

COVID19 VACCINATION FOR COUPLES UNDERGOING FERTILITY TREATMENT

A Guidance Document for Clinicians

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Philippine Society for Reproductive Medicine in collaboration with the Philippine Infectious Diseases Society for Obstetrics and Gynecology and the Philippine Society of Allergy, Asthma and Immunology¹

1. CAN COUPLES UNDERGO FERTILITY TREATMENT DURING THE COVID-19 PANDEMIC? WHAT OPTIONS DO THEY HAVE?

Yes, provided that the options for fertility treatment are discussed. Before starting fertility treatment, the physician and the couple should consider:

- Postponing pregnancy until community transmission is controlled OR
- Proceeding with fertility treatment together with risk mitigation and seek COVID-19 vaccination as soon as possible. Consider local resources for managing COVID19 infection which may complicate a pregnancy, should the fertility treatment be successful.

There should be a full explanation of the benefits and risks of fertility treatment prior to its commencement. Postponing, however, may not be ideal for women who have low ovarian reserve. Thus, if a couple is convinced that the benefit outweighs the risks of COVID 19 infection, then fertility treatment can be pursued.¹

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2. SHOULD THE COUPLE RECEIVE COVID-19 VACCINATION BEFORE TRYING TO CONCEIVE?

Yes. Although there is still limited data on the effect of COVID-19 vaccines in women undergoing assisted reproductive technique and in pregnancy, current evidence is reassuring with regards its safety during conception. ^{2,3} In contrast, available data on COVID infection in pregnant women suggest that symptomatic pregnant and recently pregnant patients with COVID-19 are at increased risk of more severe illness compared with their nonpregnant peers. These women have a higher likelihood of intensive care unit admission, a greater need for mechanical ventilation and ventilatory support (like extracorporeal membrane oxygenation), and are at a bigger risk of dying. Nonetheless, the absolute risk for severe disease is low.⁴ Women who became inadvertently pregnant while participating in COVID19 vaccine trials did not show any increased rates of miscarriage over comparable controls (Table 1).

Table 1. Accidental pregnancies in trials for the COVID-19 vaccines approved in the United Kingdom (Table adapted from Male 5,6)

			FOR OBSTETRICS AND G	YNECOLOGY, INC.		
VACCINE TYPE	Control			Vaccinated		
	Participants	Pregnancies	Miscarriages (Rate)	Participants	Pregnancies	Miscarriages (Rate)
PFIZER/BIONTECH	18,846	12	1 (8%)	18,860	11	0 (0%)
MODERNA	15,170	7 ANI A 1994	1 (14%)	15,181	6	0 (0%)
ASTRAZENECA	5,829	9	3 (33%)	5,807	12	2 (17%)
JANSSEN (J&J)	21,895	4	1 (25%)	21,888	4	1 (25%)
CORONAVAC (SINOVAC)		No d	lata available f	rom primary so	urce	

The locally available Sinovac-CoronaVac (COVID-19) vaccine is an inactivated vaccine and its adjuvant has a well-known safety profile. The World Health Organization likewise recommends use of this vaccine even among pregnant women when the benefits outweigh the potential risks.⁷ Thus, all women should be encouraged to have vaccination against COVID19 before attempting conception. However, assisted reproductive technique should not be denied to couples who opt out of vaccination or are living in areas where the vaccine is not available.²



3. CAN COUPLES START FERTILITY TREATMENT RIGHT AWAY AFTER RECEIVING COVID 19 VACCINATION?

Yes. All COVID-19 vaccines are not live virus vaccines, hence there is no need to postpone conception for those who have received or completed it, unlike live vaccines (e.g. MMR and varicella) which require a 28-day interval between vaccination and attempting conception.⁷

4. IS ROUTINE TESTING FOR PREGNANCY NECESSARY BEFORE RECEIVING THE COVID-19 VACCINATION?

No. Routine testing is not recommended since women trying to become pregnant do not need to avoid pregnancy after receiving a COVID-19 vaccine.³

5. WILL FEMALE OR MALE FERTILITY BE AFFECTED BY COVID-19 VACCINATION?

No. There is no current evidence that COVID-19 vaccination negatively affects fertility or cause sterility for either men or women.^{8, 9} Semen parameters^{10,11}, assisted reproductive technique outcomes (among these are follicular function measured by steroidogenesis, follicular response to the LH/hCG trigger, and oocyte quality biomarkers, number of oocytes retrieved, number of metaphase II (M2) oocytes produced, fertilization rate, clinical pregnancy rate)^{12,13} and pregnancy outcomes^{3, 5,14} in COVID-19 vaccinated couples show no difference compared with those without COVID-19 vaccination.

6. CAN A COUPLE RECEIVE COVID-19 VACCINATION WHILE UNDERGOING FERTILITY TREATMENT (EGG OR SPERM COLLECTION, OVULATION INDUCTION, INTRA-UTERINE INSEMINATION, IN VITRO FERTILIZATION, FRESH OR FROZEN EMBRYO TRANSFER)?

Yes, they can. However, to avoid cancellation of procedures due to the adverse effects of vaccination, it is advised to schedule oocyte retrieval, embryo transfer, intrauterine insemination and any other procedure more than 3 days after receiving the vaccine. Conversely, so as not to confuse the adverse effects of the fertility procedure with the effects of the vaccine, it is also advisable to wait at least 3 days after the procedure before receiving the vaccine.⁸

Sperm collection should be done more than 7 days after receiving the vaccine to prevent post vaccination reactions from affecting the collection.¹⁵



7. SHOULD WOMEN WITH A HISTORY OF RECURRENT MISCARRIAGES POSTPONE THEIR COVID-19 VACCINATION?

No. There is no reason to postpone receiving Covid-19 vaccinations among women who have a history of recurrent miscarriages because current data do not demonstrate that vaccination increases the risk of having another miscarriage. COVID-19 vaccination is recommended for women who are contemplating pregnancy or who are pregnant in order to minimize risks to themselves and their pregnancy.^{5,13}

8. CAN WOMEN WITH APAS AND/OR OTHER IMMUNE DISORDERS CAUSING MISCARRIAGE RECEIVE COVID-19 VACCINATION?

Yes. To date, there are no data preventing women with recurrent miscarriage due to antiphospholipid antibody syndrome (APAS) or other autoimmune diseases such as lupus, rheumatoid arthritis, thyroiditis, and psoriasis, from receiving COVID vaccines, even ChAdOx1 type of vaccines.^{16,17}

According to the Society of Thrombosis and Haemostasis Research (GTH), there is no indication in the use of routine pharmacologic thromboprophylaxis to prevent atypically located thrombosis resulting

from an immunological response possibly attributed to the ChAdOx1 (Astra Zeneca NCoV-19) vaccine.¹⁸

Note:

This document intends to provide guidance to clinicians who are deciding on the course of action to take for their patients based on current available evidence and expert recommendations. As with all clinical situations, individualized assessment is necessary.

For recommendations for vaccination in pregnancy, please refer to the POGS Practice Bulletin No. 1 (COVID19 Vaccination of Pregnant and Breastfeeding Women, 2nd update August 1, 2021) at https://pogsinc.org/practice-bulletins/

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⁴ ACOG Practice Advisory: COVID-19 Vaccination Considerations for Obstetric–Gynecologic Care. (July 2, 2021). Available through https://www.acog.org/clinical/clinical-guidance/practice-

advisory/articles/2020/12/covid-19-vaccination-considerations-for-obstetric-gynecologic-

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 ⁷ WHO team. (June 10, 2021). Update on WHO Interim recommendations on COVID-19 vaccination of pregnant and lactating women. Available through https://www.who.int/publications/m/item/update-on-who-interim-recommendations-on-covid-19-vaccination-of-pregnant-and-lactating-women.

⁸ Statement from the ASRM COVID-19 Task Force Apr 20, 2021. ASRM Press Release: ASRM Patient management and clinical recommendations during the coronavirus (covid-19) pandemic.

⁹ Morris, R. S. (2021). SARS-CoV-2 spike protein seropositivity from vaccination or infection does not cause sterility. F&s Reports.

¹⁰ Gonzalez, D. C., Nassau, D. E., Khodamoradi, K., Ibrahim, E., Blachman-Braun, R., Ory, J., & Ramasamy, R. (2021). Sperm Parameters Before and After COVID-19 mRNA Vaccination. JAMA.

¹¹ Safrai, M., Reubinoff, B., & Ben-Meir, A. (2021). BNT162b2 mRNA Covid-19 vaccine does not impair sperm parameters. medRxiv

¹² Safrai, M., Rottenstreich, A., Herzberg, S., Imbar, T., Reubinoff, B., & Ben-Meir, A. (2021). Stopping the misinformation: BNT162b2 COVID-19 vaccine has no negative effect on women's fertility. medRxiv.

¹³ Bentov, Y., Beharier, O., Moav-Zafrir, A., Kabessa, M., Godin, M., Greenfield, C., ... & Klement, A. H. (2021). Ovarian follicular function is not altered by SARS-Cov-2 infection or BNT162b2 mRNA Covid-19 vaccination. medRxiv.

¹⁴ Bowman, C. J., Bouressam, M., Campion, S. N., Cappon, G. D., Catlin, N. R., Cutler, M. W., ... & Lindemann, C. (2021). Lack of effects on female fertility and prenatal and postnatal offspring development in rats with BNT162b2, a mRNA-based COVID-19 vaccine. Reproductive Toxicology, 103, 28-35

¹⁵ The British Fertility Society and Association of Reproductive and Clinical Scientists (BFS & ARCS) on COVID 19 vaccines and fertility version 2.1(July 26, 2021). Available through https://www.britishfertilitysociety.org.uk/wp-content/uploads/2021/07/Covid19-Vaccines-FAQ-2.1.pdf.

¹⁶ Xie, C., Vincent, L., Chadwick, A., & Peschl, H. (2021). COVID-19 vaccine induced prothrombotic immune thrombocytopenia. European Heart Journal.

¹⁷ Talotta, R., & Robertson, E. S. (2021). Antiphospholipid antibodies and risk of post-COVID-19 vaccination thrombophilia: The straw that breaks the camel's back?. Cytokine & Growth Factor Reviews.

¹⁸ Oldenburg, J., Klamroth, R., Langer, F., Albisetti, M., von Auer, C., Ay, C., ... & Greinacher, A. (2021). Diagnosis and management of vaccine-related thrombosis following AstraZeneca COVID-19 vaccination: guidance statement from the GTH. Hämostaseologie.

¹ Ory, S., Veiga, A., Horton, M., & Gianaroli, L. (2021). Joint IFFS/ESHRE statement on COVID-19 vaccination for pregnant women and those considering pregnancy. Human Reproduction Open, 2021(2), hoab016.

² ESHRE COVID 19 working group. (June 8, 2021). COVID-19 vaccination and assisted reproduction – update June 2021. Available through https://www.eshre.eu/Europe/Position-statements/COVID19.

³ Shimabukuro, T. T., Kim, S. Y., Myers, T. R., Moro, P. L., Oduyebo, T., Panagiotakopoulos, L., ... & Meaney-Delman, D. M. (2021). Preliminary findings of mRNA Covid-19 vaccine safety in pregnant persons. New England Journal of Medicine, 384(24), 2273-2282.

care?utm_source=redirect&utm_medium=web&utm_campaign=int.

 ⁵ Male, V. (2021). Are COVID-19 vaccines safe in pregnancy?. Nature Reviews Immunology, 21(4), 200-201.
 ⁶ Male, V. (July 27, 2021) Explainer on COVID19 vaccination, fertility, pregnancy and breastfeeding.