

Literature screening intermediate update

Covid-19 vaccines and post-vaccination data: literature update (4)

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Preamble

A large number of scientific publications become available on a daily basis, reflecting the rapid development of knowledge and progress of science on COVID-19 related issues. Leading authorities should base decisions or policies on this knowledge; hence they need to master the actual state of this knowledge. Due to the large number of publications shared daily, decision makers heavily depend on accurate summaries of these publications, in the different public health domains. Therefore, the authors

of this update were mandated by the Swiss School of Public Health plus (SSPH+), upon request of the Federal Office of Public Health (FOPH), to inform the FOPH on recent findings from the literature.

This intermediate update shares important studies that have been published since the previous report or intermediate update. A more thorough analysis of these and other studies will be provided in the next full report.

Abstract

We report below the most important new data about Covid-19 vaccines. We highlighted the new storage conditions (now between -25 to -15 °C) for Pfizer-BioNTech Covid-19 vaccine. Many studies evaluated the variability of antibody response and potentially the effectiveness of vaccination for specific chronic care patients (e.g., inflammatory bowel disease and haemodialysis patients). Several strategies (e.g., financial incentives in individuals addicted to illicit drugs) to combat vaccine hesitancy. Some studies pointed out to healthcare workers whose reluctance to get vaccinated or their Covid-19 vaccines safety concerns would naturally impact the vaccination in the community. Other studies estimated the effectiveness of Covid-19 vaccines on long-term care residents and warned us of not relaxing other protective measures shortly after vaccination. Moreover, interim results of phase III clinical trials for CoronaVac (Sinovac) Covid-19 vaccine were released as pre-printed non-peer-reviewed manuscript. The World Health Organization (WHO) is evaluating the manufacturer's request for an emergency Use listing/prequalification (EUL/PQ), where a decision is expected end of April 2021. Of note, the European Medicines Agency (EMA) concluded a possible link to occurrences of very rare blood clots or thrombosis following vaccination with AstraZeneca/Oxford Covid-19 vaccine.

Updates

What are the most relevant data about Covid-19 vaccines?

Results:

Most importantly, new storage conditions for Pfizer-BioNTech Covid-19 vaccine (BNT162b2/COMIRNATY®) were approved by Swissmedic¹. It allows the vaccine to remain stable at lower temperatures (between -25 to -15 degrees Celsius) for two-week period. Hence, the supply and administration of the vaccine to the target population become more feasible via clinics, doctor's offices, pharmacies, and other health facilities. Therefore, we would be able to accelerate and improve our vaccination rollout at a better speed, besides other strategies.²

We started to get new data about the effectiveness of vaccination on subpopulations with specific chronic diseases. Therefore, this distinguishes them from the other 'contents of the basket' as some of them were not represented in the phase III clinical trials. For instance, a non-peer-reviewed study reported that 81 haemodialysis patients had highly diminished SARS-COV-2 S antibody titres compared to a cohort of 80 controls, all vaccinated by Pfizer-BioNTech Covid-19 vaccine [1]. Similar non-peer-reviewed study [2] showed that 50% of haemodialysis patients failed to elicit a humoral immune response after a single dose of Pfizer-BioNTech Covid-19 vaccine. As correlates of protection are not yet reliably known in Covid-19, we do not know at what level such low antibody response in haemodialysis patients would translate into a lower effectiveness of the vaccine to prevent symptomatic SARS-CoV-2 infections or severe disease in clinical settings.

Another non-peer-reviewed study [3] reported that inflammatory bowel disease (IBD) patients who were treated with infliximab had lower immunogenicity compared to a cohort of patients treated with vedolizumab after a single dose of Pfizer-BioNTech Covid-19 vaccine or AstraZeneca/Oxford vaccine. Moreover, a non-peer-reviewed study found similar adverse events in IBD patients compared to the general population at 8 days after a single or second dose vaccination with Pfizer-BioNTech Covid-19 or Moderna Covid-19 vaccines.

¹ <https://www.swissmedic.ch/swissmedic/en/home/news/coronavirus-covid-19/neue-lagerbedingungen-covid-19-impfstoff-pfizer-biontech.html> (accessed on 31.03.2021).

² See the report: Al-Gobari M. (Anti-Covid-19 vaccination in Israel: what can Switzerland learn?) 31.03.2021.

Several studies [4-12] evaluated the factors and determinants of Covid-19 vaccine hesitancy in different countries and settings. Of those studies, some addressed some strategies to combat and minimize vaccine hesitancy (sometimes simply an intentional delay in getting vaccinated). For instance, financial incentives [13, 14] were used to increase vaccination rates against Hepatitis B virus in particular groups such as individuals addicted to illicit drugs. It is likely that such incentives help increasing Covid-19 vaccines uptake in such groups.

Several studies [15-24] about effectiveness of vaccinations involving healthcare workers (HCWs) have been released. Of those, one study [15] focused on post-vaccination symptoms that were later related to covid-19 infections and not related to vaccines. A non-peer-reviewed study [16] reported that SARS-CoV-2 cases were reported in 1.4% (96/7109) and 0.3% (17/5913) after first dose and second dose of Pfizer-BioNTech Covid-19 or Moderna Covid-19 vaccines, respectively. An observational study [17] - non-peer-reviewed - of 13,109 HCWs of which 8285 received the Pfizer-BioNTech vaccine (1407 two doses) and 2738 the AstraZeneca/Oxford vaccine (49 two doses) reported that the incidence rates of laboratory-confirmed cases were 85% lower in unvaccinated previously infected individuals and 64% lower in seronegative HCWs following a first dose and 90% lower after second-dose vaccination. While the estimated effectiveness was reported for both vaccines in a pooled analysis, it is obvious that fewer participants used AstraZeneca/Oxford vaccine with less than 0.4% with two doses. A study [18] had evaluated the persistence of neutralizing antibodies among 26 HCWs who were previously infected and reported a drop to 38.5% at 3 months follow-up.

Another relatively large observational study of 36,659 HCWs (of which 28,184 received two doses of either Pfizer-BioNTech Covid-19 or Moderna Covid-19 vaccine) reported 379 SARS-CoV-2 infections at least 1-day post-vaccination. Of those infections, 342 (71%) occurred within two weeks after the first dose. Twenty-two infections occurred 1-7 days and 8 cases between day 8 and 14 after the second dose (total 37), respectively. The study [22] highlighted the elevated risk and exposure to SARS-CoV-2 among healthcare workers whose vaccination should be a top priority due to their regular contact with patients. For such reasons, it is important to identify and tackle vaccine hesitancy or reluctance among HCWs who are considered as source of vaccination information for patients. In fact, HCWs in a

study [25] in India exhibited a pre-vaccination-related anxiety [78.9% (172/218), 95% Confidence interval (CI): 72.8 to 84.1], who were vaccinated with AstraZeneca/Oxford vaccine. Similarly, A study [24] among 1,933 HCWs in the United States reported that 65% of those who received an mRNA-based vaccine had expressed Covid-19 vaccines safety concerns.

A phase III clinical trial [26] for CoronaVac (Sinovac) vaccine – an inactivated vaccine developed in China – reported preliminary results in Chilean population. Several limitations may be noted in the Chilean study. First, the analyses included only very small sample size (434 participants) of the expected 2300 enrolled participants³. Second, only limited outcomes were reported (namely, the adverse events and the presence of antibodies and cellular immune response in the study groups). Hence, we cannot infer the efficacy of the vaccine at this stage. Moreover, a non-published detailed data of phase III clinical trial in Turkey reported an immunity against SARS-CoV-2 infections of 25.3% after 28 days of the first dose and 97.92% after 28 days of the second dose of the vaccine⁴.

Several studies [27-29] evaluated the effectiveness of Covid-19 vaccination on elderly people or long-term or nursing home residents (equivalent to Alters-und Pflegeheim or Centre médico-social (CMS) in German and French respectively). Of those, one non-peer-reviewed study [27] reported 1.05% (148/14,104) laboratory-confirmed SARS-CoV-2 infections among long-term care residents within 28 days after vaccination. Another non-peer-reviewed study [28] in 39,040 Danish long-term facility residents (median age of 84 years old) reported no efficacy after first dose but 52% and 64% at 0-7 days and >7 days after the second dose of Covid-19 vaccines, respectively. On the contrary, one non-peer-reviewed study [29] in 310 long-term care facilities in England involving a total of 10,412 residents estimated an effectiveness of 56% (19-76%) at 28-34 days, and 62% (23-81%) at 35-48 days following a single dose of AstraZeneca/Oxford or Pfizer-BioNTech Covid-19 vaccines. There were many differences between the Danish [28] and the English study [29]

³ <https://clinicaltrials.gov/ct2/show/NCT04651790> (accessed on 07.04.2021).

⁴ <https://www.hurisikgazetesi.com/sinovac-asisinin-koruyuculugunu-kanitlayan-profesorler-asiyi-degerlendirdi/902597/> (accessed on 07.04.2021).

notably the timing of testing and hence the occurrence of events where the latter delayed the administration of the second dose of Pfizer-BioNTech Covid-19 vaccines.

Finally, the World health organization (WHO) is undergoing an assessment for an emergency Use listing/prequalification (EUL/PQ) for around 16 vaccine candidates (two were added recently)⁵. Among those, the WHO is evaluating CoronaVac (Sinovac) Covid-19 vaccine upon the manufacturer's request, where a decision is expected end of April 2021. Of note, the European Medicines agency (EMA)⁶ concluded a possible link to the occurrences of very rare blood clots or thrombosis following vaccination with AstraZeneca/Oxford Covid-19 vaccine, confirming previously published reports^{7,8}. The agency informs healthcare professionals and vaccinated individuals to be aware of such events and, therefore, surveillance measures should be in place. According to same source, patients should seek medical assistance immediately if they have the following symptoms:

- shortness of breath
- chest pain
- swelling in a leg
- persistent abdominal (belly) pain
- neurological symptoms, including severe and persistent headaches or blurred vision
- tiny blood spots under the skin beyond the site of injection

In France⁹, only those 55 years and over are eligible to receive AstraZeneca/Oxford Covid-19 vaccine, a strategy that may help prevent the occurrence of blood clots events where younger age and female gender represent a higher risk [30].

⁵ <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/covid-19-vaccines> (accessed on 08.04.2021).

⁶ <https://www.ema.europa.eu/en/news/astrazenecas-covid-19-vaccine-ema-finds-possible-link-very-rare-cases-unusual-blood-clots-low-blood> (accessed on 08.04.2021).

⁷ <https://www.wsj.com/articles/scientists-say-they-found-cause-of-blood-clotting-linked-to-astrazeneca-vaccine-11616169108> (accessed on 25.03.2021).

⁸ <https://www.pei.de/EN/newsroom/hp-news/2021/210315-pei-informs-temporary-suspension-vaccination-astra-zeneca.html> (accessed on 25.03.2021).

⁹ <https://www.ladepeche.fr/2021/03/19/la-vaccination-avec-astrazeneca-peut-reprendre-sans-delai-pour-les-55-ans-et-plus-annonce-la-haute-autorite-de-sante-9437802.php> (accessed on 25.03.2021).

References

All references: .ris file

1. Simon B, Rubey H, Treipl A, Gromann M, Hemedi B, Zehetmayer S, et al. Hemodialysis Patients Show a Highly Diminished Antibody Response after COVID-19 mRNA Vaccination Compared to Healthy Controls. medRxiv. 2021:2021.03.26.21254259. doi: 10.1101/2021.03.26.21254259.
2. Goupil R, Benlarbi M, Beaubien-Souligny W, Nadeau-Fredette A-C, Debashree C, Goyette G, et al. Short-term antibody response and tolerability of one dose of BNT162b2 vaccine in patients receiving hemodialysis. medRxiv. 2021:2021.03.30.21254652. doi: 10.1101/2021.03.30.21254652.
3. Kennedy NA, Lin S, Goodhand JR, Chanchlani N, Hamilton B, Bewshea C, et al. Infliximab is associated with attenuated immunogenicity to BNT162b2 and ChAdOx1 nCoV-19 SARS-CoV-2 vaccines. medRxiv. 2021:2021.03.25.21254335. doi: 10.1101/2021.03.25.21254335.
4. Batty GD, Deary IJ, Fawns-Ritchie C, Gale CR, Altschul D. Pre-pandemic Cognitive Function and COVID-19 Vaccine Hesitancy: Cohort Study. medRxiv. 2021:2021.03.16.21253634. doi: 10.1101/2021.03.16.21253634.
5. Crespo RF, Shafat M, Melas-Kyriazi N, Gould L, Jones S, Neves AL, et al. International attitudes on COVID-19 vaccination: repeat national cross-sectional surveys across 15 countries. medRxiv. 2021:2021.03.08.21252449. doi: 10.1101/2021.03.08.21252449.
6. Ghazy R, Abd ElHafeez S, Shaban R, Elbarazi I, Abdou MS, Ramadan AM, et al. Determining the cutoff points of the 5C scale for assessment of COVID-19 vaccines psychological antecedents among the Arab population: A multinational study. medRxiv. 2021:2021.03.27.21254461. doi: 10.1101/2021.03.27.21254461.
7. Hughes B, Miller-Idriss C, Piltch-Loeb R, White K, Crezizis M, Cain C, et al. Development of a Codebook of Online Anti-Vaccination Rhetoric to Manage COVID-19 Vaccine Misinformation. medRxiv. 2021:2021.03.23.21253727. doi: 10.1101/2021.03.23.21253727.
8. Iadarola S, Siegel JF, Gao Q, McGrath K, Bonuck KA. COVID-19 Vaccine Perceptions in New York State's Intellectual and Developmental Disabilities Community. medRxiv. 2021:2021.03.19.21253425. doi: 10.1101/2021.03.19.21253425.
9. Knight H, Jia R, Ayling K, Bradbury K, Baker K, Chalder T, et al. Understanding and Addressing Vaccine Hesitancy in the Context of COVID-19: Development of a Digital intervention. medRxiv. 2021:2021.03.24.21254124. doi: 10.1101/2021.03.24.21254124.
10. Kuhn R, Henwood B, Lawton A, Kleva M, Murali K, King C, et al. COVID-19 vaccine access and attitudes among people experiencing homelessness from pilot mobile phone survey in Los Angeles, CA. medRxiv. 2021:2021.03.23.21254146. doi: 10.1101/2021.03.23.21254146.
11. Qunaibi EA, Helmy M, Basheti I, Sultan I. A High Rate of COVID-19 Vaccine Hesitancy Among Arabs: Results of a Large-scale Survey. medRxiv. 2021:2021.03.09.21252764. doi: 10.1101/2021.03.09.21252764.
12. Witus LS, Larson E. A randomized controlled trial of a video intervention shows evidence of increasing COVID-19 vaccination intention. medRxiv. 2021:2021.03.26.21254433. doi: 10.1101/2021.03.26.21254433.

13. !!! INVALID CITATION !!! [2-11].
14. Herrmann ES, Matusiewicz AK, Stitzer ML, Higgins ST, Sigmon SC, Heil SH. Contingency Management Interventions for HIV, Tuberculosis, and Hepatitis Control Among Individuals With Substance Use Disorders: A Systematized Review. *J Subst Abuse Treat.* 2017;72:117-25. Epub 2016/07/11. doi: 10.1016/j.jsat.2016.06.009. PubMed PMID: 27394070; PubMed Central PMCID: PMC5386179.
15. Amit S, Beni SA, Biber A, Grinberg A, Leshem E, Regev-Yochay G. Postvaccination COVID-19 among Healthcare Workers, Israel. *Emerg Infect Dis.* 2021;27(4):1220-2. doi: 10.3201/eid2704.210016. PubMed PMID: 33522478.
16. Bouton TC, Lodi S, Turcinovic J, Weber SE, Quinn E, Korn C, et al. COVID-19 vaccine impact on rates of SARS-CoV-2 cases and post vaccination strain sequences among healthcare workers at an urban academic medical center: a prospective cohort study. *medRxiv.* 2021:2021.03.30.21254655. doi: 10.1101/2021.03.30.21254655.
17. Lumley SF, Rodger G, Constantinides B, Sanderson N, Chau KK, Street TL, et al. An observational cohort study on the incidence of SARS-CoV-2 infection and B.1.1.7 variant infection in healthcare workers by antibody and vaccination status. *medRxiv.* 2021:2021.03.09.21253218. doi: 10.1101/2021.03.09.21253218.
18. Marot S, Malet I, Leducq V, Zafilaza K, Sterlin D, Planas D, et al. Rapid decline of neutralizing antibodies against SARS-CoV-2 among infected healthcare workers. *Nat Commun.* 2021;12(1):844. Epub 2021/02/10. doi: 10.1038/s41467-021-21111-9. PubMed PMID: 33558507; PubMed Central PMCID: PMC5386179.
19. Saadat S, Tehrani ZR, Logue J, Newman M, Frieman MB, Harris AD, et al. Single Dose Vaccination in Healthcare Workers Previously Infected with SARS-CoV-2. *medRxiv.* 2021:2021.01.30.21250843. doi: 10.1101/2021.01.30.21250843.
20. Ujjainiya R, Tyagi A, Sardana V, Naushin S, Bhatheja N, Kumar K, et al. Effect Monitoring and Insights from Vaccination program of Healthcare Workforce from a tertiary level hospital in India against SARS-CoV-2. *medRxiv.* 2021:2021.02.28.21252621. doi: 10.1101/2021.02.28.21252621.
21. V Shah AS, Gribben C, Bishop J, Hanlon P, Caldwell D, Wood R, et al. Effect of vaccination on transmission of COVID-19: an observational study in healthcare workers and their households. *medRxiv.* 2021:2021.03.11.21253275. doi: 10.1101/2021.03.11.21253275.
22. Keehner J, Horton LE, Pfeffer MA, Longhurst CA, Schooley RT, Currier JS, et al. SARS-CoV-2 Infection after Vaccination in Health Care Workers in California. *N Engl J Med.* 2021. Epub 2021/03/24. doi: 10.1056/NEJMc2101927. PubMed PMID: 33755376.
23. Guijarro C, Galán I, Martínez-Ponce D, Pérez-Fernández E, José Goyanes M, Castilla V, et al. Dramatic drop of new SARS-CoV-2 infections among health care workers after the first dose of the BNT162b2 mRNA Covid-19 Vaccine. *medRxiv.* 2021:2021.03.24.21254238. doi: 10.1101/2021.03.24.21254238.
24. Oliver K, Raut A, Pierre S, Silvera L, Boulos A, Gale A, et al. Factors associated with COVID-19 vaccine receipt at two integrated healthcare systems in New York City: A Cross sectional study of healthcare workers. *medRxiv.* 2021:2021.03.24.21253489. doi: 10.1101/2021.03.24.21253489.
25. Inbaraj LR, George CE, Franklyn NN. How safe is Covishield (ChAdOx1nCoV-19) vaccine? Experience from a tertiary care hospital in South India. *medRxiv.* 2021:2021.03.16.21253744. doi: 10.1101/2021.03.16.21253744.
26. Bueno SM, Abarca K, González PA, Gálvez NMS, Soto JA, Duarte LF, et al. Interim report: Safety and immunogenicity of an inactivated vaccine against SARS-CoV-2 in healthy

chilean adults in a phase 3 clinical trial. medRxiv. 2021:2021.03.31.21254494. doi: 10.1101/2021.03.31.21254494.

27. Hollinghurst J, North L, Perry M, Akbari A, Gravenor MB, Lyons RA, et al. COVID-19 Infection Risk amongst 14,104 Vaccinated Care Home Residents: A national observational longitudinal cohort study in Wales, United Kingdom, December 2020 to March 2021. medRxiv. 2021:2021.03.19.21253940. doi: 10.1101/2021.03.19.21253940.

28. Moustsen-Helms IR, Emborg H-D, Nielsen J, Nielsen KF, Krause TG, Mølbak K, et al. Vaccine effectiveness after 1st and 2nd dose of the BNT162b2 mRNA Covid-19 Vaccine in long-term care facility residents and healthcare workers – a Danish cohort study. medRxiv. 2021:2021.03.08.21252200. doi: 10.1101/2021.03.08.21252200.

29. Shrotri M, Krutikov M, Palmer T, Giddings R, Azmi B, Subbarao S, et al. Vaccine effectiveness of the first dose of ChAdOx1 nCoV-19 and BNT162b2 against SARS-CoV-2 infection in residents of Long-Term Care Facilities (VIVALDI study). medRxiv. 2021:2021.03.26.21254391. doi: 10.1101/2021.03.26.21254391.

30. Tadi P, Behgam B, Baruffi S. Cerebral Venous Thrombosis. StatPearls. Treasure Island (FL): StatPearls Publishing Copyright © 2021, StatPearls Publishing LLC.; 2021.