Generic protocol
A prospective cohort study investigating maternal, pregnancy and neonatal outcomes for women and neonates infected with SARS-CoV-2

Version 2.6
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human reproduction programme hrp
research for impact
UNDP · UNFPA · UNICEF · WHO · THE WORLD BANK

World Health Organization

Reference:

The emergence of a new virus means that understanding transmission patterns, severity, clinical features and risk factors for infection will be limited at the start of an outbreak. To address these unknowns, WHO has provided protocols for special investigations in different settings.

Data collected using these investigation protocols will be critical to refine recommendations for case definitions and surveillance; characterize key epidemiological features of COVID-19; help understand the spread, severity and spectrum of disease and impact on the community; and inform guidance for application of countermeasures such as case isolation and contact tracing. These protocols are designed to enable the rapid and systematic collection of data in a format that facilitates comparison across different settings globally.

They are available on WHO website here: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/early-investigations

COVID-19 investigations and study protocols available include:

1. The First Few X cases and contacts (FFX) investigation protocol for coronavirus disease 2019 (COVID-19)

2. Household transmission investigation protocol for coronavirus disease 2019 (COVID-19)

3. Protocol for assessment of potential risk factors for coronavirus disease 2019 (COVID-19) among health workers in a health-care setting: cohort or case control designs

4. Population-based age-stratified seroepidemiological investigation protocol for coronavirus 2019 (COVID-19) infection

5. Surface sampling of coronavirus (COVID-19) virus: a practical "how to" protocol for health-care and public health professionals

6. Schools and other educational institutions transmission investigation protocol for coronavirus disease 2019 (COVID-19)

7. Longitudinal cohort study on pregnancy & COVID-19: maternal and neonatal transmission protocol

Please contact hrp_covid19pregnancycohort@who.int for questions related to the maternal and neonatal transmission protocol and earlyinvestigations-2019-nCoV@who.int for questions related to other early investigation protocols.

All WHO protocols for COVID-19 are available on the WHO website together with the technical guidance documents.

This protocol may be subject to revisions, pending research governance processes[1].

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For questions related to implementation or other aspects of pregnancy related SARS-CoV-2 research, please send an email to hrp_covid19pregnancycohort@who.int

[1] Version 2.2 of this protocol and its accompanying appendix dated 14 August 2020 have been approved by the WHO Ethical Review Committee. This updated version (v.2.6 dated 2 December 2020) will undergo an amendment review by the WHO Ethical Review Committee based on revised sample size calculations, including information on the pooled analysis (pp. 10–13, Appendix B), revision of the case report forms (CRFs) (Appendix B), inclusion of draft guidelines on mother-to-child transmission (MTCT) (Apndices I–L) and general revisions to improve coherence and content alignment.

Contents

Protocol summary

To better understand how severe acute respiratory coronavirus-2 (SARS-CoV-2) infection impacts outcomes in women and their neonates during pregnancy and the postpartum period, the World Health Organization (WHO) has developed a standardized research protocol for the investigation of coronavirus disease 2019 (COVID-19) in pregnant women. The protocol addresses key research questions, facilitates systematic and harmonized collection of data and biological specimens, and allows for data comparison and aggregation across different locations while minimizing potential biases. The protocol is designed to be adapted as needed in each study site based on resource availability and local circumstances.

This protocol outlines a prospective cohort study investigating the outcomes of pregnant or recently pregnant women infected with SARS-CoV-2 (exposed) compared to pregnant or recently pregnant women not infected with SARS-CoV-2 during pregnancy (unexposed). The purpose of this study is to determine if SARS-CoV-2 infection during pregnancy increases the risk of adverse pregnancy, postpartum or neonatal outcomes. Additionally, the study characterizes the clinical spectrum of COVID-19 in pregnant women, quantify (if any) the rate of in utero/intrapartum/postnatal transmission, determine the incidence of detectable SARS-CoV-2 RNA in pregnancy-related fluids (i.e. amniotic fluid), breast milk and tissues, and follow clinical outcomes of women and their newborns up to 6 weeks after childbirth.

It is expected that findings from studies implementing this protocol will be published, widely disseminated and used to develop recommendations on the surveillance, management and counselling of women during and after pregnancy, as well as their babies, in the context of the COVID-19 pandemic. Findings related to the implementation of this study protocol will help to inform public health measures, infectious disease and prevention measures, and future research protocols.

List of abbreviations

ARDS	acute respiratory distress syndrome
CIOMS	Council for International Organizations of Medical Sciences
COVID-19	coronavirus disease 2019
CRF	case report form
FGR	fetal growth restriction
GCP	good clinical practice
GDRP	general data protection regulation
HRP	UNDP/UNFPA/UNICEF/WHO/World Bank Special Programme of Research, Development and Research Training in Human Reproduction
IDMC	Independent Data Monitoring Committee
IPC	infection prevention and control
IRB	institutional review board
IUT	intrauterine transmission
LFU	loss to follow-up
LMICs	Low- and middle-income countries
MERS	Middle East respiratory syndrome
MTA	material transfer agreement
MTCT	mother-to-child transmission
NICU	neonatal intensive care unit
RDT	rapid diagnostic test
RT-PCR	reverse transcriptase polymerase chain reaction
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
TORCH	toxoplasmosis, rubella, cytomegalovirus, herpes simplex
WHO	World Health Organization
WG	working group

Preamble

This protocol is one of the WHO protocols for COVID-19 designed to enable the rapid and systematic collection of data in a format that facilitates comparison across different settings. All WHO investigation protocols for COVID-19 are available on the WHO website.

Any partner who wishes to use this protocol can do so freely and without charge or obligations. We ask implementing study sites to kindly inform the UNDP/UNFPA/UNICEF/WHO/World Bank Special Programme of Research, Development and Research Training in Human Reproduction (HRP)/World Health Organization (WHO) about their implementation of this protocol and to provide a contact point. Please share your information with hrp_covid19pregnancycohort@who.int

Implementing partners can opt to manage data onsite or through the central HRP repository subject to local circumstances. A pooled analysis bringing together all consenting and contributing sites will be discussed with sites implementing the study. Sites that agree to pool data under the coordination of WHO/HRP will have the option to independently publish their own data. The analysis of the pooled data will be made available and widely disseminated in collaboration with all contributing sites. All partners will retain control of their site data, regardless of whether or not this data is included in pooled or aggregated analyses.

All sites wishing to participate are invited to do so; however, WHO/HRP provides no guaranteed support for study implementation. Technical, financial or capacity limitations may be present. However, since this protocol proposes a study design that can be adapted to allow for smaller studies (see Appendix D for proposed methodologies), studies that follow the proposed study design may be pooled/aggregated in order to achieve an overall pooled sample size with sufficient statistical power to answer the primary research questions.

It is important to note that this protocol is designed to describe the core data variables in order to answer the key research questions and primary objectives outlined in the protocol. As such, the implementation of this study may include additional objectives or study components, as determined by each implementing site.

Comments for the user's consideration are provided in purple text throughout the document, as the user may need to modify methods slightly because of the local context in which this investigation will be carried out.