Life Cycle | The best science From birth To senescence

eISSN: 2799-8894
Life Cycle 2022;2:e5
https://doi.org/10.54724/lc.2022.e5

State-of-the-Art Review

Vaccine strategy against COVID-19 with a focus on the Omicron and stealth Omicron variants: Life Cycle Committee Recommendations

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Abstract

The Severe Acute Respiratory Syndrome Coronavirus type 2 (SARS-CoV-2), the cause of the pandemic of coronavirus disease 2019 (COVID-19), was first discovered in December 2019 in Wuhan, China, and was consequently transmitted across the world. Further, within a year of its initial discovery, vaccines against SARS-CoV-2 were developed using diverse techniques comprising mRNA-, adenoviral vector-, and recombinant DNA-technology. Researchers have assessed these vaccines in large, placebo-controlled trials and determined them to be both safe and efficient. However, there are several distinct vaccines for SARS-CoV-2 and its variants comprising Alpha, Delta Omicron, and stealth Omicron. Omicron vaccines are available to the public with reasonable safety and scientifically acceptable levels of protective effectiveness for COVID-19. Of clinical significance, it is demanding in clinical practice to precisely interpret the efficiency and the persistence of the distinct vaccines ascribed to the notion that there are no gold methods to assess neutralization levels. In this guideline, our aim is to review vaccine strategies against COVID-19 and its variants for adults, children and adolescents, and pregnant or lactating women.

Keywords: COVID-19; Omicron; Omicron stealth; guideline; vaccination

Received: date: Jan 12, 2022.
Revised date: Feb 24, 2022.
Accepted date: Mar 3, 2022.
Published date: Mar 21, 2022.

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1. Introduction

The Severe Acute Respiratory Syndrome Coronavirus type 2 (SARS-CoV-2) is the cause of the pandemic of coronavirus disease 2019 (COVID-19), first discovered in December 2019 in Wuhan, China and consequently transmitted across the world.[1] The World Health Organization (WHO) confirmed COVID-19 to be a global pandemic by March 2020 and by March 31, 2022, it accounted for more than 483 million confirmed cases and 6.0 million confirmed deaths.[2] Further, within a year of its initial discovery, vaccines against SARS-CoV-2 were developed using diverse techniques comprising mRNA-, adenoviral vector-, and recombinant DNA-technology.[3] Researchers have assessed these vaccines through large, placebo-controlled trials and determined them to be both safe and efficient.[4] In this guideline, we aimed to review vaccine strategies against COVID-19 and its variants for adults, children and adolescents, and pregnant or lactating women. The Interim COVID-19 Immunization Schedule for the Public is shown in Table 1 and Fig. 1.

Table 1. Summary of currently recommended vaccines, numbers of primary and booster doses, and their schedule for different groups as of March 30, 2022.

Product[a]		Individuals who are NOT moderately or severely immunocompromised		Individuals who are moderately or severely immunocompromised	
		Primary series[b]	Booster dose[b]	Primary series[b]	Booster dose[b]
Type of vaccine: mRNA vaccine					
Adults (≥18 years)	Pfizer/BioNTech Ages: 12 years and older (gray cap or purple cap)	Primary 2 doses (30 μg [0.3 mL] each [purple or gray cap]) Separate: Dose 1 and 2 by at least 3-8 weeks.[c]	Booster Dose 1: At least 5 months after Dose 2 (30 μg [0.3 mL]). Booster Dose 2: At least 4 months after the first booster dose (30 μg [0.3 mL]) for individuals 50 years of age and older.	Primary 3 doses. Separate: Dose 1 and 2 by at least 3 weeks. Dose 2 and 3 by at least 4 weeks.	Booster Dose 1: At least 3 months after Dose 3 Booster Dose 2: At least 4 months after the first booster (optional)
	Moderna	Primary 2 doses (100 μg [0.5 mL] each [blue cap]).[c] Separate: Dose 1 and 2 by at least 4-8 weeks.	Booster Dose 1: At least 5 months after Dose 2 (50 μg [0.25 mL] [red cap]). Booster Dose 2: At least 4 months after the first booster dose (50 μg [0.25 mL]).	Primary 3 doses. Separate: Dose 1 and 2 by at least 4 weeks. Dose 2 and 3 by at least 4 weeks.	Booster Dose 1: At least 3 months after Dose 3 Booster Dose 2: At least 4 months after the first booster dose (optional)
Adolescents (12-17 years)	Pfizer/BioNTech Ages: 12 years and older (gray cap or purple cap)	Primary 2 doses (30 μg [0.3 mL] each [purple or gray cap]). Separate: Dose 1 and 2 by at least 3-8 weeks.[c]	Booster Dose 1: At least 5 months after Dose 2 (30 μg [0.3 mL]). Booster Dose 2: At least 4 months after the first booster dose (30 μg [0.3 mL])	Primary 3 doses (30 μg [0.3 mL] each). Separate: Dose 1 and 2 by at least 3 weeks. Dose 2 and 3 by at least 4 weeks.	Booster Dose 1: At least 3 months after Dose 3 Booster Dose 2: At least 4 months after the first booster dose (optional)
	Moderna	Not recommended	Not recommended	Not recommended	Not recommended
Children (5-11 years)	Pfizer/BioNTech Ages: 5-11 years (Orange cap)	Primary 2 doses (10 μg [0.2 mL] each [orange cap]). Separate: Dose 1 and 2 by at least 3 weeks	Not recommended	Primary 3 doses. Separate: Dose 1 and 2 by at least 3 weeks. Dose 2 and 3 by at least 4 weeks.	Not recommended
Young children (6 months -4 years)	Not recommended	Not recommended	Not recommended	Not recommended	Not recommended
Infants (<2 years)	Not recommended	Not recommended	Not recommended	Not recommended	Not recommended
Pregnant women	Pfizer/BioNTech	Primary 2 doses (30 μg [0.3 mL] each [purple or gray cap]) Separate: Dose 1 and 2 by at least 3-8 weeks.	Booster Dose 1: At least 5 months after Dose 2 (30 μg [0.3 mL]).	Not applicable	Not applicable

Table 1. Continued

Product[a]		Individuals who are NOT moderately or severely immunocompromised		Individuals who are moderately or severely immunocompromised	
		Primary series[b]	Booster dose[b]	Primary series[b]	Booster dose[b]
	Moderna	Primary 2 doses (100 μg [0.5 mL] each [blue cap]). Separate: Dose 1 and 2 by at least 4-8 weeks.	Booster Dose 1: At least 5 months after Dose 2 (50 μg [0.25 mL]).	Not applicable	Not applicable
Lactating women	Pfizer/BioNTech	Primary 2 doses (30 μg [0.3 mL] each [purple or gray cap]) Separate: Dose 1 and 2 by at least 3-8 weeks.	Booster Dose 1: At least 5 months after Dose 2 (30 μg [0.3 mL]).	Not applicable	Not applicable
	Moderna	Primary 2 doses (100 μg [0.5 mL] each [blue cap]). Separate: Dose 1 and 2 by at least 4-8 weeks.	Booster Dose 1: At least 5 months after Dose 2 (50 μg [0.25 mL]).	Not applicable	Not applicable
Type of vaccine: Viral vector vaccine					
Adults (≥18 years)	Janssen[d]	Primary 1 dose (5×10^{10} viral particles [0.5 mL]). [b]	Booster Dose 1: At least 8 weeks after Dose 1 (5×10^{10} viral particles/mL [0.5 mL]).[d]	Primary 2 doses (5×10^{10} viral particles/mL [0.5 mL]). Separate: Dose 1 and 2 by at least 28 days[d] Dose 2 MUST be a mRNA vaccine.[d]	Booster Dose 1: At least 8 weeks after Dose 2 (5×10^{10} viral particles/mL [0.5 mL]). [d]
Future plan					
Young children (6 months -4 years)	Pfizer/BioNTech Ages: 6 months -4 years (Maroon cap)	Primary 2 doses (3 μg [0.2 mL] each [maroon cap]). Separate: Dose 1 and 2 by at least 3 weeks	Not recommended	Primary 3 doses. Separate: Dose 1 and 2 by at least 3 weeks. Dose 2 and 3 by at least 4 weeks.	Not recommended

[a] Administer Moderna or Pfizer-BioNTech COVID-19 Vaccine only, which are allowed under Emergency Use Instructions (EUI) for this dose. Janssen COVID-19 Vaccine is not under EUI for this dose.

[b] Administer doses as close as possible to the recommended interval. It is not necessary to restart the series if the dose is given after the recommended interval; Administer the appropriate COVID-19 vaccine product based on the recipient's age; COVID-19 vaccines may be administered on the same day as other vaccines. If multiple vaccines are administered at a single visit, administer each in a separate injection site; Complete the primary series using the same product. Every effort should be made to determine which vaccine product was received as the first dose. If the vaccine product previously administered cannot be determined or is no longer available, any age-appropriate mRNA COVID-19 vaccine product may be administered at least 28 days after the first dose; and a different COVID-19 vaccine product than the primary series may be administered. An mRNA COVID-19 vaccine is preferred.

[c] An 8 week interval may be optimal for some people, including males 12-39 years of age because of the small risk of myocarditis associated with mRNA COVID-19 vaccines. Vaccine effectiveness may also be increased with an interval longer than 3 (or 4 depending on document) weeks. See Interim Clinical Considerations for COVID-19 Vaccines (link below) for detailed information.

[d] mRNA COVID-19 vaccines are preferred over the Janssen COVID-19 Vaccine for all vaccine-eligible people. However, the Janssen COVID-19 vaccine may be offered in some situations. For male adults with a history of myocarditis or pericarditis, a Janssen vaccine can be considered.

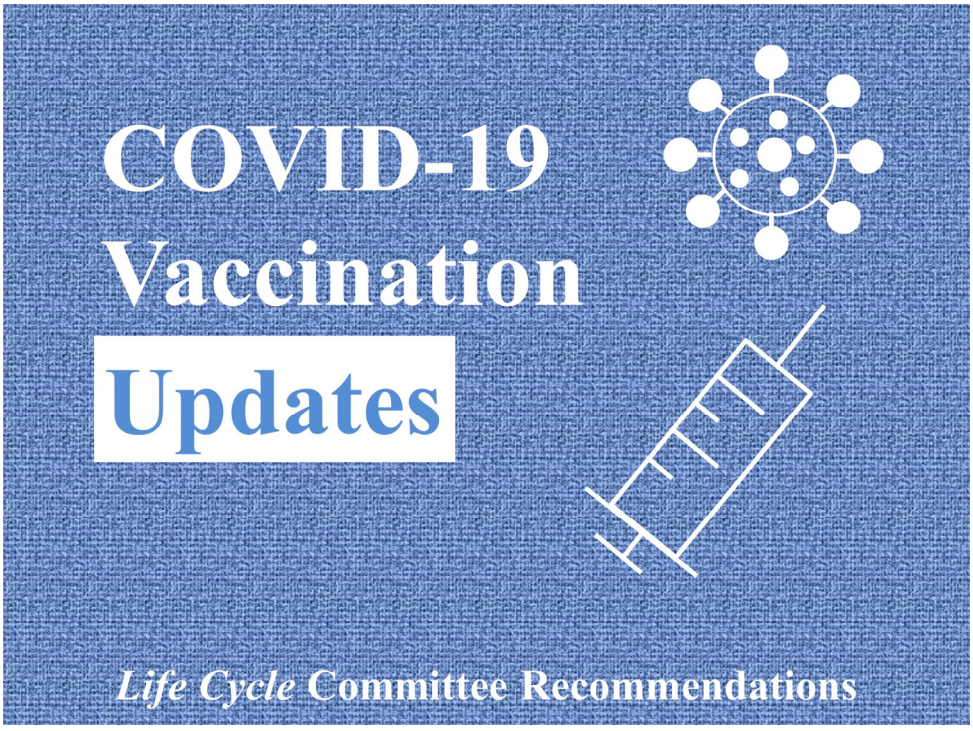

Fig. 1. Vaccine strategy against COVID-19 with a focus on the Omicron and stealth Omicron variants: Life Cycle Committee Recommendations

2. Vaccine strategies against COVID-19 and its variants

Considering the compliance and adaptability of immunogen arrangement and large-scale production, the mRNA vaccine platform has its preference as a pandemic-reaction project.[4] Soon after the SARS-CoV-2 genetic sequence was reported in January 2020, mRNA-1273, a lipid-nanoparticle-encapsulated mRNA vaccine expressing the pre-fusion-stabilized spike glycoprotein, was established by Moderna and the Vaccine Research Center at the National Institute of Allergy and Infectious Diseases by the National Institutes of Health [5], and was proven to be effective with two doses 28 days apart.[4] Further studies have indicated that they are also effective in binding and the development of neutralizing antibodies and angiotensin-converting enzyme 2-competing antibodies against spike mutants from SARS-CoV-2 variants (i.e., B.1.1.7 [Alpha], B.1.351 [Beta], P.1 [Gamma], B.1.429 [Epsilon], B.1.526 [Iota], B.1.617.2 [Delta], and B.1.1.529 [Omicron]).[6]

With the Omicron variant (B.1.1.529) originating from Botswana, and becoming the dominant variant at an astonishingly faster rate than the other variants, rising concerns have

emerged that the various vaccines currently in use may be less effective in protecting against the novel variant.[7, 8] Further, recent data on the Omicron variant has shown that it is more immunologically far from the original SARS-CoV-2 vaccine strain than the previous most distant strains, namely, Beta and Delta.[9] Besides this observation, studies have shown that the mRNA vaccine had decreased neutralization effects against the Omicron variant, but still had significant neutralization effects for this novel variant.[10, 11] In addition, a recently published paper reported that primary vaccination with two doses of ChAdOx1-S (AstraZeneca) adenoviral vector or BNT162b2 (Pfizer/BioNTech) mRNA vaccine yielded low effectiveness against symptomatic disease induced by the Omicron variant.[12] They also showed that BNT162b2 (Pfizer/BioNTech) or mRNA-1273 (Moderna) booster after either ChAdOx1-S (AstraZeneca) or BNT162b2 (Pfizer/BioNTech) primary dose significantly increased protection against the Omicron variant; however, that protection declined over time.[12] Corresponding with this finding, recent studies have demonstrated that an mRNA booster is critical in neutralizing the Omicron variant.[13, 14] In coping with the Omicron variant, Pfizer/BioNTech has stated that they could produce Omicron specialized vaccines in April 2022.[15] Further, Moderna has been developing a more effective vaccine against the new variant and stated that it could be completed with examination and fit to be available with the regulators on a similar timescale.[15] The vaccines derived from the Omicron would seemingly need only two doses to obtain efficiency for the variant.[16] Until the novel vaccines for the Omicron are available in the market, an mRNA booster shot may be the only option. Even after the novel vaccines for Omicron are developed, it would be a great economic and societal burden for underdeveloped countries in the sense that they would still have to provide their citizens with new vaccines for the Omicron variant when a great portion of them have not even had out-of-date vaccines.[16]

3. Identification of stealth Omicron sublineage BA.2

The Omicron sublineage BA.2 was originally discovered in November 2021 in Australia by a subject who traveled to South Africa.[17] This sublineage does not have the full set of polymorphisms characteristics of BA.1 (B.1.1.529) and has increased mutations exclusively observed in BA.2. One critical difference between BA.2 and BA.1 is that sublineage BA.2 has a defect in the spike gene deletion in the region ciphering amino acid 69/70, which indicates that it will not be identified by the S Gene Target Failure (SGTF) assay, which is used as a surrogate marker for the Omicron Variant of Concern.[17] Hence, it is frequently specified as the stealth Omicron variant.

4. Vaccine strategies against COVID-19 and its variants for pregnant or lactating women

Although there are public concerns about administering mRNA COVID-19 vaccines to pregnant or lactating women, studies on pregnant[18, 19] or lactating[20] women have shown its safety and effectiveness. Further evidence has suggested the trans-placental transmission of SARS-CoV-2 antibodies following maternal COVID-19 vaccination during the third trimester and the presence of SARS-CoV-2 antibodies in breast-milk sampling, thus demonstrating that

maternal vaccination may yield protection to the neonate via placenta and breast-milk to a certain degree.[20, 21] Much to our regret, there have been no studies regarding the efficacy of mRNA vaccines in pregnant or lactating women regarding the Omicron variant.

5. Vaccine strategies against COVID-19 and its variants for children

Although there are debates over whether children should be vaccinated against COVID-19,[22] studies have shown that a COVID-19 vaccination regimen comprising two 10 microgram of Pfizer/BioNTech administered 21 days apart can be safe and effective in inducing an immune response in children aged 5-11 years, the same dose of Pfizer-BioNTech COVID-19 vaccine as adults for those aged 12-15 years, and those aged 16 years and older.[23] Everyone aged 12 years and older can receive the Pfizer-BioNTech COVID-19 booster shot at least 5 to 6 months after completing their Pfizer-BioNTech COVID-19 primary series.[24]

6. Conclusions

So far, several distinct vaccines for SARS-CoV-2 and its variants comprising Alpha, Delta, and Omicron are available to the public with reasonable safety and scientifically acceptable levels of protective effectiveness for COVID-19. We speculate that further research results are warranted in terms of the competence of mRNA vaccines for the Omicron variant. Of clinical significance, it is demanding in clinical practice to precisely interpret the efficiency and persistence of the distinct vaccines due to the fact that there are no gold methods to assess neutralization levels. Further, we speculate that more scientific research is needed to determine efficient ways to promote novel COVID-19 vaccines that will provide effectiveness for the newly discovered Omicron variant and possibly more to come in order to keep the globe a safe place from this catastrophic virus.

Capsule Summary

This guideline of Life Cycle Committee summarizes vaccine strategies against COVID-19 and its variants for adults, children and adolescents, and pregnant or lactating women.

Author contribution

Dr LS, JIS, and AK contributed to the preparation of this review. Life Cycle Committee (Dong Keon Yon [Kyung Hee University] and Youn Ho Shin [CHA University] approved the final version before submission.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Competing interests

The authors have no conflicts of interest to declare for this study.

Provenance and peer review

Not commissioned; externally peer reviewed.

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