

COVID-19 Evidence Support Team EVIDENCE SEARCH REPORT

Review Question:	What is the current evidence and recommendations regarding COVID-19 vaccine booster shots (exceeding 2 doses) for the general population?		
Context:	Are third doses safe and effective? Is a third dose necessary to sustain immunogenicity?		
Review Code:	EOC210902 ESR	Complete Date:	September 29, 2021
Cite As:	Miller, L., Howell-Spooner, B. What is the current evidence and recommendations regarding COVID-19 vaccine booster shots (exceeding 2 doses) for the general population? 2021 Sep 29, Document no.: EOC210902 ESR. In: COVID-19 Rapid Evidence Reviews [Internet]. SK: SK COVID Evidence Support Team, c2021. 14 p. (CEST rapid review report).		

Librarian Notes & Comments

Hi,

Quite a lot of evidence regarding boosters/third doses is in regards to people with weakened immune systems or other comorbidities. We still have yet to see any published clinical evidence with regard to safety/immunity in the general population, though the CDC/FDA safety monitoring report cited below does provide some indication of side effects/adverse events following a third dose.

Sincerely,
Lukas & Brianna

Search Results: Guidelines, Summaries & Other Grey Literature

Government

National Advisory Committee on Immunization (Canada)

- National Advisory Committee on Immunization (NACI) rapid response: Additional dose of COVID-19 vaccine in immunocompromised individuals following 1- or 2- dose primary series. September 10, 2021. <https://www.canada.ca/en/public-health/services/immunization/national->

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[advisory-committee-on-immunization-naci/statement-september-10-2021-additional-dose-covid-19-vaccine-immunocompromised-following-1-2-dose-series.html](https://www.inspq.gc.ca/publications/3163-pertinence-dose-additionnelle-vaccin-covid-19-immunodeprimes)

Centre d'expertise et de référence en santé publique

- Avis portant sur la pertinence d'une dose additionnelle de vaccin contre la COVID-19 pour les personnes ayant une immunodépression. August 30, 2021.
<https://www.inspq.gc.ca/publications/3163-pertinence-dose-additionnelle-vaccin-covid-19-immunodeprimes>

U.K. Government

- JCVI issues updated advice on COVID-19 booster vaccination. September 14, 2021.
<https://www.gov.uk/government/news/jcvi-issues-updated-advice-on-covid-19-booster-vaccination>

UK Department of Health and Social Care

- JCVI statement regarding a COVID-19 booster vaccine programme for winter 2021 to 2022. September 14, 2021. <https://www.gov.uk/government/publications/jcvi-statement-september-2021-covid-19-booster-vaccine-programme-for-winter-2021-to-2022/jcvi-statement-regarding-a-covid-19-booster-vaccine-programme-for-winter-2021-to-2022>
- Third primary COVID-19 vaccine dose for people who are immunosuppressed: JCVI advice. September 1, 2021. <https://www.gov.uk/government/publications/third-primary-covid-19-vaccine-dose-for-people-who-are-immunosuppressed-jcvi-advice>

NHS

- Coronavirus (COVID-19) booster vaccine. September 27, 2021.
<https://www.nhs.uk/conditions/coronavirus-covid-19/coronavirus-vaccination/coronavirus-booster-vaccine/>

CDC

- Safety Monitoring of an Additional Dose of COVID-19 Vaccine — United States, August 12–September 19, 2021. Sept 28, 2021.
https://www.cdc.gov/mmwr/volumes/70/wr/mm7039e4.htm?s_cid=mm7039e4_w
- Who Is Eligible for a COVID-19 Vaccine Booster Shot?. September 27, 2021.
<https://www.cdc.gov/coronavirus/2019-ncov/vaccines/booster-shot.html>
- CDC Statement on ACIP Booster Recommendations. September 24, 2021.
<https://www.cdc.gov/media/releases/2021/p0924-booster-recommendations-.html>
- Overview of data to inform recommendations for booster doses of COVID-19 vaccines. June 23, 2021. https://stacks.cdc.gov/view/cdc/108332/cdc_108332_DS1.pdf

NIH

- The Latest on COVID-19 Boosters. September 28, 2021.
<https://directorsblog.nih.gov/2021/09/28/the-latest-on-covid-19-boosters/>

Agencies

WHO

- Interim statement on COVID-19 vaccine booster doses. August 10, 2021. <https://www.who.int/news/item/10-08-2021-interim-statement-on-covid-19-vaccine-booster-doses>

ECDC

- ECDC and EMA highlight considerations for additional and booster doses of COVID-19 vaccines. September 2, 2021. <https://www.ecdc.europa.eu/en/news-events/ecdc-and-ema-considerations-additional-and-booster-doses-covid-19-vaccines>
- Interim public health considerations for the provision of additional COVID-19 vaccine doses. September 1, 2021. <https://www.ecdc.europa.eu/en/publications-data/covid-19-public-health-considerations-additional-vaccine-doses>

National Institute for Health Research

- Data from NIHR-supported studies inform UK COVID-19 Booster Programme. September 16, 2021. <https://www.nihr.ac.uk/news/data-from-nihr-supported-studies-inform-uk-covid-19-booster-programme/28663>

CMAJ

- What's the evidence for COVID-19 booster shots?. September 7, 2021. <https://www.cmaj.ca/content/193/35/E1400>
- What's the evidence for COVID-19 booster shots?. August 20, 2021. <https://cmajnews.com/2021/08/20/covid-boosters-1095959/>

Research Centres

Prevent Epidemics

- Protecting the Immunocompromised: The Evidence for an Additional Dose of COVID-19 Vaccine. August 20, 2021. <https://preventepidemics.org/covid19/science/review/august-20-2021/>

Cleveland Clinic

- Q&A: The Differences Between a COVID Vaccine Third Dose and Booster Shot. September 9, 2021. <https://health.clevelandclinic.org/covid-booster-shot/>

American Heart Association

- What heart and stroke patients should know about COVID-19 vaccine boosters. September 28, 2021. <https://www.heart.org/en/news/2021/09/28/what-heart-and-stroke-patients-should-know-about-covid-19-vaccine-boosters>

Mayo Clinic

- Are COVID-19 vaccine boosters or extra shots recommended?. September 27, 2021. <https://www.mayoclinic.org/coronavirus-covid-19/vaccine-boosters>

Yale Medicine

- Will You Need a COVID-19 Booster? What We Know So Far. September 24, 2021. <https://www.yalemedicine.org/news/covid-19-booster>

Johns Hopkins Medicine

- Booster Shots and Third Doses for COVID-19 Vaccines: What You Need to Know. September 24, 2021. <https://www.hopkinsmedicine.org/health/conditions-and-diseases/coronavirus/booster-shots-and-third-doses-for-covid19-vaccines-what-you-need-to-know>

Search Results: News, Blogs, & Social Media

News

CBC

- Quebec to offer 3rd dose of COVID-19 vaccine to people living in long-term care, seniors' homes. September 28, 2021. <https://www.cbc.ca/news/canada/montreal/quebec-third-dose-covid-19-1.6192239>
- CDC director overrules advisory panel, paving way for wider use of COVID-19 vaccine boosters. September 24, 2021. <https://www.cbc.ca/news/health/vaccine-booster-cdc-1.6187414>
- FDA panel rejects broad use of COVID-19 boosters, approves extra doses for seniors, those at high risk. September 17, 2021. <https://www.cbc.ca/news/world/fda-pfizer-booster-shots-1.6179533>
- Third COVID-19 shots: Who needs them and why?. September 16, 2021. <https://www.cbc.ca/radio/whitecoat/third-covid-19-shots-who-needs-them-and-why-1.6175871>
- Manitoba offers 3rd dose of COVID-19 vaccine to immunocompromised people. September 15, 2021. <https://www.cbc.ca/news/canada/manitoba/covid19-vaccine-announcement-manitoba-joss-reimer-1.6176433>
- P.E.I. offering 3rd COVID-19 vaccine dose to immune-compromised Islanders. September 15, 2021. <https://www.cbc.ca/news/canada/prince-edward-island/pei-third-dose-covid-vaccine-immune-compromised-islanders-1.6175366>
- COVID-19 vaccine boosters not widely needed, top FDA and WHO scientists say. September 13, 2021. <https://www.cbc.ca/news/health/covid-vaccine-booster-shots-1.6173861>
- Advisory body recommends 3rd COVID-19 vaccine dose for some immunocompromised Canadians. September 10, 2021. <https://www.cbc.ca/news/health/third-covid-vaccine-dose-guidance-1.6171144>
- Why rushing COVID-19 booster shots for everyone could do more harm than good. September 4, 2021. <https://www.cbc.ca/news/health/canada-covid-19-booster-shots-3rd-dose-1.6164614>
- U.S. FDA vaccine advisers face thorny question: Are COVID-19 boosters needed?. September 3, 2021. <https://www.cbc.ca/news/health/us-fda-cdc-covid19-booster-sept3-1.6163549>
- Europe's health agency says no urgent need to roll out COVID-19 booster shots to fully vaccinated. September 1, 2021. <https://www.cbc.ca/news/health/europe-s-health-agency-says-no-urgent-need-to-roll-out-covid-19-booster-shots-to-fully-vaccinated-1.6161576>
- B.C. will give COVID-19 booster shots if Health Canada recommends them, health minister says. August 30, 2021. <https://www.cbc.ca/news/canada/british-columbia/bc-to-give-covid19-booster-shots-if-health-canada-recommends-them-1.6159240>
- Why countries are moving so quickly on COVID-19 booster shots — and what Canada should do next. August 21, 2021. <https://www.cbc.ca/news/health/covid-19-vaccine-booster-shots-canada-1.6148232>
- Transplant patients see boost in COVID-19 protection after 3rd vaccine dose, study suggests. August 11, 2021. <https://www.cbc.ca/news/canada/toronto/transplant-patients-see-boost-in-covid-19-protection-after-3rd-vaccine-dose-study-suggests-1.6138089>

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AM980 CJME

- Sask.-made vaccine likely to be used as a booster shot, says VIDO CEO. September 18, 2021. <https://www.cjme.com/2021/09/18/762438/>

CIDRAP

- FDA signals apprehension about COVID-19 vaccine booster shots. September 16, 2021. <https://www.cidrap.umn.edu/news-perspective/2021/09/fda-signals-apprehension-about-covid-19-vaccine-booster-shots>
- Global experts pan wider use of COVID vaccine booster dose. September 13, 2021. <https://www.cidrap.umn.edu/news-perspective/2021/09/global-experts-pan-wider-use-covid-vaccine-booster-dose>
- European officials say COVID-19 booster isn't urgent. September 2, 2021. <https://www.cidrap.umn.edu/news-perspective/2021/09/european-officials-say-covid-19-booster-isnt-urgent>
- CDC, FDA recommend 3rd COVID vaccine dose for immune-compromised. August 13, 2021. <https://www.cidrap.umn.edu/news-perspective/2021/08/cdc-fda-recommend-3rd-covid-vaccine-dose-immune-compromised>
- Study: Third COVID vaccine dose ups response in organ recipients. August 12, 2021. <https://www.cidrap.umn.edu/news-perspective/2021/08/study-third-covid-vaccine-dose-ups-response-organ-recipients>

AAP News

- Health care workers left out of COVID-19 vaccine booster recommendation. September 23, 2021. <https://www.aappublications.org/news/2021/09/23/acip-pfizer-covid-vaccine-boosters-092321>

STAT News

- Side effect rates from a third Covid-19 vaccine dose similar to those after second shot, early data indicate. September 28, 2021. <https://www.statnews.com/2021/09/28/side-effect-rates-from-a-third-covid-19-vaccine-dose-similar-to-those-after-second-shot-early-data-indicate/>
- When and how will we know if we need Covid-19 booster shots?. July 21, 2021. <https://www.statnews.com/2021/07/12/when-and-how-will-we-know-covid-19-booster-shots/>

Aljazeera

- COVID-19 vaccine boosters not widely needed, say scientists. September 13, 2021. <https://www.aljazeera.com/news/2021/9/13/covid-19-vaccine-boosters-not-widely-needed-study>

Halifax Today

- Insufficient data for third COVID vaccine booster shot necessity: infectious disease expert. August 29, 2021. <https://www.halifaxtoday.ca/local-news/insufficient-data-to-suggest-third-covid-19-vaccine-booster-shot-necessary-for-general-public-infectious-disease-expert-4262850>

Euronews

- France starts giving COVID booster jabs to its elderly and vulnerable. September 1, 2021. <https://www.euronews.com/2021/09/01/france-starts-giving-covid-booster-jabs-to-its-elderly-and-vulnerable>

Search Results: Journal Articles (includes preprints)

Sorted by newest-oldest.

1. In brief: Third dose of mRNA-based COVID-19 vaccines for immunocompromised persons. The Medical letter on drugs and therapeutics. 2021;63(1633):145-6.

URL: <https://www.ncbi.nlm.nih.gov/pubmed/34550960>

2. Albach FN, Burmester GR, Biesen R. Successful BNT162b2 booster vaccinations in a patient with rheumatoid arthritis and initially negative antibody response. Ann Rheum Dis. 2021;80(10):1361-2.

DOI: [10.1136/annrheumdis-2021-220834](https://doi.org/10.1136/annrheumdis-2021-220834)

URL: <https://www.ncbi.nlm.nih.gov/pubmed/34167947>

DOI: [10.1136/annrheumdis-2021-220834](https://doi.org/10.1136/annrheumdis-2021-220834)

3. Bar-On YM, Goldberg Y, Mandel M, et al. Protection of BNT162b2 Vaccine Booster against Covid-19 in Israel. N Engl J Med. 2021. DOI: 10.1056/NEJMoa2114255

ABSTRACT: BACKGROUND: On July 30, 2021, the administration of a third (booster) dose of the BNT162b2 messenger RNA vaccine (Pfizer-BioNTech) was approved in Israel for persons who were 60 years of age or older and who had received a second dose of vaccine at least 5 months earlier. Data are needed regarding the effect of the booster dose on the rate of confirmed coronavirus 2019 disease (Covid-19) and the rate of severe illness. METHODS: We extracted data for the period from July 30 through August 31, 2021, from the Israeli Ministry of Health database regarding 1,137,804 persons who were 60 years of age or older and had been fully vaccinated (i.e., had received two doses of BNT162b2) at least 5 months earlier. In the primary analysis, we compared the rate of confirmed Covid-19 and the rate of severe illness between those who had received a booster injection at least 12 days earlier (booster group) and those who had not received a booster injection (nonbooster group). In a secondary analysis, we evaluated the rate of infection 4 to 6 days after the booster dose as compared with the rate at least 12 days after the booster. In all the analyses, we used Poisson regression after adjusting for possible confounding factors. RESULTS: At least 12 days after the booster dose, the rate of confirmed infection was lower in the booster group than in the nonbooster group by a factor of 11.3 (95% confidence interval [CI], 10.4 to 12.3); the rate of severe illness was lower by a factor of 19.5 (95% CI, 12.9 to 29.5). In a secondary analysis, the rate of confirmed infection at least 12 days after vaccination was lower than the rate after 4 to 6 days by a factor of 5.4 (95% CI, 4.8 to 6.1). CONCLUSIONS: In this study involving participants who were 60 years of age or older and had received two doses of the BNT162b2 vaccine at least 5 months earlier, we found that the rates of confirmed Covid-19 and severe illness were substantially lower among those who received a booster (third) dose of the BNT162b2 vaccine.

URL: <https://www.ncbi.nlm.nih.gov/pubmed/34525275>

DOI: [10.1056/NEJMoa2114255](https://doi.org/10.1056/NEJMoa2114255)

4. Burki T. Booster shots for COVID-19—the debate continues. The Lancet Infectious Diseases. 2021;21(10):1359-60. DOI: 10.1016/s1473-3099(21)00574-0

URL: [https://doi.org/10.1016/S1473-3099\(21\)00574-0](https://doi.org/10.1016/S1473-3099(21)00574-0)

DOI: 10.1016/s1473-3099(21)00574-0

5. Choi A, Koch M, Wu K, et al. Safety and immunogenicity of SARS-CoV-2 variant mRNA vaccine boosters in healthy adults: an interim analysis. Nat Med. 2021;15:15. DOI: 10.1038/s41591-021-01527-y

ABSTRACT: The emergence of SARS-CoV-2 variants of concern (VOCs) and variants of interest (VOIs) with decreased susceptibility to neutralization has generated interest in assessments of booster doses and variant-specific vaccines. Clinical trial participants who received a two-dose primary series of the COVID-19 vaccine mRNA-1273 approximately 6 months earlier entered an open-label phase 2a study (NCT04405076) to evaluate the primary objectives of safety and immunogenicity of a single booster dose of mRNA-1273 or variant-modified mRNAs, including multivalent mRNA-1273.211. As the trial is currently ongoing, this exploratory interim analysis includes preliminary descriptive results only of four booster groups (n = 20 per group). Immediately before the booster dose, neutralizing antibodies against wild-type D614G virus had waned (P < 0.0001) relative to peak titers against wild-type D614G measured 1 month after the primary series, and neutralization titers against B.1.351 (Beta), P.1 (Gamma) and B.1.617.2 (Delta) VOCs were either low or undetectable. Both the mRNA-1273 booster and variant-modified boosters were safe and well-tolerated. All boosters, including mRNA-1273, numerically increased neutralization titers against the wild-type D614G virus compared to peak titers against wild-type D614G measured 1 month after the primary series; significant increases were observed for mRNA-1273 and mRNA-1273.211 (P < 0.0001). In addition, all boosters increased neutralization titers against key VOCs and VOIs, including B.1.351, P.1. and B.1.617.2, that were statistically equivalent to peak titers measured after the primary vaccine series against wild-type D614G virus, with superior titers against some VOIs. This trial is ongoing.

URL: <https://www.ncbi.nlm.nih.gov/pubmed/34526698>

DOI: 10.1038/s41591-021-01527-y

6. Flaxman A, Marchevsky NG, Jenkin D, et al. Reactogenicity and immunogenicity after a late second dose or a third dose of ChAdOx1 nCoV-19 in the UK: a substudy of two randomised controlled trials (COV001 and COV002). Lancet. 2021;398(10304):981-90. DOI: 10.1016/S0140-6736(21)01699-8

ABSTRACT: BACKGROUND: COVID-19 vaccine supply shortages are causing concerns about compromised immunity in some countries as the interval between the first and second dose becomes longer. Conversely, countries with no supply constraints are considering administering a third dose. We assessed the persistence of immunogenicity after a single dose of ChAdOx1 nCoV-19 (AZD1222), immunity after an extended interval (44-45 weeks) between the first and second dose, and response to a third dose as a booster given 28-38 weeks after the second dose. METHODS: In this substudy, volunteers aged 18-55 years who were enrolled in the phase 1/2 (COV001) controlled trial in the UK and had received either a single dose or two doses of 5 x 10(10) viral particles were invited back for vaccination. Here we report the reactogenicity and immunogenicity of a delayed second dose (44-45 weeks after first dose) or a third dose of the vaccine (28-38 weeks after second dose). Data from volunteers aged 18-55 years who were enrolled in either the phase 1/2 (COV001) or phase 2/3 (COV002), single-blinded, randomised controlled trials of ChAdOx1 nCoV-19 and who had previously received a single dose or two doses of 5 x 10(10) viral particles are used for comparison purposes. COV001 is registered with ClinicalTrials.gov, NCT04324606, and ISRCTN, 15281137, and COV002 is registered with ClinicalTrials.gov, NCT04400838, and ISRCTN, 15281137, and both are continuing but not recruiting. FINDINGS: Between March 11 and 21, 2021, 90 participants were enrolled in the third-dose boost substudy, of whom 80 (89%) were assessable for reactogenicity, 75 (83%) were assessable for evaluation of antibodies, and 15 (17%) were assessable for T-cells responses. The two-dose cohort

comprised 321 participants who had reactogenicity data (with prime-boost interval of 8-12 weeks: 267 [83%] of 321; 15-25 weeks: 24 [7%]; or 44-45 weeks: 30 [9%]) and 261 who had immunogenicity data (interval of 8-12 weeks: 115 [44%] of 261; 15-25 weeks: 116 [44%]; and 44-45 weeks: 30 [11%]). 480 participants from the single-dose cohort were assessable for immunogenicity up to 44-45 weeks after vaccination. Antibody titres after a single dose measured approximately 320 days after vaccination remained higher than the titres measured at baseline (geometric mean titre of 66.00 ELISA units [EUs; 95% CI 47.83-91.08] vs 1.75 EUs [1.60-1.93]). 32 participants received a late second dose of vaccine 44-45 weeks after the first dose, of whom 30 were included in immunogenicity and reactogenicity analyses. Antibody titres were higher 28 days after vaccination in those with a longer interval between first and second dose than for those with a short interval (median total IgG titre: 923 EUs [IQR 525-1764] with an 8-12 week interval; 1860 EUs [917-4934] with a 15-25 week interval; and 3738 EUs [1824-6625] with a 44-45 week interval). Among participants who received a third dose of vaccine, antibody titres (measured in 73 [81%] participants for whom samples were available) were significantly higher 28 days after a third dose (median total IgG titre: 3746 EUs [IQR 2047-6420]) than 28 days after a second dose (median 1792 EUs [IQR 899-4634]; Wilcoxon signed rank test $p=0.0043$). T-cell responses were also boosted after a third dose (median response increased from 200 spot forming units [SFUs] per million peripheral blood mononuclear cells [PBMCs; IQR 127-389] immediately before the third dose to 399 SFUs per million PBMCs [314-662] by day 28 after the third dose; Wilcoxon signed rank test $p=0.012$). Reactogenicity after a late second dose or a third dose was lower than reactogenicity after a first dose. INTERPRETATION: An extended interval before the second dose of ChAdOx1 nCoV-19 leads to increased antibody titres. A third dose of ChAdOx1 nCoV-19 induces antibodies to a level that correlates with high efficacy after second dose and boosts T-cell responses. FUNDING: UK Research and Innovation, Engineering and Physical Sciences Research Council, National Institute for Health Research, Coalition for Epidemic Preparedness Innovations, National Institute for Health Research Oxford Biomedical Research Centre, Chinese Academy of Medical Sciences Innovation Fund for Medical Science, Thames Valley and South Midlands NIHR Clinical Research Network, AstraZeneca, and Wellcome.

URL: <https://www.ncbi.nlm.nih.gov/pubmed/34480858>

DOI: 10.1016/S0140-6736(21)01699-8

7. Griffin S. Covid-19: Millions could be offered booster vaccinations from September. BMJ. 2021;374:n1686. DOI: 10.1136/bmj.n1686

ABSTRACT: Covid-19 booster vaccinations should be offered in England from September 2021, the Joint Committee on Vaccination and Immunisation has advised. But some experts have questioned the necessity and the practicalities of the plan. JCVI's interim advice,¹ which will be updated by September after further data analysis, could lead to millions of the people who are most vulnerable to covid-19 being offered the booster vaccination in a two stage approach alongside the annual flu vaccination programme. JCVI advised that in the first stage a third dose of covid-19 booster and annual flu vaccine should be offered as soon as possible from September 2021 to immunosuppressed adults aged 16 or over, people living in residential care homes for older adults, all adults aged 70 years or over, clinically extremely vulnerable adults aged 16 or over; and frontline health and social care workers. The second stage would see the covid ...

URL: <https://www.ncbi.nlm.nih.gov/pubmed/34215593>

DOI: 10.1136/bmj.n1686

8. Hall VG, Ferreira VH, Ku T, et al. Randomized Trial of a Third Dose of mRNA-1273 Vaccine in Transplant Recipients. N Engl J Med. 2021;385(13):1244-6. DOI: 10.1056/NEJMc2111462

URL: <https://www.ncbi.nlm.nih.gov/pubmed/34379917>

DOI: 10.1056/NEJMc2111462

9. Hause AM, Baggs J, Gee J, et al. Safety Monitoring of an Additional Dose of COVID-19 Vaccine — United States, August 12–September 19, 2021. MMWR Morbidity and Mortality Weekly Report. 2021;70(39). DOI: 10.15585/mmwr.mm7039e4
DOI: 10.15585/mmwr.mm7039e4

10. Kamar N, Abravanel F, Marion O, et al. Three Doses of an mRNA Covid-19 Vaccine in Solid-Organ Transplant Recipients. N Engl J Med. 2021;385(7):661-2. DOI: 10.1056/NEJMc2108861
URL: <https://www.ncbi.nlm.nih.gov/pubmed/34161700>
DOI: 10.1056/NEJMc2108861

11. Mahase E. Covid-19 booster vaccines: What we know and who's doing what. BMJ. 2021;374:n2082. DOI: 10.1136/bmj.n2082

ABSTRACT: The virulence of the delta variant has prompted many countries to start administering booster vaccines. Elisabeth Mahase looks at what is happening whereHow long does immunity after covid-19 vaccination last? It's something everyone would like to know, but it's a question that can't currently be answered with certainty.1There is some evidence that immunity does wane, especially against the delta variant. Researchers have found that a single dose of either the Oxford-AstraZeneca or Pfizer-BioNTech vaccine is only around 30% effective against delta, although two doses are more effective: 88% for Pfizer and 67% for AstraZeneca.2A preprint from Israeli researchers has reported that the risk of infection is significantly higher among people who were vaccinated earlier in the pandemic than among those vaccinated later (with the Pfizer vaccine only), suggesting a "possible relative decrease in the long-term protection of the BNT162b2 [Pfizer] vaccine against the delta variant of SARS-CoV-2."3 The Israeli team did not look at the effect of time of vaccination on the incidence of symptomatic infection, severe disease, or hospital admissions.But there is a view that booster doses should not be prioritised over primary vaccination. In June researchers from the University of Oxford vaccine team that developed the AstraZeneca vaccine said that although a third dose of their vaccine can provide a strong boost to the immune response there was no ...

URL: <https://www.ncbi.nlm.nih.gov/pubmed/34417167>
DOI: 10.1136/bmj.n2082

12. Mahase E. Covid-19: Booster dose will be needed in autumn to avoid winter surge, says government adviser. BMJ. 2021;372:n664. DOI: 10.1136/bmj.n664

ABSTRACT: A covid-19 booster vaccine is likely to be rolled out in the autumn to avoid another winter surge, the deputy chair of the government's vaccine advisory committee has told The BMJ.Speaking on The BMJ's Talk Evidence podcast, Anthony Harnden of the Joint Committee on Vaccination and Immunisation said he believed that the booster would be needed either to protect against a new variant or as a safety net, as the duration of protection is unknown."We certainly don't want to see a winter like we've seen ...

URL: <https://www.ncbi.nlm.nih.gov/pubmed/33687925>
DOI: 10.1136/bmj.n664

13. Mahase E. Covid-19: Booster vaccine to be rolled out in autumn as UK secures 60m more Pfizer doses. BMJ. 2021;373:n1116. DOI: 10.1136/bmj.n1116

ABSTRACT: The UK will roll out a covid-19 booster vaccine at the beginning of autumn in order to protect the most vulnerable ahead of winter, the Department of Health and Social Care (DHSC) has announced.As part of this, the government's vaccines taskforce has secured an additional 60m doses of the Pfizer BioNTech vaccine, which will be used alongside the other vaccines already purchased.Details

on how the programme will work have not yet been made public, however the DHSC said the booster dose will be given based on clinical need. The BMJ revealed in ...

URL: <https://www.ncbi.nlm.nih.gov/pubmed/33926905>

DOI: 10.1136/bmj.n1116

14. Mahase E. Covid-19: Third vaccine dose boosts immune response but may not be needed, say researchers. BMJ. 2021;373:n1659. DOI: 10.1136/bmj.n1659

URL: <https://www.ncbi.nlm.nih.gov/pubmed/34187780>

DOI: 10.1136/bmj.n1659

15. Riad A, Schunemann H, Attia S, et al. COVID-19 Vaccines Safety Tracking (CoVaST): Protocol of a Multi-Center Prospective Cohort Study for Active Surveillance of COVID-19 Vaccines' Side Effects. Int J Environ Res Public Health. 2021;18(15). DOI: 10.3390/ijerph18157859

ABSTRACT: BACKGROUND: Coronavirus disease (COVID-19) vaccine-related side effects have a determinant role in the public decision regarding vaccination. Therefore, this study has been designed to actively monitor the safety and effectiveness of COVID-19 vaccines globally. METHODS: A multi-country, three-phase study including a cross-sectional survey to test for the short-term side effects of COVID-19 vaccines among target population groups. In the second phase, we will monitor the booster doses' side effects, while in the third phase, the long-term safety and effectiveness will be investigated. A validated, self-administered questionnaire will be used to collect data from the target population; Results: The study protocol has been registered at ClinicalTrials.gov, with the identifier NCT04834869.

CONCLUSIONS: CoVaST is the first independent study aiming to monitor the side effects of COVID-19 vaccines following booster doses, and the long-term safety and effectiveness of said vaccines.

URL: <https://www.ncbi.nlm.nih.gov/pubmed/34360156>

DOI: 10.3390/ijerph18157859

16. Rubin EJ, Baden LR, Morrissey S. Audio Interview: Vaccine Efficacy and Boosters in Covid-19. N Engl J Med. 2021;385(13):e54. DOI: 10.1056/NEJMe2115556

URL: <https://www.ncbi.nlm.nih.gov/pubmed/34551238>

DOI: 10.1056/NEJMe2115556

17. Tanne JH. Covid-19: Moderna plans booster doses to counter variants. BMJ. 2021;372:n232. DOI: 10.1136/bmj.n232

ABSTRACT: The US drug company Moderna has announced that it is developing two new approaches to emerging variants of covid-19 after studies showed that its vaccine had a reduced level of neutralising titres to the South African variant, suggesting that immunity might wane. Although the studies showed that Moderna's current vaccine, known as mRNA-1273, was effective against both the UK and South African variants, a sixfold reduction was seen in neutralising titre levels to the South African variant. Moderna said that "out of an abundance of caution" it was starting a clinical programme of two booster approaches to increase immunity to the new variants. Moderna's chief executive officer, Stéphane Bancel, said, "We believe it is imperative to be proactive as the virus evolves." In the first approach Moderna said that it would see whether a third "booster dose" of the current mRNA-1273 vaccine added to the approved two dose regimen would further increase neutralising titres against the emerging variants. In a second approach the company said that ...

URL: <https://www.ncbi.nlm.nih.gov/pubmed/33500251>

DOI: 10.1136/bmj.n232

18. The Lancet Infectious D. COVID-19 vaccine equity and booster doses. The Lancet Infectious Diseases. 2021;21(9):1193. DOI: 10.1016/s1473-3099(21)00486-2

URL: [https://doi.org/10.1016/S1473-3099\(21\)00486-2](https://doi.org/10.1016/S1473-3099(21)00486-2)

DOI: 10.1016/s1473-3099(21)00486-2

19. Tre-Hardy M, Cupaiolo R, Wilmet A, et al. Six-month interim analysis of ongoing immunogenicity surveillance of the mRNA-1273 vaccine in healthcare workers: A third dose is expected. J Infect. 2021;23:23. DOI: 10.1016/j.jinf.2021.08.031

ABSTRACT: OBJECTIVES: Scarce data are currently available on the kinetics of antibodies after vaccination with mRNA vaccines as a whole and, with mRNA-1273, in particular. We report here an ad-interim analysis of data obtained after a 6-month follow-up in a cohort of healthcare workers (HCWs) who received the mRNA-1273 vaccine. These new data provide more insight into whether and in whom a 3rd dose could be necessary. METHODS: Our study compared the anti-S antibody kinetics at 2 weeks (T1), 3 months (T3) and 6 months (T4) after the first injection, and 2 weeks after the second injection (T2). The 201 participating HCWs were stratified according to their initial serological status. The vaccine effectiveness was also assessed through a medical questionnaire. RESULTS: We report here a marked and statistically significant antibody decrease ($P < 0.05$) between T3 and T4, especially in naive vaccinees. The analysis of potential confounding factors or known risk factors for severe COVID-19 disease did not reveal any influence on the drop observed. Six-month after vaccination, only one, symptomatic, infection was reported in our cohort. CONCLUSIONS: In a supply-limited environment, our results plead for reserving the 3rd dose scheme, in the upcoming months, to seronegative individuals prior to vaccination, especially when the serological status is easily accessible.

URL: <https://www.ncbi.nlm.nih.gov/pubmed/34437927>

DOI: 10.1016/j.jinf.2021.08.031

20. Villanego F, Cazorla JM, Vigara LA, et al. Protecting kidney transplant recipients against SARS-CoV-2 infection: A third dose of vaccine is necessary now. Am J Transplant. 2021;01:01. DOI: 10.1111/ajt.16829

URL: <https://www.ncbi.nlm.nih.gov/pubmed/34467623>

DOI: 10.1111/ajt.16829

21. Waldman RA, Grant-Kels JM. Dermatology Patients on Biologics and Certain Other Systemic Therapies Should Receive a 'Booster' mRNA COVID-19 Vaccine Dose: A Critical Appraisal of Recent FDA and ACIP Recommendations. J Am Acad Dermatol. 2021;23:23. DOI: 10.1016/j.jaad.2021.08.031

URL: <https://www.ncbi.nlm.nih.gov/pubmed/34437985>

DOI: 10.1016/j.jaad.2021.08.031

22. Werbel WA, Boyarsky BJ, Ou MT, et al. Safety and Immunogenicity of a Third Dose of SARS-CoV-2 Vaccine in Solid Organ Transplant Recipients: A Case Series. Ann Intern Med. 2021;174(9):1330-2. DOI: 10.7326/L21-0282

URL: <https://www.ncbi.nlm.nih.gov/pubmed/34125572>

DOI: 10.7326/L21-0282

23. Wise J. Covid-19: Booster doses to be offered to 30 million people in UK. BMJ. 2021;374:n2261. DOI: 10.1136/bmj.n2261

ABSTRACT: Booster doses of a covid-19 vaccine are to be offered to the highest risk groups in the UK as a result of new advice from the Joint Committee on Vaccination and Immunisation. A booster dose will be offered to all people who were vaccinated during phase 1 of the vaccine programme, no earlier than

six months after they received their second dose. The JCVI advises a preference for the Pfizer-BioNTech vaccine regardless of which vaccine someone had for their primary doses. This follows data from the Cov-boost trial that indicated that this vaccine is well tolerated as a third dose and provides a strong booster response. The JCVI said that it was taking a “precautionary position” and that on balance it was preferable to maintain a ...

URL: <https://www.ncbi.nlm.nih.gov/pubmed/34521637>

DOI: 10.1136/bmj.n2261

24. Wise J. Covid-19: UK will offer third vaccine dose to severely immunosuppressed people. BMJ. 2021;374:n2160. DOI: 10.1136/bmj.n2160

URL: <https://www.ncbi.nlm.nih.gov/pubmed/34475111>

DOI: 10.1136/bmj.n2160

25. Yigit M, Ozkaya-Parlakay A, Cosgun Y, et al. Should a third booster dose be scheduled after two doses of CoronaVac? A single-center experience. J Med Virol. 2021. DOI: 10.1002/jmv.27318

ABSTRACT: In the 10th month of the pandemic, coronavirus disease 2019 (COVID-19) vaccination was given first to healthcare workers in Turkey after receiving emergency use approval from the Ministry of Health. This study, which was performed at the COVID-19 reference center in Ankara (the capital of Turkey) aimed to evaluate the seroconversion rate of the CoronaVac vaccine. The anti-spike immunoglobulin G response to the two-dose vaccination was retrospectively examined in healthcare workers who had no previous history of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. The postvaccine seroconversion rate was investigated by measuring the antibody levels of healthcare workers who had received CoronaVac. Vaccination was administered as 600 SU in 28-day intervals. The healthcare workers' anti-SARS-CoV-2 immunoglobulin G levels were used to determine the seroconversion rate 2 months after the second dose of the vaccine. Of the healthcare workers, 22.9% (n = 155) were seronegative. The younger the age of the participant, the higher the level of anti-SARS-CoV-2 immunoglobulin G. Furthermore, anti-SARS-CoV-2 immunoglobulin G levels were much higher in women than men.

URL: <https://www.ncbi.nlm.nih.gov/pubmed/34487373>

DOI: 10.1002/jmv.27318

26. Yue L, Xie T, Yang T, et al. A third booster dose may be necessary to mitigate neutralizing antibody fading after inoculation with two doses of an inactivated SARS-CoV-2 vaccine. J Med Virol. 2021. DOI: 10.1002/jmv.27334

URL: <https://www.ncbi.nlm.nih.gov/pubmed/34516026>

DOI: 10.1002/jmv.27334

Appendix 1: Evidence Search Details

Filters, Limits & Exclusions:	English only 2021 – September 29 2021
Sources Searched:	<ul style="list-style-type: none">• CanCOVID• LitCovid• CBC• Medline (Ovid)• Centre for Infectious Disease Research and Policy (CIDRAP)• medRxiv• Cochrane CENTRAL (Ovid)• National Advisory Committee on Immunization (NACI)

- COVID-19 Immunity Task Force
- COVID-END
- Embase (Ovid)
- European Centre for Disease Prevention and Control
- Google
- Google Scholar
- National Collaborating Centre for Methods and Tools
- Newfoundland & Labrador Centre for Applied Health Research
- Prevent Epidemics
- Public Health Ontario
- Science Table (Ontario)

Librarian(s): Lukas Miller, Clinical Librarian, Saskatchewan Health Authority
 Brianna Howell-Spooner, Clinical Librarian, Saskatchewan Health Authority

Appendix 2: Search Strategies

Database: Ovid MEDLINE(R) ALL <1946 to September 27, 2021>

Search Strategy:

-
- 1 COVID-19/ or exp COVID-19 Testing/ or COVID-19 Vaccines/ or SARS-CoV-2/ (109644)
 - 2 (coronavirus/ or betacoronavirus/ or coronavirus infections/) and (disease outbreaks/ or epidemics/ or pandemics/) (40079)
 - 3 (nCoV* or 2019nCoV or 19nCoV or COVID19* or COVID or SARS-COV-2 or SARSCOV-2 or SARS-COV2 or SARSCOV2 or "SARS coronavirus 2" or "Severe Acute Respiratory Syndrome Coronavirus 2" or "Severe Acute Respiratory Syndrome Corona Virus 2").ti,ab,kf,nm,ot,ox,rx,px. (175008)
 - 4 ((new or novel or "19" or "2019" or Wuhan or Hubei or China or Chinese) adj3 (coronavirus* or corona virus* or betacoronavirus* or CoV or HCoV)).ti,ab,kf,ot. (53106)
 - 5 (longCOVID* or postCOVID* or postcoronavirus* or postSARS*).ti,ab,kf,ot. (19)
 - 6 ((coronavirus* or corona virus* or betacoronavirus*) adj3 (pandemic* or epidemic* or outbreak* or crisis)).ti,ab,kf,ot. (9722)
 - 7 ((Wuhan or Hubei) adj5 pneumonia).ti,ab,kf,ot. (363)
 - 8 or/1-7 (184050)
 - 9 limit 8 to yr="2019 -Current" (182569)
 - 10 exp Immunization/ or exp Vaccines/ or Immunity, Herd/ (343175)
 - 11 (vaccinat* or vaccine? or inoculat* or immunization? or immunize? or immunity or immunogenicity or variolation?).ti,kf,ot. (309563)
 - 12 (pfizer-biontech or biontech or pfizer or comirnaty or "BNT162b2" or "BNT 162B2" or tozinameran).ti,ab,kf,nm,ot,ox,rx,px. (4203)
 - 13 (astrazeneca or vaxzevria or "AZD1222" or "AZD1222" or "AZD_1222" or covishield or "ChAdOx1_nCoV-19" or "ChAdOx1 nCoV-19").ti,ab,kf,nm,ot,ox,rx,px. (1725)
 - 14 (moderna or spikevax or "mrna-1273" or "mrna 1273" or "mrna1273").ti,ab,kf,nm,ot,ox,rx,px. (1452)
 - 15 (janssen or "Ad26.COVS.2.S" or "johnson and johnson" or "johnson & johnson").ti,ab,kf,nm,ot,ox,rx,px. (2217)
 - 16 (sinovac or coronavac or gamaleya or "sputnik V" or "sputnik 5" or bharat biotech or covaxin or covovax).ti,ab,kf,nm,ot,ox,rx,px. (215)

- 17 10 or 11 or 12 or 13 or 14 or 15 or 16 (465029)
- 18 9 and 17 (14209)
- 19 (safe* or risk* or unsafe or harm* or efficacy or viability or viable or success* or valid* or evidence-based or guidance or guideline? or recommend* or best practice? or consensus or advisory or standard* or literature review? or systematic* review? or rapid review? or scoping review?).ti,kf. (1761541)
- 20 ((prevent* or control* or reduce? or reduction?) adj2 (infect* or spread* or serious* ill* or hospitaliz* or outbreak* or crossinfect* or nosocomial or severity or severe or intubat* or death? or fatal* or epidemic? or pandemic? or "loss of life" or "long covid" or intensive care or critical care)).ti,kf. (28611)
- 21 19 or 20 (1786006)
- 22 18 and 21 (1832)
- 23 limit 22 to (english language and yr="2021 -Current") (1407)
- 24 (third adj3 (dose? or dosing? or boost* or vaccin* or inoculat* or immunization?)).tw,kf. (4675)
- 25 ("3rd" adj2 (dose? or dosing? or boost* or vaccin* or inoculat* or immunization?)).tw,kf. (272)
- 26 booster?.ti. (2132)
- 27 24 or 25 or 26 (7004)
- 28 23 and 27 (20)
- 29 from 28 keep 2-5,9-11 (7)

Other Sources

booster covid vaccine
booster covid19 vaccine



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