Evidence Search Report

Review Question:	**What are the risks or benefits of extended intervals between doses of COVID-19 vaccines compared to recommended dosing in extremely vulnerable populations?**		
Context:	Clinically vulnerable populations (i.e. immunocompromised, pre-existing respiratory conditions, e.g. COPD, frail elderly, ICU, CCU) Consider patient and public health contexts		
Review ID:	**EOC210302 ESR**	**Complete Date:**	**April 1, 2021**
Cite As:	Miller, L; Howell-Spooner, B. What are the risks or benefits of extended intervals between doses of COVID-19 vaccines compared to recommended dosing in extremely vulnerable populations? 2021 Apr 01; Document no.: EOC210302 ESR. In: COVID-19 Rapid Evidence Reviews [Internet]. SK: SK COVID Evidence Support Team, c2020. 22 p. (CEST evidence search report).		

Librarian Notes & Comments

Though there is little clinical evidence available on this topic, there is no shortage of other information (reports, recommendations, expert opinion) discussing vaccine distribution amongst clinically vulnerable groups.

/Lukas & Brianna.

Disclaimer

Search Results: Guidance, Summaries & Other Grey Literature

Health Canada / PHAC / Government of Canada

- NACI rapid response: Extended dose intervals for COVID-19 vaccines to optimize early vaccine rollout and population protection in Canada. Revised 2021 March 8. https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/rapid-response-extended-dose-intervals-covid-19-vaccines-early-rollout-population-protection.html

BCCDC / British Columbia Healthcare

- Public health statement on deferral of second dose of COVID-19 vaccine in BC. 3 March 2021 http://www.bccdc.ca/Health-Info-Site/Documents/COVID-19_vaccine/Public_health_statement_deferred_second_dose.pdf
- Early findings show the first vaccine dose reduced the risk of COVID-19 by 80 per cent or more. 19 Feb 2021. http://www.bccdc.ca/about/news-stories/news-releases/2021/early-findings-show-the-first-vaccine-dose-reduced-the-risk-of-covid-19-by-80-per-cent-or-more
- Clinical Guidance on COVID- 19 Vaccines for Persons with Autoimmune Rheumatic Diseases. 29 March 2021. http://www.bccdc.ca/Health-Info-Site/Documents/COVID-19_vaccine/ARD_Clinical_Guidance.pdf
- Clinical Guidance on COVID-19 Vaccines for Solid Organ Transplant Recipients. 16 March 2021. http://www.bccdc.ca/Health-Info-Site/Documents/COVID-19_vaccine/Transplant_Clinical_Guidance.pdf
- Vaccines for people who are clinically extremely vulnerable 30 March 2021. https://www2.gov.bc.ca/gov/content/covid-19/vaccine/cev
- People deemed clinically extremely vulnerable prioritized for COVID-19 vaccine 23 March 2021. https://news.gov.bc.ca/releases/2021HLTH0022-000532

Ontario Ministry of Health

- Extension of the Second Dose Interval. 19 March 2021. https://www.health.gov.on.ca/en/pro/programs/publichealth/coronavirus/docs/vaccine/COVID_19_vaccine_dose_intervals.pdf
- Vaccine Clinical Advisory Group (VCAG) Recommendations on Exceptions to Extended Dose Intervals for COVID-19 vaccines. 26 March 2021. https://www.health.gov.on.ca/en/pro/programs/publichealth/coronavirus/docs/vaccine/COVID_19_medical_exceptions_vaccine_dose_intervals.pdf
- COVID-19 Vaccination Recommendations for Special Populations. 11 March 2021. https://www.health.gov.on.ca/en/pro/programs/publichealth/coronavirus/docs/vaccine/COVID-19_vaccination_rec_special_populations.pdf

CDC / FDA / US Gov't

- Morbidity and Mortality Weekly Report (MMWR). COVID-19 Vaccine Second-Dose Completion and Interval Between First and Second Doses Among Vaccinated Persons — United States, December 14, 2020–February 14, 2021. 19 March 2021. https://www.cdc.gov/mmwr/volumes/70/wr/mm7011e2.htm
- Vaccine Considerations for People with Underlying Medical Conditions 12 March 2021. https://www.cdc.gov/coronavirus/2019-ncov/vaccines/recommendations/underlying-conditions.html

NICE / Public Health England / UK Government

- New vaccine advice for adults living with adults who are immunosuppressed. 29 March 2021. https://www.gov.uk/government/news/new-vaccine-advice-for-adults-living-with-adults-who-are-immunosuppressed

Australian Government

- ATAGI – Provider guide to COVID-19 vaccination of people with immunocompromised. 30 March 2021. https://www.health.gov.au/resources/publications/atagi-provider-guide-to-covid-19-vaccination-of-people-with-immunocompromise
    - PDF: https://www.health.gov.au/sites/default/files/documents/2021/03/atagi-provider-guide-to-covid-19-vaccination-of-people-with-immunocompromise.pdf

UCSF Health (USA) Infection Control

- VACCINE GUIDELINES FOR IMMUNOCOMPROMISED AND OTHER SPECIAL POPULATIONS. N.d. https://infectioncontrol.ucsfmedicalcenter.org/sites/g/files/tkssra4681/f/Vaccine_Guidelines_IC_Special_Populations.pdf

COVID-NMA https://covid-nma.com/

- COVID-NMA has identified 14 of 254 trials (recruiting/ongoing/closed) of various designs/quality that involve "high risk patients" as a population group. I have copied the table including links to registry entries from the site.
    - Note that the COVID-NMA definition of "high risk patient" may be wider in scope than this question initially proposes

Vaccine (per arm)	Sample size	Type of vaccine	Phase	Sponsor/Funder	Reg. number
(1) Gam-COVID-Vac	110	Non replicating viral vector	Phase 2	Gamaleya Research Institute of Epidemiology and Microbiology, Health Ministry of the Russian Federation	NCT04587219
(1) BNT162b2	4000	RNA based vaccine	Phase 2 / Phase 3	BioNTech SE	NCT04754594
(1) SARS-CoV-2 vaccine (inactivated) *vs* (2) SARS-CoV-2 vaccine (inactivated) *vs* (3) SARS-CoV-2 vaccine (inactivated)	2067	Inactivated virus	N/A	University of Sao Paulo General Hospital	NCT04754698
(1) COVID-19 mRNA vaccine (nucleoside-modified)	120	RNA based vaccine	Phase 4	Hopital Erasme, Universit◎Libre de Bruxelles	EUCTR2021-000461-33-BE
(1) COVID-19 mRNA vaccine (nucleoside-modified)	80	RNA based vaccine	Phase 4	Hopital Erasme, Universit◎Libre de Bruxelles	EUCTR2021-000412-28-BE
(1) mRNA-1273	700	RNA based vaccine	Phase 4	Erasmus University Medical Center	EUCTR2021-000515-24-NL

(1) BNT162	540	RNA based vaccine	Phase 4	Karolinska Universitetssjukhuset	EUCTR2021-000175-37-SE
(1) mRNA-1273 *vs* (2) BNT162b2	3400	RNA based vaccine	Phase 2	National Institute of Allergy and Infectious Diseases (NIAID)	NCT04761822
(1) Ad26.COV2.S	400	Non replicating viral vector	Phase 2	Janssen Vaccines & Prevention B.V.	NCT04765384
(1) SARS-CoV-2 vaccine (inactivated) *vs* (2) AZD1222 *vs* (3) BNT162b2	900	Inactivated virus	Phase 4	Humanity & Health Medical Group Limited	NCT04775069
(1) BNT162	540	RNA based vaccine	Phase 4	Karolinska University Hospital	NCT04780659
(1) AZD1222 *vs* (2) AZD1222	2200	Non replicating viral vector	N/A	Institute of Liver and Biliary Sciences, India	NCT04794946
(1) mRNA-1273 *vs* (2) BNT162b2	380	RNA based vaccine	Phase 3	University Hospital, Basel, Switzerland	NCT04805125
(1) mRNA-1273	220	RNA based vaccine	Phase 3	McGill University Health Centre/Research Institute of the McGill University Health Centre	NCT04806113

Source: https://covid-nma.com/vaccines/mapping/ April 1 2021.

Search Results: News, Blogs, Social Media

BC Medical Journal

- (Letter/Commentary) AN UPDATED LOOK AT THE 16-WEEK WINDOW BETWEEN DOSES OF VACCINES IN BC FOR COVID-19 https://bcmj.org/letters-covid-19/updated-look-16-week-window-between-doses-vaccines-bc-covid-19
    - Response to a journal article (included in ref list below). https://bcmj.org/articles/what-evidence-extending-sars-cov-2-covid-19-vaccine-dosing-schedule

CBC News

- (Opinion) Why Canada's decision to delay 2nd doses of COVID-19 vaccines may not work for everyone 27 Mar 2021 https://www.cbc.ca/news/health/vaccine-dose-delay-canada-covid-19-research-1.5965996
- Stretch interval between COVID-19 vaccine doses up to 4 months, national advisory committee recommends 3 March 2021. https://www.cbc.ca/news/politics/naci-interval-advice-change-four-months-1.5934563
- A look at the studies from Israel, U.K. that informed B.C.'s second-dose delay 3 March 2021 https://www.cbc.ca/news/canada/british-columbia/vaccine-studies-israel-uk-informed-bc-s-second-dose-delay-1.5935865

CTV News

- Research raises questions over delayed second vaccine doses for seniors. 25 March 2021. https://www.ctvnews.ca/health/coronavirus/research-raises-questions-over-delayed-second-vaccine-doses-for-seniors-1.5362333

- Time between doses in Manitoba based on best science, but willing to pivot: health officials 24 March 2021. https://winnipeg.ctvnews.ca/time-between-doses-in-manitoba-based-on-best-science-but-willing-to-pivot-health-officials-1.5360826

CityNews (Toronto)

- Ontario revises 2nd vaccine dose timeline for transplant and some cancer patients 29 March 2021. https://toronto.citynews.ca/2021/03/29/ontario-revises-2nd-vaccine-dose-timeline-for-immunocompromised/

Global News

- New B.C. research raises questions about risks of delayed vaccine interval for the elderly. 26 March 2021. https://globalnews.ca/news/7720287/ubc-seniors-second-dose-study/

Globe & Mail

- New study casts doubt on time between COVID-19 vaccine doses 26 March 2021. https://www.theglobeandmail.com/canada/article-new-study-casts-doubt-on-time-between-covid-19-vaccine-doses/

Financial Post

- [video interview] The case for delaying the second vaccine dose 31 March 2021. https://financialpost.com/news/economy/the-case-for-delaying-the-second-vaccine-dose

Kings College London (News Centre)

- Delaying second vaccine dose leaves cancer patients vulnerable to virus 11 March 2021. https://www.kcl.ac.uk/news/delaying-second-vaccine-dose-cancer-patients-vulnerable-virus

NPR.org

- Immunocompromised And Concerned About The Vaccine? Here's What You Need To Know 29 March 2021. https://www.npr.org/sections/health-shots/2021/03/29/981767390/immunocompromised-and-concerned-about-the-vaccine-heres-what-you-need-to-know

BMJ Blog

- Vaccinated, yet still clinically extremely vulnerable 30 March 2021. https://blogs.bmj.com/bmj/2021/03/30/vaccinated-yet-still-clinically-extremely-vulnerable/

Search Results: Articles from Databases

Sorted by newest-oldest.

0. Brockman, M. A., Mwimanzi, F., Sang, Y., Ng, K., Agafitei, O., Ennis, S., Lapointe, H., Young, L., Umviligihozo, G., Burns, L., Brumme, C., Leung, V., Montaner, J. S. G., Holmes, D., DeMarco, M., Simons, J., Niikura, M., Pantophlet, R., Romney, M. G., & Brumme, Z. L. (2021). Weak humoral immune reactivity among residents of long-term care facilities following one dose of the BNT162b2 mRNA COVID-19 vaccine. *MedRxiv*, 2021.03.17.21253773. https://doi.org/10.1101/2021.03.17.21253773

1. Arnold J, Winthrop K, Emery P. COVID-19 vaccination and antirheumatic therapy. Rheumatology (Oxford). 2021. DOI: https://dx.doi.org/10.1093/rheumatology/keab223

ABSTRACT: The COVID-19 vaccination will be the largest vaccination programme in the history of the NHS. Patients on immunosuppressive therapy will be amongst the earliest to be vaccinated. Some evidence indicates immunosuppressive therapy inhibits humoral response to the influenza, pneumococcal and hepatitis B vaccines. The degree to which this will translate to impaired COVID-19 vaccine responses is unclear. Other evidence suggests withholding methotrexate for two weeks post vaccination may improve responses. Rituximab has been shown to impair humoral responses for 6 months or longer post administration. Decisions on withholding or interrupting immunosuppressive therapy around COVID-19 vaccination will need to be made prior to the availability of data on specific COVID-19 vaccine response in these patients. With this in mind, this article outlines the existing data on the effect of antirheumatic therapy on vaccine responses in patients with inflammatory arthritis and formulates a possible pragmatic management strategy for COVID-19 vaccination.
DOI: https://dx.doi.org/10.1093/rheumatology/keab223

2. Benotmane I, Gautier -Vargas G, Cognard N, et al. Weak anti-SARS-CoV-2 antibody response after the first injection of an mRNA COVID-19 vaccine in kidney transplant recipients. Kidney Int. 2021. DOI: 10.1016/j.kint.2021.03.014
URL: https://doi.org/10.1016/j.kint.2021.03.014
DOI: 10.1016/j.kint.2021.03.014

3. Boyarsky BJ, Ruddy JA, Connolly CM, et al. Antibody response to a single dose of SARS-CoV-2 mRNA vaccine in patients with rheumatic and musculoskeletal diseases. Ann Rheum Dis. 2021:annrheumdis-2021-220289. DOI: 10.1136/annrheumdis-2021-220289
ABSTRACT: The immune response to SARS-CoV-2 messenger RNA (mRNA) vaccines in patients with rheumatic and musculoskeletal diseases (RMD) is undefined because these individuals were largely excluded from phase I–III studies. To better understand the immune response to vaccination in this patient population, we studied the antibody response in patients with RMD who completed the first dose of SARS-CoV-2 mRNA vaccination.Participants with RMD across the USA were recruited to participate in this prospective cohort via social media. Those with prior SARS-CoV-2 were excluded. We collected demographics, RMD diagnoses and immunomodulatory regimens and tested for SARS-CoV-2 antibodies at baseline and prior to the second vaccine dose. Antibody testing was conducted on the semiquantitative Roche Elecsys anti-SARS-CoV-2 S enzyme immunoassay (EIA) which tests for antibodies against the receptor-binding domain (RBD) of the SARS-CoV-2 spike protein.1 We evaluated the association between demographic/clinical characteristics and positive antibody response using Fisher's exact test and Wilcoxon rank-sum test.We studied 123 participants who received their first SARS-CoV-2 vaccination dose between 8 January 2021 and 12 February 2021; 52% underwent BNT162b2, and 48% underwent mRNA-1273 (table 1). The most common reported RMD diagnoses were inflammatory arthritis (28%), systemic lupus erythematosus (SLE) (20%), Sjogren's syndrome (13%) and overlap connective tissue diseases(29%). Whereas …
URL: http://ard.bmj.com/content/early/2021/03/23/annrheumdis-2021-220289.abstract
DOI: 10.1136/annrheumdis-2021-220289

4. Chau CYC, Chow LLW, Sridhar S, et al. Ophthalmological Considerations for COVID-19 Vaccination in Patients with Inflammatory Eye Diseases and Autoimmune Disorders. Ophthalmology and therapy. 2021:1-9. DOI: 10.1007/s40123-021-00338-1
ABSTRACT: The global impact imposed by the coronavirus disease 2019 (COVID-19) pandemic may be soon alleviated by the introduction and worldwide dissemination of safe and effective vaccines. This expedited timetable for development and approval of COVID-19 vaccines is an unprecedented extraordinary, concerted achievement by the scientific community. With the pending global rollout of vaccines, each with different mechanisms of action, physicians of various specialties will need to identify vulnerable patient groups for special considerations or advice. In this commentary, we analyse the important considerations for COVID-19 vaccines in patients with inflammatory eye diseases. Scrutiny of immunogenicity and adverse effects, particularly antibody-dependent enhancement, would better help in counselling these patients undergoing vaccination. More research on pharmacovigilance would allow for tailored guidelines and personalised management strategies.

URL: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7936587/
DOI: 10.1007/s40123-021-00338-1

5. Corti C, Crimini E, Tarantino P, et al. SARS-CoV-2 vaccines for cancer patients: a call to action. Eur J Cancer. 2021;148:316-27. DOI: 10.1016/j.ejca.2021.01.046
ABSTRACT: Coronavirus disease 2019 (COVID-19) has affected more than 96 million people worldwide, leading the World Health Organization (WHO) to declare a pandemic in March 2020. Although an optimal medical treatment of COVID-19 remains uncertain, an unprecedented global effort to develop an effective vaccine hopes to restore pre-pandemic conditions. Since cancer patients as a group have been shown to be at a higher risk of severe COVID-19, the development of safe and effective vaccines is crucial. However, cancer patients may be underrepresented in ongoing phase 3 randomised clinical trials investigating COVID-19 vaccines. Therefore, we encourage stakeholders to provide real-time data about the characteristics of recruited participants, including clearly identifiable subgroups, like cancer patients, with sample sizes large enough to determine safety and efficacy. Moreover, we envisage a prompt implementation of suitable registries for pharmacovigilance reporting, in order to monitor the effects of COVID-19 vaccines and immunisation rates in patients with cancer. That said, data extrapolation from other vaccine trials (e.g. anti-influenza virus) showed a favourable safety and efficacy profile for cancer patients. On the basis of the evidence discussed, we believe that the benefits of the vaccination outweigh the risks. Consequently, healthcare authorities should prioritise vaccinations for cancer patients, with the time-point of administration agreed on a case-by-case basis. In this regard, the American Society of Clinical Oncology and the European Society of Medical Oncology are advocating for cancer patients a high priority status, in the hope of attenuating the consequences of the pandemic in this particularly vulnerable population.
URL: https://doi.org/10.1016/j.ejca.2021.01.046
DOI: 10.1016/j.ejca.2021.01.046

6. Fanciullino R, Ciccolini J, Milano G. COVID-19 vaccine race: watch your step for cancer patients. Br J Cancer. 2021;124(5):860-1. DOI: https://dx.doi.org/10.1038/s41416-020-01219-3
ABSTRACT: Patients with cancer should benefit from COVID-19 vaccination. Some of the most advanced vaccine candidates are mRNAs encapsulated into lipid carriers, and small liposomes are expected to accumulate in tumour tissues through the enhanced and permeation retention effect. However, to what extent solid tumours could take up a significant part of the vaccine dose as well remains unknown. This calls for a careful evaluation of the efficacy of these promising mRNA COVID-19 vaccines administered as lipid carriers for patients with solid tumours, including a possible re-appraisal of the dosing for optimal protection of this specific and frail population.
DOI: https://dx.doi.org/10.1038/s41416-020-01219-3

7. Felten R, Dubois M, Ugarte-Gil MF, et al. Vaccination against COVID-19: Expectations and concerns of patients with autoimmune and rheumatic diseases. Lancet Rheumatol. 2021;3(4):e243-e5. DOI: 10.1016/S2665-9913(21)00039-4
URL: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7906671/
DOI: 10.1016/S2665-9913(21)00039-4

8. Furer V, Rondaan C, Agmon-Levin N, et al. Point of view on the vaccination against COVID-19 in patients with autoimmune inflammatory rheumatic diseases. RMD open. 2021;7(1):e001594. DOI: 10.1136/rmdopen-2021-001594
ABSTRACT: In view of the COVID-19 pandemic, there is an unmet clinical need for the guidelines on vaccination of patients with autoimmune inflammatory rheumatic diseases (AIIRD). This position paper summarises the current data on COVID-19 infection in patients with AIIRD and development of vaccines against COVID-19, discusses the aspects of efficacy and safety of vaccination, and proposes preliminary considerations on vaccination against COVID-19 in patients with AIIRD, mainly based on the expert opinion and knowledge on the use of other vaccines in this population of patients.
URL: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7907831/
DOI: 10.1136/rmdopen-2021-001594

9. Geisen UM, Berner DK, Tran F, et al. Immunogenicity and safety of anti-SARS-CoV-2 mRNA vaccines in patients with chronic inflammatory conditions and immunosuppressive therapy in a monocentric cohort. Ann Rheum Dis. 2021. DOI: https://dx.doi.org/10.1136/annrheumdis-2021-220272

ABSTRACT: INTRODUCTION: In light of the SARS-CoV-2 pandemic, protecting vulnerable groups has become a high priority. Persons at risk of severe disease, for example, those receiving immunosuppressive therapies for chronic inflammatory cdiseases (CIDs), are prioritised for vaccination. However, data concerning generation of protective antibody titres in immunosuppressed patients are scarce. Additionally, mRNA vaccines represent a new vaccine technology leading to increased insecurity especially in patients with CID., OBJECTIVE: Here we present for the first time, data on the efficacy and safety of anti-SARS-CoV-2 mRNA vaccines in a cohort of immunosuppressed patients as compared with healthy controls., METHODS: 42 healthy controls and 26 patients with CID were included in this study (mean age 37.5 vs 50.5 years). Immunisations were performed according to national guidelines with mRNA vaccines. Antibody titres were assessed by ELISA before initial vaccination and 7 days after secondary vaccination. Disease activity and side effects were assessed prior to and 7 days after both vaccinations., RESULTS: Anti -SARS-CoV-2 antibodies as well as neutralising activity could be detected in all study participants. IgG titres were significantly lower in patients as compared with controls (2053 binding antibody units (BAU)/mL +/-1218 vs 2685+/-1102). Side effects were comparable in both groups. No severe adverse effects were observed, and no patients experienced a disease flare., CONCLUSION: We show that SARS-CoV-2 mRNA vaccines lead to development of antibodies in immunosuppressed patients without considerable side effects or induction of disease flares. Despite the small size of this cohort, we were able to demonstrate the efficiency and safety of mRNA vaccines in our cohort. Copyright © Author(s) (or their employer(s)) 2021. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.
DOI: https://dx.doi.org/10.1136/annrheumdis-2021-220272

10. Gray KJ, Bordt EA, Atyeo C, et al. COVID-19 vaccine response in pregnant and lactating women: a cohort study. Am J Obstet Gynecol. 2021. DOI: 10.1016/j.ajog.2021.03.023

ABSTRACT: BACKGROUND: Pregnant and lactating women were excluded from initial COVID-19 vaccine trials; thus, data to guide vaccine decision-making are lacking. OBJECTIVES: To evaluate the immunogenicity and reactogenicity of COVID-19 mRNA vaccination in pregnant and lactating women compared to: (1) non-pregnant controls and (2) natural COVID-19 infection in pregnancy. STUDY DESIGN: 131 reproductive-age vaccine recipients (84 pregnant, 31 lactating, and 16 non-pregnant) were enrolled in a prospective cohort study at two academic medical centers. Titers of SARS-CoV-2 Spike and RBD IgG, IgA and IgM were quantified in participant sera (N=131) and breastmilk (N=31) at baseline, second vaccine dose, 2-6 weeks post second vaccine, and at delivery by Luminex. Umbilical cord sera (N=10) titers were assessed at delivery. Titers were compared to those of pregnant women 4-12 weeks from natural infection (N=37) by ELISA. A pseudovirus neutralization assay was used to quantify neutralizing antibody titers for the subset of women who delivered during the study period. Post-vaccination symptoms were assessed via questionnaire. Kruskal-Wallis tests and a mixed effects model, with correction for multiple comparisons, were used to assess differences between groups. RESULTS: Vaccine-induced antibody titers were equivalent in pregnant and lactating compared to non-pregnant women (median [IQR] 5.59 [4.68-5.89] pregnant, 5.74 [5.06-6.22] lactating, 5.62 [4.77-5.98] non-pregnant, p = 0.24). All titers were significantly higher than those induced by SARS-CoV-2 infection during pregnancy (p < 0.0001). Vaccine-generated antibodies were present in all umbilical cord blood and breastmilk samples. Neutralizing antibody titers were lower in umbilical cord compared to maternal sera, although this finding did not achieve statistical significance (median [IQR] 104.7 [61.2-188.2] maternal sera, 52.3 [11.7-69.6] cord sera, p=0.05). The second vaccine dose (boost dose) increased SARS-CoV-2-specific IgG, but not IgA, in maternal blood and breastmilk. No differences were noted in reactogenicity across the groups. CONCLUSIONS: COVID-19 mRNA vaccines generated robust humoral immunity in pregnant and lactating women, with immunogenicity and reactogenicity similar to that observed in non-pregnant women. Vaccine-induced immune responses were significantly greater than the response to natural infection. Immune transfer to neonates occurred via placenta and breastmilk.
URL: https://www.ajog.org/article/S0002-9378(21)00187-3/pdf
DOI: 10.1016/j.ajog.2021.03.023

11. Kronbichler A, Anders H-J, Fernandez-Juárez GM, et al. Recommendations for the use of COVID-19 vaccines in patients with immune-mediated kidney diseases. Nephrology Dialysis Transplantation. 2021. DOI: 10.1093/ndt/gfab064

ABSTRACT: Coronavirus Disease 19 (COVID-19) vaccine platforms are becoming available and are the most promising strategy to curb the spread of SARS-CoV-2 infections. However, numerous uncertainties exist regarding the pros and cons of vaccination, especially in patients with (immune-mediated) kidney diseases on immunosuppressive drugs. Here, members of the Immunonephrology Working Group (IWG) of the European Renal Association-European Dialysis and Transplant Association (ERA-EDTA) discuss thirteen frequently-asked questions regarding safety and efficacy of the most promising vaccine candidates. Post-marketing surveillance should be performed to estimate the rate of vaccine response (humoral and cellular) of different vaccine platforms, and surveillance of disease activity following administration of COVID-19 vaccines. Some of the candidates induce signaling pathways which also promote autoimmune kidney diseases, e.g. type I interferons in systemic lupus erythematosus. Efficacy estimates would thus far favor the use of selected COVID-19 vaccines, such as BNT162b2, mRNA-1273 or Gam-COVID-Vac. Humoral immune response after vaccination should be monitored using appropriate assays. Even in the absence of neutralizing antibodies patients might be protected by a sufficient cellular immune response capable to reduce severity of COVID-19. A reduced vaccine response after the use of CD20-depleting agents is anticipated, and it is particularly important to discuss strategies to improve vaccine response with these patients. Distancing and shielding measures remain important as not all vaccines fully protect from coronavirus infection. In-depth information about the most pressing vaccine questions is essential to reduce vaccine hesitancy of patients.
URL: https://doi.org/10.1093/ndt/gfab064
DOI: 10.1093/ndt/gfab064

12. Kuderer NM, Hill JA, Carpenter PA, et al. Challenges and Opportunities for COVID-19 Vaccines in Patients with Cancer. Cancer Invest. 2021;39(3):205-13. DOI: https://dx.doi.org/10.1080/07357907.2021.1885596

ABSTRACT: Given the rapidly expanding global spread of the SARS-Co-V-2 virus and the expanding number of individuals with the serious and potentially fatal illness, COVID-19, there is an urgent need for safe and effective vaccines. Based on compelling evidence that patients with cancer are at increased risk for greater morbidity and mortality with COVID-19, several professional organizations have provided early guidance on the role of COVID-19 vaccines in patients with malignant disease. In this commentary we review the available data on the efficacy and safety of the approved and forthcoming vaccines in patients with cancer. Based on a review of the totality of available evidence, we recommend that most patients with cancer should receive the recommended dose and schedule of one of the COVID-19 vaccines when available. We encourage industry, regulators and professional research organizations to carefully track the efficacy and safety of COVID-19 vaccination in patients with cancer in the real world setting and routinely report unanticipated adverse events and signs of loss of efficacy. Particular attention is needed for patients on active cancer therapy to carefully evaluate efficacy and safety in relationship to the timing of vaccination relative to that of active cancer treatment and immunosuppression.
DOI: https://dx.doi.org/10.1080/07357907.2021.1885596

13. Moghadas SM, Vilches TN, Zhang K, et al. Evaluation of COVID-19 vaccination strategies with a delayed second dose. medRxiv. 2021:2021.01.27.21250619. DOI: 10.1101/2021.01.27.21250619

ABSTRACT: Two of the COVID-19 vaccines currently approved in the United States require two doses, administered three to four weeks apart. Constraints in vaccine supply and distribution capacity, together with a deadly wave of COVID-19 from November 2020 to January 2021 and the emergence of highly contagious SARS-CoV-2 variants, sparked a policy debate on whether to vaccinate more individuals with the first dose of available vaccines and delay the second dose, or to continue with the recommended two-dose series as tested in clinical trials. We developed an agent-based model of COVID-19 transmission to compare the impact of these two vaccination strategies, while varying the temporal waning of vaccine efficacy following the first dose and the level of pre-existing immunity in the population. Our results show that for Moderna vaccines, a delay of at least 9 weeks could maximize vaccination program effectiveness and avert at least an additional 17.3 (95% CrI: 7.8 – 29.7) infections, 0.71 (95% CrI: 0.52 - 0.97) hospitalizations, and 0.34 (95% CrI: 0.25 - 0.44) deaths per 10,000 population compared to the recommended 4-week interval between the two doses. Pfizer-BioNTech vaccines also averted an additional 0.61 (95% CrI: 0.37 - 0.89) hospitalizations and 0.31 (95% CrI: 0.23 - 0.45) deaths per 10,000 population in a 9-week

delayed second dose strategy compared to the 3-week recommended schedule between doses. However, there was no clear advantage of delaying the second dose with Pfizer-BioNTech vaccines in reducing infections, unless the efficacy of the first dose did not wane over time. Our findings underscore the importance of quantifying the characteristics and durability of vaccine-induced protection after the first dose in order to determine the optimal time interval between the two doses.Competing Interest StatementThe authors have declared no competing interest.Funding StatementCanadian Institutes of Health Research [OV4-170643, COVID-19 Rapid Research]; São Paulo Research Foundation [18/24811-1]; the National Institutes of Health [1RO1AI151176-01; 1K01AI141576-01], and the National Science Foundation [RAPID 2027755; CCF-1918784].Author DeclarationsI confirm all relevant ethical guidelines have been followed, and any necessary IRB and/or ethics committee approvals have been obtained.YesThe details of the IRB/oversight body that provided approval or exemption for the research described are given below:No ethics approval required.All necessary patient/participant consent has been obtained and the appropriate institutional forms have been archived.YesI understand that all clinical trials and any other prospective interventional studies must be registered with an ICMJE-approved registry, such as ClinicalTrials.gov. I confirm that any such study reported in the manuscript has been registered and the trial registration ID is provided (note: if posting a prospective study registered retrospectively, please provide a statement in the trial ID field explaining why the study was not registered in advance).Yes I have followed all appropriate research reporting guidelines and uploaded the relevant EQUATOR Network research reporting checklist(s) and other pertinent material as supplementary files, if applicable.YesThe computational system and parameters are available under an open source license at: https://github.com/thomasvilches/delayed_dose.
URL: http://medrxiv.org/content/early/2021/03/26/2021.01.27.21250619.abstract
DOI: 10.1101/2021.01.27.21250619

14. Otero-Romero S, Ascherio A, Lebrun-Frenay C. Vaccinations in multiple sclerosis patients receiving disease-modifying drugs. Curr Opin Neurol. 2021. DOI: https://dx.doi.org/10.1097/WCO.0000000000000929
ABSTRACT: PURPOSE OF REVIEW: This review focuses on new evidence supporting the global immunization strategy for multiple sclerosis (MS) patients receiving disease-modifying drugs (DMDs), including the recently available vaccines against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection., RECENT FINDINGS: New data strengthen the evidence against a causal link between MS and vaccination. Recent consensus statements agree on the need to start vaccination early. Timings for vaccine administration should be adjusted to ensure safety and optimize vaccine responses, given the potential interference of DMDs. Patients treated with Ocrelizumab (and potentially other B-cell depleting therapies) are at risk of diminished immunogenicity to vaccines. This has relevant implications for the upcoming vaccination against SARS-CoV-2., SUMMARY: An early assessment and immunization of MS patients allows optimizing vaccine responses and avoiding potential interference with treatment plans. Vaccinations are safe and effective but some specific considerations should be followed when vaccinating before, during, and after receiving immunotherapy. A time-window for vaccination taking into account the kinetics of B cell repopulation could potentially improve vaccine responses. Further understanding of SARS-CoV-2 vaccine response dynamics in MS patients under specific therapies will be key for defining the best vaccination strategy. Copyright © 2021 Wolters Kluwer Health, Inc. All rights resereved.
DOI: https://dx.doi.org/10.1097/WCO.0000000000000929

15. Park JK, Lee EB, Shin K, et al. COVID-19 Vaccination in Patients with Autoimmune Inflammatory Rheumatic Diseases: Clinical Guidance of the Korean College of Rheumatology. J Korean Med Sci. 2021;36(12):e95. DOI: https://dx.doi.org/10.3346/jkms.2021.36.e95
ABSTRACT: The coronavirus disease 2019 (COVID-19) pandemic has caused more than 100 million infections and 2 million deaths worldwide. In up to 20% of cases, COVID-19 infection can take a severe, life-threatening course. Therefore, preventive measures such as mask-wearing, hand hygiene, and social distancing are important. COVID-19 vaccines that use novel vaccine technology can prevent up to 95% of infections. However, the uncertainty regarding the efficacy and safety of vaccination in patients with autoimmune inflammatory rheumatic disease (AIIRD), who are immunocompromised due to underlying immune dysfunction and concomitant immunosuppressive treatment, warrants clear guidance. A task force of the Korean College of Rheumatology formulated a set of vaccination guidance based on the currently available data and expert consensus. The currently available COVID-19 vaccines are considered to be safe and effective. Every patient with AIIRD should receive one of the available COVID-19 vaccines unless contraindicated for medical reasons such as prior allergy/anaphylaxis to the

COVID-19 vaccine or its components. Patients should continue immunosuppressive treatment for their underlying AIIRD, including biological and targeted synthetic disease-modifying anti-rheumatic drugs (b/tsDMARDs). Corticosteroids should be reduced to the lowest dose possible without aggravating the AIIRD. To improve the vaccine response, methotrexate can be withheld for 1-2 weeks after each vaccination, and the timing of rituximab and abatacept infusion should be adjusted if clinically acceptable. Rheumatologists should play a leading role in educating and vaccinating patients with AIIRD. Copyright © 2021 The Korean Academy of Medical Sciences.
DOI: https://dx.doi.org/10.3346/jkms.2021.36.e95

16. Pimenta D, Yates C, Pagel C, et al. Delaying the second dose of covid-19 vaccines. BMJ (Clinical research ed). 2021;372:n710. DOI: https://dx.doi.org/10.1136/bmj.n710
DOI: https://dx.doi.org/10.1136/bmj.n710

17. Salmeron Rios S, Mas Romero M, Cortes Zamora EB, et al. Immunogenicity of the BNT162b2 vaccine in frail or disabled Nursing Home residents: COVID-A Study. J Am Geriatr Soc. 2021. DOI: https://dx.doi.org/10.1111/jgs.17153
ABSTRACT: BACKGROUND/OBJECTIVES: The safety and immunogenicity of the BNT162b2 COVID-19 vaccine in older adults with different frailty and disability profiles has not been well determined. Our objective was to analyze immunogenicity of the BNT162b2 mRNA COVID-19 vaccine in older adults across frailty and disability profiles., DESIGN: Multicenter longitudinal cohort study., SETTING AND PARTICIPANTS: 134 residents, >65 years with different frailty and disability profiles in 5 long-term care facilities (LTCFs) in Albacete, Spain., INTERVENTION AND MEASUREMENTS: Residents were administered 2 vaccine doses as per the label, and antibody levels were determined 21.9 days (SD 9.3) after both the first and second dose. Functional variables were assessed using activities of daily living (Barthel index) and frailty status was determined with the FRAIL instrument. Cognitive status and comorbidity were also evaluated., RESULTS: Mean age was 82.9 years (range 65-99) and 71.6% were female. The mean antibody titers in residents with and without previous COVID-19 infection were 49,878 AU/mL and 15,274 AU/mL respectively (mean difference 34,604. 95% CI: 27,699 to 41,509). No severe adverse reactions were observed, after either vaccine dose. Those with pre-vaccination COVID-19 had an increased antibody level after the vaccine (B=31,337; 95% CI: 22,725 to 39,950; p<0.001). Frailty, disability, older age, sex, cognitive impairment or comorbidities were not associated with different antibody titers., CONCLUSIONS: The BNT162b2 mRNA COVID-19 vaccine in older adults is safe and produces immunogenicity, independently of the frailty and disability profiles. Older adults in LTCFs should receive a COVID-19 vaccine. This article is protected by copyright. All rights reserved. Copyright This article is protected by copyright. All rights reserved.
DOI: https://dx.doi.org/10.1111/jgs.17153

18. Salmerón Ríos S, Mas Romero M, Cortés Zamora EB, et al. Immunogenicity of the BNT162b2 vaccine in frail or disabled Nursing Home residents: COVID-A Study. J Am Geriatr Soc. 2021;n/a(n/a). DOI: https://doi.org/10.1111/jgs.17153
ABSTRACT: Abstract Background/Objectives The safety and immunogenicity of the BNT162b2 COVID-19 vaccine in older adults with different frailty and disability profiles has not been well determined. Our objective was to analyze immunogenicity of the BNT162b2 mRNA COVID-19 vaccine in older adults across frailty and disability profiles. Design Multicenter longitudinal cohort study. Setting and participants 134 residents, >65?years with different frailty and disability profiles in 5 long-term care facilities (LTCFs) in Albacete, Spain. Intervention and measurements Residents were administered 2 vaccine doses as per the label, and antibody levels were determined 21.9?days (SD 9.3) after both the first and second dose. Functional variables were assessed using activities of daily living (Barthel index) and frailty status was determined with the FRAIL instrument. Cognitive status and comorbidity were also evaluated. Results Mean age was 82.9?years (range 65-99) and 71.6% were female. The mean antibody titers in residents with and without previous COVID-19 infection were 49,878 AU/mL and 15,274 AU/mL respectively (mean difference 34,604. 95% CI: 27,699 to 41,509). No severe adverse reactions were observed, after either vaccine dose. Those with pre-vaccination COVID-19 had an increased antibody level after the vaccine (B=31,337; 95% CI: 22,725 to 39,950; p<0.001). Frailty, disability, older age, sex, cognitive impairment or comorbidities were not associated with different antibody titers. Conclusions The BNT162b2 mRNA COVID-19 vaccine in older adults is safe and produces immunogenicity, independently of the frailty and disability profiles. Older adults in LTCFs should receive a COVID-19 vaccine. This article is protected by copyright. All rights reserved.

URL: https://doi.org/10.1111/jgs.17153
DOI: https://doi.org/10.1111/jgs.17153

19. Soy M, Keser G, Atagunduz P, et al. A practical approach for vaccinations including COVID-19 in autoimmune/autoinflammatory rheumatic diseases: a non-systematic review. Clin Rheumatol. 2021. DOI: https://dx.doi.org/10.1007/s10067-021-05700-z
ABSTRACT: The COVID-19 pandemic has occupied the world agenda since December 2019. With no effective treatment yet, vaccination seems to be the most effective method of prevention. Recently developed vaccines have been approved for emergency use only and are currently applied to large populations. Considering both the underlying pathogenic mechanisms of autoimmune/autoinflammatory rheumatological diseases (AIIRDs) and the immunosuppressive drugs used in treatment, vaccination for COVID-19 deserves special attention in such patients. In this article, we aimed to give simple messages to the clinicians for COVID-19 vaccination in patients with AIIRDs based upon the current evidence regarding the use of other vaccines in this patient group. For this purpose, we conducted a "Pubmed search" using the following keywords: Influenza, Hepatitis B, Pneumococcal, and Shingles vaccines and the frequently used conventional and biologic disease-modifying antirheumatic drugs (DMARDs). Likewise, an additional search was performed for the COVID-19 immunization in patients with AIIRDs and considering such drugs. In summary, patients with AIIRDs should also be vaccinated against COVID-19, preferably when disease activity is under control and when there is no concurrent infection. Low-degree immunosuppression does not appear to decrease antibody responses to vaccines. Ideally, vaccinations should be done before the initiation of any biological DMARDs. Patients receiving rituximab should be vaccinated at least 4 weeks before or 6 months after treatment. Since tofacitinib may also reduce antibody responses, especially in combination with methotrexate, it may be appropriate to discontinue this drug before vaccination and to restart after 14 days of immunization. Key points * COVID-19 vaccinations should preferably be made during remission in patients with autoimmune/autoinflammatory rheumatological diseases. * Low-degree immunosuppression may not interfere with antibody response to vaccines. * Ideally, vaccinations should be made before the initiation of any biological DMARDs. * Timing of vaccination is especially important in the case of rituximab.
DOI: https://dx.doi.org/10.1007/s10067-021-05700-z

20. Subbarao S, Warrener LA, Hoschler K, et al. Robust antibody responses in 70–80-year-olds 3 weeks after the first or second doses of Pfizer/BioNTech COVID-19 vaccine, United Kingdom, January to February 2021. Eurosurveillance. 2021;26(12):2100329. DOI: doi:https://doi.org/10.2807/1560-7917.ES.2021.26.12.2100329
ABSTRACT: In the United Kingdom (UK), the Joint Committee on Vaccination and Immunisation (JCVI) recommended extending the interval between coronavirus disease (COVID-19) vaccine doses from the authorised 3–4 weeks up to 12 weeks in order to maximise the roll-out of the first dose of vaccine to those at highest risk of death due to COVID-19 [1]. The COVID-19 vaccine responses after extended immunisation schedules (CONSENUS) evaluation aimed to assess immune responses to the extended immunisation schedule which was implemented across the UK from 8 December 2020. In this report, we present severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) antibody responses in the first 185 adults aged 70–90 years, recruited from the end of January 2021 through North London primary care networks, who were tested ca 3 weeks either after their first or second Pfizer/BioNTech (Mainz, Germany) vaccine dose received as part of the national programme. Responses were compared with 100 convalescent samples collected from clinically mild-to-moderate PCR-confirmed adult COVID-19 cases, ca 3–6 weeks after onset of symptoms.
URL: https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2021.26.12.2100329
DOI: doi:https://doi.org/10.2807/1560-7917.ES.2021.26.12.2100329

21. Tauh T, Mozel, M., Meyler, P., & Lee, S. M. WHAT IS THE EVIDENCE FOR EXTENDING THE SARS-COV-2 (COVID-19) VACCINE DOSING SCHEDULE? BB Medical Journal. 2021;63(2):67-70.
ABSTRACT: ABSTRACT: Vaccine rollout for SARS-CoV-2 (COVID-19) in British Columbia is underway with two approved mRNA vaccines (Pfizer-BioNTech and Moderna). Traditionally, an inactivated or attenuated pathogen may have been used as a vaccine, whereas mRNA and DNA vaccines provide genetic material that instruct the body's cells to produce a viral spike protein antigen. Presently, both mRNA vaccines are approved for use as a two-dose schedule given either 21 days or 28 days apart. However, there is a relative scarcity of vaccine compared to the population of British Columbia. BC's public health officials have proposed a delay between the primary

vaccination and booster to 35 days from the recommended 21 and 28 days. Based on unpublished data available to the National Advisory Committee on Immunization through Health Canada for both the Pfizer-BioNTech and Moderna vaccines, there was no difference in vaccine efficacy between the people who got their second dose at day 19 and the people who got it at day 42. Various jurisdictions around the world are permitting a prolonged second dosing interval. Despite the paucity of clinical trial data, it is likely that increasing the interval between the first and second doses of COVID-19 mRNA vaccines by Pfizer-BioNTech and Moderna is safe, both in the intervening period between doses and for long-term efficacy. Extending the vaccine schedule is likely warranted in order to allow the widest population to receive the first dose.
URL: https://bcmj.org/articles/what-evidence-extending-sars-cov-2-covid-19-vaccine-dosing-schedule

22. Anderson EJ, Rouphael NG, Widge AT, et al. Safety and immunogenicity of SARS-CoV-2 mRNA-1273 vaccine in older adults. N Engl J Med. 2020;383(25):2427-38. DOI: http://dx.doi.org/10.1056/NEJMoa2028436
ABSTRACT: BACKGROUND Testing of vaccine candidates to prevent infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in an older population is important, since increased incidences of illness and death from coronavirus disease 2019 (Covid-19) have been associated with an older age. METHODS We conducted a phase 1, dose-escalation, open-label trial of a messenger RNA vaccine, mRNA-1273, which encodes the stabilized prefusion SARS-CoV-2 spike protein (S-2P) in healthy adults. The trial was expanded to include 40 older adults, who were stratified according to age (56 to 70 years or >=71 years). All the participants were assigned sequentially to receive two doses of either 25 mug or 100 mug of vaccine administered 28 days apart. RESULTS Solicited adverse events were predominantly mild or moderate in severity and most frequently included fatigue, chills, headache, myalgia, and pain at the injection site. Such adverse events were dose-dependent and were more common after the second immunization. Binding-antibody responses increased rapidly after the first immunization. By day 57, among the participants who received the 25-mug dose, the anti-S-2P geometric mean titer (GMT) was 323,945 among those between the ages of 56 and 70 years and 1,128,391 among those who were 71 years of age or older; among the participants who received the 100-mug dose, the GMT in the two age subgroups was 1,183,066 and 3,638,522, respectively. After the second immunization, serum neutralizing activity was detected in all the participants by multiple methods. Binding- and neutralizing-antibody responses appeared to be similar to those previously reported among vaccine recipients between the ages of 18 and 55 years and were above the median of a panel of controls who had donated convalescent serum. The vaccine elicited a strong CD4 cytokine response involving type 1 helper T cells. CONCLUSIONS In this small study involving older adults, adverse events associated with the mRNA-1273 vaccine were mainly mild or moderate. The 100-mug dose induced higher binding- and neutralizing-antibody titers than the 25-mug dose, which supports the use of the 100-mug dose in a phase 3 vaccine trial.
DOI: http://dx.doi.org/10.1056/NEJMoa2028436

23. Ciotti JR, Valtcheva MV, Cross AH. Effects of MS disease-modifying therapies on responses to vaccinations: A review. Multiple sclerosis and related disorders. 2020;45:102439. DOI: https://dx.doi.org/10.1016/j.msard.2020.102439
ABSTRACT: BACKGROUND: Development of long-term immunologic memory relies upon humoral and cellular immune responses. Vaccinations aim to stimulate these responses against pathogens. Several studies have evaluated the impact of multiple sclerosis disease-modifying therapies on immune response to vaccines. Findings from these studies have important implications for people with multiple sclerosis who require vaccination and are using disease-modifying therapies., METHODS: Searches using PubMed and other engines were conducted in May 2020 to collect studies evaluating the impact of various disease-modifying therapies on immune responses to vaccination., RESULTS: Several studies demonstrated preserved immune responses in people treated with beta-interferons to multiple vaccine types. Limited data suggest vaccine responses to be preserved with dimethyl fumarate treatment, as well. Vaccine responses were reduced to varying degrees in those treated with glatiramer acetate, teriflunomide, sphingosine-1-phosphate receptor modulators, and natalizumab. The timing of vaccination played an important role in those treated with alemtuzumab. Humoral vaccine responses were significantly impaired by B cell depleting anti-CD20 monoclonal antibody therapies, particularly to a neoantigen. Data are lacking on vaccine responses in patients with multiple sclerosis taking cladribine and high-dose corticosteroids. Notably, the majority of these studies have focused on humoral responses, with few examining cellular immune responses to vaccination., CONCLUSIONS: Prior investigations into the effects of individual disease-modifying

therapies on immune responses to existing vaccines can serve as a guide to expected responses to a SARS-CoV-2 vaccine. Responses to any vaccination depend on the vaccine type, the type of response (recall versus response to a novel antigen), and the impact of the individual disease-modifying therapy on humoral and cellular immunity in response to that vaccine type. When considering a given therapy, clinicians should weigh its efficacy against MS for the individual patient versus potential impact on responses to vaccinations that may be needed in the future.

DOI: https://dx.doi.org/10.1016/j.msard.2020.102439

24. Spassiani I, Gubian L, Palu G, et al. Vaccination Criteria Based on Factors Influencing COVID-19 Diffusion and Mortality. Vaccines. 2020;8(4). DOI: https://dx.doi.org/10.3390/vaccines8040766

ABSTRACT: SARS-CoV-2 is highly contagious, rapidly turned into a pandemic, and is causing a relevant number of critical to severe life-threatening COVID-19 patients. However, robust statistical studies of a large cohort of patients, potentially useful to implement a vaccination campaign, are rare. We analyzed public data of about 19,000 patients for the period 28 February to 15 May 2020 by several mathematical methods. Precisely, we describe the COVID-19 evolution of a number of variables that include age, gender, patient's care location, and comorbidities. It prompts consideration of special preventive and therapeutic measures for subjects more prone to developing life-threatening conditions while affording quantitative parameters for predicting the effects of an outburst of the pandemic on public health structures and facilities adopted in response. We propose a mathematical way to use these results as a powerful tool to face the pandemic and implement a mass vaccination campaign. This is done by means of priority criteria based on the influence of the considered variables on the probability of both death and infection.
DOI: https://dx.doi.org/10.3390/vaccines8040766

Appendix 1: Evidence Search Details

Filters, Limits & Exclusions:	English only 2020-Current ...	
Sources Searched:	Embase LitCOVID Medline MedRvix ECRI Alberta Health Services BCCDC BC Health Manitoba Health Ontario Health Google Google Scholar COVID-NMA European CDC	WHO Global Literature on Novel Coronavirus WHO Website CDC Website FDA Website CPG Infobase TRIP CADTH CEP Health Canada Government of Canada McMaster NCCMT CEBM (UK) NICE Guidance (UK) Australian Gov't
Librarian(s):	**Brianna Howell-Spooner, Clinical Librarian, Saskatchewan Health Authority** **Lukas Miller, Clinical Librarian, Saskatchewan Health Authority**	

Appendix 2: Search Strategies

Search Strategies

Medline – March 30, 2021

#	Searches	Results
1	(coronavirus/ or betacoronavirus/ or coronavirus infections/) and (disease outbreaks/ or epidemics/ or pandemics/)	39965
2	(nCoV* or 2019nCoV or 19nCoV or COVID19* or COVID or SARS-COV-2 or SARSCOV-2 or SARSCOV2 or Severe Acute Respiratory Syndrome Coronavirus 2 or Severe Acute Respiratory Syndrome Corona Virus 2).ti,ab,kf,nm,ox,rx,px.	113729
3	((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.	37346
4	((coronavirus* or corona virus* or betacoronavirus*) adj3 (pandemic* or epidemic* or outbreak* or crisis)).ti,ab,kf.	7126
5	((Wuhan or Hubei) adj5 pneumonia).ti,ab,kf.	318

6	or/1-5	119380
7	limit 6 to yr="2019 -Current"	117912
8	exp *Immunosuppression/ or exp *Immunocompromised Host/ or (immunocompromised or immunosuppress* or (weak* adj2 immun*)).ti,kf,kw.	66052
9	risk factors/ or exp age factors/ or exp comorbidity/ or race factors/ or sex factors/ or exp diabetes mellitus/ or exp cardiovascular diseases/ or hypertension/ or exp smoking/ or exp lung diseases, obstructive/	4172400
10	(risk factor* or comorbidit* or diabetes or cardiovascular disease* or heart disease* or hypertension or smoking or asthma* or chronic lung disease or chronic respiratory disease or chronic obstructive pulmonary disease or COPD or cancer* or renal disease? or kidney disease? or heart failure? or pulmonary disease? or peripheral vascular disease? or stroke? or dementia? or alzheimer* or myocardial infarction? or liver disease? or rheumatologic* disease? or hemiplegia? or paraplegia? or peptic ulcer? or ((extremely or clinical* or medical*) adj1 vulnerable)).ti,kf,tw.	4626596
11	8 or 9 or 10	7035395
12	(vaccinat* or vaccine? or inoculat* or immunization? or immunize? or immunogenicity).ti,kf. or (vaccinat* or vaccine? or inoculat* or immunization? or immunize? or immunogenicity).ab. /freq=2	337745
13	7 and 12	4870
14	(moderna? or mrna-1273 or mrna1273).mp.	1121
15	(pfizer* or biontech* or tozinameran or BNT162b2).mp.	3208
16	(astrazeneca or astra zeneca or "ChAdOx1-S" or ChAdOx1* or COVISHIELD or (oxford adj3 astrazeneca)).mp.	1328
17	(janssen? or "ad26.cov2.s" or ad26cov2s or ad26cov2* or (johnson adj2 johnson)).mp.	16191
18	or/14-17	21513
19	13 or 18	26114
20	time/ or time factors/ or (interval? or timing? or time? or period* or week? or day? or month?).ti,kf,tw.	8477447
21	7 and 11 and 19 and 20	128

Medline – March 31, 2021

#	Searches	Results
1	(coronavirus/ or betacoronavirus/ or coronavirus infections/) and (disease outbreaks/ or epidemics/ or pandemics/)	39966

2	(nCoV* or 2019nCoV or 19nCoV or COVID19* or COVID or SARS-COV-2 or SARSCOV-2 or SARSCOV2 or Severe Acute Respiratory Syndrome Coronavirus 2 or Severe Acute Respiratory Syndrome Corona Virus 2).ti,ab,kf,nm,ox,rx,px.	114058
3	((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.	37437
4	((coronavirus* or corona virus* or betacoronavirus*) adj3 (pandemic* or epidemic* or outbreak* or crisis)).ti,ab,kf.	7141
5	((Wuhan or Hubei) adj5 pneumonia).ti,ab,kf.	318
6	or/1-5	119713
7	limit 6 to yr="2019 -Current"	118245
8	exp *Immunosuppression/ or exp *Immunocompromised Host/ or (immunocompromised or immunosuppress* or (weak* adj2 immun*)).ti,kf,kw.	66070
9	risk factors/ or exp age factors/ or exp comorbidity/ or race factors/ or sex factors/ or exp diabetes mellitus/ or exp cardiovascular diseases/ or hypertension/ or exp smoking/ or exp lung diseases, obstructive/	4173239
10	(risk factor* or comorbidit* or diabetes or cardiovascular disease* or heart disease* or hypertension or smoking or asthma* or chronic lung disease or chronic respiratory disease or chronic obstructive pulmonary disease or COPD or cancer* or renal disease? or kidney disease? or heart failure? or pulmonary disease? or peripheral vascular disease? or stroke? or dementia? or alzheimer* or myocardial infarction? or liver disease? or rheumatologic* disease? or hemiplegia? or paraplegia? or peptic ulcer? or ((extremely or clinical* or medical*) adj1 vulnerable)).ti,kf,tw.	4627454
11	8 or 9 or 10	7036632
12	(vaccinat* or vaccine? or inoculat* or immunization? or immunize? or immunogenicity).ti,kf. or (vaccinat* or vaccine? or inoculat* or immunization? or immunize? or immunogenicity).ab. /freq=2	337823
13	7 and 12	4908
14	(moderna? or mrna-1273 or mrna1273).mp.	1125
15	(pfizer* or biontech* or tozinameran or BNT162b2).mp.	3215
16	(astrazeneca or astra zeneca or "ChAdOx1-S" or ChAdOx1* or COVISHIELD or (oxford adj3 astrazeneca)).mp.	1329
17	(janssen? or "ad26.cov2.s" or ad26cov2s or ad26cov2* or (johnson adj2 johnson)).mp.	16193
18	or/14-17	21522

19	13 or 18	26154
20	time/ or time factors/ or (interval? or timing? or time? or period* or week? or day? or month?).ti,kf,tw.	8478879
21	7 and 11 and 19 and 20	132
22	hiv/ or acquired immunodeficiency syndrome/ or exp *Immunosuppression/ or exp *Immunocompromised Host/ or abatacept/ or adalimumab/ or "Interleukin 1 Receptor Antagonist Protein"/ or Certolizumab pegol/ or etanercept/ or infliximab/ or rituximab/ or tocilizumab/ or Ustekinumab/ or Azathioprine/ or cladribine/ or cyclophosphamide/ or cyclosporine/ or Fingolimod Hydrochloride/ or Leflunomide/ or methotrexate/ or Mycophenolic Acid/ or Sirolimus/ or prednisone/ or exp leukemia/ or exp immune system diseases/	1797837
23	(abatacept or orencia or adalimumab or humira or Interleukin 1 Receptor Antagonist Protein or kineret or Brodalumab or siliq or Certolizumab pegol or cimzia or etanercept or enbrel or simponi or etanercept or infliximab or remicade or atumumab or ocrevus or ocrelizumab or rituxan or rituximab or kevzara or sarilumab or cosentyx or secukinumab or tocilizumab or atlizumab or actemra or satralizumab or ustekinumab or stelara or Azathioprine or imurel or imuran or immuran or cladribine or mavenclad or cyclophosphamide or sendoxan or procytox or cyclosporine or neoral or Fingolimod Hydrochloride or gilenya or gilenia or Leflunomide or arava or methotrexate or Mycophenolic Acid or cellcept or Mycophenolate Mofetil or myfortic or Sirolimus or rapamune or rapamycin or xeljanz or tasocitinib or tofacitinib or prednisone or leukemia? or immunodeficienc* or immunocompromised or immunosuppress* or (weak* adj2 immun*) or immune system disease? or immune system disorder? or immune disorder? or immunologic disease? or immunologic disorder? or immune disease? or graves disease or addison disease).ti,ab,kf.	742454
24	22 or 23	2107271
25	7 and 19 and 20 and 24	68

#	Searches	Results
1	(coronavirus/ or betacoronavirus/ or coronavirus infections/) and (disease outbreaks/ or epidemics/ or pandemics/)	39966
2	(nCoV* or 2019nCoV or 19nCoV or COVID19* or COVID or SARS-COV-2 or SARSCOV-2 or SARSCOV2 or Severe Acute Respiratory Syndrome Coronavirus 2 or Severe Acute Respiratory Syndrome Corona Virus 2).ti,ab,kw,nm,rx,px.	112763
3	((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.	37437
4	((coronavirus* or corona virus* or betacoronavirus*) adj3 (pandemic* or epidemic* or outbreak* or	7141

	crisis)).ti,ab,kf.	
5	((Wuhan or Hubei) adj5 pneumonia).ti,ab,kf.	318
6	or/1-5	118996
7	limit 6 to yr="2019 -Current"	117528
8	exp *Immunosuppression/ or exp *Immunocompromised Host/ or (immunocompromised or immunosuppress* or (weak* adj2 immun*)).ti,kf,kw.	66070
9	risk factors/ or exp age factors/ or exp comorbidity/ or race factors/ or sex factors/ or exp diabetes mellitus/ or exp cardiovascular diseases/ or hypertension/ or exp smoking/ or exp lung diseases, obstructive/	4173239
10	(risk factor* or comorbidit* or diabetes or cardiovascular disease* or heart disease* or hypertension or smoking or asthma* or chronic lung disease or chronic respiratory disease or chronic obstructive pulmonary disease or COPD or cancer* or renal disease? or kidney disease? or heart failure? or pulmonary disease? or peripheral vascular disease? or stroke? or dementia? or alzheimer* or myocardial infarction? or liver disease? or rheumatologic* disease? or hemiplegia? or paraplegia? or peptic ulcer? or ((extremely or clinical* or medical*) adj1 vulnerable)).ti,kf,tw.	4627454
11	8 or 9 or 10	7036632
12	(vaccinat* or vaccine? or inoculat* or immunization? or immunize? or immunogenicity).ti,kf. or (vaccinat* or vaccine? or inoculat* or immunization? or immunize? or immunogenicity).ab. /freq=2	337823
13	7 and 12	4880
14	(moderna? or mrna-1273 or mrna1273).mp.	1125
15	(pfizer* or biontech* or tozinameran or BNT162b2).mp.	3215
16	(astrazeneca or astra zeneca or "ChAdOx1-S" or ChAdOx1* or COVISHIELD or (oxford adj3 astrazeneca)).mp.	1329
17	(janssen? or "ad26.cov2.s" or ad26cov2s or ad26cov2* or (johnson adj2 johnson)).mp.	16193
18	or/14-17	21522
19	13 or 18	26126
20	time/ or time factors/ or (interval? or timing? or time? or period* or week? or day? or month?).ti,kf,tw.	8478879
21	7 and 11 and 19 and 20	132
22	hiv/ or acquired immunodeficiency syndrome/ or exp *Immunosuppression/ or exp *Immunocompromised Host/ or abatacept/ or adalimumab/ or "Interleukin 1 Receptor Antagonist Protein"/ or Certolizumab pegol/ or etanercept/ or infliximab/ or rituximab/ or tocilizumab/ or	1797837

	Ustekinumab/ or Azathioprine/ or cladribine/ or cyclophosphamide/ or cyclosporine/ or Fingolimod Hydrochloride/ or Leflunomide/ or methotrexate/ or Mycophenolic Acid/ or Sirolimus/ or prednisone/ or exp leukemia/ or exp immune system diseases/	
23	(abatacept or orencia or adalimumab or humira or Interleukin 1 Receptor Antagonist Protein or kineret or Brodalumab or siliq or Certolizumab pegol or cimzia or etanercept or enbrel or simponi or etanercept or infliximab or remicade or atumumab or ocrevus or ocrelizumab or rituxan or rituximab or kevzara or sarilumab or cosentyx or secukinumab or tocilizumab or atlizumab or actemra or satralizumab or ustekinumab or stelara or Azathioprine or imurel or imuran or immuran or cladribine or mavenclad or cyclophosphamide or sendoxan or procytox or cyclosporine or neoral or Fingolimod Hydrochloride or gilenya or gilenia or Leflunomide or arava or methotrexate or Mycophenolic Acid or cellcept or Mycophenolate Mofetil or myfortic or Sirolimus or rapamune or rapamycin or xeljanz or tasocitinib or tofacitinib or prednisone or leukemia? or immunodeficienc* or immunocompromised or immunosuppress* or (weak* adj2 immun*) or immune system disease? or immune system disorder? or immune disorder? or immunologic disease? or immunologic disorder? or immune disease? or graves disease or addison disease).ti,ab,kf.	742454
24	22 or 23	2107271
25	7 and 19 and 20 and 24	68
26	autoimmune.tw,kf.	159934
27	7 and 19 and 21 and 26	5
28	((first adj5 second) and ((first or second) adj1 dose?)).ti,ab,kf.	736
29	11 or 24 or 26	8459820
30	7 and 19 and 28 and 29	1
31	7 and 28 and 29	2
32	19 and 28 and 29	1

Embase

#	Searches	Results
1	(coronavirus/ or betacoronavirus/ or coronavirus infections/) and (disease outbreaks/ or epidemics/ or pandemics/)	2380
2	[(nCoV* or 2019nCoV or 19nCoV or COVID19* or COVID or SARS-COV-2 or SARSCOV-2 or SARSCOV2 or Severe Acute Respiratory Syndrome Coronavirus 2 or Severe Acute Respiratory Syndrome Corona Virus 2).ti,ab,kw,ox,rx,px.]	0

3	((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,kw.	36205
4	((coronavirus* or corona virus* or betacoronavirus*) adj3 (pandemic* or epidemic* or outbreak* or crisis)).ti,ab,kw.	6919
5	((Wuhan or Hubei) adj5 pneumonia).ti,ab,kw.	373
6	or/1-5	39768
7	limit 6 to yr="2019 -Current"	38514
8	exp *Immunosuppression/ or exp *Immunocompromised Host/ or (immunocompromised or immunosuppress* or (weak* adj2 immun*)).ti,ab,kw.	314084
9	risk factors/ or exp age factors/ or exp comorbidity/ or race factors/ or sex factors/ or exp diabetes mellitus/ or exp cardiovascular diseases/ or hypertension/ or exp smoking/ or exp lung diseases, obstructive/	6456618
10	(risk factor* or comorbidit* or diabetes or cardiovascular disease* or heart disease* or hypertension or smoking or asthma* or chronic lung disease or chronic respiratory disease or chronic obstructive pulmonary disease or COPD or cancer* or renal disease? or kidney disease? or heart failure? or pulmonary disease? or peripheral vascular disease? or stroke? or dementia? or alzheimer* or myocardial infarction? or liver disease? or rheumatologic* disease? or hemiplegia? or paraplegia? or peptic ulcer? or ((extremely or clinical* or medical*) adj1 vulnerable)).ti,ab,kw.	6631397
11	8 or 9 or 10	10130227
12	[(vaccinat* or vaccine? or inoculat* or immunization? or immunize? or immunogenicity).ti,kf. or (vaccinat* or vaccine? or inoculat* or immunization? or immunize? or immunogenicity).ab. /freq=2]	0
13	7 and 12	0
14	(moderna? or mrna-1273 or mrna1273).mp.	833
15	(pfizer* or biontech* or tozinameran or BNT162b2).mp.	52295
16	(astrazeneca or astra zeneca or "ChAdOx1-S" or ChAdOx1* or COVISHIELD or (oxford adj3 astrazeneca)).mp.	22224
17	(janssen? or "ad26.cov2.s" or ad26cov2s or ad26cov2* or (johnson adj2 johnson)).mp.	57566
18	or/14-17	121255
19	13 or 18	121255
20	time/ or time factors/ or (interval? or timing? or time? or period* or week? or day? or month?).ti,ab,tw.	10960758
21	7 and 11 and 19 and 20	22

Other Search Terms:
COVID vaccine schedule immunocompromised