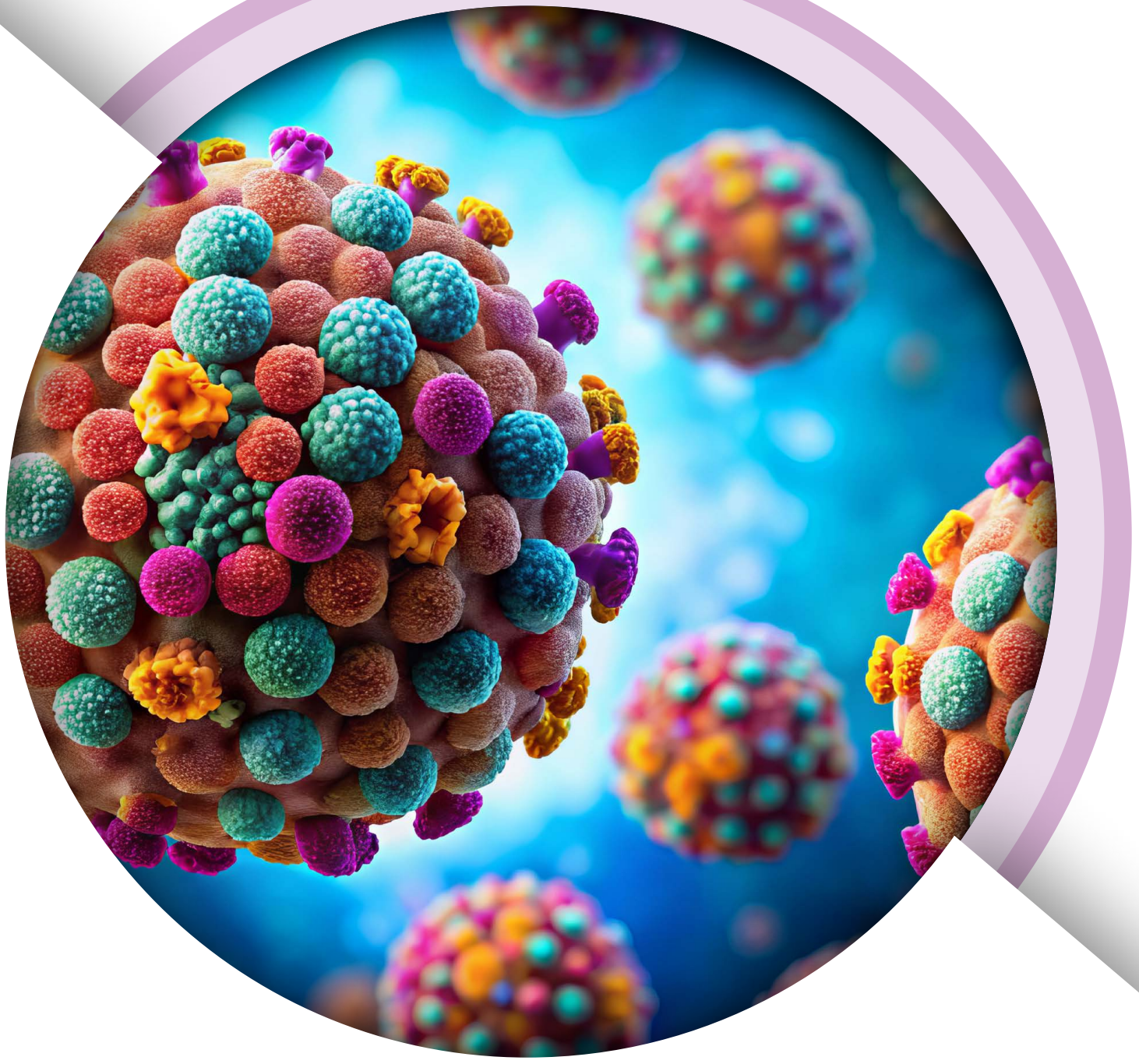
2025
WINTER•VOLUME 58



BIOTHERAPEUTICS QUARTERLY

A HENRY SCHEIN® MEDICAL PUBLICATION

Diagnostic and Pharmaceutical News for You and Your Medical Practice

BIOTHERAPEUTICS QUARTERLY

Diagnostic and Pharmaceutical News for You and Your Medical Practice

2025/Winter/Volume 58

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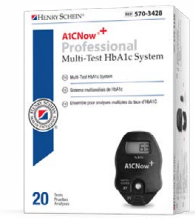

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Date of Approval: August 14, 2024
Company: Incyte and Syndax Pharmaceuticals
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Niktimvo (axatilimab-csfr) is a colony stimulating factor-1 receptor (CSF-1R)-blocking antibody used for the treatment of chronic graft-versus-host disease.

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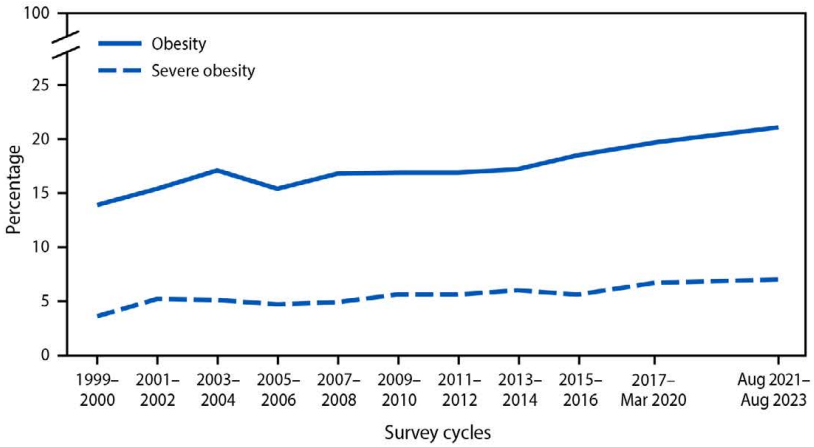
QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Prevalence of Obesity* and Severe Obesity† Among Persons Aged 2–19 Years — United States, 1999–2000 Through 2021–2023§



Abbreviation: BMI = body mass index.

* Obesity was defined as BMI ≥95th percentile for age and sex on CDC growth charts (https://www.cdc.gov/growthcharts/cdc_charts.htm). BMI is calculated as weight in kilograms divided by height in meters squared.

† Severe obesity was defined as BMI ≥120% of the 95th percentile for age and sex on CDC growth charts.

§ After National Health and Nutrition Examination Survey operations were suspended in March 2020 because of the COVID-19 pandemic, field operations resumed from August 2021 until August 2023.

From 1999–2000 through August 2021–August 2023, the prevalence of obesity among persons in the United States aged 2–19 years increased from 13.9% to 21.1%, and the prevalence of severe obesity increased from 3.6% to 7.0%.

Supplementary Table: https://stacks.cdc.gov/view/cdc/164014

Source: National Center for Health Statistics, National Health and Nutrition Examination Survey, 1999–2000 through August 2021–August 2023. https://www.cdc.gov/nchs/nhanes/index.htm

Reported by: Samuel D. Emmerich, DVM, semmerich@cdc.gov; Cynthia L. Ogden, PhD.

For more information on this topic, CDC recommends the following link: https://www.cdc.gov/obesity/family-action/index.html.

National Institutes of Health
Turning Discovery Into Health

October 1, 2024

Childhood obesity linked to limited food options

At a Glance

- Children living in neighborhoods with low access to grocery stores early in life, even before birth, were at increased risk for obesity later.
- The findings hint that improving early access to healthy foods might help to reduce the risk of childhood obesity.

Childhood obesity is a growing public health problem, affecting about 1 in 5 children nationwide, according to the Centers for Disease Control and Prevention. Limited access to grocery stores and healthy foods may be one reason. Several studies have found links between obesity and neighborhood food access among people of varying ages. But few studies have assessed the impact of food insufficiency during the earliest stages of life, when interventions might have the greatest impact.

A growing body of research suggests that access to healthy foods early in life can improve children's health years later. *MillaF / Shutterstock*

A research team led by Dr. Izzuddin M. Aris of Harvard University set out to assess the potential long-term impact of poor food access during early life stages, including the weeks before birth. The scientists drew on nationwide data gathered between 1994 and 2003 as part of the NIH-supported Environmental influences on Child Health Outcomes (ECHO) consortium.

The researchers focused on data from more than 28,000 children (48% female, 52% male). About 23% of them had been in low-income, low-food access neighborhoods before birth, at about 34 weeks of pregnancy. And about 24% of the children were living in similarly disadvantaged neighborhoods at a young age, before age 5. Neighborhoods with low food access were defined as those in which the nearest supermarket was more than a half-mile away in urban areas, or more than 10 miles away in rural regions.

The researchers calculated each child's body mass index (BMI) over time, from birth to age 15. BMI is a ratio of weight to height. For children and adolescents, BMI can be adjusted based on age, gender, and expected growth and weight patterns. This is known as the BMI z score. Results appeared in *JAMA Pediatrics* on September 16, 2024.

Overall, the scientists found that early-life residence in neighborhoods with limited food access was associated with a greater than 50% higher risk of obesity (defined as BMI at or above the 95th percentile for age and sex) or severe obesity (BMI at or above 120% of the 95th percentile) later in life. The risks were similar whether the children had been living in food-restricted neighborhoods before birth or during childhood. BMI z scores were elevated at

ages 5, 10, and 15 among those with limited food access early in life. The association was strongest among those who had lived in food-limited regions during both pregnancy and early childhood.

The researchers also assessed the data by adjusting for numerous factors. These included differing distances to supermarkets and considering vehicle ownership, which might increase access to healthy foods. Even with these adjustments, the increased risks for obesity and higher child BMI remained into adolescence.

"Living in neighborhoods with access to healthy foods during these stages may be an important factor in preventing the development of obesity later in childhood and adolescence," Aris says. "Our findings support the need for further research on strategies to improve access to healthy food in early life."

—by Vicki Contie

References: Neighborhood Food Access in Early Life and Trajectories of Child Body Mass Index and Obesity. Aris IM, Wu AJ, Lin PD, Zhang M, Farid H, Hedderson MM, Zhu Y, Ferrara A, Chehab RF, Barrett ES, Carnell S, Camargo CA Jr, Chu SH, Mirzakhani H, Kelly RS, Comstock SS, Strakovsky RS, O'Connor TG, Ganiban JM, Dunlop AL, Dabelea D, Breton CV, Bastain TM, Farzan SF, Call CC, Hartert T, Snyder B, Santarossa S, Cassidy-Bushrow AE, O'Shea TM, McCormack LA, Karagas MR, McEvoy CT, Alshawabkeh A, Zimmerman E, Wright RJ, McCann M, Wright RO, Coull B, Amutah-Onukagha N, Hacker MR, James-Todd T, Oken E; ECHO Cohort Consortium. *JAMA Pediatr.* 2024 Sep 16:e243459. doi: 10.1001/jamapediatrics.2024.3459. Online ahead of print. PMID: 39283628.

Funding: NIH's Office of the Director (OD) and National Institute of Environmental Health Sciences (NIEHS).

Source: https://nih.gov/news-events/nih-research-matters/childhood-obesity-linked-limited-food-options

Human Papillomavirus Vaccination Coverage Among Adolescent Girls Aged 13–17 Years — U.S.-Affiliated Pacific Islands, 2013–2023

Ashley Tippins, MPH[1]; Glodi Mutamba, MD[2]; E.M. Boyd, MHCA[2]; Kelsey C. Coy, MPH[2]; Jennifer L. Kriss, PhD[1]

Abstract

Worldwide, cervical cancer is the fourth most common cancer among women, and the World Health Organization (WHO) Western Pacific Region, where the U.S.-affiliated Pacific Islands (USAPI) are located, accounts for one quarter of all estimated cases. Human papillomavirus (HPV) vaccines are recommended at age 11–12 years to prevent most cervical cancers. HPV vaccines were introduced across USAPI during 2007–2016, predominantly provided through school-located vaccination programs. Retrospective analysis using data from jurisdictional immunization information systems was used to estimate vaccination coverage among adolescent girls as of the last day of each calendar year during 2013–2023. This analysis measured progress toward the WHO 2030 vaccination coverage goal of ≥90% completion of the HPV vaccination series among girls by age 15 years. As of December 2023, initiation of the HPV vaccination series among adolescent girls aged 13–17 years ranged from 58.0% in Palau to 97.2% in the Northern Mariana Islands, and HPV vaccination series completion coverage ranged from 43.4% in Palau to 91.8% in the Northern Mariana Islands. HPV vaccination series completion coverage is >90% in the Northern Mariana Islands and is on track to meet WHO goals by 2030 in American Samoa. Assessment of adolescent vaccination coverage can help immunization programs monitor progress toward regional goals and identify populations and areas with low coverage. Implementing evidence-based strategies to increase vaccine access and coverage would benefit jurisdictions with lagging coverage.

Introduction

Worldwide, cervical cancer is the fourth most common cancer among women, and the World Health Organization (WHO) Western Pacific region* accounts for one quarter of all estimated cases (*1*); the age-standardized rate of cervical cancer in the Marshall Islands (74 per 100,000 women) is the highest in the world (*2*). Nearly all cervical cancers are caused by human papillomaviruses (HPV). HPV vaccines, which have been licensed for use since 2006, are estimated to have the potential to prevent approximately 75% of all cervical cancers (*3*). CDC recommends HPV vaccination for both boys and girls at age 11–12 years.† However, to assess progress toward reaching vaccination goals in the 2020 WHO Global Strategy to Accelerate the Elimination of Cervical Cancer as a Public Health Problem,§ this report focuses on HPV vaccination coverage among adolescent girls. The WHO strategy recommends that HPV vaccines be included in all national immunization programs; the goal is for ≥90% of girls to complete the HPV vaccination series by age 15 years, by 2030 (*4*).

HPV vaccines were introduced across the U.S.-affiliated Pacific Islands (USAPI)¶ during 2007–2016,** predominantly provided through school-located vaccination programs.†† Assessment of vaccination coverage among adolescent girls can help immunization programs monitor progress toward regional goals and identify populations and areas with low coverage. These data can be used to guide evidence-based interventions, adapted to the local context, to improve vaccination coverage. This report describes annual HPV vaccination coverage among adolescent girls in five of the six USAPI§§ jurisdictions during 2013–2023.

* WHO member countries are grouped into six regions: Africa, Americas, Eastern Mediterranean, Europe, South-East Asia, and Western Pacific. The Western Pacific Region consists of 37 countries and areas, including the six U.S.-affiliated Pacific Islands. https://www.who.int/westernpacific/about/where-we-work

† https://www.cdc.gov/vaccines/imz-schedules/adolescent-easyread.html

§ Three of the six USAPI jurisdictions offer the vaccine to girls (American Samoa, Guam, and the Northern Mariana Islands), and three offer the vaccine to both boys and girls (Federated States of Micronesia, Marshall Islands, and Palau). Coverage among adolescent girls is included in this report for consistency across jurisdictions and to assess progress toward WHO goals, which include vaccination goals only for girls. https://www.cdc.gov/vaccines/hcp/imz-schedules/child-adolescent-notes.html#note-hpv

¶ USAPI comprise three U.S. territories (American Samoa, Guam, and the Northern Mariana Islands) and three freely associated nations (Federated States of Micronesia, Marshall Islands, and Palau). All jurisdictions receive Section 317 Immunization Program funding, which is a discretionary program funded by the U.S. Congress to purchase vaccines and support immunization infrastructure. The U.S. territories (American Samoa and Northern Mariana Islands) also receive Vaccines for Children (VFC) funding; VFC is an entitlement program for children aged ≤18 years that provides vaccines at no cost to VFC program–eligible children through public and private health care providers that are enrolled in the VFC program.

** Implementation of the HPV vaccine program varied by jurisdiction. Northern Mariana Islands implemented the program in 2007, Palau in 2008, Marshall Islands in 2009, and American Samoa in 2011. Federated States of Micronesia implemented the program in three states (Kosrae, Pohnpei, and Yap) in 2009, and the fourth state (Chuuk) in 2016.

†† American Samoa provided a mixed clinic- and school-located HPV program during 2011–2018. The school-located program ended in 2018.

§§ Jurisdictions in this report include American Samoa, Northern Mariana Islands, Federated States of Micronesia, Marshall Islands, and Palau. Vaccination coverage among adolescents in Guam has been assessed via the National Immunization Survey since 2013; immunization Information system (IIS)–based coverage assessment was not conducted for Guam. Information on adolescent vaccination coverage in Guam is available at https://www.cdc.gov/vaccines/imz-managers/coverage/teenvaxview/data-reports/index.html.

Methods

Data Sources and Inclusion and Exclusion Criteria

Patient-level data from jurisdictional immunization information systems (IISs) were aggregated at the jurisdiction level for this retrospective analysis. Persons were included in the denominator for annual analyses if they 1) were adolescent girls aged 13–17 years as of January 1 of the assessment year, 2) had an active patient status[¶¶] in the IIS through the end of the assessment year, and 3) had received any vaccine within the most recent 5 years. Exclusion criteria consistent with the Modeling of Immunization Registry Operations Work Group managing active patient status guidance was retrospectively applied to mitigate IIS denominator inflation (5). Patients were excluded from all analyses if they had zero vaccine doses recorded in the IIS or if the last vaccination date recorded in the IIS was before January 1, 2006.

Estimation of HPV Vaccination Coverage

Retrospective point-in-time analysis (i.e., coverage as of a specific date) was used to estimate vaccination coverage as of December 31 of each year during 2013–2023. All HPV vaccine doses received as of the end of the assessment year were included in coverage estimates. Vaccination coverage indicators included receipt of ≥1 HPV vaccine dose and HPV vaccination series completion status.[***] Completion of the HPV vaccination series is defined as receipt of ≥3 HPV vaccine doses, or receipt of 2 doses if the series was initiated at age <15 years, and if ≥5 months minus 4 days have elapsed between receipt of the first and second dose.

HPV vaccination series dropout was measured as the proportion of adolescents who had not completed the HPV vaccination series by the end of the assessment year, among those who received the first dose. SAS software (version 9.4; SAS Institute) was used to conduct all analyses. This activity was reviewed by CDC, deemed not research, and was conducted consistent with applicable federal law and CDC policy.[†††]

[¶¶] Patient active or inactive status in the IIS establishes a classification of individual patients within a health care organization. Health care providers are responsible for vaccinating patients with an "active" status within their clinic population or geographic catchment area. Patient status is changed to "inactive" when the patient changes providers, moves, or is lost to follow-up or "deceased" if patient death is confirmed through manual review or system linkage with vital statistics or other health records. https://repository.immregistries.org/files/resources/5835adc2dad8d/mirow_pais_mini-guide.pdf

[***] In 2016, the HPV vaccine recommendations changed from a 3-dose series for all to a 2-dose series among children and adolescents who initiate the vaccination series before age 15 years. Completion of the HPV vaccination series is defined as receipt of ≥3 HPV vaccine doses or receipt of 2 doses if the series is initiated at age <15 years, and ≥5 months minus 4 days have elapsed between the first and second dose. This measure was applied retrospectively for all years 2013–2023. https://www.cdc.gov/vaccines/hcp/imz-schedules/child-adolescent-notes.html#note-hpv

[†††] 45 C.F.R. part 46, 21 C.F.R. part 56; 42 U.S.C. Sect. 241(d); 5 U.S.C. Sect. 552a; 44 U.S.C. Sect. 3501 et seq.

Results

Jurisdictional HPV Vaccination Coverage Among Adolescent Girls Aged 13–17 Years

Coverage with ≥1 HPV vaccine dose and HPV vaccination series completion status varied by jurisdiction (Table). As of December 2023, coverage with ≥1 HPV dose among adolescent girls aged 13–17 years ranged from 58.0% in Palau to 97.2% in the Northern Mariana Islands. HPV vaccination series completion coverage ranged from 43.4% in Palau to 91.8% in the Northern Mariana Islands. As of 2023, the Northern Mariana Islands is the only jurisdiction to have already met the WHO 2030 HPV 90% vaccination coverage goal.

Trends in HPV Vaccination Coverage Among Adolescent Girls, 2013–2023

During 2013–2023, coverage with ≥1 HPV vaccine dose increased by 35.2–72.8 percentage points across jurisdictions (Figure 1), and HPV vaccination series completion coverage increased by 35.3–72.9 percentage points (Figure 2). The percentage of adolescent girls who had received ≥1 HPV vaccine dose and who completed the vaccination series increased each year from 2013 to 2023 in all jurisdictions except Palau, where ≥1-dose coverage and HPV vaccination series completion coverage peaked in 2020 at 71.6% and 59.0%, respectively, and have since declined to 58.0% and 43.4%, respectively, in 2023 (Table). In American Samoa, HPV vaccination series completion coverage increased from 78.0% to 82.8% (4.8 percentage points) from 2022 to 2023. If coverage continues to increase at the same rate, American Samoa will meet the WHO 2030 ≥90% HPV vaccination series completion coverage goal by 2025.

HPV vaccination series dropout varied across jurisdictions and years; during 2013–2023, dropout decreased in all jurisdictions except in Palau, where it increased from a low of 17.2% in 2021 to a high of 25.2% in 2023 (Table). Dropout was lowest in the Northern Mariana Islands, where only 5.6% of adolescent girls aged 13–17 years who initiated the HPV vaccination series had not completed it in 2023.

Discussion

HPV vaccines are a critical public health tool to prevent most cervical cancers. HPV vaccination coverage has increased markedly in USAPI since the vaccination programs commenced, and HPV vaccination series completion coverage in the Northern Mariana Islands currently exceeds the ≥90% WHO 2030 goal. If the current coverage trends continue, American Samoa will also be on track to meet the WHO 2030 coverage goal. The 2023 rates of initiation of the HPV vaccination series among adolescent girls aged 13–17 years in American Samoa

TABLE. Human papillomavirus vaccination coverage among adolescent girls aged 13–17 years, by jurisdiction — U.S.-affiliated Pacific Islands,* 2013–2023

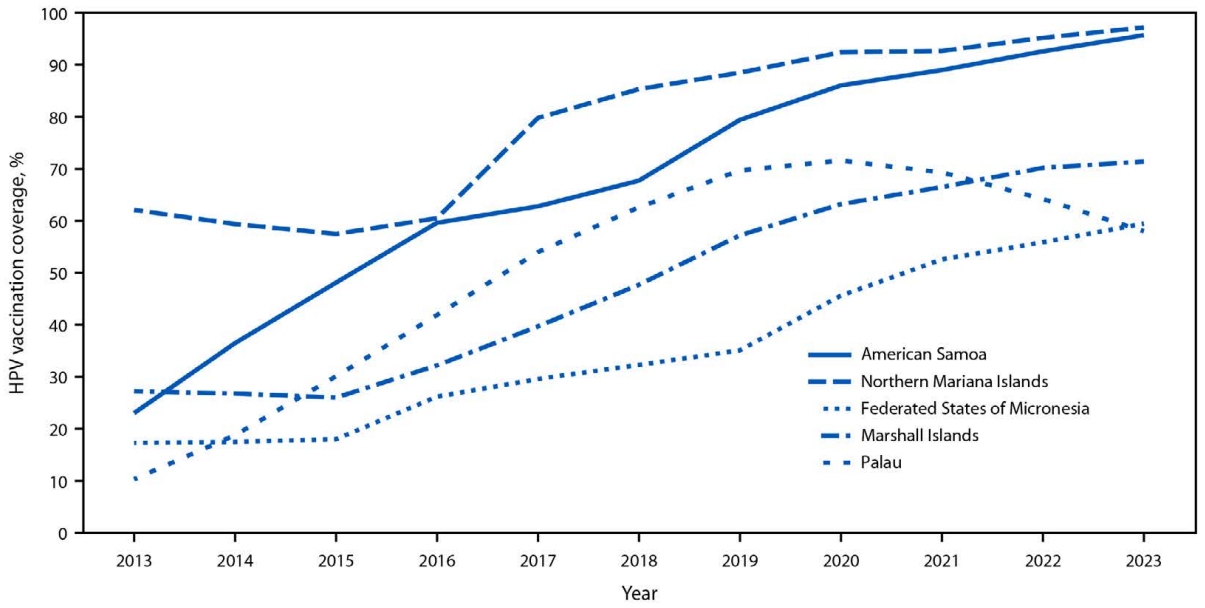
Jurisdiction/Year	Population,† no.	Coverage, %		
		Received ≥1 HPV vaccine dose	HPV vaccination series completion§	HPV vaccination series dropout¶
American Samoa				
2013	3,785	23.0	4.9	78.8
2014	3,888	36.5	12.9	64.7
2015	3,937	48.1	25.2	47.6
2016	3,608	59.6	34.6	42.0
2017	3,580	62.8	36.0	42.7
2018	3,578	67.7	39.1	42.2
2019	3,492	79.4	50.0	37.1
2020	3,291	86.0	61.0	29.0
2021	3,194	89.0	67.6	24.0
2022	3,027	92.6	78.0	15.8
2023	2,921	95.7	82.8	13.4
Northern Mariana Islands				
2013	3,142	62.1	44.2	28.8
2014	3,155	59.4	43.0	27.5
2015	3,053	57.5	40.6	29.3
2016	2,904	60.5	44.2	26.8
2017	2,733	79.8	56.1	29.7
2018	2,673	85.3	72.1	15.5
2019	2,591	88.5	79.7	9.9
2020	2,476	92.4	87.0	5.9
2021	2,511	92.7	87.6	5.5
2022	2,314	95.2	90.2	5.3
2023	2,289	97.2	91.8	5.6
Federated States of Micronesia				
2013	6,807	17.3	9.4	45.8
2014	6,914	17.5	9.7	44.2
2015	6,854	18.0	10.2	43.1
2016	6,853	26.2	12.6	52.1
2017	6,769	29.6	16.0	45.9
2018	6,800	32.3	19.5	39.7
2019	6,789	35.1	23.6	32.8
2020	5,956	45.6	33.9	25.5
2021	5,766	52.6	40.9	22.2
2022	5,539	55.9	45.6	18.5
2023	5,507	59.5	48.4	18.5
Marshall Islands				
2013	3,358	27.2	13.6	49.8
2014	3,400	26.8	13.8	48.4
2015	3,373	26.0	13.0	50.2
2016	3,368	32.2	16.4	49.0
2017	3,402	39.7	22.3	43.9
2018	3,475	47.7	30.7	35.6
2019	3,528	57.2	39.7	30.6
2020	3,518	63.2	45.3	28.3
2021	3,476	66.5	48.1	27.7
2022	3,231	70.2	52.2	25.6
2023	2,981	71.4	53.6	24.9
Palau				
2013	893	10.3	8.1	21.7
2014	786	18.8	12.2	35.1
2015	721	30.1	19.6	35.0
2016	673	41.9	27.8	33.7
2017	683	54.0	35.4	34.4
2018	650	62.6	45.8	26.8
2019	647	69.7	54.7	21.5
2020	630	71.6	59.0	17.5
2021	639	69.3	57.4	17.2
2022	623	64.2	52.2	18.8
2023	629	58.0	43.4	25.2

See table footnotes on the next page.

TABLE. (*Continued*) Human papillomavirus vaccination coverage among adolescent girls aged 13–17 years, by jurisdiction — U.S.-affiliated Pacific Islands,* 2013–2023

Abbreviations: HPV = human papillomavirus; IIS = immunization information system.
* Jurisdictions in this report include American Samoa, Northern Mariana Islands, Federated States of Micronesia, Marshall Islands, and Palau. Vaccination coverage among adolescents in Guam has been assessed via the National Immunization Survey since 2013; IIS-based coverage assessment was not conducted for Guam. Information on adolescent vaccination coverage in Guam is available at https://www.cdc.gov/vaccines/imz-managers/coverage/teenvaxview/data-reports/index.html.
† Total number of adolescent girls aged 13–17 years with an active patient status in the IIS, ≥1 dose of any vaccine ever recorded in the IIS, and ≥1 dose of any vaccine recorded in the IIS within 5 years of the assessment year.
§ In December 2016, the HPV vaccination recommendations changed from a 3-dose series for all to a 2-dose series among children and adolescents who initiate the vaccination series before age 15 years. Completion of the HPV vaccination series is defined as receipt of ≥3 HPV vaccine doses, or receipt of 2 doses if the series is initiated at age <15 years, and ≥5 months minus 4 days have elapsed between the first and second dose. This measure was applied retrospectively for all years 2013–2023. https://www.cdc.gov/vaccines/hcp/imz-schedules/child-adolescent-notes.html#note-hpv
¶ The percentage of adolescents who started the HPV vaccination series but did not complete it as of the end of the assessment year.

FIGURE 1. Trends in ≥1-dose human papillomavirus vaccination coverage among adolescent girls aged 13–17 years, by jurisdiction — U.S.-affiliated Pacific Islands,* 2013–2023



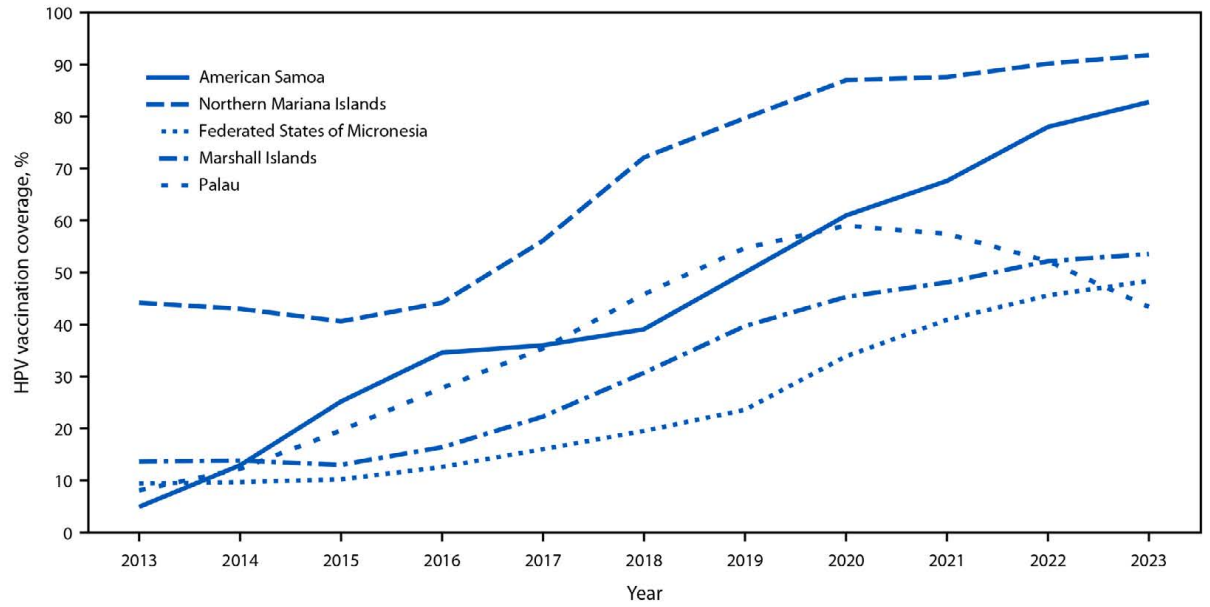
Abbreviation: HPV = human papillomavirus.
* Jurisdictions include American Samoa, Northern Mariana Islands, Federated States of Micronesia, Marshall Islands, and Palau. Vaccination coverage among adolescents in Guam has been assessed via the National Immunization Survey since 2013; immunization information system–based coverage assessment was not conducted for Guam. https://www.cdc.gov/vaccines/imz-managers/coverage/teenvaxview/data-reports/index.html

(95.7%) and the Northern Mariana Islands (97.2%) are higher than those in the three freely associated USAPI jurisdictions (Federated States of Micronesia, Marshall Islands, and Palau) (range = 58.0%–71.4%).

The differences in coverage among the USAPI jurisdictions might be attributed, at least in part, to differences in access to the vaccine. Both American Samoa and the Northern Mariana Islands have offered the vaccine through a mix of school-located vaccination programs as well as in public health clinics. These two jurisdictions receive vaccination program funding and vaccine supply through the Section 317 Immunization Program and the U.S. Vaccines for Children (VFC) program. The three freely associated jurisdictions are not eligible to receive VFC funding and thus have a more limited vaccine supply; therefore, these jurisdictions have not consistently been able to offer HPV vaccine in clinics or other locations outside the school setting.

The school-located HPV vaccination program is an evidence-based intervention to increase HPV vaccination coverage, particularly in low- and middle-income settings; however,

FIGURE 2. Trends in human papillomavirus vaccination series completion* coverage among adolescent girls aged 13–17 years, by jurisdiction† — U.S.-affiliated Pacific Islands, 2013–2023



Abbreviation: HPV = human papillomavirus.

* In December 2016, the HPV vaccination recommendations changed from a 3-dose series for all to a 2-dose series among children and adolescents who initiate the vaccination series before age 15 years. Completion of the HPV vaccination series is defined as receipt of ≥3 HPV vaccine doses, or receipt of 2 doses if the series is initiated at age <15 years, and ≥5 months minus 4 days have elapsed between the first and second dose. This measure was applied retrospectively for all years 2013–2023. https://www.cdc.gov/vaccines/hcp/imz-schedules/child-adolescent-notes.html#note-hpv

† Jurisdictions include American Samoa, Northern Mariana Islands, Federated States of Micronesia, Marshall Islands, and Palau. Vaccination coverage among adolescents in Guam has been assessed via the National Immunization Survey since 2013; immunization information system–based coverage assessment was not conducted for Guam. https://www.cdc.gov/vaccines/imz-managers/coverage/teenvaxview/data-reports/index.html

jurisdiction-level coverage is constrained when the vaccine is only available in the school setting (*6*). For example, secondary school enrollment§§§ among girls is approximately 66% in Federated States of Micronesia, 83% in Marshall Islands, and 80% in Palau, compared with approximately 97% in American Samoa and the Northern Mariana Islands (*7–9*). Strategies to reach out-of-school adolescent girls are needed to improve vaccination coverage in these settings. Providing vaccine access to girls who are not enrolled in school is also an important health equity consideration. Some research suggests that girls who drop out of school are more likely to contract sexually transmitted infections, such as HPV, than are those who remain in school (*10*).

§§§ Gross enrollment ratio, measured as the ratio of total enrollment, regardless of age, to the population of the age group that officially corresponds to the level of education shown. Data for American Samoa and the Northern Mariana Islands are available from the U.S. Census Bureau. https://data.census.gov/table?q=school%20enrollment%20and%20sex%20american%20samoa; https://data.census.gov/table?q=school%20enrollment%20and%20sex%20commonwealth%20of%20the%20northern%20mariana%20islands

In addition to challenges associated with accessing adolescent girls who are not in school, school-based HPV vaccination programs in some areas might have been suspended while schools were closed during the COVID-19 pandemic. The decline in coverage after 2020 in Palau might be evidence of the pandemic's impact because coverage was trending up among girls who reached the target vaccination age of 11–12 years before 2020, compared with girls who reached age 11–12 years in 2020 and later. More research is needed to assess the underlying reasons for the lower coverage in the freely associated USAPI and to design and implement evidence-based interventions to improve vaccination outcomes adapted to the local context. Specific strategies might be needed to increase vaccination coverage among populations that have recently experienced larger declines in coverage, including those who would have been within the recommended age for vaccination during the pandemic.

Limitations

The findings in this report are subject to at least three limitations. First, accuracy of coverage estimates in this assessment is

Summary

What is already known about this topic?

Cervical cancer is the fourth most common cancer among women worldwide, and the World Health Organization Western Pacific Region, where the U.S.-affiliated Pacific Islands (USAPI) are located, accounts for one quarter of all estimated cases. Human papillomavirus (HPV) vaccines prevent most cervical cancers and are recommended for girls at age 11–12 years.

What is added by this report?

This is the first comprehensive report of trends in HPV vaccination coverage among adolescent girls since the vaccines were introduced in USAPI jurisdictions. Coverage with HPV vaccine is on track to meet 2030 goals in two jurisdictions, but disparities need to be addressed.

What are the implications for public health practice?

Adolescent vaccination coverage assessment identifies progress toward regional goals. To target increased vaccine access and coverage, this assessment identifies populations and areas with low coverage.

dependent upon completeness and accuracy of jurisdictional IIS data. Working with the jurisdictions, CDC has found high levels of completeness and accuracy of vaccination data (i.e., consistency in recorded dose dates and product types between paper and IIS records) across the five USAPI IISs included in this assessment through evaluations conducted since 2016. However, IIS data completeness before 2016 has not been evaluated. Second, the active patient population size could be inflated in IISs compared with census estimates because of difficulties tracking out-migration and deaths, which can lead to an underestimation of vaccination coverage. However, recent U.S. Census Bureau data were not available for denominator estimation for all jurisdictions included in this assessment. For this reason, exclusion criteria consistent with the Modeling of Immunization Registry Operations Work Group managing active patient status guidance were applied to retrospectively classify likely active patient status to patients in the IIS for each assessment year. Finally, vaccination coverage for Guam is assessed via the National Immunization Survey and was not included in this analysis. Differences in vaccination coverage estimation methods might mean that results are not directly comparable with IIS-based estimates for the other USAPI presented in this report.

Implications for Public Health Practice

Only two of the five USAPI have met or are on track to meet the WHO 2030 goal of ≥90% completion of the HPV vaccination series among girls by age 15 years. Identifying and implementing evidence-based strategies to increase vaccine access and coverage would benefit jurisdictions with lagging coverage. The USAPI immunization programs partner with various international governmental, nongovernmental, and academic organizations on immunization and comprehensive cancer control initiatives. Vaccination coverage data can support development of their activities by providing performance indicators and data for modeling health outcomes related to HPV vaccination, promoting health equity, and attaining the WHO 2030 goal of 90% HPV vaccination series completion coverage.

Acknowledgments

Peter Judicpa, Michelle Ruslavage, Alex Turner, CDC; Carter Apaisam, Midion Neth, Jr., Federated States of Micronesia Department of Health and Social Affairs; Merlyn Basilius, Landon Decherong, Palau Ministry of Health and Human Services; Silimusa Masui, Yolanda Masunu, American Samoa Department of Health; Shaun Kileleman, Heather Pangelinan, Emman Parian, Cyji Tenorio, Commonwealth Healthcare Corporation; Edlen Anzures, Daisy Pedro, Marshall Islands Ministry of Health.

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All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. No potential conflicts of interest were disclosed.

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Standing orders for other vaccines are available at www.immunize.org/standing-orders. NOTE: This standing orders template may be adapted per a practice's discretion without obtaining permission from Immunize.org. As a courtesy, please acknowledge Immunize.org as its source.

STANDING ORDERS FOR
Administering Human Papillomavirus Vaccine to Children and Teens

Purpose

To reduce morbidity and mortality from human papillomavirus (HPV) infection by vaccinating all children and teens who meet the criteria established by the Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices (ACIP).

Policy

Where allowed by state law, standing orders enable eligible nurses, pharmacists, and other healthcare professionals to assess the need for and vaccinate children and teens who meet any of the criteria below.

Procedure

1 Assess children and teens for need of vaccination against human papillomavirus infection based on the following criteria:

- Age 11 or 12 years (may start at age 9 or 10, if preferred)
- Age 13 through 26 years who have not completed an HPV vaccination series
- Age 9 years and older with any history of sexual abuse or assault

2 Screen for contraindications and precautions

Contraindication

Do not give HPV vaccine to a child or teen who has experienced a serious systemic or anaphylactic reaction to a prior dose of HPV vaccine or to any of its components (e.g., yeast). For information on vaccine components, refer to the manufacturers' package insert (www.fda.gov/vaccines-blood-biologics/vaccines/vaccines-licensed-use-united-states) or go to www.cdc.gov/vaccines/pubs/pinkbook/downloads/appendices/B/excipient-table-2.pdf.

Precaution

Moderate or severe acute illness with or without fever

Pregnancy

Delay vaccination until after completion of the pregnancy.

3 Provide Vaccine Information Statements

Provide all patients (or, in the case of minors, their parent, or legal representative) with a copy of the most current federal Vaccine Information Statement (VIS). Provide non-English speaking patients with a copy of the VIS in their native language, if one is available and desired; these can be found at www.immunize.org/vis. (For information about how to document that the VIS was given, see section 6 titled "Document Vaccination.")

4 Prepare to Administer Vaccine

Choose the needle gauge, needle length, and injection site according to the following chart:

AGE OF INFANT/CHILD	NEEDLE GAUGE	NEEDLE LENGTH	INJECTION SITE
9 through 10 years	22–25	5/8*–1"	Deltoid muscle of arm**
		1–1¼"	Anterolateral thigh muscle
11 through 18 years	22–25	5/8*–1"	Deltoid muscle of arm**
		1–1½"	Anterolateral thigh muscle

* A 5/8" needle may be used for children for IM injection in the deltoid muscle only if the skin is stretched tight, the subcutaneous tissue is not bunched, and the injection is made at a 90-degree angle.

** Preferred site.

CONTINUED ON THE NEXT PAGE ▶

5 Administer HPV vaccine, 0.5 mL, via the intramuscular (IM) route, according to the following tables:

Schedule for routine vaccination

TYPE OF VACCINE	AGE WHEN FIRST DOSE IS ADMINISTERED[1,2]	DOSE	SCHEDULE
HPV (Gardasil 9)	9 through 14 years	0.5 mL	Two doses, 6–12 months apart[2]
	15 years or older	0.5 mL	Three doses at 0, 1–2, and 6 months

Note: For individuals who failed to complete either the 2-dose or 3-dose schedule as stated above, do not start over. Simply follow the schedule shown below.

Schedule for catch-up vaccination

HISTORY OF PREVIOUS HPV VACCINATION	SCHEDULE FOR ADMINISTRATION OF HPV VACCINE
0 documented doses, or none known	Follow schedule as per above table.
1 previous dose when younger than age 15 years	Give dose #2 with minimum interval of 5 months[2]
2 previous doses given less than 5 months apart and dose #1 given when younger than age 15 years	Give dose #3 with minimum interval of 12 weeks after dose #2 and at least 5 months after dose #1.
1 previous dose when age 15 or older	Give dose #2 at least 4 weeks after dose #1, then give dose #3 at least 12 weeks after dose #2 and at least 5 months after dose #1.
2 previous doses when age 15 or older	Give dose #3 at least 12 weeks after dose #2 and at least 5 months after dose #1.

[1] Only two doses are recommended for anyone who begins the schedule before the 15th birthday, regardless of age at series completion.

[2] Immunocompromised persons, including those with HIV infection, should receive a 3-dose series at 0, 1–2, and 6 months, regardless of age at vaccine initiation.

6 Document Vaccination

Document each patient's vaccine administration information and follow-up in the following places:

Medical record: Record the date the vaccine was administered, the manufacturer and lot number, the vaccination site and route, and the name and title of the person administering the vaccine. You must also document, in the patient's medical record or office log, the publication date of the VIS and the date it was given to the patient. Note that medical records/charts should be documented and retained in accordance with applicable state laws and regulations. If vaccine was not administered, record the reason(s) for non-receipt of the vaccine (e.g., medical contraindication, patient refusal); discuss the need for vaccine with the patient (or, in the case of a minor, their parent or legal representative) at the next visit.

Personal immunization record card: Record the date of vaccination and the name/location of the administering clinic.

Immunization Information System (IIS) or "registry": Report the vaccination to the appropriate state or local IIS, if available.

7 Be Prepared to Manage Medical Emergencies

Be prepared for management of a medical emergency related to the administration of vaccine by having a written emergency medical protocol available, as well as equipment and medications. For Immunize.org's "Medical Management of Vaccine Reactions in Children and Teens in a Community Setting," go to www.immunize.org/catg.d/p3082a.pdf. For "Medical Management of Vaccine Reactions in Adults in a Community Setting," go to www.immunize.org/catg.d/p3082.pdf. To prevent syncope, vaccinate patients while they are seated or lying down and consider observing them for 15 minutes after receipt of the vaccine.

CONTINUED ON THE NEXT PAGE ▶

8 Report Adverse Events to VAERS

Report all adverse events following the administration of HPV vaccine to the federal Vaccine Adverse Event Reporting System (VAERS). To submit a VAERS report online (preferred) or to download a writable PDF form, go to https://www.vaers.hhs.gov/reportevent.html. Further assistance is available at (800) 822-7967.

Standing Orders Authorization

This policy and procedure shall remain in effect for all patients of the _____ (NAME OF PRACTICE OR CLINIC)

effective _____ (DATE) until rescinded or until _____ (DATE).

Medical Director _____ (PRINT NAME) / _____ (SIGNATURE) _____ (DATE)

PREVENTING CHRONIC DISEASE
PUBLIC HEALTH RESEARCH, PRACTICE, AND POLICY
Volume 21, E81 OCTOBER 2024

ORIGINAL RESEARCH

Prevalence of Self-Reported Diagnosed Diabetes Among Adults, by County Metropolitan Status and Region, United States, 2019–2022

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Accessible Version: www.cdc.gov/pcd/issues/2024/24_0221.htm

Suggested citation for this article: Onufrak S, Saelee R, Zaganjor I, Miyamoto Y, Koyama AK, Xu F, et al. Prevalence of Self-Reported Diagnosed Diabetes Among Adults, by County Metropolitan Status and Region, United States, 2019–2022. Prev Chronic Dis 2024;21:240221. DOI: https://doi.org/10.5888/pcd21.240221.

PEER REVIEWED

Summary

What is already known on this topic?

Rural–urban disparities in diabetes mortality, hospitalization, and incidence rates may manifest differently across US regions.

What is added by this report?

We found that the association of metropolitan residence with diabetes prevalence differs across regions of the US. Diabetes prevalence ranged from 7.0% in large fringe metro counties in the Northeast to 14.8% in nonmetro counties in the South.

What are the implications for public health practice?

These findings can help guide efforts in areas where diabetes prevention and care resources may be better directed.

Abstract

Introduction

Previous research suggests that rural–urban disparities in diabetes mortality, hospitalization, and incidence rates may manifest differently across US regions. However, no studies have examined disparities in diabetes prevalence by metropolitan residence and region.

Methods

We used data from the 2019–2022 National Health Interview Survey to compare diabetes status, socioeconomic characteristics, and weight status among adults in each census region (Northeast, Midwest, South, West) according to county metropolitan status of residence (large central metro, large fringe metro, small/medium metro, and nonmetro). We used χ^2 tests and logistic regression models to assess the association of metropolitan residence with diabetes prevalence in each region.

Results

Diabetes prevalence ranged from 7.0% in large fringe metro counties in the Northeast to 14.8% in nonmetro counties in the South. Compared with adults from large central metro counties, those from small/medium metro counties had significantly higher odds of diabetes in the Midwest (age-, sex-, and race and ethnicity–adjusted odds ratio [OR] = 1.24; 95% CI, 1.06–1.45) and South (OR = 1.15; 95% CI, 1.02–1.30). Nonmetro residence was also associated with diabetes in the South (OR = 1.62 vs large central metro; 95% CI, 1.43–1.84). After further adjustment for socioeconomic and body weight status, small/medium metro associations with diabetes became nonsignificant, but nonmetro residence in the South remained significantly associated with diabetes (OR = 1.22; 95% CI, 1.07–1.39).

Conclusion

The association of metropolitan residence with diabetes prevalence differs across US regions. These findings can help to guide efforts in areas where diabetes prevention and care resources may be better directed.

Introduction

Diabetes is a costly chronic disease that shortens lifespans and leads to substantial illness that negatively affects quality of life. In

2021, approximately 8.5% of the US adult population had diagnosed diabetes, although prevalence varied widely among states and territories, ranging from 14.4% in Puerto Rico to 6.5% in Colorado (1). The substantial geographic variation of prevalence estimates may be driven partly by differences in age, race and ethnicity, and socioeconomic status (2). However, other contextual factors such as access to health care, the built environment, behavioral risk factors such as physical inactivity, and cultural elements such as dietary patterns may further affect diabetes prevalence. Rural areas in the US have higher prevalence of obesity (3), heart disease (4), stroke mortality (5), and chronic disease risk factors such as cigarette smoking (6), physical inactivity (7), and poor nutrition (8). Diabetes mortality rates are also higher in rural counties than urban counties and have declined more slowly than in urban counties in recent decades (9).

Rural areas in the US are diverse in terms of land use, employment, and culture. Previous research suggests that rural–urban disparities in diabetes mortality, hospitalization, and incidence rates may manifest differently across different US regions. For example, urban–rural disparities in diabetes mortality rates appear to be greater in the South census region and lesser in the West region compared with the Northeast and Midwest regions (10). Similar patterns have also been observed in diabetes-related hospitalization rates following an emergency department visit (11). Finally, health care data from the Veterans Administration also suggests higher incidence of type 2 diabetes in the rural South and in higher-density urban environments of the Northeast and West than in other areas of the US (12). Although diabetes prevalence is a function of both diabetes incidence (new cases) and mortality (survival of existing cases), no recent studies have examined how disparities of diabetes prevalence according to urban/rural status may vary according to region. Therefore, the purpose of this study was to examine differences in the association of diabetes prevalence and urban/rural status of residence by region, as well as how demographic and socioeconomic factors and weight status may help to explain any observed disparities.

Methods

We used data from the 2019–2022 National Health Interview Survey (NHIS), an annual survey of US households and noninstitutional group quarters (eg, college dormitories, group homes) from the 50 states and the District of Columbia (13). The sample is drawn using a geographically clustered design in a manner such that each month's sample is nationally representative. A sample adult from each household responds to various survey questions regarding health status and behaviors and demographic and socioeconomic characteristics. Most interviews are conducted face-to-face using a computer-aided personal interview, although some interviews are conducted, in part or whole, over the telephone. For 2019–2022, NHIS sample sizes and final response rates for sample adults were 31,997 (59.1%) for 2019; 21,153 (48.9%) for 2020; 29,482 (50.9%) for 2021; and 27,651 (47.7%) for 2022 (13). Participants from the 2019 NHIS who were reinterviewed in 2020 as part of a one-time NHIS longitudinal data collection were only included in the 2019 sample. For the present study, 110,283 participants were included across all years. A total of 725 participants were excluded due to missing data for diabetes status (n = 135), educational attainment (n = 590), sex (n = 9), or a combination of these variables, resulting in a final analytic sample of 109,558.

The primary outcome, diabetes status, was based on self-report of physician diagnosis ascertained with the question, "(Not including gestational diabetes or prediabetes) Has a doctor or other health professional EVER told you that you had diabetes?" The primary predictor variables were region, which was classified according to the US census regions (Northeast, Midwest, South, and West) and metropolitan residence, which was based on the county of residence of the household and serves as a proxy for urban/rural status. Metropolitan residence was classified based on the 6 categories of the 2013 National Center for Health Statistics (NCHS) Urban–Rural Classification Scheme, which are collapsed into 4 categories in NHIS public use data sets: large central metro, large fringe metro, medium and small metro, and nonmetro (includes micropolitan and noncore) (14). Demographic variables were age (18–44 y, 45–64 y, 65–74 y, and ≥75 y), sex (female, male), and race and ethnicity (Hispanic, non-Hispanic [NH] Asian, NH Black, NH White, or NH Other). Socioeconomic status variables were educational attainment (less than high school, high school or equivalent, some college or associate degree, or bachelor's degree and above) and family income-to-poverty ratio (<100%, 100%–199%, 200%–299%, 300%–399%, 400%–499%, or ≥500%), the ratio of annual family income to the poverty threshold for household size. Because of missing or incomplete data on family income, approximately 23% to 24% of family income-to-poverty ratio values for each survey year were replaced with a single imputation provided by NCHS. Body weight status was based on self-reported height and weight and classified according to body mass index (BMI, kg/m^2) as underweight or normal weight (<25.0), overweight (25.0–29.9), obese (≥30.0), or missing.

Statistical analysis

Analysis was conducted using SAS version 9.4 (SAS Institute) with survey procedures to account for sample weights and survey design variables. Significance was set at $P < .05$. Diabetes status, demographic and socioeconomic characteristics, and body weight status were compared within each region according to metropolitan residence using the Rao-Scott F-adjusted χ^2 test. Odds ratios

(ORs) with 95% CIs from logistic regression models were used to assess the association between metropolitan residence and diabetes prevalence within each region. In all models, the interaction between region and metropolitan residence was tested using type 3 analysis of effects F-test, and a SLICE statement was used to perform a partitioned analysis to estimate the effect of metropolitan residence on diabetes prevalence within each region. In addition to region and metropolitan residence, the first model also included age, sex, and race and ethnicity as covariates. The second model additionally included income-to-poverty ratio and educational attainment, and the third model included variables from the second model plus body weight status.

Results

Age differed significantly by metropolitan residence for all regions, with large central and fringe metro counties containing a younger population compared with nonmetro counties (Table 1a and Table 1b). Race and ethnicity distribution also differed according to metropolitan residence across all regions, with NH White adults constituting most (≥71%) residents of nonmetro areas in every region. For all regions, educational attainment was lower among adults from nonmetro counties compared with those from large metro counties. Income and body weight status also differed by metropolitan residence across all regions, with residents from nonmetro counties having lower incomes and greater prevalence of obesity.

Unadjusted diabetes prevalence differed by metropolitan residence in the Northeast and South, with prevalence highest among adults residing in nonmetro counties and lowest among those in large fringe metro counties (Figure). Unadjusted diabetes prevalence among adults from nonmetro counties ranged from 9.0% (95% CI, 7.0%–11.1%) in the West to 14.8% (95% CI, 13.5%–16.1%) in the South.

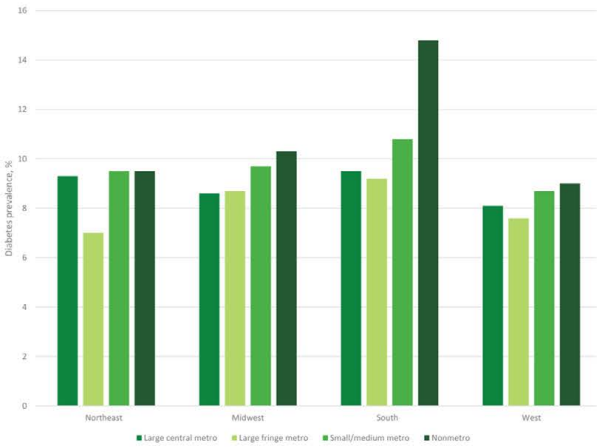

Figure. Unadjusted prevalence of self-reported diagnosed diabetes according to US census region and metropolitan status of county of residence, United States, 2019–2022.

A significant interaction was detected between region and metropolitan residence in the logistic regression model adjusting for age, sex, and race and ethnicity ($P = .01$, Table 2). Compared with adults from large central metro counties, those from small/medium metro counties had significantly higher odds of diabetes in both the Midwest (OR = 1.24; 95% CI, 1.06–1.45) and South (OR = 1.15; 95% CI, 1.02–1.30). In the South region only, adults from nonmetro counties had significantly higher odds of diabetes compared with those from large central metro counties (OR = 1.62; 95% CI, 1.43–1.84). After further adjustment for socioeconomic status variables, the interaction between region and metropolitan residence remained significant ($P = .01$) and small/medium metro counties had significantly higher odds of diabetes only in the Northeast (OR = 1.16; 95% CI, 1.00–1.34). Nonmetro county residence remained significantly associated with diabetes in the South (OR = 1.30; 95% CI, 1.15–1.47). After further adjustment for body weight status, this interaction remained significant and only nonmetro county residence in the South remained significantly associated with diabetes (OR = 1.22; 95% CI, 1.07–1.39).

Discussion

The results of our study suggest that the association of metropolitan status with diabetes prevalence is not homogenous across the US. Rather, the highest unadjusted prevalence of diabetes was observed among adults residing in nonmetro counties in the South (14.8%). The odds of having diabetes were 62% higher among Southern nonmetro residents compared with those from large central metro counties after adjustment for age, sex, and race and eth-

nicity, and this association remained significant, though reduced, after further adjustment for income, education, and body weight status. By contrast, residence in nonmetro counties in other regions of the US was not associated with higher odds of diabetes. Higher odds of diabetes were also observed among residents of small and medium metro counties in the Northeast, Midwest, and South as compared with large metro counties within their respective regions, although these associations became nonsignificant after further adjustment for income, education, and body weight status.

Numerous disparities in health (15,16), health behaviors (6,17), socioeconomic status (18), and access to health care (19) have been reported among those living in rural areas. However, relatively fewer studies have examined how rural health disparities may differ across regions of the US. Although all rural, nonmetro counties in the US typically share characteristics such as lower population density and distance from large metropolitan areas, they may differ in terms of racial and ethnic distribution, socioeconomic status, the environment, and economy. For example, although nonmetro counties across every region have larger proportions of non-Hispanic White residents compared with large metro counties, Southern and Western nonmetro counties have smaller majorities of non-Hispanic White residents with greater proportions of Black residents in the South and Hispanic, Asian, and NH Other residents in the West (20). Furthermore, although rural–urban disparities in poverty and educational attainment are observed across all US regions, they manifest more severely in the rural South. Similar patterns in race and ethnicity, poverty, and educational attainment across region and metropolitan status were observed in our study. However, controlling for these variables in multivariable models did not fully explain the association of nonmetro county status with greater diabetes prevalence in the South. Regarding environment and economy, nonmetro counties can vary from those with tourist economies based on natural amenities such as mountains and lakes, to agricultural areas where cultivated fields or range land stretch for large distances, to places where mining or manufacturing is the key economic activity (19). These differences in environment and economy may further affect employment opportunities and commuting distances, access to health care, the retail food environment, and opportunities for physical activity (19). Unfortunately, exploring the potential effect of these environmental and economic contextual factors was not possible in this study because these data are not available in the NHIS data set.

This finding of elevated diabetes prevalence in the nonmetro South is consistent with research regarding diabetes mortality rates (10), diabetes incidence among the Veterans Administration patient population (12), and hospitalization rates following diabetes-related emergency department visits (11). Furthermore, the Southeastern region has long been designated as the "stroke belt" due to elevated stroke mortality rates observed since the middle of the 20th century, and stroke incidence has been observed to be particularly high among nonmetro areas in the South (21). Likewise, more recent research using Bayesian multilevel modeling of Behavioral Risk Factor Surveillance System data has also proposed a "diabetes belt" that occurs in the South (22). The factors contributing to the elevated prevalence of stroke and diabetes in the rural South are not entirely understood (21,22) but could include greater prevalence of risk factors such as lower socioeconomic status, obesity (3), poor diet (23), and insufficient physical activity (7). Although the association of diabetes with nonmetro county residence in the South was attenuated when we controlled for age, race and ethnicity, socioeconomic status, and body weight status, these factors did not entirely explain the association. Unfortunately, we were not able to assess whether physical activity or dietary quality explained the increased prevalence because data on these variables were not available for the entirety of the study period. However, in previous research by Barker et al regarding the "diabetes belt," sociodemographic factors, body weight status, and sedentary lifestyle did not fully account for increased diabetes prevalence observed (22). Some literature also suggests that other unmeasured social factors such as discrimination and institutional racism could help explain the increased prevalence in the rural South, but information on these factors was also unavailable in our data (24). Finally, higher diabetes prevalence in the nonmetro South may also be linked to limited health insurance access among low-income populations, who are disproportionately concentrated there. As of May 2024, 7 of the 10 states that have not adopted Medicaid expansion under the Affordable Care Act to cover adults with incomes up to 138% of the poverty line are in the South census region (25). However, data on state of residence is unavailable in public use data, so we were unable to assess the potential impact of state Medicaid eligibility criteria on the results.

We also observed greater prevalence of diabetes among adults living in small and medium metro counties in the Midwest and South. However, our results suggest that this increased prevalence was largely explained by disparities in socioeconomic status, as these associations became nonsignificant when we controlled for income and education and further attenuated when we controlled for body weight status. Smaller cities in the Midwest and South, particularly those reliant on manufacturing, have been disrupted in recent decades by foreign trade and automation and have seen slower growth in employment and income compared with larger cities (26). We also observed a significant association of small and medium metro residence with diabetes in the Northeast after con-

trolling for socioeconomic status, although the odds ratio remained of similar magnitude as in the previous model. This association may have been due to increased prevalence of risk factors such as body weight status, as the association became insignificant and attenuated after controlling for this variable.

Our study has several limitations. We relied on self-report of diabetes, which may be subject to misclassification; self-report also does not capture undiagnosed diabetes, which may occur more frequently among people without sufficient access to health care such as in nonmetro areas, although research suggests that diabetes screening rates are similar in urban and rural counties (27). Furthermore, we did not have adequate data on physical activity, dietary intake, or distance from health care resources, which could help elucidate potential mechanisms by which metropolitan residence could be associated with diabetes. Nonetheless, the large sample size allowed us to examine how the association of metropolitan residence with diabetes differs across US regions. In addition, our use of county metropolitan status as a proxy measure for rurality may limit the generalizability of the results since counties across metropolitan status categories may contain both urban and rural places and populations (28).

In conclusion, we found that the association of metropolitan residence with diabetes prevalence differs across regions of the US. These findings can help to guide efforts in areas where diabetes prevention and care resources may be better directed. Future research on rural–urban health disparities may consider examining how these disparities differ across US regions.

Acknowledgments

The authors received no external financial support for the research, authorship, or publication of this article. The authors declare no potential conflicts of interest with respect to the research, authorship, or publication of this article. No copyrighted material, surveys, instruments, or tools were used in this research. 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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Tables

Table 1a. Demographic Characteristics of Adults, by Region and County Metropolitan Status, US Northeast and Midwest Regions, National Health Interview Survey, 2019–2022

Characteristic	Northeast (n = 18,461), % (95% CI)				Midwest (n = 24,081), % (95% CI)			
	Large central metro (n = 5,250)	Large fringe metro (n = 6,788)	Small/ medium metro (n = 5,005)	Nonmetro (n = 1,418)	Large central metro (n = 5,110)	Large fringe metro (n = 6,005)	Small/ medium metro (n = 7,180)	Nonmetro (n = 5,786)
Age, y								
18–44	48.0 (45.8–50.2)	43.0 (41.3–44.6)	40.3 (38.3–42.3)	36.6 (33.5–39.7)	50.8 (48.8–52.8)	44.6 (42.8–46.3)	48.4 (45.8–50.9)	37.8 (35.9–39.7)
45–64	31.4 (29.9–32.9)	34.1 (32.9–35.3)	35.1 (33.5–36.7)	36.1 (33.8–38.4)	30.7 (28.9–32.5)	34.2 (32.7–35.7)	30.2 (28.3–32.1)	34.7 (33.3–36.1)
65–74	12.1 (11.1–13.2)	13.3 (12.5–14.1)	14.5 (13.0–16.1)	16.5 (15.3–17.7)	11.7 (10.7–12.7)	12.8 (11.8–13.7)	12.6 (11.8–13.5)	15.4 (14.5–16.4)
≥75	8.5 (7.5–9.4)	9.7 (8.9–10.4)	10.1 (9.3–10.9)	10.7 (9.0–12.5)	6.9 (6.1–7.7)	8.5 (7.5–9.5)	8.8 (7.9–9.7)	12.1 (11.0–13.2)
Sex								
Female	51.9 (50.1–53.6)[a]	51.1 (49.6–52.6)[a]	51.8 (50.0–53.6)[a]	51.0 (46.4–55.6)[a]	51.1 (49.6–52.6)[a]	52.0 (50.4–53.5)[a]	51.5 (49.9–53.1)[a]	50.2 (48.2–52.1)[a]
Male	48.1 (46.4–49.9)[a]	48.9 (47.4–50.4)[a]	48.2 (46.4–50.0)[a]	49.0 (44.4–53.6)[a]	48.9 (47.4–50.4)[a]	48.0 (46.5–49.5)[a]	48.5 (46.9–50.1)[a]	49.8 (47.9–51.8)[a]
Race and ethnicity								
Hispanic	19.9 (16.3–23.5)	11.1 (8.8–13.4)	8.9 (6.7–11.1)	2.8 (0.1–5.5)	11.5 (8.9–14.1)	6.8 (5.0–8.5)	6.7 (4.4–9.0)	3.0 (2.0–4.0)
Non-Hispanic Asian	13.1 (10.6–15.6)	7.2 (6.1–8.2)	3.1 (2.0–4.1)	1.1 (0.6–1.7)	5.3 (4.3–6.4)	3.7 (2.9–4.6)	2.8 (2.0–3.5)	0.9 (0.5–1.3)
Non-Hispanic Black	19.9 (17.1–22.7)	6.3 (4.6–8.0)	6.0 (4.2–7.8)	1.2 (0.4–1.9)	18.5 (15.9–21.1)	6.3 (4.9–7.7)	6.7 (5.6–7.8)	1.8 (0.7–2.9)
Non-Hispanic White	45.7 (39.1–52.3)	74.2 (70.9–77.4)	80.8 (76.7–85.0)	92.9 (89.4–96.5)	62.8 (59.1–66.5)	81.2 (78.7–83.8)	80.8 (77.9–83.7)	91.8 (89.8–93.9)
Non-Hispanic Other	1.4 (1.0–1.8)	1.3 (0.9–1.6)	1.3 (0.8–1.7)	2.0 (1.2–2.7)	1.9 (1.3–2.4)	2.0 (1.5–2.5)	3.0 (2.4–3.6)	2.5 (1.5–3.5)
Education level								
Less than high school	12.1 (9.7–14.4)	7.3 (6.2–8.4)	8.6 (7.2–10.0)	10.0 (7.2–12.8)	9.0 (7.5–10.4)	6.0 (5.0–7.0)	8.2 (6.6–9.8)	11.1 (8.9–13.3)
High school diploma/GED	26.0 (24.2–27.9)	26.0 (24.3–27.7)	31.4 (28.4–34.4)	34.8 (30.0–39.5)	22.2 (20.4–23.9)	26.9 (25.3–28.5)	30.9 (28.1–33.8)	37.9 (35.0–40.8)
Some college/associate degree	22.9 (20.9–24.9)	25.5 (24.1–26.8)	26.9 (25.0–28.8)	31.2 (27.5–34.9)	28.3 (26.6–30.0)	31.3 (29.6–33.0)	31.8 (29.9–33.6)	31.9 (29.7–34.2)
Bachelor's degree or higher	39.0 (36.6–41.3)	41.3 (39.0–43.6)	33.1 (29.4–36.7)	24.0 (18.5–29.5)	40.6 (38.1–43.1)	35.8 (33.3–38.3)	29.2 (25.4–32.9)	19.1 (16.9–21.2)
Family income-to-poverty ratio, %								
<100	13.5 (11.4–15.5)	5.0 (4.1–5.8)	7.7 (6.3–9.1)	10.4 (7.4–13.3)	10.8 (9.3–12.3)	5.2 (4.3–6.0)	10.0 (8.5–11.6)	10.2 (8.2–12.3)
100–199	18.4 (16.3–20.4)	12.2 (10.8–13.5)	15.5 (13.5–17.6)	20.0 (16.4–23.5)	16.9 (15.3–18.5)	12.1 (10.8–13.4)	17.0 (15.4–18.7)	21.1 (19.3–22.8)

Abbreviation: GED, general educational development.
[a] Not significant according to χ^2 test ($P > .05$). All other values significant at $P < .05$ of characteristic differing according to county metropolitan status within region.

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Table 1a. Demographic Characteristics of Adults, by Region and County Metropolitan Status, US Northeast and Midwest Regions, National Health Interview Survey, 2019–2022

Characteristic	Northeast (n = 18,461), % (95% CI)				Midwest (n = 24,081), % (95% CI)			
	Large central metro (n = 5,250)	Large fringe metro (n = 6,788)	Small/ medium metro (n = 5,005)	Nonmetro (n = 1,418)	Large central metro (n = 5,110)	Large fringe metro (n = 6,005)	Small/ medium metro (n = 7,180)	Nonmetro (n = 5,786)
200–299	14.6 (13.5–15.8)	12.1 (11.1–13.2)	16.1 (14.3–18.0)	18.1 (16.0–20.3)	15.4 (14.0–16.8)	14.8 (13.4–16.2)	18.0 (16.9–19.1)	20.1 (18.7–21.5)
300–399	11.5 (10.3–12.7)	12.6 (11.5–13.6)	14.3 (13.1–15.5)	15.2 (12.2–18.2)	11.9 (10.8–13.1)	15.0 (14.0–16.0)	15.3 (14.3–16.3)	16.6 (15.4–17.8)
400–499	9.2 (7.9–10.6)	11.7 (10.7–12.8)	12.1 (10.6–13.6)	12.2 (10.0–14.4)	10.5 (9.6–11.3)	14.2 (13.1–15.2)	12.5 (11.6–13.5)	13.1 (11.7–14.5)
≥500	32.8 (30.1–35.4)	46.4 (44.1–48.8)	34.2 (31.0–37.5)	24.1 (18.3–30.0)	34.5 (32.0–37.0)	38.8 (36.0–41.5)	27.1 (24.5–29.7)	18.9 (16.7–21.1)
Body weight status								
Underweight/normal weight	36.5 (34.8–38.3)	35.9 (34.3–37.4)	32.3 (29.8–34.8)	28.5 (25.8–31.3)	34.5 (32.7–36.4)	32.8 (32.2–34.3)	30.3 (28.5–32.1)	26.2 (24.5–27.8)
Overweight	33.7 (32.3–35.1)	35.1 (33.6–36.7)	33.3 (31.8–34.8)	30.4 (27.9–32.8)	35.0 (33.4–36.5)	32.6 (31.1–34.1)	31.5 (30.3–32.7)	32.4 (30.6–34.2)
Obese	26.3 (24.8–27.9)	26.2 (24.3–28.0)	31.3 (28.9–33.6)	38.1 (35.1–41.1)	28.5 (26.3–30.7)	32.6 (30.8–34.3)	36.0 (34.3–37.7)	39.0 (37.3–40.6)
Missing	3.5 (2.8–4.2)	2.8 (2.2–3.5)	3.1 (2.4–3.8)	3.0 (1.9–4.2)	2.0 (1.4–2.5)	2.1 (1.6–2.6)	2.2 (1.6–2.9)	2.4 (1.8–3.0)

Abbreviation: GED, general educational development.
[a] Not significant according to χ^2 test ($P > .05$). All other values significant at $P < .05$ of characteristic differing according to county metropolitan status within region.

Table 1b. Demographic Characteristics of Adults, by Region and County Metropolitan Status, US South and West Regions, National Health Interview Survey, 2019–2022

Characteristic	South (n = 39,671), % (95% CI)				West (n = 27,345), % (95% CI)			
	Large central metro (n = 10,167)	Large fringe metro (n = 9,572)	Small/ medium metro (n = 13,108)	Nonmetro (n = 6,824)	Large central metro (n = 12,056)	Large fringe metro (n = 3,434)	Small/ medium metro (n = 9,291)	Nonmetro (n = 2,564)
Age, y								
18–44	52.0 (50.4–53.7)	45.2 (43.8–46.6)	43.7 (41.9–45.6)	36.4 (36.0–40.7)	50.4 (49.0–51.8)	49.0 (46.3–51.8)	47.2 (44.2–50.3)	40.9 (36.8–44.9)
45–64	30.5 (29.1–31.9)	33.8 (32.6–35.0)	32.4 (31.3–33.6)	34.5 (33.0–36.0)	31.1 (29.9–32.3)	30.9 (28.9–32.8)	30.2 (28.5–32.0)	34.5 (31.9–37.2)
65–74	10.4 (9.7–11.2)	12.6 (11.8–13.3)	13.9 (13.0–14.8)	15.8 (14.5–17.1)	10.6 (9.9–11.3)	11.7 (10.7–12.8)	13.8 (12.5–15.1)	15.3 (13.3–17.4)
≥75	7.0 (6.4–7.7)	8.4 (7.7–9.1)	10.0 (9.1–10.9)	11.3 (10.2–12.5)	7.9 (7.3–8.5)	8.4 (6.9–9.8)	8.7 (7.8–9.6)	9.3 (8.0–10.6)
Sex								
Female	52.3 (51.2–53.4)	51.2 (50.1–52.4)	53.7 (52.6–54.8)	53.4 (52.0–54.8)	49.8 (48.8–50.8)[a]	51.3 (49.2–53.4)[a]	51.1 (50.0–52.2)[a]	50.9 (48.1–53.7)[a]
Male	47.7 (45.6–48.8)	48.8 (47.6–49.9)	46.3 (45.2–47.4)	46.6 (45.2–48.0)	50.2 (49.2–51.2)[a]	48.7 (46.6–50.8)[a]	48.9 (47.8–50.0)[a]	49.1 (46.3–51.9)[a]
Race and ethnicity								
Hispanic	29.4 (24.9–33.9)	14.5 (12.2–16.7)	13.4 (8.4–18.4)	8.2 (1.5–14.9)	33.1 (29.8–36.4)	25.8 (20.0–31.6)	26.6 (20.2–32.9)	11.5 (6.6–13.3)
Non-Hispanic Asian	5.8 (4.9–6.7)	6.6 (5.3–7.9)	1.6 (1.3–2.0)	0.6 (0.4–0.8)	15.7 (13.4–17.9)	9.2 (7.2–11.3)	6.5 (3.4–9.7)	2.5 (0.1–4.9)
Non-Hispanic Black	22.7 (19.8–25.7)	18.3 (15.5–21.1)	18.8 (15.6–22.1)	15.4 (10.5–20.3)	5.7 (4.8–6.6)	5.4 (4.4–6.5)	2.2 (1.4–2.9)	0.5 (0.1–0.8)
Non-Hispanic White	40.2 (33.4–43.9)	58.6 (55.1–62.1)	63.9 (59.4–68.4)	71.6 (64.4–78.8)	42.6 (38.9–46.3)	56.1 (49.6–62.7)	60.6 (53.3–67.9)	72.0 (55.5–88.5)
Non-Hispanic Other	1.9 (1.5–2.3)	2.0 (1.5–2.4)	2.2 (1.5–3.0)	4.2 (1.9–6.4)	3.0 (2.5–3.4)	3.4 (2.6–4.2)	4.2 (3.0–5.4)	13.6 (0.0–29.9)
Education level								
Less than high school	13.2 (11.7–14.6)	9.4 (8.4–10.4)	12.7 (11.2–14.2)	19.3 (17.0–21.7)	12.2 (10.9–13.5)	10.1 (7.6–12.6)	12.5 (9.7–15.3)	13.1 (9.9–16.2)
High school diploma/GED	24.6 (22.9–26.4)	25.2 (23.6–26.8)	31.4 (29.8–33.0)	36.0 (34.1–37.9)	22.5 (20.9–24.0)	23.2 (21.5–25.0)	25.3 (23.0–27.6)	31.6 (28.9–34.3)
Some college/associate degree	26.3 (25.0–27.7)	29.4 (27.7–31.0)	30.6 (29.3–32.0)	28.9 (26.8–31.0)	28.2 (26.8–29.5)	32.3 (29.5–35.2)	34.9 (32.8–37.0)	34.7 (31.6–37.9)
Bachelor's degree or higher	35.9 (33.1–38.7)	36.0 (33.4–38.6)	25.3 (23.5–27.1)	15.8 (13.9–17.7)	37.2 (34.5–39.9)	34.3 (30.8–37.9)	27.3 (24.3–30.3)	20.6 (15.4–25.8)
Family income-to-poverty ratio, %								
<100	12.2 (10.9–13.5)	7.0 (6.2–7.9)	12.9 (11.4–14.5)	17.3 (14.8–19.8)	8.9 (7.9–9.8)	7.0 (5.8–8.1)	9.9 (8.2–11.5)	12.8 (6.4–19.3)
100–199	19.4 (17.9–20.9)	14.7 (13.2–16.3)	21.8 (20.6–23.0)	26.7 (25.3–28.2)	16.9 (15.4–18.4)	14.5 (12.2–16.7)	19.0 (17.2–20.9)	20.1 (17.0–23.2)
200–299	17.0 (15.9–18.2)	15.6 (14.3–16.8)	17.5 (16.6–18.5)	19.8 (18.5–21.1)	15.2 (14.1–16.2)	16.1 (14.3–18.0)	17.8 (16.6–19.1)	19.2 (17.1–21.4)

Abbreviation: GED, general educational development.
[a] Not significant according to χ^2 test ($P > .05$). All other values significant at $P < .05$ of characteristic differing according to county metropolitan status within region.

(continued on next page)

(continued)

Table 1b. Demographic Characteristics of Adults, by Region and County Metropolitan Status, US South and West Regions, National Health Interview Survey, 2019–2022

Characteristic	South (n = 39,671), % (95% CI)				West (n = 27,345), % (95% CI)			
	Large central metro (n = 10,167)	Large fringe metro (n = 9,572)	Small/ medium metro (n = 13,108)	Nonmetro (n = 6,824)	Large central metro (n = 12,056)	Large fringe metro (n = 3,434)	Small/ medium metro (n = 9,291)	Nonmetro (n = 2,564)
300–399	12.0 (11.1–12.8)	13.9 (12.9–14.9)	13.6 (12.8–14.3)	12.6 (11.4–13.8)	12.5 (11.7–13.4)	13.8 (11.9–15.6)	14.1 (12.9–15.2)	13.4 (10.8–16.0)
400–499	9.9 (9.1–10.8)	12.0 (11.0–12.9)	11.1 (10.4–11.8)	9.5 (8.4–10.6)	9.7 (8.9–10.5)	11.2 (9.7–12.7)	11.6 (10.6–12.6)	9.9 (7.7–12.1)
≥500	29.5 (27.0–32.0)	36.8 (34.1–39.5)	23.1 (21.3–24.9)	14.1 (12.7–15.5)	36.8 (34.2–39.3)	37.4 (33.4–41.4)	27.6 (24.6–30.5)	24.5 (17.5–31.5)
Body weight status								
Underweight/normal weight	33.1 (31.7–34.6)	32.8 (31.5–34.1)	28.4 (27.2–29.5)	26.0 (24.3–27.6)	38.6 (37.2–40.0)	33.3 (30.9–35.6)	34.1 (32.1–36.1)	31.2 (25.7–36.7)
Overweight	33.2 (31.9–34.5)	33.2 (31.9–34.5)	32.7 (31.6–33.8)	31.0 (29.7–32.3)	33.6 (32.5–34.7)	34.8 (32.6–36.9)	33.4 (32.1–34.7)	31.7 (29.4–34.0)
Obese	31.1 (29.7–32.4)	31.8 (30.5–33.1)	36.5 (35.1–37.9)	40.9 (39.1–42.7)	25.8 (24.3–27.2)	30.1 (27.6–36.7)	30.4 (29.0–31.9)	35.1 (28.6–41.5)
Missing	2.6 (2.2–3.0)	2.2 (1.8–2.6)	2.4 (2.0–2.9)	2.1 (1.6–2.6)	2.0 (1.7–2.4)	1.8 (1.3–2.4)	2.0 (1.5–2.5)	2.0 (1.3–2.8)

Abbreviation: GED, general educational development.
[a] Not significant according to χ^2 test ($P > .05$). All other values significant at $P < .05$ of characteristic differing according to county metropolitan status within region.

Table 2. Association Between County Metropolitan Status and Prevalence of Self-Reported Diagnosed Diabetes, by US Census Region, National Health Interview Survey, 2019–2022

Census region	Large fringe metro	Small/medium metro	Nonmetro
	Odds ratio[a] (95% CI)		
Model 1[b]			
Northeast	0.84 (0.72–0.99)[c]	1.15 (0.99–1.34)	1.18 (0.95–1.45)
Midwest	1.04 (0.87–1.25)	1.24 (1.06–1.45)[c]	1.17 (0.97–1.40)
South	0.97 (0.86–1.11)	1.15 (1.02–1.30)[c]	1.62 (1.43–1.84)[c]
West	1.00 (0.84–1.19)	1.13 (0.98–1.30)	1.16 (0.90–1.48)
Model 2[b]			
Northeast	0.91 (0.78–1.07)	1.16 (1.00–1.34)[c]	1.05 (0.89–1.25)
Midwest	1.05 (0.88–1.26)	1.15 (0.99–1.34)	0.99 (0.82–1.20)
South	1.00 (0.88–1.13)	1.05 (0.94–1.18)	1.30 (1.15–1.47)[c]
West	1.00 (0.85–1.17)	1.06 (0.93–1.21)	1.00 (0.79–1.26)
Model 3[b]			
Northeast	0.90 (0.76–1.06)	1.10 (0.95–1.28)	0.94 (0.79–1.12)
Midwest	1.00 (0.83–1.20)	1.06 (0.92–1.23)	0.89 (0.74–1.07)
South	0.99 (0.87–1.12)	1.00 (0.89–1.13)	1.22 (1.07–1.39)[c]
West	0.95 (0.80–1.12)	1.04 (0.91–1.19)	0.94 (0.77–1.16)

[a] Odds ratios and confidence intervals shown for each model reflect parameterization of region and metropolitan status main effect coefficients and corresponding interaction terms. Estimates represent the association of metropolitan residence and diabetes prevalence within each region. Model 1 joint interaction, $P = .002$; model 2 joint interaction, $P = .01$; model 3 joint interaction, $P = .008$.
[b] Model 1 adjusted for age, sex, and race and ethnicity; model 2 adjusted for model 1 covariates plus income-to-poverty ratio and educational attainment; model 3 adjusted for model 2 covariates plus body weight status; reference group for each region is large central metro.
[c] $P < .05$.

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National Institutes of Health
Turning Discovery Into Health

October 8, 2024

How heat from fever and inflammation affects immune cells

At a Glance

- Scientists showed that fever temperatures boost activity in certain immune cells but also promote DNA damage.
- The findings suggest how chronic inflammation might contribute to cancer risk.

Fever raises the temperature of the body, and local inflammation can raise the temperature of surrounding tissues. But it's not clear how these temperature changes affect the immune cells that fight infection and mediate inflammation. Among the most critical cells in the immune response are T cells. A variety of T cell types with different functions help recognize pathogens, control inflammation, and kill infected cells.

Fevers may help us fight disease, but might also contribute to cancer risk. *Lightfield Studios / Adobe Stock*

A team of researchers, led by Dr. Jeffrey Rathmell at Vanderbilt University Medical Center, carefully examined how higher temperatures affect T cells. The results of the study, which was funded in part by NIH, appeared in *Science Immunology* on September 20, 2024.

The team cultured mouse T cells at a normal body temperature (37 °C or 98.6 °F) and at fever temperature (39 °C or 102.2 °F). At the higher temperature, T helper cells, which direct other immune cells by releasing signaling molecules called cytokines, produced more cytokines than at the lower temperature. At the same time, regulatory T cells, which suppress immune responses, were less effective at the higher temperature. All the types of T cells evaluated proliferated more at the higher temperature. These led to an enhanced inflammatory state at fever temperature.

Higher temperatures also enhanced metabolism in various types of T cells. The exception was in the T helper 1 (T_H1) cell subset, whose metabolic rate was largely unaffected. T_H1 cells developed stress and DNA damage at high temperature, making them less likely to survive. Those that did survive, however, had more mitochondria—the energy-generating compartments of the cell—and greater activity.

Further experiments showed that higher temperatures impaired a protein called electron transport chain complex 1 (ETC1) in T_H1 cells. ETC1 is part of the process by which mitochondria convert fuel to energy. Impairing ETC1 led to formation of reactive byproducts, mitochondrial stress, and DNA damage. In response, the cells activated mechanisms to repair DNA or, failing that, to self-destruct.

The team wanted to find out if these results were relevant to human inflammation. They examined sequencing data from patients with Crohn's disease and rheumatoid arthritis, two inflammatory autoimmune diseases. They found signs of increased DNA damage and ETC1 impairment in T_H1 cells like they saw in the cultured cells.

These findings suggest how fever and inflammation can enhance the immune response, but also increase DNA damage. DNA damage results in mutations when the damage isn't properly repaired. This could explain why chronic inflammation increases the risk of cancer.

"People ask me, 'Is fever good or bad?'" Rathmell says. "The short answer is, a little bit of fever is good, but a lot of fever is bad. We already knew that, but now we have a mechanism for why it's bad."

—by Brian Doctrow, Ph.D.

References: Subset-specific mitochondrial stress and DNA damage shape T cell responses to fever and inflammation. Heintzman DR, Sinard RC, Fisher EL, Ye X, Patterson AR, Elasy JH, Voss K, Chi C, Sugiura A, Rodriguez-Garcia GJ, Chowdhury NU, Arner EN, Krystoviak ES, Mason FM, Toudji YT, Steiner KK, Khan W, Olson LM, Jones AL, Hong HS, Bass L, Beier KL, Deng W, Lyssiotis CA, Newcomb DC, Bick AG, Rathmell WK, Wilson JT, Rathmell JC. *Sci Immunol*. 2024 Sep 20;9(99):eadp3475. doi: 10.1126/sciimmunol.adp3475. Epub 2024 Sep 20. PMID: 39303018.

Funding: NIH's National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Heart, Lung, and Blood Institute (NHLBI), National Cancer Institute (NCI), National Institute of Allergy and Infectious Diseases (NIAID), National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), and National Eye Institute (NEI); Lupus Research Alliance; Waddell Walker Hancock Cancer Discovery Fund; National Science

Source: https://www.nih.gov/news-events/nih-research-matters/how-heat-fever-inflammation-affects-immune-cells

PREVENTING CHRONIC DISEASE
PUBLIC HEALTH RESEARCH, PRACTICE, AND POLICY
Volume 21, E32 MAY 2024

GIS SNAPSHOTS

Geographic Disparities in Cancer Incidence in the US Population Aged 20 to 49 Years, 2016–2020

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Accessible Version: www.cdc.gov/pcd/issues/2024/23_0335.htm

Suggested citation for this article: DuBois TD, Henry KA, Siegel SD, Lynch SM. Geographic Disparities in Cancer Incidence in the US Population Aged 20 to 49 Years, 2016–2020. Prev Chronic Dis 2024;21:230335. DOI: https://doi.org/10.5888/pcd21.230335.

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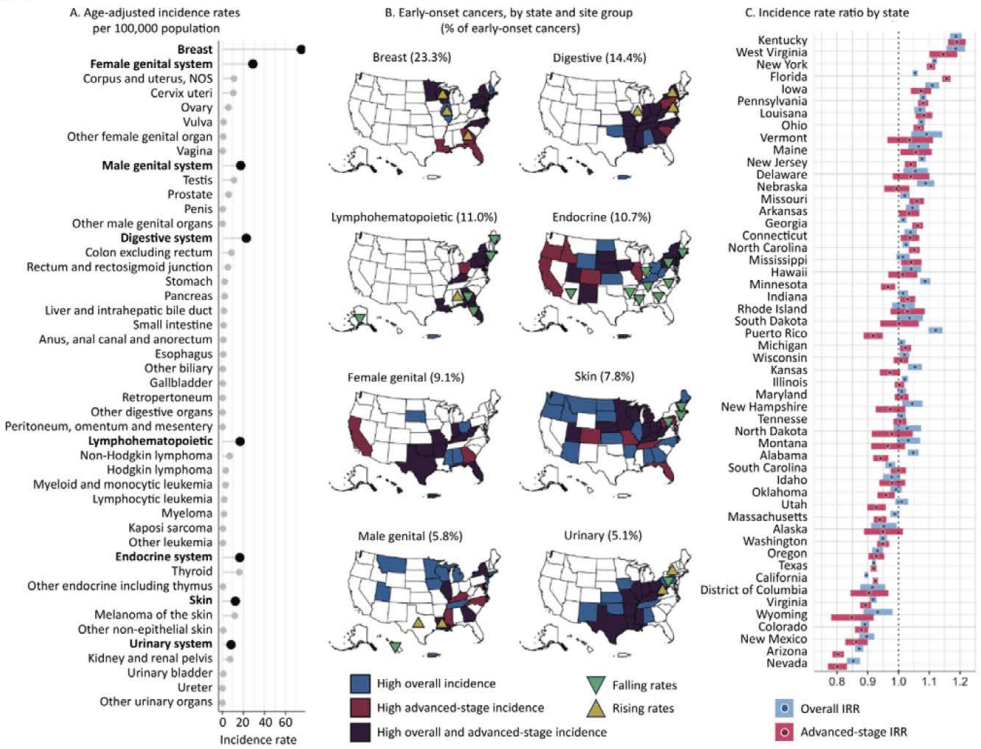

Geographic disparities in cancer incidence in the US population aged 20 to 49 years, 2016–2020. The most prevalent cancer site groups diagnosed among adults aged <50 years are female breast, female genital, male genital, digestive, lymphohematopoietic, endocrine, skin, and urinary. The incidence of early-onset cancers is not distributed evenly across the US. Differing geographic patterns emerge by cancer site group as measured by overall incidence rates, advanced-stage incidence rates, and recent temporal trends. Some states have significantly higher rates of early-onset cancer than the nation overall. In A, dark circles indicate a group of cancer sites; light circles indicate cancer sites within the group. The category Skin excludes basal cell and squamous cell carcinomas. In B, for the male genital group, data on cancer stage were not available for cancer of the testis. In C, shaded bars indicate 95% CIs, and the vertical dashed line indicates the reference group, the US, excluding Puerto Rico. Abbreviations: IRR, incident rate ratio; NOS, not otherwise specified. Data source: Centers for Disease Control and Prevention (1).

Background

A growing awareness of the increase in the incidence of early-onset cancer, defined as cancer diagnosed in adults aged 50 years or younger (2), has prompted researchers to investigate the underlying drivers of this trend (3). These investigations have focused on racial and ethnic disparities (4) and colorectal (5–8) and breast cancers (9,10). The objective of our analysis was to describe the geospatial patterns of states with a high incidence of early-onset cancer. By identifying priority states and cancer types, our analysis can generate hypotheses about drivers of early-onset cancer and guide prevention and screening interventions.

Data and Methods

Data for this analysis are from the US Cancer Statistics Public Use Research Database, provided by the National Program of Cancer Registries and the Surveillance, Epidemiology, and End Results programs (1). The analysis included adults aged 20 to 49 with invasive cancer (excluding in situ cases) diagnosed during the 6-year period from 2015 through 2020. We calculated age-adjusted incidence rates (IRs) per 100,000 population for each cancer site by using the 2000 US standard population and, separately, for each cancer site for each state for the 5-year period from 2016 through 2020. Breast cancer and female genital cancer rates were based on the female population, and male genital cancer rates were based on the male population. We calculated incidence rate ratios (IRRs) and associated 95% CIs for the same period for each state by using the national rate as the reference. We calculated a second set of IRs, IRRs, and 95% CIs for advanced-stage early-onset cancer cases diagnosed at regional and distant stages, demonstrating how each state compares to the US in overall incidence and advanced-stage incidence for all early-onset cancers; we considered states whose 95% CIs did not cross 1 to be significantly different from the US rate. We calculated trends as the average annual percentage change (APC) in the 5-year period before the COVID-19 pandemic (2015–2019) to avoid the effect of postponed diagnoses. Trends were significant when the 95% CI for the APC did not cross zero. Negative APCs indicate falling rates, and positive APCs indicate rising rates. The percentage of early-onset cancer cases contributed by each site group and all visualizations were produced in R Statistical Computing Language version 4.3.1. All other analyses were conducted in SEER*Stat version 8.4.2 (R Core Team).

Highlights

In our study, early-onset cancer (IR = 158.2) accounted for 11.4% of all cancer cases (IR = 599.9), including 17.3% of female breast cancers (overall IR = 177.9) and 8.8% of digestive cancers (overall IR = 108.7). We found that 87.2% of early-onset cancer cases fell into 8 groups of early-onset cancer sites (Panels A and B). Breast cancer contributed 23.3% of all early-onset cancer. Digestive cancers, including colon and rectum sites, contributed 14.4%. Lymphohematopoietic cancers (or "blood cancers"), which include lymphomas and leukemias, contributed 11.0%. Endocrine cancers, predominately thyroid cancer, contributed 10.7%. Female genital cancers, including uterus and cervix sites, contributed 9.1%, and skin (excluding basal and squamous) cancers, predominately melanoma, contributed 7.8%. Male genital cancers, including testis and prostate, contributed 5.8%, and urinary cancers, including kidney and renal pelvis, contributed 5.1%. Three prevalent early-onset cancer sites were not represented in the 8 site groups: lung and bronchus (IR = 4.7), brain (IR = 3.5), and tongue (IR = 1.3).

Our maps of high overall incidence and high advanced-stage incidence indicate that the incidence of early-onset cancer is not evenly distributed (Panel B). States that have worse-than-national rates are frequently near each other geographically. States with changing rates only sometimes have the highest incidence.

The rate of early-onset female breast cancer (IR = 75.1) was worse than the national rate in 17 states, which, except for Hawaii, are located in the eastern half of the US, and rates were rising in 3 states (Georgia, Illinois, Wisconsin) (Panels A and B). Eighteen states had worse-than-national rates of digestive cancers (IR = 22.7). Aside from Hawaii and Puerto Rico, these states are located in the eastern half of the US, with a concentration in the South. Rates of digestive cancers were rising in 3 states (Illinois, Maryland, New York). The incidence of lymphohematopoietic cancers (IR = 16.9) was highest in 3 states in the Southeast, 7 states in the Northeast, and Puerto Rico. Rates were rising in 1 state (Alabama) and falling in 5 (Alaska, Connecticut, Florida, Georgia, Maine). Rates of endocrine cancers (IR = 16.5) were worse than national rates in 25 states, which form a horizontal core of the country running from east to west, plus Puerto Rico. Rates of endocrine cancers were falling in 9 states (Arizona, Arkansas, Georgia, Indiana, Massachusetts, Mississippi, North Carolina, Pennsylvania, Tennessee) and not rising in any. Rates of female genital cancers (IR = 14.5) were worse than national rates in 16 states, largely in the Midwest and South, plus California and Puerto Rico; rates were not rising or falling in any state. Rates of skin cancer (IR = 12.3) were worse than national rates in 32 states, concentrated in the northern portion of the country. Three states had falling rates of skin cancer (Connecticut, New Hampshire, Pennsylvania), and none had rising rates. Rates of male genital cancers (IR = 8.7) were worse than national rates in 18 states, mostly in the eastern half of the country, plus Montana, Nebraska, and Puerto Rico. These rates were rising in 2 states (Louisiana, Texas) and falling in one (Hawaii). Rates of urinary system can-

cers (IR = 8.2) were worse than national rates in 17 contiguous states, from New Mexico to Pennsylvania. Rates were rising in 2 states (New York, West Virginia) and falling in one (Pennsylvania).

The states with the highest overall and advanced-stage incidence rates of early-onset cancer for all cancer sites combined were Kentucky and West Virginia (Panel C), followed by 13 others that also had worse-than-national rates on both (Arkansas, Connecticut, Florida, Georgia, Iowa, Louisiana, Maine, Missouri, New Jersey, New York, North Carolina, Ohio, and Pennsylvania).

Action

This study provides the first analysis of age-adjusted rates of early-onset cancer based on state-level population and case counts. Geographic patterns in early-onset cancer indicate possible similarities that could relate to demographic, socioeconomic, behavioral, or environmental risks. By uncovering geospatial patterns across various cancer sites, this analysis informs hypotheses about factors driving early-onset cancer. Because important local patterns may be masked in a state-level analysis, future analyses may consider a more granular geographic unit such as county or zip code. However, focusing prevention efforts on the highest-incidence states for the most prevalent sites may reduce the rate of early-onset cancer nationally.

Acknowledgments

The authors received no external financial support for the research, authorship, or publication of this article. The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article. No copyrighted materials were used in this article.

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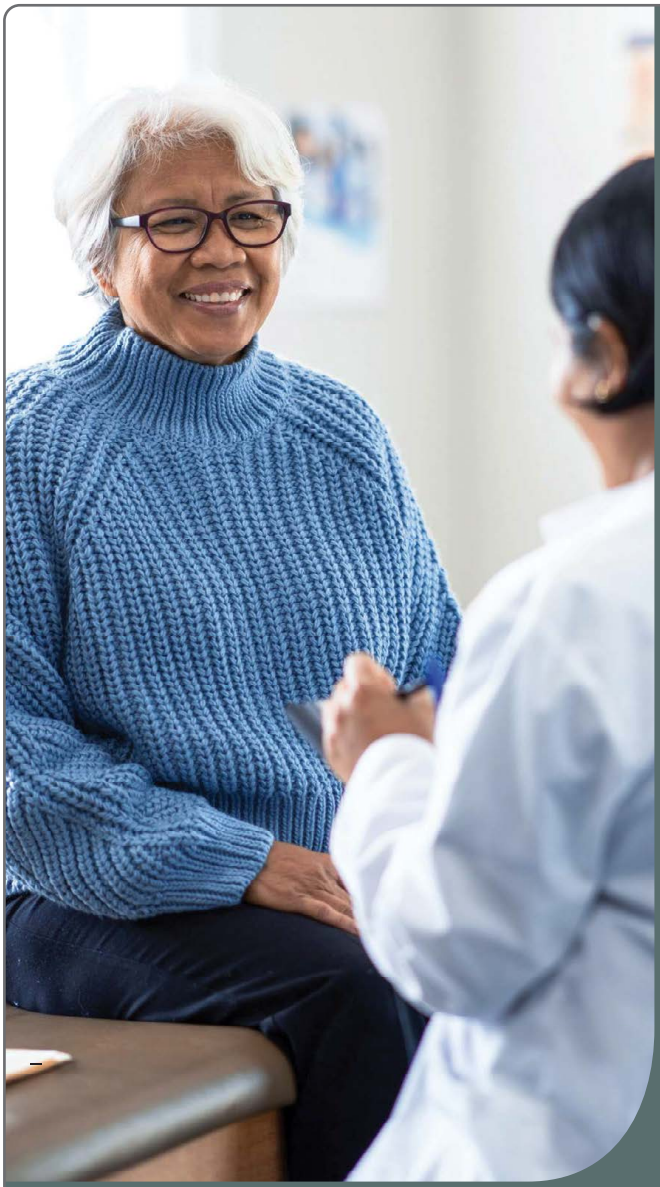

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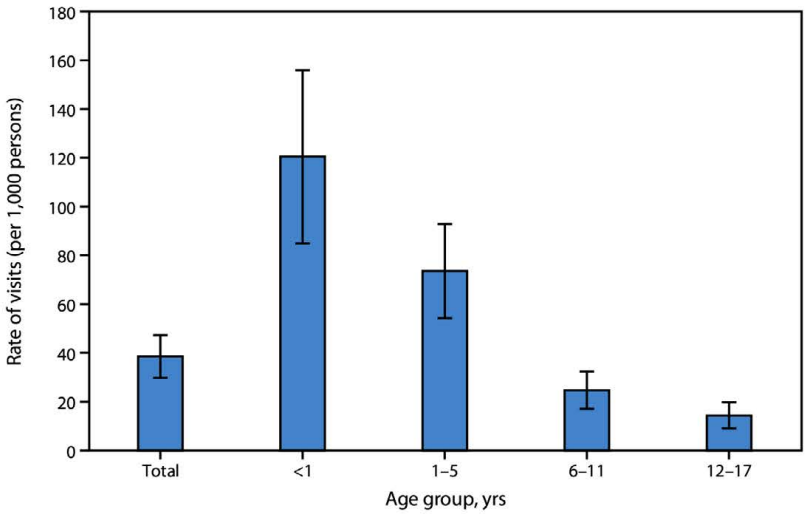
FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Rates of Emergency Department Visits* for Children and Adolescents with Acute Upper Respiratory Infection,† by Age Group — United States, 2021–2022



* With 95% CIs indicated by error bars. Visit rates are based on U.S. Census Bureau estimates of the U.S. civilian, noninstitutionalized population as of July 1 of each year. Estimates are based on a sample of visits to emergency departments in noninstitutional general and short-stay hospitals, exclusive of federal, military, and Veterans Administration hospitals, located in the 50 states and the District of Columbia.

† Visits with an acute upper respiratory infection (viral or bacterial) recorded as first listed diagnosis using *International Classification of Diseases, Tenth Revision, Clinical Modification* codes J00–J06.

In 2021–2022, the rate for emergency department (ED) visits for children and adolescents with acute upper respiratory infection was 38.6 per 1,000 persons aged <18 years. The ED visit rate was highest for infants aged <1 year (120.5) and decreased by age, with the lowest rate among adolescents aged 12–17 years (14.4).

Supplementary Table: https://stacks.cdc.gov/view/cdc/162215

Source: National Center for Health Statistics, National Hospital Ambulatory Medical Care Survey, 2021–2022.

Reported by: Loredana Santo, MD, lsanto@cdc.gov; Jill J. Ashman, PhD; Michelle Olton, MPH.

For more information on this topic, CDC recommends the following links: https://www.cdc.gov/respiratory-viruses/about/index.html and https://www.cdc.gov/pneumonia/prevention/index.html.

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Visit www.henryschein.com/flu

*Offer good on minimum purchase of 7 vials and/or packs of Flucelvax, Afluria, Fluad, Fluzone, Flublok, Fluarix and Flulaval. Returns must be in complete unopened vials or packs of syringes and allowable return percentage is specific to brand. Ask your sales consultant for more information. Returns will be in a form of a credit toward next year's flu purchases. Allowable flu vaccine returns must be received back to Henry Schein, Inc. between March 1, 2026 and April 30, 2026 for full returns credit.

**Subject to availability. ***Not available in California. †Subject to credit approval.

HENRY SCHEIN® MEDICAL

To Order: **1-800-772-4346** 8am–8pm (et) or visit: **henryschein.com/medical**

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