

The Medical Letter[®]

on Drugs and Therapeutics

Volume 63

November 29, 2021

ISSUE No.
1638

IN THIS ISSUE

Booster Doses of COVID-19 Vaccinesp 186

Important Copyright Message

FORWARDING OR COPYING IS A VIOLATION OF U.S. AND INTERNATIONAL COPYRIGHT LAWS

The Medical Letter, Inc. publications are protected by U.S. and international copyright laws. Forwarding, copying or any distribution of this material is prohibited.

Sharing a password with a non-subscriber or otherwise making the contents of this site available to third parties is strictly prohibited.

By accessing and reading the attached content I agree to comply with U.S. and international copyright laws and these terms and conditions of The Medical Letter, Inc.

For further information click: [Subscriptions](#), [Site Licenses](#), [Reprints](#)
or call customer service at: 800-211-2769

The Medical Letter[®]

on Drugs and Therapeutics

Volume 63 (Issue 1638)

November 29, 2021

[Take CME Exams](#)

▶ **Booster Doses of COVID-19 Vaccines**

Revised 11/29/21: This article originally went to press on 11/10/21. On 11/19/21 the FDA changed their recommendations. We have included a revision note to reflect these changes.

The FDA has expanded the Emergency Use Authorizations (EUAs) for the mRNA-based COVID-19 vaccines manufactured by Pfizer/BioNTech (*Comirnaty*) and Moderna (*Spikevax*) and the adenovirus-based vaccine manufactured by Johnson & Johnson/Janssen to include administration of a booster dose in select populations after primary immunization with either the same COVID-19 vaccine or a different one.

RECOMMENDATIONS — A single booster dose of any COVID-19 vaccine can now be administered ≥ 6 months after a primary series of an mRNA-based vaccine in adults who are ≥ 65 years old or at high risk for severe COVID-19 because of an underlying medical condition or frequent institutional or occupational exposure to SARS-CoV-2, or ≥ 2 months after a single primary dose of the Johnson & Johnson vaccine in any adult (see Table 1).^{1,2} **Revised:** As of November 19, 2021, the FDA has expanded the EUAs for the mRNA-based COVID-19 vaccines (*Comirnaty* and *Spikevax*) to include administration of a booster dose for all adults ≥ 18 years old after primary immunization with either the same COVID-19 vaccine or a different one.¹⁹

DOSAGE — The booster dose is the same as the dose for primary immunization for both *Comirnaty* (30 mcg [0.3 mL] IM) and the Johnson & Johnson vaccine (5×10^{10} viral particles [0.5 mL] IM); it is half the dose for primary immunization for *Spikevax* (50 mcg [0.25 mL] vs 100 mcg [0.5 mL] IM).³⁻⁵

CLINICAL STUDIES — Waning Immunity — In a retrospective cohort study of ~ 3.4 million persons ≥ 12 years old in the US, those who received two doses of *Comirnaty* were significantly less likely to be infected with SARS-CoV-2 than those who were not vaccinated, but the relative risk reduction associated with vaccination declined from 88% at ≤ 1 month to 47% at ≥ 5 months after the second dose.

Vaccination was also associated with a lower risk of hospitalization due to COVID-19; the relative risk reduction did not change significantly over time (87% at ≤ 1 month; 88% at ≥ 5 months).⁶

In a study in Israel that examined positive PCR test results for SARS-CoV-2 infection over 3 weeks in July 2021, adults ≥ 60 years old who completed a 2-dose primary series of the Pfizer/BioNTech vaccine in the second half of January 2021 had a significantly higher rate of infection than those who completed their series in the second half of March 2021 (3.3 vs 1.7 cases/1000 persons). Similarly, adults ≥ 60 years old who completed their series in January had a significantly higher rate of severe COVID-19 than those who completed it in March (0.34 vs 0.15 cases/1000 persons).⁷

In a US study of breakthrough infection rates between July 1 and August 27, 2021 in $\sim 26,000$ adults who had received primary immunization with *Spikevax*, the rate in an earlier-vaccinated (median 13 months since first dose) cohort was 36.4% higher than that in a later-vaccinated (median 8 months since first dose) cohort (77.1 vs 49.0 cases/1000 person-years).⁸

The efficacy of the Johnson & Johnson vaccine appears to be sustained through at least 6 months post-dose, but the peak efficacy of a single Johnson & Johnson dose seems to be lower than that of a 2-dose primary series of an mRNA-based vaccine.⁹⁻¹¹

Booster Immunogenicity — Longitudinal immunogenicity studies (unpublished; summarized in FDA Fact Sheets) compared titer levels of anti-SARS-CoV-2 neutralizing antibodies after a booster dose to those achieved after completion of primary immunization in adults with no evidence of prior SARS-CoV-2 infection. In 210 adults 18-55 years old who received a booster dose of *Comirnaty* about 6 months after completion of a 2-dose primary series, the geometric mean titer (GMT) 1 month after the booster dose was 3.29-fold higher than it was 1 month after the second primary-series dose.³ In 149 adults

Table 1. Indications and Dosage Regimens for COVID-19 Vaccines¹

Indication	Pfizer-BioNTech (<i>Comirnaty</i>)	Moderna (<i>Spikevax</i>)	Johnson & Johnson/Janssen
Primary immunization	≥16 yrs: 30 mcg (0.3 mL) IM at 0 and 3 weeks 12-15 yrs: 30 mcg (0.3 mL) IM at 0 and 3 weeks	≥18 yrs: 100 mcg (0.5 mL) IM at 0 and 4 weeks	≥18 yrs: 5x10 ¹⁰ vp (0.5 mL) IM once
Additional primary dose for immunocompromised persons	≥12 yrs: 30 mcg (0.3 mL) IM ≥4 weeks after second primary dose	≥18 yrs: 100 mcg (0.5 mL) IM ≥4 weeks after second primary dose	N.A.
Booster dose in at-risk adults ² after a Pfizer-BioNTech or Moderna primary series ³	30 mcg (0.3 mL) IM ≥6 months after last primary dose	50 mcg (0.25 mL) IM ≥6 months after last primary dose	5x10 ¹⁰ vp (0.5 mL) IM ≥6 months after last primary dose
Booster dose in adults after a Johnson & Johnson primary dose	30 mcg (0.3 mL) IM ≥2 months after primary dose	50 mcg (0.25 mL) IM ≥2 months after primary dose	5x10 ¹⁰ vp (0.5 mL) IM ≥2 months after primary dose

N.A. = not authorized; vp = viral particles

1. The Pfizer-BioNTech vaccine has received full FDA licensure for use as a 2-dose primary series in patients ≥16 years old. All other recommendations are based on FDA Emergency Use Authorizations (EUAs).

2. Aged ≥65 years or at high risk for severe COVID-19 because of an underlying medical condition or frequent institutional/occupational exposure to SARS-CoV-2.

3. After either a 2- or 3-dose primary series. CDC. Considerations for use of a COVID-19 vaccine booster dose. October 25, 2021. Available at: <https://bit.ly/3EnjXZ8>. Accessed October 29, 2021.

who received a 50-mcg booster dose of *Spikevax* ≥6 months after completion of a 2-dose primary series, the GMT 4 weeks after a 50-mcg booster dose was 1.8-fold higher than it was 4 weeks after the second primary-series dose.⁵ In 38 adults who received a booster dose of the Johnson & Johnson vaccine 12 weeks after a primary dose, the GMT 4 weeks after the booster dose was 1.6-fold higher than it was 4 weeks after the primary dose.⁴

Booster Efficacy – In a one-month cohort study in ~1.1 million Israeli residents who had completed a 2-dose primary series of the Pfizer/BioNTech vaccine ≥5 months previously, persons who received a booster dose had significantly lower rates of SARS-CoV-2 infection (by 11.3-fold) and severe COVID-19 (by 19.5-fold) beginning 12 days after administration compared to those who did not.¹² In a follow-up analysis, relative reductions in the rates of symptomatic and severe COVID-19 associated with booster immunization persisted through ~2 months after the booster dose, and among persons ≥60 years old, the rate of death due to COVID-19 was 14.7-fold lower beginning 12 days after administration in patients who received a booster dose than it was in those who did not receive one.¹³

In an unpublished double-blind trial (ENSEMBLE 2; summarized in an FDA presentation), 31,300 persons were randomized to receive two doses of the Johnson & Johnson vaccine or placebo 8 weeks apart. After a median follow-up of 36 days, the vaccine efficacy rate for prevention of moderate to severe COVID-19 from 14 days after the second dose, the primary endpoint, was 75% (94% in the US). There were no cases of

severe or critical COVID-19 in vaccine recipients versus 8 in the placebo group. This data analysis was performed in June 2021, before the Delta variant of SARS-CoV-2 became predominant in the US.¹¹

Heterologous (“Mix-and-Match”) Boosters – In an unpublished nonrandomized trial (summarized in an FDA presentation), 458 adults who had received primary immunization with one of the three FDA-authorized COVID-19 vaccines ≥12 weeks previously were given a booster dose of either the same vaccine or one of the two other vaccines (for *Spikevax*, 100-mcg rather than 50-mcg booster doses were used). For all vaccine combinations, the GMT of anti-SARS-CoV-2 neutralizing antibodies increased significantly in the 2 weeks after the booster dose.¹⁴

ADVERSE EFFECTS – Adverse effects with a third dose of an mRNA-based COVID-19 vaccine appear to be similar to those with the second primary-series dose.¹⁵ Lymphadenopathy occurs more frequently with a booster dose. Booster immunization with mRNA-based COVID-19 vaccines has not been associated with increased rates of hypersensitivity reactions, Bell's palsy, or myocarditis/pericarditis compared to primary immunization.^{16,17}

Adverse effects with a booster dose of the Johnson & Johnson vaccine appear to be similar to those with the primary dose. Booster immunization has not been associated with a higher rate of thrombosis with thrombocytopenia syndrome (TTS) compared to primary immunization with the vaccine. In the UK, the rate of TTS with the second dose of the

adenovirus-based COVID-19 vaccine manufactured by AstraZeneca (not authorized for use in the US) has been lower than the rate with the first dose.^{11,18}

No vaccine-related serious adverse effects were reported in the heterologous booster trial. Adverse effects with heterologous and homologous booster immunization appear to be similar.¹⁴

CONCLUSION – Booster immunization has been associated with decreased rates of SARS-CoV-2 infection and severe COVID-19. The FDA has authorized use of a single booster dose of a COVID-19 vaccine in certain adults who received a primary series with the Pfizer-BioNTech vaccine (*Comirnaty*) or the Moderna vaccine (*Spikevax*) ≥ 6 months previously and in all adults who received a primary dose of the Johnson & Johnson/Janssen vaccine ≥ 2 months previously. The vaccine used for the booster dose can be different from the one used for primary immunization. ■

1. FDA News Release. Coronavirus (COVID-19) update: FDA takes additional actions on the use of a booster dose for COVID-19 vaccines. October 20, 2021. Available at: <https://bit.ly/3vJjPLy>. Accessed October 29, 2021.
2. CDC News Release. CDC expands eligibility for COVID-19 booster shots. October 21, 2021. Available at: <https://bit.ly/3CpoXft>. Accessed October 29, 2021.
3. FDA. Fact sheet for health care providers administering vaccine (vaccination providers). Emergency Use Authorization (EUA) of the Pfizer-BioNTech COVID-19 vaccine to prevent coronavirus disease 2019 (COVID-19). October 20, 2021. Available at: <https://bit.ly/37fX1NG>. Accessed October 29, 2021.
4. FDA. Fact sheet for healthcare providers administering vaccine (vaccination providers). Emergency Use Authorization (EUA) of the Janssen COVID-19 vaccine to prevent coronavirus disease 2019 (COVID-19). October 20, 2021. Available at: <https://bit.ly/3e6KEaD>. Accessed October 29, 2021.
5. FDA. Fact sheet for healthcare providers administering vaccine (vaccination providers). Emergency Use Authorization (EUA) of the Moderna COVID-19 vaccine to prevent coronavirus disease 2019

(COVID-19). October 20, 2021. Available at: <https://bit.ly/3nosylA>. Accessed October 29, 2021.

6. SY Tartof et al. Six-month effectiveness of BNT162b2 mRNA COVID-19 vaccine in a large US integrated health system: a retrospective cohort study. 2021 August 23 (preprint). Available at: <https://bit.ly/3CJwzJ8>. Accessed October 29, 2021.
7. Y Goldberg et al. Waning immunity after the BNT162b2 vaccine in Israel. *N Engl J Med* 2021 October 27 (epub).
8. LR Baden et al. Covid-19 in the phase 3 trial of mRNA-1273 during the Delta-variant surge. medRxiv 2021 September 22 (preprint). Available at: <https://bit.ly/3Gk9q2N>. Accessed October 29, 2021.
9. J Sadoff et al. Safety and efficacy of single-dose Ad26.COV2.S vaccine against Covid-19. *N Engl J Med* 2021; 384:2187.
10. JM Polinski et al. Effectiveness of the single-dose Ad26.COV2.S COVID vaccine. medRxiv 2021 September 16 (preprint). Available at: <https://bit.ly/3EdYPVk>. Accessed October 29, 2021.
11. R Zhang and T Brennan. FDA review of effectiveness and safety of Janssen COVID-19 vaccine (Ad26.COV2.S) booster dose. Emergency Use Authorization amendment. Vaccines and Related Biological Products Advisory Committee Meeting. October 14-15, 2021. Available at: <https://bit.ly/3k6a9eD>. Accessed October 29, 2021.
12. YM Bar-On et al. Protection of BNT162b2 vaccine booster against Covid-19 in Israel. *N Engl J Med* 2021; 385:1393.
13. YM Bar-On et al. Protection across age groups of BNT162b2 vaccine booster against Covid-19. medRxiv 2021 October 7 (preprint). Available at: <https://bit.ly/3jy9h1Q>. Accessed October 29, 2021.
14. KE Lyke. DMID 21-0012 – heterologous platform boost study: mix and match. Vaccines and Related Biological Products Advisory Committee Meeting. October 14-15, 2021. Available at: <https://bit.ly/2Zk5NcB>. Accessed October 29, 2021.
15. AM Hause et al. Safety monitoring of an additional dose of COVID-19 Vaccine – United States, August 12–September 19, 2021. *MMWR Morb Mortal Wkly Rep* 2021; 70:1379.
16. J Lee. FDA review of effectiveness and safety of COMIRNATY (COVID-19 vaccine, mRNA) booster dose. Biologics License Application supplement. Vaccines and Related Biological Products Advisory Committee Meeting. September 17, 2021. Available at: <https://bit.ly/2ZhqsgQ>. Accessed October 29, 2021.
17. T Mongeau. FDA review of effectiveness and safety of Moderna COVID-19 vaccine (mRNA-1273) booster dose. Emergency Use Authorization amendment. Vaccines and Related Biological Products Advisory Committee Meeting. October 14, 2021. Available at: <https://bit.ly/3Be97mq>. Accessed October 29, 2021.
18. UK Medicines & Healthcare products Regulatory Agency. Coronavirus vaccine – weekly summary of Yellow Card reporting. October 21, 2021. Available at: <https://bit.ly/3pFVH01>. Accessed October 29, 2021.
19. In Brief: Booster doses of mRNA-based COVID-19 vaccines for all adults. *Med Lett Drugs Ther* 2021; 63:202.

PRESIDENT: Mark Abramowicz, M.D.; **VICE PRESIDENT AND EXECUTIVE EDITOR:** Gianna Zuccotti, M.D., M.P.H., F.A.C.P., Harvard Medical School
VICE PRESIDENT AND EDITOR IN CHIEF: Jean-Marie Pflomm, Pharm.D.; **ASSOCIATE EDITORS:** Susan M. Daron, Pharm.D., Amy Faucard, MLS, Corinne Z. Morrison, Pharm.D., Michael P. Viscusi, Pharm.D. **CONSULTING EDITORS:** Joanna Esterow, PA-C, Mordechai Sacks, DMSc, PA-C, Brinda M. Shah, Pharm.D., F. Peter Swanson, M.D.

CONTRIBUTING EDITORS: Carl W. Bazil, M.D., Ph.D., Columbia University College of Physicians and Surgeons; Ericka L. Crouse, Pharm.D., B.C.P.P., C.G.P., F.A.S.H.P., F.A.S.C.P., Virginia Commonwealth University; Vanessa K. Dalton, M.D., M.P.H., University of Michigan Medical School; Eric J. Epstein, M.D., Albert Einstein College of Medicine; David N. Juurlink, BPhm, M.D., Ph.D., Sunnybrook Health Sciences Centre; Richard B. Kim, M.D., University of Western Ontario; Sandip K. Mukherjee, M.D., F.A.C.C., Yale School of Medicine; Dan M. Roden, M.D., Vanderbilt University School of Medicine; Esperance A.K. Schaefer, M.D., M.P.H., Harvard Medical School; Neal H. Steigbigel, M.D., New York University School of Medicine; Arthur M. F. Yee, M.D., Ph.D., F.A.C.R., Weill Medical College of Cornell University

MANAGING EDITOR AND DIRECTOR OF CONTENT OPERATIONS: Susie Wong; **EDITORIAL ASSISTANT:** Karrie Ferrara

FULFILLMENT AND SYSTEMS MANAGER: Cristine Romatowski; **EXECUTIVE DIRECTOR OF SALES:** Elaine Reaney-Tomaselli

EXECUTIVE DIRECTOR OF MARKETING AND COMMUNICATIONS: Joanne F. Valentino; **INTERIM PUBLISHER:** Jean-Marie Pflomm, Pharm.D.

Founded in 1959 by Arthur Kallet and Harold Aaron, M.D.

Copyright and Disclaimer: The Medical Letter, Inc. is an independent nonprofit organization that provides healthcare professionals with unbiased drug prescribing recommendations. The editorial process used for its publications relies on a review of published and unpublished literature, with an emphasis on controlled clinical trials, and on the opinions of its consultants. The Medical Letter, Inc. does not sell advertising or receive any commercial support. No part of the material may be reproduced or transmitted by any process in whole or in part without prior permission in writing. The editors do not warrant that all the material in this publication is accurate and complete in every respect. The editors shall not be held responsible for any damage resulting from any error, inaccuracy, or omission.

Subscription Services

Address:

The Medical Letter, Inc.
145 Huguonot St. Ste. 312
New Rochelle, NY 10801-7537
www.medicalletter.org

Customer Service:

Call: 800-211-2769 or 914-235-0500
Fax: 914-632-1733
E-mail: custserv@medicalletter.org

Permissions:

To reproduce any portion of this issue, please e-mail your request to: permissions@medicalletter.org

Subscriptions (US):

1 year - \$159; 2 years - \$298;
3 years - \$398. \$65 per year
for students, interns, residents,
and fellows in the US and Canada.
Reprints - \$45 per issue or article

Site License Inquiries:

E-mail: SubQuote@medicalletter.org
Call: 800-211-2769
Special rates available for bulk
subscriptions.

