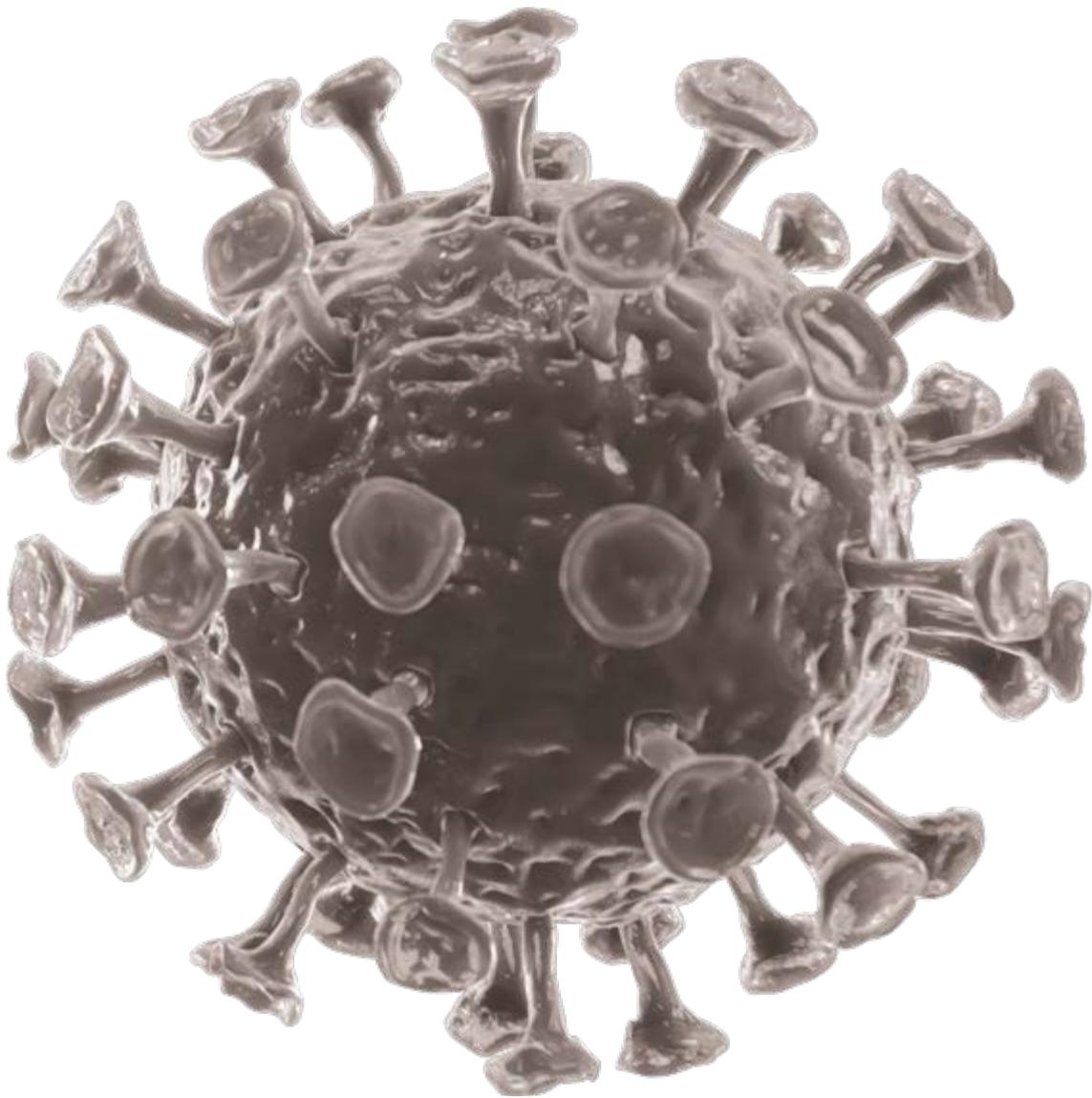


COVID-19 VACCINES:

SAFETY SURVEILLANCE MANUAL

**MODULE: SAFETY
SURVEILLANCE OF
COVID-19 VACCINES
IN PREGNANT AND
BREASTFEEDING WOMEN**

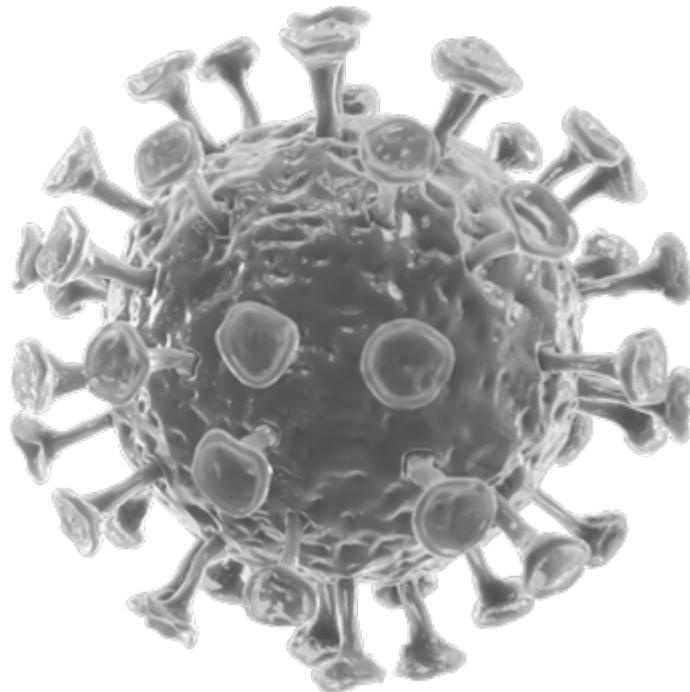


World Health
Organization

COVID-19 VACCINES:

**SAFETY
SURVEILLANCE
MANUAL**

**MODULE: SAFETY
SURVEILLANCE OF
COVID-19 VACCINES
IN PREGNANT AND
BREASTFEEDING WOMEN**



World Health
Organization

WHO/MHP/RPQ/PVG/2021.1

© World Health Organization 2021

Some rights reserved. This work is available under the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 IGO licence (CC BY-NC-SA 3.0 IGO; <https://creativecommons.org/licenses/by-nc-sa/3.0/igo>).

Under the terms of this licence, you may copy, redistribute and adapt the work for non-commercial purposes, provided the work is appropriately cited, as indicated below. In any use of this work, there should be no suggestion that WHO endorses any specific organization, products or services. The use of the WHO logo is not permitted. If you adapt the work, then you must license your work under the same or equivalent Creative Commons licence. If you create a translation of this work, you should add the following disclaimer along with the suggested citation: "This translation was not created by the World Health Organization (WHO). WHO is not responsible for the content or accuracy of this translation. The original English edition shall be the binding and authentic edition".

Any mediation relating to disputes arising under the licence shall be conducted in accordance with the mediation rules of the World Intellectual Property Organization (<http://www.wipo.int/amc/en/mediation/rules/>).

Suggested citation. COVID-19 Vaccines: safety surveillance manual. Module on safety surveillance of COVID-19 vaccines in pregnant and breastfeeding women. Geneva: World Health Organization; 2021 (WHO/MHP/RPQ/PVG/2021.1). Licence: [CC BY-NC-SA 3.0 IGO](https://creativecommons.org/licenses/by-nc-sa/3.0/igo).

Cataloguing-in-Publication (CIP) data. CIP data are available at <http://apps.who.int/iris>.

Sales, rights and licensing. To purchase WHO publications, see <http://apps.who.int/bookorders>. To submit requests for commercial use and queries on rights and licensing, see <http://www.who.int/about/licensing>.

Third-party materials. If you wish to reuse material from this work that is attributed to a third party, such as tables, figures or images, it is your responsibility to determine whether permission is needed for that reuse and to obtain permission from the copyright holder. The risk of claims resulting from infringement of any third-party-owned component in the work rests solely with the user.

General disclaimers. The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of WHO concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement. The mention of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by WHO in preference to others of a similar nature that are not mentioned. Errors and omissions excepted, the names of proprietary products are distinguished by initial capital letters.

All reasonable precautions have been taken by WHO to verify the information contained in this publication. However, the published material is being distributed without warranty of any kind, either expressed or implied. The responsibility for the interpretation and use of the material lies with the reader. In no event shall WHO be liable for damages arising from its use.

Contents

Key points	iv
1. Introduction	1
1.1 COVID-19 disease and vaccination in pregnant and breastfeeding women.....	1
1.2 WHO recommendations for COVID-19 vaccination in pregnant and breastfeeding women.....	2
1.3 Pregnancy and vaccine safety surveillance.....	3
1.4 Vaccine safety surveillance methods for COVID-19 vaccination in pregnant women	5
2. Routine (passive) AEFI surveillance following COVID-19 vaccination in pregnant women	7
2.1 Considerations for reporting of AEFIs after administration of a COVID-19 vaccine to pregnant women.....	7
2.2 Investigation of serious AEFIs and AESIs.....	9
2.3 Profile of the AEFI investigation team.....	10
3. Active surveillance following COVID-19 immunization in pregnant women	11
3.1 Standardized case definitions.....	12
3.2 Methods for active safety surveillance.....	12
3.2.1 General principles.....	13
3.2.2 Prospective cohort studies.....	13
3.2.3 Record linkage studies – retrospective cohorts.....	15
4. Communication	16
5. Appendices	18
Appendix 5.1.....	18
Appendix 5.2.....	20
Appendix 5.3.....	23

Key points

- Evidence suggests that pregnant women with COVID-19 are at higher risk of developing severe disease compared to non-pregnant women of reproductive age.
- COVID-19 infection may increase the risk of preterm delivery. Studies are underway globally to assess the risk-benefit profile of COVID-19 vaccines in pregnant and breast-feeding women.
- Immunization programmes need to incorporate surveillance of women who have been vaccinated either intentionally or inadvertently during pregnancy, and their children.
- Passive surveillance approaches need to take into consideration three potential scenarios:
 - maternal AEFIs not directly related to the pregnancy;
 - obstetric adverse events believed to be linked to COVID-19 vaccination during pregnancy; and
 - adverse events in the fetus (in the case of pregnancy loss), neonate, infant or child suspected to be associated with COVID-19 vaccination during pregnancy.
 - late/delayed adverse event in a child believed to be linked to COVID-19 vaccination during pregnancy.
- Prompt investigations and causality assessment involving health care workers knowledgeable in maternal and neonatal health are needed to mitigate any adverse consequences for the mother-infant pair, as well as the vaccination programme itself.
- Currently, there is a lack of adequate data on the performance of COVID-19 vaccines in pregnant women. Therefore, both active and passive surveillance approaches are recommended.
- National AEFI monitoring programmes designed for routine immunization will need to be adapted to include COVID-19 vaccinations in adults, including pregnant women. For this the AEFI reporting forms, case investigation procedures, as well as causality assessment procedures will need to be adapted to take into account the specific characteristics of AEFIs following maternal immunization.
- There are challenges in assessing causality in individual cases of adverse birth outcomes due to the specific characteristics of pregnancy exposure to vaccine.
- Active surveillance approaches such as pregnancy exposure registries, cohort event monitoring studies, nested case-control and linkage studies may be used to assess the potential risks of adverse birth outcomes in vaccinated compared with unvaccinated women.
- Embedding AEFI surveillance for COVID-19 vaccines in existing surveillance programmes, such as pregnancy exposure registries for other medicines, may be an efficient way of harnessing existing resources for this purpose.
- Communication strategies for the AEFI programme need to be adapted to take into consideration the different stakeholders that need to be engaged when pregnant and breast-feeding women are vaccinated with COVID-19 vaccines.

01 Introduction

1.1 COVID-19 disease and vaccination in pregnant and breastfeeding women

While there is no indication that pregnant women have an increased susceptibility to infection with SARS-CoV-2, evidence suggests that pregnant women with COVID-19 are at higher risk of developing severe disease compared to non-pregnant women of reproductive age.¹ As seen with non-pregnant women, a high proportion of pregnant women have asymptomatic SARS-CoV-2 infection and severe disease is associated with recognized medical (e.g., high body-mass index (BMI), diabetes, pre-existing pulmonary or cardiac conditions^{1,2,3,4}) and social (e.g., social deprivation, ethnicity) risk factors. Pregnant women with symptomatic COVID-19 appear to have an increased risk of intensive care unit admission, mechanical ventilation and death in comparison with non-pregnant women of reproductive age, although the absolute risks remain low.¹ COVID-19 may increase the risk of preterm birth, compared with pregnant women without COVID-19, although the evidence is inconclusive.⁵

SARS-CoV-2 has been observed in placenta and some case reports suggest that vertical transmission of the virus to infants born to infected women may occur (as opposed to postpartum infection).³ However, congenital COVID-19 infections have not been reported so far during the pandemic.⁴ The acute effects of the disease on neonates and infants have been secondary to complications arising from severe maternal illness and medically-indicated preterm delivery or caesarean delivery due to clinician concerns.

There is no evidence that SARS-CoV-2 can be transmitted via human breast milk.^{4,5,6,7}

-
- 1 Allotey J, Stallings E, Bonet M, Yap M, Chatterjee S, Kew T, et al. for PregCOV-19 Living Systematic Review Consortium. 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. doi: 10.1136/bmj.m3320.
 - 2 Khalil A, Kalafat E, Benlioglu C, O'Brien P, Morris E, Draycott T, et al. SARS-CoV-2 infection in pregnancy: A systematic review and meta-analysis of clinical features and pregnancy outcomes. *EClinicalMedicine*. 2020;25:100446. doi: 10.1016/j.eclinm.2020.100446.
 - 3 Raschetti R, Vivanti A, Vauloup-Fellous C. et al. Synthesis and systematic review of reported neonatal SARS-CoV-2 infections. *Nat Commun*. 2020;11:5164. doi.org/10.1038/s41467-020-18982-9.
 - 4 Gale C, Quigley MA, Placzek A, Knight M, Ladhani S, Draper ES, et al. Characteristics and outcomes of neonatal SARS-CoV-2 infection in the UK: a prospective national cohort study using active surveillance. *Lancet Child Adolesc Health*. 2021; 5:113-21. doi: 10.1016/S2352-4642(20)30342-4.
 - 5 Centeno-Tablante E, Medina-Rivera M, Finkelstein JL, Rayco-Solon P, Garcia-Casal MN, Rogers L, et al. Transmission of SARS-CoV-2 through breast milk and breastfeeding: a living systematic review. *Ann N Y Acad Sci*. 2021 Jan;1484:32-54. doi: 10.1111/nyas.14477.
 - 6 World Health Organization. COVID-19 clinical management: living guidance, 25 January 2021. Available from: <https://apps.who.int/iris/handle/10665/338882>, accessed 26 March 2021.
 - 7 Rollins N, Minckas N, Jehan F, Lodha R, Raiten D, Thorne C, et al. A public health approach for deciding policy on infant feeding and mother–infant contact in the context of COVID-19. *Lancet Glob Health*. 2021;9:e552-7. doi.org/10.1016/S2214-109X(20)30538-6.

Women of reproductive age represent a very large group of the categories of workers who have been prioritized to receive COVID-19 vaccination globally, i.e., health care workers, carers, educators and other front-line essential workers. Several COVID-19 vaccines are under development using various technological platforms and some are already authorized for use under emergency use approval in response to the pandemic. For more information on each platform, and links to relevant, updated information on the status of development refer to the module, [COVID-19 vaccines: description and general safety considerations for implementation](#) in this manual.

To date, pregnant women have not been included in Phase II and III clinical trials of COVID-19 vaccines. Hence data on COVID-19 vaccines in pregnant women are insufficient to assess vaccine efficacy or vaccine-associated risks in pregnancy, although studies are underway. Section 1.2 summarizes WHO's current recommendations for COVID-19 vaccination in pregnant and breastfeeding women.

Pregnant women may be exposed to COVID-19 vaccines in two ways:

1. inadvertent vaccination before the woman knows she is pregnant, i.e., at an early gestational stage; or
2. vaccination offered to a woman with confirmed pregnancy who is at high risk of COVID-19 exposure and infection or at risk of severe disease should they become infected, and who choose to be vaccinated.

The risks and benefits of COVID-19 vaccine exposure apply to both the pregnant woman and her fetus, and the timing of exposure during pregnancy may have an impact on the outcomes. It is important that vaccine safety monitoring programmes proactively include pregnant women that have been either inadvertently or knowingly exposed to COVID-19 vaccines, to collect information on associated maternal and neonatal outcomes.

1.2 WHO recommendations for COVID-19 vaccination in pregnant and breastfeeding women

预览已结束，完整报告链接和二维码如下：

https://www.yunbaogao.cn/report/index/report?reportId=5_23724

