COVID-19

CONSOLIDATED REGIONAL AND GLOBAL INFORMATION ON ADVERSE EVENTS FOLLOWING IMMUNIZATION (AEFI) AGAINST COVID-19 AND OTHER UPDATES

Thirty-sixth report

WASHINGTON, DC

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PAHO Pan American Health Organization World Health Organization Americas

In partnership with Canada

CONTENTS

CANADA

As of 13 May 2022, 57,011,324 doses of the Pfizer-BioNTech COVID-19 vaccine, 23,707,288 doses of the Moderna vaccine, 2,812,881 doses of the AstraZeneca and Covishield vaccine (AstraZeneca manufactured by the Serum Institute of India), and 20,950 doses of the Janssen vaccine had been administered.

To date, there have been 46,149 individual reports of one or more AEFI (55.2 reports per 100,000 doses administered), of which 9,515 events were considered serious (11.4 reports per 100,000 doses administered).

The majority of individual case reports were of non-serious adverse events. The most frequently reported adverse events were: paresthesia, injection-site pain, headache, pruritus, dyspnea, fatigue, urticaria, chest pain, and fever.

Number of reports and reporting rate of AEFI (per 100,000 doses administered), by vaccine, as of 13 May 2022 (n=46,246)						
Vaccine	Number of reports of non-serious AEFI		Number of reports of serious AEFI		Total number of reports of AEFI	
	N*	Rate/100,000 doses administered	N*	Rate/100,000 doses administered	N*	Rate/100,000 doses administered
Pfizer-BioNTech	20,910	36.68	6,547	11.48	27,457	48.16
Moderna	12,566	53.00	1,848	7.80	14,414	60.80
Covishield and AstraZeneca	3,071	109.18	896	31.85	3,967	141.03
Janssen	36	171.84	23	109.79	59	281.62
Unknown	54	N/A	295	N/A	349	N/A
Total	36,637	43.85	9,609	11.50	46,246	55.35

*N=number of reports

The following table shows information, included in the above total, regarding adverse events associated with the Pfizer-BioNTech vaccine in children between ages 5 and 18:

Number of reports and reporting rate of AEFI (per 100,000 doses administered) for the Pfizer-BioNTech vaccine in the under-18-year-old population, as of 13 May 2022						
Age group (doses administered, ds)	Number of reports of non-serious AEFI		Number of reports of serious AEFI		Total number of reports of AEFI	
	N*	Rate/100,000 doses administered	N*	Rate/100,000 doses administered	N*	Rate/100,000 doses administered
Ages 12 to 17	1,136	23.16	376	7.66	1,512	30.82
4,905,661						
Ages 5 to 11	473	15.75	85	2.83	558	18.58
3,002,761						
Total	1,609	20.35	461	5.83	2,070	26.17
7,908,422						

*N=number of reports

Reports for the 5-11-year-old age group included those born in 2017 who were not yet 5 years old at the time of vaccination.

Note: The 5-11-year-old age group includes those who were born in 2017 but were not yet 5 years old at the time of vaccination.

Lastly, the following table details the number and rate (per 100,000 doses administered) of the main adverse events of special interest (AESI), by vaccine.

Number of reports and reporting rate of the main adverse events of special interest (AESI) (per 100,000 doses administered), by vaccine, in the general population, as of 13 May 2022						
AESI	Vaccine					
	Pfizer-BioNTech		Moderna		Covishield and AstraZeneca	
	N*	Rate/100,000 doses administered	N*	Rate/100,000 doses administered	N*	Rate/100,000 doses administered
Anaphylaxis	620	1.09	187	0.79	29	1.03
Guillain-Barré syndrome	60	0.11	30	0.13	39	1.39
Myocardial infarction	80	0.14	25	0.11	6	0.21
Myocarditis/pericarditis	639	1.12	714	3.01	32	1.14
Deep vein thrombosis	170	0.30	74	0.31	73	2.60
Pulmonary embolism	241	0.42	100	0.42	135	4.80
Thrombosis with thrombocytopenia syndrome (TTS)	30	0.05	13	0.05	71	2.52
Bell's palsy/facial paralysis	613	1.08	226	0.95	55	1.96
Cerebrovascular accident	136	0.24	57	0.24	37	1.32
Acute renal injury	35	0.06	23	0.10	7	0.25
Miscarriage	63	0.11	16	0.07	1	0.04
Fatal events	339* post-vaccination deaths					
*Following a medical review of the 339 deaths, it was determined that 108 were most likely unrelated to administration of the COVID-19 vaccine, while 49 are still under investigation; in 182 cases, the cause of death could not be classified, due to insufficient information.						

*N=number of reports

Note: Information on the Janssen vaccine was not included, due to the small number of reported cases.

Source: Public Health Agency of Canada. Canadian COVID-19 vaccine safety report. Ottawa: Public Health Agency of Canada; May 30, 2022. https://health-infobase.canada.ca/covid-19/vaccine-safety/. Data reproduced by PAHO/WHO.

ENGLISH-SPEAKING CARIBBEAN

As of 15 May 2022, VigiBase, the global Individual Case Safety Report (ICSR) database, had received 1,472 reports of AEFI associated with COVID-19 vaccines in the English-speaking Caribbean.

Reports came from Barbados, Jamaica, and Saint Vincent and the Grenadines, mainly in people under 65 years of age (84.9%), and females (74.4%). To date, the most frequent reactions were headache n=442 (30%), fever n=293 (19.9%), dizziness n=291 (19.8%), fatigue n=245 (16.6%), chills n=242 (16.4%), and myalgia n=215 (14.6%). Of total reported events, 249 (16.9%) were classified as serious.

Individual cases reported were associated with the following COVID-19 vaccines: AstraZeneca, COVISHIELD, Sputnik V, Pfizer-BioNTech, J&J/Janssen, BIBP-Sinopharm, Moderna, and unspecified COVID-19 vaccines.

Number of reports and reporting rate of adverse events (per 100,000 doses administered), by vaccine and by reporting country, as of 13 May 2022 (n=1,472)

Country	Total doses administered	Non-serious events		Serious events		Total events	
		N*	Rate/100,000 doses administered	N*	Rate/100,000 doses administered	N*	Rate/100,000 doses administered
Barbados	362,338	510	140.75	77	21.25	587	162.00
Jamaica	1,424,600	697	48.93	166	11.65	863	60.58
Saint Vincent and the Grenadines	70,331	16	22.75	6	8.53	22	31.28
Total	1,857,269	1,223	65.85	249	13.41	1,472	79.26

*N=number of events

Note: Individual case safety reports (ICSR) describe events that occurred following vaccination, and may include coincident events not attributable to the vaccine(s).

Source: The Caribbean Public Health Agency (CARPHA). Caribbean Regulatory System. Vigicarib News, 18 May 2022. Additional information available at: https://carpha.org/What-We-Do/CRS/VigiCarib.

COLOMBIA

As of 16 May 2022, 84,035,139 doses of COVID-19 vaccines had been administered. As of the same date, 51,137 individual case reports of AEFI had been received through VigiFlow©. An individual case report may include one or more adverse events. The national reporting rate was 61 reports per 100,000 doses administered.

Of total individual case reports, 3% (1,515 reports) included serious AEFI, and 66% (33,934 reports) were in women. Analyzing the distribution of reports by age, the highest percentage of reports, 12.5% (6,389) was in the 25-to-29-year-old age group, followed by those between the ages of 30 and 34, representing 11.3% (5,783 reports).

The most frequently reported signs and symptoms, without indication as to the type of vaccine, were: headache (17.2%), fever (8.8%), malaise (7.4%), muscle pain (7.2%), injection-site pain (6.4%), and weakness (5.6%).

Source: Colombia Ministry of Health, National Food and Drug Surveillance Institute (INVIMA), National Institute of Health (INS). Bulletin #13: May 2022. Surveillance of Adverse Events Following Immunization (AEFI) with COVID-19 vaccines in Colombia. Reporting period: 17 February 2021 to 16 May 2022. Available at: https://www.minsalud.gov.co/sites/rid/Lists/BibliotecaDigital/RIDE/VS/ED/PSP/boletin13-farmacovigilancia-vacunas-may2022.pdf.

UNITED STATES

The following is updated information from the U.S. Centers for Disease Control and Prevention (CDC) regarding serious adverse events of special interest:

Anaphylaxis following COVID-19 vaccination is rare, with approximately five cases per million people vaccinated in the United States. Anaphylaxis can occur after administration of any type of vaccine. CDC scientists have conducted detailed reviews of cases of anaphylaxis, and have made the information available to health care providers and the public at the following links:

- Allergic Reactions Including Anaphylaxis After Receipt of the First Dose of Pfizer-BioNTech COVID-19 Vaccine
  https://pubmed.ncbi.nlm.nih.gov/33475702/
- Allergic Reactions Including Anaphylaxis After Receipt of the First Dose of Moderna COVID-19 Vaccine — United States, December 21, 2020–January 10, 2021
  https://www.cdc.gov/mmwr/volumes/70/wr/mm7004e1.htm

Thrombosis with thrombocytopenia syndrome (TTS) after COVID-19 vaccination with the Janssen (J&J/Janssen) vaccine is rare, with approximately four cases per million people vaccinated in the United States. A case series review indicates a causal relationship between Janssen's COVID-19 vaccine and TTS. CDC scientists have made detailed reviews of cases of TTS, and have published the results in: U.S. Case Reports of Cerebral Venous Sinus Thrombosis

With Thrombocytopenia After Ad26.COV2.S Vaccination, March 2 to April 21, 2021. https://jamanetwork.com/journals/jama/fullarticle/2779731

Guillain-Barré syndrome (GBS) in people who have received the J&J/Janssen COVID-19 vaccine is rare. According to a recent analysis of data from the Vaccine Safety Datalink, the rate of GBS within the first 21 days after administration of the J&J/Janssen COVID-19 vaccine was 21 times higher than after administration of the Pfizer-BioNTech or Moderna mRNA COVID-19 vaccines; and after the first 42 days, the rate was 11 times higher than for the mRNA vaccines. Most of the reported cases were in individuals who received the Pfizer-BioNTech or Moderna mRNA COVID-19 vaccines, and occurred particularly in adolescent males and young adults.

A review of vaccine safety data in the VAERS database from December 2020 to August 2021 detected a small increase in the risk of myocarditis after administration of the mRNA COVID-19 vaccines. More than 350 million mRNA vaccines were administered during the study period, and CDC scientists found that myocarditis rates were higher after administering the second dose of mRNA vaccine among males in the following age groups:

- Ages 12 to 15 (70.7 cases per million doses of Pfizer-BioNTech)
- Ages 16 to 17 (105.9 cases per million doses of Pfizer-BioNTech)
- Ages 18 to 24 (52.4 and 56.3 cases per million doses of the Pfizer-BioNTech and Moderna vaccines, respectively)

Reports of deaths after COVID-19 vaccination are rare. Between 14 December 2020 and 6 June 2022, more than 589 million doses of COVID-19 vaccine were administered in the United States. During this time, VAERS received 14,980 reports of deaths (0.0025%) among people who received a COVID-19 vaccine. Follow-up indicated that nine of these deaths were causally associated with the J&J/Janssen COVID-19 vaccine.

Source: Centers for Disease Control and Prevention (CDC). Selected Adverse Events Reported after COVID-19 Vaccination. Updated 11 July 2022. Available at: https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/adverse-events.html.

Note: The page is updated weekly, and the data may differ at the time this newsletter is published.

PARAGUAY

As of 13 May 2022, 8,677,814 doses of COVID-19 vaccines had been administered. A total of 2,710 AEFI have been reported since the start of the vaccination program (22 February 2021 to 13 May 2022), representing 0.03% of doses administered. A total of 453 events were considered serious (16.7% of total reported cases), representing 0.005% of total doses administered.

The highest rate of reported AEFI is associated with the Covaxin COVID-19 vaccine (80.26/100,000 doses administered), followed by AstraZeneca (63.61/100,000 doses administered) and CoronaVac (55.67/100,000 doses

administered). Of the total AEFI reports (n=2,710), 71% (1,919) were in women, and 67% (1,811) were in the 25-to-49-year-old age group.

Source: Paraguay Ministry of Public Health and Social Welfare. AEFI Surveillance Information Bulletin #61 Regarding COVID-19 Vaccination. National Program on Immunopreventable Diseases and Expanded Program on Immunization, 13 May 2022. Available at: https://pai.mspbs.gov.py/wp-content/uploads/2022/05/61-Boletin-Epidemiologico-ESAVI.pdf.

PERU

As of 30 April 2022, 72,543,665 doses of COVID-19 vaccines had been administered nationwide. As of that date, 40,860 reports of one or more AEFI had been recorded in the national pharmacovigilance database (VigiFlow©). More than 60% of reported events were of headache, injection-site pain, pyrexia, malaise, dizziness, drowsiness, pain in a limb, and myalgia.

Number of reports and reporting rate of AEFI (per 100,000 doses administered), by vaccine, as of 30 April 2022 (n=40,860)

Vaccine	Total doses administered	Number of reports of non-serious AEFI		Number of reports of serious AEFI		Total number of reports of AEFI	
		N*	Rate/100,000 doses administered	N*	Rate/100,000 doses administered	N*	Rate/100,000 doses administered
Sinopharm	20,640,284	18,939	91.76	70	0.34	19,009	92.10
Comirnaty/Pfizer	43,752,688	16,664	38.09	136	0.31	16,800	38.40
Vaxzevria/ AstraZeneca	7,950,204	2,871	36.11	17	0.21	2,888	36.33
Spikevax/Moderna	200,489	2,163	1078.86	-	-	2,163	1078.86
Total	72,543,665	40,637	56.02	223	0.31	40,860	56.32

*N=number of reports

Source: Ministry of Health. General Directorate of Medicines, Supplies, and Drugs. Pharmacovigilance report. Reported adverse events following immunization (AEFI) attributed to vaccination with COVID-19 vaccine. Period: 9 February 2021 to 30 April 2022. Available at:

https://repositorio.digemid.minsa.gob.pe/bitstream/handle/DIGEMID/273/Informe_de_ESAVI_vacunas_COVID_30_abril_2022_1.pdf?sequence=3&isAllowed=y.

MEXICO

As of 29 April 2022, a total of 38,100 AEFI had been reported, of which 97.10% (36,994) were for non-serious events. The highest proportion of AEFI, both serious (59.2%) and non-serious (71.4%), occurred in women. The non-serious AEFI occurred primarily in the 30-to-39-year-old age group, while the serious AEFI were mostly in the over-60-year-old age group.

The most frequently reported non-serious AEFI signs and symptoms were headache, 66% (24,365), injection-site pain or tenderness, 46.38% (17,158), and myalgia, 41.96% (15,521), while the most commonly reported serious AEFI were headache, 44% (490), asthenia, 37% (409), and dyspnea, 31% (347).

Number of reports and reporting rate of AEFI (per 100,000 doses administered), by vaccine, as of 29 April 2022 (n=38,100)

Vaccine	Total doses administered	Non-serious events		Serious events		Total events	
		N*	Rate per 100,000 doses administered	N*	Rate per 100,000 doses administered	N*	Rate per 100,000 doses administered
Pfizer-BioNTech	35,874,667	18,996	52.95	338	0.94	19,334	53.89
AstraZeneca	49,783,383	12,213	24.53	457	0.92	12,670	25.45
Sinovac	18,456,001	1,695	9.18	109	0.59	1,804	9.77
Sputnik V	10,257,589	1,077	10.50	61	0.59	1,138	11.09
CanSino	15,177,016	1,571	10.35	64	0.42	1,635	10.77
Janssen	1,242,211	830	66.82	9	0.72	839	67.54
Moderna	3,181,399	560	17.60	54	1.70	614	19.30
Unknown	-	9	-	2	-	11	-
Vaccinated abroad	-	43	-	12	-	55	-
Total	133,972,266	36,994	27.61	1,106	0.83	38,100	28.44

*N=number of events

Source: Undersecretariat of Prevention and Health Promotion, General Directorate of Epidemiology. Office of Epidemiological Surveillance of Communicable Diseases. April 2022. AEFI COVID-19 Report. Published 13 May 2022. Available at: https://www.gob.mx/cms/uploads/attachment/file/725076/REPORTE_ESAVI_04_2022.pdf.

Publications on potential safety signals detected with the use of COVID-19 vaccines

Efficacy and Safety of a Recombinant Plant-Based Adjuvanted COVID-19 Vaccine: CoVLP+AS03

On 4 May 2022, a multinational, randomized, placebo-controlled phase 3 study was published. The study was conducted at 85 sites in Argentina, Brazil, Canada, United States, Mexico, and the United Kingdom.

For the trial, which was conducted from 15 March to 2 September 2021, adults (≥18 years) were randomly assigned in a 1:1 ratio to receive two intramuscular injections of the CoVLP+AS03 vaccine (coronavirus virus-like particle vaccine) grown in the Australian grass, expressed in *Nicotiana benthamiana* + AS03 (adjuvant), or placebo 21 days apart. Participants had not been previously vaccinated against SARS-CoV-2 and had no history of confirmed COVID-19.

The primary objective of the trial was to determine the efficacy of the CoVLP+AS03 vaccine in preventing symptomatic COVID-19, beginning at least seven days after the second trial injection, with the analysis performed after the detection of at least 160 laboratory-confirmed cases.

Vaccine efficacy results were calculated after a median follow-up of at least two months.

A total of 24,141 volunteers, with a median age of 29 years, participated in the trial.

COVID-19 was confirmed by PCR assay in 165 participants in the target population; all viral samples that could be sequenced contained variants of the original strain.

Vaccine efficacy was 69.5% (95% confidence interval [CI], 56.7 to 78.8) against any symptomatic COVID-19 caused by any of five variants that were identified by sequencing (Alpha, Gamma, Delta, Lambda, and Mu).

In a post hoc analysis, vaccine efficacy was 78.8% (95% CI, 55.8 to 90.8) against moderate-to-severe disease and 74.0% (95% CI, 62.1 to 82.5) among the participants who were seronegative at baseline.

Vaccine efficacy among adults who were 65 years or older could not be determined because of the limited enrollment of participants in this age group.

No severe or critically ill cases occurred in the vaccinated group.

The safety population included 24,076 participants (12,036 in the vaccine group and 12,040 in the placebo group). Solicited adverse events up to seven days after each dose were analyzed in 7,819 participants (4,136 participants in the vaccinated group and 3,683 in the placebo group).

Local and systemic adverse events were predominantly mild to moderate and transient (duration one to three days).

In the two groups, local reactogenicity consisted primarily of injection-site pain. The most common systemic adverse events were headache, myalgia, fatigue, and a feeling of general discomfort. Local adverse events occurred in 92.3% of the vaccine group and 45.5% of the placebo group, with systemic events in 87.3% and 65.0%, respectively.

Grade 2 and 3 local and systemic adverse events occurred more frequently after the second dose. Grade 3 (severe) local adverse events were reported in 2.1% of the participants in the vaccine group and in less than 0.1% of those in the placebo group after the second dose. Grade 3 systemic reactions were reported in 3.1% and 0.5%, respectively.

No grade 4 (life-threatening) local adverse events were reported, but 3 participants reported grade 4 systemic adverse events after the second dose: two in the vaccine group (chills, headache, muscle aches, and a feeling of general discomfort in one participant, and fever in the other) and one in the placebo group (headache).

The incidence of unsolicited adverse events after the first or second dose was slightly higher in the vaccine group than in the placebo group (22.7% vs. 20.4% up to 21 days after the second dose; 4.2% vs. 4.0% from day 43 to day 201).

The incidence of serious adverse events was similar in the two groups up to 21 days after the first or second doses (24 participants in the vaccine group [0.2%] vs. 16 in the placebo group [0.1%]) and between days 43 and 201 (19 [0.2%] vs. 22 [0.2%], respectively). One participant in the placebo group reported two serious adverse events (aortic thrombosis and peripheral artery thrombosis). There were four (<0.1) serious events with fatal outcomes in the vaccine group and 5 (<0.1) in the placebo group. The deaths were not considered vaccine-related.

The authors conclude that the CoVLP+AS03 vaccine was effective in preventing COVID-19 caused by a spectrum of variants, with efficacy ranging from 69.5% against symptomatic infection to 78.8% against moderate to severe disease.

Source: Karen J. Hager, et al. Efficacy and Safety of a Recombinant Plant-Based Adjuvanted COVID-19 Vaccine. N Engl J Med 2022; 386:2084–96. DOI: 10.1056/NEJMoa2201300.
https://www.nejm.org/doi/pdf/10.1056/NEJMoa2201300?articleTools=true

Safety, immunogenicity and reactogenicity of BNT162b2 and mRNA-1273 COVID-19 vaccines given as fourth-dose boosters after two doses of ChAdOx1 nCoV-19 or BNT162b2 and a third dose of BNT162b2 (VOC-BOOST): a multicentre, blinded, phase 2, randomized trial

This study, published 9 May 2022, is a randomized sub-trial nested within the main COV-BOOST trial (a blinded, multicenter, randomized, controlled, phase 2 trial of seven COVID-19 vaccines given as third-dose boosters at 18 sites in the UK).

Its objective was to investigate the safety, reactogenicity, and immunogenicity of fourth-dose boosters against COVID-19.

Participants aged 30 years or older who had received two doses of BNT162b2 or ChAdOx1 nCoV-19 and a third-dose booster of BNT162b2 vaccine in the COV-BOOST trial during June 2021 were eligible for inclusion, unless they had a previous severe adverse reaction to mRNA vaccines or had acquired an additional COVID-19 vaccine outside of the study since enrolling.

Participants were randomly assigned (1:1) to receive a fourth dose of BNT162b2 (30 µg in 0.30 mL) or mRNA-1273 (Moderna; 50 µg in 0.25 ml).

The coprimary outcomes were safety, reactogenicity, and immunogenicity (anti-spike protein IgG titers by ELISA and cellular immune response by ELISpot).

Immunogenicity was compared at 28 days after the third dose versus 14 days after the fourth dose and compared at day 0 versus day 14 (primary outcome timepoint) relative to the fourth dose.

Between 11 and 25 January 2022, 166 participants were screened, randomly assigned, and received either a full-dose of BNT162b2 (n=83) or a half-dose of mRNA-1273 (n=83) as a fourth dose. The median age of participants was 70.1 years (IQR 51.6–77.5), and 52% were female.

The median interval between the third and fourth doses was 208.5 days (IQR 203.3–214.8).

Safety and reactogenicity results showed that the most commonly reported local adverse event was pain, while fatigue was the most frequently reported systemic adverse event after booster doses of BNT162b2 or mRNA-1273.

None of three serious adverse events reported after a fourth dose with BNT162b2 were related to the study vaccine.

With regard to the results on immunogenicity and cellular immunity:

- In the group that received BNT162b2, geometric mean anti-spike protein IgG concentration at day 28 after the third dose was 23,325 ELISA laboratory units (ELU)/mL (95% CI: 20,030–27,162), which increased to 37,460 ELU/mL (31,996–43,857) on day 14 after the fourth dose; this represented a significant fold change (geometric mean 1.59, 95% CI 1.41–1.78).
- The fold changes in anti-spike protein IgG titers from before (day 0) to after (day 14) the fourth dose were 12.19 (95% CI 10·37–14.32) and 15.90 (12.92–19.58) in the BNT162b2 and mRNA-1273 groups, respectively.
- T-cell responses were also boosted after the fourth dose (e.g., the fold changes for the wild-type variant from before to after the fourth dose were 7.32 [95% CI 3.24–16.54] in the BNT162b2 group and 6.22 [3.90–9.92] in the mRNA-1273 group).

Based on the results in this sub-study, the authors conclude that a fourth dose of COVID-19 mRNA vaccines is well tolerated and provide a boost to both humoral and cellular immunity. The maximum responses after the fourth dose were similar and possibly better than the peak responses after the third dose.

Source: Alasdair P S Munro et al. Safety, immunogenicity, and reactogenicity of BNT162b2 and mRNA-1273 COVID-19 vaccines given as fourth-dose boosters following two doses of ChAdOx1 nCoV-19 or BNT162b2 and a third dose

of BNT162b2 (COV-BOOST): a multicenter, blinded, phase 2, randomized trial. Lancet Infect Dis. 2020. Published online 9 May 2022. https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(22)00271-7/fulltext.

Association of Prior BNT162b2 COVID-19 Vaccination with Symptomatic SARS-CoV-2 Infection in Children and Adolescents During Omicron Predominance

On 13 May 2022, a test-negative, case-control analysis was conducted using data from 6,897 pharmacy-based, drive-through SARS-CoV-2 testing sites across the U.S. from a single pharmacy chain in the Increasing Community Access to Testing platform.

The objective was to evaluate the association of symptomatic SARS-CoV-2 infection with a history of previous vaccination with BNT162b2 vaccine in order to estimate vaccine effectiveness (VE) in children and adolescents during the period of Omicron variant predominance.

This analysis included 74,208 tests from children 5 to 11 years of age, and 47,744 tests from adolescents 12 to 15 years of age with COVID-19–like illness who underwent SARS-CoV-2 PCR testing from 26 December 2021 to 21 February 2022.

The following were compared:

- Children with two doses of BNT162b2 (two weeks or more before the SARS-CoV-2 test) versus unvaccinated children; and
- Adolescents with two or three doses (2 weeks or more before the test and for whom a booster dose is recommended) versus unvaccinated adolescents.

The main outcome was symptomatic SARS-CoV-2 infection. A total of 30,999 test-positive cases and 43,209 test-negative controls were included from children 5 to 11 years of age. Within the group of adolescents ages 12 to 15 there were 22,273 positive cases and 25,471 controls with negative tests.

Among all participants, the mean age was 10 years (IQR, 7–13); 61,189 (50.2%) were female, 75,758 (70.1%) were White, and 29,034 (25.7%) were Hispanic/Latino.

At 2 to 4 weeks after the second dose: among children, the adjusted odds ratio (OR) was 0.40 (95% CI, 0.35-0.45; estimated VE: 60.1% [95% CI, 54.7%-64.8%]); and among adolescents, the OR was 0.40 (95% CI, 0.29–0.56;estimated VE:59.5 % [95% CI, 44.3%-70.6%]).

During month 2 after dose 2, among children, the OR was 0.71 (95% CI, 0.67-0.76;estimated VE: 28.9% [95% CI, 24.5%-33.1%]); and among adolescents, the OR was 0.83 (95% CI, 0.76-0.92; estimated VE: 16.6% [95% CI, 8.1%-24.3%]).

Among adolescents, after the booster dose, from 2 to 6.5 weeks after the dose, OR was 0.29 (95% CI, 0.24-0.35; estimated VE: 71.1% [95% CI, 65.5%-75.7%]).

The authors conclude that, among children and adolescents, estimated VE for two doses of BNT162b2 against symptomatic infection was modest and decreased rapidly. Among adolescents, the estimated effectiveness increased after a booster dose.

Source: Fleming-Dutra KE, Britton A, Shang N, et al. Association of Prior BNT162b2 COVID-19 Vaccination With Symptomatic SARS-CoV-2 Infection in Children and Adolescents During Omicron Predominance. JAMA. Published online 13 May 2022. https://jamanetwork.com/journals/jama/fullarticle/2792524.

Protection and waning of natural and hybrid immunity to SARS-CoV-2

On 25 May 2022, a study was published based on data from the Israeli Ministry of Health from 1 August to 30 September 2021, when B.1.617.2 (Delta) variant was predominant, on all persons who had been previously infected with SARS-CoV-2 or who had received Coronavirus 2019 vaccine referring toBNT162b2.

The study used Poisson regression with adjustment for confounding factors to compare the rates of infection as a function of time since the last immunity-conferring event (vaccination or infection).

In this study, an estimate was made of the incidence of confirmed SARS-CoV-2 infection in cohorts of people 16 years of age and over:

- Previously infected, unvaccinated;
- Previously infected, vaccinated with BNT162b2;
- Not previously infected, vaccinated with BNT162b2. .

For each cohort, the association between the time elapsed since infection or vaccination and the confirmed infection rate was quantified. By comparing infection rates among these groups, it was possible to assess the level of protection provided by hybrid immunity compared with that provided by immunity conferred by vaccination.

The adjusted rate of SARS-CoV-2 infection per 100,000 person-days at risk increased over time since vaccination with BNT162b2 or since previous infection.

The adjusted rate of confirmed infections among recovered, unvaccinated persons four to less than six months after infection was 10.5 per 100,000 person-days at risk (95% CI, 8.8 to 12.4); this rate increased to 30.2 (95% CI, 28.5 to 32.0) among persons in this cohort 12 months or more after infection.

In people who had received a single dose of vaccine less than two months after a previous infection, the adjusted rate was 3.7 (95% CI, 3.1 to 4.5), but increased to 11.6 (95% CI, 10.0 to 13.5) among those who had been vaccinated at

least six months previously. Among previously uninfected people who had received two doses of vaccine, the adjusted rate increased from 21.1 (95% CI, 20.0 to 22.4) among those who had been vaccinated less than two months earlier to 88.9 (95% CI, 88.2 to 89.5) among those who had been vaccinated at least six months earlier.

During the study period, most infections were dominated by the Delta variant, and the analysis provides no information regarding protection against newer variants such as B.1.1.529 (Omicron).

The authors conclude that among persons who had been previously infected with SARS-CoV-2 (regardless of whether they had received any dose of vaccine or whether they had received one dose before or after infection), protection against reinfection decreased as the time increased since the last immunity-conferring event (infection or vaccination); however, this protection was higher than that conferred after the same time had elapsed since receipt of a second dose of vaccine among previously uninfected persons. A single dose of vaccine after infection reinforced protection against reinfection by SARS-CoV-2.

Source: Yair Goldberg et al. Protection and Waning of Natural and Hybrid Immunity to SARS-CoV-2. N Engl J Med 2022; 386:2201–12. DOI: 10.1056/NEJMoa2118946.

U.S. Food and Drug Administration (FDA) Pfizer-BioNTech COVID-19 vaccine authorization for children 12 to 15 years of age

On 7 May 2022, the U.S. Food and Drug Administration (FDA) amended the emergency use authorization (EUA) for the Pfizer-BioNTech COVID-19 vaccine, authorizing the use of a single booster dose (10 µg/0.2 mL) for administration to individuals 5 through 11 years of age at least five months after completion of a primary series with the Pfizer-BioNTech COVID-19 vaccine. On 3 January 2022, the FDA authorized the use of a single booster dose (30 µg/0.3 mL) of the Pfizer-BioNTech COVID-19 vaccine for administration to individuals 12 through 15 years of age.

The authorization was based on safety data from a total of 401 participants ages 5 to 11 who received the booster dose in an extension of the Phase 2/3 trial, C4591007. Immunogenicity (inferred vaccine effectiveness) was assessed by determining SARS-CoV-2 neutralizing antibody titers.

The increase in neutralizing antibody titers caused by the booster dose in children ages 5 to 11 was similar in magnitude to the increase seen with the booster dose in adults. The most frequently reported solicited adverse reactions were injection-site pain (73.9%), fatigue (45.6%), and headache (34.0%). All local and systemic reactions were mild to moderate in severity, with a median onset within two days of vaccination and a median duration of approximately two days after onset. The most frequently reported unsolicited adverse event was lymphadenopathy (2.5%), which occurred within two days of vaccination and had a median duration of six days. No vaccine-related hypersensitivity reactions, myocarditis/pericarditis, anaphylaxis, or serious adverse events or deaths were reported.

Additional information available at:

https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-expands-eligibility-pfizer-biontech-covid-19-vaccine-booster-dose

https://www.fda.gov/media/158575/download

The U.S. Centers for Disease Control and Prevention Strengthens Recommendations and Expands Eligibility for Booster Doses of COVID-19 Vaccines

On 19 May 2022, the U.S. Centers for Disease Control and Prevention (CDC) recommended that:

- Children ages 5 through 11 receive a booster shot of 0.2 mL (10 µg BNT162b2) five months after their initial Pfizer-BioNTech vaccination series.
- People over the age of 12 who are immunocompromised, and those over the age of 50, as previously recommended, receive a second booster dose at least four months after the first booster.
- Regarding the interval between doses of the primary COVID-19 immunization series, the CDC indicates that people between the ages of 5 and 64, and particularly males between the ages of 12 and 39, may consider

receiving a second primary dose of an mRNA vaccine (Pfizer-BioNTech or Moderna; for children aged 5 to 17 years, Pfizer-BioNTech only) eight weeks after the first dose. A longer interval between first and second primary doses can increase the protection offered by these vaccines and further minimize the risk of rare heart problems, including myocarditis and pericarditis.

- People 65 years of age or older, those who are more likely to become severely ill from COVID-19, and those who require increased protection due to high levels of community transmission, should receive a second dose of the primary immunization series of the Pfizer-BioNTech vaccine three weeks after the first dose, or a second dose of the primary immunization series of the Moderna vaccine four weeks after the first dose.
- People who have COVID-19 should wait until they recover and complete their period of isolation before receiving any vaccine, including the COVID-19 vaccine. People who recently had COVID-19 may consider delaying the next dose of vaccine (primary or booster dose) three months from the onset of symptoms or from the date of the first positive diagnostic test, since reinfection is less likely in the weeks or months after infection. However, certain factors, such as personal risk of severe disease, local COVID-19 community level, and the most common COVID-19 variant currently causing illness, could be reasons to get a vaccine sooner rather than later.

Additional information available at:

https://www.cdc.gov/media/releases/2022/s0519-covid-booster-acip.html

https://www.cdc.gov/coronavirus/2019-ncov/vaccines/stay-up-to-date.html#recommendations

CLARIFICATIONS/CONCLUSIONS ON EVENTS PRESENTED IN PREVIOUS COMMUNICATIONS

Interim statement on the use of additional booster doses of Emergency Use Listed mRNA vaccines against COVID-19

On 17 May 2022, WHO, with the support of the Strategic Advisory Group of Experts (SAGE) on Immunization and its COVID-19 Vaccines Working Group, provided an updated interim statement on booster doses for COVID-19 vaccines that have received Emergency Use Listing (EUL). The following is a summary of the Group's report.

- Booster doses should be considered for all EUL COVID-19 vaccines. The optimal interval between completion of a primary series and administration of additional doses has yet to be determined, and depends on epidemiological setting, vaccine product, targeted age groups, background seroprevalence, and circulation and frequency of specific variants of concern (VOCs). However, as a general principle, an interval of four to six months since completion of the primary series could be considered, especially in the context of Omicron.
- Booster doses should be prioritized for higher-risk groups, people who are unable to mount and maintain an adequate immune response, and health care workers, ahead of lower priority-use groups, unless there is sufficient justification for doing otherwise.
- In immunocompromised individuals, the available data suggest that the efficacy and immunogenicity of these vaccines are lower; for these individuals, therefore, WHO has recommended an extended primary series (three doses) and one booster dose (fourth dose) using homologous (same platform) or heterologous (different platform) vaccines.
- With regard to additional booster doses, the only current data are on an additional booster dose (fourth dose) of an mRNA vaccine, based on six studies from Israel[1,2,3,4,5,6] and one study from Canada[7] conducted during the time when the Omicron VOC was the predominant circulating strain worldwide. Taken together, these studies show short-term benefit from an additional booster dose of mRNA vaccine in healthcare workers, people over the age of 60, and immunocompromised individuals.
- Administering an additional booster dose likely comes with considerable programmatic challenges in terms of vaccine delivery in many settings. In those most at risk for severe disease or death (i.e., adults above the age of 60, or those who are not able to mount a full immune response), the added benefit of an additional booster dose of mRNA vaccine might be warranted.
- For longer-term considerations, there are significant uncertainties related to the evolution of the virus and the characteristics of future variants. Given widespread transmission of Omicron globally, and continued viral evolution with the emergence of new variants or sub lineages, development of a pan-SARS-CoV-2 or pan-sarbecovirus vaccine is needed, but the timeframe for their development is uncertain. It may therefore be necessary to update the composition of COVID-19 vaccines to include VOCs that are antigenically distinct, to obtain a broader immune response against circulating and emerging variants, as well as to retain protection against severe disease and death.

- Evidence from the past two years supports the idea of increased transmission of SARS-COV-2 during the winter season. Countries with a winter season should take seasonality into account when updating their vaccination plans.

Both SAGE and the Technical Advisory Group on COVID-19 Vaccine Composition continue to monitor the situation carefully, and the WHO position will be updated accordingly.

Additional information available at: https://www.who.int/news/item/17-05-2022-interim-statement-on-the-use-of-additional-booster-doses-of-emergency-use-listed-mrna-vaccines-against-covid-19.

1. Bar-On YM, Goldberg Y, Mandel M, Bodenheimer O, Amir O, Freedman L et al. Protection by a Fourth Dose of BNT162b2 against Omicron in Israel. New England Journal of Medicine. 2022. DOI: 10.1056/NEJMoa2201570.
2. Magen O, Waxman JG, Makov-Assif M, Vered R, Dicker D, Hernán MA et al. Fourth Dose of BNT162b2 mRNA COVID-19 Vaccine in a Nationwide Setting. N Engl J Med 2022; DOI: 10.1056/NEJMoa2201688.
3. Sivan Gazit, Yaki Saciuk, Galit Perez, Asaf Peretz, Virginia E. Pitzer, Tal Patalon. Relative Effectiveness of Four Doses Compared to Three Dose of the BNT162b2 Vaccine in Israel. 2022.03.24.22272835. DOI: 10.1101/2022.03.24.22272835.
4. Ronen Arbel, Ruslan Sergienko, et al. Effectiveness of a second BNT162b2 booster vaccine against hospitalization and death from COVID-19 in adults aged over 60 years. Nature Medicine. 2020. DOI: 10.1038/s41591-020-0877-5.
5. Matan J Cohen, View ORCID Profile Yonatan Oster, Allon E Mose and et al. Effectiveness of the BNT162b vaccine fourth dose in reducing SARS-CoV-2 infection among healthcare workers in Israel, a multi-center cohort study. 2022.04.11.22273327. DOI: 10.1101/2022.04.11.22273327.
6. Gili Regev-Yochay, Tal Gonen, Mayan Gilboa and et al. Efficacy of a Fourth Dose of COVID-19 mRNA Vaccine against Omicron. New England Journal of Medicine. 2022;386:1377–80. DOI: 10.1056/NEJMc2202542.
7. Grewal R, Kitchen SA, Nguyen L, Buchan SA, Wilson SE, Costa AP and et al. Effectiveness of a Fourth Dose of COVID-19 Vaccine among Long-Term Care Residents in Ontario, Canada. medRxiv. 2022.04.15.22273846. DOI: 10.1101/2022.04.15.22273846.

U.S. Food and Drug Administration authorizes a booster dose of the Pfizer-BioNTech COVID-19 vaccine for certain populations

On 5 May 2022, the U.S. Food and Drug Administration (FDA) reported that once the risk of thrombosis with thrombocytopenia syndrome (TTS) has been assessed after administration of the Janssen COVID-19 vaccine, limiting authorization of its use to persons 18 years and older is warranted:

- with contraindication for receiving mRNA COVID-19 vaccines;

- if, otherwise, they would not be vaccinated against COVID-19 due to limited access to mRNA vaccines;
- for those who want to receive the Janssen COVID-19 vaccine despite identified safety concerns.

The FDA and the U.S. Centers for Disease Control and Prevention (CDC) investigated all suspected cases of TTS reported to the Vaccine Adverse Event Reporting System (VAERS) following administration of the Janssen COVID-19 vaccine through 18 March 2022, and identified 60 confirmed cases, including nine cases resulting in death, equivalent to a TTS reporting rate of 3.23 per million doses administered, and a TTS death reporting rate of 0.48 per million doses administered in the U.S.

The factors considered by the FDA in limiting authorized use of the Janssen COVID-19 vaccine include the following:

- As of 18 March 2022, the rates of reporting and of deaths from TTS following administration of this vaccine were not significantly lower than those previously reported;
- Risk factors for developing TTS following administration of the Janssen COVID-19 vaccine remain unknown;
- TTS can cause debilitating long-term health consequences, and has a high mortality rate;
- There are authorized and approved alternative COVID-19 vaccines available in the country, for which no risk of TTS has been reported.

Additional information available at:

https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-limits-use-janssen-covid-19-vaccine-certain-individuals

https://www.cdc.gov/coronavirus/2019-ncov/vaccines/different-vaccines/janssen.html

Inclusions in the WHO Emergency Use Listing (EUL)

On 19 May 2022, WHO added an eleventh COVID-19 vaccine to the Emergency Use List (EUL). The product description is as follows:

Name	CONVIDECIA COVID-19 [recombinant] vaccine (Ad26.COV2-S)
EUL holder	CanSino Biologics Inc.
Responsible NRA*	National Medical Products Administration (NMPA), China
WHO/EUL recommendation issued	19 May 2022
Platform/Type of vaccine	Viral vector (non-replicating)
Presentation	2 mL / Vial; 1 and 3 doses of 0.5 mL
Pharmaceutical form	Sterile solution for injection
Diluent	None
Shelf life and temperature	12 months, 2°C to 8°C (35° to 46°F)

*The NRA that first authorized the vaccine and that is responsible for supervision of the vaccine.

Additional information available at: https://extranet.who.int/pqweb/vaccines/convidecia.

Decisions of Regulatory Authorities in the Region

Chile

Chile's Institute of Public Health (ISP) updates the AstraZeneca COVID-19 vaccine factsheet

The ISP published the fifth version of AstraZeneca's VAXZEVRIA (ChAdOx1-S, recombinant) COVID-19 vaccine factsheet, with updated information on precautions for use; among them, coagulation disorders (thrombosis with thrombocytopenia syndrome [TTS], cerebral venous sinus, and thrombocytopenia); neurological events; and capillary leak syndrome.

Additional information available at: https://www.ispch.cl/wp-content/uploads/2022/04/FIV-AstrazenecaV05-08042022B.pdf.