



# Covid-19 and Vaccines in Pregnancy

**SBRA**  
SOCIEDADE BRASILEIRA DE  
REPRODUÇÃO ASSISTIDA

# Covid-19 and Vaccines in Pregnancy

## SUMMARY

1. Types of vaccines
2. Vaccines during pregnancy
3. Vaccines against Covid-19
4. Repercussions on the pregnant woman and the fetus
5. Position of international medical societies
6. Sars-CoV-2 (Covid-19), vaccines, assisted reproduction and pregnant women  
(Position of the Brazilian Society for Assisted Reproduction – SBRA and REDLARA)

## 1. Types of vaccines

### What is immunization?

Immunization is a set of therapeutic methods aiming to give the body a state of resistance, that is, immunity against certain infectious diseases.

There are two types of immunization: passive and active.

#### Passive immunization

It is called serum, or human immunoglobulin. Passive immunization is achieved by administering previously formed antibodies (immunoglobulins).

Passive immunization indication:

- Patients with defects in antibody formation.
- Immunodepressed individuals (who have low immunity).
- Those who have not been immunized (such as children who are not yet old enough to receive a certain vaccine).
- Individuals who have any contraindications to the vaccine, being susceptible to the disease.

The serum provides emergency and temporary protection for a risky situation but does not offer an immunity memory. If the person later has again contact with that infectious agent, he/she may become infected and become ill.

### **Active immunization**

These are called vaccines. They can protect against one or more of a disease and can be made from:

- Pieces of microorganisms.
- Dead microorganisms.
- Live attenuated (weakened) microorganisms.
- Inactivated living microorganisms.
- Proteins of the microorganism.

Vaccines aim to simulate what would be a “weak disease” so that our body has time to produce antibodies and already have the defense built in case it ever comes into contact with the real infectious agent, preventing it from making us ill.

This immunity brings a memory that can be for a lifetime or decrease with time, requiring boosters, depending on the vaccine.

### **Live attenuated virus vaccine**

- They are made of live viruses that have undergone procedures that have weakened them.
- They have a higher risk of causing adverse effects.
- Its adverse effects may occur later (5 to 20 days after the vaccine).
- The adverse effects are more similar to that of wild disease, although milder.
- The immune response to a live attenuated virus vaccine can interfere with another of the same type.

- They are contraindicated for pregnant women and people with low immunity.
- They suffer interference from specific immune cells. That is why people who receive immunoglobulins, serums, whole blood, etc., should wait 3 to 11 months before receiving a vaccine of this type.

#### **Examples of live attenuated virus vaccines:**

- BCG.
- Dengue.
- Yellow fever.
- Herpes zoster.
- Oral polio.
- Rotavirus.
- Tetra viral (measles, mumps, rubella and chickenpox).
- Viral trivalent (measles, mumps and rubella).
- Chickenpox.

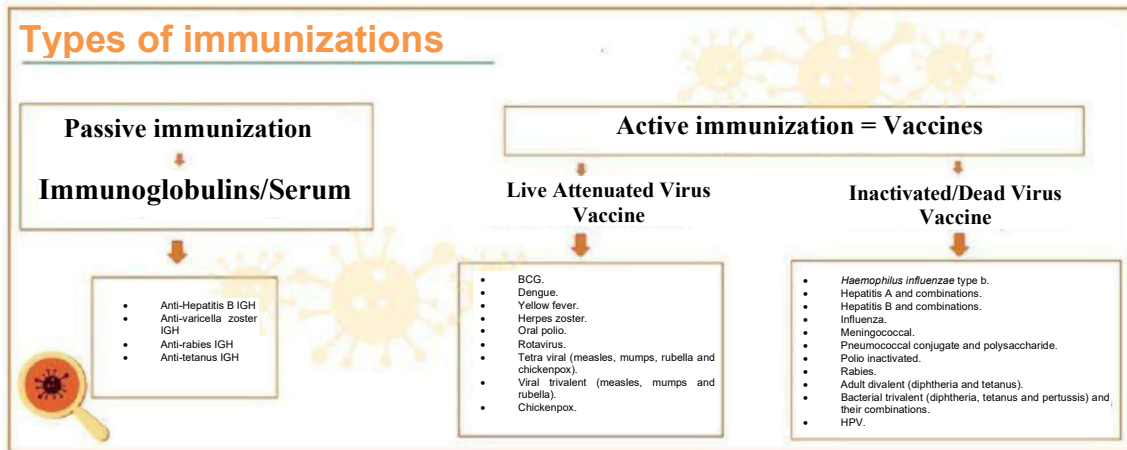
#### **Inactivated or killed virus vaccines**

- They are composed of whole viruses that are not alive, or just part of those viruses.
- Adverse events are usually early, 24 to 48 hours after vaccination.
- Since these viruses are not able to multiply, these vaccines are not capable of producing disease.
- Adverse effects are related to an inflammatory response, such as pain, swelling, heat or redness at the application site.
- They usually need several applications to be able to generate a lasting response.
- The response of one vaccine does not interfere with the other and, therefore, can be applied without a minimum interval between them or at the same time.
- Can be used on pregnant women or immunocompromised people.

#### **Examples of inactivated or killed virus vaccines**

- Adult divalent (diphtheria and tetanus).
- *Haemophilus influenzae* type b.
- Hepatitis A and combinations.
- Hepatitis B and combinations.
- Influenza.
- Meningococcal.
- Pneumococcal conjugate and polysaccharide.
- Polio inactivated.

- Rabies.
- Bacterial trivalent (diphtheria, tetanus and pertussis) and their combinations.
- HPV.



## 2. Vaccines in pregnancy

### Recommended vaccines

#### *Influenza (flu)*

The flu vaccine is one of the most important during pregnancy. In addition to immunizing against the flu virus, it also protects against more severe conditions with pneumonia, since the risk of pneumonia in pregnant women is greater due to the decrease in immunity. The flu vaccine is the only one that can be taken at any time during pregnancy. It should be applied even if the woman has already been vaccinated in the previous pregnancy.

**Moment to get it:** the dose of the influenza vaccine can be prescribed any month of pregnancy or up to 45 days after the baby is born for those who have not taken it during the 9 months, in a single dose. If the pregnant woman suspects flu, she should start treatment as soon as possible.

#### **H3 bacterial trivalent (DTPa-diphtheria, tetanus and pertussis)**

The adult bacterial trivalent vaccine (DTPa) protects against pertussis, tetanus and diphtheria. Pertussis is the fifth leading cause of death in children, being especially severe in babies up to 6 months. Tetanus is a disease known in the prenatal period due to contamination of the umbilical cord. Diphtheria is a disease that can cause respiratory obstruction, with a high mortality rate among newborns.

**Moment to get it:** The pregnant woman must take this vaccine between 27 and 36 weeks, since any immunizing agent takes 7 to 15 days to develop antibodies in the individual. It is essential that the mother received the vaccine on due time, so that there is time to create and transmit the antibodies to the fetus. If born prematurely, the baby will have received protection from the mother.

### **Hepatitis B**

The disease does not present well-defined symptoms, but the person who manifests it may experience vomiting, muscle pain, nausea and malaise (symptoms pertinent to other complications as well). Infection during pregnancy is a common route of transmission, so it is important to prevent the mother from becoming infected and transmitting it to the fetus or newborn.

Vaccination against hepatitis B is also very important. In the case of perinatal transmission, almost 25% of infected children will develop chronic liver disease. Babies can die of hepatocellular carcinoma (a type of cancer that affects the liver) or cirrhosis.

Vaccination against hepatitis B is on the official children's calendar and those taking the three doses, in general, are already protected for life. However, it is important for women, even before becoming pregnant, to be sure whether or not they have already been vaccinated. If she has not taken all three doses (or is not sure about that), she should undergo disease serology to make sure she is immunized.

**Moment to get it:** hepatitis B vaccine should be administered in three doses, preferably from the second trimester of pregnancy. If the pregnant woman has been vaccinated before, there is no need for booster.

## **Vaccines recommended in special situations**

### **Hepatitis A and hepatitis A and B**

As in Brazil situations of risk of exposure to the hepatitis A transmitting agent are frequent, vaccination should be considered. In addition, as it is an inactivated vaccine, it has no contraindication.

### **Pneumococcal**

The sequential scheme of pneumococcal vaccines can be performed in pregnant women at risk for invasive pneumococcal disease.

### **Conjugated meningococcal ACWY and meningococcal B**

In this case, the epidemiological situation is considered, which varies from region to region.

### **Yellow fever**

It is usually contraindicated for pregnant women. However, in situations where the risk of infection outweighs the potential risks of vaccination, it can be done during pregnancy.

### **Contraindicated for pregnant women**

Pregnant women cannot take live virus and bacteria vaccines, as is the case of the viral trivalent – against measles, mumps and rubella – varicella (chickenpox), yellow fever and BCG (against tuberculosis). These vaccines are made from **live** and attenuated viruses or bacteria (in the case of BCG). So, there is a risk, even if it is low, of the pregnant woman, who already has the immunity altered due to pregnancy, to develop the disease.

### **Viral trivalent (measles, mumps and rubella)**

The viral trivalent vaccine cannot be taken by pregnant women, but it can be applied during the puerperium and during breastfeeding.

<b>RECOMMENDED</b>	<b>RECOMMENDED IN SPECIAL SITUATIONS</b>	<b>CONTRAINDICATED</b>
Influenza/flu	Hepatitis A and hepatitis A + B	Viral trivalent (measles/mumps/rubella)
Trivalent DTPa (diphtheria/tetanus/pertussis)	Pneumococcal/meningococcal	Varicella (chicken pox)
Hepatitis B	Yellow fever	HPV
		Yellow fever
		BCG (tuberculosis)
		Dengue

### **HPV and varicella (chickenpox)**

They can also only be applied during the puerperium and during breastfeeding.

### **Dengue**

This is contraindicated not only for pregnant women, but also during breastfeeding.

**References:**

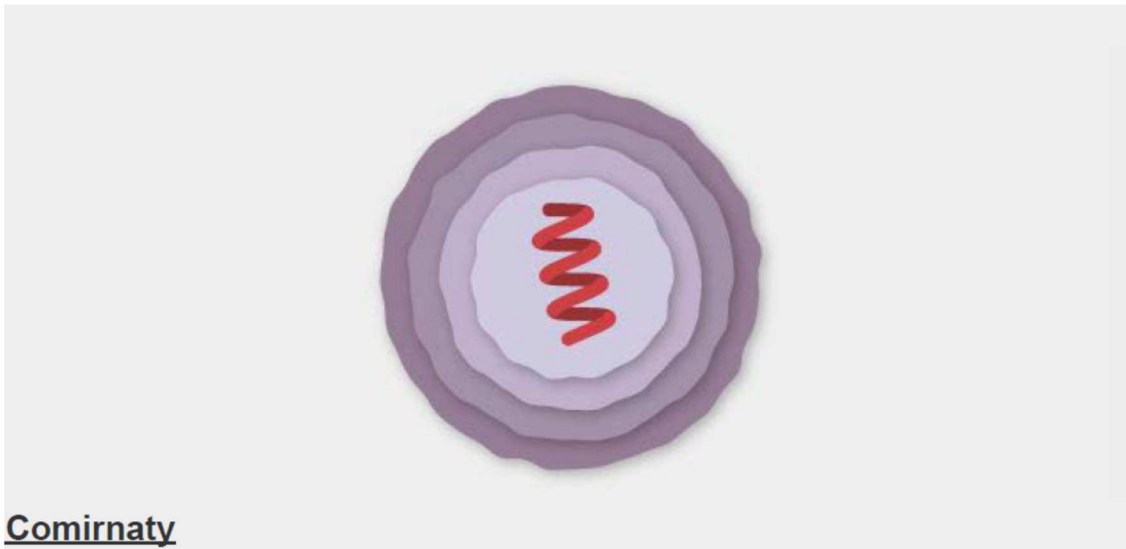
Programa vacinal para mulheres. Ed. rev. atual. São Paulo: Federação Brasileira das Associações de Ginecologia e Obstetrícia; 2019. 172 p. (Série Orientações e Recomendações FEBRASGO n. 2/ Comissão Nacional Especializada de Vacinas).

ACOG Committee Opinion. Maternal immunization. Am J Obstetr Gynecol 741, 2018.

### **3. Covid-19 vaccines**

Vaccines typically require years of research and testing before reaching the clinic, but in 2020, scientists embarked on a race to produce safe and effective coronavirus vaccines in record time. The researchers are currently testing **65 vaccines** in human clinical trials, and 20 of them have reached the final stages of testing. At least 85 preclinical vaccines are under active investigation in animals.

#### **Vaccines with messenger RNA**







**BIONTECH**

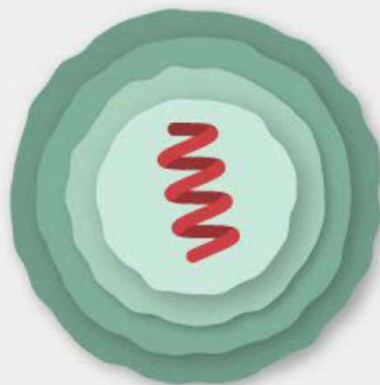
VACCINE NAME: Comirnaty (also known as  
tozinameran or BNT162b2)

EFFICACY: 95%

DOSE: **2 doses, 3 weeks apart**

TYPE: **Muscle injection**

STORAGE: **Freezer storage only at -94°F (-70°C)**



mRNA-1273

moderna



VACCINE NAME: [mRNA-1273](#)

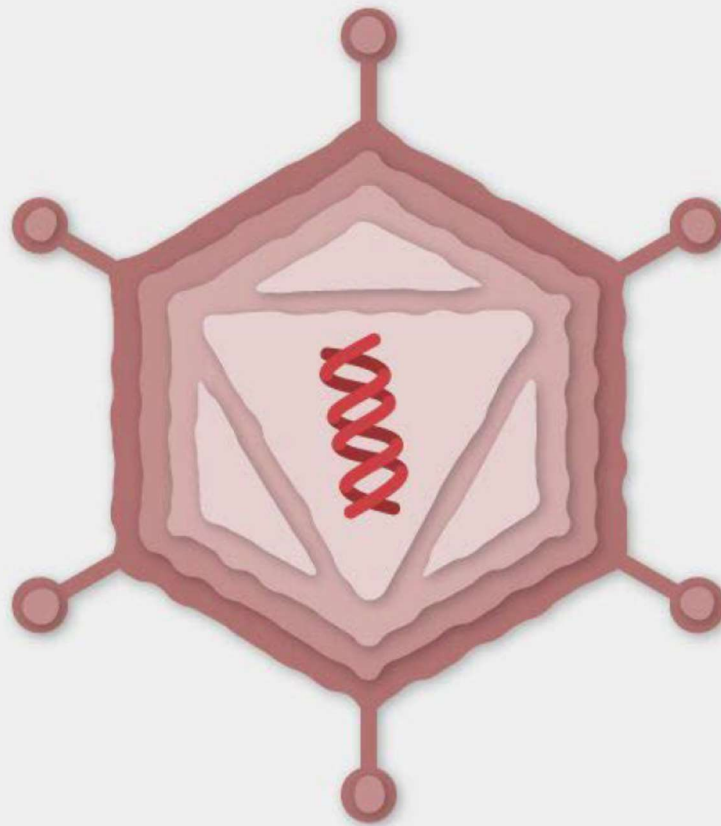
EFFICACY: [94.5%](#)

DOSE: **2 doses, 4 weeks apart**

TYPE: **Muscle injection**

STORAGE: **30 days with refrigeration, 6 months at -4°F (-20°C)**

## Adenovirus vaccines



**AZD1222**



UNIVERSITY OF  
**OXFORD**

**AstraZeneca** 

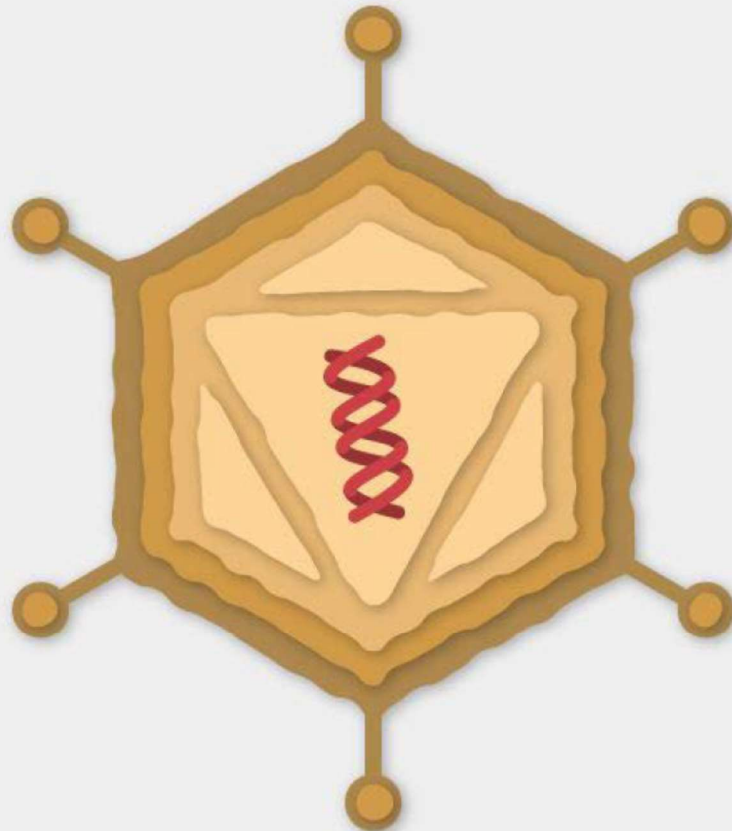
**VACCINE NAME: AZD1222 (also known as Covishield in India)**

**EFFICACY: 62% to 90%, depending on the dosage**

**DOSE: 2 doses, 4 weeks apart**

**TYPE: Muscle injection**

**STORAGE: Stable in refrigerator for at least 6 months**



**Ad26.COV2.S**

**Johnson & Johnson**

Beth Israel Lahey Health   
Beth Israel Deaconess Medical Center

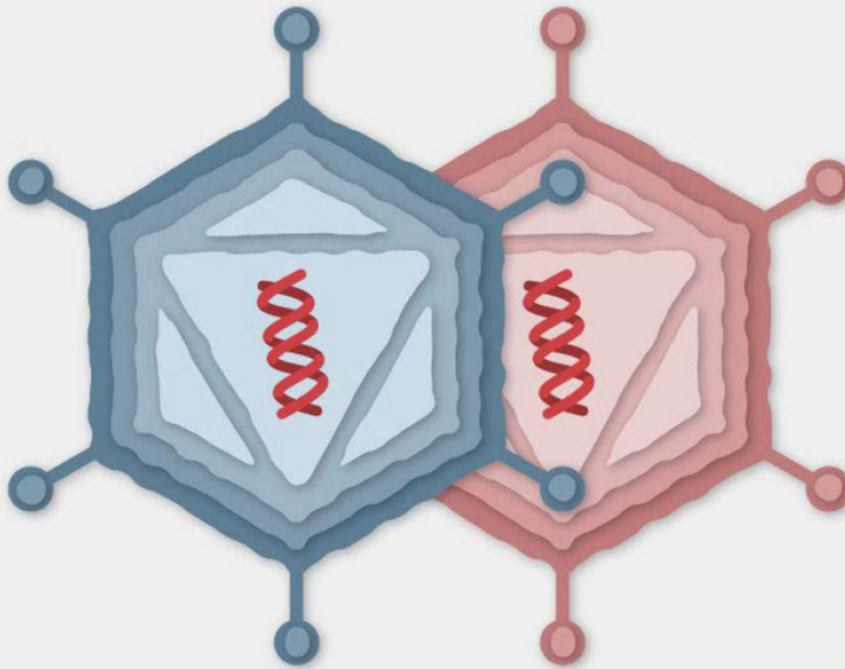
VACCINE NAME: Ad26.COV2.S

EFFICACY: Unknown

DOSE: 1 dose

TYPE: Muscle injection

STORAGE: Up to two years frozen at  $-4^{\circ}\text{F}$  ( $-20^{\circ}\text{C}$ ), and up to three months refrigerated at  $36-46^{\circ}\text{F}$  ( $2-8^{\circ}\text{C}$ ).



Sputnik V (Ad5)

Sputnik V (Ad26)



**МИНИСТЕРСТВО  
ЗДРАВООХРАНЕНИЯ  
РОССИЙСКОЙ ФЕДЕРАЦИИ**

**Gamaleya Research Institute**

VACCINE NAME: Sputnik V (also known as Gam-Covid-Vac)

EFFICACY: 91.4%

DOSE: 2 doses, 3 weeks apart

TYPE: Muscle injection

STORAGE: Freezer storage. Developing an alternative formulation that can be refrigerated.

## Protein vaccines



NVX-CoV2373  
nanoparticle

# NOVAVAX

Creating Tomorrow's Vaccines Today

VACCINE NAME: NVX-CoV2373

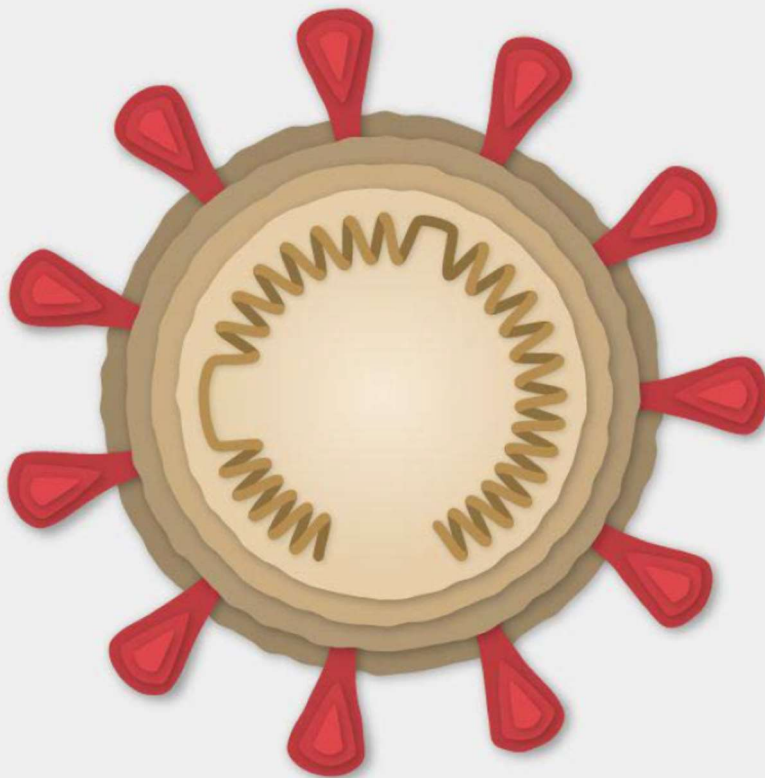
EFFICACY: **Unknown**

DOSE: 2 doses, 3 weeks apart

TYPE: **Muscle injection**

STORAGE: **Stable in refrigerator.**

## Inactivated coronavirus vaccines



**BBIBP-CorV**

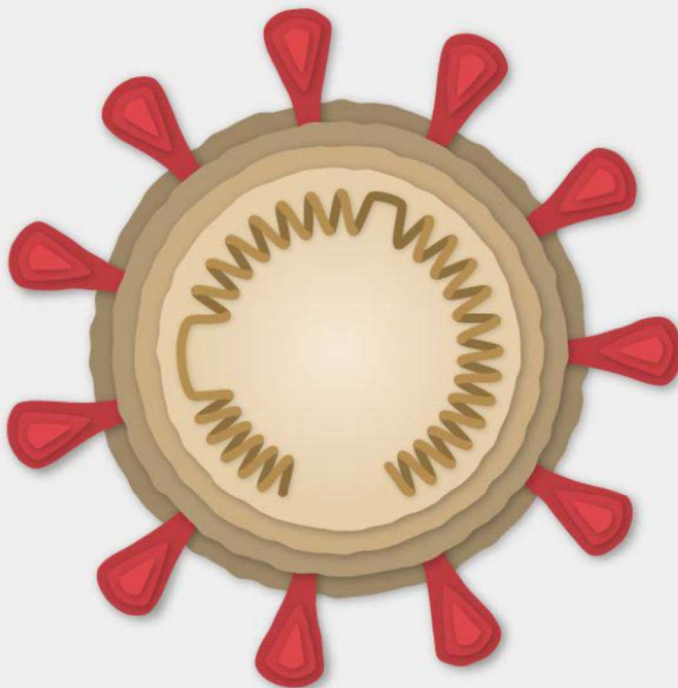


VACCINE NAME: **BBIBP-CorV**

EFFICACY: **79.34%**

DOSE: **2 doses, 3 weeks apart**

TYPE: **Muscle injection**



CoronaVac



# sinovac

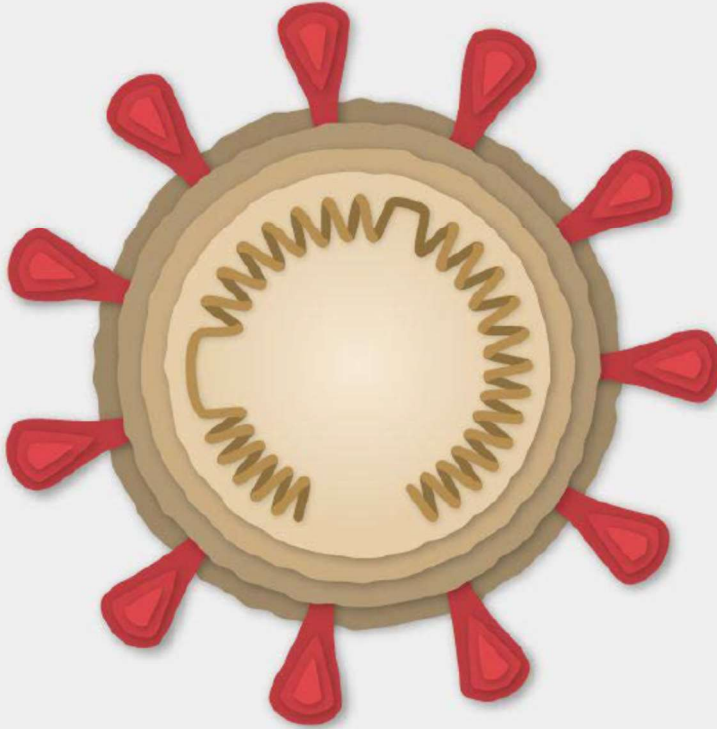
VACCINE NAME: CoronaVac (formerly PiCoVacc)

EFFICACY: Less than 78 percent

DOSE: 2 doses, 2 weeks apart

TYPE: Muscle injection

STORAGE: Refrigerated



Covaxin












VACCINE NAME: Covaxin (also known as BBV152 A, B, C)









EFFICACY: Unknown

DOSE: 2 doses, 2 weeks apart

STORAGE: At least a week at room temperature

## Main vaccines

Developer	How it works	Stage	Status
  Pfizer-BioNTech	mRNA	23	Approved in Saudi Arabia and other countries. Emergency use in the USA, the EU and other countries.
 Moderna	mRNA	3	Emergency use in the USA, the EU and other countries.
 Gamaleja	Ad26, Ad5	3	Initial use in Russia. Emergency use in Belarus and other countries.
  Oxford-AstraZeneca	ChAdOx1	23	Emergency use in Great Britain, India and other countries.
 CanSino	Ad5	5	Use limited to China.

 Johnson &			
 Johnson	Ad26		3
 Vector	Protein		3 Initial use in Russia.
Institute			
 Novavax	Protein		3
Approved in China, UAE and Bahrain.			
 Sinopharm	Inactivated		3 Emergency use in Egypt.
Use limited to China, Indonesia and Pakistan.			
 Sinovac	Inactivated		3
 Sinopharm-	Inactivated		3 Use limited to China and UAE.
Wuhan			
 Bharat	Inactivated		3 Emergency use in India.
Biotech			

## 4. Repercussions on pregnant women and fetuses

***Reproduced from THE ROYAL COLLEGE OF MIDWIVES and THE ROYAL COLLEGE OF OBSTETRICIANS AND GYNECOLOGISTS***

***October 14<sup>th</sup>, 2020***

Most pregnant women infected with Sars-CoV-2 will experience only mild or moderate cold/flu symptoms.

The systematic review of PregCOV-19 Living to date has included more than 11,000 pregnant women worldwide with suspected or confirmed Covid-19 (reported before June 26<sup>th</sup>, 2020).

In this review, the most common symptoms of Covid-19 in pregnant women were fever (40%) and cough (39%). The less frequent symptoms were dyspnea, myalgia, loss of taste and diarrhea, each present in more than 10% of women.

Pregnant women with Covid-19 were less likely to have a fever or myalgia than non-pregnant women of the same age.

A significant proportion of pregnant women with Covid-19 may be asymptomatic: an estimated 74% (95% CI 51-93) are asymptomatic, based on studies that reported universal screening for a total of 162 pregnant women.

### **Serious disease in pregnant women**

Severe symptoms, suggesting pneumonia and marked hypoxia, are more common in the elderly, immunosuppressed people and people with chronic diseases, such as diabetes, cancer or chronic lung disease.

Serious disease, such as one that requires admission to the intensive care unit (ICU), is relatively uncommon in young women of reproductive age.

In the United Kingdom's National Intensive Care Research and Audit Center report of patients admitted from the first reported case in the United Kingdom to 31 August 2020, a total of 70 women who were currently or recently (within 6 weeks) pregnant were admitted to intensive care, representing 8.9% of all 785 women admitted aged 16-49 years.

Serious disease appears to be more common in late pregnancy. In the UKOSS study, most women were hospitalized in the third trimester or peripartum (n = 342, 81%). The median gestational age at hospital admission was 34 + 0 weeks of pregnancy (interquartile range [IQR] 29-38 weeks of pregnancy).

Likewise, an analysis of women in French hospitals showed that women in the second half of pregnancy, after 20 weeks of pregnancy, were five times more likely to be admitted to the ICU than in the first half of pregnancy.

In the analysis of the PregCOV-19 Living Systematic Review Consortium, 73/11 580 women with confirmed Covid-19 were registered as having died of any cause, and 16/1935 women required ECMO (extracorporeal membrane oxygenation – a device that works as a lung and heart).

The MBRRACE-UK consortium published an expedited report on maternal deaths in the UK between March and May 2020. During that period, nine women died during pregnancy or in the immediate postpartum period (6 weeks postpartum) and one woman died during the prolonged postpartum period (up to 1 year).

Of these ten women, seven died from Covid-19, in one the cause of death was undetermined, but it was thought to be probably related to Covid-19, and two died from unrelated causes. It is not clear at this point whether the pandemic will result in a statistically significant impact on the overall maternal mortality rate in the UK.

### **Effect on pregnancy**

Maternal Covid-19 is associated with an approximately three times greater risk of premature delivery. A systematic review estimated the risk at approximately 17%. Most of these premature births (94%) were iatrogenic. In the UKOSS study, 58% of women gave birth during the data collection period; the median gestational age at birth was 38 weeks (IQR 36–39 weeks).

Of the women who gave birth, 27% had premature births: 47% of these were iatrogenic for maternal impairment and 15% were iatrogenic for fetal impairment.

### **Risk factors for hospitalization with Covid-19 during pregnancy**

Risk factors that appear to be associated with both infection and hospitalization with Covid-19 include:

1. Black, Asian and minority ethnic origin.
2. Being overweight (BMI 25-29 kg/m<sup>2</sup>) or obese (BMI 30 kg/m<sup>2</sup> or more).
3. Pre-pregnancy comorbidity, such as pre-existing diabetes and chronic hypertension.
4. Maternal age of 35 years or more.
5. Living in areas or families with greater socioeconomic deprivation.

In the PregCOV-19 Living Systematic Review, the association estimates were: for the age of 35 or older, OR 1.78 (95% CI 1.25–2.55); for BMI of 30 kg/m<sup>2</sup> and above, OR 2.38 (95% CI 1.67–3.39); for chronic hypertension, OR 2.0 (95% CI 1.14–3.48); and for pre-existing diabetes, OR 2.51 (95% CI 1.31–4.80).

## **Covid-19 effect on the fetus**

For Covid-19, there was no significant increase reported in the incidence of congenital anomalies. In the PregCOV-19 Living Systematic Review, there was no evidence of an increase in stillbirths or neonatal deaths among women with Covid-19, although there was insufficient evidence available to comment on the risk of miscarriage.

There has also been no evidence to date that fetal growth restriction (FGR) is a consequence of Covid-19; however, this is considered a theoretical possibility, as two thirds of pregnancies with SARS were affected by FGR.

For babies born to women with Covid-19, the overall results are positive, with more than 95% of newborns included in a systematic review reported as being born in good condition. In the UKOSS study, 10% of babies born at term in the UK, children of women with Covid-19, were admitted to the neonatal unit. Six (2.5% of the total) babies tested positive for Sars-CoV-2 during the first 12 hours after birth; three of these babies were born by caesarean section and one required admission to a neonatal unit.

A large New York study also reported reassuring neonatal results during the pandemic. Of 1,481 births overall, 116 (8%) mothers (giving birth to 120 newborns) tested positive for Sars-CoV-2. All 120 newborns were tested at 24 hours of life and none were positive for Sars-CoV-2. Of the 79 neonates who were repeated using the Sars-CoV-2 polymerase chain reaction test at the age of 5 to 7 days (follow-up rate of 66%), all evolved with a negative test; 72 neonates were also tested at 14 days of life and, again, none were positive. None of the neonates showed signs of Covid-19.

## **References**

Walker KF, O'Donoghue K, Grace N, et al. Maternal transmission of Sars-CoV-2 to the neonate, and possible routes for such transmission: a systematic review and critical analysis. *BJOG* 2020;127(11):1324-36.

Salvatore CM, Han JY, Acker KP, et al. Neonatal management and outcomes during the Covid-19 pandemic: an observation cohort study. *Lancet Child Adolesc Health* 2020;4(10):721-27.

Docherty AB, Harrison EM, Green CA, et al. Features of 20 133 UK patients in hospital with covid-19 using the ISARIC WHO Clinical

Characterisation Protocol: prospective observational cohort study. *BMJ* 2020;369:m1985.

Public Health England. Covid-19: investigation and initial clinical management of possible cases 2020 [Available from: <https://www.gov.uk/government/publications/wuhan-novel-coronavirus-initial-investigation-of-possible-cases/investigation-and-initial-clinical-management-of-possible-cases-of-wuhannovel-coronavirus-wn-cov-infection>] Accessed 2020 Mar 2.

Allotey J, Stallings E, Bonet M, et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. *BMJ* 2020;370:m3320.

Guan W-j, Ni Z-y, Hu Y, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. *NEMJ* 2020; 382:1708-1720.

ICNARC. Report on Covid-19 in critical care 2020 [updated 25 September 2020. Available from: <https://www.icnarc.org/Our-Audit/Audits/Cmp/Reports>] Accessed 2020 Sep 28.

Knight M, Bunch K, Vousden N, et al. Characteristics and outcomes of pregnant women admitted to hospital with confirmed Sars-CoV-2 infection in UK: national population-based cohort study. *BMJ* 2020;369:m2107.

Badr DA, Mattern J, Carlin A, et al. Are clinical outcomes worse for pregnant women at  $\geq 20$  weeks' gestation infected with coronavirus disease 2019? A multicenter case-control study with propensity score matching. *Am J Obstet Gynecol* 2020 Jul 27 [Epub ahead of print]

Ellington S, Strid P, Tong VT, et al. Characteristics of Women of Reproductive Age with Laboratory-Confirmed Sars-CoV-2 Infection by Pregnancy Status - United States, January 22-June 7, 2020. *MMWR Morb Mortal Wkly Rep* 2020;69(25):769-75.

Liu Y, Chen H, Tang K, et al. Clinical manifestations and outcome of Sars-CoV-2 infection during pregnancy. *J Infect* 2020 Mar 5 [Epub ahead of print]

Nakamura-Pereira M, Andreucci CB, de Oliveira Menezes M, et al. Worldwide maternal deaths due to Covid-19: A brief review. *Int J Gynaecol Obstet* 2020;151(1):148-50.

MBRRACE-UK. Rapid report: Learning from Sars-CoV-2-related and associated maternal deaths in the UK. 2020 [Available from: [https://www.npeu.ox.ac.uk/assets/downloads/mbrrace-uk/reports/MBRRACE-UK\\_Maternal\\_Report\\_2020\\_v10\\_FINAL.pdf](https://www.npeu.ox.ac.uk/assets/downloads/mbrrace-uk/reports/MBRRACE-UK_Maternal_Report_2020_v10_FINAL.pdf)] Accessed 2020 Sep 28.

Williamson EJ, Walker AJ, Bhaskaran K, et al. Factors associated with Covid-19-related death using OpenSAFELY. *Nature* 2020;584(7821):430-36.

Knight M, Bunch K, Tuffnell D, et al. Saving Lives, Improving Mothers' Care 2019 [Available from: <https://www.npeu.ox.ac.uk/downloads/files/mbrrace-uk/reports/MBRRACE-UK%20Maternal%20Report%202019%20-20WEB%20VERSION.pdf>] Accessed 2020 Jul 10.

Office for National Statistics. Coronavirus (Covid-19) related deaths by ethnic group, England and Wales: 2 March 2020 to 10 April 2020 [Available from: <https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/articles/coronavirusrelateddeathsbyethnicgroupenglandandwales/2march2020to10april2020>] Accessed 2020 May 11.

Khunti K, Singh AK, Pareek M, et al. Is ethnicity linked to incidence or outcomes of covid-19? *BMJ* 2020;369:m1548.

Pal BR, Marshall T, James C, et al. Distribution analysis of vitamin D highlights differences in population subgroups: preliminary observations from a pilot study in UK adults. *J Endocrinol* 2003;179(1):119-29.

Marik PE, Kory P, Varon J. Does vitamin D status impact mortality from Sars-CoV-2 infection? *Med Drug Discov* 2020; 6:100041.

Mitchell F. Vitamin D and Covid-1: do deficient risk a poorer outcome? *The Lancet Diabetes Endocrinol* 2020; 8:570.

Grant WB, Lahore H, McDonnell SL, et al. Evidence that Vitamin D Supplementation Could Reduce Risk of Influenza and Covid-19 Infections and Deaths. *Nutrients* 2020; 12:988.

National Health Service. Vitamin D 2017 [Available from: <https://www.nhs.uk/conditions/vitaminsand-minerals/vitamin-d/>] Accessed 2020 Jun 1.

National Institute for Health and Care Excellence. Vitamin D: supplement use in specific population groups. Public Health Guideline 56. London; NICE:2017.

Royal College of Obstetricians & Gynaecologists. Vitamin D in Pregnancy: Scientific Impact Paper No. 43. London; RCOG:2014.

Schwartz DA, Graham AL. Potential Maternal and Infant Outcomes from Coronavirus 2019-nCoV (Sars-CoV-2) Infecting Pregnant Women: Lessons from Sars, MERS, and Other Human Coronavirus Infections. *Viruses* 2020; 12:194.

Alserehi H, Wali G, Alshukairi A, et al. Impact of Middle East Respiratory Syndrome coronavirus (MERS-CoV) on pregnancy and perinatal outcome. *BMC Infect Dis* 2016; 16:105.

## **Considerations**

There are several other publications that go against the cited findings.

The repercussion for the fetus, vertical transmission and increased morbidity for pregnancy do not seem to be significantly increased in the pregnant woman.

In a recent study published by Cour Freiesleben et al., Maternal Sars-CoV-2 infection had no effect on the thickness of the nuchal translucency and there was no significant increase in the risk of pregnancy loss for women with Sars-CoV-2 infection in the first trimester of pregnancy.

These data indicate that infection with Sars-CoV-2 in non-hospitalized women does not pose a significant threat in first trimester pregnancies.

In another Canadian study, recently published by Madjunkov et al., data reported in pregnant women, although limited, suggest that Covid-19 symptoms and disease severity during pregnancy are similar to those in non-pregnant women, with pregnancy outcomes closely related to the severity of maternal illness.

Thus, the worst morbidity seems to be related to risk factors such as diabetes, hypertension, obesity, old age, immunocompromised patients, with respiratory problems and a higher risk of exposure to Covid-19.



## References

Madjunkov et al. Journal of Ovarian Research (2020) 13:140. doi: 10.1186/s13048-020-00737-1.

Cour Freiesleben et al. Hum Reprod (2021) 36 (1) 40–47. doi :10.1093/humrep/deaa311

Centers for Disease Control and Prevention. Covid-19 (coronavirus disease): people with certain medical conditions. Available at : <https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html> . Retrieved December 11, 2020.

[www.thelancet.com/infection](http://www.thelancet.com/infection) Published online August 11, 2020  
[https://doi.org/10.1016/S1473-3099\(20\)30638-1](https://doi.org/10.1016/S1473-3099(20)30638-1)

Maru S, Patil U, Carroll-Bennett R, et al. Universal screening for sars-cov-2 infection among pregnant women at Elmhurst Hospital Center, Queens, New York. PLoS One. 2020;15:e0238409. Available at <https://www.ncbi.nlm.nih.gov/pubmed/33301498>.

Allotey J, Stallings E, Bonet M, et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: Living systematic review and meta-analysis. BMJ. 2020;370:m3320. Available at <https://www.ncbi.nlm.nih.gov/pubmed/32873575>.

Money D. Canadian surveillance of covid-19 in pregnancy: Epidemiology, maternal and infant outcomes. Report #1: Released December 2nd, 2020early release: Maternal and infant outcomes (March 1, 2020 to September 30, 2020) from three Canadian provinces 2020. Available at [https://med-fom-ridresearch.sites.olt.ubc.ca/files/2020/12/CANCOVID-Preg-report-1-BC-AB-ON-data\\_02DEC2020-V2.pdf](https://med-fom-ridresearch.sites.olt.ubc.ca/files/2020/12/CANCOVID-Preg-report-1-BC-AB-ON-data_02DEC2020-V2.pdf).

Zambrano LD, Ellington S, Strid P, et al. Update: Characteristics of symptomatic women of reproductive age with laboratory-confirmed sars-cov-2 infection by pregnancy status - united states, January 22–october 3, 2020. MMWR Morb Mortal Wkly Rep. 2020;69:1641-7. Available at <https://www.ncbi.nlm.nih.gov/pubmed/33151921>

## 5. Position of some international medical societies



**Version 1:** Published 12 January 2021

Vaccination against Covid-19 is only offered to two groups of pregnant women:

1. Those with high-risk medical conditions (clinically extremely vulnerable) who are at an increased risk of serious Covid-19 disease.

Medical conditions are:

- organ transplantation;
- cancer treatment;
- bone marrow or stem cell transplantation in the last 6 months;
- significant lung condition, e.g., cystic fibrosis or severe asthma;
- conditions that significantly increase the risk of infection, e.g., severe combined immunodeficiency (SCID) or homozygous sickle cell disease;
- use of drugs to suppress the immune system enough to increase the risk of infection;
- conditions that affect the spleen, including prior removal;
- Down syndrome;
- significant kidney conditions and/or on dialysis;
- significant heart disease; or

- your doctor thinks there are other reasons why you may have a more serious disease if you develop Covid-19
2. Health or social care assistants – who are at very high risk of Covid-19.

## **COVID-19 vaccination and assisted reproduction**

*Statement from the ESHRE COVID-19 Working Group  
Date of publication: 12 January 2021  
Last update: 12 January 2021*



### **Should men and women receive the vaccine against Covid-19 before trying conception?**

There is a lack of information about the possible effect of vaccination against Covid-19 in the treatment of assisted reproduction or future pregnancy. The drug information for the vaccine Moderna Comirnaty and Covid-19 states that animal studies “do not show any harmful effects on pregnancy”. However, data during pregnancy are reported as “very limited”, without knowledge about breastfeeding. As a result, ESHRE cannot make recommendations as to whether men and women trying to conceive through assisted reproduction should receive the vaccine before starting treatment.

For women with comorbidities, which put them at greater risk for Covid-19 and/or complications in pregnancy, encouraging vaccination before attempting conception should be considered. The same applies to women in whom the risk of exposure to Sars-CoV-2 infection is high and cannot be avoided.

ESHRE recommends that men and women living in countries where the vaccine is not available or who have chosen not to be vaccinated should not be prevented from having access to assisted reproduction treatments.

### **Should couples who received Covid-19 vaccination postpone conception and, if so, for how long?**

There are different points of view regarding the need to postpone conception after vaccination. It seems prudent to delay the start of assisted reproduction treatments (sperm collection, ovarian stimulation, embryo transfer) for at least a few days after the completion of the vaccination (i.e., after the second dose) to allow time for the immune response to establish. In the absence of information about the effect of the Covid-19 vaccine on oocytes and sperm, embryo implantation and early stages of pregnancy, and to allow time for the development of antibodies, a more cautious approach could be considered (i.e. postponing start of treatment for up to 2 months).

Assisted reproduction treatments should not be started in women who have had any significant side effects from vaccination against Covid-19 (as an allergic reaction) and until they are considered fit for pregnancy by their doctor.

### **Should pregnant women be vaccinated?**

As stated in previous ESHRE guidance documents, pregnant patients with Covid-19 are at a higher risk of more serious disease than non-pregnant women. Vaccines against diseases such as tetanus, pertussis and influenza have been described as safe during pregnancy. However, the safety of Covid-19 vaccines in human pregnancy has not been evaluated so far.

For the Moderna Comirnaty and Covid-19 vaccine, the decision on its use in pregnant women should be made in close consultation with a healthcare professional after considering the individual benefits and risks.

Similar advice is provided on the administration of the Oxford/AstraZeneca vaccine (ChAdOx1-Sars-CoV-2), recently authorized in the UK, during pregnancy and breastfeeding.

Pregnant women should be informed about the lack of long-term human studies on vaccination against Covid-19, but should not be excluded from vaccination programs.



AMERICAN SOCIETY FOR REPRODUCTIVE MEDICINE (ASRM)  
PATIENT MANAGEMENT AND CLINICAL RECOMMENDATIONS DURING THE  
CORONAVIRUS (COVID-19) PANDEMIC

**UPDATE No. 11 – COVID-19 Vaccination**  
***December 16, 2020***

The task force does not recommend suspending the vaccine for patients planning to become pregnant, who are pregnant or breastfeeding. These recommendations are in line with those of the Advisory Committee on Immunization Practices (ACIP) of the US Centers for Disease Prevention and Control (CDC), the American College of Obstetricians and Gynecologists (ACOG) and the Society of Maternal-Fetal Medicine (SMFM).

- Patients undergoing fertility treatment and pregnant patients should be encouraged to receive vaccination based on the eligibility criteria. Since the vaccine is not a live virus, there is no reason to delay pregnancy attempts due to its administration or to delay treatment until the second dose is administered.
- A decision-making model shared between patients and healthcare providers should be used when considering vaccination and should take into account the ethical principles of autonomy, beneficence and non-maleficence. Consideration of local Covid-19 transmission and acquisition risk, personal risk of contracting Covid-19, risks of Covid-19 for the patient and potential risks to the fetus, vaccine efficacy and known side effects, and the lack of data on the vaccine during pregnancy should be taken into account when patients make decisions about vaccination. Some individuals may choose to delay conception attempts until both doses of the vaccine have been administered.
- Recent studies have suggested that pregnancy is a risk factor for severe Covid-19. In addition, many women who are pregnant or planning to become pregnant have additional risk factors, such as obesity, hypertension or diabetes, which can further increase the chance of serious Covid-19 disease. These considerations should be included in vaccination decisions.



AMERICAN SOCIETY FOR REPRODUCTIVE MEDICINE (ASRM) PATIENT  
MANAGEMENT AND CLINICAL RECOMMENDATIONS DURING THE  
CORONAVIRUS (COVID-19) PANDEMIC

**UPDATE No. 12 – January 18<sup>th</sup>, 2021**  
**Testing and Vaccine Truths**

- Since Covid-19 mRNA vaccines are not composed of live viruses, they are not believed to cause an increased risk of infertility, pregnancy loss in the first or second trimester, stillbirth or congenital anomalies.

The latest update of the task force demystifies some points for patients willing to conceive or pregnant women and include:

- Available data indicate that Covid-19 vaccines do not cause infertility in women or men.
- The vaccine does not induce an immune reaction against placental sicitin-1 protein (which mediates placental cell fusion).
- In mRNA vaccines, as soon as the protein is synthesized, it is degraded in the muscle cells at the injection site, **not** crossing the placental barrier.
- Immunization against Covid-19 is recommended for women who are planning to become pregnant or who are pregnant, in order to minimize the risks to themselves and their pregnancies.

## Vaccinating Pregnant and Lactating Patients Against COVID-19

Practice Advisory 

December 2020

- Vaccines currently available in the USA have not been tested on pregnant women. Therefore, there is no specific safety data for its use in pregnancy.
- Pregnancy testing should not be a requirement before receiving any US approved Covid-19 vaccine.
- Pregnant patients who refuse vaccination should be supported in their decision. Regardless of their decision to receive the vaccine or not, these conversations provide an opportunity to remind patients about the importance of other preventive measures, such as hand washing, physical distance and wearing a mask.
- The expected side effects should be explained as part of patient counseling, including that they are a normal part of the body's reaction to the vaccine and develop antibodies to protect against Covid-19 disease.
- mRNA vaccines are not live virus vaccines, nor do they use an adjuvant to increase their efficacy. These vaccines do not enter the core and do not alter the human DNA of those immunized. As a result, mRNA vaccines cannot cause any genetic changes.



### SOGC Statement on COVID-19 Vaccination in Pregnancy

Version Date: December 18<sup>th</sup>, 2020

### **Consensus statement:**

For individuals who are at high risk of Covid-19 infection and/or morbidity, it is the position of the SOGC that the documented risk of not receiving the Covid-19 vaccine outweighs the theorized and non-described risk of being vaccinated during pregnancy or during breastfeeding and vaccination should be offered.

### **Sars-CoV-2 and the impact on pregnancy**

Most pregnant women infected with Sars-CoV-2 will have mild to moderate symptoms and many can be asymptomatic. However, Canadian and international data from large studies covering multiple jurisdictions demonstrate that approximately 8-11% of pregnant women will require hospitalization for Covid-19-related morbidity and between 2-4% of pregnant women will need admission to an intensive care unit (ICU). Compared to non-pregnant women with Covid-19, pregnant women are at higher risk for invasive ventilation and mortality equivalent to peers of the same age. The risk of severe Covid-19 morbidity in pregnant women appears to be associated with risk factors, including age  $\geq$  35 years, asthma, obesity, hypertension, pre-existing heart disease and diabetes.

SOGC Statement on Covid-19 Vaccination in Pregnancy. Poliquin V, Castillo E, Boucoiran I, Watson H, Yudin M, Money D, Van Schalkwyk, Elwood, C on behalf of the Infectious Disease Committee of the Society of Obstetricians and Gynaecologists of Canada. Disponível em:  
[https://sogc.org/common/Uploaded%20files/Latest%20News/SOGC\\_Statement\\_COVID-19\\_Vaccination\\_in\\_Pregnancy.pdf](https://sogc.org/common/Uploaded%20files/Latest%20News/SOGC_Statement_COVID-19_Vaccination_in_Pregnancy.pdf) . Access: 01/30/2021.





## SARS-Cov-2 (Covid-19): vaccines, assisted reproduction and pregnant women

- Joint current position •



Major advances in collaborative studies today include at least 85 preclinical vaccines in active animal research, 65 in human clinical trials, with 20 vaccines that have reached the final stages of testing, 12 of which are already in use in different countries/situations. The main vaccines available are composed of messenger RNA particles (Pfizer-BioNTech and Moderna), inactivated virus (CoronaVac, Sinopharma and Covaxin, Bharat Biotech), with adenovirus (Oxford-AstraZeneca, Johnson & Johnson and Sputnik V, Gamaleya).



The pandemic continues, and at this time the discussion is centered on the use of available vaccines and on patients undergoing assisted reproduction techniques, pregnant women and populations at risk among pregnant women. Our companies, also evaluating the guidelines issued by global companies such as ESHRE, ASRM, IFFS and ACOG (SOGC), consider that, within the possible availability:



1 - Vaccination is effective and does not induce an increased risk of contracting Covid-19 infection. Although there are still no long-term human studies on Covid-19 vaccination and pregnancy, none of the vaccines contain live SARS-CoV-2 viruses.



2 - For vulnerable individuals, who are at high risk of infection and/or morbidity by Covid-19, among which are pregnant women, not receiving the vaccine outweighs the risk of being vaccinated, either before or during pregnancy. This group also includes health professionals and those in the front line who are at greatest risk of exposure.



3 - There is no reason to delay pregnancy attempts or assisted reproduction treatments if the vaccine is not available or in the case of patients outside the risk group.

4 - Decisions regarding the use (or not) of vaccines must be shared between patients and doctors, respecting the ethical principles of autonomy, beneficence and non-maleficence.



5 - This vaccine information should be included as a specific item in an existing informed consent.

6 - Updates will follow, whenever new knowledge support the current data.

**REDCLARA – Red Latinoamericana de Reproducción Asistida**  
**SBRA – Sociedade Brasileira de Reprodução Assistida**  
**SAMeR - Sociedad Argentina de Medicina Reproductiva**  
**AMMR – Asociación Mexicana de Medicina de la Reproducción**  
**PRONÚCLEO – Associação Brasileira de Embriologistas em Medicina Reprodutiva**  
**SAEC – Sociedad Argentina de Embriología Clínica**  
**SOCMER - Sociedad Chilena de Medicina Reproductiva**  
**ACCERH – Asociación de Centros Colombianos de Reproducción Humana**  
**SURH – Sociedad Uruguaya de Reproducción Humana**  
**AVEMERE – Asociación Venezolana de Medicina Reproductiva y Embriología**  
**FEBRASGO - Federação Brasileira das Associações de Ginecologia e Obstetrícia**  
**SBRH – Sociedade Brasileira de Reprodução Humana**

#### References:

American Society for Reproductive Medicine (ASRM). Patient management and clinical recommendations during the Coronavirus (COVID-19) pandemic. Statement from ASRM Coronavirus/COVID-19 Task Force (the “Task Force”). Update No. 11 – COVID-19 Vaccination, December 16, 2020. Disponível em: <https://www.asrm.org/globalassets/asrm/asrm-content/news-and-publications/covid-19/covidtaskforceupdate11.pdf>. Acesso 29-01-2021.

American Society for Reproductive Medicine (ASRM). Patient management and clinical recommendations during the Coronavirus (COVID-19) pandemic. ASRM Coronavirus/COVID-19 Task Force (the “Task Force”). Update No. 12 - Testing and Vaccine Truths - January 18, 2021. Disponível em:

<https://www.asrm.org/globalassets/asrm/asrm-content/news-and-publications/covid-19/covidtaskforceupdate12.pdf>. Acesso 29-01-2021.

American College of Obstetrics and Gynecology. Vaccinating Pregnant and Lactating Patients Against COVID-19, January 27, 2021. Disponível em: <https://www.acog.org/clinical/clinical-guidance/practice-advisory/articles/2020/12/vaccinating-pregnant-and-lactating-patients-against-covid-19>. Acesso: 29-01-2021.

Centers for Disease Control and Prevention. COVID-19 (coronavirus disease): people with certain medical conditions. Disponível em: <https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html>. Acesso: December 11, 2020

European Society of Human Reproduction and Embryology (ESHRE). COVID-19 vaccination and assisted reproduction. Statement from ESHRE COVID-19 Working Group. Disponível em: <https://www.eshre.eu>. Acesso 29-01-2021.

SOGC Statement on COVID-19 Vaccination in Pregnancy POLIQUIN, V; CASTILLO, E; BOUCOIRAN, I; WATSON, H; YUDIN, M; MONEY, D; VAN SCHALKWYK, J; ELWOOD, C on behalf of the Infectious Disease Committee of the Society of Obstetricians and Gynaecologists Canada. Disponível em: [https://sogc.org/common/Uploaded%20files/of Latest%20News/SOGC\\_Statement\\_COVID-19\\_Reaffirmed](https://sogc.org/common/Uploaded%20files/of Latest%20News/SOGC_Statement_COVID-19_Reaffirmed) Jan 28,2021. Acesso:30/01/2021.

The Royal College of Obstetricians and Gynecologists (RCOG) and the Royal College of Midwives (RCM). I am pregnant and have been offered a COVID-19 vaccination. What are my options? Version 1: Published 12 January 2021. Disponível em: <https://www.rcog.org.uk/globalassets/documents/guidelines/2021-01-12-covid-19-vaccine-info-sheet.pdf>. Acesso em 29-01-2021.

The Royal College of Obstetricians and Gynecologists (RCOG) and the Royal College of Midwives (RCM). The RCOG and the RCM misinformation around Covid-19 vaccine and fertility. Disponível em: respond to <https://www.rcog.org.uk/en/news/RCOG-and-RCM-respond-to-misinformation-around-Covid-19-vaccine-and-fertility/>. Acesso em 29-01-2021.