strategies for balancing public health priorities and individual autonomy.[44, 45]

Variation in vaccine hesitancy across states may also offer insight into differences in vaccination rates and, consequently, trends in cervical cancer incidence among young women.[46] A National Immunization Survey study reported an 80% nationwide increase from 2015 to 2018 in parents of unvaccinated adolescents, citing safety concerns as the primary reason for not initiating the HPV vaccine.[47] Despite extensive data from prelicensure vaccine trials and over 15 years of post-licensure surveillance through the U.S. vaccination safety monitoring system and specialized evaluations that affirm the safety of the HPV vaccine,[48] hesitancy driven by safety concerns increased across 30 states, with the fastest rises in Mississippi and South Dakota and also in California and Hawaii, where the current vaccination rates are relatively high. Given the concerning trends, targeted campaigns addressing misinformation among vaccine-hesitant parents are crucial for improving HPV vaccine uptake. Evidence has shown that provider-patient education programs incorporating culturally appropriate and religiously acceptable content can effectively reduce hesitancy and improve HPV vaccine initiation or completion rates.[49]

In shaping public perceptions and behaviors regarding vaccination, healthcare providers play a pivotal role as trusted sources of health information for patients and their children. A national survey study found that HPV vaccine initiation was nine times higher among individuals who received high-quality recommendations from healthcare providers compared with those who did not.[50] However, provider recommendations are less common in Southern than in Northeastern states.[51, 52] In 2018, Mississippi (59.5%) and Arkansas (63.5%) had the lowest provider recommendations rates, substantially lower than those in Massachusetts (90.7%) or DC (90.4%).[52] Equipping providers with training and resources to educate parents about the benefits of HPV vaccination as a key method for cancer prevention, especially in states with low recommendation rates, could help narrow the gap in vaccination rates and, in turn, mitigate the disparate progress against cervical cancer across states.

Additionally, herd immunity effects and interstate migration may partially account for state-level variations in progress that are not fully explained by HPV vaccination rates. Larger reductions in cervical cancer incidence in Washington, Louisiana, Hawaii, and Wisconsin, compared to states with similar vaccination rates, may partly reflect the herd effects, given earlier and broader uptake of HPV vaccination among girls and boys.[53] States with lower HPV vaccination rates among girls are estimated to benefit the most from improving vaccination coverage among boys,[54] highlighting opportunities to advance progress against cervical cancer. Over the past decade, southern states have gained young migrants, while northeastern states such as New York and New Jersey have experienced losses.[55] In particular, South Carolina, with consistently lower-than-national-average vaccination rates but the highest net migration per capita, may show faster progress partly due to the in-migration of vaccinated individuals.

Differences in cervical cancer screening rates across states likely also play a role in state-level variation in progress against cervical cancer.[56, 57] However, data comparing state-level screening uptake among women under 30 are limited, possibly reflecting increasing recognition of the higher harm-to-benefit ratio associated with screening and immediate invasive treatment in this age group.[58-60] This evidence prompted guidelines revisions toward more conservative screening and less intensive management: In 2012, the US Preventive Service Task Force raised the recommended initiation age to 21 years and extended the screening interval from annual to triennial testing,[61] and the American Society for Colposcopy and Cervical Pathology supported observation rather than immediate treatment for women under 25 years.[62] In 2020, the American Cancer Society further raised the initiation age to 25 years.[63] The potential impact of varying compliance with these guidelines changes on cervical cancer burden among young women remains uncertain, and residual confounding by state-level screening practices may not be fully excluded. Nevertheless, states with lower HPV vaccination coverage and persistently high cancer incidence are likely to benefit most from improving screening uptake.[28]

States exhibiting patterns unexplained by aforementioned factors or those excluded from the study warrant further investigation. In Vermont, incidence rate changed from 4.36 to 4.82 per 100,000, yielding an RR of 1.11 (95% CI=0.21 to 2.00), appearing as an outlier given its relatively high vaccination coverage. While the wide CI, reflecting small case counts, warrants cautious interpretation, this pattern may also reflect limited potential for further reduction, given the low baseline incidence and early achievement of high vaccination coverage, consistent with a modeling exercise showing smaller incremental gains in highly vaccinated states.[28] Mississippi, omitted from this study, had the nation's lowest HPV vaccination rate (58.6% in 2024) and a high cervical cancer burden,[5, 64] highlighting the need for targeted intervention and continued surveillance. Meanwhile, HPV vaccination rates among adolescents were higher in South Dakota (82.5%) and lower in Indiana (73.2%) compared with the national level (78.2%).[5]

This study has several important limitations. First, given the ecological nature of the study, the association between HPV vaccination rates and cancer incidence rates does not establish causality. Second, RDs and RRs in states with small case counts have wide CIs and should be interpreted cautiously. Combining six years of diagnoses improved data stability and comparability across states but may obscure changes detectable in yearly analyses. Third, the low household response rate in NIS-Teen may introduce selection bias if respondents differ systematically from nonrespondents. Although weighting adjustments were applied for selection probability, residual bias may persist.[65] Additionally, NIS-Teen was partly based on parental reports and is subject to recall and social desirability biases. Fourth, we used HPV vaccine initiation (≥1 dose) rates to measure population-level coverage, rather than completion of the multi-dose schedule recommended by ACIP. While a single dose has been shown to offer protection lasting up to 16 years,[21] we note that if future evidence indicates waning immunity in the longer term, a ≥1 dose measure may overestimate the true level of protection compared with full-dose vaccination. Fifth, hysterectomy correction was not applied, but given the low prevalence among young women (0.4-1.1% at ages 20-29), its impact on the results is expected to be minimal.[66, 67] Finally, state-level assessment masks intrastate disparities such as differences between urban and rural areas and across race and ethnicity subgroups, where both cancer incidence and HPV vaccination rates likely differ, underscoring the need for more granular analyses to guide more locally relevant interventions.

In conclusion, despite the national decline in cervical cancer incidence rates among young women, state-level progress has diverged sharply, ranging from more than 50% reduction to no progress between 2000-2005 and 2016-2022. The association across states suggests that the disparate progress may be attributed to differences in HPV vaccination rates, underscoring the crucial roles of state-level factors in ensuring the effective implementation of HPV vaccination programs. Without a more equitable implementation of HPV vaccination, the existing disparities may widen when cervical cancer becomes more common among these young women as they age. To ensure that all states benefit equally from a proven preventive measure, strengthening political commitment will be crucial, especially in states with slower progress in reducing disease burden and low vaccination rates.

Data Availability Statement: These data were provided by central cancer registries participating in the National Program of Cancer Registries (NPCR) and submitted to the Centers for Disease Control and Prevention (CDC) in the 2023 data submission and/or the Surveillance, Epidemiology and End Results (SEER) Program and submitted to NCI in the 2023 data

submission. The data can be obtained from CDC upon request. CDC does not endorse any one particular organization, service, or product and this publication does not necessarily represent the views and/or position of CDC.

Funding: This work was supported by the Intramural Research Department of the American Cancer Society (CJ, JS, PB, AJ, and HS) and by the Intramural Research Program of the National Cancer Institute, Division of Cancer Epidemiology and Genetics (PSR).

Conflict of interest: We declare no competing interests.

Acknowledgment: The American Cancer Society had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

References

1. Siegel RL, Kratzer TB, Giaquinto AN, *et al.* Cancer statistics, 2025. CA Cancer J Clin 2025; https://doi.org/10.3322/caac.21871.
2. Adegoke O, Kulasingam S, Virnig B. Cervical cancer trends in the United States: a 35-year population-based analysis. J Womens Health (Larchmt) 2012;21(10):1031–7.
3. Meites E, Szilagyi PG, Chesson HW, *et al.* Human Papillomavirus Vaccination for Adults: Updated Recommendations of the Advisory Committee on Immunization Practices. MMWR Morb Mortal Wkly Rep 2019;68(32):698–702.
4. Chido-Amajuoyi OG, Talluri R, Wonodi C, *et al.* Trends in HPV Vaccination Initiation and Completion Within Ages 9–12 Years: 2008–2018. Pediatrics 2021;147(6).
5. Pingali C, Yankey D, Elam-Evans LD, *et al.* Vaccination Coverage Among Adolescents Aged 13–17 Years — National Immunization Survey-Teen, United States, 2024. MMWR Morb Mortal Wkly Rep 2025 2025;74(30):466–472.
6. Silverberg MJ, Leyden WA, Lam JO, *et al.* Effectiveness of catch-up human papillomavirus vaccination on incident cervical neoplasia in a US health-care setting: a population-based case-control study. Lancet Child Adolesc Health 2018;2(10):707–714.
7. Wheeler CM, Adcock R, Hunt WC, *et al.* Human papillomavirus genotype-specific prevalence and infection risks: a 10-year population-based study from the United States. J Natl Cancer Inst 2024;117(5):924–933.

8. Guo F, Cofie LE, Berenson AB. Cervical Cancer Incidence in Young U.S. Females After Human Papillomavirus Vaccine Introduction. Am J Prev Med 2018;55(2):197–204.
9. Tabibi T, Barnes JM, Shah A*, et al.* Human Papillomavirus Vaccination and Trends in Cervical Cancer Incidence and Mortality in the US. JAMA Pediatr 2022;176(3):313–316.
10. Dorali P, Damgacioglu H, Clarke MA*, et al.* Cervical Cancer Mortality Among US Women Younger Than 25 Years, 1992-2021. JAMA 2024; 10.1001/jama.2024.22169.
11. National Program of Cancer Registries and Surveillance, Epidemiology, and End Results Program SEER*Stat Database: US Cancer Statistics Incidence Analytic Database with single ages - 1998-2021. United States Department of Health and Human Services, Centers for Disease Control and Prevention. In. Released June 2024, based on the 2023 submission ed: United States Department of Health and Human Services, Centers for Disease Control and Prevention; 2024.
12. *Site Recode ICD-O-3/WHO 2008 Definition*. https://seer.cancer.gov/siterecode/icdo3_dwhoheme/index.html.
13. *Registries That Met U.S. Cancer Statistics Publication Criteria*. https://www.cdc.gov/united-states-cancer-statistics/technical-notes/publication-criteria.html.
14. Suk R, Hong Y-R, Rajan SS*, et al.* Assessment of US Preventive Services Task Force Guideline–Concordant Cervical Cancer Screening Rates and Reasons for Underscreening by Age, Race and Ethnicity, Sexual Orientation, Rurality, and Insurance, 2005 to 2019. JAMA Network Open 2022;5(1):e2143582–e2143582.
15. Watson M, Benard V, Flagg EW. Assessment of trends in cervical cancer screening rates using healthcare claims data: United States, 2003-2014. Prev Med Rep 2018;9:124–130.
16. Center for Disease Control and Prevention. *National Immunization Survey*.
17. Basu P, Malvi SG, Joshi S*, et al.* Vaccine efficacy against persistent human papillomavirus (HPV) 16/18 infection at 10 years after one, two, and three doses of quadrivalent HPV vaccine in girls in India: a multicentre, prospective, cohort study. The Lancet Oncology 2021;22(11):1518–1529.
18. Baisley KJ, Whitworth HS, Changalucha J*, et al.* A dose-reduction HPV vaccine immunobridging trial of two HPV vaccines among adolescent girls in Tanzania (the DoRIS trial) - Study protocol for a randomised controlled trial. Contemp Clin Trials 2021;101:106266.
19. Bénard É, Drolet M, Laprise J-F*, et al.* Potential population-level effectiveness of one-dose HPV vaccination in low-income and middle-income countries: a mathematical modelling analysis. The Lancet Public Health 2023;8(10):e788–e799.
20. Barnabas RV, Brown ER, Onono MA*, et al.* Efficacy of Single-Dose Human Papillomavirus Vaccination among Young African Women. NEJM Evidence 2022;1(5):EVIDoa2100056.
21. Porras C, Romero B, Kemp T*, et al.* HPV16/18 antibodies 16-years after single dose of bivalent HPV vaccination: Costa Rica HPV vaccine trial. JNCI Monographs 2024;2024(67):329–336.
22. Kreimer AR, Porras C, Liu D*, et al.* Noninferiority of One HPV Vaccine Dose to Two Doses. New England Journal of Medicine 2025;393(24):2421–2433.

23. Epanechnikov VA. Non-Parametric Estimation of a Multivariate Probability Density. Theory of Probability & Its Applications 1969;14(1):153–158.
24. Markowitz LE, Dunne EF, Saraiya M*, et al.* Human papillomavirus vaccination: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep 2014;63(RR-05):1–30.
25. MathWorks. *Delta-method & parametric bootstrap in nonlinear regression*. https://www.mathworks.com/matlabcentral/fileexchange/158541-delta-method-parametric-bootstrap-in-nonlinear-regression.
26. Gargano JW, Stefanos R, Dahl RM*, et al.* Trends in Cervical Precancers Identified Through Population-Based Surveillance — Human Papillomavirus Vaccine Impact Monitoring Project, Five Sites, United States, 2008–2022. MMWR Morb Mortal Wkly Rep 2025;2025(74):96–101.
27. Alarid-Escudero F, Gracia V, Wolf M*, et al.* State-level disparities in cervical cancer prevention and outcomes in the U.S.: a modeling study. J Natl Cancer Inst 2024; 10.1093/jnci/djae298.
28. Zhao R, Kulasingam S, Alarid-Escudero F*, et al.* Public-health impact of increasing human papillomavirus vaccination and cervical cancer screening: A United States state-level decision analysis. J Natl Cancer Inst 2025; 10.1093/jnci/djaf311.
29. Markowitz LE, Dunne EF, Saraiya M*, et al.* Quadrivalent Human Papillomavirus Vaccine: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep 2007;56(Rr-2):1–24.
30. World Health Organization. Human Papillomavirus Vaccines: WHO Position Paper. In. Weekly Epidemiological Record No 50; 2022, 645–672.
31. Department of Health & Social Care. JCVI statement on a one-dose schedule for the routine HPV immunisation programme. In; 2022.
32. World Health Organization Africen Region. *Africa immunization advisory group urges single-dose HPV vaccine adoption to advance vaccination efforts*. https://www.afro.who.int/news/africa-immunization-advisory-group-urges-single-dose-hpv-vaccine-adoption-advance-vaccination.
34. Asturias EJ, Chen LH, Shaw AC*, et al.* Science for vaccine policy: Independent review of the September 2025 ACIP processes, deliberations and votes. Vaccine 2025;67:127876.
35. Asturias EJ, Brewer NT, Brooks O*, et al.* Advisory Committee on Immunization Practices at a Crossroads. JAMA 2025;334(8):667–668.
36. Center for Disease Control and Prevention. *The Vaccines for Children (VFC) Program: A Retrospective of the Program's First 30 Years*.
37. Alden J, Crane K, Robinson R*, et al.* Expansion of community pharmacies' role in public vaccine delivery to children: Opportunities and need. J Am Pharm Assoc (2003) 2022;62(5):1514–1517.
38. Hoff BM, Livingston MD 3rd, EL T. The association between state Medicaid expansion and human papillomavirus vaccination. Vaccine 2020;38(38):5963–5965.
39. Calo WA, Lennon RP, Ruffin Iv MT*, et al.* Support for HPV vaccine school-entry requirements in the United States: The role of exemption policies. Vaccine 2022;40(51):7426–7432.
40. McKeithen MC, Gilkey MB, Kong WY*, et al.* Policy Approaches for Increasing Adolescent HPV Vaccination Coverage: A Systematic Review. Pediatrics 2024;153(5).

41. James Colgrove, Sara Abiola, Mello MM. HPV vaccination mandates--lawmaking amid political and scientific controversy. N Engl J Med 2010;363(8):785–791.
42. Ko JS, Goldbeck CS, Baughan EB*, et al.* Association Between Human Papillomavirus Vaccination School-Entry Requirements and Vaccination Initiation. JAMA Pediatr 2020;174(9):861–867.
43. Cuff RD, Buchanan T, Pelkofski E*, et al.* Rates of human papillomavirus vaccine uptake amongst girls five years after introduction of statewide mandate in Virginia. Am J Obstet Gynecol 2016;214(6):752 e1–6.
44. U.S Department of Health and Human Service. Vaccine National Stratefic Plan 2021-2025. In. Washington, DC; 2021.
45. Zolot J. Mandatory Parental Counseling Reduces Vaccine Exemptions. AJN The American Journal of Nursing 2018;118(4):13.
46. Szilagyi PG, Albertin CS, Gurfinkel D*, et al.* Prevalence and characteristics of HPV vaccine hesitancy among parents of adolescents across the US. Vaccine 2020;38(38):6027–6037.
47. Sonawane K, Lin YY, Damgacioglu H*, et al.* Trends in Human Papillomavirus Vaccine Safety Concerns and Adverse Event Reporting in the United States. JAMA Netw Open 2021;4(9):e2124502.
48. Markowitz LE, Unger ER. Human Papillomavirus Vaccination. N Engl J Med 2023;388(19):1790–1798.
49. Rani U, Darabaner E, Seserman M*, et al.* Public Education Interventions and Uptake of Human Papillomavirus Vaccine: A Systematic Review. J Public Health Manag Pract 2022;28(1):E307–E315.
50. Oh NL, Biddell CB, Rhodes BE*, et al.* Provider communication and HPV vaccine uptake: A meta-analysis and systematic review. Prev Med 2021;148:106554.
51. Mohammed KA, Geneus CJ, Osazuwa-Peters N*, et al.* Disparities in Provider Recommendation of Human Papillomavirus Vaccination for U.S. Adolescents. J Adolesc Health 2016;59(5):592–598.
52. Walker TY, Elam-Evans LD., Yankey D.*, et al.* National, Regional, State, and Selected Local Area Vaccination Coverage Among Adolescents Aged 13-17 Years - United States, 2018. MMWR Morb Mortal Wkly Rep 2019;68(33):718–723.
53. Hirth J. Disparities in HPV vaccination rates and HPV prevalence in the United States: a review of the literature. Hum Vaccin Immunother 2019;15(1):146–155.
54. Brisson M, Benard E, Drolet M*, et al.* Population-level impact, herd immunity, and elimination after human papillomavirus vaccination: a systematic review and meta-analysis of predictions from transmission-dynamic models. Lancet Public Health 2016;1(1):e8–e17.
55. United States Census Bureau. State-to-State Migration Flows. In: United States Census Bureau, (ed); 2024.
56. Amboree TL, Montealegre JR, Damgacioglu H*, et al.* County-Level Cervical Cancer Screening Coverage and Differences in Incidence and Mortality. JAMA Netw Open 2025;8(8):e2526709.
57. Kish JK, Rolin AI, Zou Z*, et al.* Prioritizing US Cervical Cancer Prevention With Results From a Geospatial Model. Journal of Global Oncology 2016;2(5):275–283.

58. Kyrgiou M, Koliopoulos G, Martin-Hirsch P*, et al.* Obstetric outcomes after conservative treatment for intraepithelial or early invasive cervical lesions: systematic review and meta-analysis. Lancet 2006;367(9509):489–98.
59. McAllum B, Sykes PHH, Sadler L*, et al.* Is the treatment of CIN 2 always necessary in women under 25 years old? American Journal of Obstetrics & Gynecology 2011;205(5):478.e1–478.e7.
60. Benard VB, Watson M, Castle PE*, et al.* Cervical carcinoma rates among young females in the United States. Obstet Gynecol 2012;120(5):1117–23.
61. U.S. Preventive Service Task Force. *Cervical Cancer: Screening*. https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/cervical-cancer-screening-2012.
62. Massad LS, Einstein MH, Huh WK*, et al.* 2012 Updated Consensus Guidelines for the Management of Abnormal Cervical Cancer Screening Tests and Cancer Precursors. Journal of Lower Genital Tract Disease 2013;17:S1–S27.
63. Fontham ETH, Wolf AMD, Church TR*, et al.* Cervical cancer screening for individuals at average risk: 2020 guideline update from the American Cancer Society. CA: A Cancer Journal for Clinicians 2020;70(5):321–346.
64. National Cancer Institute. State Cancer Profiles. In; 2023.
65. Pingali; C, Yankey; D, Elam-Evans; LD*, et al.* Vaccination Coverage Among Adolescents Aged 13–17 Years — National Immunization Survey–Teen, United States, 2022. MMWR Morb Mortal Wkly Rep 2023;72(34):912–919.
66. Adam EE, White MC, Saraiya M. US hysterectomy prevalence by age, race and ethnicity from BRFSS and NHIS: implications for analyses of cervical and uterine cancer rates. Cancer Causes Control 2022;33(1):161–166.
67. Hysterectomy Among Women Age 18 and Older: United States, 2021. In. Hyattsville, MD; 2024.

Figure Legends

Figure 1. Trends in age-standardized cervical cancer incidence rates (2000-2021) and vaccination rates (2008-2022) by state

NOTE Trend lines represented the three-year moving average incorporating the Epanechnikov kernel function weights.[23] Shade represented the 95% confidence interval for the denoised age-standardized incidence rates and vaccination rates.

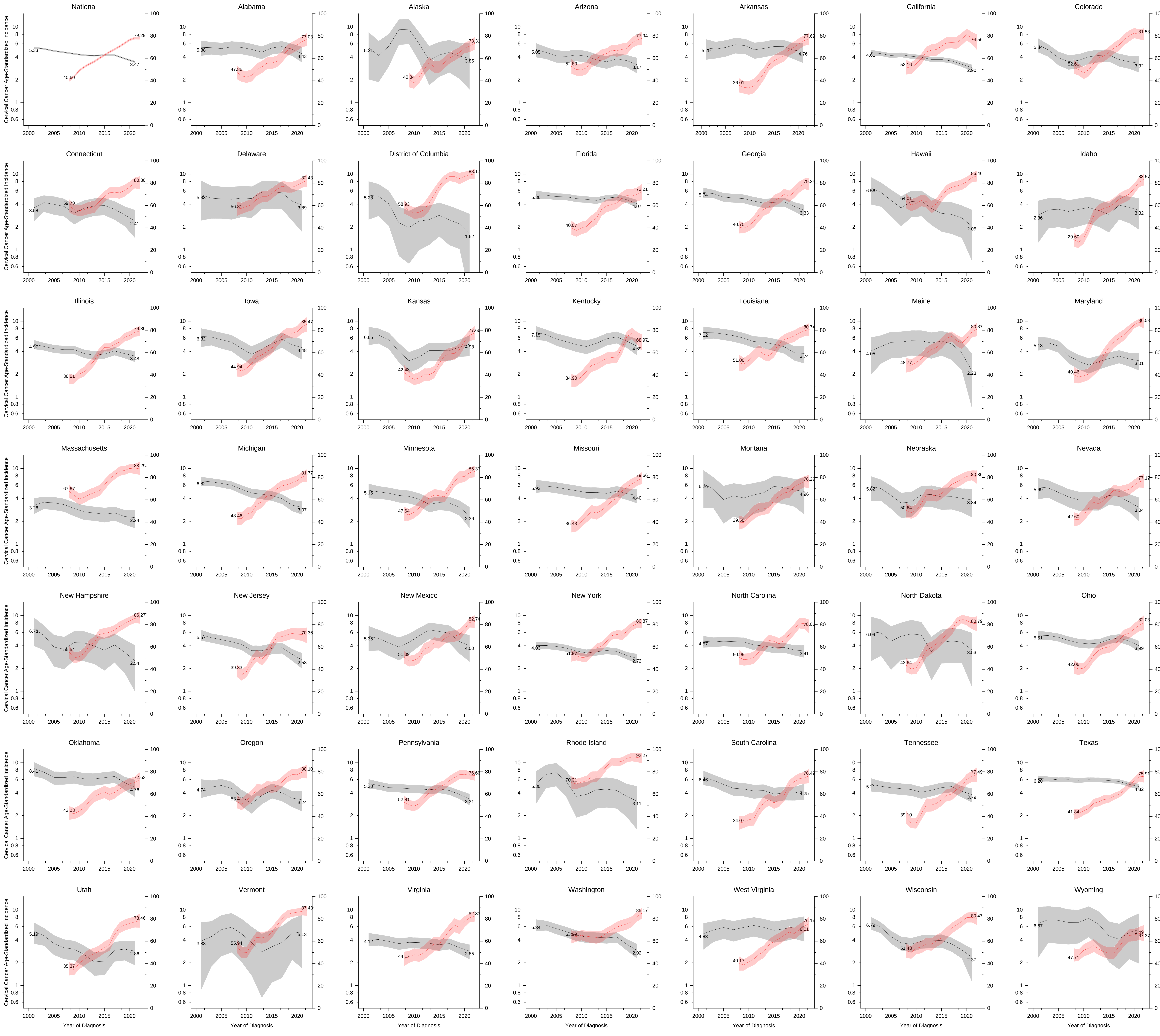
Figure 2. Cervical cancer incidence rate differences and incidence rate ratios during 2000-2005 and 2016-2021 by state

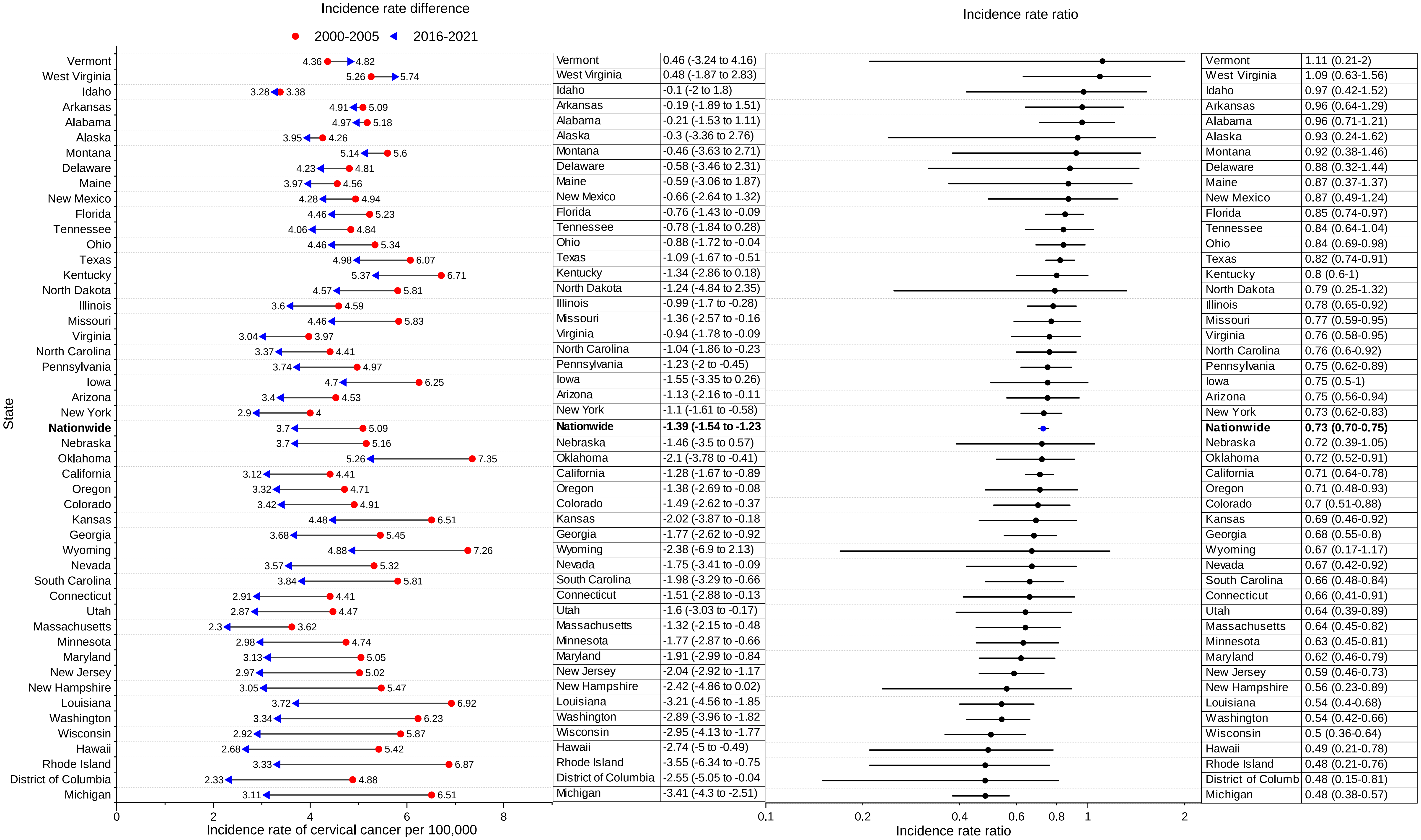
NOTE Rate differences and rate ratios, comparing 2016-2021 to 2000-2005, were calculated, along with corresponding 95% confidence intervals using the Delta method. Case counts by states for each period are provided in Supplementary Table S2 to aid interpretation of the estimates.

Figure 3. State-level HPV vaccination rates (2010) and cervical cancer incidence rate ratios comparing 2016-2021 vs 2000-2005

NOTE Rate ratios, comparing 2016-2021 to 2000-2005, were calculated across states, along with corresponding 95% confidence intervals using the Delta method. HPV vaccination rates were smoothed using a three-year moving average with Epanechnikov weight.[23] Regions were defined based on census regions designated by the US Census Bureau. Available from https://www2.census.gov/geo/pdfs/maps-data/maps/reference/us_regdiv.pdf. Dot size is scaled proportionally to the population size of each state, obtained from the US Census Bureau. Available from https://www.census.gov/topics/population.html. The black line represents the fitted linear regression line, and the gray shaded area indicates the corresponding 95% confidence interval.

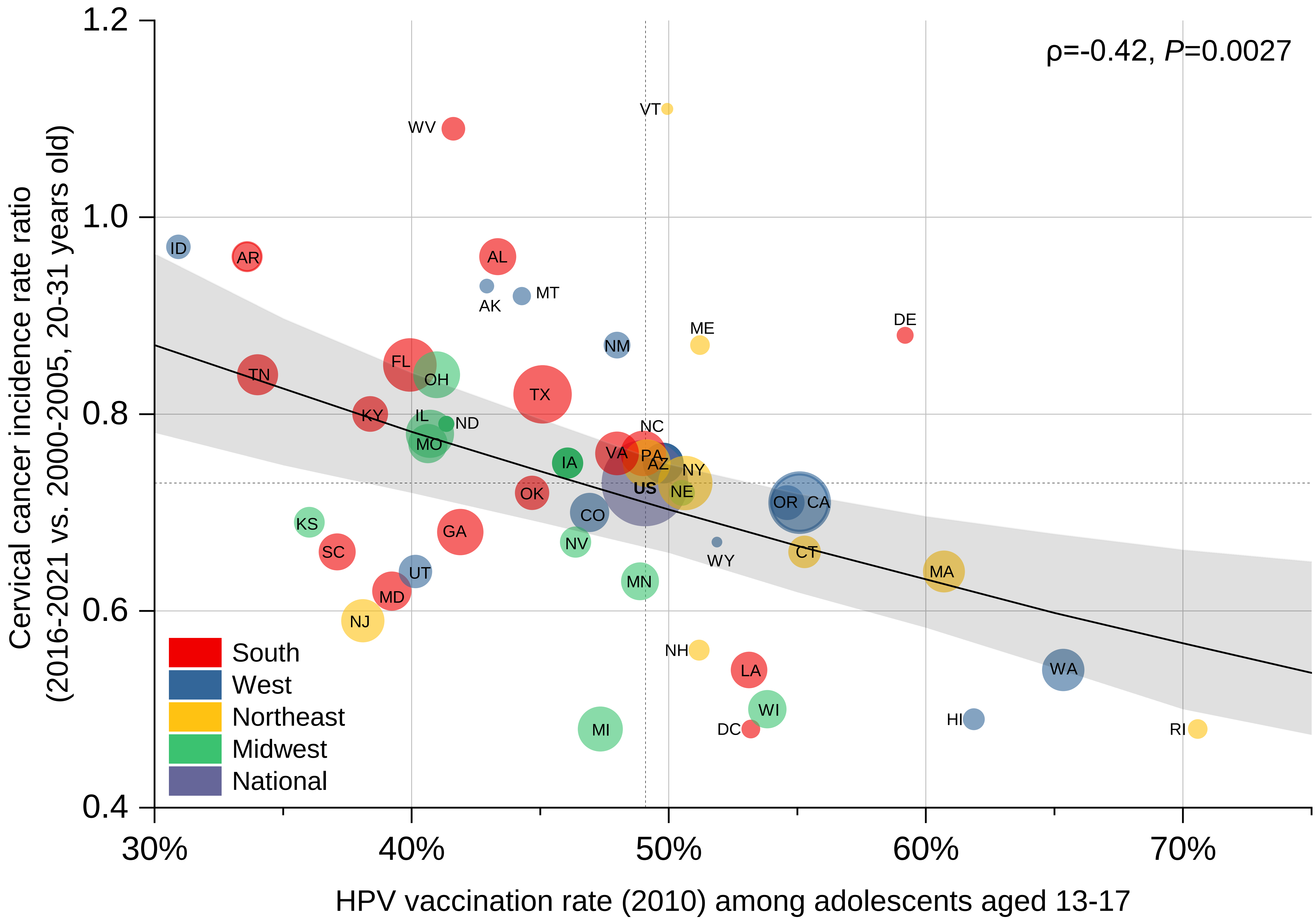
Figure - Color





Vermont	0.46 (-3.24 to 4.16)
West Virginia	0.48 (-1.87 to 2.83)
Idaho	-0.1 (-2 to 1.8)
Arkansas	-0.19 (-1.89 to 1.51)
Alabama	-0.21 (-1.53 to 1.11)
Alaska	-0.3 (-3.36 to 2.76)
Montana	-0.46 (-3.63 to 2.71)
Delaware	-0.58 (-3.46 to 2.31)
Maine	-0.59 (-3.06 to 1.87)
New Mexico	-0.66 (-2.64 to 1.32)
Florida	-0.76 (-1.43 to -0.09
Tennessee	-0.78 (-1.84 to 0.28)
Ohio	-0.88 (-1.72 to -0.04
Texas	-1.09 (-1.67 to -0.51
Kentucky	-1.34 (-2.86 to 0.18)
North Dakota	-1.24 (-4.84 to 2.35)
Illinois	-0.99 (-1.7 to -0.28)
Missouri	-1.36 (-2.57 to -0.16
Virginia	-0.94 (-1.78 to -0.09)
North Carolina	-1.04 (-1.86 to -0.23
Pennsylvania	-1.23 (-2 to -0.45)
Iowa	-1.55 (-3.35 to 0.26)
Arizona	-1.13 (-2.16 to -0.11
New York	-1.1 (-1.61 to -0.58)
Nationwide	**-1.39 (-1.54 to -1.23**
Nebraska	-1.46 (-3.5 to 0.57)
Oklahoma	-2.1 (-3.78 to -0.41)
California	-1.28 (-1.67 to -0.89
Oregon	-1.38 (-2.69 to -0.08
Colorado	-1.49 (-2.62 to -0.37
Kansas	-2.02 (-3.87 to -0.18
Georgia	-1.77 (-2.62 to -0.92
Wyoming	-2.38 (-6.9 to 2.13)
Nevada	-1.75 (-3.41 to -0.09
South Carolina	-1.98 (-3.29 to -0.66
Connecticut	-1.51 (-2.88 to -0.13
Utah	-1.6 (-3.03 to -0.17)
Massachusetts	-1.32 (-2.15 to -0.48
Minnesota	-1.77 (-2.87 to -0.66
Maryland	-1.91 (-2.99 to -0.84
New Jersey	-2.04 (-2.92 to -1.17
New Hampshire	-2.42 (-4.86 to 0.02)
Louisiana	-3.21 (-4.56 to -1.85
Washington	-2.89 (-3.96 to -1.82
Wisconsin	-2.95 (-4.13 to -1.77
Hawaii	-2.74 (-5 to -0.49)
Rhode Island	-3.55 (-6.34 to -0.75
District of Columbia	-2.55 (-5.05 to -0.04
Michigan	-3.41 (-4.3 to -2.51)

Vermont	1.11 (0.21-2)
West Virginia	1.09 (0.63-1.56)
Idaho	0.97 (0.42-1.52)
Arkansas	0.96 (0.64-1.29)
Alabama	0.96 (0.71-1.21)
Alaska	0.93 (0.24-1.62)
Montana	0.92 (0.38-1.46)
Delaware	0.88 (0.32-1.44)
Maine	0.87 (0.37-1.37)
New Mexico	0.87 (0.49-1.24)
Florida	0.85 (0.74-0.97)
Tennessee	0.84 (0.64-1.04)
Ohio	0.84 (0.69-0.98)
Texas	0.82 (0.74-0.91)
Kentucky	0.8 (0.6-1)
North Dakota	0.79 (0.25-1.32)
Illinois	0.78 (0.65-0.92)
Missouri	0.77 (0.59-0.95)
Virginia	0.76 (0.58-0.95)
North Carolina	0.76 (0.6-0.92)
Pennsylvania	0.75 (0.62-0.89)
Iowa	0.75 (0.5-1)
Arizona	0.75 (0.56-0.94)
New York	0.73 (0.62-0.83)
Nationwide	**0.73 (0.70-0.75)**
Nebraska	0.72 (0.39-1.05)
Oklahoma	0.72 (0.52-0.91)
California	0.71 (0.64-0.78)
Oregon	0.71 (0.48-0.93)
Colorado	0.7 (0.51-0.88)
Kansas	0.69 (0.46-0.92)
Georgia	0.68 (0.55-0.8)
Wyoming	0.67 (0.17-1.17)
Nevada	0.67 (0.42-0.92)
South Carolina	0.66 (0.48-0.84)
Connecticut	0.66 (0.41-0.91)
Utah	0.64 (0.39-0.89)
Massachusetts	0.64 (0.45-0.82)
Minnesota	0.63 (0.45-0.81)
Maryland	0.62 (0.46-0.79)
New Jersey	0.59 (0.46-0.73)
New Hampshire	0.56 (0.23-0.89)
Louisiana	0.54 (0.4-0.68)
Washington	0.54 (0.42-0.66)
Wisconsin	0.5 (0.36-0.64)
Hawaii	0.49 (0.21-0.78)
Rhode Island	0.48 (0.21-0.76)
District of Columb	0.48 (0.15-0.81)
Michigan	0.48 (0.38-0.57)


ρ=-0.42, P=0.0027
Cervical cancer incidence rate ratio
(2016-2021 vs. 2000-2005, 20-31 years old)
HPV vaccination rate (2010) among adolescents aged 13-17
1.2
1.0
0.8
0.6
0.4
30%
40%
50%
60%
70%
South
West
Northeast
Midwest
National
VT
WV
ID
AR
AL
AK
MT
DE
ME
NM
FL
OH
TN
TX
KY
IL
ND
MO
NC
VA
PA
AZ
NY
IA
US
NE
OK
OR
CA
CO
KS
GA
NV
WY
CT
SC
MA
UT
MN
MD
NJ
NH
LA
WA
WI
HI
MI
DC
RI