Literature screening report

Covid-19 vaccines and post-vaccination data: literature update (7)

Report submission date:	**12.07.2021**

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Abstract

We report below the most relevant data on Covid-19 vaccines literature as of July 9, 2021. The current report addressed the prevalence or incidence rate of SARS-CoV-2 breakthrough infections among fully vaccinated people and the importance of children and adolescent's timely vaccination.

We also reported on the current data about safety of vaccines, gave a reminder about the efficacy of vaccines on emerged variants and highlighted the latest news about 'new' SARS-CoV-2 vaccines.

Content

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 report 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.

Background

The current epidemiological situation is evolving in many countries where new SARS-CoV-2 variants (e.g., delta) are dominant even in countries with high vaccination rate as the United Kingdom (66% of the adult population). Indeed, one global threat remains the emergence of new Covid-19 variants or strains that may - at the worst scenario- become more harmful to children. In this report, we focused on published studies that covered the following questions/points:

- What is the percentage or incidence rate of breakthrough covid-19 infections among fully vaccinated people?
- Is it time to vaccinate children and adolescents against Covid-19?
- What are the current safety data about Covid-19 vaccines?
- Reminder about the efficacy of Covid-19 vaccines against variants
- What is the status of new SARS-CoV-2 vaccines?

Methodology

Please refer to the previous reports if needed. The current report screened the Covid-19 vaccine-related literature as of July 09, 2021. We focused on those studies that would help to discuss the points raised above.

Synthesis of information

We analysed the data based on the specific questions cited in the introduction and tried to answer them as part of this report.

Results and Findings

What is the prevalence or incidence rate of breakthrough covid-19 infections among fully vaccinated people?

Summary of results:

SARS-CoV-2 infections that occur in fully vaccinated people are termed breakthrough infections. In a study[1] in the United States, there were 10,262 SARS-CoV-2 vaccine breakthrough infections between January 1 and April 30, 2021, of which 6,446 (63%) occurred in females, 2,725 (27%) were asymptomatic, 995 (10%) patients were hospitalized, and 160 (2%) patients died. In a cohort [1] of 417 fully vaccinated individuals with Pfizer-BioNTech COVID-19 vaccine (BNT162b2/COMIRNATY®) or Moderna COVID-19 vaccine (Spikevax/mRNA-1273), two breakthrough infections occurred. Both cases involved virus mutations such as E484K, T95I, del142–144, and D614G. Another study [2] showed that mutations (i.e., deletion of the N-Terminal protein (NTD)) were behind the surges of SARS-CoV-2 breakthrough infections in India and Chile. A cross-sectional study [3] estimated the incidence rate of breakthrough infections at 11.3% (95% CI 8.3 to 15.3) in a small sample of 325 healthcare workers who were vaccinated with either Bharat vaccine or AstraZeneca/Oxford (AZD1222) vaccine in a medical institution in India. It is noteworthy that 94.4% (34.9 out of 37) of the cases were mild and did not require hospitalizations.

In Israel, data showed a 7-day rolling average of 324 new confirmed COVID-19 cases as of July 5. It is assumed that 55% (178) of these cases were among vaccinated people (i.e., breakthrough infections)[2]. Moreover, it is believed that 90% of the cases were caused by the variant B.1.617.2 (delta)[3].

[1] https://www.cdc.gov/mmwr/volumes/70/wr/mm7021e3.htm (accessed on 09.07.2021).
[2] https://www.medscape.com/viewarticle/954357 (accessed on 09.07.2021).
[3] https://www.wsj.com/articles/vaccinated-people-account-for-half-of-new-covid-19-delta-cases-in-israeli-outbreak-11624624326 (accessed on 09.7.2021).

In the United Kingdom[4], an incidence rate of ≈ 298.1 SARS-CoV-2 infections per 100,000 – compared to 27 in Switzerland[5]- was reported while almost 50% daily increase in hospitalizations and deaths was observed as of July 11, 2021. At an earlier stage of Covid-19 vaccination rollout, experts estimated that vaccinating 60-70% of a population would be enough to reach herd immunity. Although this could have happened in Israel and the United Kingdom, several reasons might explain why it does not. Of those, two main reasons may elucidate this phenomenon, namely the ability of the vaccines to prevent SARS-CoV-2 transmission and the emergence of new variants that escape vaccine-induced immunity [4].

Is it time to vaccinate children and adolescents against Covid-19?

Summary of results:

Small phase II/III clinical trials involving participants (12-17) have shown an efficacy of 100% to prevent symptomatic SARS-CoV-2 infections for Pfizer-BioNTech COVID-19 vaccine (BNT162b2) [5] or Moderna COVID-19 vaccine (Spikevax/mRNA-1273)[6]. Currently, rollout of Covid-19 vaccination in children has started in some countries after the approval of US FDA, the EMA, and the local health authorities including Swissmedic.

In Israel, at least 50% of recent SARS-CoV-2 infections (as of July 5, 2021) occurred in children and adolescents under the age of 19 years old that forced the local authorities to further encourage the vaccination of those aged 12-15 years old [6].

Several key factors and elements can play an important role in the decision to initiate teenager's vaccination: ''the current vaccination uptake in the older age groups, the

[4] https://coronavirus.data.gov.uk/ (accessed on 10.07.2021).
[5] https://www.covid19.admin.ch/en/overview (accessed on 10.07.2021
[6] https://investors.modernatx.com/news-releases/news-release-details/moderna-announces-teencove-study-its-covid-19-vaccine (accessed on 09.07.2021).

incidence of Covid-19 in the population, and the availability and access of vaccines on a global scale"[7]. Other related factors would be related to the level of herd immunity with or without vaccinating children, the level of protection of vaccines against viral transmission, the risk of transmission from infected children to naïve adults, and the actual non-pharmacological public health intervention in place (e.g., opening or closure of schools). In fact, a good proportion of SARS-CoV-2 infections in children and adolescent were reported asymptomatic and the ability of vaccines to stop the transmission is crucial to fully justify the vaccination of this overall subpopulation [7]. Of note, the Covid-19 vaccines were able to curb the transmission at least indirectly. Children who are prone to severe covid-19 should be prioritized[8] as it was the case for the adult population. While children have good prognosis [8] in case of infection and even low transmission in some settings [9], they were still heavily impacted by the non-pharmacological public health interventions to curb the pandemic, notably the closure of schools. The question of how much benefits the community gains from vaccinating children remains unanswered.

What are the current safety data about Covid-19 vaccines?
Summary of results: Safety data generated by surveillance programs showed that the benefits of vaccination outweigh the risks at the population level[9]. Cases of thrombosis and thrombocytopenia as post-vaccination adverse events were reported in many studies but repeatedly judged as coincidental onset not attributable to mRNA vaccines. However, the possibility of a link between mRNA vaccination and de novo immune thrombocytopenia (ITP) cannot be excluded [10], but also secondary ITP [11].

[7] https://www.ecdc.europa.eu/en/news-events/ecdc-report-outlines-considerations-covid-19-vaccination-adolescents (accessed on 10.07.2021).

[8] https://www.tdg.ch/bientot-des-vaccins-pour-les-12-a-15-ans-572751804132 (accessed on 10.07.2021).

[9] https://www.swissmedic.ch/swissmedic/en/home/news/coronavirus-covid-19/covid-19-vaccines-safety-update-2.html (accessed on 09.07.2021).

It is noteworthy that cases of cerebral venous sinus thrombosis and thrombocytopenia – mostly fatal [12, 13] but rare [14]- were linked to Vaxzevria (AstraZeneca/Oxford) vaccination. Future studies that aim to understand the mechanisms of such relationship and the potential risk factors are of vital importance [15-18]. Vaccination may probably be discouraged to known susceptible persons such as those with hereditary thrombocytopenia or documented abnormal platelet counts after benefits/risk evaluation.

In addition, rare cases of myocarditis and pericarditis have recently been linked[10] to mRNA vaccines [namely, Pfizer-BioNTech COVID-19 vaccine (BNT162b2) or Moderna COVID-19 vaccine (Spikevax/mRNA-1273)]. In case of post vaccination symptoms such as breathlessness, a forceful heartbeat that may be irregular, or chest pain, the patient should seek help immediately.

Reminder about the efficacy of Covid-19 vaccines against variants

Summary of results:

As with other viruses, mutations of SARS-CoV-2 have been reported in many countries [19-21]. Compared to the wild-type, SARS-CoV-2 variants (due to a single or multiple mutations) may minimize immune responses triggered by vaccines. Practically speaking, clinical trials conducted in countries with variant dominance have shown variable efficacy as low as 52% in South Africa to as high as 74.4 in the United States (for Janssen Covid-19 vaccine at least 14 days after vaccination)[11].
Several studies [22-28] reported a partial loss of virus-neutralizing activity caused by such variants after vaccination. Vaxzevria (AstraZeneca/Oxford) vaccine was

[10] https://www.ema.europa.eu/en/news/comirnaty-spikevax-possible-link-very-rare-cases-myocarditis-pericarditis (accessed on 10.07.2021).

[11] https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/janssen-covid-19-vaccine (04.03.2021)

deemed ineffective [21.9% (95% CI (-49.9 to 59.8))] to prevent mild and moderate Covid-19 infections in patients with the B.1.351 variant in South Africa [29], causing a halt to an ongoing rollout[12]. It is noteworthy that subgroup analyses of phase III clinical trial in South Africa reported an efficacy of approximately 75% after a single dose but that was before the dominance of the variant in the country[13]. One study [25] showed a moderate yet significant resistance of N501Y/K417N/E484K mutants to convalescent or post-vaccine sera. This may translate to lower vaccine efficacy to prevent infection but not necessarily the severity of the disease. A non-peer reviewed study [30] conducted in the UK demonstrated that single doses of AstraZeneca/Oxford and Pfizer-BioNTech Covid-19 vaccines reduced symptomatic cases against the variant B.1.617.2 with an effectiveness of 32.9% and 33.2%, respectively. However, two-dose vaccinations were respectively more efficacious with 59.8% and 87.9%. A comparison among emergency-authorized vaccines would be interesting but an 'upgrade' of currently available vaccines would be expectedly necessary in the coming months/years.

What is the status of new SARS-CoV-2 vaccines?

Summary of results:

As of July 2, 2021, the World Health Organization (WHO) has authorized 6 vaccines [namely, Pfizer-BioNTech, USA), Spikevax/Moderna COVID-19 Vaccine/ mRNA-1273 (Moderna, USA), Vaxzevria/ChAdOx1 nCoV-19/AZD1222/Covishield (AstraZeneca/Oxford, UK, India), Janssen Covid-19 vaccine/Johnson & Johnson (Janssen, USA), Sinopharm/BIBP (China), and Sinovac/CoronaVac (China)]. Among those under assessment, three vaccines [Gam-COVID-Vac/SPUTNIK V, Novavax (NVX-CoV2373/Covovax), and CUREVAC (CVnCoV)] have reached an advanced clinical and marketing stage.

[12] https://www.cidrap.umn.edu/news-perspective/2021/02/south-africa-share-covid-vaccine-europe-weighs-jj-vaccine (accessed on 04.03.2021).

[13] https://www.theguardian.com/world/2021/feb/08/oxford-covid-vaccine-10-effective-south-african-variant-study (accessed on 04.03.2021).

Interim results from phase III clinical trials [31] showed that the efficacy of Gam-COVID-Vac/SPUTNIK V (Gamaleya Research Institute, Russia) was 91.6% ((95% CI 85·6–95·2) with a median follow-up of 48 days.

Most common adverse events were flu-like illness, injection site reactions, headache, and asthenia. Most of the reported adverse events (7485 [94.0%] of 7966) were grade 1; 451 were grade 2 (5.66%) and 30 were grade 3 (0.38%) [see terms in https://www.meddra.org/user-groups]. One hundred twenty-two rare adverse events were reported in the study (91 in the vaccine group and 31 in the placebo group).

A phase III clinical trial [32] for Novavax (NVX-CoV2373/Covovax) involved 14,039 participants and showed an efficacy of 89.7% (95% CI 80.2 to 94.6) against symptomatic SARS-CoV-2 infection >7 days after the 2nd dose. In a phase II clinical trial [33] in South Africa, Novavax (NVX-CoV2373/Covovax) had an efficacy of 49.4% (95% CI 6.1 to 72.8) against the B.1.351 variant.

CUREVAC (CVnCoV) showed a disappointing efficacy results of 47% or 48% in phase III clinical trials[14]. A partial explanation of such findings was the presence of 15 circulating strains in the studied population of 40,000. An efficacy of 77% was reported for prevention of moderate to severe disease[15].

For Sinovac/CoronaVac (China) inactivated SARS-CoV-2 vaccine, a prospective cohort of 10.2 million participants in Chile showed an effectiveness of 65.9% (95% CI 65.2 to 66.6) against symptomatic SARS-CoV-2 infections. 87.5% (95% CI, 86.7 to 88.2) and 86.3% (95% CI, 84.5 to 87.9) for the prevention of hospitalization and death, respectively [34].

[14] https://www.nature.com/articles/d41586-021-01694-5 (accessed on 10.07.2021).

[15] https://www.curevac.com/en/2021/06/30/curevac-final-data-from-phase-2b-3-trial-of-first-generation-covid-19-vaccine-candidate-cvncov-demonstrates-protection-in-age-group-of-18-to-60/ (accessed on 10.09.2021).

Ongoing studies

Booster doses (i.e., 2nd or 3rd doses after a first dose) are scientifically established in other licensed vaccines as polio, hepatitis B, or tetanus. Unlike those diseases, the timing of a booster dose is still to be optimized for Covid-19 vaccines.

Pfizer-BioNTech has recently announced the end of its study about a booster dose (3rd dose) to combat new variants of SARS-CoV-2 (e.g., the delta variant) and its intention to seek an authorization from the US FDA[16].

More studies are needed to establish whether current emergency-authorized vaccines would directly reduce virus transmissibility among individuals while being asymptomatic.

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[16] https://www.theguardian.com/world/2021/jul/08/pfizer-covid-19-vaccine-booster-us (accessed on 10.07.2021).

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