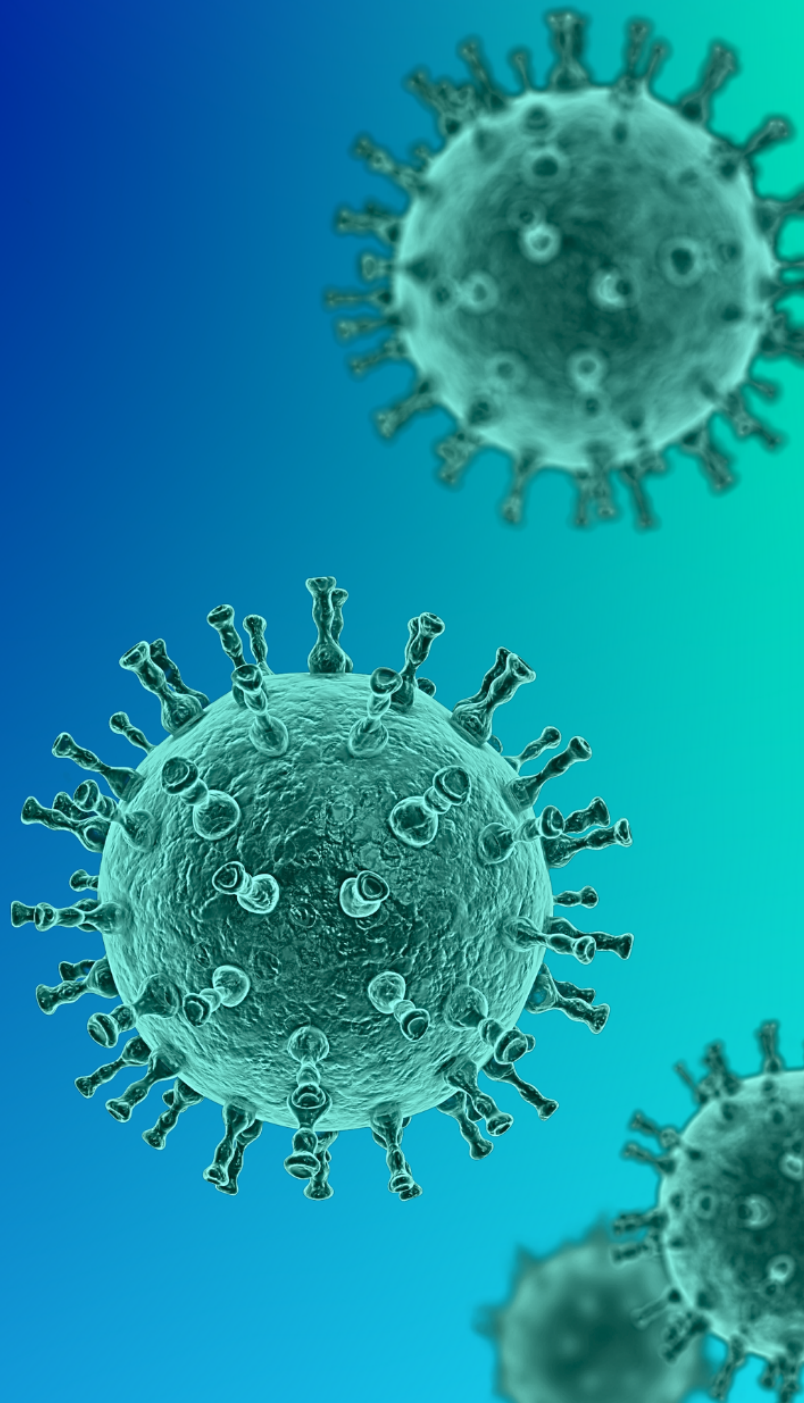


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VARICELLA ZOSTER SURVEILLANCE REPORT

Key Trends & Insights in 2024



Varicella Zoster Surveillance Report

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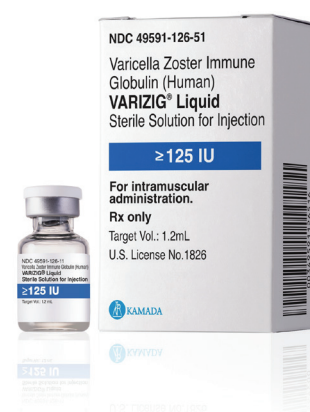
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REDUCING VARICELLA SEVERITY COULD MEAN THE WORLD TO HIGH-RISK PATIENTS¹

Varicella-zoster virus (VZV) infection remains a significant concern for high-risk populations lacking immunity to VZV.

VARIZIG[®] was proven to reduce varicella disease severity and is recommended as a first-line treatment by leading guidelines for VZV post-exposure prophylaxis in high-risk patients, including immunocompromised patients, pregnant women, and infants.¹⁻³



INDICATION AND USAGE¹

VARIZIG[®], Varicella Zoster Immune Globulin (Human), is indicated for post-exposure prophylaxis of varicella in high-risk individuals. High-risk groups include: immunocompromised children and adults, newborns of mothers with varicella shortly before or after delivery, premature infants, neonates, and infants less than one year of age, adults without evidence of immunity, and pregnant women. VARIZIG administration is intended to reduce the severity of varicella.

TIMING OF ADMINISTRATION¹

Administer as soon as possible after exposure to VZV, ideally within 96 hours (4 days), and up to 10 days post-exposure.

DOSING GUIDELINES

Weight (kg)	Weight (lbs)	Dose (IU)
≤2.0	≤4.4	62.5 IU
2.1-10.0	4.5-22.0	125 IU
10.1-20.0	22.1-44.0	250 IU
20.1-30.0	44.1-66.0	375 IU
30.1-40.0	66.1-88.0	500 IU
≥40.1	≥88.1	625 IU

ORDER VARIZIG¹

VARIZIG is widely available. To order VARIZIG, please get in touch with your specialty distributor or visit: <https://varizig.com/ordering-reimbursement/>

IMPORTANT SAFETY INFORMATION:

VARIZIG® contains trace amounts of IgA. Individuals known to have anaphylactic or severe systemic (hypersensitivity) reactions to human immune globulin preparations should not receive VARIZIG®. IgA-deficient patients with antibodies against IgA and a history of hypersensitivity may have an anaphylactoid reaction. Thrombotic events may occur during or following treatment with immune globulin products. Administer VARIZIG® intramuscularly only. In patients who have severe thrombocytopenia or any coagulation disorder that would contraindicate intramuscular injections, only administer VARIZIG® if the expected benefits outweigh the potential risks. Severe hypersensitivity reactions may occur following VARIZIG® administration. In case of hypersensitivity, discontinue the administration of VARIZIG® immediately and provide appropriate treatment. Because VARIZIG® is made from human plasma, it may carry a risk of transmitting infectious agents, e.g., viruses, the variant Creutzfeldt-Jakob disease agent, and, theoretically, the Creutzfeldt-Jakob disease agent. The most serious adverse drug reactions observed in clinical trials for all subjects and patients include pyrexia, nausea, and vomiting. The most common adverse drug reactions observed in clinical trials for all subjects and patients were injection site pain, headache, chills, fatigue, rash, and nausea.

Please see full Prescribing Information for complete prescribing details. To report SUSPECTED ADVERSE REACTIONS, contact Kamada at pharmacovigilance@kamada.com

References:

1. VARIZIG [package insert]. Kamada Inc September 2022.
2. Bialek SR, Perella D, Zhang J, Mascola L, Viner K, Jackson C, et al. Impact of a routine two-dose varicella vaccination program on varicella epidemiology. *Pediatrics*. 2013;132(5): e1134-e1140.
3. Anne M. Lachiewicz, Megan L. Srinivas, Varicella-zoster virus post-exposure management and prophylaxis: A review, *Preventive Medicine Reports*, Volume 16,2019,101016, ISSN 2211-3355.



For more information about VARIZIG visit www.VARIZIG.com

VARIZIG® [Varicella Zoster Immune Globulin (Human)] and all Kamada brand, product, service and feature names, logos, and slogans are trademarks or registered trademarks of Kamada in the United States and/or other countries.

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Key Takeaways

US trends:

- Nationally, varicella cases have been **increasing steadily since 2020**, when the country reported a **10-year low during the COVID-19 pandemic**.¹
- In 2024, Colorado, Illinois, Wisconsin, North Dakota, and New Hampshire reported the **highest incidence of cases** while Mississippi and Hawaii reported the **greatest increase in cases** when comparing reported cases from 2023 and 2024.¹
- State-level **vaccine coverage is significantly correlated with varicella incidence**, whereby lower vaccine coverage is associated with higher incidence rates.²
- States reporting **low coverage and high incidence** include Colorado, Wisconsin, and Florida.²
- Countries with **high migration into the US** that **do not** have an **establish vaccination program at the national level** include: Cuba, India, Dominican Republic, China, Philippines, Vietnam, United Kingdom, and Puerto Rico.^{3, 4}

Global trends:

- In 2024, **varicella cases continue to increase** in most countries globally following the steep decline in cases reported in 2020-2021 during the COVID-19 pandemic emergency.
- However, in many countries, 2024 case totals have **not reached levels reported prior to 2020** despite some countries reporting a resurgence in cases with increasing trends in recent years.
- Routine childhood immunization schedules against varicella have not been introduced in many countries, making their populations more susceptible to infection.⁵

Research:

- **Vaccine coverage** for varicella **declined year-over-year** among kindergarten students since the onset of the COVID-19 pandemic, while **school exemptions are continuing to increase**.^{6, 7}
- **Vaccine coverage** has been **improving** among **children born to military families**, up until the cohort of infants born during the onset of the pandemic.⁸
- Continuity of care remains a challenge affecting the timeliness of vaccine completion in military children.⁸
- **Gaps remain in prescribing the recommended PEP (VARIZIG®) for vulnerable children with varicella exposure**, despite a reduced risk of varicella among those receiving VARIZIG® over acyclovir.⁹
- Please see VARIZIG® Important Safety Information on page 21.
 - For full prescribing information please refer to:
<https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=f367f996-aafa-4b8b-8cb4-63a009cd2015>

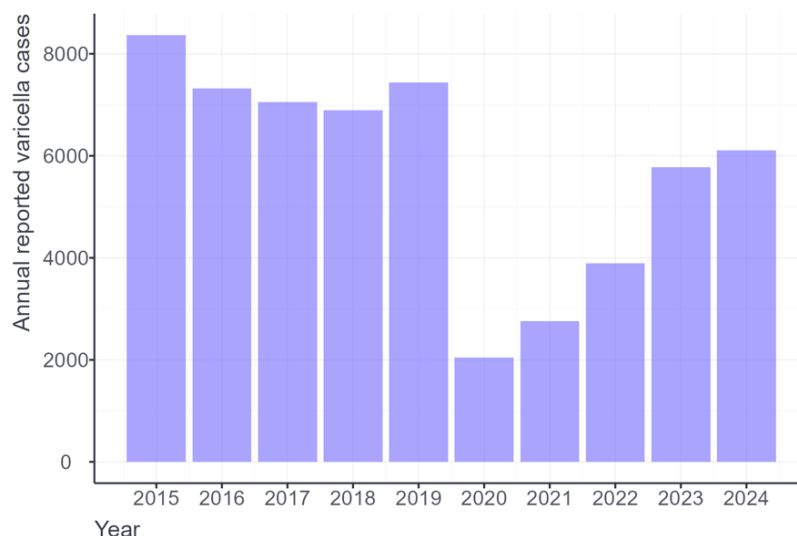
Key Takeaways References:

1. <https://stacks.cdc.gov/cbrowse?pid=cdc%3A49375&parentId=cdc%3A49375>
2. <https://pmc.ncbi.nlm.nih.gov/articles/PMC11486350/>
3. BlueDot Population Air Travel Forecasted/Historical Volumes API
4. Ward, A. (2024) U.S. Lawful Permanent Residents: 2023. Office of Homeland Security Statistics. https://ohss.dhs.gov/sites/default/files/2024-09/2024_0906_plcy_lawful_permanent_residents_fy2023.pdf
5. https://immunizationdata.who.int/global/wiise-detail-page/introduction-of-varicella-vaccine?ISO_3_CODE=&YEAR=
6. Coverage with Selected Vaccines and Exemption Rates Among Children in Kindergarten — United States, 2023–24 School Year. Seither R, Yusuf OB, Dramann D, et al., MMWR Morb Mortal Wkly Rep. 2024;73(41):925–932.
7. Impact of the COVID-19 pandemic on routine childhood vaccination in 9 US jurisdictions. Treharne A, Patel Murthy B, Zell ER, et al., Vaccine. 2024 Sep 17;42(22):125997.
8. Vaccine completion and timeliness among children in the Military Health System: 2010–2019 Romano CJ, Burrell M, Bukowinski AT, et al., Pediatrics. 2024 Oct 1;154(4):e2023064965.
9. Post-Exposure Prophylaxis for Varicella-Zoster Virus Exposure in High-Risk Children. Shteynberg E, Sun S, Jhaveri R, Patel SJ. J Pediatric Infect Dis Soc. 2024 Jan 29;13(1):69–74.

Spotlight: United States

US National Cases

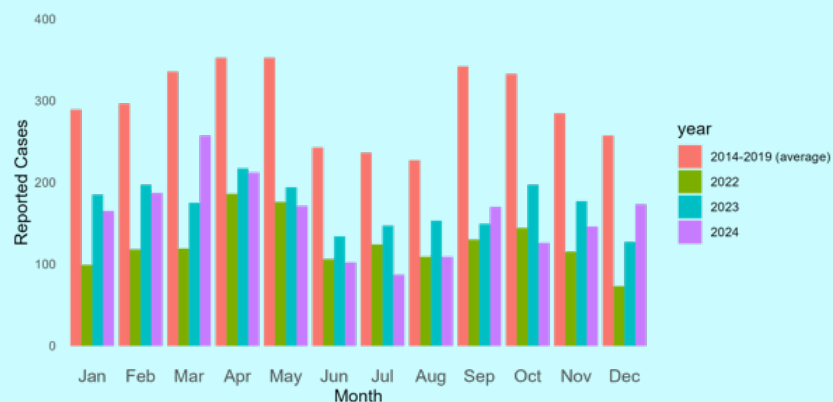
Year	Varicella Cases	% Change from Previous Year
2015	8,370	-
2016	7,319	-12.6
2017	7,059	-3.6
2018	6,892	-2.4
2019	7,439	7.9
2020	2,049	-72.5
2021	2,755	34.5
2022	3,890	41.2
2023	5,774	48.4
2024	6,112	5.9



Data Source: Centers for Disease Control and Prevention. National Notifiable Diseases Surveillance System, Weekly Tables of Infectious Disease Data. Atlanta, GA. CDC Division of Health Informatics and Surveillance. Available at: <https://stacks.cdc.gov/cbrowse?pid=cdc%3A49375&parentId=cdc%3A49375>

Year-over-Year US National Trends

Key Statistics	
Reported cases in 2024	6,112
Comparison to reported cases in 2023 (relative change compared to 2024)	5,774 (-5.9%)
Comparison to average of 2015 to 2019 (relative change compared to 2024)	7,415 (+21.3%)

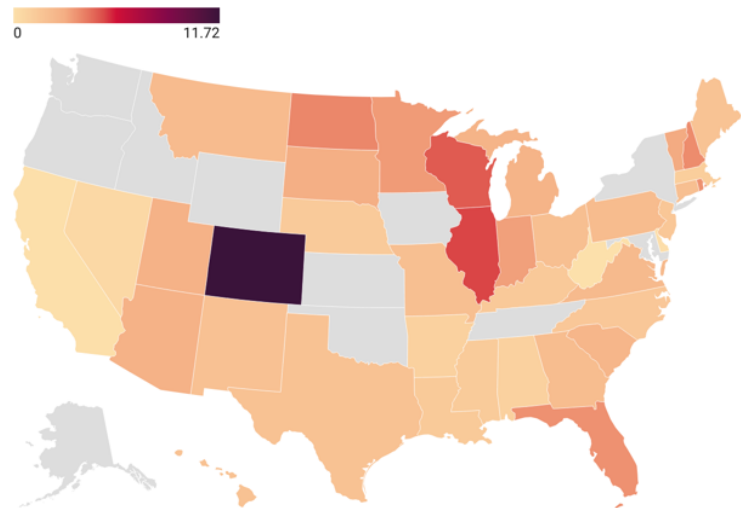


Data Source: Centers for Disease Control and Prevention. National Notifiable Diseases Surveillance System, Weekly Tables of Infectious Disease Data. Atlanta, GA. CDC Division of Health Informatics and Surveillance. Available at: <https://stacks.cdc.gov/cbrowse?pid=cdc%3A49375&parentId=cdc%3A49375>

Subnational Trends

States reporting the highest number of cases per 100,000 in 2024	Number of reported cases per 100,000
Colorado	11.7
Illinois	5.2
Wisconsin	4.8
North Dakota	3.9
New Hampshire	3.7

Cumulative cases of varicella, per 100,000 in 2024

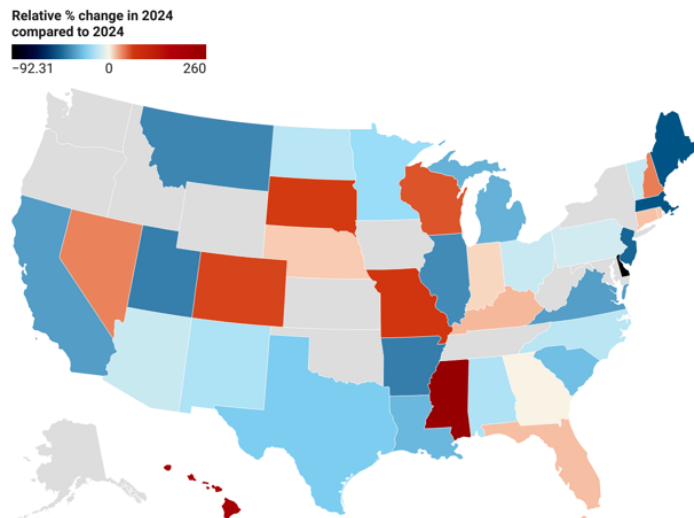


Data Source: Centers for Disease Control and Prevention. National Notifiable Diseases Surveillance System, Weekly Tables of Infectious Disease Data. Atlanta, GA. CDC Division of Health Informatics and Surveillance. Available at: <https://stacks.cdc.gov/cbrowse?pid=cdc%3A49375&parentId=cdc%3A49375>

Subnational Trends – Change in Cases

States reporting the highest increase in reported case data from 2023 to 2024	Percent change
Mississippi	260%
Hawaii	213%
Missouri	66%
South Dakota	56%
Colorado	54%

Relative percent change in cumulative yearly cases per 100,000 in 2024 compared to 2023

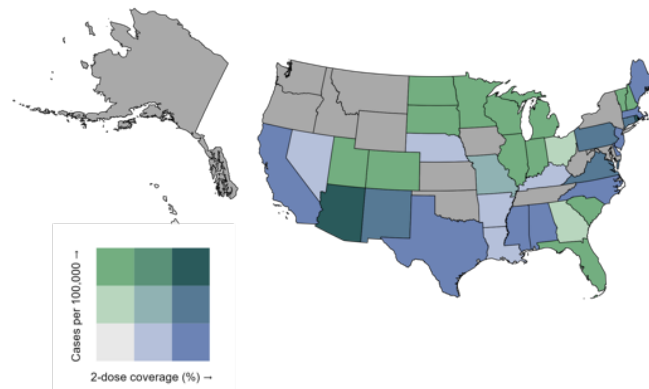


Data Source: Centers for Disease Control and Prevention. National Notifiable Diseases Surveillance System, Weekly Tables of Infectious Disease Data. Atlanta, GA. CDC Division of Health Informatics and Surveillance. Available at: <https://stacks.cdc.gov/cbrowse?pid=cdc%3A49375&parentId=cdc%3A49375>

Subnational Trends – Vaccine Coverage and Varicella Incidence

- When comparing vaccine coverage and case incidence, a significant moderate negative correlation was observed (-0.48 , $p\text{-value} < 0.005$)*.
- As vaccine coverage increased within the state, the lower the cumulative cases per 100,000.
- The map on the right categorizes states based on lowest, moderate, and highest vaccine coverage and reported incidence in comparison to all states.
- States with higher incidence rates and lower coverage are concentrated in the southeast and north-central states.

Reported incidence of varicella and 2-dose vaccine coverage in 2024



Notes: Grey states indicates no data available; *See Appendix

Data Source: <https://pmc.ncbi.nlm.nih.gov/articles/PMC11486350/>

Observations: US Spotlight

- At the national level, varicella cases demonstrated an overall decreasing trend between 2015 to 2018. Reported cases increased in 2019, after which the **US observed a 10-year low in 2020**. This finding is likely due to factors related to the start of the COVID-19 pandemic including social distancing measures, healthcare seeking behaviour changes, and changes in healthcare access and diagnostics capacity. Nationally, **varicella cases have been increasing steadily since 2020**, though they remain **lower than pre-pandemic levels**.
- The top five states with the highest cases per 100,000 in 2024 reported **two dose vaccination** coverage of **less than 91%**.
- Similarly, the top five states that reported the highest increases in case incidence between 2023 and 2024 had equal to or less than 90% vaccination coverage with two doses in 2024.
- Additionally, of those states that reported a **high increase in case incidence** between 2023 and 2024, Mississippi, Missouri, and South Dakota demonstrated a **decrease** in vaccination coverage from 2023 to 2024.
- The proportion of the population with **at least two doses** of the varicella vaccine was **moderately correlated** with a lower reported **incidence of cases**.
- States categorized as **having low vaccine coverage and high incidence** include Colorado, Wisconsin, and Florida.
- Although reported cases remain below pre-pandemic levels, vaccination trends indicate continued increasing rates of varicella should be expected, especially in communities with low vaccination uptake.

Migration to the US and Varicella Vaccination Status of Origin Country

Lawful Permanent Residents to the US by Country of Birth Top 20 Countries: 2023 Fiscal Year

Country of Birth	Number of New Lawful Permanent Residents 2023	Percent of New Lawful Permanent Residents for the US in 2023	Varicella Vaccination Program
Mexico	180,530	15.4	Mandatory for children entering schools
Cuba	81,600	7.0	No vaccination schedule
India	78,070	6.7	Mandatory and enforced in some states, but not in all
Dominican Republic	68,870	5.9	No vaccination schedule
China, People's Republic	59,260	5.1	Federally, no mandatory vaccines. Some requirement from schools
Philippines	49,200	4.2	Recommended
Vietnam	36,000	3.1	Recommended
Afghanistan	30,300	2.6	Mandatory
Brazil	28,880	2.5	Mandatory
El Salvador	26,210	2.2	Mandatory administration at 15 months and 4 years

Sources:

- Ward, A. (2024) U.S. Lawful Permanent Residents: 2023. Office of Homeland Security Statistics. https://ohss.dhs.gov/sites/default/files/2024-09/2024_0906_plcy_lawful_permanent_residents_fy2023.pdf
- https://immunizationdata.who.int/global/wise-detail-page/vaccination-schedule-for-varicella?ISO_3_CODE=MEX&TARGETPOP_GENERAL=
- <https://www.sciencedirect.com/science/article/abs/pii/S0264410X21005478#preview-section-snippets>
- https://www.pidsphil.org/home/wp-content/uploads/2021/05/11-Vol-22-No-1_Childhood_Immunization_Schedule_2021_v3.pdf

Highest Air Travel Passenger Volume by Origin Country to the US, 2024

Country of Origin	Total Forecasted Passenger Volume Jan-Dec 2024	Varicella Vaccination Program
Mexico	19,107,507	Mandatory
Canada	14,318,478	Mandatory in some provinces, recommended In others
United Kingdom	7,511,223	Recommended
Puerto Rico	5,748,561	No vaccination schedule
Dominican Republic	4,768,186	No vaccination schedule
Italy	4,550,652	Mandatory, enforced for minors up to the age of 16
Japan	3,678,312	Mandatory
France	3,596,495	Mandatory, enforced
Germany	3,570,060	Mandatory, administered at 11 and 15 months with catch up administered before 17 years of age
India	3,154,277	Mandatory and enforced in some states, but not in all

Sources:

- BlueDot Population Air Travel Forecasted Volumes API
- BlueDot Population Air Travel Historical Volumes API
- <https://www.sciencedirect.com/science/article/abs/pii/S0264410X21005478#preview-section-snippets>
- <https://www.city.hiroshima.lg.jp/english/everyday/1029818/1009645.html>

Observations: Migration to the US and Varicella Vaccination Status of Origin Country

- Countries with high migration into the US, defined as being among either the top 10 countries contributing the greatest number of new lawful residents in the US in 2023 or among the top 10 countries with the highest forecasted air travel volumes for 2024 to the US, that do not have an established vaccination program at the national level include:
 - Cuba
 - China
 - United Kingdom
 - India
 - Philippines
 - Puerto Rico
 - Dominican Republic
 - Vietnam
- Although several countries do not list the varicella vaccine as mandatory, several (Philippines, Vietnam, and the United Kingdom) list the vaccine as a recommendation as part of a child's vaccination schedule.
- While the threat of imported cases of varicella is evident, high vaccine coverage leading herd immunity at the state level in the United States is needed in order to prevent further outbreak from imported cases.

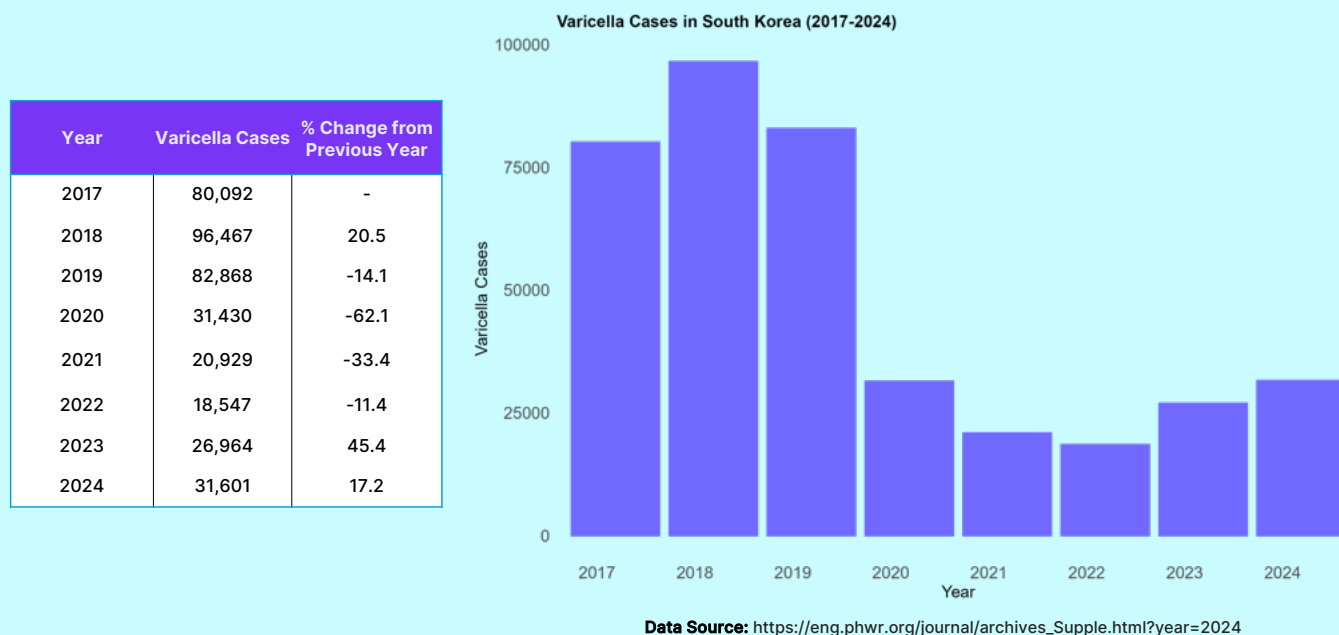
Global Varicella Trends

Global Trends

Country	Reported cases (2024)	Reported cases per 100,000 population (2024)*	% Change from Previous Year (2023)	Data Source
US	6,112	1.8	5.9	https://stacks.cdc.gov/cbrowse?pid=cdc%3A49375&parentId=cdc%3A49375
South Korea	31,601	61.3	17.2	https://eng.phwr.org/journal/archives_Supple.html?year=2024
Japan	28,326	22.9	74.3	https://www.niid.go.jp/niid/en/surveillance-data-table-english.html
Australia	35,096	137.4	1.63	https://nindss.health.gov.au/pbi-dashboard/
Estonia	5,321	444.0	-50.8	https://www.terviseamet.ee/nakkushaigused/statistika#nakkushaigused
Germany	19,616	23.3	9.93	https://www.rki.de/DE/Content/Infekt/EpidBull/epid_bull_node.html
Hungary	11,934	123.1	-23.3	https://www.antsz.hu/felso_menu/temaink/jarvany/Fertozo_betegsegek/Fertozo_eves_jelentesk
Colombia	24,470	49.8	-21.8	https://www.ins.gov.co/buscador-eventos/Paginas/Vista-Boletin-Epidemiologico.aspx
Mexico	54,843	42.3	32.2	https://www.gob.mx/salud/acciones-y-programas/direccion-general-de-epidemiologia-boletin-epidemiologico

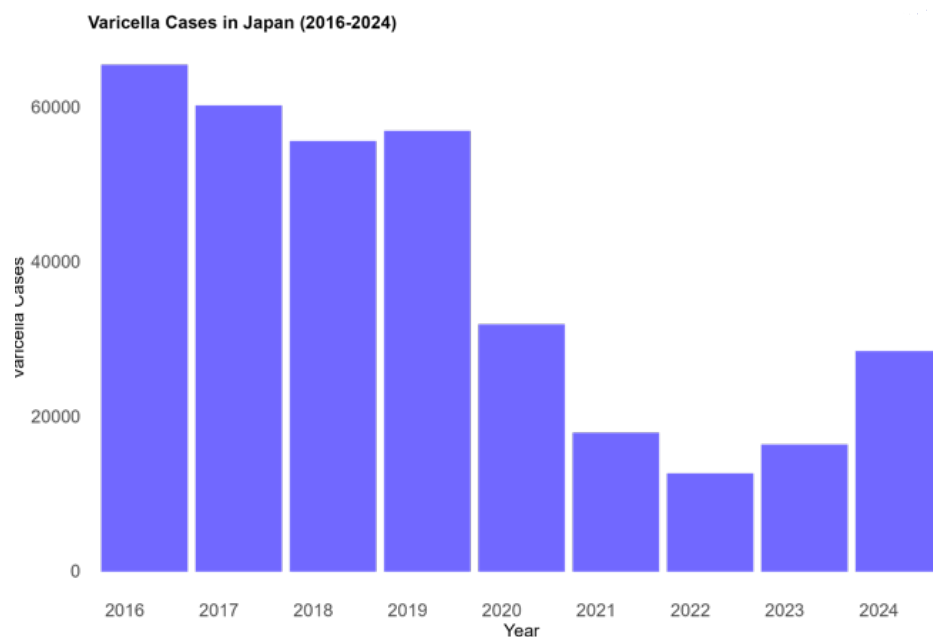
Note: Not all countries are reporting historical data for varicella; hence, comparisons to last year and pre-pandemic averages will be made only where data are available. *Population adjusted estimates were calculated using the total population variable available for 2022 (the most recent data available) from the BlueDot Population Density API.

Country Profile – South Korea



Country Profile – Japan

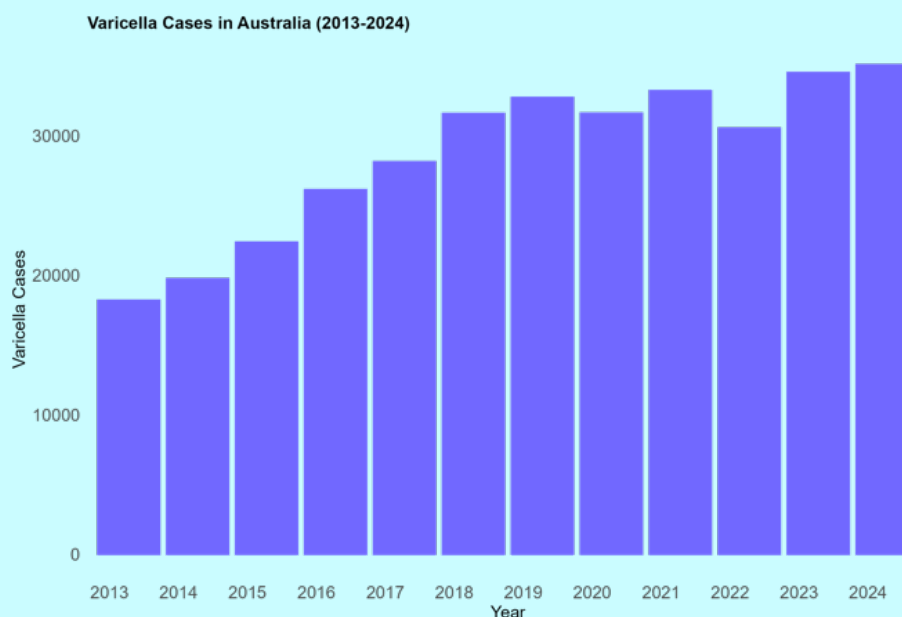
Year	Varicella Cases	% Change from Previous Year
2016	65,353	-
2017	60,084	-8.05
2018	55,480	-7.67
2019	56,796	2.37
2020	31,785	-44.0
2021	17,776	-44.1
2022	12,511	-29.6
2023	16,247	29.9
2024	28,326	74.3



Data Source: <https://www.niid.go.jp/niid/en/surveillance-data-table-english.html>

Country Profile – Australia

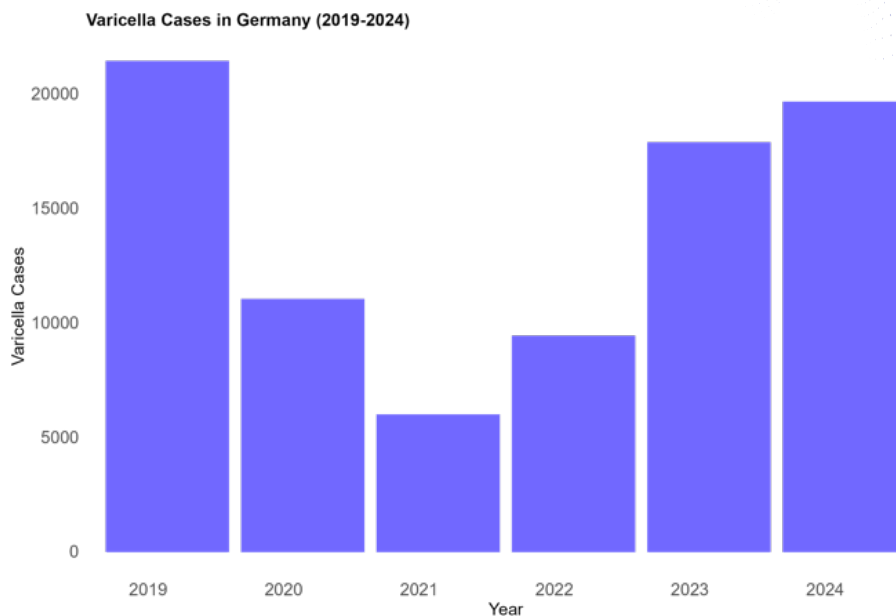
Year	Varicella Cases	% Change from Previous Year
2013	18,211	-
2014	19,756	8.48
2015	22,376	13.3
2016	26,134	16.8
2017	28,141	7.68
2018	31,597	12.3
2019	32,749	3.65
2020	31,619	-3.45
2021	33,239	5.12
2022	30,555	-8.07
2023	34,532	13.0
2024	35,096	1.63



Data Source: <https://nindss.health.gov.au/pbi-dashboard/>

Country Profile – Germany

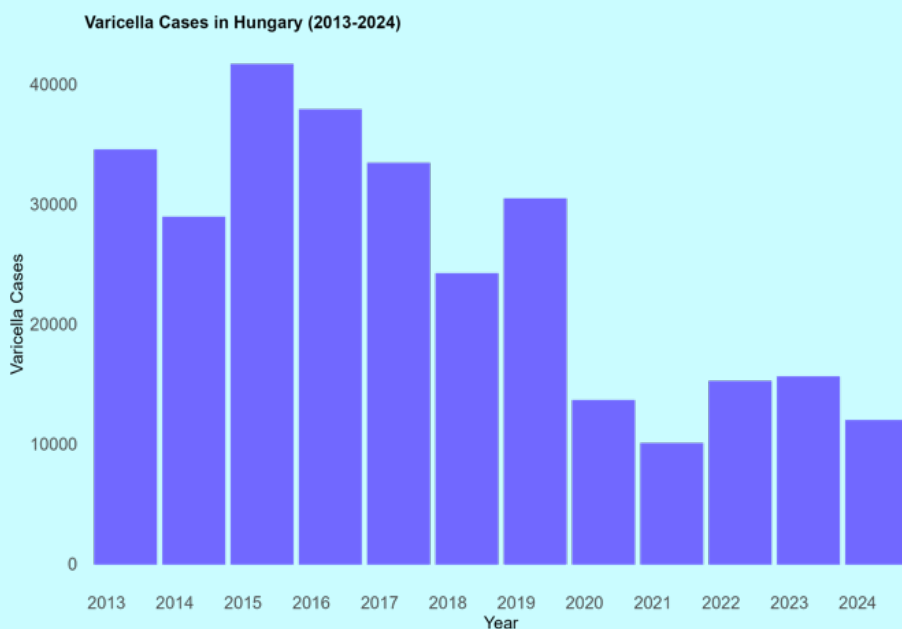
Year	Varicella Cases	% Change from Previous Year
2019	21,398	-
2020	10,998	-48.6
2021	5,954	-45.8
2022	9,393	57.7
2023	17,843	90.0
2024	19,616	9.92



Data Source: https://www.rki.de/DE/Content/Infekt/EpidBull/epid_bull_node.html

Country Profile – Hungary

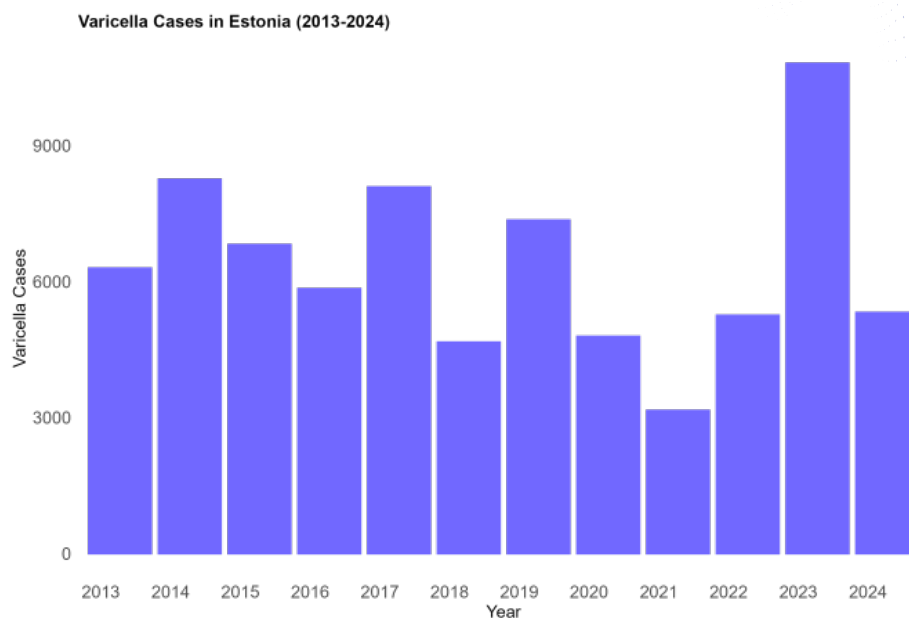
Year	Varicella Cases	% Change from Previous Year
2013	34,498	-
2014	28,882	-16.3
2015	41,620	44.1
2016	37,843	-9.08
2017	33,381	-11.8
2018	24,176	-27.6
2019	30,412	25.8
2020	13,600	-55.3
2021	10,016	-26.4
2022	15,196	51.7
2023	15,577	2.5
2024	11,934	-23.3



Data Source: https://www.antsz.hu/felso_menu/temaink/jarvany/Fertozo_betegsegek/Fertozo_eves_jelentesk

Country Profile – Estonia

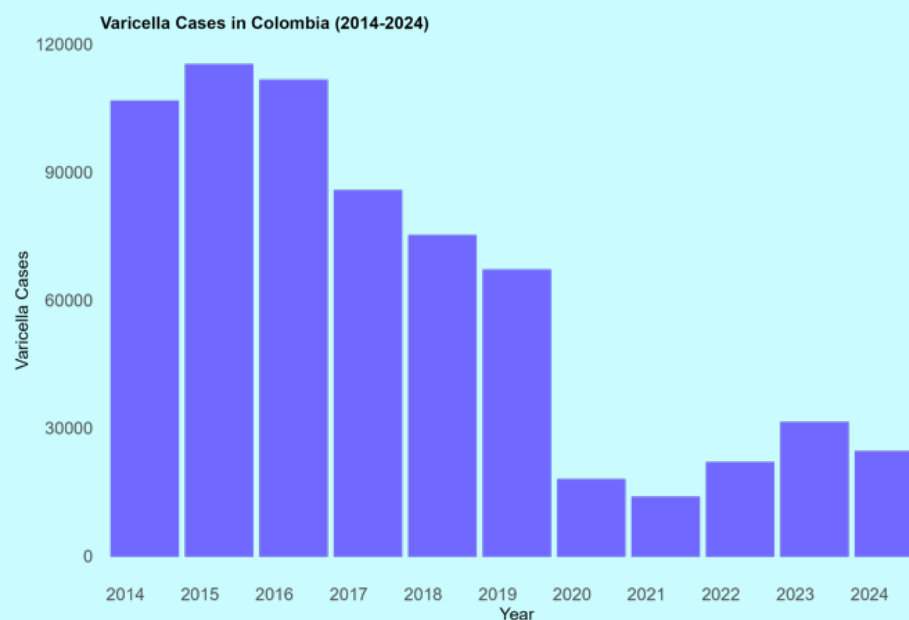
Year	Varicella Cases	% Change from Previous Year
2013	6,299	-
2014	8,258	31.1
2015	6,819	-17.4
2016	5,846	-14.3
2017	8,088	38.4
2018	4,667	-42.3
2019	7,357	57.6
2020	4,794	-34.8
2021	3,162	-34.0
2022	5,259	66.3
2023	10,815	106
2024	5,321	-50.8



Data Source: <https://www.terviseamet.ee/nakkushaigused/statistika#nakkushaigused>

Country Profile – Colombia

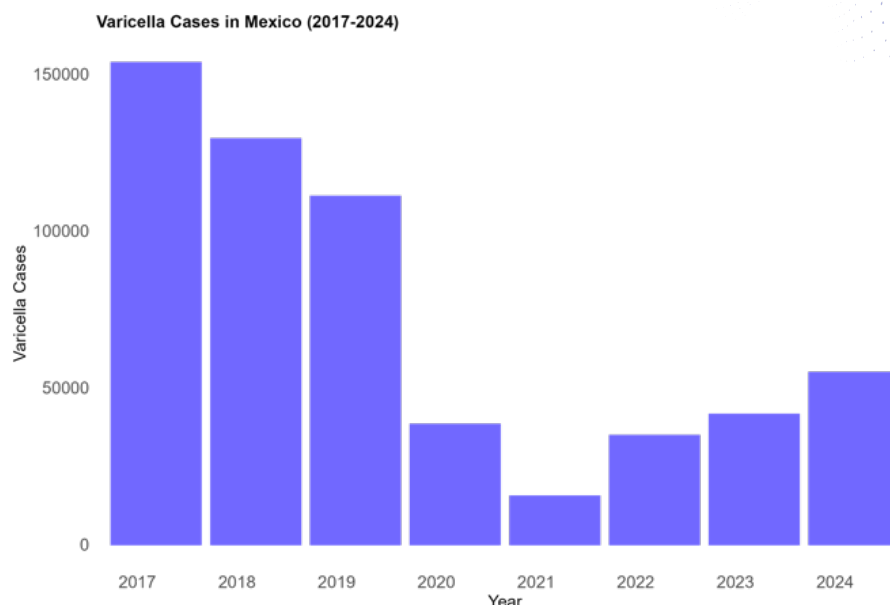
Year	Varicella Cases	% Change from Previous Year
2014	106,592	-
2015	115,148	8.0
2016	111,521	-3.1
2017	85,622	-23.2
2018	75,109	-12.3
2019	67,020	-10.8
2020	17,923	-73.3
2021	13,784	-23.1
2022	21,889	58.8
2023	31,295	43.0
2024	24,470	-21.8



Data Source: <https://www.ins.gov.co/buscador-eventos/Paginas/Vista-Boletin-Epidemiologico.aspx>

Country Profile – Mexico

Year	Varicella Cases	% Change from Previous Year
2017	153,596	-
2018	129,311	-15.8
2019	110,986	-14.2
2020	38,315	-65.5
2021	15,438	-59.7
2022	34,759	125.2
2023	41,488	19.4
2024	54,843	32.2



Data Source: <https://www.gob.mx/salud/acciones-y-programas/direccion-general-de-epidemiologia-boletin-epidemiologico>

Vaccine Coverage

Country (Year*)	2024	2023	2022	2021	2020	2019	2018	2017	2016	2015
United States (1995)				90.1%	89.7%	91.1%	91.2%	89.9%	90.3%	90.2%
Australia (2005)	92.4%	92.8%	93.3%	94.1%	94.4%	93.9%	92.7%	93.0%	93.3%	92.0%
Germany (2004)					88.9%					
Hungary (2019)		99.1%	99.7%	99.6%						
South Korea (2005)						96.3%				

*Year of introduction of at least one dose of a national varicella vaccination program.
Grey boxes indicate lack of availability of vaccine coverage estimates.

Sources and Notes:

United States: Years represent birth year. Vaccine coverage estimates represent coverage (at least one dose) at 24 months. <https://www.cdc.gov/childvaxview/about/interactive-reports.html>

Australia: Vaccine coverage estimates (one dose) from all Primary Health Networks (PHNs) were averaged to calculate a national average. <https://www.health.gov.au/resources/collections/childhood-immunisation-coverage-data-phn-and-sa3#phn-data-by-year>

Germany: Vaccine coverage estimates only easily available for 2020. Value represents vaccine coverage estimate (one dose) among 4- to 7-year-olds in 2020. <https://pmc.ncbi.nlm.nih.gov/articles/PMC10631171/>

Hungary: Vaccine coverage estimates (one dose) represent vaccines administered among 13-month olds in a specific year. https://www.antsz.hu/felso_menu/temaink/jarvany/vedooltasok/Vedooltasok_eves_jelentesek

South Korea: Value represents vaccine coverage estimate (one dose) in 2019 among 12- to 15- month olds. <https://pmc.ncbi.nlm.nih.gov/articles/PMC9621034/>

Global Event-Based Surveillance

- Event-based surveillance (EBS) incorporates information from news media, which typically sources data from official and unofficial reports.
- While these media reports can provide timely insights and often originate from official sources, such as local or subnational ministries of health.
- EBS offers additional context and coverage of locations that may lack accessible indicator-based surveillance (IBS) data.
- The following slide provides a summary of 2024 varicella trends identified by BlueDot's EBS system.
- Additional details are available through the BlueDot event alert and assessments API.

Country	Cases Reported	News Article Highlights
Poland	153,640	<u>30-Dec-2024</u> <ul style="list-style-type: none"> • 153,640 cases reported in 2024. • Represents a 20% decrease in cases compared to 2023 when more than 190,000 cases were reported.
Vietnam	627	<u>11-Jun-2024</u> <ul style="list-style-type: none"> • 627 cases reported in Hanoi since the beginning of 2024. • Represents a decrease of more than 2.6x compared to the same period in 2023.
South Korea	13,277	<u>10-Jun-2024</u> <ul style="list-style-type: none"> • As of the first week of June, 13,277 people reported to be infected. • This is nearly double the number reported by the first week of June 2022 (7,069 cases). June 2022 represented the lowest number reported in the past five years. • 82,868 cases were reported in 2019. In subsequent years, cases decreased but trends began to increase in 2023 and continues to increase in 2024.
India	6,744	<u>17-Mar-2024</u> <ul style="list-style-type: none"> • 6,744 cases reported in state of Kerala, including nine related deaths, between 01-Jan-2024 and 15-Mar-2024. • In 2023, the state of Kerala reported a total of 26,363 confirmed cases and four deaths.
Peru	1	<u>10-Jan-2024</u> <ul style="list-style-type: none"> • Varicella fatality among a two-year-old girl in Trujillo. • The child had not received a varicella vaccine. • This was the first serious case recorded in Trujillo since 2018. • Vaccination campaigns were promoted after 2017 when nearly 60 children were affected by a varicella outbreak that included five deaths. • Previously, vaccination was not available nationwide.
Bulgaria	432	<u>25-Mar-2024</u> <ul style="list-style-type: none"> • 432 cases registered in the region of Montana, up from 29 reported in 2023 during the same period.

	131	<u>12-Jan-2024</u> <ul style="list-style-type: none"> 131 cases reported in Yambol since 01-Jan-2024. In Dec-2023, 247 cases were reported, up from 20 cases reported in Dec-2022.
Mongolia	14	<u>19-Jan-2024</u> <ul style="list-style-type: none"> 14 cases registered in Bayan-Ulgii aimag since the beginning of the year. In 2023, 205 cases were registered in Bayan-Ulgii aimag. This was a 2.5x increase compared to 2022.

Sources:

Poland: <https://www.rynekzdrowia.pl/Polityka-zdrowotna/W-2024-roku-w-Polsce-rekordowo-duzo-zakazen-krztuscem-ponad-trzydziestokrotny-skok,266802,14.html>

Vietnam: <https://hanoimoi.vn/so-ca-mac-sot-xuat-huyet-thuy-dau-tai-ha-noi-tang-tro-lai-669008.html>

South Korea: <https://www.news1.kr/bio/pharmaceutical-bio/5442519>

India: <https://www.newindianexpress.com/states/kerala/2025/Feb/04/cardamom-prices-highest-in-five-years-but-declining-production-hit-small-farmers>

Peru: <https://larepublica.pe/sociedad/2024/01/10/trujillo-nina-de-2-anos-fallece-por-varicela-en-trujillo-no-tenia-la-vacuna-del-ano-la-libertad-lrsd-293110>

Bulgaria: <https://dariknews.bg/novini/bylgariia/skok-na-zarazenite-s-varicela-v-montansko-2378926>;

<https://dariknews.bg/regioni/yambol/pik-na-varicela-i-skarlatina-v-iambol-2372238>

Mongolia: <https://montsame.mn/mn/read/335863>

Observations: Global Trends

- Varicella cases plummeted in most countries during the COVID-19 pandemic (2020-2021) compared to pre-pandemic levels likely due to pandemic preventative measures that reduced population exposure to varicella zoster virus.
- However, a **resurgence** of varicella cases has been reported in many countries since ~2022 (post-pandemic).
- In 2024, varicella cases continue to be reported with **increasing trends in most countries** when compared to pandemic years (2020-2021), but cumulative yearly cases have not reached pre-pandemic levels (pre-2019) in most countries.
- Most countries globally **do not** include varicella in the routine immunization schedules for children.¹ As of 2023, **45 countries** have introduced **at least one dose** of the varicella vaccine into their routine vaccination program.

Sources:

- https://immunizationdata.who.int/global/wiise-detail-page/introduction-of-varicella-vaccine?ISO_3_CODE=&YEAR=

Research Spotlight

Notable Observations



Declining vaccination rates:

Varicella vaccine coverage among kindergarteners continues to decline.¹
10.4% decrease in routine vaccination in 2020 and 2021 cohorts compared to 2016-2020 cohorts.²



Rising non-medical exemptions:

Significant contributor to reduced coverage and increased outbreak risk among kindergarten-aged cohorts.¹



Rising coverage rates among children of military families until the pandemic onset:

Lower coverage by two years of age was found among children born during 2018-2019, consistent with the onset of the COVID-19 pandemic.³



Continuity of care gap for military children:

Changes in healthcare location affect large proportions of children in the military health system and are associated with delayed completion of the recommended childhood vaccine series.³



Post-exposure prophylaxis:

VARIZIG®, Varicella Zoster Immune Globulin (Human), is indicated for post-exposure prophylaxis of varicella in high-risk individuals. High-risk groups include: Immunocompromised children and adults, newborns of mothers with varicella shortly before or after delivery, premature infants, neonates, and infants less than one year of age, adults without evidence of immunity, and pregnant women.^{4, 5}

VARIZIG® administration is intended to reduce the severity of varicella.

VARIZIG® is the recommended first-line for varicella zoster post-exposure prophylaxis among high-risk populations, according to all relevant associations such as the CDC, American Society of Transplantation (AST) Infectious Diseases Community of Practice, American Academy of Pediatrics (AAP), and American College of Obstetricians and Gynecologists (ACOG).^{5, 6, 7}

VARIZIG® prescribing for vulnerable children exposed to varicella has increased since 2012.⁸

VARIZIG® PEP was associated with a lower rate of varicella compared to acyclovir among exposed children.⁸

Sources:

1. Coverage with Selected Vaccines and Exemption Rates Among Children in Kindergarten — United States, 2023–24 School Year. Seither R, Yusuf OB, Dramann D, et al., *MMWR Morb Mortal Wkly Rep.* 2024;73(41):925–932.
2. Impact of the COVID-19 pandemic on routine childhood vaccination in 9 US jurisdictions. Trehan A, Patel Murthy B, Zell ER, et al., *Vaccine.* 2024 Sep 17;42(22):125997.
3. Vaccine completion and timeliness among children in the Military Health System: 2010–2019 Romano CJ, Burrell M, Bukowski AT, et al., *Pediatrics.* 2024 Oct 1;154(4):e2023064965.
4. VARIZIG [package insert]. Kamada Inc September 2022.
5. The CDC updated Recommendations for Use of VARIZIG®—United States, 2013.
6. Varicella Zoster virus in solid organ transplantation: Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice, 2019.
7. Red-Book: 2021–2024 Report of the Committee on Infectious Diseases.
8. Post-Exposure Prophylaxis for Varicella-Zoster Virus Exposure in High-Risk Children. Shteynberg E, Sun S, Jhaveri R, Patel SJ. *J Pediatric Infect Dis Soc.* 2024 Jan 29;13(1):69–74.

*Please see page 21 for VARIZIG® Important Safety information.

Study 1

Coverage with Selected Vaccines and Exemption Rates Among Children in Kindergarten — United States, 2023–24 School Year

Seither R, Yusuf OB, Dramann D, et al., *MMWR Morb Mortal Wkly Rep.* 2024;73(41):925-932.

TAKEAWAYS	<ul style="list-style-type: none">• Since 2019–2020, vaccine coverage for varicella declined year-over-year among kindergarten students, while school exemption rates (medical and non-medical) have increased across most US states.• Coverage levels and exemption rates vary widely among states; 15 states show vaccination rates below 90% for the 2023-2024 school year. The lowest coverage of under 80%, and highest exemption rate of 14.3%, both occur in Idaho.• Two-dose varicella coverage is lower on average across US states than both two-dose measles, mumps and rubella vaccine and four-dose polio vaccine coverage among kindergarten-aged children.		
IMPLICATIONS	<ul style="list-style-type: none">• Declining varicella coverage increases the susceptibility of communities to outbreaks, particularly where there are clusters of unvaccinated children such as at schools and other public settings.• Increased varicella disease trends should be anticipated in states where vaccine exemptions have increased and vaccination coverage has decreased.		
PUBLISHED	17-Oct-2024	STUDY PERIOD	2023-2024 School Year
POPULATION	US kindergarteners from public schools in 49 states and the District of Columbia (DC), and private schools in 48 states and DC (Montana did not report data).		
ANALYSIS	Cross-sectional study assessing vaccine coverage and exemption rates among kindergartners.		
KEY FINDINGS	National Varicella Coverage (2023-24)	92.4%, a decline from 92.9% (2022–23) and 94.8% (pre-pandemic, 2019–20).	
	Healthy People 2030 Target	Coverage remains above the target of 90% nationally.	
	Jurisdictions Below 90% Coverage	15 jurisdictions; lowest coverage reported in Idaho (79.1%).	
	Jurisdictions with ≥95% Coverage	12 jurisdictions achieved coverage ≥95%.	
	Exemption Rate Trend	Exemptions increased to 3.3% from 3.0% (2022–23) and 2.6% (2021–22).	
	Jurisdictions with Exemption Increases	41 jurisdictions reported increased exemption rates; 14 jurisdictions exceed 5%.	
	Contribution of Non-Medical Exemptions	94% were non-medical, accounting for most of the increase in exemptions.	
LIMITATIONS	Inter-state variability in data collection methods, exemption types and grace periods. Proportion of population surveyed differs by state. Exclusion of some groups like home-schooled children and jurisdictions (e.g. Montana), and survey sampling differences may impact representativeness among states. Errors in vaccine documentation/records may result in under- or over-estimation of vaccine coverage.		

Study 2

Impact of the COVID-19 pandemic on routine childhood vaccination in 9 US jurisdictions. Treharne A, Patel Murthy B, Zell ER, et al., *Vaccine*. 2024 Sep 17;42(22):125997.

TAKEAWAYS	<ul style="list-style-type: none">There was a 10.4% decrease in routine vaccination in 2020 and 2021 cohorts compared to 2016-2020 cohorts. The range of percent decreases across the jurisdictions was 8.7-13.7%.		
IMPLICATIONS	<ul style="list-style-type: none">The declines in vaccination coverage for routine children's vaccines could foreshadow outbreaks of vaccine-preventable diseases in the future. Concerted efforts to educate about the importance of staying up to date on routine vaccines, and getting children caught up to vaccines are needed at all levels (practitioner, state, and federal) to reverse declines experienced due to the COVID-19 pandemic.		
PUBLISHED	25-May-2024	STUDY PERIOD	2016-2022
POPULATION	A study was conducted in nine jurisdictions (New York City, Iowa, Louisiana, Michigan, Minnesota, North Dakota, Oregon, Washington, Wisconsin) with high quality vaccine data based on IIS functional standards, using routine high-quality immunization data. Data was collected from 2016-2022.		
ANALYSIS	Childhood vaccine coverage was measured between birth cohorts in 2020, 2021, and 2022 compared to a baseline from 2016-2020. Population size for each age group was obtained from the National Center for Health Statistics' Bridging Population estimates.		
KEY FINDINGS	<p>Several Reasons are stated behind vaccine hesitancy:</p> <ul style="list-style-type: none">The most common reasons stated behind vaccine hesitancy included: a lack of available information, perceived low risk of disease, side effects, community influence, religion, family, concerns about vaccine schedules, efficacy, cost, and access.During the pandemic 42.9% of parents in New York City reported delaying children's preventative health services due to limited appointments. Additionally, 42.2% of parents reported delaying appointments due to concerns of COVID-19 exposure.Additionally, communities moved away from urban, densely populated areas – changes in NYC addresses increased by 36% in 2020, which was 65% higher than rates seen in 2019. This reason was cited to be a potential reason for coverage decline in 2020.		
LIMITATIONS	<ul style="list-style-type: none">Only about 30% of the US population is covered in this study, so the study may not be generalizable to the entire population.2020 population denominators were used for the 2021 birth cohort calculations, which could affect vaccine estimates.		

Study 3

Vaccine completion and timeliness among children in the Military Health System: 2010-2019

Romano CJ, Burrell M, Bukowinski AT, et al., *Pediatrics*. 2024 Oct 1;154(4):e2023064965.

TAKEAWAYS	<ul style="list-style-type: none">• Completion of the 7-vaccine series recommended by ACIP reached a peak of 78.7% among children born from 2016-2017, exceeding national estimates.• However, over 1/3 (36.2%) experienced delays in the recommended timeliness.• Varicella vaccination was not among the most common vaccines contributing to non-completion or delays in completion.• Lower coverage was found among children born during 2018-2019, which would be the cohort with vaccine eligibility occurring during the onset of the COVID-19 pandemic, and consistent with national trends.• Elevated risk for noncompletion and delays was linked to changes in healthcare location, which affected a large proportion (64%) of the study population.		
IMPLICATIONS	<ul style="list-style-type: none">• Children of military families face unique circumstances that can impact the completion and timeliness of vaccinations, although varicella was one of the less commonly-implicated vaccines in terms of incomplete or delayed coverage.• Continuity of care can be improved upon to ensure children in military families receive all recommended doses on time.• Similar to national trends, gaps remain following the onset of the COVID-19 pandemic, which indicates the need to continue efforts to improve coverage for childhood vaccines.		
PUBLISHED	19-Sept-2024	STUDY PERIOD	2010-2019
POPULATION	Over one million children born between 2010-2019 in the Military Health System database.		
ANALYSIS	Modified Poisson regression models were used to calculate risk ratios (RRs) and 95% confidence intervals (CIs) for noncompletion and delays in completing the recommended vaccine series by age two years, adjusting for demographic characteristics.		
KEY FINDINGS	Full 7-vaccine series coverage and timeliness	Of 275,967 children, 74.4% completed the combined 7-vaccine series, with 36.2% of completers experiencing delays.	
	Yearly trends	The risk for noncompletion of the combined 7-vaccine series by age 24 months was highest among children born in 2010-2011 (adjusted risk ratio [aRR] = 1.44). This risk generally decreased over time, though the COVID-19 pandemic disrupted this trend for children born in 2018-2019.	
	Individual vaccine trends	Completion rates were lowest for rotavirus (77.5%), diphtheria, tetanus, and pertussis (83.1%), Haemophilus influenzae type b (86.6%), and pneumococcal conjugate (88.4%).	
	Risks for noncompletion and delays	Associated with children born to younger parents (aRR = 1.33) and those with a well-child care location change (aRR = 1.10).	
LIMITATIONS	<ul style="list-style-type: none">• Inclusion criteria limited the study to children receiving care mainly at civilian facilities and those with inconsistent TRICARE health insurance enrollment.• The MHS immunization database captures vaccinations at military clinics well, but vaccines received outside this context may be less documented.• Children with dual insurance coverage are less likely to have vaccinations billed to TRICARE, as it serves as a secondary payor source.		

Study 4

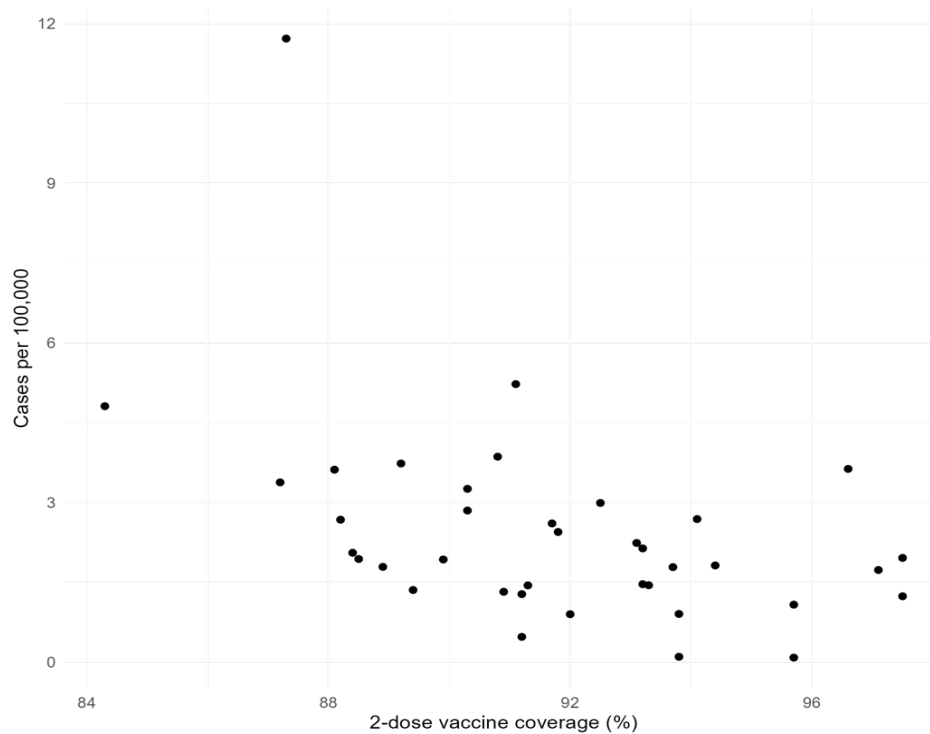
Post-Exposure Prophylaxis for Varicella-Zoster Virus Exposure in High-Risk Children. Shteynberg E, Sun S, Jhaveri R, Patel SJ. *J Pediatric Infect Dis Soc*. 2024 Jan 29;13(1):69-74.

TAKEAWAYS	<ul style="list-style-type: none">• Post-exposure prophylaxis (PEP) prescribing patterns in pediatric patients show considerable variation by regimen and risk condition and vary widely by institution.• Varicella zoster-specific immune globulin (VARIZIG®) use has increased since 2012, but acyclovir is still commonly used for PEP, especially among oncology/stem cell transplant and NICU/nursery patients.• Although a smaller proportion of patients in the acyclovir group had at least one risk condition, the rate of subsequent varicella disease codes was more than four times higher in those who received acyclovir (15.4%, 30/195) compared to those who received VARIZIG® (3.4%, 5/146).		
IMPLICATIONS	<ul style="list-style-type: none">• There were likely missed opportunities for VARIZIG® administration.• Provider awareness of recommended post-exposure treatment, cost barriers, provider comfort and familiarity with VARIZIG®, and willingness to consult infectious disease specialists may be some reasons for the prescribing patterns found.• Better adherence to CDC guidelines with increased receipt of VARIZIG® could reduce complications of varicella infection in high-risk children.		
PUBLISHED	21-Nov-2023	STUDY PERIOD	2009-2019
POPULATION	Pediatric patients with first clinical encounters for varicella among a network of 47 public children's hospitals in the US		
ANALYSIS	Retrospective cohort study assessing PEP prescribing practices over time and the rate of varicella disease clinical encounters up to 30 days following PEP prescription.		
ANALYSIS	This study was conducted on varicella post-exposure prophylaxis (PEP) among children at high risk following varicella exposure, using data from 47 not-for-profit, tertiary care pediatric hospitals in the US. The researchers analyzed PEP regimens, variations based on underlying conditions and institutions, and the incidence of varicella disease.		
LIMITATIONS	<ul style="list-style-type: none">• Inclusion and exclusion criteria may have led to missed study subjects:• A 10-day window was specified for administering PEP from the clinical encounter date, though the actual exposure could have occurred earlier.• ICD-9/10 codes were used for determination of varicella zoster virus exposure, and significant details about underlying conditions were lacking.• Variations in PEP practices may have arisen due to different clinical assessments by treating clinicians.• Care received outside of the hospital network could not be evaluated, and findings may be more relevant among not-for-profit tertiary care hospitals.		

*Please see page 21 for VARIZIG® Important Safety information.

Appendix

- A Spearman's rank correlation was performed to assess the relationship between vaccine coverage and case incidence in 2024, as shown in the plot to the right. A **significant moderate negative correlation** was observed (-0.48 , $p\text{-value} < 0.005$).
- The map depicting reported incidence of varicella and two-dose vaccine coverage in 2024 (on page 5) was created by taking the value for vaccine coverage and case incidence for each state, and separating them each into three equal sized categories, or quantiles, per variable. The states were then mapped based on the combined assigned quantile for both vaccine coverage and case incidence.



VARIZIG INDICATION AND IMPORTANT SAFETY INFORMATION

INDICATION:

VARIZIG®, Varicella Zoster Immune Globulin (Human), is indicated for post-exposure prophylaxis of varicella in high-risk individuals. High-risk groups include: Immunocompromised children and adults, newborns of mothers with varicella shortly before or after delivery, premature infants, neonates, and infants less than one year of age, adults without evidence of immunity, and pregnant women.

VARIZIG® administration is intended to reduce the severity of varicella.

IMPORTANT SAFETY INFORMATION:

VARIZIG® contains trace amounts of IgA. Individuals known to have anaphylactic or severe systemic (hypersensitivity) reactions to human immune globulin preparations should not receive VARIZIG®. IgA-deficient patients with antibodies against IgA and a history of hypersensitivity may have an anaphylactoid reaction. Thrombotic events may occur during or following treatment with immune globulin products.

Administer VARIZIG® intramuscularly only.

In patients who have severe thrombocytopenia or any coagulation disorder that would contraindicate intramuscular injections, only administer VARIZIG® if the expected benefits outweigh the potential risks. Severe hypersensitivity reactions may occur following VARIZIG® administration.

In case of hypersensitivity, discontinue the administration of VARIZIG® immediately and provide appropriate treatment. Because VARIZIG® is made from human plasma, it may carry a risk of transmitting infectious agents, e.g., viruses, the variant Creutzfeldt-Jakob disease agent, and, theoretically, the Creutzfeldt-Jakob disease agent.

The most serious adverse drug reactions observed in clinical trials for all subjects and patients include pyrexia, nausea, and vomiting. The most common adverse drug reactions observed in clinical trials for all subjects and patients were injection site pain, headache, chills, fatigue, rash, and nausea.

For full prescribing information please refer to:

<https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=f367f996-aafa-4b8b-8cb4-63a009cd2015>

To report SUSPECTED ADVERSE REACTIONS, contact Kamada at pharmacovigilance@kamada.com.

VARIZIG® [Varicella Zoster Immune Globulin (Human)] and all Kamada brand, product, service and feature names, logos, and slogans are trademarks or registered trademarks of Kamada in the United States and/or other countries.

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