

Topical Antifungal Prescribing for Medicare Part D Beneficiaries — United States, 2021

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Abstract

Incorrect use of topical antifungals and antifungal-corticosteroid combinations is likely contributing to the global emergence and spread of severe antimicrobial-resistant superficial fungal infections, which have recently been detected in the United States. Understanding prescribing patterns is an initial step in establishing and promoting recommended use of these medications. Using 2021 Medicare Part D data, CDC examined prescription volumes, rates, and costs for topical antifungals (including topical combination antifungal-corticosteroid medications). Total prescription volumes were compared between higher-volume prescribers (top 10% of topical antifungal prescribers by volume) and lower-volume prescribers. During 2021, approximately 6.5 million topical antifungal prescriptions were filled (134 prescriptions per 1,000 beneficiaries), at a total cost of \$231 million. Among 1,017,417 unique prescribers, 130,637 (12.8%) prescribed topical antifungals. Primary care physicians wrote the highest percentage of prescriptions (40.0%), followed by nurse practitioners or physician assistants (21.4%), dermatologists (17.6%), and podiatrists (14.1%). Higher-volume prescribers wrote 44.2% (2.9 million) of all prescriptions. This study found that enough topical antifungal prescriptions were written for approximately one of every eight Medicare Part D beneficiaries in 2021, and 10% of antifungal prescribers prescribed nearly one half of these medications. In the setting of emerging antimicrobial resistance, these findings highlight the importance of expanding efforts to understand current prescribing practices while encouraging judicious prescribing by clinicians and providing patient education about proper use.

Introduction

Superficial fungal skin infections have an estimated lifetime prevalence of more than 20% worldwide and are particularly common among adults aged ≥65 years (1–3). The emergence

and spread of antimicrobial-resistant superficial fungal infections, especially dermatophytosis (also known as ringworm or tinea), has led to large outbreaks of extensive, recalcitrant skin infections in South Asia that frequently do not respond to topical antifungals or first-line oral therapies. This emergence and spread are likely exacerbated by the overuse and misuse of topical antifungals, particularly antifungal-corticosteroid combination creams (1,4). Cases of antimicrobial-resistant dermatophytosis have been identified in at least 11 U.S. states (5), with patients experiencing extensive lesions and delays in diagnosis (6). In the United States, nonrecommended topical antifungal prescribing is likely common, because diagnosis of cutaneous fungal infections by visual inspection is frequently incorrect, including among board-certified dermatologists (7), and clinicians across

INSIDE

- 6 Advisory Committee on Immunization Practices Recommended Immunization Schedule for Children and Adolescents Aged 18 Years or Younger — United States, 2024
- 11 Advisory Committee on Immunization Practices Recommended Immunization Schedule for Adults Aged 19 Years or Older — United States, 2024
- 16 Effectiveness of Bivalent mRNA COVID-19 Vaccines in Preventing COVID-19–Related Thromboembolic Events Among Medicare Enrollees Aged ≥65 Years and Those with End Stage Renal Disease — United States, September 2022–March 2023
- 24 Notice to Readers: Change in Publication Date of *MMWR* Series
- 25 QuickStats

Continuing Education examination available at https://www.cdc.gov/mmwr/mmwr_continuingEducation.html



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specialties rarely perform confirmatory diagnostic testing (2,8). Understanding prescribing patterns, including identification of clinicians who prescribe a disproportionate volume of topical antifungals, might help establish and promote correct use of these medications (9). Centers for Medicare & Medicaid Services (CMS) data were used to characterize prescribing volume of topical antifungal medications among Medicare Part D beneficiaries in the United States during 2021.

Methods

Data Source

Approximately 48.8 million (76%) Medicare beneficiaries were enrolled in the Part D prescription drug benefit program in 2021,^{*,†} the most recent year of data available for this study. The publicly available CMS Medicare Part D Prescribers-by-Provider and Drug data set[§] contains information on the total number of prescriptions (including refills) and total drug

costs,[¶] aggregated by National Provider Identifier number and drug name. The data set excludes clinician records with <11 prescriptions. Prescribers from outside the United States or whose U.S. Census Bureau region was unknown were excluded from the analysis.^{**} The Medicare Monthly Enrollment dataset^{††} was used to ascertain the total number of Medicare Part D beneficiaries.

Data Analysis

Prescription volume (i.e., number of prescriptions), total costs, and average costs for topical antifungal and topical antifungal-corticosteroid drugs covered by Medicare Part D^{§§} were assessed. Prescription rates per 1,000 beneficiaries were calculated by drug and region and to calculate prescription rates per 1,000 beneficiaries by drug and region. Prescription rates per prescriber were calculated by tabulating number of providers overall and by provider type (primary care physician [internal medicine or family medicine physician], nurse

*Medicare, the federal health insurance program, is available to most persons aged ≥65 years, certain persons aged <65 years who are receiving disability benefits, and persons with end stage renal disease. Medicare Part D is the part of Medicare that helps cover the cost of prescription drugs. <https://www.medicare.gov/what-medicare-covers/your-medicare-coverage-choices/whats-medicare>

† <https://data.cms.gov/summary-statistics-on-beneficiary-enrollment/medicare-and-medicare-reports/cms-program-statistics-medicare-part-d-enrollment>

§ <https://data.cms.gov/provider-summary-by-type-of-service/medicare-part-d-prescribers/medicare-part-d-prescribers-by-provider-and-drug>

¶ Cost includes the ingredient cost, dispensing fee, and sales tax and is based on the amounts paid by the Part D plan, Medicare beneficiary, government subsidies, and any other third-party payers. <https://data.cms.gov/resources/medicare-part-d-prescribers-by-provider-and-drug-data-dictionary>

** https://www2.census.gov/geo/pdfs/maps-data/maps/reference/us_regdiv.pdf

†† <https://data.cms.gov/summary-statistics-on-beneficiary-enrollment/medicare-and-medicare-reports/medicare-monthly-enrollment>

§§ Butenafine, butoconazole, ciclopirox, clotrimazole, clotrimazole-betamethasone dipropionate, econazole, efinaconazole, ketoconazole, luliconazole, miconazole, naftifine, nystatin, nystatin-triamcinalone, oxiconazole, sertaconazole, sulconazole, tavaborole, and terconazole.

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practitioner or physician assistant, dermatologist, podiatrist, and other) in the Medicare Part D Prescribers—by Provider and Drug data set as the denominator.

Higher-volume prescribers were defined as those within the top 10th percentile of prescriber-level topical antifungal prescriptions by volume. The volume and percentage of topical antifungal prescriptions written by higher-volume prescribers compared with lower-volume prescribers (bottom 90th percentile) were assessed overall and by prescriber type. Analyses were conducted using SAS software (version 9.4; SAS Institute). This activity was reviewed by CDC, deemed not research, and was conducted consistent with applicable federal law and CDC policy.^{¶¶}

Results

Prescriptions

During 2021, a total of 6.5 million topical antifungal prescriptions were filled by Part D beneficiaries (overall rate = 134.0 prescriptions per 1,000 beneficiaries) (Table 1). By volume, the most common prescriptions were for ketoconazole (2.4 million [36.6%]), nystatin (1.9 million [29.0%]), and clotrimazole-betamethasone dipropionate (0.9 million [14.7%]). The total cost for all topical antifungal prescriptions was \$231 million. The highest average per prescription costs

were for efinaconazole (\$1,035.38), tavaborole (\$784.63), and oxiconazole (\$729.84); the lowest average costs were for nystatin (\$25.66), clotrimazole-betamethasone dipropionate (\$27.82), clotrimazole (\$30.36), and ketoconazole (\$30.69). By U.S. Census Bureau region, the highest prescription rate was in the Northeast (188.0 prescriptions per 1,000 beneficiaries), followed by the South (138.1 per 1,000).

Prescribers

Among 1,017,417 unique prescribers, 130,637 (12.8%) prescribed topical antifungals (Table 2). The number of prescriptions per provider was highest for dermatologists (87.1), followed by podiatrists (67.2), and primary care physicians (12.3). Among 6.5 million topical antifungal prescriptions, the most were written by primary care physicians (2.6 million [40.0%]), followed by nurse practitioners or physician assistants (1.4 million [21.4%]), dermatologists (1.1 million [17.6%]), and podiatrists (0.9 million [14.1%]). Among all topical antifungal prescriptions, 44.2% (2.9 million) were written by the top 10% (13,106) of topical antifungal prescribers. By provider type, the percentage of topical antifungal prescriptions written by higher-volume topical antifungal prescribers ranged from 35.5% for dermatologists to 54.8% for podiatrists.

Discussion

This analysis of publicly available CMS data found that 6.5 million topical antifungal prescriptions (enough to provide

^{¶¶} 45 C.F.R. part 46.102(l)(2), 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.

TABLE 1. Number of topical antifungal prescriptions, prescriptions per 1,000 beneficiaries, and cost, by drug and U.S. Census Bureau region — United States, 2021

Characteristic	No. of prescriptions (% of all prescriptions)	Prescriptions per 1,000 beneficiaries	Aggregate cost, all prescriptions, USD*	Avg. cost per prescription, USD*
Antifungal drug				
Ketoconazole [†]	2,364,169 (36.6)	49.1	72,556,081.61	30.69
Nystatin	1,871,368 (29.0)	38.9	48,025,095.10	25.66
Clotrimazole-betamethasone dipropionate	945,838 (14.7)	19.6	26,311,901.12	27.82
Ciclopirox	657,986 (10.2)	13.7	22,739,088.92	34.56
Clotrimazole	397,603 (6.2)	8.3	12,070,066.47	30.36
Econazole	75,675 (1.2)	1.6	4,414,180.46	58.33
Nystatin-triamcinolone	55,276 (0.9)	1.1	2,928,976.33	52.99
Terconazole	32,203 (0.5)	0.7	1,051,091.05	32.64
Efinaconazole	17,881 (0.3)	0.4	18,513,585.90	1,035.38
Oxiconazole	14,892 (0.2)	0.3	10,868,838.98	729.84
Naftifine	13,532 (0.2)	0.3	5,018,673.14	370.87
Tavaborole	8,317 (0.1)	0.2	6,525,735.61	784.63
Other [§]	400 (—)	—	185,439.42	463.60
U.S. Census Bureau region				
Northeast	1,677,727 (26)	188.0	78,235,437.54	46.63
Midwest	1,198,093 (19)	112.2	34,204,692.89	28.55
South	2,489,321 (39)	138.1	74,554,713.01	29.95
West	1,089,999 (17)	103.5	44,213,910.67	40.56
Total	6,455,140 (100)	134.0	231,208,754.11	35.82

* All costs are in U.S. dollars.

[†] It was not possible to distinguish oral from topical ketoconazole, but ketoconazole was included in the analysis because oral ketoconazole use is discouraged because of safety concerns. <https://www.fda.gov/drugs/drug-safety-and-availability/fda-drug-safety-communication-fda-warns-prescribing-nizoral-ketoconazole-oral-tablets-unapproved>

[§] Butenafine (41 prescriptions), luliconazole (169), miconazole (155), and sertaconazole (35).

TABLE 2. Number of topical antifungal prescriptions per provider and prescribing volume among higher-volume* and lower-volume† prescribers, by provider type for Medicare Part D beneficiaries — United States, 2021

Provider type (no.)	No. of prescriptions per provider	All topical antifungal prescribers		Higher-volume prescribers (top 10%)		Lower-volume prescribers (bottom 90%)	
		No. of prescribers	No. of prescriptions (% of total)§	No. of prescribers	No. of prescriptions (% of total)¶	No. of prescribers	No. of prescriptions (% of total)¶
Primary care physician (209,169)	12.3	61,735	2,579,045 (40.0)	6,200	973,824 (37.8)	55,535	1,605,221 (62.2)
NP or PA (263,999)	5.2	34,476	1,379,981 (21.4)	3,428	570,577 (41.3)	31,048	809,404 (58.7)
Dermatologist (13,029)	87.1	10,735	1,134,347 (17.6)	1,068	402,750 (35.5)	9,667	731,597 (64.5)
Podiatrist (13,527)	67.2	8,401	909,569 (14.1)	838	498,210 (54.8)	7,563	411,359 (45.2)
Other (517,693)	0.9	15,290	452,198 (7.0)	1,507	165,742 (36.7)	13,783	286,456 (63.3)
Total (1,017,417)	6.3	130,637	6,455,140 (100.0)	13,106	2,851,394 (44.2)	117,531	3,603,746 (55.8)

Abbreviations: NP = nurse practitioner; PA = physician assistant.

* Top 10% of topical antifungal providers, by volume.

† Bottom 90% of topical antifungal providers, by volume.

§ Column percentage.

¶ Row percentage.

one prescription to more than one eighth of all beneficiaries) were written for Medicare Part D beneficiaries in 2021, at a cost of \$231 million. The actual volume of topical antifungal use among the study population is likely considerably higher than that identified in this study because most topical antifungals can be purchased over the counter without a prescription; such topical antifungal use is not recorded in CMS data and is an important consideration for potential antifungal stewardship efforts. The large volume of topical antifungals used in the United States warrants increased attention given the infrequent use of confirmatory testing, inaccuracy of diagnosis made by physical examination alone, and the recent emergence of severe and antimicrobial-resistant superficial skin infections (1,5,6). To help control the emergence and spread of antimicrobial-resistant superficial fungal infections and help promote the appropriateness of topical antifungal prescribing, health care providers could use diagnostic testing*** whenever possible to confirm suspected superficial fungal infections. Further, health care providers can educate patients about prognosis, benefits, and harms of topical antifungal and combination antifungal-corticosteroid treatment (both prescription and over-the-counter), and the importance of using these medications as prescribed or according to manufacturer instructions.

Variation in Prescribing by Prescriber Type and Region

The largest number of topical antifungal prescriptions was written by primary care physicians, nurse practitioners, or physician assistants, suggesting that efforts to determine and improve appropriateness of prescribing could prioritize these groups. Although dermatologists and podiatrists had lower prescribing volumes compared with other groups, they had higher per-provider prescribing rates. This observation could reflect that dermatologists and podiatrists might see patients

with superficial fungal infections more frequently than do other provider types. In contrast to systemic antibiotic prescribing, which is highest in the South (9), topical antifungal prescribing rates were highest in the Northeast. Reasons for this finding are unclear but could reflect a higher prevalence of superficial fungal infections, more ready access to medical care, or less frequent use of over-the-counter topical antifungal medications in the Northeast compared with that in other regions.

High Volume Prescribers and Prescriptions

As with antibiotic prescribing for Medicare Part D beneficiaries, 10% of prescribers wrote a disproportionately large percentage (>40%) of topical antifungal prescriptions (9). Among podiatrists, the top 10% of prescribers wrote more than one half of topical antifungal prescriptions. These findings suggest potential opportunities to prioritize higher-volume topical antifungal prescribers for antimicrobial stewardship interventions using evidence-based techniques such as peer comparison audit and feedback; however, additional data are needed to determine whether topical antifungal prescribing rates correlate with rates of incorrect prescribing, as shown for systemic antibiotics in primary care settings (9).

The large volume of clotrimazole-betamethasone dipropionate prescriptions (0.9 million; 15% of all topical antifungal prescriptions) is potentially concerning, as use of combination topical medications containing corticosteroids and antifungal agents has been proposed as a potential driver of emerging antimicrobial-resistant dermatophytosis (10). In addition, clotrimazole-betamethasone dipropionate contains a high-potency steroid that can cause skin damage if applied to intertriginous areas as well as hypothalamic-pituitary-adrenal axis suppression if used for a prolonged time or over a large body surface area.††† Clinicians should be aware of the potential risks

*** <https://www.cdc.gov/fungal/diseases/ringworm/health-professionals.html>

††† https://www.accessdata.fda.gov/drugsatfda_docs/label/2014/018827s046lbl.pdf

Summary

What is already known about this topic?

Severe antimicrobial-resistant superficial fungal infections have recently been detected in the United States; evaluating topical antifungal use is an initial step in developing strategies to prevent the global emergence and spread of these infections.

What is added by this report?

A total of 6.5 million topical antifungal prescriptions, costing \$231 million, were filled for Medicare Part D beneficiaries in 2021, approximately one prescription for every eight beneficiaries. Most prescriptions were written by primary care physicians, nurse practitioners, or physician assistants.

What are the implications for public health practice?

The large volume of topical antifungal prescriptions in the context of emerging resistance highlights the need to better understand current prescribing practices and to encourage judicious prescribing by clinicians and improve patient education about recommended use.

associated with clotrimazole-betamethasone dipropionate use and consider alternatives such as antifungal monotherapy, with a short course of low-potency corticosteroid treatment added if needed for symptoms such as severe pruritis. §§§

Limitations

The findings in this report are subject to at least four limitations. First, the data set does not contain information on individual patients, drug indication (i.e., candidiasis versus dermatophytosis), or diagnostic testing, so prescribing appropriateness could not be determined. Second, the data set analyzed only identifies prescriptions for Medicare Part D beneficiaries and therefore does not represent all Medicare beneficiaries; topical antifungal prescribing patterns might differ among other populations. Third, the data set only contained information on prescription topical antifungals and did not capture over-the-counter topical antifungal use; therefore, actual topical antifungal use is likely underestimated. Finally, this study likely underestimates the total volume of topical antifungal drug prescribing among Medicare Part D beneficiaries because records for some lower-volume prescribers (those with <11 prescriptions per year for any given drug) are not included in the data set, and prescribers whose census region was unknown were excluded.

Implications for Public Health Practice

The substantial volume of topical antifungal and antifungal-corticosteroid prescriptions among Medicare Part D beneficiaries in the setting of emerging resistant infections underscores

the need to evaluate current practices of topical antifungal use. Health care providers should be judicious in prescribing topical antifungals and combination antifungal-corticosteroid medications for suspected superficial fungal infections, using testing when feasible to confirm diagnoses, and can educate patients about the correct use of topical antifungals and combination antifungal-corticosteroids.

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§§§ <https://www.aafp.org/pubs/afp/collections/choosing-wisely/471.html>

Advisory Committee on Immunization Practices Recommended Immunization Schedule for Children and Adolescents Aged 18 Years or Younger — United States, 2024

A. Patricia Wodi, MD¹; Neil Murthy, MD¹; Veronica V. McNally, JD²; Matthew F. Daley, MD³; Sybil Cineas, MD⁴

At its October 2023 meeting, the Advisory Committee on Immunization Practices* (ACIP) approved the Recommended Child and Adolescent Immunization Schedule for Ages 18 Years or Younger, United States, 2024. The child and adolescent immunization schedule, which can be found on the CDC immunization schedule website (<https://www.cdc.gov/vaccines/schedules>), is published annually to consolidate and summarize updates to ACIP recommendations on the vaccination of children and adolescents and to assist health care providers in implementing current ACIP recommendations. The 2024 immunization schedule includes several changes to the cover page, tables, notes, and appendix from the 2023 immunization schedule.[†] In addition, the 2024 child and adolescent immunization schedule includes a new addendum section to summarize new or updated ACIP recommendations that will occur before the next annual update to the child and adolescent immunization schedule. Health care providers are advised to use the cover page, tables, notes, appendix, and addendum together to identify the recommended immunizations for patient populations.

The 2024 child and adolescent immunization schedule is recommended by ACIP (<https://www.cdc.gov/vaccines/acip>) and approved by CDC (<https://www.cdc.gov>), the American Academy of Pediatrics (<https://www.aap.org>), the American Academy of Family Physicians (<https://www.aafp.org/home.html>), the American College of Obstetricians and Gynecologists (<https://www.acog.org/>), the American College of Nurse-Midwives (<https://www.midwife.org>), the American Academy of Physician Associates (<https://www.aapa.org>),

and the National Association of Pediatric Nurse Practitioners (<https://www.napnap.org>).

ACIP's recommendations for the use of each vaccine and other immunizing agents are developed after in-depth reviews of product-related data, including the epidemiology and societal impacts of the vaccine-preventable disease, efficacy and effectiveness of the vaccine or other immunizing agent, safety of the vaccine or other immunizing agent, quality of evidence, feasibility of program implementation, impact on health equity, and economic analyses of immunization policy (1,2). Health care providers should be aware that changes in recommendations for specific vaccines and related agents occur between these annual updates to the child and adolescent immunization schedule.[§] Such changes will be summarized in the new addendum section; however, health care providers are encouraged to refer to ACIP vaccine recommendations for detailed guidance on the use of each product (<https://www.cdc.gov/vaccines/hcp/acip-recs>). An online version of the 2024 child and adolescent immunization schedule and instructions for downloading the schedule app are available on the immunization schedule website (<https://www.cdc.gov/vaccines/schedules>). The use of trade names in the child and adolescent immunization schedule and in this report is for identification purposes only and does not imply endorsement by ACIP or CDC.

Changes in the 2024 Child and Adolescent Immunization Schedule

Changes to the recommendations for vaccines and related agents in the 2024 immunization schedule for children and adolescents aged ≤18 years include new or updated recommendations for influenza vaccine (3), pneumococcal vaccines (4), respiratory syncytial virus monoclonal antibody

* Recommendations for routine immunization of children and adolescents are developed by ACIP, a federal advisory committee chartered to provide expert external advice and guidance to the CDC director on use of vaccines and related agents for the control of vaccine-preventable diseases in the civilian population of the United States. Recommendations for routine immunization of children and adolescents are harmonized to the greatest extent possible with recommendations made by the American Academy of Pediatrics, the American Academy of Family Physicians, the American College of Obstetricians and Gynecologists, the American College of Nurse-Midwives, the American Academy of Physician Associates, and the National Association of Pediatric Nurse Practitioners. ACIP recommendations become official agency guidelines once the recommendation has been adopted by the CDC Director. Additional information about ACIP is available at <https://www.cdc.gov/vaccines/acip>.

[†] Past immunization schedules are available at <https://www.cdc.gov/vaccines/schedules/hcp/schedule-related-resources.html>.

[§] CDC encourages organizations to use syndication as a more reliable method for displaying the most current and accurate immunization schedules on an organization's website rather than copying these schedules to their websites. Use of content syndication requires a one-time step that ensures an organization's website displays current schedules as soon as they are published or revised; instructions for syndication code are available on CDC's website (<https://www.cdc.gov/vaccines/schedules/resource-library/syndicate.html>). CDC also offers technical assistance for implementing this form of content syndication (requests can be emailed to ncirdwebteam@cdc.gov).

(RSV-mAb) (5), respiratory syncytial virus vaccines (RSV) (6), COVID-19 vaccines (7), inactivated poliovirus vaccine (IPV) (8), Mpox vaccine (Mpox) (<https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2023-10-25-26/04-MPOX-Rao-508.pdf>), and meningococcal serogroups A, B, C, W, Y vaccine (MenACWY-TT/MenB-FHbp) (<https://www.cdc.gov/vaccines/acip/recommendations.html>). Diphtheria and tetanus toxoid adsorbed vaccine (DT), 13-valent pneumococcal conjugate vaccine (PCV13), bivalent COVID-19 mRNA vaccines, and meningococcal serogroups A, C, W, Y polysaccharide diphtheria toxoid conjugate vaccine (MenACWY-D, Menactra) were deleted from all sections of the schedule, because these products are no longer distributed or recommended for use in children and adolescents in the United States.

Other changes include clarification of the recommendations for diphtheria, tetanus, and acellular pertussis vaccine (DTaP), *Haemophilus influenzae* type b vaccine (Hib), human papillomavirus vaccine (HPV), measles, mumps, and rubella vaccine (MMR), serogroup B meningococcal vaccine (MenB), and tetanus, diphtheria, and acellular pertussis vaccine (Tdap). Substantial revisions were made to Table 3, which outlines the immunization schedule by medical indication. The definitions for the legend colors were revised to better highlight additional vaccination recommendations for each medical condition and to harmonize with the adult immunization schedule. Finally, a new addendum section was added, which will list new and updated ACIP recommendations that occur before the next annual update to the child and adolescent immunization schedule.

Cover page

- In the table of abbreviations and trade names, the column header was changed from “vaccine” to “vaccines and other immunizing agents” to account for the inclusion of the newly licensed RSV monoclonal antibody (nirsevimab).
- A sixth step in the “How to Use the Child and Adolescent Immunization Schedule” box was added directing health care providers to review the new Addendum section that lists new or updated ACIP recommendations that occur before the next annual update of the child and adolescent immunization schedule.
- 20-valent pneumococcal conjugate vaccine (PCV20), RSV-mAb (nirsevimab), RSV for maternal vaccination (Abrysvo), Mpox (Jynneos), and pentavalent meningococcal vaccine (MenACWY-TT/MenB-FHbp, [Penbraya]) have been added to the table listing abbreviations and trade names of vaccines and other immunizing agents.
- Diphtheria and Tetanus Toxoid Adsorbed vaccine (DT), 13-valent pneumococcal conjugate vaccine (PCV13), MenACWY-D (Menactra), and bivalent mRNA COVID-19 vaccines were removed from the table listing

abbreviations and trade names of vaccines and other immunizing agents, because they are no longer distributed or recommended for use in the United States.

Table 1 (Routine Immunization Schedule)

- The column header was changed from “vaccine” to “vaccines and other immunizing agents” to account for the inclusion of the newly licensed RSV monoclonal antibody (nirsevimab).
- **COVID-19 row:** The text overlay was revised to reflect updated vaccination recommendations. This text overlay now states, “1 or more doses of updated (2023–2024 Formula) vaccine.”
- **MenACWY row:** Menactra has been deleted.
- **Mpox row:** A new row was added for Jynneos with the column for age 18 years highlighted in purple reflecting the risk-based recommendation for this age group.
- **Pneumococcal conjugate row:** PCV20 has been added and PCV13 has been deleted.
- **Pneumococcal polysaccharide vaccine (PPSV23) row:** This row has been deleted because PPSV23 is no longer routinely recommended for all children and adolescents aged ≥ 2 years at increased risk for invasive pneumococcal disease. It is still recommended in certain circumstances.
- **RSV-mAb row:** A new row has been added with the columns for ages birth–7 months highlighted in yellow to indicate the recommended age for routine immunization. The overlaying text, “1 dose depending on maternal RSV vaccination status” was also added. In addition, age 8–19 months is highlighted in purple to reflect the risk-based recommendation for this age group.
- **RSV row:** A new row was added for Abrysvo (Pfizer Inc.) and ages 11–18 years are highlighted in purple with the overlaying text, “Seasonal administration during pregnancy” added to reflect the recommendation for the use of Abrysvo (Pfizer Inc.) during pregnancy.

Table 2 (Catch-up Immunization Schedule)

- **DTaP row:** Language for the minimum interval between doses 4 and 5 was added to clarify when a fifth dose is indicated. The text reads, “A fifth dose is not necessary if the fourth dose was administered at age ≥ 4 years and ≥ 6 months after dose 3.”
- **MenACWY row:** Menactra has been deleted.

Table 3 (Immunization by Medical Indication Schedule)

- A sentence was added to the header of Table 3 stating that medical conditions are often not mutually exclusive and that health care providers should review all relevant columns in the Table if multiple conditions are present.

- The column header was changed from “vaccine” to “vaccines and other immunizing agents” to account for the inclusion of the newly licensed RSV monoclonal antibody (nirsevimab).
- **Legend:** The definitions of the yellow, purple, and gray colors boxes in the legend were revised. Based on the revised definitions, the colors for many of the rows in this table have changed. In addition, the checked yellow color was changed to a brown color to harmonize with the 2024 adult immunization schedule.
- **Mpox row:** A new row was added for Jynneos. Across all medical indications listed, the entire row is purple reflecting the risk-based recommendation for Mpox vaccination. In the pregnancy column, an overlaying text, “See Notes” has been added, directing health care providers to review the pregnancy bullet in the Mpox vaccination notes.
- **RSV-mAb row:** A new row was added to summarize nirsevimab immunization recommendations by medical condition. The columns for both immunocompromised status (excluding HIV infection) and HIV infection with CD4 <15% or <200 cells per mm³ is highlighted in brown and an overlaying text “2nd RSV season” was added. In addition, the column for heart disease or chronic lung disease is also highlighted in brown with the overlaying text “2nd RSV season for chronic lung disease.”
- **RSV row:** A new row was added for use of Abrysvo (Pfizer Inc.) during 32–36 weeks’ gestation. The pregnancy column is highlighted in yellow with overlaying text of “seasonal administration” added to indicate that the maternal RSV vaccination recommendation is on the basis of RSV seasonality.

Vaccine Notes

The notes for each vaccine and related agent are presented in alphabetical order. Edits have been made throughout the Notes section to harmonize language, to the greatest extent possible, with that in the adult immunization schedule.

- **Additional information:** The text for vaccine injury compensation was revised to add Mpox and RSV to the list of vaccines not covered by the National Vaccine Injury Compensation Program. Mpox is covered by the Countermeasures Injury Compensation Program.
- **COVID-19:** The language in the “Routine vaccination” and “Special situations” sections was revised to reflect the current COVID-19 vaccination recommendations for children and adolescents. The number of doses needed and intervals between doses might vary on the basis of a patient’s previous vaccination history, immunocompromised status, and the vaccine product used. The “Routine vaccination” section describes the recommendations for

the general population, and the “Special situations” section describes the recommendations for persons who are moderately or severely immunocompromised. In addition, hyperlinks to the current COVID-19 vaccination schedules as well as Emergency Use Authorization indications for COVID-19 vaccines are included.

- **DTaP:** Language in the “Routine vaccination” section was revised to clarify primary and booster doses.
- **HPV:** In the “Routine vaccination” section, the recommendation for interrupted schedules was removed because that information is also presented on the Cover Page and applicable to all vaccines. In addition, to improve clarity, the words, “of any valency” were added to the bullet, “No additional dose recommended when any HPV vaccine series *of any valency* has been completed using the recommended dosing intervals.”
- **Influenza:** A hyperlink to the 2023–24 influenza recommendations and a bullet for the 2024–25 influenza recommendations were added. In the “Special situations” section, all bullets describing recommendations for persons with a history of egg allergy were removed. Persons with a history of egg allergy of any severity can be vaccinated with any influenza vaccine indicated for the recipient’s age and health status, with no additional safety considerations. A note describing this recommendation was added at the end of the “Special situations” section.
- **MMR:** The bullet, “If MMRV is used, the minimum interval between MMRV doses is 3 months” was moved to the end of the notes section. In addition, the “Routine vaccination,” “Catch-up vaccination,” and “Special situations” sections were revised to clarify that this minimal interval is applicable to all sections.
- **MenACWY:** All reference to Menactra was removed because this vaccine is no longer distributed in the United States, and any remaining doses of this product expired in October 2023. In addition, information about the use of the newly licensed pentavalent meningococcal vaccine (Penbraya) is included at the end of the MenACWY notes.
- **MenB:** A note summarizing recommendations for Penbraya was added. In addition, a link to a resource to assist health care providers with shared clinical decision-making recommendations for MenB vaccination was added.
- **Mpox:** A new section describing the recommendations for use of Jynneos in adolescents aged 18 years, including sexual risk factors and vaccination during pregnancy, was added.
- **Pneumococcal:** The “Routine vaccination,” “Catch-up vaccination,” and “Special situations” sections have been updated with the new recommendations for use of 15-valent pneumococcal conjugate vaccine (PCV15), PCV20, and PPSV23. PCV13 was deleted from all

sections. Chronic kidney disease, chronic liver disease, and moderate persistent or severe persistent asthma were added to the list of medical conditions that increase the risk for invasive pneumococcal disease.

- **Poliovirus:** The “Catch up vaccination” section has been revised to include updated recommendations for adolescents aged 18 years. Language was added stating that most adolescents aged 18 years who were born and raised in the United States can assume to be vaccinated against poliovirus as children. The “Special situations” section was revised to describe administering a one-time, lifetime IPV booster to adolescents aged 18 years who have completed the primary series and are at increased risk for exposure to poliovirus.
- **RSV-mAb:** A new section was added to provide details on the use of nirsevimab in infants and young children. The “Routine immunization” section outlines the recommendations for infants aged <8 months. The “Special situations” section describes recommendations for age-eligible children who are undergoing cardiac surgery with cardiopulmonary bypass, and children aged 8–19 months who are at increased risk for severe RSV disease. Information describing timing of immunization, including guidance for jurisdictions with RSV seasonality that differs from most of the continental United States, was included.
- **RSV:** A new section was added outlining recommendations for maternal RSV vaccination with Abrysvo (Pfizer Inc.) using seasonal administration. Language was added to clarify that health care providers should take one of two approaches to prevent severe respiratory syncytial virus disease in infants: either administer Abrysvo (Pfizer Inc.) to pregnant persons at 32–36 weeks’ gestation or administer nirsevimab to the infant. Information describing vaccination timing, including guidance for jurisdictions with RSV seasonality that differs from most of the continental United States, was included.
- **Tdap:** The “Routine vaccination” and “Catch-up vaccination” sections were revised to clarify that the Tdap dose recommended at age 11–12 years is the adolescent Tdap booster dose.

Appendix (Contraindications and Precautions)

- The header sentence of the Appendix was revised to include all the sources used to create the Appendix.
- The column header was changed from “Vaccine” to “Vaccines and other immunizing agents” to account for the inclusion of the newly licensed RSV monoclonal antibody (nirsevimab).

- **COVID-19 row:** Two new rows for COVID-19 vaccines were added to describe contraindications and precautions to COVID-19 vaccination. The first row lists contraindications and precautions to receipt of mRNA vaccines (Pfizer-BioNTech and Moderna), and the second row lists contraindications and precautions to receipt of the protein subunit vaccine (Novavax).
- **DTaP and DT row:** DT was deleted because this vaccine is no longer distributed in the United States.
- **Hib row:** In the “Contraindicated or Not Recommended” column, the bullet describing history of severe allergic reaction to dry natural latex was removed because most vials of Hib products no longer contain latex.
- **Meningococcal ACWY row:** Menactra was removed because this product is no longer distributed in the United States. Any remaining doses expired in October 2023.
- **Meningococcal ABCWY row:** A new row was added to describe contraindications and precautions to vaccination with the new pentavalent meningococcal vaccine, Penbraya.
- **RSV-mAb row:** A new row for nirsevimab was added to describe contraindications and precautions to nirsevimab.
- **RSV row:** A new row for RSV (Abrysvo [Pfizer Inc.]) was added describing the contraindications and precautions to RSV vaccination.

Addendum

A new Addendum section was added to the child and adolescent immunization schedule to summarize new and updated ACIP recommendation(s) that occur before the next annual update to the child and adolescent immunization schedule.

Additional Information

The Recommended Child and Adolescent Immunization Schedule, United States, 2024 is available at <https://www.cdc.gov/vaccines/schedules/hcp/imz/child-adolescent.html>. The full ACIP recommendations for each vaccine are also available at <https://www.cdc.gov/vaccines/hcp/acip-recs>. All vaccines and immunizing agents identified in Tables 1, 2, and 3 (except DTaP, rotavirus, and nirsevimab) also appear in the Recommended Adult Immunization Schedule for Ages 19 Years or Older, United States, 2024, available at <https://www.cdc.gov/vaccines/schedules/hcp/imz/adult.html>. The notes and appendix for vaccines that appear in both the child and adolescent immunization schedule and the adult immunization schedule have been harmonized to the greatest extent possible.

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Rosters of current and past members of the Advisory Committee on Immunization Practices are available at <https://www.cdc.gov/vaccines/acip/members/index.html>.

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Advisory Committee on Immunization Practices Recommended Immunization Schedule for Adults Aged 19 Years or Older — United States, 2024

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At its October 2023 meeting, the Advisory Committee on Immunization Practices* (ACIP) approved the Recommended Adult Immunization Schedule for Ages 19 Years or Older, United States, 2024. The adult immunization schedule, which can be found on the CDC immunization schedule website (<https://www.cdc.gov/vaccines/schedules>), is published annually to consolidate and summarize updates to ACIP recommendations on the vaccination of adults and to assist health care providers in implementing current ACIP recommendations. The 2024 immunization schedule includes several changes to the cover page, tables, notes, and appendix from the 2023 immunization schedule.[†] In addition, the 2024 adult immunization schedule includes a new addendum section that summarizes new or updated ACIP recommendations that will occur before the next annual update to the adult immunization schedule. Health care providers are advised to use the cover page, tables, notes, appendix, and addendum together to determine recommended vaccinations for patient populations.

This adult immunization schedule is recommended by ACIP (<https://www.cdc.gov/vaccines/acip>) and approved by CDC (<https://www.cdc.gov>), the American College of Physicians (<https://www.acponline.org>), the American Academy of Family Physicians (<https://www.aafp.org>), the American College of Obstetricians and Gynecologists (<https://www.acog.org>), the American College of Nurse-Midwives (<https://www.midwife.org>), the American Academy of Physician Associates (<https://www.aapa.org>), the American Pharmacists Association (<https://www.pharmacist.com>), and the Society for Healthcare Epidemiology of America (<https://shea-online.org>).

ACIP's recommendations on the use of each vaccine are developed after in-depth reviews of vaccine-related data, including disease epidemiology and societal impacts, vaccine

efficacy and effectiveness, vaccine safety, quality of evidence, feasibility of program implementation, impact on health equity, and economic analyses of immunization policy (1,2). Health care providers should be aware that changes in recommendations for specific vaccines occur between these annual updates to the adult immunization schedule.[§] Such changes will be summarized in the new addendum section; however, health care providers are encouraged to refer to ACIP recommendations for detailed guidance on the use of each vaccine (<https://www.cdc.gov/vaccines/hcp/acip-recs>). An online version of the 2024 adult immunization schedule and instructions for downloading the schedule app to use on mobile devices are available on the immunization schedule website (<https://www.cdc.gov/vaccines/schedules>). The use of vaccine trade names in this report and in the adult immunization schedule is for identification purposes only and does not imply endorsement by ACIP or CDC.

Changes in the 2024 Adult Immunization Schedule

Vaccine-specific changes in the 2024 immunization schedule for adults aged ≥19 years include new and updated recommendations for respiratory syncytial virus vaccines (RSV) (3), influenza vaccines (4), COVID-19 vaccines (5), inactivated poliovirus vaccine (IPV) (6), Mpox vaccine (Mpox) (<https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2023-10-25-26/04-MPOX-Rao-508.pdf>), and meningococcal serogroups A, B, C, W, Y pentavalent vaccine (MenACWY-TT/MenB-FHbp) (<https://www.cdc.gov/vaccines/acip/recommendations.html>). Any reference to meningococcal serogroups A, C, W, Y polysaccharide diphtheria toxoid conjugate vaccine (MenACWY-D [Menactra]) was removed from the schedule because this product is no longer distributed in the United States. Other changes include clarification of the recommendations for hepatitis A vaccine (HepA), hepatitis B vaccine

* Recommendations for routine use of vaccines in adults are developed by ACIP, a federal advisory committee chartered to provide expert external advice and guidance to the CDC director on use of vaccines and related agents for the control of vaccine-preventable diseases in the civilian population of the United States. Recommendations for routine use of vaccines in adults are harmonized to the greatest extent possible with recommendations made by the American Academy of Pediatrics, the American Academy of Family Physicians, and the American College of Obstetricians and Gynecologists. ACIP recommendations become official agency guidelines once the recommendation has been adopted by the CDC Director. Additional information about ACIP is available at <https://www.cdc.gov/vaccines/acip/>.

[†] Past immunization schedules are available at <https://www.cdc.gov/vaccines/schedules/hcp/schedule-related-resources.html>.

[§] CDC encourages organizations to use syndication as a more reliable method for displaying the most current and accurate immunization schedules on an organization's website rather than copying these schedules to their websites. Use of content syndication requires a one-time step that ensures an organization's website displays current schedules as soon as they are published or revised; instructions for the syndication code are available on CDC's website (<https://www.cdc.gov/vaccines/schedules/resource-library/syndicate.html>). CDC also offers technical assistance for implementing this form of content syndication (requests can be e-mailed to ncirdwebteam@cdc.gov).

(HepB), human papillomavirus vaccine (HPV), measles, mumps, and rubella vaccine (MMR), pneumococcal vaccines, and tetanus, diphtheria, and pertussis vaccine (Tdap).

Cover page

- A fifth step in the “How to Use the Adult Immunization Schedule” box was added directing health care providers to review the new addendum section that lists new or updated ACIP recommendations that occur before the next annual update to the adult immunization schedule.
- Information on injury claims, travel vaccine recommendations and a hyperlink to the 2024 child and adolescent immunization schedule was removed from the Cover Page and moved to a new “Additional Information” section on the first page of the Notes. This was done to harmonize presentation of this information with the 2024 child and adolescent immunization schedule.
- Mpox (Jynneos), pentavalent meningococcal vaccine (MenACWY-TT/MenB-FHbp [Penbraya]), and RSV vaccines (Abrysvo [Pfizer Inc.] and Arexvy [GSK]) were added to the table of vaccine abbreviations and trade names.
- MenACWY-D (Menactra) was removed from the table of vaccine abbreviations and trade names because it is no longer distributed in the United States, and any remaining doses of this product expired in October 2023.
- The bivalent mRNA COVID-19 vaccines were removed from the table of vaccine abbreviations and trade names because current mRNA COVID-19 vaccines are all monovalent, and the bivalent mRNA COVID-19 vaccines used in the United States during 2022–2023 are no longer recommended.

Table 1 (Routine Immunization Schedule)

- **COVID-19 row:** The text overlay was revised to reflect updated vaccination recommendations. This text overlay now states, “1 or more doses of updated (2023–2024 Formula) vaccine.”
- **RSV row:** The RSV vaccination is a new addition to this table. The color of this row is purple for adults aged 19–49 years, with overlaying text “seasonal administration during pregnancy,” reflecting the recommendation for the use of Abrysvo (Pfizer Inc.) during 32–36 weeks’ gestation. The row is light blue for adults aged ≥60 years, indicating that the recommendation for RSV vaccination with either Abrysvo (Pfizer Inc.) or Arexvy (GSK) among adults aged ≥60 years is based on shared clinical decision-making.
- **Mpox row:** A new row was added for Jynneos, with a purple bar across all ages reflecting the risk-based recommendation for Mpox vaccination.

Table 2 (Immunization by Medical Indication Schedule)

- A header sentence was added to Table 2 stating that medical conditions or indications are often not mutually exclusive and advising health care providers to review all relevant columns in the table if multiple conditions or indications are present.
- **Legend:** The definitions of the yellow, purple, and gray colors in the legend were revised. The new definitions of these colors are intended to be more focused and narrower, such that the recommendation for vaccination based on that medical indication is more readily apparent. In addition, brown was introduced as a new legend color, indicating that additional doses of vaccine might be necessary based on medical condition or other indication. To account for these revised color definitions, many of the vaccine rows in Table 2 were recolored.
- **HepB row:** Under the diabetes column, a blue bar was added to indicate that the recommendation for vaccination for persons aged ≥60 years with diabetes is based on shared clinical decision-making.
- **RSV row:** The RSV vaccination is a new addition to this table. For use during pregnancy, the color is yellow with overlaying text of “seasonal administration” to indicate that the use of Abrysvo (Pfizer Inc.) in pregnancy is based on RSV seasonality. For the rest of the medical indications listed, the color is light blue reflecting that the recommendation for vaccination among adults aged ≥60 years is based on shared clinical decision-making.
- **Mpox row:** A new row was added for Jynneos. Across all medical indications listed, the entire row is purple reflecting the risk-based recommendation for Mpox vaccination. In the pregnancy column, an overlaying text “See Notes” was added to encourage health care providers to review the pregnancy bullet in the Mpox vaccination notes.

Vaccine Notes

The notes for each vaccine are presented in alphabetical order. Edits have been made throughout the Notes section to harmonize language, to the greatest extent possible, with that in the child and adolescent schedule.

- A new “Additional Information” section now begins the Notes section of the 2024 adult immunization schedule. This section mirrors the “Additional Information” section in the Notes section of the 2024 child and adolescent immunization schedule and contains similar information. Bullets that were previously on the Cover Page (such as injury claims and travel vaccine recommendations, etc.) have now been incorporated into the new “Additional Information” section of the Notes section. The text for vaccine injury compensation was revised to add Mpox and

RSV to the list of vaccines not covered by the National Vaccine Injury Compensation Program. Mpox is covered by the Countermeasures Injury Compensation Program.

- **COVID-19:** All adults are now recommended to receive at least 1 dose of an updated (2023–2024 Formula) COVID-19 vaccine. The number of doses needed and intervals between doses might vary based on a patient's previous vaccination history, immunocompromise status, and the vaccine product used. In addition, the COVID-19 notes section is divided into a "Routine vaccination" section that describes the vaccination recommendations for the general population and a "Special situations" section that describes the vaccine recommendations for persons who are moderately or severely immunocompromised.
- **HepA:** To better align the language with ACIP policy, the bullet in the "Routine vaccination" section was revised to, "Any person who is not fully vaccinated and requests vaccination." The HepA vaccine regimen is described in detail later in that bullet.
- **HepB:** In the "Routine vaccination" section, additional context and details were added to the bullets describing the risk-based vaccination recommendation for persons aged ≥ 60 years. In addition, a note was added at the end of the "Routine vaccination" section describing the shared clinical decision-making recommendation for persons aged ≥ 60 years with diabetes.
- **HPV:** In the "Routine vaccination" section, the guidance on interrupted schedules was removed because that information is presented on the Cover Page. Age ranges were reordered to be in chronological order. In addition, to improve clarity, the words "of any valency" were added to the bullet, "No additional dose recommended when any HPV vaccine series *of any valency* has been completed using the recommended dosing intervals." Lastly, a link to a resource was added to assist health care providers with shared clinical decision-making recommendations for HPV vaccination.
- **Influenza:** A hyperlink to the 2023–24 influenza recommendations and a bullet regarding the 2024–25 influenza recommendations were added. In the "Special situations" section, all bullets that discuss history of egg allergy were removed, and a note was added at the end of the "Special situations" section stating that persons with a history of egg allergy can be vaccinated with any influenza vaccine indicated for the recipient's age and health status (4). Finally, the bullet describing Guillain-Barré syndrome was removed because this information is presented in the Appendix section on contradictions and precautions.
- **MMR:** Minor changes were made to the "Routine vaccination" section to improve language clarity.
- **Meningococcal:** All references to Menactra were removed because this product is no longer distributed in the United States. A link to a resource was added to assist health care providers with shared clinical decision-making recommendations for MenB vaccination. Lastly, information about the use of the newly licensed pentavalent meningococcal vaccine (Penbraya) is provided at the end of the meningococcal notes section.
- **Mpox:** Mpox vaccination is a new addition to the Notes section of the adult immunization schedule. Risk factors that warrant routine Jynneos vaccination are listed. Bullets about the use of Jynneos among health care providers and in pregnant persons are provided at the end of the Mpox notes section.
- **Pneumococcal:** Minor edits were made throughout the "Routine vaccination" and "Special situations" sections to provide clarity on the guidance and minimum intervals between doses of pneumococcal vaccines.
- **Poliovirus:** Additional context was added to the "Routine vaccination" section. This section now calls for adults who are known or suspected to be unvaccinated or incompletely vaccinated to complete the 3-dose IPV primary vaccination series. A statement was added stating that most adults who were born and raised in the United States can assume that they were vaccinated against polio as children. The "Special situations" section describes administering a one-time, lifetime IPV booster dose to adults who have completed the primary series and who are at increased risk for exposure to poliovirus.
- **RSV:** A new RSV notes section was added this year. The section begins with a "Routine vaccination" section that describes the use of Abrysvo (Pfizer Inc.) in pregnant persons during 32–36 weeks' gestation from September through January in most of the continental United States. In addition, a sub-bullet was added stating that either maternal RSV vaccination or infant immunization with nirsevimab (RSV monoclonal antibody) is recommended to prevent respiratory syncytial virus lower respiratory tract infection in infants. A note was added at the end of the RSV notes section to acknowledge that certain jurisdictions might have RSV seasonality that differs from most of the continental United States, and that providers should follow guidance from public health authorities regarding the timing of maternal RSV vaccine administration, based on local RSV seasonality. The "Special situations" section describes the shared clinical decision-making recommendation for vaccination of persons aged ≥ 60 years; either Abrysvo (Pfizer Inc) or Arexvy (GSK) may be used. In addition, a link to a resource was added to assist health care providers with shared clinical decision-making

recommendations for RSV vaccination. Finally, a note was added that lists risk factors and medical conditions that health care providers should consider when thinking through a patient's risk for severe RSV disease and potential benefit from vaccination.

- **Tdap:** A note was added at the end of the Tdap section to clarify that a dose of Tdap received at age 10 years may be counted as the adolescent dose routinely recommended at age 11–12 years.

Appendix (Contraindications and Precautions)

- The header sentence of the Appendix was revised to include all the sources used to create the Appendix.
- **COVID-19 row:** Two new rows for COVID-19 vaccines were added describing the contraindications and precautions to COVID-19 vaccination. The first row lists the contraindications and precautions to mRNA vaccines (Pfizer-BioNTech and Moderna), and the second row lists the contraindications and precautions to the protein subunit vaccine (Novavax).
- **Hib row:** In the “Contraindicated or Not Recommended” column, the bullet describing history of severe allergic reaction to dry natural latex was removed because vials of Hib products no longer contain latex.
- **Meningococcal rows:** All references to Menactra were removed because this product is no longer distributed in the United States. Contraindications and precautions to vaccination with the new pentavalent meningococcal vaccine (MenACWY-TT/MenB-FHbp [Penbraya]) were added.
- **Mpox row:** A new row for Mpox was added describing the contraindications and precautions to Mpox vaccination.
- **RSV row:** A new row for RSV was added describing the contraindications and precautions to RSV vaccination.

Addendum

- A new addendum section was added to the adult immunization schedule to summarize new and updated ACIP recommendations that occur before the next annual update to the adult immunization schedule.

Additional Information

The Recommended Adult Immunization Schedule, United States, 2024, is available at <https://www.cdc.gov/vaccines/schedules/hcp/adult.html>, and in the *Annals of Internal Medicine* (7). The full ACIP recommendations for each vaccine are also available at <https://www.cdc.gov/vaccines/hcp/acip-recs/index.html>. All vaccines identified in Tables 1 and 2 (except Zoster vaccine) also appear in the Recommended Immunization Schedule for Children and Adolescents, United States, 2024

(<https://www.cdc.gov/vaccines/schedules/hcp/imz/child-adolescent.html>). For vaccines that appear in both the adult immunization schedule and the child and adolescent immunization schedule, the language in both schedules has been harmonized to the greatest extent possible.

Acknowledgments

Rosters of current and past members of the Advisory Committee on Immunization Practices are available at <https://www.cdc.gov/vaccines/acip/members/index.html>.

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Effectiveness of Bivalent mRNA COVID-19 Vaccines in Preventing COVID-19–Related Thromboembolic Events Among Medicare Enrollees Aged ≥65 Years and Those with End Stage Renal Disease — United States, September 2022–March 2023

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Abstract

COVID-19 has been associated with an increased risk for thromboembolic events, including ischemic stroke, venous thromboembolism, and myocardial infarction. Studies have reported lower rates of COVID-19–related thromboembolic events among persons who received the COVID-19 vaccine compared with persons who did not, but rigorous estimates of vaccine effectiveness (VE) in preventing COVID-19–related thromboembolic events are lacking. This analysis estimated the incremental benefit of receipt of a bivalent mRNA COVID-19 vaccine after receiving an original monovalent COVID-19 vaccine. To estimate VE of a bivalent mRNA COVID-19 dose in preventing thromboembolic events compared with original monovalent COVID-19 vaccine doses only, two retrospective cohort studies were conducted among Medicare fee-for-service enrollees during September 4, 2022–March 4, 2023. Effectiveness of a bivalent COVID-19 vaccine dose against COVID-19–related thromboembolic events compared with that of original vaccine alone was 47% (95% CI = 45%–49%) among Medicare enrollees aged ≥65 years and 51% (95% CI = 39%–60%) among adults aged ≥18 years with end stage renal disease receiving dialysis. VE was similar among Medicare beneficiaries with immunocompromise: 46% (95% CI = 42%–49%) among adults aged ≥65 years and 45% (95% CI = 24%–60%) among those aged ≥18 years with end stage renal disease. To help prevent complications of COVID-19, including thromboembolic events, adults should stay up to date with COVID-19 vaccination.

Introduction

Complications of COVID-19 include an increased risk for thromboembolic events, including ischemic stroke, venous thromboembolism, and myocardial infarction (1). Adults aged ≥65 years and persons with end stage renal disease (ESRD) receiving dialysis are at increased risk for thromboembolic events, including COVID-19–related thromboembolic events (2). COVID-19 vaccination has been shown to be protective against severe COVID-19–associated outcomes, including hospitalization, mechanical ventilation, and death (3,4). In

addition, rates of COVID-19–related thromboembolic events have been reported to be lower among vaccinated persons than among unvaccinated persons (5); however, rigorous estimates of COVID-19 vaccine effectiveness (VE) in preventing COVID-19–related thromboembolic events are not available. This analysis aimed to assess relative effectiveness of bivalent COVID-19 mRNA vaccines compared with original monovalent COVID-19 vaccines alone against COVID-19–related thromboembolic events, stratified by time since dose, among Medicare fee-for-service beneficiaries aged ≥65 years and among those aged ≥18 years with ESRD receiving dialysis.

Methods

Two retrospective cohort studies were conducted, one among Medicare fee-for-service beneficiaries aged ≥65 years and one among Medicare beneficiaries aged ≥18 years with ESRD receiving dialysis.* Medicare Parts A and B enrollment and claims records were used to obtain information on study participation eligibility,[†] COVID-19 vaccination status,[§] covariates,[¶]

* Defined as having at least one dialysis encounter (excluding acute kidney injury) in the 90 days before the index date. Persons with ESRD receiving dialysis are eligible for Medicare benefits, regardless of age.

[†] Eligible beneficiaries were continuously enrolled in Medicare Parts A and B but not part C for at least 365 days before the index date and were eligible to receive a bivalent mRNA COVID-19 vaccine dose. In addition, beneficiaries must not have received a kidney transplant (ESRD cohort), dialysis encounter (Medicare beneficiaries aged ≥65 years cohort), hospice care, or COVID-19 monoclonal antibody treatment within 90 days of the index date, resided in a nursing home consecutively for ≥100 days within 365 days of the index date, or had a COVID-19 diagnosis within 30 days of index date.

[§] Defined as receipt of a bivalent mRNA COVID-19 vaccine dose at least 7 days earlier or receipt of original monovalent doses only. Bivalent doses were identified using codes from the Healthcare Common Procedure Coding System and Current Procedural Terminology and must have been administered after August 31, 2022. Beneficiaries could change vaccination status during the study period.

[¶] Covariates included demographics (age, sex, race, Social Vulnerability Index, and state and rural/urban classification) and underlying medical conditions. Underlying medical conditions were treated as binary variables and required at least one encounter with the appropriate *International Classification of Diseases, Tenth Revision* code within 365 days from the index date. Time-varying covariates included receipt of an original monovalent booster dose, whether time since last COVID-19 vaccine dose was >150 days, receipt of monoclonal antibody or antiviral treatment, and previous medical claims listing a COVID-19 diagnosis.

and outcomes.** Beneficiaries included^{††} in this study were eligible to receive the bivalent COVID-19 mRNA vaccine.^{§§} All beneficiaries entered the study cohorts on September 4, 2022 (the index date); vaccination status was updated daily, and beneficiaries began contributing time to the bivalent vaccine cohorts beginning 7 days after receipt of a bivalent vaccine dose. Follow-up continued until the earliest occurrence of a censoring event,^{¶¶} study end (March 4, 2023), or COVID-19–related thromboembolic event (ischemic stroke, venous thromboembolism, or myocardial infarction from 7 days before through 30 days after COVID-19 diagnosis). A marginal structural Cox model^{***} was used to estimate relative VE,^{†††} which can be interpreted as the incremental benefit of a bivalent dose compared with only the original monovalent vaccine doses without a bivalent dose, by immunocompromise

status^{§§§} and time since vaccination. Two-sided 95% CIs were calculated for each VE estimate, with 95% CIs that excluded zero considered statistically significant. Nonoverlapping CIs were interpreted as statistically significantly different effectiveness estimates. This activity was reviewed by CDC, deemed not research, and was conducted consistent with applicable federal law and CDC policy.^{¶¶¶}

Results

Bivalent Vaccine Coverage

During September 4, 2022–March 4, 2023, among 12,706,176 immunocompetent Medicare beneficiaries aged ≥65 years who had previously received an original COVID-19 vaccine, 5,683,208 (44.7%) received a bivalent dose (Table 1). Overall, higher percentages of bivalent vaccine recipients than nonrecipients resided in an urban area (83% versus 78%), had received an influenza vaccine during the 2021–22 season (82% versus 55%) and 2022–23 season (87% versus 50%), and had received an original monovalent booster vaccine dose (96% versus 73%).

Among 78,618 Medicare beneficiaries aged ≥18 years with ESRD receiving dialysis who did not have additional immunocompromising conditions and had previously received original COVID-19 vaccine, 23,229 (29.5%) received a bivalent dose, including 7,239 (31.2%) aged 18–64 years and 15,990 (68.8%) aged ≥65 years. Similar to beneficiaries aged ≥65 years, among recipients with ESRD receiving dialysis, a higher percentage of those who received a bivalent vaccine dose compared with those who had not, had also received an influenza vaccine during the 2021–22 season (90% versus 82%) and the 2022–23 season (92% versus 79%) and had received an original monovalent booster vaccine dose (90% versus 74%). In addition, a higher percentage of bivalent COVID-19–vaccinated ESRD beneficiaries were older (69% were aged ≥65 years) and non-Hispanic White (53%) compared with those who did not receive the bivalent COVID-19 vaccine (59% and 47%, respectively).

^{§§§} Immunocompromise was defined as at least two encounters within 183 days before the index date for one or more of the following conditions: hematologic malignancy, other intrinsic immune conditions or immunodeficiency, solid malignancy, transplant, or rheumatologic/inflammatory disorders. Immunocompetent was defined as absence of immunocompromise. ESRD alone was not considered an immunocompromising condition, as persons with ESRD were not considered to be moderately or severely immunocompromised in COVID-19 vaccine recommendations.

^{¶¶¶} 45 C.F.R. part 46.102(l)(2), 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.

** COVID-19–related thromboembolic events were defined as the first occurrence of such events in the inpatient setting after the index date and 7 days before to 30 days after COVID-19 diagnosis. Occurrence of myocardial infarction or ischemic stroke was defined as the presence of a diagnosis code in any position on an inpatient claim; venous thromboembolism was defined as a venous thromboembolism diagnosis in any position on an inpatient claim reported as present on admission, combined with a relevant procedure code in any claim setting within 7 days before or after admission date. COVID-19–related thromboembolic events occurring in the first 7 days after vaccination were not counted. A supplementary analysis considered all-cause thromboembolic events, regardless of relation to COVID-19.

^{††} Because many COVID-19 primary vaccination series doses among Medicare beneficiaries were administered at mass vaccination clinics where Medicare claims might not be filed, determining whether beneficiaries were in fact unvaccinated was not possible. Thus, this study was limited to beneficiaries with documented evidence of receipt of original COVID-19 vaccine doses.

^{§§} Beneficiaries had documented claims for ≥2 original monovalent mRNA vaccine doses, ≥2 Novavax vaccine doses, or ≥1 Janssen vaccine dose. A single dose (i.e., Janssen), second dose, third dose, or monovalent booster administration code was considered adequate to meet the inclusion criteria.

^{¶¶} Follow-up continued until the earliest occurrence of an outcome, death, disenrollment in Medicare Parts A or B, enrollment in Medicare Part C, a nursing home stay lasting ≥100 days or admission to a hospice facility, a dialysis encounter (aged ≥65 years cohort) or a kidney transplant (ESRD cohort), receipt of multiple bivalent booster doses or a dose received <60 days from the last COVID-19 vaccine dose, or end of study period.

^{***} To adjust for confounders between the bivalent and original-only cohorts, inverse probability of treatment weights was estimated using a proportional hazards model to estimate the propensity for receiving a bivalent dose based on covariates. A marginal structural Cox model estimated the hazard ratio and 95% CIs among the bivalent cohort versus the original cohort, using a doubly robust approach: implementing inverse probability treatment weights and adjusting for influenza vaccination status, receipt of original monovalent booster, whether time since original monovalent vaccine was >150 days, and urban/rural residence (aged ≥65 years cohort) and adjusting for age, race, receipt of original monovalent booster, and time since original monovalent vaccine >150 days (ESRD cohort).

^{†††} Vaccine effectiveness was calculated as $(1 - \text{hazard ratio}) \times 100\%$, where hazard ratio is the estimated hazard ratio comparing bivalent mRNA COVID-19 vaccine recipients to original monovalent-only COVID-19 vaccine recipients.

TABLE 1. Characteristics of immunocompetent Medicare fee-for-service beneficiaries aged ≥65 years and beneficiaries aged ≥18 years with end stage renal disease receiving dialysis* without additional immunocompromising conditions, by receipt of bivalent mRNA COVID-19 vaccine — United States, September 2022–March 2023

Characteristic	Beneficiaries aged ≥65 yrs (N = 12,706,176)				Beneficiaries aged ≥18 yrs with ESRD receiving dialysis (N = 78,618)			
	Overall no. (column %)	Original vaccine only [†] No. (column %)	Bivalent vaccine [§] No. (column %)	SMD [¶]	Overall no. (column %)	Original vaccine only No. (column %)	Bivalent vaccine No. (column %)	SMD
Age group, yrs								
18–64	—	—	—	—	30,240 (38.5)	23,001 (41.5)	7,239 (31.2)	0.22
≥65	12,706,176 (100)	7,022,968 (100)	5,683,208 (100)	—	48,378 (61.5)	32,388 (58.5)	15,990 (68.8)	0.22
Sex								
Men	5,324,511 (41.9)	2,940,150 (41.9)	2,384,361 (42.0)	0	45,347 (57.7)	31,751 (57.3)	13,596 (58.5)	0.02
Women	7,381,665 (58.1)	4,082,818 (58.1)	3,298,847 (58.0)	0	33,271 (42.3)	23,638 (42.7)	9,633 (41.5)	0.02
Race and ethnicity								
Asian or Pacific Islander, NH	299,359 (2.4)	175,013 (2.5)	124,346 (2.2)	0.02	4,647 (5.9)	3,269 (5.9)	1,378 (5.9)	0
Black or African American, NH	639,186 (5.0)	404,907 (5.8)	234,279 (4.1)	0.08	22,731 (28.9)	16,698 (30.1)	6,033 (26.0)	0.09
White, NH	10,971,824 (86.4)	6,007,977 (85.5)	4,963,847 (87.3)	0.05	38,226 (48.6)	25,857 (46.7)	12,369 (53.2)	0.13
Hispanic or Latino	136,672 (1.1)	103,341 (1.5)	33,331 (0.6)	0.09	6,729 (8.6)	5,220 (9.4)	1,509 (6.5)	0.11
Other, NH	659,135 (5.2)	331,730 (4.7)	327,405 (5.8)	0.05	6,285 (8.0)	4,345 (7.8)	1,940 (8.4)	0.02
Social Vulnerability Index ranking**								
≥1 to ≤10	1,426,615 (11.2)	678,323 (9.7)	748,292 (13.2)	0.11	3,793 (4.8)	2,362 (4.3)	1,431 (6.2)	0.09
>10 to ≤20	1,534,203 (12.1)	765,545 (10.9)	768,658 (13.5)	0.08	4,979 (6.3)	3,205 (5.8)	1,774 (7.6)	0.07
>20 to ≤30	1,601,416 (12.6)	820,302 (11.7)	781,114 (13.7)	0.06	5,942 (7.6)	3,854 (7.0)	2,088 (9.0)	0.08
>30 to ≤40	1,502,011 (11.8)	804,184 (11.5)	697,827 (12.3)	0.03	6,741 (8.6)	4,585 (8.3)	2,156 (9.3)	0.04
>40 to ≤50	1,411,576 (11.1)	782,312 (11.1)	629,264 (11.1)	0	7,149 (9.1)	4,850 (8.8)	2,299 (9.9)	0.04
>50 to ≤60	1,265,748 (10.0)	721,828 (10.3)	543,920 (9.6)	0.02	7,308 (9.3)	5,070 (9.2)	2,238 (9.6)	0.02
>60 to ≤70	1,275,330 (10.0)	748,934 (10.7)	526,396 (9.3)	0.05	8,619 (11.0)	6,203 (11.2)	2,416 (10.4)	0.03
>70 to ≤80	1,096,430 (8.6)	671,164 (9.6)	425,266 (7.5)	0.07	9,650 (12.3)	6,984 (12.6)	2,666 (11.5)	0.03
>80 to ≤90	928,621 (7.3)	584,906 (8.3)	343,715 (6.0)	0.09	11,475 (14.6)	8,413 (15.2)	3,062 (13.2)	0.06
>90 to ≤100	642,510 (5.1)	428,758 (6.1)	213,752 (3.8)	0.11	12,406 (15.8)	9,380 (16.9)	3,026 (13.0)	0.11
Missing	21,716 (0.2)	16,712 (0.2)	5,004 (0.1)	0.04	556 (0.7)	483 (0.9)	73 (0.3)	0.07
HHS Region^{††}								
1	796,402 (6.3)	352,686 (5.0)	443,716 (7.8)	0.11	3,196 (4.1)	1,923 (3.5)	1,273 (5.5)	0.10
2	1,129,459 (8.9)	616,638 (8.8)	512,821 (9.0)	0.01	7,203 (9.2)	5,206 (9.4)	1,997 (8.6)	0.03
3	1,472,982 (11.6)	772,703 (11.0)	700,279 (12.3)	0.04	8,135 (10.3)	5,454 (9.8)	2,681 (11.5)	0.05
4	2,542,060 (20.0)	1,587,467 (22.6)	954,593 (16.8)	0.15	16,108 (20.5)	12,412 (22.4)	3,696 (15.9)	0.17
5	2,143,140 (16.9)	1,084,671 (15.4)	1,058,469 (18.6)	0.08	11,893 (15.1)	7,446 (13.4)	4,447 (19.1)	0.15
6	1,253,738 (9.9)	793,820 (11.3)	459,918 (8.1)	0.11	10,517 (13.4)	7,726 (13.9)	2,791 (12.0)	0.06
7	676,509 (5.3)	346,395 (4.9)	330,114 (5.8)	0.04	2,806 (3.6)	1,873 (3.4)	933 (4.0)	0.03
8	433,653 (3.4)	231,531 (3.3)	202,122 (3.6)	0.01	1,694 (2.2)	1,073 (1.9)	621 (2.7)	0.05
9	1,608,310 (12.7)	885,149 (12.6)	723,161 (12.7)	0	13,495 (17.2)	9,758 (17.6)	3,737 (16.1)	0.04
10	585,995 (4.6)	311,662 (4.4)	274,333 (4.8)	0.02	2,745 (3.5)	1,882 (3.4)	863 (3.7)	0.02
Missing	63,928 (0.5)	40,246 (0.6)	23,682 (0.4)	0.02	826 (1.1)	636 (1.1)	190 (0.8)	0.03
Rural/Urban classification^{§§}								
Rural	2,566,503 (20.2)	1,581,607 (22.5)	984,896 (17.3)	0.13	14,092 (17.9)	10,475 (18.9)	3,617 (15.6)	0.09
Urban	10,139,673 (79.8)	5,441,361 (77.5)	4,698,312 (82.7)	0.13	64,526 (82.1)	44,914 (81.1)	19,612 (84.4)	0.09
Respiratory disease								
Asthma	904,139 (7.1)	478,798 (6.8)	425,341 (7.5)	0.03	7,680 (9.8)	5,393 (9.7)	2,287 (9.8)	0
COPD	1,377,175 (10.8)	825,581 (11.8)	551,594 (9.7)	0.07	15,652 (19.9)	11,066 (20.0)	4,586 (19.7)	0.01
Other chronic lung disease	863,446 (6.8)	507,600 (7.2)	355,846 (6.3)	0.04	24,094 (30.6)	17,396 (31.4)	6,698 (28.8)	0.06
Cardiovascular disease								
Heart failure	1,099,317 (8.7)	665,610 (9.5)	433,707 (7.6)	0.07	36,985 (47.0)	26,223 (47.3)	10,762 (46.3)	0.02
Ischemic heart disease	2,689,861 (21.2)	1,529,106 (21.8)	1,160,755 (20.4)	0.03	39,285 (50.0)	27,497 (49.6)	11,788 (50.7)	0.02
Hypertension	8,765,015 (69.0)	4,893,880 (69.7)	3,871,135 (68.1)	0.03	68,951 (87.7)	48,479 (87.5)	20,472 (88.1)	0.02
Other	4,465,517 (35.1)	2,499,783 (35.6)	1,965,734 (34.6)	0.02	56,368 (71.7)	39,466 (71.3)	16,902 (72.8)	0.03
Cerebrovascular disease								
Stroke	412,153 (3.2)	248,517 (3.5)	163,636 (2.9)	0.04	6,978 (8.9)	5,091 (9.2)	1,887 (8.1)	0.04
Other	201,661 (1.6)	125,875 (1.8)	75,786 (1.3)	0.04	4,447 (5.7)	3,230 (5.8)	1,217 (5.2)	0.03

See table footnotes on the next page.

TABLE 1. (Continued) Characteristics of immunocompetent Medicare fee-for-service beneficiaries aged ≥65 years and beneficiaries aged ≥18 years with end stage renal disease receiving dialysis* without additional immunocompromising conditions, by receipt of bivalent mRNA COVID-19 vaccine — United States, September 2022–March 2023

Characteristic	Beneficiaries aged ≥65 yrs (N = 12,706,176)				Beneficiaries aged ≥18 yrs with ESRD receiving dialysis (N = 78,618)			
	Overall no. (column %)	Original vaccine only [†] No. (column %)	Bivalent vaccine [§] No. (column %)	SMD [¶]	Overall no. (column %)	Original vaccine only No. (column %)	Bivalent vaccine No. (column %)	SMD
HIV								
HIV Infection ^{¶¶}	14,740 (0.1)	6,814 (0.1)	7,926 (0.1)	0.01	915 (1.2)	627 (1.1)	288 (1.2)	0.01
Neurologic and musculoskeletal disease								
Dementia (including Alzheimer disease)	613,704 (4.8)	397,074 (5.7)	216,630 (3.8)	0.09	4,563 (5.8)	3,407 (6.2)	1,156 (5.0)	0.05
Other	2,696,976 (21.2)	1,532,313 (21.8)	1,164,663 (20.5)	0.03	28,662 (36.5)	20,407 (36.8)	8,255 (35.5)	0.03
Mental health condition								
Depression	1,883,167 (14.8)	1,044,477 (14.9)	838,690 (14.8)	0	15,605 (19.8)	10,960 (19.8)	4,645 (20.0)	0.01
Hematologic disease								
Blood disorders	364,164 (2.9)	203,907 (2.9)	160,257 (2.8)	0.01	10,696 (13.6)	7,585 (13.7)	3,111 (13.4)	0.01
Endocrine or metabolic disease								
Diabetes type I	135,667 (1.1)	75,941 (1.1)	59,726 (1.1)	0	8,895 (11.3)	6,423 (11.6)	2,472 (10.6)	0.03
Diabetes type II	3,297,417 (26.0)	1,921,942 (27.4)	1,375,475 (24.2)	0.07	56,024 (71.3)	39,574 (71.4)	16,450 (70.8)	0.01
Diabetes due to underlying condition or other specified diabetes	189,711 (1.5)	110,823 (1.6)	78,888 (1.4)	0.02	9,430 (12.0)	6,841 (12.4)	2,589 (11.1)	0.04
Other	9,927,282 (78.1)	5,389,421 (76.7)	4,537,861 (79.8)	0.08	71,473 (90.9)	50,227 (90.7)	21,246 (91.5)	0.03
Gastrointestinal and hepatic disease								
Chronic liver disease	690,767 (5.4)	386,244 (5.5)	304,523 (5.4)	0.01	10,979 (14.0)	7,800 (14.1)	3,179 (13.7)	0.01
Obesity								
Clinical obesity	2,296,440 (18.1)	1,280,953 (18.2)	1,015,487 (17.9)	0.01	26,447 (33.6)	18,654 (33.7)	7,793 (33.5)	0
Disability status								
Disabled	1,640,013 (12.9)	878,602 (12.5)	761,411 (13.4)	0.03	15,708 (20.0)	11,099 (20.0)	4,609 (19.8)	0
Influenza vaccination status								
Received 2021–22 flu vaccine	8,505,872 (66.9)	3,853,154 (54.9)	4,652,718 (81.9)	0.61	66,330 (84.4)	45,489 (82.1)	20,841 (89.7)	0.22
Received 2022–23 flu vaccine	8,460,188 (66.6)	3,492,915 (49.7)	4,967,273 (87.4)	0.89	64,918 (82.6)	43,480 (78.5)	21,438 (92.3)	0.40
Received 2022–23 flu vaccine and COVID-19 vaccine on same date	1,924,540 (15.1)	0 (—)	1,924,540 (33.9)	1.01	2,280 (2.9)	0 (—)	2,280 (9.8)	0.47
Original monovalent COVID-19 booster vaccine status								
Received***	10,540,003 (83.0)	5,089,503 (72.5)	5,450,500 (95.9)	0.68	61,680 (78.5)	40,733 (73.5)	20,947 (90.2)	0.44

Abbreviations: COPD = chronic obstructive pulmonary disease; ESRD = end stage renal disease; flu = influenza; HHS = U.S. Department of Health and Human Services; MS = musculoskeletal; NH = non-Hispanic; SMD = standardized mean or proportion difference.

* Defined as having at least one dialysis encounter (excluding acute kidney injury) in the 90 days preceding the index date. Persons with ESRD receiving dialysis are eligible for Medicare benefits, regardless of age.

[†] Beneficiaries had documented claims for ≥2 original monovalent mRNA vaccine doses, ≥2 Novavax vaccine doses, or ≥1 Janssen vaccine dose. A single dose (i.e., Janssen), second dose, third dose, or monovalent booster administration code was considered adequate to meet inclusion criteria.

[§] Defined as receipt of a bivalent mRNA COVID-19 vaccine dose at least 7 days earlier or receipt of original monovalent doses only. Bivalent doses were identified using codes from the Healthcare Common Procedure Coding System and Current Procedural Terminology and must have been administered after August 31, 2022. Beneficiaries' vaccination status could change during the study period.

[¶] A standardized mean difference of ≤0.1 indicates a negligible difference in means or proportions between groups.

** <https://www.atsdr.cdc.gov/placeandhealth/svi/index.html>

†† <https://www.hhs.gov/about/agencies/iea/regional-offices/index.html>

^{§§} https://www.cdc.gov/nchs/data_access/urban_rural.htm#Use_of_the_Urban-Rural_Classification_with_Nativity_and_Mortality_Files

^{¶¶} Defined as ≥2 encounters with *International Classification of Diseases, Tenth Revision, Clinical Modification* code consistent with HIV diagnosis within 183 days before index date.

*** Documentation of third dose or original monovalent vaccine booster administration code. Because there was documentation of receipt of original monovalent booster doses after the index date for some beneficiaries, this variable was considered time-varying. Data presented reflect status as of censoring date.

Vaccine Effectiveness in Preventing COVID-19–related Thromboembolic Events

During the study period, COVID-19–related thromboembolic events were recorded among 22,001 immunocompetent beneficiaries aged ≥ 65 years and 1,040 immunocompetent beneficiaries aged ≥ 18 years with ESRD receiving dialysis (Table 2). A total of 1,505,533,898 original-vaccine-only person-days were contributed by immunocompetent beneficiaries aged ≥ 65 years, during which 17,746 COVID-19–related thromboembolic events were identified (Table 3). Among adults aged ≥ 65 years, 694,184,995 bivalent-vaccine person-days were contributed, during which 4,255 COVID-19–related thromboembolic events were identified. Adjusted VE against COVID-19–related thromboembolic events among immunocompetent beneficiaries aged ≥ 65 years was 47%, with lower VE estimates ≥ 60 days after bivalent vaccine receipt (42%) compared with VE estimates 7–59 days after bivalent vaccine receipt (54%).

Similarly, a total of 10,395,534 original-vaccine-only person-days were contributed by beneficiaries aged ≥ 18 years with ESRD receiving dialysis, during which 917 COVID-19–related

thromboembolic events were identified. A total of 2,394,731 bivalent vaccine person-days were contributed, during which 123 COVID-19–related thromboembolic events were identified. Adjusted VE against COVID-19–related thromboembolic events was 51%, with lower VE estimates ≥ 60 days after bivalent vaccine receipt (45%) than 7–59 days after bivalent vaccine receipt (56%); however, these differences were not statistically significant (i.e., the 95% CIs overlapped).

Similar results were seen among beneficiaries aged ≥ 65 years with immunocompromise (overall bivalent VE = 46%, with 55% VE 7–59 days after receipt of vaccine, and 39% VE ≥ 60 days post-vaccination) and among beneficiaries with ESRD receiving dialysis and who had additional immunocompromising conditions (overall bivalent VE = 45%, with 60% VE 7–59 days after receipt of vaccine, and nonsignificant 30% VE at ≥ 60 days post-vaccination) (Supplementary Table 1; <https://stacks.cdc.gov/view/cdc/140316>). A supplementary analysis estimating VE against all-cause thromboembolic events also indicated a protective effect of bivalent vaccination (Supplementary Table 2; <https://stacks.cdc.gov/view/cdc/140315>).

TABLE 2. Summary of COVID-19–related thromboembolic events* among Medicare fee-for-service beneficiaries aged ≥ 65 years and beneficiaries aged ≥ 18 years with end stage renal disease receiving dialysis,† by immunocompromise status, age group, and event type — United States, September 2022–March 2023

Age group/Event type [§]	Beneficiaries by age group, ESRD, and immunocompromise status, No. (%)			
	Beneficiaries aged ≥ 65 yrs		Beneficiaries aged ≥ 18 yrs with ESRD receiving dialysis	
	Immunocompetent	With immunocompromise [¶]	Immunocompetent	With immunocompromise
≥ 18 yrs				
Total no. of persons	—	—	78,618 (100)	22,391 (100)
Any thromboembolic event	—	—	1,040 (1.32)	365 (1.63)
Ischemic stroke	—	—	308 (0.39)	102 (0.46)
Myocardial infarction	—	—	650 (0.83)	230 (1.03)
Venous thromboembolism	—	—	82 (0.1)	33 (0.15)
18–64 yrs				
Total no. of persons	—	—	30,240 (100)	7,349 (100)
Any thromboembolic event	—	—	275 (0.91)	87 (1.18)
Ischemic stroke	—	—	93 (0.31)	26 (0.35)
Myocardial infarction	—	—	155 (0.51)	49 (0.67)
Venous thromboembolism	—	—	27 (0.09)	12 (0.16)
≥ 65 yrs				
Total no. of persons	12,706,176 (100)	2,346,581 (100)	48,378 (100)	15,042 (67.18)
Any thromboembolic event	22,001 (0.17)	7,432 (0.32)	765 (1.58)	278 (1.85)
Ischemic stroke	8,382 (0.07)	2,316 (0.1)	215 (0.44)	76 (0.51)
Myocardial infarction	10,339 (0.08)	3,627 (0.15)	495 (1.02)	181 (1.2)
Venous thromboembolism	3,280 (0.03)	1,489 (0.06)	55 (0.11)	21 (0.14)

Abbreviation: ESRD = end stage renal disease.

* Defined as the first occurrence of clotting outcomes (i.e., myocardial infarction, ischemic stroke, or venous thromboembolism) after index date and 7 days before to 30 days after COVID-19 diagnosis.

† Defined as having at least one dialysis encounter (excluding acute kidney injury) in the 90 days before the index date. Persons with end stage renal disease receiving dialysis are eligible for Medicare benefits, regardless of age.

§ Individual thromboembolic events are mutually exclusive. If two thromboembolic events occurred on the same day, the following hierarchy is applied: 1) venous thromboembolism, 2) ischemic stroke, 3) myocardial infarction.

¶ Defined as at least two encounters within 183 days before the index date for one or more of the following conditions: hematologic malignancy, other intrinsic immune conditions or immunodeficiency, solid malignancy, transplant, or rheumatologic/inflammatory disorders.

Discussion

During September 4, 2022–March 4, 2023, effectiveness of a bivalent COVID-19 vaccine compared with receipt of original monovalent vaccine alone against COVID-19–related thromboembolic events was 47% among Medicare beneficiaries aged ≥65 years and 51% among Medicare beneficiaries aged ≥18 years with ESRD receiving dialysis. These findings can be interpreted as the incremental benefit of a recent bivalent dose

compared with earlier receipt of original monovalent doses and are consistent with reported lower rates of COVID-19–related thromboembolic events among vaccinated than among unvaccinated persons (5).

Context to Risk-Benefit Considerations

The findings that bivalent COVID-19 vaccine provided protection against COVID-19–related thromboembolic events

TABLE 3. Vaccine effectiveness* of bivalent compared with original monovalent vaccination against COVID-19–related thromboembolic events† among immunocompetent Medicare fee-for-service beneficiaries aged ≥65 years and beneficiaries aged ≥18 years with end stage renal disease receiving dialysis‡ without additional immunocompromising conditions, by age group and time since vaccination — September 2022–March 2023

Age group/ Vaccination status	Immunocompetent beneficiaries aged ≥65 years					Beneficiaries aged ≥18 years with ESRD receiving dialysis without additional immunocompromising conditions				
	No. of beneficiaries	No. of COVID-19– related TE	Total no. of person-days	Median follow-up days contributed to category¶	aVE (95% CI)**	No. of beneficiaries	No. of COVID-19– related TE	Total no. of person-days	Median follow-up days contributed to category¶	aVE (95% CI)††
≥18 yrs										
Original vaccine only (Ref)§§	—	—	—	—	—	55,389	917	10,395,534	181	Ref
Bivalent vaccine overall¶¶	—	—	—	—	—	23,229	123	2,394,731	114	51 (39–60)
7–59 days since vaccination	—	—	—	—	—	2,822	53	1,165,617	53	56 (40–68)
≥60 days since vaccination	—	—	—	—	—	20,407	70	1,229,114	61	45 (28–58)
18–64 yrs										
Original vaccine only (Ref)	—	—	—	—	—	23,001	255	4,215,882	181	Ref
Bivalent vaccine overall¶¶	—	—	—	—	—	7,239	20	694,039	101	56 (33–71)
7–59 days since vaccination	—	—	—	—	—	—	—	—	—	—
≥60 days since vaccination	—	—	—	—	—	—	—	—	—	—
≥65 yrs										
Original vaccine only (Ref)	7,022,968	17,746	1,505,533,898	181	Ref	32,388	662	6,179,652	181	Ref
Bivalent vaccine overall¶¶	5,683,208	4,255	694,184,995	130	47 (45–49)	15,990	103	1,700,692	116	49 (35–60)
7–59 days since vaccination	350,021	1,492	294,516,234	53	54 (51–56)	1,768	45	806,703	53	52 (32–66)
≥60 days since vaccination	5,333,187	2,763	399,668,761	77	42 (39–45)	14,222	58	893,989	63	43 (23–58)

Abbreviations: aVE = adjusted vaccine effectiveness; ESRD = end stage renal disease; Ref = referent group; TE = thromboembolic events.

* Vaccine effectiveness was calculated as $(1 - \text{hazard ratio}) \times 100\%$.

† Defined as the first occurrence of clotting outcomes (i.e., myocardial infarction, ischemic stroke, or venous thromboembolism) after index date and 7 days before to 30 days after COVID-19 diagnosis.

‡ Defined as having at least one dialysis encounter (excluding acute kidney injury) in the 90 days preceding the index date. Persons with ESRD receiving dialysis are eligible for Medicare benefits, regardless of age.

¶ A single beneficiary can contribute follow-up time in multiple categories. The maximum number of post-bivalent vaccination follow-up days = 181.

** aVE was estimated using a doubly robust approach: implementing inverse probability of treatment weighting and further adjusting for adjusting for influenza vaccination status, receipt of original monovalent booster, time since original monovalent vaccine >150 days, and urban/rural residence.

†† aVE was estimated using a doubly robust approach: implementing inverse probability of treatment weighting and further adjusting for age, race, receipt of original monovalent booster, and time since original monovalent vaccine >150 days.

§§ Beneficiaries had documented claims for ≥2 original monovalent mRNA vaccine doses, ≥2 Novavax vaccine doses, or ≥1 Janssen vaccine dose. A single dose (i.e., Janssen), second dose, third dose, or monovalent booster administration code was considered adequate to meet the inclusion criteria.

¶¶ Defined as receipt of a COVID-19 bivalent mRNA vaccine dose at least 7 days earlier or receipt of original monovalent doses only. Bivalent doses were identified using codes from the Healthcare Common Procedure Coding System and Current Procedural Terminology and must have been administered after August 31, 2022. Beneficiaries could change vaccination status during the study period.

are important considering a January 13, 2023, joint statement^{****} by CDC and the Food and Drug Administration regarding a rapid-response investigation of a preliminary safety signal detected in the Vaccine Safety Datalink (VSD), a vaccine safety monitoring system. The signal was detected in a vaccinated concurrent comparator analysis and raised a question about whether receipt of a Pfizer-BioNTech bivalent COVID-19 mRNA vaccine increased the risk for an ischemic stroke event in the 21 days following vaccination in persons aged ≥ 65 years. As additional data accumulated in VSD in early 2023, the signal attenuated and was no longer statistically significant; review of additional studies have not provided clear and consistent evidence of a safety problem with ischemic stroke and bivalent mRNA COVID-19 vaccines.^{†††} Factors other than vaccination, such as unmeasured confounding or selection bias, might have contributed to the VSD signal. The findings in this report provide important context to risk-benefit considerations and highlight the protective effect of bivalent COVID-19 vaccination against COVID-19–related thromboembolic events among adults aged ≥ 65 years and among adults aged ≥ 18 years with ESRD receiving dialysis. The supplementary analysis estimating VE against all-cause thromboembolic events, irrespective of COVID-19 diagnosis, also indicated a protective effect of bivalent vaccination. Persons with ESRD receiving dialysis are at high risk for thromboembolic events (6). The findings in this report suggest that recent receipt of a COVID-19 bivalent vaccine dose was protective against COVID-19–related thromboembolic events among this high-risk population.

Duration of Protection

In this analysis, protection afforded by a bivalent dose against COVID-19–related thromboembolic events appeared to wane, with VE decreasing over time since the last dose. However, these results should be interpreted with caution, as only two periods since last dose were assessed in this study. Furthermore, VE estimates by time since dose among beneficiaries with ESRD receiving dialysis did not differ substantially. Previous CDC studies have shown that VE against COVID-19–associated hospitalization wanes, but more durable protection against critical illness (i.e., intensive care unit admission or death), persists for up to 179 days postvaccination (4).

**** <https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/cdc-and-fda-identify-preliminary-covid-19-vaccine-safety-signal-persons-aged-65-years-and-older>

††† <https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2023-10-25-26/01-VaxSafety-Shimabukuro-508.pdf>

Limitations

The findings in this study are subject to at least five limitations. First, the results of this analysis should be interpreted in the context of underlying immunity as the incremental benefit provided by COVID-19 vaccination. Because of underascertainment of COVID-19 vaccine receipt in medical claims data during the early period of vaccine distribution, assessing absolute VE (i.e., comparing vaccinated and unvaccinated persons) was not possible. Models were adjusted for previous COVID-19 illness reported through Medicare fee-for-service claims data; however, the analysis cannot account for previous SARS-CoV-2 infection among persons without medical encounters. According to a national seroprevalence survey, a large proportion of the population has now experienced SARS-CoV-2 infection ($>70\%$ by the third quarter of 2022)^{§§§§}; infection-induced immunity decreases the risk for future medically attended COVID-19 illness and might affect observed VE against COVID-19–related thromboembolic events. Second, because of timing of COVID-19 vaccine policy implementation (7), this analysis compared recent receipt of a bivalent dose with earlier receipt of an original monovalent vaccine dose. Thus, a direct comparison between bivalent doses and original vaccine doses by similar time since dose was not feasible within the same calendar period. Third, although models were adjusted for relevant confounders such as age and calendar time, residual confounding is possible, including by behavioral differences, history of previous SARS-CoV-2 infection not requiring a medical encounter, history of COVID-19 illness >365 days before the index date, and use of COVID-19 treatments such as nirmatrelvir-ritonavir (Paxlovid). Fourth, COVID-19–related thromboembolic events were ascertained using medical claims data, which might have limitations compared with imaging or other diagnostic test results (8). COVID-19–related thromboembolic events in this analysis were limited to events recorded in the inpatient setting to reduce likelihood of misclassification. Finally, because only Medicare beneficiaries enrolled in Part A (hospital insurance) and Part B (medical insurance) are included, the results of this analysis might not be representative of the entire U.S. population aged ≥ 65 years or all persons aged ≥ 18 years with ESRD receiving dialysis.

Implications for Public Health

Among adults aged ≥ 65 years, a recent bivalent mRNA COVID-19 vaccine dose helped provide protection against COVID-19–related thromboembolic events compared with

§§§§ <https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2023-04-19/06-COVID-Oliver-508.pdf>

References

Summary

What is already known about this topic?

Thromboembolic complications of COVID-19 include ischemic stroke, venous thromboembolism, and myocardial infarction. COVID-19 vaccines are effective in preventing severe outcomes, including hospitalization and death.

What is added by this report?

During September 2022–March 2023, receipt of bivalent mRNA COVID-19 vaccine was 47% effective in preventing thromboembolic events among immunocompetent persons aged ≥ 65 years and 51% effective among adults aged ≥ 18 years with end stage renal disease (ESRD) receiving dialysis, compared with receipt of the original monovalent vaccines alone.

What are the implications for public health practice?

COVID-19 vaccines helped provide protection against COVID-19–related thromboembolic events. Persons aged ≥ 65 years and adults with ESRD should receive all recommended COVID-19 vaccine doses to prevent COVID-19–associated complications, including thromboembolic events.

more distant receipt of original monovalent doses alone. This pattern of protection was also observed among adults with ESRD receiving dialysis, a population particularly susceptible to thromboembolic events. To prevent COVID-19–related complications, including thromboembolic events, adults should stay up to date with recommended COVID-19 vaccination (9).

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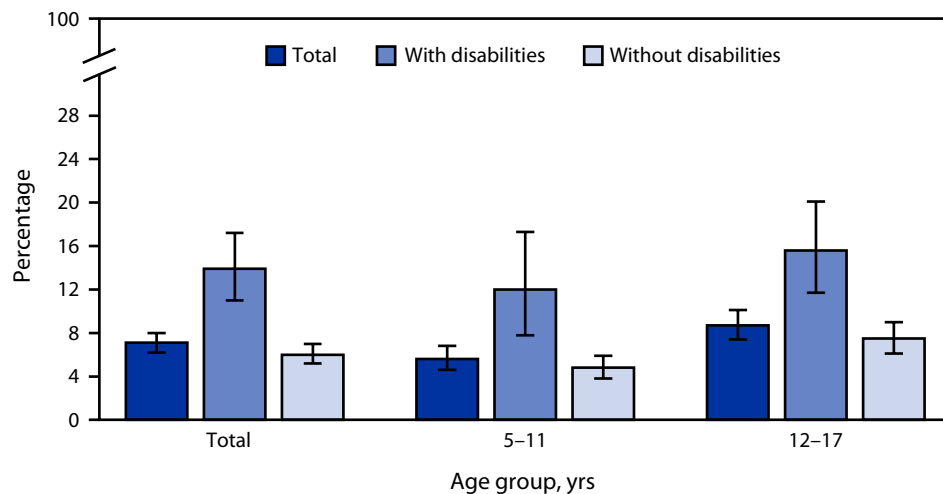
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QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Percentage* of Children and Adolescents Aged 5–17 Years Who Had Been the Victim of Violence or Witnessed Violence in Their Neighborhood,[†] by Disability Status[§] and Age Group — National Health Interview Survey, United States, 2022[¶]



* With 95% CIs indicated with error bars.

[†] Based on an affirmative response to the survey question, “Has (child) ever been the victim of violence or witnessed violence in his/her neighborhood?”

[§] Disability is defined by responses in 13 core functioning domains: 1) seeing, 2) hearing, 3) mobility, 4) self-care, 5) communication, 6) learning, 7) remembering, 8) concentrating, 9) accepting change, 10) controlling behavior, 11) making friends, 12) anxiety, and 13) depression. Children and adolescents who were reported to have “a lot of difficulty” or “cannot do at all” to at least one of the domains 1–11 or “daily” to domains 12 or 13 are classified in the with disabilities category. Children and adolescents with “no difficulty” or “some difficulty” to all domains 1–11 and “never,” “a few times a year,” “monthly,” or “weekly” to domains 12 and 13 are classified in the without disabilities category.

[¶] Estimates are based on household interviews of a sample of the civilian, noninstitutionalized U.S. population.

In 2022, 7.1% of children and adolescents aged 5–17 years had been the victim of violence or witnessed violence in their neighborhood. Percentages were higher among children and adolescents with disabilities (13.9%) than children and adolescents without disabilities (6.0%). This pattern was observed among children and adolescents aged 5–11 years (12.0% versus 4.8%) and those aged 12–17 years (15.6% versus 7.5%). Percentages increased with age among children and adolescents without disabilities from 4.8% among those aged 5–11 years to 7.5% among those aged 12–17 years. Percentages also increased with age for those with disabilities, but the observed difference (12.0% versus 15.6%) was not significant.

Source: National Center for Health Statistics, National Health Interview Survey, 2022. <https://www.cdc.gov/nchs/nhis.htm>

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