Protocol for PRIORITY (**P**regnancy Co**R**onav**I**rus **O**utcomes **R**egIs**T**r**Y**)
COVID-19 Pregnancy Registry

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Version Date: May 5, 2020

Protocol Revision History

Version Date: 3/15/2020

Version Date: 3/24/2020
- Section 5.2: Added Surrogate Consent procedures

Version Date: 4/7/2020
- Section 5.2: Added Biospecimen Consent procedures
- Section 6.1: Added Depression and Anxiety measures
- Section 6.2: Added Pregnancy Arm: added gestational age 36 week and 38 week survey
  - Added Month 6 and Month 12 time points
  - Added Biospecimen substudy (pregnancy arm, postpartum arm, and neonatal measures)

Version Date: 5/5/2020
- Section 1.0: Added rationale for 12 months post pregnancy data collection and need for Health Equity and Birth Justice Core
- Section 2.1: Added Study Team and Organization overview
- Section 3.0: Clarified Study Aims
- Section 6.2: Change Pregnancy Arm: gestational age 36 week and 38 week contact points to 38 week and 42 week
- Section 9.1: Updated sample size consideration

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1.0 BACKGROUND AND STUDY RATIONALE

Coronavirus disease, or COVID-19, is a novel influenza-like infection that has now reached WHO criteria for a global pandemic. Pregnant women have alterations in the immune system that likely increase their risk for adverse outcomes of COVID-19. In previous outbreaks of influenza, pregnant women have had higher morbidity and mortality compared with nonpregnant women.[1,2] Pregnant women with influenza are more likely to be hospitalized and receive care in the intensive care unit than the general population.[3,4] In the 2009 HINI pandemic, pregnant women accounted for 5% of all deaths, although they were only 1% of the general population.[5] Severe illness and mortality may be higher in the COVID-19 pandemic because there is no antiviral therapy yet available.

In addition to increased maternal risks, COVID-19 infection may increase adverse obstetric and fetal outcomes. Although transplacental transmission of influenza is rare, infection with influenza has been associated with increased risk of miscarriage, preterm delivery, and fetal death, as well as congenital abnormalities such as cleft lip, neural tube defects, and congenital heart defects.[6-10] In addition, hyperthermia that results from fever from any source in pregnancy increases risk for neural tube defects and increase risk for other teratogenic outcomes.[11]

Some subgroups of pregnant women with COVID-19 may have an even higher risk of adverse outcomes due to inequalities in social determinants of health that are amplified during this pandemic. For instance, prior to the pandemic, Black women were 3-4 times more likely to die from pregnancy related causes than white women. In the first several weeks of the pandemic, state health departments began reporting higher death rates among Black people infected with COVID-19 than any other racial or ethnic group. Given the existing disparities in maternal mortality, we posit that COVID-19 infection may widen these health inequalities with higher rates of severe illness, death, and obstetric complications among Black women compared with white women.

Data is very limited on short and long-term clinical outcomes of neonates born to mothers with COVID-19. To date, the largest series reporting deliveries to COVID-19 positive women has reported on 68 live births, all of which occurred in the context of third trimester infection.[5] Reported pathology for infants born to COVID-19 positive mothers includes demise, prematurity and cyanosis.[6-12] There is also very limited information on preterm infants, who may be at particular risk of perinatal COVID-19 infection. The fetus is primed towards immunologic tolerance in a semi-allogeneic uterine environment and may not mount effective inflammatory responses to infection. Additionally, passive transfer of protective maternal immunoglobulins does not reach maximum until term, with 28-30 week infants having about 50% of maternal IgG levels. The immature skin integrity of preterm infants may also be a risk factor for perinatal transmission. Given the abrupt onset of the COVID-19 pandemic and the potential effects of COVID-19 on the 3.8 million U.S. births each year, more data is urgently needed on neonatal outcomes associated with maternal COVID-19 infection and their relationship to gestational age at onset of infection.

Despite the likely increased risks of COVID-19 for pregnant women and the newborn, little is known about the clinical course, disease prognosis, obstetric or neonatal outcomes. In addition, no studies have evaluated health disparities in COVID-19 outcomes among pregnant women by race/ethnicity or other demographic factors. Our goal is to close this knowledge gap as COVID-19 is emerging broadly within the United States. We propose a nationwide registry to enroll pregnant women or those who have recently been pregnant (within 6 weeks) who are under investigation for COVID-19 or have a confirmed diagnosis. We will assess the full range of disease course and outcomes for the patient and her pregnancy, including neonatal outcomes

when applicable for women who have live births. Outcome data from this registry will provide critical evidence needed to help improve care for pregnant women during this time of a global pandemic of novel disease.

2.0 STUDY OVERVIEW

We propose PRIORITY (**P**regnancy Co**R**onav**I**rus **O**utcomes **R**eg**I**s**T**r**Y**), a prospective cohort study of pregnant and recently pregnant women and their infants who are: either patients under investigation for COVID-19 or a confirmed case of COVID-19. Data from PRIORITY will be used to evaluate the impact of COVID-19 on the clinical course and pregnancy outcomes of pregnant women and women within 6 weeks of pregnancy and their infants.

We will recruit women age 13 or older under investigation for COVID-19 or with confirmed COVID-19 at any clinical state across the United States. Eligible participants will be identified through voluntary physician referrals or self-referrals. We will advertise and promote PRIORITY through professional societies and academic listservs, and through existing research collaborations within Obstetrics and Gynecology networks.

When an eligible patient is referred to the PRIORITY Coordinating Center at UCSF, a UCSF study coordinator will follow-up by phone or email with the patient and complete a verbal or electronic consent. The participant will be asked to complete an approval to release of medical information. We will then use patient questionnaires to assess symptoms, maternal clinical course, pregnancy outcomes, and neonatal outcomes from initial investigation of COVID-19 to 12 months. We will also obtain all medical records for the participant to data abstract key clinical, pregnancy, and neonatal outcomes. Specimens from a subgroup of eligible women and their neonates may be collected to evaluate COVID-19 transmission and/or immune studies.

UCSF will serve as the Coordinating Center and have oversight of all scientific and administrative aspects of the study. All study data will be stored securely in a HIPAA compliant, secure database monitored by the UCSF Women's Health Clinical Research Center.

2.1 Study Team and Organization

PRIORITY is a nationwide registry with an organizational structure to provide efficient and accurate data collection and analysis to produce high impact results during this global pandemic. We will utilize a multi-disciplinary leadership plan in which 5 investigators from the University of California closely collaborate to oversee all scientific and administrative aspects of the study (**Figure 1**). The *Executive Committee* will consist of the leads of each Core, the lead of Coordinating Center, and the Senior Program Manager. The *Executive Committee* meets at least twice weekly to discuss overall strategy and operations. The *Steering Committee* is comprised of 20 stakeholders with diverse expertise and experience to serve as the governing body of the

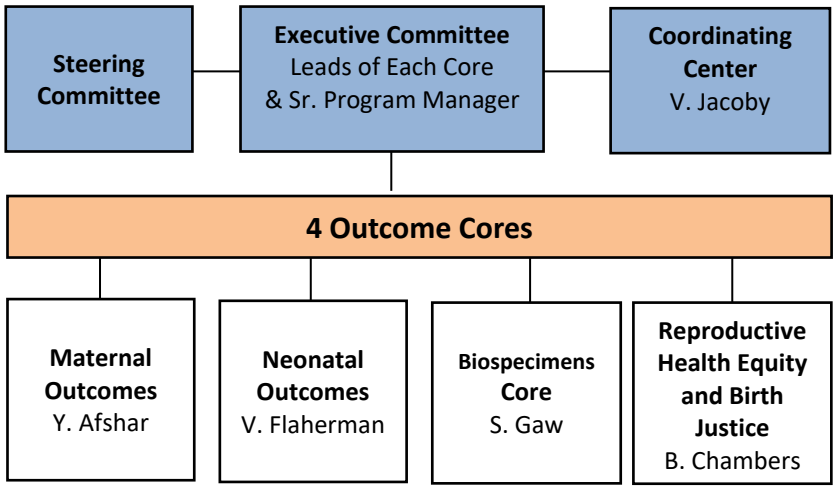

Figure 1. Study Team Organization

registry and provide overall guidance and scientific input (see Appendix for membership). The UCSF Women's Health Clinical Research Center (WHCRC) will serve as the ***Coordinating Center*** for this registry. The WHCRC is a multi-disciplinary research unit that serves as a coordinating center for large multi-centered studies and has highly trained and experienced staff and the necessary infrastructure to support the proposed study. There are 4 ***Outcome Cores*** to collect and integrate essential data to accomplish our Specific Aims: Maternal Outcomes, Neonatal Outcomes, Biospecimen Core, and Reproductive Health Equity and Birth Justice. The Co-PIs bring diverse expertise needed for the success of this registry:

1) Dr. Vanessa Jacoby (lead, Coordinating Center), an Obstetrician Gynecologist and clinical researcher with a strong track record of experience as Principal Investigator and Co-Investigator for multiple national registries including a current nationwide fibroid treatment registry that uses the same recruitment and data collection approach that we use in PRIORITY;
2) Dr. Yalda Afshar (lead, Maternal Outcomes), a specialist in Maternal-Fetal Medicine who conducts basic and translational studies of pregnancy complications;
3) Dr. Valerie Flaherman, (lead, Neonatal Outcomes), a pediatrician and clinical researcher with expertise in breast feeding research who directs the UCSF Well Baby Nursery;
4) Dr. Stephanie Gaw (lead, Biospecimens Core), a translational researcher in Maternal-Fetal Medicine and perinatal infectious diseases, with active clinical and laboratory-based research in malaria and Zika in pregnancy, who led the perinatal core of a prospective cohort of mother-baby dyads during the 2015 Rio de Janeiro outbreak; and
5) Dr. Brittany Chambers (lead, Reproductive Health Equity and Birth Justice), an Epidemiologist with Public Health expertise with a focus on health equity and Black women's maternal health.

3.0 STUDY AIMS

The aim of PRIORITY is to assess the impact of COVID-19 on pregnant women and those who have been pregnant within the last 6 weeks and, when applicable, their newborns. The specific aims of PRIORITY are:

Aim 1: 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.

Specific Aim 1A. Describe pregnancy and obstetric outcomes among women infected with COVID-19 versus those that are COVID-19 negative.

Areas of assessment include: 1) pregnancy completion, 2) antepartum complications and indicators of severe morbidity (as defined by the Center for Disease Control (CDC), 3) laboratory and radiographic changes, and 4) obstetric outcomes.

Specific Aim 1B. Identify high-risk subgroups with increased risk for clinical and obstetric adverse outcomes among pregnant women diagnosed with COVID-19.

We will identify what baseline clinical and demographic characteristics may be associated with adverse pregnancy and obstetric outcomes among women diagnosed with COVID-19.

Aim 2: Neonatal outcomes: To assess fetal/neonatal outcomes among infants born to women with COVID-19 compared with those that are COVID-19 negative.

Specific Aim 2A: To describe morbidity and mortality among infants born to mothers with COVID-19 diagnosed during pregnancy or within 14 days after birth**.**

We will determine gestational age at birth, use of respiratory support, length of stay, and incidence of readmission and will compare these outcomes to outcomes among infants with mothers testing negative for COVID-19. We will also report a neonatal mortality rate for deaths in the first 28 days and an age-specific mortality rate for deaths occurring day 29-162.

Specific Aim 2B: To report prevalence of congenital anomalies by gestational age at time of COVID-19 infection.

Using data collected from both maternal and physician report, we will determine the prevalence of major birth defects or other congenital anomalies such as orofacial clefts, neural tube defects, congenital heart disease and hearing loss among infants born to mothers testing positive for COVID-19.

Specific Aim 2C: To describe health outcomes of children at 6 and 12 months chronological age born to women with COVID-19 infection during pregnancy and how these are associated with postpartum care practices including maternal-infant separation.

We will follow infants through 12 months to determine the incidence of upper and lower respiratory tract infection and wheezing illness, as well as breastfeeding duration, postpartum depression and emergency room and inpatient utilization.

Aim 3: Biospecimen analysis. To characterize the molecular epidemiology of COVID-19 in pregnant women and the mother-infant dyad.

We have established a network of 11 academic centers from around the country that have existing IRBs in place and have agreed to collect and share biospecimens for molecular investigations. Through this network we aim to collect samples and analyze 200 mother/infant dyads during the study period to address outstanding questions regarding the kinetics of viral shedding in pregnant women and neonates, and the potential for maternal-fetal transmission.

Specific Aim 3A: Determine if COVID-19 is detected in diverse samples collected from pregnant women and their infants to generate relevant data regarding the timing and degree of viral shedding in bodily fluids/tissues of direct relevance to maternal-child transmission.

Quantitative reverse-transcriptase PCR (qRT-PCR) will be applied to detect viral load of SARS-CoV-2 in biologic samples. Samples that test positive for SARS-CoV-2 will be cultured to determine whether infectious virus is present in the sample.

Specific Aim 3B: Describe the kinetics of viral shedding over time, including passage to extrapulmonary sites as well as duration of viral shedding.

In women with acute COVID infection, we will collect serial blood (up to weekly), nasopharyngeal (up to every 4 days), stool (up to 3 times per week), and breast milk (daily for up to 1 week) samples. These samples will be analyzed with qRT-PCR to determine the kinetics of viral load during the course of infection. Samples that test positive for SARS-CoV-2 will be cultured to determine whether infectious virus is present (in a BSL-3 facility at UCSF).

Specific Aim 3C: Establish a biobank of maternal-fetal-infant biologic specimens for future studies of immunologic responses.

This biorepository will be a valuable source of paired specimens from which to understand the pathophysiology of COVID-19 disease as it relates to the pregnant woman and her neonate. Our biorepository will draw from women with a spectrum of disease severity and gestational timing of illness.

Aim 4. Health Equity: To assess if there are racial and ethnic inequities associated with social determinants of health, clinical characteristics, and adverse pregnancy and obstetric outcomes among pregnant and recently pregnant women with COVID-19.

The COVID-19 pandemic is widening existing health inequities by race and ethnicity including significant increased risks of death among Black and Latinx people infected with COVID-19 compared with white people. We will focus on recruitment of a racially and ethnically diverse study population and query participants on a diverse range of social determinants of health that are known to impact health outcomes including structural racism.

Specific Aim 4A: To assess if Black, Latina, or Native American women with COVID-19 are at increased risk for an adverse clinical course based on social determinants of health including structural racism and community-level poverty compared to white women.

Specific Aim 4B: To assess if Black, Latina, or Native American women with COVID-10 are at increased risk for negative care experiences during pregnancy and delivery including interpersonal racism compared to white women.

Specific Aim 4C: To determine if Black, Latina, or Native American women with COVID-19 are at increased risk of miscarriage, preterm delivery, stillbirth, and adverse neonatal outcomes compared with white women.

4.0 STUDY SITES

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.

5.0 STUDY POPULATION

We will recruit women under investigation for COVID-19 or who have tested positive for COVID-19 who meet the following criteria:

INCLUSION CRITERIA

1. Pregnant women or women who have been pregnant within the last 6 weeks
2. Able to give informed consent, or by surrogate
3. Diagnosed with COVID-19; or being evaluated for COVID-19 (“patient under investigation”) since January 1, 2020

EXCLUSION CRITERIA

1. <13 years of age.

5.1 Participant Recruitment

PRIORITY participants will be recruited through referrals from physicians treating pregnant women with COVID-19. We will advertise and promote PRIORITY through professional societies and academic listservs, and through existing research collaborations within Obstetrics and Gynecology networks. Physicians will identify potential participants and provide them with a recruitment pamphlet about the study. Participants will be asked if they are willing to be contacted by UCSF about PRIORITY and, if they agree, their contact information will be given to the study coordinator at UCSF. The referring physician may place a note in the patient's medical record stating that the patient has given permission for their contact information (phone number, email, address) to be sent to UCSF. Participants can also inquire about PRIORITY by contacting the UCSF study coordinator directly by phone, email, or through the PRIORITY website.

5.2 Informed Consent

A trained research coordinator from UCSF will contact a study eligible patient who has been referred by her physician to the UCSF research staff. A UCSF trained study coordinator will contact the eligible patient to explain the study aims and procedures. If the patient is interested, the coordinator will then confirm that the patient meets the inclusion and exclusion criteria and will review in detail the study consent form and protocol with emphasis on the length of follow-up and required follow-up procedures. The participant will be asked to verbally or electronically consent to participate in the study. After the participant agrees to participate in the study, the study coordinator will mail, fax, or send electronically via Docu-Sign the HIPAA form and release of medical records form for completion.

Surrogate consent: If the patient is in the intensive care unit (ICU) and cannot consent herself, surrogate consent will be obtained on the patient’s behalf. The surrogate will be sent a Self-Certification Form for completion. If/When the patient is able to consent herself, the study coordinator will consent the participant to continue in the study.

Sub-study Biospecimen Consent: If the participant agrees to provide biospecimens, the participant will be asked to sign or Docu-sign the biospecimens consent form.

6.0 MEASURED VARIABLES

6.1 Outcome Variables: Clinical presentation, prognosis, and outcome

The clinical course of disease from presentation to resolution of symptoms will be assessed through patient report using self-reported questionnaires and through review of the medical record. Broad outcomes of interest include: presenting symptoms and testing, disease course including hospitalizations and interventions, clinical outcomes with resolution of illness (morbidity and mortality), and neonatal and infant clinical outcomes.

6.1.a CDC Human Infection with COVID-19 Person Under Investigation (PUI) and Case Report Form

We will use the Center for Disease Control (CDC) COVID-19 Person Under Investigation (PUI) Case Report Form as a clinical outcome template. This is a standardized form to assess disease presentation, what diagnostic evaluation has occurred, and baseline demographic characteristics.

6.1.b Questionnaires for Health History

We will ask participants to complete a questionnaire to assess general medical and reproductive history and disease assessment and treatment at baseline and at each follow-up point of contact. We will include covariate measures tobacco, alcohol, and drug use.

6.1.c Outcome Variables: Pregnancy and Neonatal Outcomes

We will query participants on all pregnancy events and outcomes through self-reported questionnaires and adjudicate this data with review of the medical record. Areas of assessment include: 1) Pregnancy completion: miscarriage, abortion, ectopic pregnancy, or continued pregnancy that results in delivery of term or preterm infant or fetal demise, 2) Antepartum complications such as, but not limited to: development of hypertension, diabetes, pre-eclampsia, placental abruption, and 3) Obstetric outcomes; gestational age at birth, mode of delivery (vaginal or cesarean), and complications (e.g. postpartum hemorrhage). We will request delivery records to adjudicate obstetric outcomes.

For participants reporting births of a live infant, we will assess neonatal complications or adverse health outcomes. In a subset of participants, we will collect neonatal specimens including nasopharyngeal swab, blood, stool and urine.

6.1.d Depression and Anxiety

To evaluate depression and anxiety symptoms that may be associated with COVID-19, participants will complete the following validated questionnaires:

- Edinburgh Postnatal Depression Scale (EPDS) – The EDPS was developed to identify women who may have postpartum depression**.** Each answer is given a score of 0 to 3. The scores range from 0 to 30, with higher scores indicating more severe depression.

- The Generalized Anxiety Disorder-7 (GAD-7) - Anxiety symptoms will be assessing using the GAD-7, a 7-item structured questionnaire designed to assess the severity of anxiety symptoms over a 2-week period in primary care populations (Spitzer, Kroenke et al. 2006). Total scores range from 0 to 21, with higher scores indicating more severe anxiety.

6.2 Schedule of Outcome Assessment

6.2.a Pregnant Participant

Outcomes will be assessed at varying time points from initial presentation of COVID-19 symptoms, at 6 weeks post-delivery/miscarriage/abortion, 6 months and 12 months (Table 1). All data will be collected through by phone, mail, or on-line questionnaires.

Baseline/Enrollment Survey:

- Complete surveys about their demographic, medical, and reproductive history

- Complete surveys about their symptoms
- Complete structured questionnaires about depression and anxiety

Weekly Follow-up Surveys:
- Complete surveys about their symptoms and pregnancy status

Surveys once per trimester:
- Complete surveys about their symptoms and pregnancy status
- Complete structured questionnaires about depression and anxiety

38 weeks pregnant and 42 weeks pregnant:
- We will ask women "Are you still pregnant?" at 38 weeks and 42 weeks, to capture the infant birthdate. Neonatal outcomes are based on the infant's chronological age, so it is important to know when the mother delivers.

6 weeks post-partum:
- Complete surveys about their symptoms, pregnancy and neonatal outcomes
- Complete structured questionnaires about depression and anxiety

Month 6 and Month 12:
- Complete surveys about their symptoms and health status
- Complete surveys about their infant
- Complete structured questionnaires about depression and anxiety

Table 1. Schedule of Outcome Assessment

	PUI/ COVID-19 Baseline	Once a week for 4 weeks	2nd Trimester Survey (24 wks)	3rd Trimester Survey (34 wks)	Gestational age 38* weeks	Gestational age 42* weeks	6 weeks after pregnancy	6 Months	12 Months
COVID-19 PUI Case Report Form (Demographics, Medical History, symptoms)	X								
Questionnaires to Assess Symptoms		X	X	X			X		
Depression and Anxiety	X		X	X			X	X	X
Pregnancy Status		X	X	X	X	X			
Pregnancy Outcomes							X		
Neonatal/Infant Outcomes							X	X	X

*Frequency of contact will depend on gestational age of the participant at the time of enrollment.

6.2.a.1 Pregnancy Biospecimen Sub-study

Biospecimen collection will occur for a subset of consenting women. Trained staff will collect the specimens per standard operating procedures. In some cases, specimen collection may occur through patient self-collect and sent in by mail (ie for stool).

- Blood draws: Participants will receive blood draws of 10ml maximum based on the following criteria for each blood draw: 1) last hemoglobin ≥8.0 and 2) amount to be drawn may be decreased at the discretion of the clinical team. When possible, blood draws will be combined with other blood draws for clinical care. Blood draws may occur at the following time points:

1) within 48 hours of enrollment/initial PUI evaluation,
2) up to weekly, if hospitalized or presenting for acute clinical evaluation of COVID-19- or pregnancy-related condition,
3) 4 weeks after enrollment,
4) in conjunction with routine prenatal lab draws (ie third trimester prenatal labs),
5) on admission to the labor and delivery unit

We expect most individuals will not be hospitalized for more than 4 weeks. Blood draws for pregnant women will not exceed the lesser of 50ml OR 3ml/kg in an 8 week period.

- Respiratory samples: Participants may have nasal/throat swabs, saliva, sputum, bronchoalveolar lavage (BAL) or other fluid (e.g., pleural) collected up to 3 times per week. BAL and other fluid will only be collected if available in those with clinical indications for the procedure.

- Urine: 10ml of urine may be collected up to 3 times per week

- Rectal swabs: Rectal swabs may be collected up to 3 times per week

- Stool collection: Stool may be collected up to 3 times per week

- Amniotic fluid: Amniotic fluid may be collected at the time of amniocentesis performed for clinical indication, or at the time of pregnancy termination or cesarean delivery, if applicable.

- Placenta: Placental swabs and/or biopsies may be collected at the completion of pregnancy.

- Cord blood: Cord blood may be collected at the time of completion of pregnancy.

- Other specimens: In cases of pregnancy termination, miscarriage, or stillbirth, other specimens may be collected, such as swabs/samples from the remains of the fetus.

6.2.b Postpartum Participant

Outcomes will be assessed at Baseline, once a week for 4 weeks, at 8 weeks, Month 6, and Month 12 (Table 2). All data will be collected through by phone, mail, or on-line questionnaires.

<u>Baseline/Enrollment Survey</u>:
- Complete surveys about their demographic, medical and reproductive history, and coronavirus symptoms, pregnancy and neonatal outcomes
- Complete structured questionnaires about depression and anxiety

<u>Weekly Follow-up Surveys:</u>
- Complete surveys about their symptoms

<u>8 Week Survey:</u>
- Complete surveys about their symptoms and neonatal outcomes
- Complete structured questionnaires about depression and anxiety

Month 6 and Month 12:

- Complete surveys about their symptoms and health status
- Complete surveys about their infant
- Complete structured questionnaires about depression and anxiety

Table 2. Schedule of Outcome Assessment								
	PUI COVID-19 (Baseline)	Week 1	Week 2	Week 3	Week 4	Week 8	Month 6	Month 12
COVID-19 PUI Case Report Form (Demographics, Medical History, symptoms)	X							
Depression and Anxiety	X					X	X	X
Questionnaires to Assess Clinical outcomes		X	X	X	X	X	X	X
Pregnancy Outcomes	X							
Neonatal/Infant Outcomes	X					X	X	X

6.2.b.1 Postpartum Biospecimen Sub-study

Biospecimen collection will occur for a subset of consenting women. Trained staff will collect the specimens per standard operating procedures. In some cases, specimen collection may occur through patient self-collect and sent in by mail (ie for stool or breastmilk).

- Blood draws: Participants will receive blood draws of 10ml maximum based on the following criteria for each blood draw: 1) last hemoglobin ≥8.0 and 2) amount to be drawn may be decreased at the discretion of the clinical team. When possible, blood draws will be combined with other blood draws for clinical care. Blood draws may occur at the following time points:
  1) within 48 hours of enrollment/initial PUI evaluation,
  2) up to weekly, if hospitalized or presenting for acute clinical evaluation of COVID-19- or postnatal-related condition,
  3) 4 weeks after enrollment or 6 weeks postpartum, whichever is later,
  4) up to one year after the completion of pregnancy.

  We expect most individuals will not be hospitalized for more than 4 weeks. Blood draws for postpartum women will not exceed the lesser of 50ml OR 3ml/kg in an 8 week period.

- Respiratory samples: Participants may have nasal/throat swabs, saliva, sputum, bronchoalveolar lavage (BAL) or other fluid (e.g., pleural) collected up to 3 times per week. BAL and other fluid will only be collected if available in those with clinical indications for the procedure.

- Urine: 10ml of urine may be collected up to 3 times per week

- Rectal swabs: Rectal swabs may be collected up to 3 times per week

- Stool collection: Stool may be collected up to 3 times per week

- Breastmilk collection: Breastmilk may be collected up to 3 times per week.

6.2.c Neonatal Biospecimen Sub-study

Biospecimen collection will occur for a subset of neonates with consenting mothers at select sites, where trained staff will collect the specimens per standard operating procedures. In some cases, specimen collection may occur through patient self-collect and sent in by mail (ie for stool).

- Respiratory samples: Participants may have nasal/throat swabs, saliva, sputum, bronchoalveolar lavage (BAL) or other fluid (e.g., pleural) collected up to 3 times per week. BAL and other fluid will only be collected if available in those with clinical indications for the procedure.

- Heelstick/Dried Blood Spot: Participants may have dried blood spot (DBS) collected at the time of routine newborn heelstick.

- Urine: 10ml of urine may be collected up to 3 times per week

- Rectal swabs: Rectal swabs may be collected up to 3 times per week

- Stool collection: Stool may be collected up to 3 times per week

7.0 PARTICIPANT REMUNERATION

Study participants will be provided with small values of electronic or plastic gift cards for their time and commitment to the study as follows: $20 at enrollment, $20 at Week 6 postpartum or Week 8, $20 at month 6, and $20 Final Visit, for a total of $80.

Sub-study participants that are eligible and consent to biospecimen collection will be provided with small values of electronic or plastic gift cards for their time and commitment to the study as follows: $20 at initial blood draw; $20 at the time of pregnancy completion/delivery or postpartum arm 4 weeks after enrollment or 6 weeks postpartum, whichever is later; and $20 at the final visit, for an additional $60.

8.0 TIME COMMITMENT

8.1 Pregnant Participants

Participation in the study will last up to 2 years. There will be between 8 and 12 times that we contact you to complete questionnaires, depending on how far along you are during your pregnancy when you enroll (enrollment, once a week for 4 weeks, once each trimester, at gestational age 38 weeks, gestational age 42 weeks, end of pregnancy, month 6 and month 12). All together, the total time it may take to complete all of the questionnaires over the two years is 2 hours and 35 minutes.

8.2 Postpartum Participants

Participation in the study will last about 1 year. There will be 8 times that we contact you to complete questionnaires (enrollment, then once a week for 4 weeks, 8 Weeks, 6 months, and

12 months). All together, the total time it may take to complete all of the questionnaires over the year is 2 hour 15 minutes.

9.0 STATISTICAL ANALYSIS

9.1 Sample size

Sample Size Considerations: PRIORITY is a prospective cohort with the goal of enrolling at least 1,500 women through the pandemic, to have a robust sample size to assess all key outcomes and conduct important subgroup analyses. Based on current recruitment rates with almost 500 enrolled to date, we anticipate that we will reach our goal of 1,500 women enrollees by July 30, 2020. Based on a sample size of 1,500 women, of which an estimated 60% will be confirmed to have COVID-19, we have projected power calculations for select maternal and perinatal outcomes listed in Table 1.

Table 1: Projected power calculations based on total cohort size of 1500.

Outcome	Estimated incidence		Power to detect difference in COVID- vs. COVID+ participants with alpha=.05
	COVID-	COVID+	
Maternal hospitalization	1%	15%	>99%
Maternal ICU admission	0.1%	3%	99.5%
Preterm birth	10%	15%	81.4%
Fetal Growth Restriction	10%	15%	81.4%

10.0 RISK AND BENEFITS

There are minimal risks for pregnant women under investigation for COVID-19 and agree to be in the Registry. The risks include:

- *Anxiety while completing study questionnaires:* Participants may be asked questions about their health that make them feel uncomfortable or cause anxiety. They may skip any questions they are not comfortable answering.
- *Confidentiality:* Participation in research may involve a loss of privacy, but information will be handled as confidentially as possible. Names will not be used in any published reports about this study.
- *Pain during blood draw:* Participants will feel brief pain during this procedure. To reduce unnecessary pain, study blood draws will be timed with clinical blood draws as possible.

There are minimal risks for neonates enrolled in this study. The risks include:

- *Pain during heelstick blood sampling:* Participants will feel brief pain during this procedure. To reduce the risk of pain, infants will be comfortably swaddled and when possible held by parent during the procedure.

- *Confidentiality:* participation in research may involve a loss of privacy, but information will be handled as confidentially as possible. Names will not be used in any published reports about this study.

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