Title: Protocol for a Sequential, Prospective Meta-Analysis to Describe COVID-19 in Pregnancy and Newborn Periods

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Conflict of Interest: The authors have none to declare.
Abstract
Background. We urgently need answers to basic epidemiological questions regarding COVID-19 infection in pregnant women and newborns. While many national registries, health facilities, and research groups are collecting relevant data, we need a collaborative and methodologically appropriate approach to utilize these data to generate answers.

Methods. We propose that a sequential, prospective meta-analysis (PMA) is the best approach to rapidly generate policy and practice-oriented guidelines. As the pandemic is rapidly evolving, studies identified retrospectively through a living systematic review will also be invited to participate. The primary analysis will pool data using a two-stage meta-analysis with generic inverse-variance methods. The meta-analyses will be updated as additional data accrues in each contributing study and as additional studies meet study-specific time or data accrual thresholds for sharing.

Participating Studies. At the time of publication, there are 19 studies being conducted in 21 countries that prospectively agreed to pool data for this analysis. Among the 19 included studies, ten are COVID-19 registry studies, seven are cohort or surveillance studies, and two are case-control studies. More than 74,000 pregnant women are expected to contribute to the completed analysis.

Dissemination: Protocols and updates will be maintained publicly. Results will be shared with key stakeholders including the World Health Organization (WHO) Maternal, Newborn, Child, and Adolescent Health (MNCAH) Research Working Group. Scientific publications will be published in open access journals on an ongoing basis.

Keywords: SARS-CoV-2, Coronavirus Disease 2019, COVID-19, Pregnancy, Perinatal, Newborn, Maternal Mortality, Neonatal Mortality, Preterm Birth, Small-for-gestational Age
Background

The coronavirus disease 2019 (COVID-19) has led to over 43 million confirmed cases and claimed more than 1.1 million lives globally as of October 27, 2020 (1). The Centers for Disease Control and Prevention (2) notes that pregnant women may be at higher risk of developing severe illness due to COVID-19. The concern was initially based on the fact that pregnant women are generally at increased risk for severe illness with many infectious diseases including influenza, hepatitis E, malaria, and herpes simplex virus (3). The specific mechanisms as to why this might also be the case for SARS-CoV-2 infection are currently unclear, though may be related to physiologic and immunologic changes during pregnancy (4,5). A living systematic review suggests that pregnant women, compared with non-pregnant women, are 62% more likely to be admitted to an intensive care unit and 88% more likely to require invasive ventilation (last updated: August 2020) (5). However, these data should be interpreted with caution, because the vast majority came from the United States surveillance program with high rates of missing data (4). To date, evidence suggests that most reported COVID-19 cases in pregnancy occurred in the later stages of gestation, particularly in the third trimester (6). In a US study of 64 hospitalized pregnant women, iatrogenic preterm delivery was reported in 75% of the patients with critical COVID-19 illness (7). Another two studies (313 women) reported a two-fold higher risk of preterm birth in COVID-infected versus uninfected pregnancies (5). There is limited evidence suggest potential risk to neonates as well. A study of 1121 neonates in the UK reported a three-fold increased odds of neonatal intensive care unit (NICU) admission among infants born to mothers with COVID-19, compared to historical controls (5).

Despite the urgent need to accurately document the number of cases, severe illness, and deaths in pregnant people, as well as transmission rates and consequences of SARS-CoV-2 infection in newborns, relevant data are limited (4). Further, pregnant people have been systematically excluded from clinical trials assessing the efficacy of COVID-related treatment and preventives in an effort to avoid this medically complex population (8). There are also misplaced ethical concerns that actually creates an ethical dilemma: the exclusion of pregnant people at the stage of developing vaccines or treatments may ultimately pose harm to this very population (8). There are also challenges in establishing mother-to-child transmission of SARS-CoV-2 because there is no consensus case definition for intrauterine versus intrapartum or early peripartum transmission, and proposed definitions require researchers to follow complex protocols; WHO is expected to share an expert consensus on the case definition before the end of 2020 (6,9–12). Given the scarcity of COVID data in pregnancy, differences in data collection protocols globally, and potential risks for severe illnesses in this population, there is an urgent need to rapidly generate high quality information to make evidence-based decisions and create guidelines on the prevention and treatment of COVID-19 illness in pregnant women and infants.

We propose that a sequential, prospective meta-analysis (PMA) is the best approach to rapidly accrue harmonized global data to generate policy and practice-relevant data regarding the epidemiology of COVID-19 in the pregnancy, peripartum, and postnatal period.

Methods Background
A prospective meta-analysis identifies studies that will contribute data to the meta-analysis, as well as establishes the analysis plans, before the results of the individual studies are known (13). This approach is similar to a multi-site registry or cohort in the sense that studies work to harmonize collection of key outcomes, but differs from multi-site studies in that each site will implement a study design and local protocol that is appropriate for their context (13).

Benefits of our Approach
There are many benefits to our approach. One major benefit of a PMA in the context of COVID-19 is that we were able to standardize some data collection components while a number of participating studies were starting. Early efforts to plan for pooling can also reduce research waste (e.g. incompatible data, duplication of efforts) and improve the collective value of data in a collaborative way (14). Using individual participant data also allows us to avoid duplicate case counting. This has been a major issue in COVID-related meta-analyses because much scientific literature is based on case reports or case series; the same cases sometimes appear in multiple published papers.

Methods
The protocol was registered with PROSPERO (ID: 188955) on May 28, 2020.

Research Questions
The study aims to answer basic epidemiological questions about COVID-19 and about maternal and newborn health in the context of COVID-19.

Specific objectives regarding COVID-19 among pregnant or recently pregnant women include:
- Describe the natural history of disease (COVID-19);
- Estimate the incidence of disease severity-related healthcare utilization including hospitalization, admittance to the intensive care unit, and use of invasive ventilation (for COVID-19);
- Estimate infection and case fatality rate.

Specific objectives regarding maternal health among pregnant or recently pregnant women with COVID-19 include:
- Estimate the incidence of maternal morbidities;
- Estimate the maternal mortality ratio;
- Describe the incidence of adverse pregnancy outcomes.

Specific objectives regarding newborn health among newborns born to women with COVID-19 including:
- Describe the incidence of congenital anomalies;
- Estimate the perinatal and (early) neonatal mortality rate;
- Estimate the incidence of transmission of SARS-CoV-2 from mother to child.
Specific objectives regarding SARS-CoV-2 in biospecimens include:

- Estimate the proportion of biospecimens with detectable SARS-COV2 virus and median viral load;
- Estimate the association between virus or viral load in biospecimen and a) severity of disease, b) maternal morbidity, c) maternal mortality, d) vertical transmission.

Search Strategy & Study Inclusion

We recruited study sites to join the proposed PMA first via professional research networks, and subsequently via key stakeholder networks. Stakeholders at the National Institute of Child Health and Human Development (NICHD) at the U.S. National Institutes of Health (NIH) supported recruitment of NIH-funded maternal and child health network groups and other US government funded projects. Stakeholders at WHO in the Maternal, Newborn, Child and Adolescent health (MNCAH) Department and Department of Sexual and Reproductive Health and Research groups supported recruitment based on the current group of researchers engaged in the COVID-19 MNCAH research network. Stakeholders from the International Federation of Gynecology and Obstetrics (FIGO) supported recruitment by issuing an invitation through their international network. Studies were invited to participate based solely on study design. Eligible study designs included a) registries enrolling all suspected or confirmed pregnant or recently postpartum women, b) cohorts enrolling all pregnant women, or c) a case-control studies enrolling cases of pregnant or recently postpartum women with COVID. There were no a priori sample size limitations due the dynamic epidemiology of the pandemic. Study investigators confirmed their intent to contribute to the PMA by signing a letter of intent.

At the time of publication, there were 19 studies taking place in 21 countries that prospectively agreed to pool data for this analysis (Supplementary Table 1). Among these 19 prospectively included studies, ten are COVID-19 registry studies, seven are cohort or surveillance studies, and two are case-control studies. More than 74,000 pregnant women are expected to contribute to the completed analysis (Supplementary Table 1). These studies include data from 21 countries: Australia, Bangladesh, Canada, Chile, China and Hong Kong, Colombia, The Democratic Republic of Congo, Guatemala, India, Kenya, Malawi, Mali, Mexico, Mozambique, Pakistan, Spain, The Gambia, Uganda, United Kingdom, United States, Zambia. A description of each participating study is presented in Supplementary Table 2.

Building off of the concepts laid out in the Framework for Adaptive Meta-analyses (FAME) (15), we will also collaborate with a living systematic review (LSR) project to identify studies that might be eligible for post-publication inclusion into the proposed meta-analysis. The search strategy for the LSR has been previously published (5). LSR project team members will screen all studies for potential inclusion in the PMA using the following criteria: i) The study conforms to the study designs outlined above; ii) There is a defined catchment area (e.g. certain hospitals,
states, etc.); iii) More than 25 pregnant or recently postpartum women were consecutively recruited.

**Exposure (Suspected or Confirmed SARS-CoV-2 Infection)**

Confirmed cases of COVID-19 will be defined as those with laboratory-confirmed SARS-CoV-2 via a nucleic acid amplification test, regardless of clinical signs or symptoms. The protocol may be expanded to included cases confirmed via antigen or other tests as they are validated and become widely available. Suspected cases will be defined according to the WHO August 7, 2020 case definition based on either clinical and epidemiological criteria or the severe acute respiratory illness (SARI) case definition (16). Probable COVID-19 infections will also be defined according to the WHO August 7, 2020 case definition (16).

**Comparison Group**

Analyses will be done in three groups. First descriptive epidemiology regarding COVID-19 in pregnancy and the perinatal period will be presented without a comparison group. Second, some analyses regarding morbidity and mortality will assess outcomes comparing pregnant women with confirmed or suspected COVID-19 to other pregnant women without COVID-19. Third, we will compare women with confirmed or suspected COVID-19 to non-pregnant women with confirmed or suspected COVID-19.

**Outcomes of Interest - Maternal Health**

- Mortality outcomes of interest for women include: all-cause mortality, COVID-19 specific mortality, and pregnancy-related mortality.
- Morbidity outcomes of interest for women include COVID-19 related clinical signs and symptoms (fever, cough, shortness of breath, dizziness or fainting, body aches, runny nose, sore throat, loss of sense of smell, loss of sense of taste, sneezing, fatigue, nausea, vomiting, diarrhea, headache) and pregnancy-related clinical signs and symptoms (hypertensive disease of pregnancy (including preeclampsia/eclampsia), gestational diabetes, hyperemesis, intrauterine growth restriction, abnormal placentation (placental previa/accreta/percreta), placental abruption, bacterial infection prior to hospital visit, preterm contractions (not in labor), preterm labor, preterm rupture of membranes, hemorrhage (antepartum/intrapartum; postpartum; abortion-related), embolic disease, anesthetic complications).
- Other morbidity-related healthcare outcomes include hospitalization, admittance to an intensive care unit or requiring critical care, and requiring intensive ventilation. Adverse pregnancy outcomes of interest include: stillbirth (categorized as both fetal death ≥28 weeks per WHO), early preterm birth (<34 weeks gestation), preterm birth (<37 weeks gestation), small-for-gestational-age birth (<10th percentile per the Intergrowth newborn reference values), and low birthweight (<2500 g). We will assess SARS-CoV-2 viral load in maternal biological specimens including: amniotic fluid, placenta (maternal or fetal side), cord blood, vaginal swab, feces or rectal swab, nasopharyngeal swab, pregnancy
tissue (fetus or pregnancy sac and placenta) in the case of fetal demise or induced abortion, breastmilk, and maternal blood.

Outcomes of Interest - Neonatal Health

- Neonatal outcomes of interest include congenital anomalies, namely neural tube defects, microcephaly, congenital malformations of ear, congenital heart defects, orofacial clefts, congenital malformations of digestive system, congenital malformations of genital organs, abdominal wall defects, chromosomal abnormalities, reduction defects of upper and lower limbs, talipes equinovarus/clubfoot.
- We will measure early neonatal (7 day), neonatal (28 day), and six-week infant mortality (42 days). We will also measure perinatal death defined as a stillbirth or early neonatal death.
- Mother-to-child transmission of SARS-CoV-2 will also be measured, with an effort to differentiate intrauterine versus intrapartum or early peripartum infection. These definitions will be aligned with the WHO consensus case definitions once they become available.

Data Harmonization

We developed the draft data modules and questions in April 2020 based on a proposed set of questions from the Pregnancy CoRonavIrus Outcomes RegIsTrY (PRIORITY) study. We also reviewed and included questions from the data collection forms developed by the World Health Organization (WHO) and the U.S. Center for Disease Control (CDC). We requested two rounds of feedback via a survey and by email from the >50 participants of the bi-monthly informal meeting established at the beginning of the pandemic called the “Perinatal COVID-19 Global Gathering”. The current data modules reflect feedback and general consensus among survey respondents. The final draft of the data modules and core variables was finalized and shared broadly on June 2, 2020 (Supplementary File 2). We updated the data modules in September 2020 to reflect evolving understanding of SARS-CoV-2 infection in newborns and to reflect an updated generic protocol developed by WHO for COVID-related pregnancy cohort studies (Supplementary File 3).

Study-Specific Data Analysis

We will develop a codebook and statistical codes for each study to map original study variables to the PMA core variables. The same data quality and consistency checks will be performed for each study, and any issues will be resolved with study investigators. Studies will be eligible to contribute data to the PMA when they have accrued at least 25 confirmed cases with completed follow up including obtaining maternal and neonatal outcomes.

Study-specific estimates for the two-stage meta-analysis will be produced using standardized analytical codes, and aggregated measures will be exported into a standardized database to be used for the meta-analysis.

Methods for Data Synthesis
Ideally all individual-level data would be combined for one-stage meta-analysis. However, we anticipate that the ability to quickly share data and the degree of willingness to share individual patient data may vary by country and across collaborators. Thus, we will plan for a step-wise statistical analysis plan where the most feasible and simple analyses (that contribute directly to our research questions) are prioritized, and more advanced statistical modelling will be conducted subsequently.

For the first stage of analysis, data for each research question will be pooled using a two-stage, random-effects meta-analysis using conventional DerSimonian-Laird methods (17). For analyses where only proportions or crude incidence rates are used, the Arcsine method may be applied to stabilize the statistics and ensure approximate asymptotic normality (18). We will assess forest plots visually for heterogeneity. When at least ten studies are being pooled, we will also quantify heterogeneity by $I^2$. Further model fit analyses may also include inspection of the impact on the former two heterogeneity statistics when excluding apparent outlier studies.

Analysis of Subgroups
Where appropriate and as sample size allows, we will consider meta-regression or subgroup analyses by the following study level characteristics: study design and sampling strategy, proportion of confirmed COVID-19 cases (out of suspected and confirmed cases), national maternal mortality ratio, national neonatal mortality rate. We will also consider subgroup analysis by the following individual patient characteristics: Confirmed versus suspected COVID case status; gestational age at COVID onset (by week, by trimester), COVID severity, pre-pregnancy health conditions, maternal morbidity, time since first COVID diagnosis in the study area, gravidity, parity, maternal age, race or ethnicity, and maternal education.

Governance
The steering committee will consist of at least one member from each participating site, key stakeholders (Supplementary Table 3), and the technical coordinating team. In the case a formal vote is needed, the following can each cast one official vote: each participating study, each key stake holder organization, and the technical coordinating team. The steering committee will prioritize research questions and agree on common elements of data collection. They will disseminate results, including rapid reports to key stakeholders, webinars, and submission of manuscripts to preprint servers and scientific journals. The technical coordinating team will develop protocols for data transfer and ensuring data quality; write the statistical analysis plans; and conduct meta-analyses.

Conclusion
Prospective meta-analyses offer a rigorous way to generate definitive answers to emerging questions. Given the current state of limited, high-quality evidence to inform public health guidance and healthcare strategies for pregnant women and newborn, the proposed study will contribute timely and necessary evidence-based data for decision-making in the context of COVID-19 and maternal and neonatal health.
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**List of Supplementary Files**

Supplementary Table 1. List of participating studies, country, study design, and anticipated sample size

Supplementary Table 2. Description of participating studies

Supplementary Table 3. Key stakeholders

Supplementary File 1. Data modules and core variables - version June 2, 2020

Supplementary File 2. Data modules and core variables - version November 8, 2020

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**Supplementary Table 1. List of participating studies, country, study design, and anticipated sample size**

| Study Name (Principle Investigators) | Registry (Cases Only) | Cohort (All Pregnancies) | Case Control | N Pregnancies |
|-------------------------------------|-----------------------|---------------------------|--------------|---------------|
| ARC Kenya (Akelo/Barr/Onyango)      |                       |                           |              | 2500          |
| PRIORITY USA (Gaw/Flaherman/Jacoby/Afshar) |                       |                           |              | 1,500         |
| Madrid Hospital Registry (Gil/Fernandez Buhigas) |                       |                           |              | 54            |
| GESTACOVID Chile (Hernandez/Carrillo) |                       |                           |              | 1200          |
| UKOSS (Knight)*                     |                       |                           |              | 1700          |
| UK Neonatal Complications UK (Kurinczuk/Gale)* |                       |                           |              |               |
| Mali ANC-1 and DSS Surveillance (Kotloff) |                       |                           |              | 3000          |
| Mali Case-Control: ANC illness (Kotloff) |                       |                           | X            | 1500          |
| Mali Case-Control: L&D (Kotloff)    |                       |                           | X            | 7,500         |
| PERICOVID (PREPARE) (Le Doare)      |                       |                           |              | 10,000        |
| Mexico National Registry (Martinez-Portilla) |                       |                           |              | 5,249         |
| NICHD Global Network (McClure)      |                       |                           | X            | 16,000        |
| NICHD MFMU Network (Metz)           |                       |                           | X            | 16,000        |
| CANCOVID-Preg Canada (Money)        |                       |                           |              | 1000          |
| China & Hong Kong (Poon/ Yang)      |                       |                           |              | 125           |
| RECOGEST Colombia (Sanin)           |                       |                           |              | 400           |
| PERICOVID (PRECISE) (Von Dadelszen) |                       |                           | X            | 6,000         |
| WA Collaborative USA (Waldorf/Lokken) |                       |                           |              | 240           |
| CHOPAN Australia (Whitehead)        |                       |                           |              | 50            |

*This registry is a population-based surveillance system capturing all pregnant cases in the study area or country.*
**Supplementary Table 2. Description of participating studies**

### Supplementary Table 2-1: ARC Kenya

| Study Site/Name | ARC Kenya |
|-----------------|-----------|
| Investigators | Victor Akelo, Beth Tippett Barr, Dickens Onyango |
| Institutional Affiliations | CDC Kenya, Kisumu County Department of Health |
| Study Design | Prospective cohort study |
| Participants | Pregnant women both positive and negative for SARS-COV-2 |
| Sample Size | 2,500 |
| Timeline | Ongoing (anticipating recruitment beginning in August 2020 through April 2021) |
| Outcomes | Primary Outcome Measures: Adverse maternal outcomes |
| Notes | |

### Supplementary Table 2-2: USA PRIORITY

| Study Site/Name | USA PRIORITY: Pregnancy Coronavirus Outcomes Registry |
|-----------------|-----------------------------------------------------|
| Investigators | Valerie Flaherman¹, Stephanie Gaw¹, Yalda Afshar², Vanessa Jacoby¹ |
| Institutional Affiliations | ¹UCSF; ²UCLA |
| Study Design | Registry |
| Participants | Women will be recruited from all clinical sites across the United States where pregnant women are under investigation for COVID-19 or have received a COVID-19 diagnosis. All participants in PRIORITY will be enrolled remotely through the UCSF Coordinating Center. We will recruit women under investigation for COVID-19 or who have tested positive for COVID-19 who meet the inclusion and exclusion criteria (see study protocol). |
| Sample Size | 1,500 women, 60% of whom will be confirmed to have COVID-19 |
| Timeline | Ongoing, opened enrollment March 2020. Following up newborns through 6 and 12 months |
| Outcomes | Maternal outcomes: To evaluate the presentation, disease course, and clinical outcomes for pregnant women infected with COVID-19 compared with those that are COVID-19 negative. We will query participants on disease presentation, course of infection, treatments received, incidence and risk of hospitalization and/or ICU stay, and time to complete recovery. Neonatal outcomes: To assess fetal/neonatal outcomes among infants born to women with COVID-19 compared with those that are COVID-19 negative. |
| Notes | [Priority UCSF](https://priority.ucsf.edu/researchers) |
Supplementary Table 2-3: Neonatal Complications of Coronavirus Disease (COVID-19) (United Kingdom)

| Study Site/Name | Neonatal Complications of Coronavirus Disease (COVID-19) |
|-----------------|---------------------------------------------------------|
| Investigators   | Christopher Gale¹ and Jenny Kurinczuk²                 |
| Institutional Affiliations | ¹Imperial College London, ²University of Oxford |
| Study Design    | Prospective cohort study/National active surveillance |
| Participants    | 1. Neonates COVID-19 positive: Neonatal COVID-19 in babies (<29 days old) in neonatal units, paediatric intensive care units and other in-patient locations.  
                2. Neonates born to COVID-19 positive mothers: Neonates (<29 days old) born to COVID-19 positive mothers requiring neonatal care |
| Sample Size     | 500                                                    |
| Timeline        | Ongoing (April 2020 through March 2021)                |
| Outcomes        | Primary Outcome Measures:  
                1. Incidence of neonatal COVID-19 [Time Frame: April 2020 to March 2021]  
                    Number of neonatal participants with COVID-19 divided by the total number of live births in the population  
                2. Incidence of vertically transmitted COVID-19 [Time Frame: April 2020 to March 2021]  
                    Number of neonatal participants with COVID-19 following vertically transmission of the Coronavirus divided by the total number of live births in the population  
                Secondary Outcome Measures:  
                1. Presentation and natural history of neonatal COVID-19 [Time Frame: April 2020 to March 2021]  
                    Questionnaire data  
                2. Presentation of neonates with COVID-19 positive mothers [Time Frame: April 2020 to March 2021]  
                    Questionnaire data  
                3. Outcomes for neonates with COVID-19 [Time Frame: April 2020 to March 2021]  
                    Proportion of neonate participants who died and the proportion who were discharged home alive.  
                4. Clinical treatment of neonatal COVID-19 [Time Frame: April 2020 to March 2021]  
                    Questionnaire data  
                5. Neonatal secondary impacts of maternal COVID-19 [Time Frame: April 2020 to March 2021]  
                    Questionnaire data |
| Notes           | These data reflect neonatal outcomes of pregnant cases identified by the UKOSS study.  
                 https://clinicaltrials.gov/ct2/show/NCT04386109 |
### Supplementary Table 2-4: Madrid Hospital-Based Registry

| Study Site/Name | Madrid Hospital-based registry |
|-----------------|-------------------------------|
| Investigators    | Dr. Mar Gil; Dr. Irene Fernandez Buhigas |
| Institutional Affiliations | Torrejon University Hospital |
| Study Design     | Registry                      |
| Participants     | Pregnant women                |
| Sample Size      | 54 cases as of August 2020    |
| Timeline         | Ongoing                       |
| Outcomes         | Primary Outcome Measures: effect of COVID-19 on the pregnancy outcomes and the effect of the pregnancy on the COVID-19 evolution. |

### Supplementary Table 2-5: Gestacovid Registro Chileno de Embarazadas con Covid-19

| Study Site/Name | Gestacovid Registro Chileno de Embarazadas con Covid-19 |
|-----------------|--------------------------------------------------------|
| Investigators    | Olivia Hernandez, Jorge Carillo                        |
| Institutional Affiliations | Multicenter Study with patients recruited at hospitals from all the country |
| Study Design     | Registry                                               |
| Participants     | Active cases (pregnant women); new sites may add controls |
| Sample Size      | 1,200                                                  |
| Timeline         | Began in April 2020 and recruit last patients by August 31, 2020, with follow-up completed by March 2021 |
| Outcomes         | Presentation and natural history of neonatal COVID-19   |

Notes
Supplementary Table 2-6: Maternal and perinatal outcomes of pandemic influenza or novel coronavirus in pregnancy in the U.K. (UKOSS)

| Study Site/Name | Maternal and perinatal outcomes of pandemic influenza or novel coronavirus in pregnancy in the U.K. (UKOSS) |
|-----------------|-----------------------------------------------------------------------------------------------------------|
| Investigators   | Marian Knight                                                                                              |
| Institutional Affiliations | National Perinatal Epidemiology Unit, Nuffield Department of Population Health, University of Oxford |
| Study Design    | National population-based cohort study using the UK Obstetric Surveillance System/International Network of Obstetric Survey Systems |
| Participants    | Cases will be identified through the UKOSS network of nominated reporting clinicians in each consultant led maternity unit in the UK (194 maternities total). Nominated reporting clinicians will be asked to report all pregnant women with confirmed pandemic influenza or novel coronavirus admitted to their unit |
| Sample Size     | 1,000 infected pregnant women admitted to hospital and 700 comparison women (1,700 total)                   |
| Timeline        | Next interim results: August and published in September. Going through March 2021.                          |
| Outcomes        | Primary Outcome Measures: Maternal death; Maternal level 3 critical care unit admission; Other major maternal complication; Preterm birth; Congenital anomaly; Perinatal death |
| Notes           | [https://www.npeu.ox.ac.uk/ukoss/current-surveillance/covid-19-in-pregnancy](https://www.npeu.ox.ac.uk/ukoss/current-surveillance/covid-19-in-pregnancy) |
**Supplementary Table 2-7: COVID-19 Surveillance to Inform Public Health Action in Mali**

| Study Site/Name | COVID-19 Surveillance to Inform Public Health Action in Mali |
|----------------|------------------------------------------------------------|
| Investigators | Karen Kotloff\(^1\), Milagritos Tapia\(^1\), Amanda Driscoll\(^1\), Samba Sow\(^2\), Fadima Cheick Haidara\(^2\), Adama Mamby Keita\(^2\), Uma Onwuchekwa\(^2\) |
| Institutional Affiliations | \(^1\)University of Maryland, Baltimore \(^2\)Centre pour le Developpement des Vaccins du Mali (CVD-Mali) |
| Study Design | Prospective cohort: mother-infant linked pregnancy surveillance |
| Participants | Cohorts: (see protocol for full inclusion/exclusion criteria) |
| | 1. Antenatal surveillance cohort (ANC-1): pregnant women recruited at ANC-1 visit |
| | 2. Antenatal surveillance cohort (DSS): pregnant women recruited from the community (DSS area) |
| | 3. Antenatal illness surveillance cohort: pregnant women who meet COVID-19 testing criteria and pregnant women who do not meet COVID-19 testing criteria |
| | 4. Labor and delivery surveillance cohort: women in labor/at delivery who meet COVID-19 testing criteria and women in labor/at delivery who do not meet COVID-19 testing criteria |
| Sample Size | 1. ANC-1 pregnant woman cohort: 2,000 pregnant women and their infants |
| | 2. DSS pregnant women cohort: 1,000 pregnant women and their infants |
| | 3. ANC illness surveillance cohort: up to 1,500 pregnant women and their infants (up to 500 symptomatic women + 1000 asymptomatic controls) |
| | 4. Labor and Delivery Surveillance cohort: Up to 7,500 pregnant women and their infants (up to 2,500 symptomatic women + 5,000 asymptomatic controls) |
| Timeline | From August 2020 through 6 weeks postpartum and 6 months postnatal for infants |
| Outcomes | Primary Outcomes: Mother-Infant linked Pregnancy Surveillance |
| | ● Life-threatening or potentially life-threatening maternal complications (e.g. stroke, hemorrhage, seizure, etc.) |
| | ● Maternal death |
| | ● Fetal loss prior to 22 weeks gestation |
| | ● Preterm birth (birth at <37 weeks gestation) |
| | ● Low birth weight (<2500g) |
| | ● Stillbirth |
| | ● Infant death within the first 6 months of life |
| | Secondary outcomes: Pregnancy cohort: |
| | ● Maternal antenatal or postpartum requirement for hospitalization (excluding the delivery visit) |
| | ● Infant requirement for hospitalization within the first six months of life |
| | ● Congenital malformation at birth |
| | ● SARS-CoV-2 microbiologically confirmed infection during pregnancy |
| | ● SARS-CoV-2 microbiologically confirmed infection during the postpartum period |
| | ● SARS-CoV-2 infection in the first six months of life |
- SARS-CoV-2 microbiologically confirmed infection in health care workers
- SARS-CoV-2 seropositivity at delivery
- SARS-CoV-2 seropositivity at the ANC-1 visit

Notes

The ANC-1 and DSS prospective surveillance cohorts are mutually exclusive but are designed to be analyzed together.

Supplementary Table 2-8: PERICOVID – PREPARE

| Study Site/Name | PERICOVID – PREPARE |
|-----------------|----------------------|
| Investigators   | Dr Kirsty Le Doare   |
| Institutional Affiliations | St George’s, University of London |
| Study Design    | Prospective cohort study |
| Participants    | Pregnant women at any gestation attending designated study centres for ANC and delivery |
| Sample Size     | 10,000 (from Uganda and Malawi) |
| Timeline        | 12 months (September 2020 to August 2021) |
| Outcomes        |                                     |
| Notes           | [https://www.pericovid.com/pericovid-in-africa](https://www.pericovid.com/pericovid-in-africa) |
Supplementary Table 2-9: Washington State COVID-19 in Pregnancy Collaborative

| Study Site/Name | Washington State COVID-19 in Pregnancy Collaborative |
|----------------|--------------------------------------------------------|
| Investigators  | Kristina Adams Waldorf (PI); Erica Lokken (Co-I)      |
| Institutional Affiliations | University of Washington, Seattle, WA |
| Study Design   | Retrospective medical records review of PCR confirmed SARS-CoV-2 infections in pregnancy (case-only) |
| Participants   | Pregnant patients with PCR confirmed SARS-CoV-2 infections during any trimester of pregnancy detected through June 30, 2020 at 35 hospitals and clinics in Washington State. |
| Sample Size    | ~240 cases in pregnancy; not all cases will have delivered by completion of data collection |
| Timeline       | Data collection complete September 2020, data sharing with PMA team by Dec 2020 or early 2021. |
| Outcomes       | Pregnancy, delivery, and some neonatal outcomes. COVID-19 disease severity and hospitalization data. |
| Notes          | If our cases are included, we recommend dropping WA state cases from the PRIORITY registry (those occurring prior to June 30, 2020) to reduce duplication. There is also a potential for a few duplicate cases with the “Inter-COVID” project; we are not sure if this group is contributing data to the PMA. |

Supplementary Table 2-10: NICHD Global Network

| Study Site/Name | NICHD Global Network |
|----------------|----------------------|
| Investigators  | Beth McClure         |
| Institutional Affiliations | RTI International (data coordinating center); ICDDR,B (Bangladesh); Moi University (Kenya); INCAP (Guatemala); Kinshasa School of Public Health (DRC); Lata Medical Research Foundation (India); KLE University (India); Aga Khan University (Pakistan); University of Zambia (Zambia); US Partners: University of Alabama at Birmingham; Boston University; Columbia University; University of Colorado; University of Virginia; University of North Carolina at Chapel Hill; Thomas Jefferson University; Indiana University |
| Study Design   | Prospective cohort   |
| Participants   | All pregnancies within the catchment area are recruited; questionnaires used to identify suspected COVID-19, as well as ongoing antibody testing at delivery. A subset of women will also have antibody testing conducted at the first ANC visit |
| Sample Size    | Target of 2,000 pregnancies per study site (16,000 total) |
| Timeline       | Expected 1-year timeline |
| Outcomes       | Maternal morbidity and mortality; stillbirth; neonatal morbidity and mortality |
| Notes          |                                                     |
### Supplementary Table 2-11: NICHD Maternal-Fetal Medicine Units (MFMU) Network

| Study Site/Name | NICHD Maternal-Fetal Medicine Units (MFMU) Network |
|-----------------|--------------------------------------------------|
| Investigators   | Torri Metz¹ (Protocol Chair), Rebecca Clifton² (Data Coordinating Center PI) |
| Institutional Affiliations | ¹University of Utah, ²George Washington University |
| Study Design   | Registry and prospective cohort study |
| Participants   | Pregnant women confirmed to have COVID-19 in participating network sites; the cohort component of the study includes random deliveries from 2020 at selected study sites for comparison. |
| Sample Size    | Approximately 2,000 COVID-19 cases; the cohort study component will include approximately 14,000 random deliveries from the same study sites as unexposed. |
| Timeline       | Actively recruiting as of June 2020; completing follow-up through February 2021 |
| Outcomes       | The primary endpoint is a maternal composite defined as at least one of the following during pregnancy and through 6 weeks postpartum: mortality, morbidity related to hypertensive disorders of pregnancy, morbidity related to postpartum hemorrhage, morbidity related to infection. |
| Notes          | [https://mfmunetwork.bsc.gwu.edu/PublicBSC/MFMU/MFMUPublic/](https://mfmunetwork.bsc.gwu.edu/PublicBSC/MFMU/MFMUPublic/) |

### Supplementary Table 2-12: Canadian Surveillance of COVID-19 in Pregnancy

| Study Site/Name | Canadian Surveillance of COVID-19 in Pregnancy: Epidemiology, Maternal and Infant Outcomes (CANCOVID-Preg) |
|-----------------|------------------------------------------------------------------------------------------------------------------|
| Investigators   | Deborah Money |
| Institutional Affiliations | University of British Columbia |
| Study Design   | National surveillance: prospective observational/surveillance cohort |
| Participants   | Women currently pregnant or delivered, living in Canada, documented SARS-CoV-2 infection in pregnancy |
| Sample Size    | 1,000 |
| Timeline       | April 2020-December 2023 |
| Outcomes       | Primary Outcome Measures: Maternal outcomes will include the risk for preterm birth and delivery complications. Fetal outcomes will include Apgar scores at 1 and 5 minutes, birthweight, admission to NICU, positive test for SARS-CoV-2, and need for resuscitation at delivery |
| Notes          | [https://ridprogram.med.ubc.ca/cancovid-preg/](https://ridprogram.med.ubc.ca/cancovid-preg/) |
**Supplementary Table 2-13: China and Hong Kong COVID Registry**

| Study Site/Name | China and Hong Kong COVID Registry |
|-----------------|-------------------------------------|
| Investigators   | Liona Poon¹; Huixia Yang²           |
| Institutional Affiliations | ¹The Chinese University of Hong Kong; ²Peking University Health Science Center |
| Study Design    | Registry                            |
| Participants    | Pregnant women. Hong Kong: PCR positive. Original China data used probable infection definition, but new cases will be PCR. |
| Sample Size     | 116 participants initially recruited in January 2020; potential to recruit more for China and Hong Kong sites. Following pregnant women and infants. |
| Timeline        | Contribute initial data by August 2020. |
| Outcomes        |                                     |
| Notes           |                                     |

**Supplementary Table 2-14: RECOGEST Colombia**

| Study Site/Name | RECOGEST Colombian registry: COVID and pregnancy |
|-----------------|-------------------------------------------------|
| Investigators   | Jose Sanin, Nataly Velasquez, Jorge Tolosa      |
| Institutional Affiliations | Colombia, Clinica Universitaria Bolivariana, FUNDARED-MATERNA |
| Study Design    | Multicenter study: prospective, longitudinal observational |
| Participants    | Pregnant and puerperal women with confirmed SARS cOV2/ COVID |
| Sample Size     | All COVID-19 positive pregnant women in the participating institutions. 82 recruited as of August 2020, expected to be 400 patients total. |
| Timeline        | Recruiting until December 2020                  |
| Outcomes        | Primary Outcome Measures: Maternal, perinatal and fetal outcomes and socioeconomic characteristics. Emphasis in COVID positive admitted to Intensive Care Unit |
| Notes           | [https://www.clinicauniversitariabolivariana.org.co/clinica/es/recogest?resolvetemplatefordevice=true](https://www.clinicauniversitariabolivariana.org.co/clinica/es/recogest?resolvetemplatefordevice=true) |


Supplementary Table 2-15: PERICOVID Africa – PRECISE

| Study Site/Name | PERICOVID – PRECISE |
|----------------|---------------------|
| Investigators  | Peter von Dadelszen |
| Institutional Affiliations | King’s College London |
| Study Design | Prospective cohort study |
| Participants | Pregnant women at any gestation attending designated study centres for ANC and delivery in the Gambia, Kenya, and Mozambique. |
| Sample Size | Tentative target: 6,000 |
| Timeline | Tentative: August 2020 through June 2021 |
| Outcomes | Key outcomes include: |
| | ● Stillbirth |
| | ● Pre-term birth |
| | ● Hypertension |
| Notes | [https://www.pericovid.com/pericovid-in-africa](https://www.pericovid.com/pericovid-in-africa) |

Supplementary Table 2-16:

| Study Site/Name | Coronavirus Health Outcomes in Pregnancy and Newborns (CHOPAN) Registry |
|----------------|-----------------------------------------------------------------------|
| Investigators  | Clare Whitehead |
| Institutional Affiliations | University of Melbourne |
| Study Design | Registry of pregnant women who are infect with COVID-19 in Australia and New Zealand |
| Participants | Pregnant people with confirmed COVID-19 (suspected cases are not included) |
| Sample Size | 50 cases as of August 2020 (expecting 100 new cases through end of 2020) |
| Timeline | Ongoing (began April 2020) |
| Outcomes | Obstetric, perinatal and neonatal outcomes after coronavirus infection |
| Notes | CHOPAN is collaborating with EpiCentre on neonatal outcomes. |
Supplementary Table 3. Key stakeholders

| Organization                                                                 | Steering Committee Members                                      |
|------------------------------------------------------------------------------|------------------------------------------------------------------|
| American College of Obstetrics and Gynecology (ACOG)                         | Maria Diaz, Sara Homayouni, Nadia Ramey, Alireza A. Shamshirsaz |
| International Federation of Gynecology and Obstetrics (FIGO)                 | Jeanne Conry, Lesley Regan                                        |
| Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) | Daniel Raiten, Nahida Chakhtoura, Caroline Signore                |
| The World Health Organization (WHO)                                          | Rajiv Bahl, Mercedes Bonet Semenas, Karen M. Edmond, Christine Godwin, Caron Rahn Kim, Olufemi Taiwo Oladapo, Anna Thorson, Soe Soe Thwin |
Global Data Harmonization: Data Modules and Core Questions / Variables for Pregnancy & Perinatal COVID-19 Registries or Cohorts (Last Updated June 2, 2020)

Prepared by Emily R. Smith¹ (EmilySmith@GWU.edu) and Siran He, in collaboration with Yalda Afshar² and Valerie Flaherman³

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Objective: Our objective is to provide a harmonized set of high priority, core questions / variables for pregnancy and perinatal COVID-19 registry or cohort studies. These are not intended to be a survey or case report form. Each study has or will develop local protocols and data collection forms. However, each study will ideally collect the data outlined here. This will enable future collaborations to answer high priority questions or to pool data where studies investigators are willing and able.

Harmonization Process: We developed the draft data modules and questions based on a proposed set of questions from the PRIORITY study. We also reviewed and included questions from the data collection forms developed by the World Health Organization (WHO) and the U.S. Center for Disease Control (CDC). We requested feedback via a survey and by email from the >50 participants of the bi-monthly “Perinatal COVID-19 Global Gathering”. The current data modules reflect feedback and general consensus among survey respondents.

Which studies should harmonize data? Any registry or cohort study collecting data regarding pregnant or postpartum people suspected or confirmed to have COVID-19 (as well as their fetus / infant) should consider collecting harmonized data, whether or not they are population-based. The studies may collect data from health records, by directly questioning the participant, or both. Differences in the way participants are sampled/recruited or the way data is collected can be reconciled when specific data analyses are planned.

Participant Inclusion Criteria: Participants enrolled in the study should meet the following inclusion criteria:

- Pregnant person, or person who was pregnant within the past 6 weeks (Note: 42 days / 6 weeks reflects the postpartum period / maternal mortality definition);
- diagnosed with (or suspected to be infected with) COVID-19;
- provides informed consent.

What is a Data Module: We define a "Data Module" as a group of questions (variables) that: 1) are thematically related; 2) are asked at the same time and with the same frequency; 3) AND refer to EITHER mother or baby (not both). These modules are organized for the purpose of prioritizing variables and themes, and do NOT reflect the order in which they should/would appear in actual data collection forms.
**Core Data Modules**

| Module | Research Objective |
|--------|--------------------|
| Module 1: Maternal COVID-19 Information (n=7 questions) | To evaluate the clinical presentation and natural history of disease for women infected with (or suspected to be infected with) COVID-19 who are pregnant or have been pregnant within the last 6 weeks / 42 days. *(e.g., symptoms, testing, treatment, clinical course)* |
| Module 2: Pregnancy Status & Pregnancy-Related Morbidity (n=16 questions) | To confirm pregnancy status and to document pregnancy-related basic information among women infected with COVID-19 *(e.g., due date, singleton/multiple pregnancy, etc.)* |
| Module 3: Pregnancy Outcomes (n=6 questions) | To document the endpoint of the registered pregnancy among women infected with COVID-19 *(e.g., abortion, stillbirth, live birth, etc.)* |
| Module 4: Birth Characteristics (n=14 questions) | To document various characteristics related to live birth. *(e.g., place of birth, birthweight, gestational age, etc. Information about the infant, if recorded during/right after delivery, will be in this module)* |
| Module 5: Infant Morbidity & Mortality (n=12 questions) | To evaluate infant outcomes among those born to women who have had COVID-19 (if live birth) *(e.g., COVID-like symptoms up till 12mo, etc.)* |
| Module 6: Core socio-demographic information (n=6 questions) | To identify high-risk subgroups with increased pregnancy, delivery, and infant adverse outcomes that are potentially associated with COVID-19 |

Time intervals (e.g. gestational age, time from symptom onset to testing) should be calculated directly from dates where possible. **The dates (and ages) recorded in these modules include:**

- Module 1-Q1: Date of onset of COVID-like symptoms
- Module 1-Q2: Date of COVID diagnosis
- Module 2-Q1: Date of study/registry enrollment
- Module 2-Q3: Gestational age upon enrollment
- Module 3-Q1: Date of pregnancy outcome
- Module 3-Q4: Date of maternal death
- Module 4-Q1: Date of birth & time of birth
  - Same as Module 3-Q1 (if live birth)
- Module 4-Q5: Age of infant (in hours) for weighing
- Module 4-Q6: Infant gestational age estimation
  - Can calculate this from Module 3-Q1 (if live birth)
  - Note this question asks about estimation method, which is important in order to address measurement error in analysis stage
- Module 4-Q13: Date of facility discharge after birth (for infant)
- Module 5-Q2: Date of neonatal death
- Module 5-Q6: Date of neonatal COVID testing
**Module 1: Maternal COVID-19 Information**

What: COVID symptoms, testing, treatment, clinical course  
When: At regular interval until disease resolution or chart abstraction

| Questionnaire-based data collection | Medical record data extraction |
|------------------------------------|--------------------------------|
| Q1. Date of onset of COVID-like symptoms (DD:MM:YY) | Q1. Extract from medical record:  
  - First date of COVID-like symptoms (DD:MM:YY) |
| Q2. Have you been diagnosed with COVID-19?  
  - Yes, confirmed  
  - Not confirmed, under investigation | Q2. Extract from medical record:  
  - COVID-19 diagnosis notes:  
    - Confirmed  
    - Patient under investigation (PUI) |
| Q3. If answered “Yes” to Q2:  
  - Date of COVID-19 diagnosis (DD:MM:YY) | Q3. Extract from medical record:  
  - Date of COVID-19 diagnosis, or Date PUI status was documented (DD:MM:YY) |
| Q4. What symptoms did you have that led you to be tested or suspected of Coronavirus/COVID19? (Check all that apply)  
  - Fever  
  - Cough  
  - Shortness of breath  
  - Dizziness or fainting  
  - Body aches  
  - Runny nose  
  - Sore throat  
  - Loss of sense of smell or taste  
  - Sneezing  
  - Fatigue  
  - Nausea  
  - Vomiting  
  - Diarrhea  
  - Headache  
  - Other symptoms (please specify)  
  - None / Asymptomatic | Q4. Extract from medical record:  
  - All symptoms listed in the record that are related to COVID investigation / diagnosis |
| Q5. Do you work in healthcare or provide direct patient care?  
  - Yes  
  - No  
  - Other, please specify | Q5. Extract from medical record:  
  - If occupation data is available,  
    - Note down “Y” for healthcare/direct patient care,  
    - “N” for other occupations,  
    - “NA” for unknown |
| Q6. Have you received any medication for the treatment of COVID-19 (e.g. anti-viral, immunomodulators, convalescent plasma, IL6 mAb, other)  
  - Yes, I have  
  - No, I have not  
  - Maybe / uncertain  
  - Other, please specify | Q6. Extract from medical record:  
  - Has the patient been given any medication for the treatment of COVID-19  
    - Yes  
    - No  
    - Other, please specify |
| Q7. If answered “Yes” to Q6: if possible, document more details about the medication:  
  - Type / Name  
  - Dose  
  - Duration  
  - Indications  
  - Clinical trial registration | Q7. Extract from medical record:  
  - Details about COVID-19 treatment regime, including medications, dose, duration, clinical trial inclusion, etc. | 
Module 2: Pregnancy Status & Pregnancy-Related Morbidity

What: Pregnancy registration information and non-COVID morbidity among participants
When: At pregnancy registration

| Questionnaire-based data collection | Medical record data extraction |
|------------------------------------|-------------------------------|
| **Q1. Date of study enrolment (DD:MM:YY)** | **Q1. Extract from medical record: Date of study enrolment (DD:MM:YY)** |
| **Q2. Status upon enrolment** | **Q2. Extract from medical record:**
| • Pregnant (confirmed by healthcare provider), not in labor | • Pregnancy status:
| • Pregnant (not confirmed by healthcare provider), not in labor | ○ Pregnant (confirmed by healthcare provider) not in labor
| • Pregnant in labor | ○ Pregnant in labor
| • Postpartum [days] --> if yes, breastfeeding Y/N | ○ Postpartum [days] --> if yes, breastfeeding Y/N
| • Post-abortion, miscarriage | ○ Post-abortion, miscarriage |
| **Q3. If answered “postpartum” in Q2: are you breastfeeding?** | **Q3. Extract from medical record:**
| • Yes | • Breastfeeding status for postpartum women
| • No | |
| **Q4. Gestational age at enrollment. Do you know your due date?** | **Q4. Extract from medical record:**
| • Yes → document due date (or how far along you are in pregnancy) (DD:MM:YY) | • Gestation age at enrollment
| • No | |
| • Maybe / uncertain | |
| **Q5. If answered “Yes” to Q4:** | **Q5. Extract from medical record:**
| • What is the method of due date assessment? | • Method of gestational age assessment
| **Q6. Number of fetuses:** | **Q6. Extract from medical record:**
| • Singleton | • Number of fetuses
| • Twins | |
| • Other, specify | |
| **Q7. (Pre-pregnancy) BMI (can document BMI or weight and height):** | **Q7. Extract from medical record:**
| • Weight (Kg) | • Pre-pregnancy weight and height (if available, be sure to note down units)
| • Height (m) | |
| **Q8. (At the time of registration) BMI (can document BMI or weight and height):** | **Q8. Extract from medical record:**
| • Weight (Kg) | • At the time of clinical visit, weight and height (if available, note down units)
| • Height (m) | |
| **Q9. Gravidity: Is this your first pregnancy?** | **Q9. Extract from medical record:**
| • Yes | • Gravidity information
| • No | |
| **Q10. If answered “No” to Q9:** | **Q10. NA**
| • How many times have you been pregnant? | |
| **Q11. Parity: Is this your first child birth?** | **Q11. Extract from medical record:**
| • Yes | • Parity information
| • No | |
| **Q12. If answered “Not” to Q11:** | **Q12. NA**
| • How many live births have you had previously? | |
Q13. Has a doctor or other healthcare provider told you that you have any of the following conditions before you were pregnant? (check all that apply) *(local sites should describe conditions in a way that women will understand and self-report)*

- Asthma
- Obesity
- Sleep apnea
- Anemia (Hb < 11g/dL per WHO)
- Chronic high blood pressure (hypertension)
- Thyroid disease
- Immune suppression (due to underlying disease or meds)
- Neurological disease
- Chronic lung disease (excluding asthma)
- Autoimmune disease
- Cardiovascular disease (excluding hypertension)
- Other, please note

Q13. Extract from medical record:
- List all pregnancy-related conditions documented in the record

Q14. Has a doctor or other healthcare provider told you that you have any of the following conditions during pregnancy? (check all that apply) *(local sites should describe conditions in a way that women will understand and self-report)*

- Hypertensive disease of pregnancy (including preeclampsia/eclampsia)
- Hyperemesis
- Intrauterine growth restriction
- Abnormal placentation (placental previa/accreta/percreta)
- Placental abruption
- Bacterial infection prior to hospital visit
- Preterm contractions (not in labor)
- Preterm labor
- Preterm rupture of membranes
- Haemorrhage
- If haemorrhage, which type: antepartum/intrapartum; Postpartum; Abortion-related
- Embolic disease
- Anesthetic complications

Q14. Extract from medical record:
- List all pregnancy-related conditions documented in the record

Q15. If any sample was collected for research, what was/were the sample(s)?

- Amniotic fluid
- Placenta
- Cord blood
- Vaginal swab
- Feces/rectal swab
- Pregnancy tissue in the case of fetal demise/induced abortion
- Breastmilk
- Maternal blood
- Not applicable (no sample collected)

Q15. Extract from medical record:
- Document collection of any biological sample

Q16. If selected any sample(s) in Q15:

- If possible, please document for each type of sample collected:
  - Tests done with the samples
  - Results of the tests

Q16. Extract from medical record:
- Separately for each sample documented:
  - Tests done
  - Results of the tests
**Module 3: Pregnancy Outcomes**

What: Information about how the pregnancy ended; maternal mortality will be recorded in this module

When: Once, after pregnancy outcome is known

| Questionnaire-based data collection | Medical record data extraction |
|------------------------------------|--------------------------------|
| Q1. Date of pregnancy outcome (DD:MM:YY) [Allows calculation of gestational age (in weeks) when pregnancy ended] | Q1. Extract from medical record:  
  - Date of pregnancy outcome (DD:MM:YY) |
| Q2. Please indicate the end point of this pregnancy:  
  - Live birth  
  - Stillbirth  
  - SAB (spontaneous abortion) → expectant, medical management, D&C/E (3 choices)  
  - TAB (therapeutic abortion) → expectant, medical management, D&C/E (3 choices) | Q2. Extract from medical record:  
  - The end point of this pregnancy (note down based on the format in the record, such as live birth, stillbirth, etc.) |
| Q3. Maternal death?  
  - Yes  
  - No  
  - Unknown | Q3. Extract from medical record:  
  - If maternal death occurred (yes/no/unknown) |
| Q4. If answered “Yes” for Q3:  
  - Date of maternal death? (DD:MM:YY) | Q4. Extract from medical record:  
  - If maternal death, date of death (DD:MM:YY) |
| Q5. If answered “Yes” for Q3:  
  - Gestational age in weeks at death? | Q5. Extract from medical record:  
  - If maternal death, gestational age in weeks at death |
| Q6. If answered “Yes” for Q3:  
  - Cause of death  
    - COVID-19  
    - Obstetric hemorrhage  
    - Hypertensive disorder (including preeclampsia and eclampsia)  
    - Pregnancy-related infection  
    - Abortion/ectopic pregnancy  
    - Other direct cause (obstetric complications)  
    - Indirect cause (pre-existing medical condition exacerbated by pregnancy)  
    - Coincidental cause (e.g. motor vehicle cause, accidental injury, assault)  
    - Unknown | Q6. Extract from medical record:  
  - If maternal death, cause of maternal death (COVID or other causes, document as appeared in medical record) |
Module 4: Birth Characteristics

What: Information related to labor and delivery/birth and other data collected on the day of birth
When: To be asked on or soon after the day of birth, at enrollment if enrollment occurs postpartum, or directly extracted from chart

| Questionnaire-based data collection | Medical record data extraction |
|------------------------------------|-------------------------------|
| **Q1. Date** and time, if available of birth (DD:MM:YY) (HH:MM) | **Q1. Extract from medical record:**
  - Date of birth (and time of birth, if available) (DD:MM:YY) (HH:MM) |
| **Q2. Where was the infant born?** *
  - Home
  - Birthing facility/hospital
  - Other location, please specify | **Q2. Extract from medical record:**
  - Location of birth:
    - Hospital (indicate which hospital)
    - Other (specify location, if delivery did not occur at this facility)
    - “NA” if unknown |
| * If your registry collects only hospital-based births, please record “facility/hospital” for all records | **Q3. Mode of delivery?**
  - Spontaneous vaginal
  - Operative vaginal - forceps or vacuum
  - Cesarean section (scheduled)
  - Cesarean section (intrapartum)
  - Unknown |
| **Q4. What was the infant’s weight at birth (grams)?** | **Q4. Extract from medical record:**
  - Infant weight at birth (grams) |
| **Q5. Has the infant’s gestational age been estimated?**
  - Yes
  - No | **Q5. NA** |
| **Q6. If answered “Yes” to Q6:**
  - What was the estimated gestational age (weeks) | **Q6. Extract from medical record:**
  - Gestational age of infant |
| **Q7. If answered “Yes” to Q6:**
  - What method was used to determine gestational age?
    - Ultrasound
    - Estimated date of delivery based on last menstrual period (EDD)
    - Ballard/Dubowitz;
    - Other, please specify | **Q7. Extract from medical record:**
  - Estimation method exactly as documented in the record |
| **Q8. On the day of birth, did your infant have any difficulty breathing?**
  - Yes
  - No
  - Maybe / Uncertain | **Q8. Extract from medical record:**
  - On the day of birth, did the infant have any difficulty breathing, as documented in the record |
| **Q9. At the time of birth, was your infant admitted to the neonatal intensive care unit or the special care unit?**
  - Yes
  - No | **Q9. Extract from medical record:**
  - At the time of birth, was the infant admitted to the neonatal intensive care unit/special care unit (Y/N/NA) |
| **Q10. At the time of birth, did your infant receive oxygen?**
  - Yes
  - No | **Q10. Extract from medical record:**
  - At the time of birth, did the infant receive oxygen? (Y/N/NA) |
| Q11. What type of resuscitation was provided at delivery? |
|---------------------------------|
| • None                           |
| • Warm/dry/stimulation          |
| • Blow by oxygen                |
| • Continuous positive airway pressure |
| • Positive pressure ventilation |
| • Intubation                    |
| • Chest compressions            |
| • Surfactant                    |
| • Unknown                       |

| Q11. Extract from medical record: |
|---------------------------------|
| • Resuscitation? (Y/N/NA)       |
| • If yes → type of resuscitation, as documented in the record |

| Q12. Did the infant breastfeed or receive any breast milk on the day of birth? |
|---------------------------------|
| • Yes                            |
| • No                             |
| • Maybe / Uncertain              |

| Q12. Extract from medical record: |
|---------------------------------|
| • Breastfeeding or breast milk on the day of birth (Y/N/NA) |

| Q13. Date of infant discharge from labor and delivery event (DD:MM:YY) |
|------------------------------------------------------------------------|
|                                                                        |

| Q13. Extract from medical record: |
|---------------------------------|
| • Date of infant discharge (DD:MM:YY) |

| Q14. Newborn outcome at discharge: |
|---------------------------------|
| • Expired                       |
| • Home                          |
| • Transfer to another acute care facility |
| • Transfer to a chronic care facility |

| Q14. Extract from medical record: |
|---------------------------------|
| • Newborn outcomes at discharge as documented in the record |
Module 5: Infant Mortality and Morbidity

What: Information related to infant health, particularly related to COVID-19
When: At regular interval until up to 12 months after birth (or until chart extraction)

| Questionnaire-based data collection | Medical record data extraction |
|------------------------------------|-------------------------------|
| Q1. Neonatal/infant death?         | Q1. Extract from medical record: |
| • Yes                              | • Neonatal/infant death? (Y/N/NA) |
| • No                               | Q2. Extract from medical record: |
|                                    | • If neonatal/infant death, date-time of death (DD:MM:YY) (HH:MM) |
| Q2. If answered “Yes” to Q1:       | Q3. Extract from medical record: |
| • Date-time of neonatal/infant death? | • If neonatal/infant death, cause of death (COVID or other causes, document as appeared in medical record) |
| (DD:MM:YY) (HH:MM)                 |                                    |
| Q3. If answered “Yes” to Q1:       | Q4. Extract from medical record: |
| • Cause of death?                  | • Was the infant documented by clinicians to have any of the symptoms of COVID-19? (document exactly as in the record) |
| o COVID-19                         |                                    |
| o Preterm/low birth weight         |                                    |
| o Birth asphyxia                   |                                    |
| o Infection                        |                                    |
| o Birth trauma                     |                                    |
| o Congenital/birth defects         |                                    |
| o Unknown                          |                                    |
| o Other, please specify            |                                    |
| Q4. Was the infant documented by clinicians to have any of the following symptoms of COVID-19? |
| - Fever (T>37.5)                   |                                    |
| - Respiratory distress             |                                    |
| - Cough                            |                                    |
| - Nasal congestion/runny nose      |                                    |
| - Vomiting                         |                                    |
| - Diarrhea                         |                                    |
| - Lethargy                         |                                    |
| - Rapid heart rate (>160 bpm) (record bpm if available) | Q5. Extract from medical record: |
|                                    | • Any COVID-19 test for the infant? (Y/N) |
| Q5. Was the baby tested for COVID-19? | Q6. Extract from medical record: |
| • Yes                              | • Testing date and time (DD:MM:YY) (HH:MM) |
| • No                               |                                    |
| • Maybe / Uncertain                |                                    |
| Q6. If answered “Yes” to Q5:       | Q7. Extract from medical record: |
| • When was the baby tested?        | • Which tests were conducted |
| o Immediately after birth          |                                    |
| o Other, please specify date (DD:MM:YY) (HH:MM) | Q8. Extract from medical record: |
|                                    | • Test result – exactly as documented |
| Q7. If answered “Yes” to Q5:       |                                    |
| • What tests were conducted?       |                                    |
| o Viral PCR test                   |                                    |
| o Chest image or X-ray             |                                    |
| o Other, please specify            |                                    |
| Q8. If answered “Yes” to Q5:       |                                    |
| • What was the test result?        |                                    |
| o Confirmed COVID-19               |                                    |
| o Not COVID-19                     |                                    |
| o Other, specify                   |                                    |
| Q9. Has the baby received antiviral medications? | Q9. Extract from medical record: |
|                                    |                                    |
| Q10. If answered “Yes” to Q9: If antiviral medication was administered? | Did the infant receive antiviral medication? (Y/N/NA) |
|---|---|
| • Which antiviral medication was administered? If possible, document:  
  o Name  
  o Dosage  
  o Duration | |
| Q10. Extract from medical record:  
  • If antiviral medication was used, note down exactly as in the record:  
    o Which medication  
    o Dosage  
    o Duration | |
| Q11. Has your infant breastfed or received any breast milk in the last 24 hours?  
  • Yes  
  • No  
  • Other, please specify | |
| Q11. Extract from medical record:  
  • Has the infant been breastfed or received any breast milk in the past 24 hours (Y/N/NA)?  
  • If information is available for longer periods, note it down as well | |
| Q12. Any congenital anomalies?  
  • Neural tube defects  
  • Microcephaly  
  • Congenital malformations of ear  
  • Congenital heart defects  
  • Orofacial clefts  
  • Congenital malformations of digestive system  
  • Congenital malformations of genital organs  
  • Abdominal wall defects  
  • Chromosomal abnormalities  
  • Reduction defects of upper and lower limbs  
  • Talipes equinovarus/clubfoot | |
| Q12. Extract from medical record:  
  • Any congenital anomalies in the record? (Note it down exactly as in the record) | |
### Module 6: Core Sociodemographic Information

**What:** Socio-demographic information about the study participant  
**When:** Once at the beginning of the study (maternal information); Once after birth (for infant information)

| Questionnaire-based data collection | Medical record data extraction |
|-------------------------------------|--------------------------------|
| Q1. Country | Site ID | Q1. Indicate the site / facility |
| Q2. Age of the mother (years) | | Q2. Extract from medical record:  
| | | ● Mother’s age (years), or  
| | | ● Mother’s date of birth (DD:MM:YY) |
| Q3. Sex of the child (if applicable) | | Q3. Extract from medical record:  
| | | ● Sex of the child |
| Q4. Race/Ethnicity of the mother * | | Q4. Extract from medical record:  
| * Each site to define appropriate categories for their context | | ● Mother’s race/ethnicity (if available) |
| Q5. Race/Ethnicity of the child (if applicable) * | | Q5. Extract from medical record:  
| * Each site to define appropriate categories for their context | | ● Child’s race/ethnicity (if available) |
| Q6. Years/level of education completed by the mother  
(choose highest level completed) | | Q6. Extract from medical record:  
| | | ● Mother’s education level (if available)  
| • No formal education | |  
| • Some primary education | |  
| • Primary education completed | |  
| • Secondary education completed | |  
| • University/College completed | |  
| • Graduate education / Terminal degree completed | |  

* Each site to define appropriate categories for their context
Global Data Harmonization
Data Modules and Core Questions / Variables for
Pregnancy & Perinatal COVID-19 Registries or Cohorts
(Last Updated November 8, 2020)

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Objective: Our objective is to provide a harmonized set of high priority, core questions / variables for pregnancy and perinatal COVID-19 registry or cohort studies. These are not intended to be a survey or case report form. Each study has or will develop local protocols and data collection forms. However, each study will ideally collect the data outlined here. This will enable future collaborations to answer high priority questions or to pool data where studies investigators are willing and able.

Harmonization Process: We developed the draft data modules and questions based on a proposed set of questions from the PRIORITY study. We also reviewed and included questions from the data collection forms developed by the World Health Organization (WHO) and the U.S. Center for Disease Control (CDC). We requested feedback via a survey and by email from the >50 participants of the bi-monthly “Perinatal COVID-19 Global Gathering”. The current data modules reflect feedback and general consensus among survey respondents.

Which studies should harmonize data? Any registry or cohort study collecting data regarding pregnant or postpartum people suspected or confirmed to have COVID-19 (as well as their fetus / infant) should consider collecting harmonized data, whether or not they are population-based. The studies may collect data from health records, by directly questioning the participant, or both. Differences in the way participants are sampled/recruited or the way data is collected can be reconciled when specific data analyses are planned.

Participant Inclusion Criteria: Participants enrolled in the study should meet the following inclusion criteria:
- Pregnant person, or person who was pregnant within the past 6 weeks (Note: 42 days / 6 weeks reflects the postpartum period / maternal mortality definition);
- diagnosed with (or suspected to be infected with) COVID-19;
- provides informed consent.
**What is a Data Module:** We define a "Data Module" as a group of questions (variables) that: 1) are thematically related; 2) are asked at the same time and with the same frequency; 3) AND refer to EITHER mother or baby (not both). These modules are organized for the purpose of prioritizing variables and themes, and do NOT reflect the order in which they should/would appear in actual data collection forms.

**Updates:** Updates to the data modules in August and September 2020 reflect efforts to harmonize these modules with updated World Health Organization (WHO) case definitions and ongoing multi-site study protocols developed by WHO. Additions are highlight in yellow. Questions that have been removed are crossed out.

### Core Data Modules

| Module                                      | Research Objective                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
|---------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Module 1: Maternal COVID-19 Information     | To evaluate the clinical presentation and natural history of disease for women infected with (or suspected to be infected with) COVID-19 who are pregnant or have been pregnant within the last 6 weeks / 42 days. *(e.g., symptoms, testing, treatment, clinical course)*                                                                                                                                                                                                                             |
| *(n=14 questions)*                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| Module 2: Pregnancy Status                  | To confirm pregnancy status and to document pregnancy-related basic information among women infected with COVID-19 *(e.g., due date, singleton/multiple pregnancy, etc.)*                                                                                                                                                                                                                                                                                                  |
| & Pregnancy-Related Morbidity               | *(n=14 questions)*                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| Module 3: Pregnancy Outcomes                | To document the endpoint of the registered pregnancy among women infected with COVID-19 *(e.g., abortion, stillbirth, live birth, etc.)*                                                                                                                                                                                                                                                                                                  |
| *(n=5 questions)*                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| Module 4: Birth Characteristics             | To document various characteristics related to live birth. *(e.g., place of birth, birthweight, gestational age, etc. Information about the infant, if recorded during/right after delivery, will be in this module)*                                                                                                                                                                                                                                  |
| *(n=15 questions)*                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| Module 5: Infant Morbidity & Mortality      | To evaluate infant outcomes among those born to women who have had COVID-19 *(if live birth)* *(e.g., COVID-like symptoms up till 12mo, etc.)*                                                                                                                                                                                                                                                                                                    |
| *(n=8 questions)*                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| Module 6: Core socio-demographic information | To identify high-risk subgroups with increased pregnancy, delivery, and infant adverse outcomes that are potentially associated with COVID-19                                                                                                                                                                                                                                                                                                    |
| *(n=6 questions)*                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| Module 7: Biospecimens and Diagnostic Testing| To clearly document all biospecimens collected related to COVID-19 in a pregnancy and delivery and diagnostic testing for COVID-19 completed for the mother and infant, with a focus on identifying any instances of vertical transmission of COVID-19.                                                                                                                                                                                                                             |
| *(n=unlimited responses based on collected samples)* |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
Time intervals (e.g. gestational age, time from symptom onset to testing) should be calculated directly from dates where possible. The dates (and ages) recorded in these modules include:

- **Module 1-Q1**: Date of onset of COVID-like symptoms
- **Module 1-Q3**: Date of COVID diagnosis
- **Module 1-Q8**: Date of hospital admission
- **Module 1-Q13**: Date of ICU admission / critical care receipt
- **Module 2-Q1**: Date of study/registry enrollment
- **Module 2-Q4**: Expected date of delivery
- **Module 3-Q1**: Date of pregnancy outcome
- **Module 3-Q4**: Date of maternal death
- **Module 4-Q1**: Date of birth & time of birth
  - Same as Module 3-Q1 (if live birth)
- **Module 4-Q6**: Infant gestational age estimation
  - Note this question asks about estimation method, which is important in order to address measurement error in analysis stage
- **Module 4-Q14**: Date of facility discharge after birth (for infant)
- **Module 5-Q2**: Date of neonatal death
- **Module 5-Q4**: Date of neonatal COVID-19 signs/symptoms
- **Module 7-Q2a**: Collection date of maternal biospecimen(s)
- **Module 7-Q4a**: Collection date of biospecimen(s) at delivery
- **Module 7-Q6a**: Collection date of neonatal/infant biospecimen(s)

### Module 1: Maternal COVID-19 Information

**What**: COVID symptoms, testing, treatment, clinical course

**When**: At regular interval until disease resolution or chart abstraction

| Questionnaire-based data collection | Medical record data extraction |
|------------------------------------|--------------------------------|
| **Q1. Date of onset of COVID-like symptoms (DD:MM:YY)** | **Q1. Extract from medical record:**
  - First date of COVID-like symptoms (DD:MM:YY) |
| **Q2. Have you been diagnosed with COVID-19?**
  - Yes, laboratory confirmed COVID-19
  - Yes, probable COVID-19 case (see 2a)
  - Suspected COVID-19 case (see 2b)
  - No, COVID-19 negative | **Q2. Extract from medical record:**
  -COVID-19 diagnosis notes:
    - Laboratory Confirmed
    - Probable COVID-19 case (see 2a)
    - Suspected COVID-19 case (see 2b)
    - No, COVID-19 negative |
| **Q2a. If diagnosed as a probable COVID-19 case, by which criteria where you diagnosed?**
  - A patient who meets clinical criteria above AND is a contact of a probable or confirmed case, or epidemiologically linked to a cluster with at least one confirmed case. | **Q2a. If diagnosed as a probable COVID-19 case, by which criteria was diagnosis made?**
  - A patient who meets clinical criteria above AND is a contact of a probable or confirmed case, or epidemiologically linked to a cluster with at least one confirmed case. |
### Q2b. If diagnosed as a probable COVID-19 case, by which criteria were you diagnosed?
- A person who meets the clinical AND epidemiological criteria by WHO
- A patient with severe acute respiratory illness

### Q3. If answered ‘Yes’ to Q2:
- Date of COVID-19 diagnosis (DD:MM:YY)

### Q4. What symptoms did you have that led you to be tested or suspected of Coronavirus/COVID19? (Check all that apply)
- Fever
- Cough
- Shortness of breath
- Dizziness or fainting
- Body aches
- Runny nose
- Sore throat
- Loss of sense of smell
- Loss of sense of taste
- Sneezing
- Fatigue
- Nausea
- Vomiting
- Diarrhea
- Headache
- Other symptoms (please specify)
- None / Asymptomatic

### Q5. Do you work in healthcare or provide direct patient care?
- Yes
- No
- Other, please specify

### Q6. Have you received any medication for the treatment of COVID-19 (e.g. anti-viral, immunomodulators, convalescent plasma, IL6 mAb, other)
- Yes, I have
- No, I have not
- Maybe / uncertain
- Other, please specify

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Module 2: Pregnancy Status & Pregnancy-Related Morbidity

What: Pregnancy registration information and non-COVID morbidity among participants
When: At pregnancy registration

| Questionnaire-based data collection | Medical record data extraction |
|------------------------------------|-------------------------------|
| Q1. Date of study enrolment (DD:MM:YY) | Q1. Extract from medical record: |
|                                    | • Details about COVID-19 treatment regime, including medications, dose, duration, clinical trial inclusion, etc. |

Q7. If answered “Yes” to Q6: if possible, document more details about the medication:
• Type / Name
• Dose
• Duration
• Indications
• Clinical trial registration

Q7. Extract from medical record:
• Details about COVID-19 treatment regime, including medications, dose, duration, clinical trial inclusion, etc.

Q8. Were you ever admitted to the hospital for COVID-19
• Yes
• No
• Unknown

Q8. Extract from medical record: Ever admitted to the hospital for COVID-19
• Yes
• No
• Unknown

Q9. If answer “Yes” to Q8: What was the date of hospital admission? (DD:MM:YY)

Q9. Extract from medical record: What was the date of hospital admission? (DD:MM:YY)

Q10. If answer “Yes” to Q8: What was the date of hospital discharge? (DD:MM:YY) (in the case of death, enter date of death).

Q10. If answer “Yes” to Q8: Extract from medical record: What was the date of hospital discharge? (DD:MM:YY) (in the case of death, enter date of death).

Q11. If answer “Yes” to Q8: what was the respiratory status of the patient while hospitalized?
• Self ventilating in room air
• Self ventilating with oxygen support
• Non-invasive respiratory support (CPAP, NIV)
• Mechanically ventilated, intubation
• Unknown

Q11. If answer “Yes” to Q8: Extract from medical record: what was the respiratory status of the patient while hospitalized?
• Self ventilating in room air
• Self ventilating with oxygen support
• Non-invasive respiratory support (CPAP, NIV)
• Mechanically ventilated, intubation
• Unknown

Q12. If answer “Yes” to Q8: Was the mother admitted to an intensive care unit (ICU) or administered critical care for COVID-19?

Q12. If answer “Yes” to Q8: Extract from medical record: Was the patient admitted to an intensive care unit (ICU) or administered critical care for COVID-19?

Q13. If answer “Yes” to Q12: What was the date of ICU admission / critical care? (DD:MM:YY)

Q13. If answer “Yes” to Q12: Extract from medical record: What was the date of ICU admission / critical care? (DD:MM:YY)

Q14. If answer “Yes” to Q8: What was the date of ICU discharge / end of critical care? (DD:MM:YY) (in the case of death, enter date of death).

Q14. If answer “Yes” to Q8: Extract from medical record: What was the date of ICU discharge / end of critical care? (DD:MM:YY) (in the case of death, enter date of death).
| Question                                                                 | Date of study enrolment (DD:MM:YY) | Extract from medical record:                                                                 |
|------------------------------------------------------------------------|------------------------------------|---------------------------------------------------------------------------------------------|
| Q2. Status upon enrolment                                              |                                    | ● Pregnant (confirmed by healthcare provider), not in labor                                  |
|                                                                       |                                    | ● Pregnant (not confirmed by healthcare provider), not in labor                              |
|                                                                       |                                    | ● Pregnant in labor                                                                         |
|                                                                       |                                    | ● Postpartum [days] --> if yes, breastfeeding Y/N                                           |
|                                                                       |                                    | ● Post-abortion, miscarriage                                                                |
| Q2. Extract from medical record:                                        |                                    | ● Pregnancy status:                                                                         |
|                                                                       |                                    |   ○ Pregnant (confirmed by healthcare provider) not in labor                                 |
|                                                                       |                                    |   ○ Pregnant in labor                                                                        |
|                                                                       |                                    |   ○ Postpartum [days] --> if yes, breastfeeding Y/N                                         |
|                                                                       |                                    |   ○ Post-abortion, miscarriage                                                              |
| Q3. If answered “postpartum” in Q2: are you breastfeeding?             |                                    | ● Yes                                                                                       |
|                                                                       |                                    | ● No                                                                                        |
| Q3. Extract from medical record:                                       |                                    | ● Breastfeeding status for postpartum women                                                  |
| Q4. What is your due date (expected date of delivery)?                 |                                    | ● DD/MM/YYYY = Date                                                                         |
|                                                                       |                                    | ● 08/08/1908 = Unknown                                                                      |
|                                                                       |                                    | ● 09/09/1909 = Not applicable                                                                |
| Q4. Extract from medical record:                                       |                                    | ● Gestational age at enrollment                                                              |
| Q5. If answered “Yes” to Q4: What is the method of due date assessment?|                                    | ● Method of gestational age assessment                                                      |
| Q6. Number of fetuses:                                                 |                                    | ● Singleton                                                                                  |
|                                                                       |                                    | ● Twins                                                                                     |
|                                                                       |                                    | ● Triplet                                                                                   |
|                                                                       |                                    | ● Higher order                                                                              |
| Q6. Extract from medical record:                                       |                                    | ● Number of fetuses                                                                         |
| Q7. (Pre-pregnancy) BMI (can document BMI or weight and height):       |                                    | ● Weight (Kg)                                                                               |
|                                                                       |                                    | ● Height (m)                                                                                |
| Q7. Extract from medical record:                                       |                                    | ● Pre-pregnancy weight and height (if available, be sure to note down units)                |
| Q8. (At the time of registration) BMI (can document BMI or weight and height): |                                    | ● Weight (Kg)                                                                               |
|                                                                       |                                    | ● Height (m)                                                                                |
| Q8. Extract from medical record:                                       |                                    | ● At the time of clinical visit, weight and height (if available, note down units)          |
| Q9. Gravidity: Is this your first pregnancy?                           |                                    | ● Yes                                                                                       |
|                                                                       |                                    | ● No                                                                                        |
| Q9. Extract from medical record:                                       |                                    | ● Gravidity information                                                                     |
| Q10. If answered “No” to Q9: How many times have you been pregnant?   |                                    | Q10. NA                                                                                    |
| Q11. Parity: Is this your first child birth?                           |                                    | ● Yes                                                                                       |
|                                                                       |                                    | ● No                                                                                        |
| Q11. Extract from medical record:                                      |                                    | ● Parity information                                                                        |
| Q12. If answered “Not” to Q11: How many live births have you previously? |                                    | Q12. NA                                                                                    |
| Q13. Has a doctor or other healthcare provider told you that you have any of the following conditions before you were pregnant? (check all that apply) (local sites should) |                                    | ● List all pregnancy-related conditions documented in the record                             |
### Module 3: Pregnancy Outcomes

**What:** Information about how the pregnancy ended; maternal mortality will be recorded in this module

**When:** Once, after pregnancy outcome is known

| Questionnaire-based data collection | Medical record data extraction |
|------------------------------------|--------------------------------|
| Q1. Date of pregnancy outcome (DD:MM:YY) [Allows calculation of gestational age (in weeks) when pregnancy ended] | Q1. Extract from medical record:  
- Date of pregnancy outcome (DD:MM:YY) |
| Q2. Please indicate the end point of this pregnancy:  
- Live birth | Q2. Extract from medical record:  
- The end point of this pregnancy (note down) |
| Questionnaire-based data collection | Medical record data extraction |
|------------------------------------|--------------------------------|
| Q1. Date (and time, if available) of birth (DD:MM:YY) (HH:MM) | Q1. Extract from medical record:  
- Date of birth (and time of birth, if available) (DD:MM:YY) (HH:MM) |
| Q2. Where was the infant born? * | Q2. Extract from medical record:  
- Location of birth:  
  - Hospital (indicate which hospital)  
  - Other (specify location, if delivery did not occur at this facility)  
  - “NA” if unknown |
| - Home  
- Birthing facility/hospital  
- Other location, please specify | * If your registry collects only hospital-based births, please record “facility/hospital” for all records |
### Q3. Mode of delivery?
- Spontaneous vaginal
- Operative vaginal - forceps or vacuum
- Cesarean section (scheduled)
- Cesarean section (intrapartum)
- Unknown

### Q3. Extract from medical record:
- Mode of delivery exactly as documented in the record

### Q4a. What was the infant's weight at birth (grams)?

### Q4a. Extract from medical record:
- Infant weight at birth (grams)

### Q4b. What was the infant's length at birth (cm)?

### Q4b. Extract from medical record:
- Infant length at birth (cm)

### Q4c. What was the head circumference at birth (cm)?

### Q4c. Extract from medical record:
- Infant head circumference at birth (cm)

### Q5. Has the infant's gestational age been estimated?
- Yes
- No

### Q5. NA

### Q6. If answered “Yes” to Q6:
- What was the estimated gestational age at birth (weeks)

### Q6. Extract from medical record:
- Gestational age of infant

### Q7. If answered “Yes to Q6:
- What method was used to determine gestational age?
  - Ultrasound
  - Estimated date of delivery based on last menstrual period (EDD)
  - Ballard/Dubowitz;
  - Other, please specify

### Q7. Extract from medical record:
- Estimation method exactly as documented in the record

### Q8. On the day of birth, did your infant have any difficulty breathing?
- Yes
- No
- Maybe / Uncertain

### Q8. Extract from medical record:
- On the day of birth, did the infant have any difficulty breathing, as documented in the record

### Q9. At the time of birth, was your infant admitted to the neonatal intensive care unit or the special care unit?
- Yes
- No

### Q9. Extract from medical record:
- At the time of birth, was the infant admitted to the neonatal intensive care unit/special care unit (Y/N/NA)

### Q10. At the time of birth, did your infant receive oxygen?
- Yes
- No

### Q10. Extract from medical record:
- At the time of birth, did the infant receive oxygen? (Y/N/NA)

### Q11. What type of resuscitation was provided at delivery?
- None
- Warm/dry/stimulation
- Blow by oxygen
- Continuous positive airway pressure
- Positive pressure ventilation
- Intubation
- Chest compressions
- Surfactant

### Q11. Extract from medical record:
- Resuscitation? (Y/N/NA)
- If yes → type of resuscitation, as documented in the record
Core Variables, Prospective Meta-Analyses for Perinatal COVID-19
Version Date: 08-NOV-20

| Question | Medical record data extraction |
|--------------------------|-----------------------------|
| **Q12. Did the infant breastfeed or receive any breast milk on the day of birth?**<br>● Yes<br>● No<br>● Maybe / Uncertain | **Q12. Extract from medical record:**<br>● Breastfeeding or breast milk on the day of birth (Y/N/NA) |
| **Q13: Was the newborn isolated away from mother in another area in hospital (postnatal ward, special care nursery, NICU or special ward)?** | **Q13: Extract from medical record:**<br>● Was the newborn isolated away from mother in another area in hospital (postnatal ward, special care nursery, NICU or special ward)? |
| **Q14. Date of infant discharge from labor and delivery event (DD:MM:YY)** | **Q14. Extract from medical record:**<br>● Date of infant discharge (DD:MM:YY) |
| **Q15. Newborn outcome at discharge:**<br>● Expired<br>● Home<br>● Transfer to another acute care facility due to clinical needs<br>● Transfer to a chronic care facility | **Q15. Extract from medical record:**<br>● Newborn outcomes at discharge as documented in the record |

**Module 5: Infant Mortality and Morbidity**

What: Information related to infant health, particularly related to COVID-19
When: At regular interval until up to 12 months after birth (or until chart extraction)

| Questionnaire-based data collection | Medical record data extraction |
|-------------------------------------|--------------------------------|
| **Q1. Neonatal/infant death?**<br>● Yes<br>● No | **Q1. Extract from medical record:**<br>● Neonatal/infant death? (Y/N/NA) |
| **Q2. If answered “Yes” to Q1:**<br>● Date-time of neonatal/infant death?<br>  (DD:MM:YY) (HH:MM) | **Q2. Extract from medical record:**<br>● If neonatal/infant death, date-time of death<br>  (DD:MM:YY) (HH:MM) |
| **Q3. If answered “Yes” to Q1:**<br>● Cause of death?<br>  ○ COVID-19<br>  ○ Preterm/low birth weight<br>  ○ Birth asphyxia<br>  ○ Infection<br>  ○ Birth trauma<br>  ○ Congenital/birth defects<br>  ○ Unknown<br>  ○ Other, please specify | **Q3. Extract from medical record:**<br>● If neonatal/infant death, cause of death<br>  (COVID or other causes, document as appeared in medical record) |
| **Q4. Was the infant documented by clinicians to have any of the following symptoms of COVID-19?**<br>  - Fever (T>37.5)<br>  - Respiratory distress | **Q4. Extract from medical record:**<br>● Was the infant documented by clinicians to have any of the symptoms of COVID-19?<br>  (document exactly as in the record) |
| Symptoms                                      |
|----------------------------------------------|
| Cough                                        |
| Nasal congestion/runny nose                  |
| Vomiting                                     |
| Diarrhea                                     |
| Lethargy                                     |
| Rapid heart rate (>160 bpm) (record bpm if available) |
| Seizure                                      |
| Paralysis                                    |
| Hypotonia (floppiness)                       |
| Hypertonia or Stiffness or spasticity of limbs |
| Other neurological signs                     |
| Rash                                         |
| Oedema                                       |
| Eye redness/conjunctivitis                   |
| Other condition                              |

If yes, date of onset?

Q5. Was the baby tested for COVID-19?
   - Yes
   - No
   - Maybe / Uncertain

Q5. Extract from medical record:
   - Any COVID-19 test for the infant? (Y/N)

If answered “Yes” go to Module 7 to record details.

Q6. If answered “Yes” to Q5:
   - What tests were conducted?
     - Biospecimen: viral, antibody, or antigen test (record details in Module 7)
     - Chest image or X-ray
     - Lung ultrasound
     - Echocardiogram
     - Cerebral ultrasound
     - Abdominal ultrasound
     - Other, please specify

Q6. Extract from medical record:
   - Which tests were conducted

If answered “Yes” to “Biospecimen” - go to Module 7 to record details.

Q7. Has your infant breastfed or received any breast milk in the last 24 hours?
   - Yes
   - No
   - Unknown

Q7. Extract from medical record:
   - Has the infant been breastfed or received any breast milk in the past 24 hours (Y/N/NA)?
   - If information is available for longer periods, note it down as well

Q8. Any congenital anomalies?
   - Neural tube defects
   - Microcephaly
   - Congenital malformations of ear
   - Congenital heart defects
   - Orofacial clefts
   - Congenital malformations of digestive system
   - Congenital malformations of genital organs
   - Abdominal wall defects
   - Chromosomal abnormalities
   - Reduction defects of upper and lower limbs

Q8. Extract from medical record:
   - Any congenital anomalies in the record?
     - Note it down exactly as in the record

Core Variables, Prospective Meta-Analyses for Perinatal COVID-19
Version Date: 08-NOV-20
Module 6: Core Sociodemographic Information

What: Socio-demographic information about the study participant
When: Once at the beginning of the study (maternal information); Once after birth (for infant information)

| Questionnaire-based data collection | Medical record data extraction |
|-------------------------------------|--------------------------------|
| Q1. Country | Site ID | Q1. Indicate the site / facility |
| Q2. Age of the mother (years) | Q2. Extract from medical record: |
| Q3. Sex of the child (if applicable) | |
| Q4. Race/Ethnicity of the mother * | |
| Q5. Race/Ethnicity of the child (if applicable) * | |
| Q6. Years/level of education completed by the mother (check highest level completed) | |

Module 7: Biospecimens and Diagnostic Testing

What: Biological specimens collected from mother and infant during pregnancy, at delivery, and postpartum, with a focus on indicators of vertical transmission of COVID-19.
When: Maternal biospecimens collected during the pregnancy, at the time of delivery, or after delivery, as well as biospecimens collected during delivery and from the infant at birth and during the first 6 weeks of life.
Questionnaire-based data collection | Medical record data extraction
---|---
Q1. Were any biospecimens collected for COVID-19 diagnostic testing from the mother during pregnancy, at the time of delivery, or in the postpartum period? | Q1. Extract from medical record:  
- Any biospecimen/diagnostic testing for the mother? (Y/N)
Q2. If answered “Yes” to Q1: Proceed to maternal biospecimen table below | See Q2 Maternal Biospecimen Table below
Q3. Were any biospecimens collected for COVID-19 diagnostic testing at the time of the delivery? | Q3. Extract from medical record:  
- Any biospecimen/diagnostic testing at delivery? (Y/N)
Q4. If answered “Yes” to Q3: Proceed to delivery-related biospecimen table below | See Q3 Delivery-Related Biospecimen Table below
Q5. Were any biospecimens collected for COVID-19 diagnostic testing from the infant? | Q5. Extract from medical record:  
- Any biospecimen/diagnostic testing for the infant? (Y/N)
Q6. If answered “Yes” to Q5: Proceed to infant biospecimen table below | See Q3 Infant Biospecimen Table below

### Q2. Maternal Biospecimen Table

| Sample Number (as needed) | 2a. Date of Biospecimen Collection | 2b. Type of Biospecimen | 2c. Type of Testing Conducted | 2d. Qualitative Results | 2e. Quantitative Result (e.g., viral load) | 2f. Specify units for Quantitative Results |
|---------------------------|----------------------------------|-------------------------|-------------------------------|------------------------|-----------------------------------------|------------------------------------------|
| SM1. | DD:MM:YY | Nasopharyngeal swab  
Vaginal swab  
Feces/rectal swab  
Maternal blood  
Breast milk  
Pregnancy tissue (in the case of fetal demise/induced abortion)  
Other, specify | Viral PCR  
IgM  
IgG  
Other, specify | Positive  
Negative  
Other, specify |  |  |
| SM2. | | | | | | |
| SM3. | | | | | | |
| SM4. | | | | | | |

### Q4. Delivery-Related Biospecimen Table

| Sample Number (as needed) | 4a. Date of Biospecimen Collection | 4b. Type of Biospecimen | 4c. Type of Testing Conducted | 4d. Qualitative Results | 4e. Quantitative Result (e.g., viral load) | 4f. Specify units for Quantitative Results |
|---------------------------|----------------------------------|-------------------------|-------------------------------|------------------------|-----------------------------------------|------------------------------------------|
| SD1. | DD:MM:YY | Amniotic fluid  
Placental swab (any side)  
Placental swab (fetal side)  
Cord blood  
Other, specify | Viral PCR  
IgM  
IgG  
Other, specify | Positive  
Negative  
Other, specify |  | |
| SD2. | | | | | | |
| SD3. | | | | | | |
### Q6. Infant Biospecimen Table

| Sample Number (as needed) | 6a. Date of Biospecimen Collection | 6b. Type of Biospecimen | 6c. Type of Testing Conducted | 6d. Qualitative Results | 6e. Quantitative Result (e.g., viral load) | 6f. Specify units for Quantitative Results |
|--------------------------|-----------------------------------|-------------------------|-------------------------------|------------------------|------------------------------------------|-------------------------------------------|
| SI1. DD:MM:YY             | • Nasopharyngeal swab             | • Viral PCR             | • Positive                   | ___                    |                                          |                                           |
|                          | • Feces/rectal swab              | • IgM                   | • Negative                   | ___                    |                                          |                                           |
|                          | • Gastric swab                   | • IgG                   | • Other, specify             | ___                    |                                          |                                           |
|                          | • Neonatal peripheral blood      |                         |                               | ___                    |                                          |                                           |
|                          | • Other, specify                 |                         |                               | ___                    |                                          |                                           |

SI2.
SI3.
SI4.