



# Promoting Data Harmonization to Accelerate COVID-19 Pregnancy Research

Post-Acute Sequelae of SARS-CoV-2 Infection and Vaccine Attitudes Working Group Addendum



# Post COVID–19 Public Health Emergency Addendum

*Published: October 2023*

# CONTEXTUALIZING PREGNANCY COVID-19 CDEs

## TRANSITION FROM PANDEMIC TO ENDEMIC COVID-19

The Public Health Emergency for COVID-19 officially expired in the United States on May 11th, 2023. This marked the transition of COVID-19 from a pandemic to endemic disease. During the three-year COVID-19 pandemic, the research community made significant achievements towards the global understanding of how COVID-19 affects maternal (pregnancy and postpartum) and neonatal health outcomes (e.g., risks of vertical transmission, transplacental antibody transfer, changes during the perinatal period through delivery etc.). In the current endemic COVID-19 phase, research on the effects of COVID-19 related to maternal and neonatal health outcomes will continue to evolve and advance our understanding of the pandemic's long-term impacts on pregnant people and neonates, with an added focus on the effects of Post-Acute Sequelae of COVID-19 (PASC), also known as Long COVID, and long-term psychosocial consequences of the pandemic.

While the common data elements (CDEs) in this report were originally designed and intended for use by researchers during the acute phase of the pandemic, many CDEs may remain applicable in future COVID-19 research. This report serves as a historical archive of CDEs for COVID-19 research in pregnant populations during the acute COVID-19 pandemic; the CDEs in this report will not be updated to an endemic COVID-19 research context. The content and tiers of these CDEs will remain as originally designed; most of them could be useful in ongoing COVID-19 studies.

## USING THESE CDEs IN FUTURE COVID-19 RESEARCH

Although the research community moving forward may have different needs, priorities, and research questions than they did during the acute phase of the pandemic, we encourage researchers to incorporate these CDEs into research studies as applicable. Going forward, real-time studies of COVID-19 will have different needs than retrospective studies that research the pandemic period from 2020 – 2023.

Some CDEs are unlikely to apply in a future real-time COVID-19 study but could be used in a retrospective study with slight modification. Consider, for example, the following Psychosocial CDE:

- As a result of COVID-19 have you received...
  - Enrollment in the Special Supplemental Nutrition Program for Women, Infants, and Children, known as WIC?
    - Yes
    - No
    - Not sure
    - Decline to answer
  - One or more stimulus checks from the government?
    - Yes
    - No
    - Not sure
    - Decline to answer
  - Any amount of unemployment benefits from the government?
    - Yes
    - No

- Not sure
- Decline to answer

This question is unlikely to apply to future COVID-19 studies because pandemic-era government assistance policies have ended. However, this question could apply to a retrospective study by changing “have you received” to “did you receive”.

On the other hand, the following CDE in the Biomedical domain is reasonable to ask subjects in any future research study:

- Have [you/the participant] received a vaccination for COVID-19?
  - No (*if no, skip to... “if not vaccinated, why?”*)
  - Yes

This question is reasonable because the COVID-19 vaccine will continue to be available to the public and is likely to be updated seasonally. COVID-19 vaccination status is likely to be of interest in any future COVID-19 study. We encourage researchers to use their best judgment in identifying COVID-19 pregnancy CDEs that apply to their research goals and study populations.

## USING THESE CDEs IN RESEARCH STUDYING FUTURE PUBLIC HEALTH EMERGENCIES

CDEs in this report may also apply to research on future public health emergencies. Measures in both the Biomedical and Psychosocial domains are likely to be of interest in any public health emergency. Many questions can be easily modified for use in a future infectious or other public health emergency by replacing the reference to SARS-CoV-2, COVID-19, or coronavirus with a reference to the new public health emergency. An example is the following CDE in the Psychosocial domain:

- How has the COVID-19 outbreak affected your regular childcare? (Mark all that apply)
  - I had difficulty arranging for childcare
  - I had to pay more for childcare
  - My spouse/partner or I had to change our work schedule to care for our children ourselves
  - My regular childcare has not been affected by the COVID-19 outbreak
  - I do not have a child in childcare

This question could be easily modified for use in a future pandemic by replacing “COVID-19 outbreak” with a different disease or exposure.


We encourage researchers to study pregnant, maternal, and neonatal populations during future health emergencies and to modify and utilize these CDEs in their research. Researchers should use their best judgment in selecting and modifying CDEs in a way that best applies to future public health emergencies in their study population. For example, given the nature of the COVID-19 pandemic, these CDEs apply well to infectious disease outbreaks, but could easily apply to other exposures with minor adaptations. For example, in the event of a major hurricane, the following modified CDE could be asked:

- Since you gave birth, has the **hurricane emergency** led to any of the following problems accessing medical care?
  - Yes
  - No

## DATA HARMONIZATION AND OTHER RESOURCES

Across all biomedical research, data harmonization remains a key priority to answer complex questions about diseases and pool information on rare outcomes to improve statistical power. While this report is a historical

document that sought to accelerate COVID-19 research in pregnant, maternal, and neonatal populations in the midst of the COVID-19 pandemic, these CDEs can be applied to future COVID-19 research and research in future public health emergencies. We encourage the use of these and other CDEs to promote data harmonization in all pregnancy research. Other resources to access CDEs include the [NIH CDE Repository](#) and the [PhenX Toolkit](#).



# Promoting Data Harmonization to Accelerate COVID-19 Pregnancy Research

Post-Acute Sequelae of SARS-CoV-2 Infection and Vaccine  
Attitudes Working Group Addendum

*Published: June 2021*



## INTRODUCTION

Given the global pandemic and growing body of research on Post-Acute Sequelae of COVID-19 (PASC) and vaccinations in pregnant and lactating research participants, the collective impact of pregnancy studies in these areas can be amplified by planning for future analyses using combined datasets. Data harmonization will be especially helpful to address more complex questions about the effects of PASC and vaccines on individuals of reproductive age, pregnant and lactating individuals, postpartum people, and their neonates, and will help investigators to study rare outcomes for which individual studies may be underpowered.

To address this, The Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) convened researchers across several NIH-funded pregnancy cohort studies to recommend considerations for PASC and vaccination data harmonization. These recommendations build from previous efforts to recommend biomedical and psychosocial common data elements (CDEs) for researchers studying COVID-19 in pregnancy or any study enrolling participants of reproductive age, which can be found here: [Promoting Data Harmonization to Accelerate COVID-19 Pregnancy Research report](#). This group recommends that PASC studies enrolling pregnant people include both the original set of biomedical and psychosocial CDEs, and this additional PASC/Vaccine set.

Taken together, these two sets of CDEs are intended to facilitate data harmonization in studies that include pregnant and postpartum individuals who may have or be at risk of having PASC. It is important to note that **these CDEs are not designed to diagnose or characterize the PASC phenotype in adults**. Rather, they are meant to complement sets of general PASC CDEs that are under development by other groups by collecting **data on unique issues that may face people who experience PASC while pregnant or postpartum**.

The vaccine attitude CDEs recommended here apply generally to adults. Their inclusion reflects the working group's recognition that COVID-19 vaccination is a topic of critical public and scientific interest for pregnant and lactating people.

The PASC/Vaccine Working Group used the modified Delphi approach described in the previous report to prioritize methodologies for addressing PASC and vaccine attitudes and outcomes specifically.

COVID-19 studies with PASC/vaccine elements in pregnant and lactating individuals or any study enrolling participants of reproductive age each have their own unique research questions, protocols, and analysis strategies. Given this diversity, our recommendations are broken into two tiers which build on the original two tiers of data elements.

## TIER 1

**All COVID-19 and PASC Studies:** Baseline CDEs for any study related to PASC and vaccine attitudes that may include pregnant participants, postpartum participants, or participants of reproductive age. Because around 5% of individuals of reproductive age are pregnant at any given point in time and roughly 50% of pregnancies in the US are unplanned, it is important for non-pregnancy-focused studies to be prepared to collect key data specific to pregnancy when it occurs in the course of a study. Our Tier 1 recommendations provide guidance to do so.

## TIER 2

**COVID-19 and PASC Studies Focusing on Pregnant, Postpartum, and/or Lactating Populations:** CDEs that can be used to collect more detailed information on COVID-19 and/or PASC in these groups. Together, Tier 1 and Tier 2 comprise the baseline recommended CDEs to collect for any study focused on PASC and vaccine attitudes during pregnancy and postpartum.



# APPROACH

A detailed approach can be found in the [Promoting Data Harmonization to Accelerate COVID - 19 Pregnancy Research report on pg. 6](#). In summary:

1

**Conducted Landscape Analysis:** The research team collected available case report forms (CRFs), instruments, and protocols related to PASC in pregnant individuals. At the time of this review (March 2021), research on PASC and the COVID-19 vaccine in pregnant people was still very limited. The group therefore relied more heavily on Working Group member expertise, experience in the field, and related surveys.

2

**Defined Key Scientific Questions:** The key research questions decided on by the Working Group did not intend to cover or define the course of PASC in adults generally, rather, this group leveraged its expertise to discern those elements specific to the effects of PASC during pregnancy or postpartum, including lactation. Research questions can be found in the appendix.

3

**Prioritized Data Elements:** Data elements from four Biomedical Domains and six Psychosocial Domains were prioritized after creating inventories of data elements from existing questionnaires and tools.

4

**Defined Data Measures:** The research team identified potential measures for Tier 1 and Tier 2 elements based on CRFs, questionnaires, and validated measures from COVID-19 specific and non-COVID-19-specific studies. We employed a hierarchal approach for measure selection with top preference for 1) known, validated instruments, followed by 2) measures from COVID-19 studies already in the field, 3) modified versions of existing measures, and 4) measures developed by our Working Group(s).

# KEY FINDINGS

The summary below provides details on the number of domains and CDEs prioritized by the Biomedical and Psychosocial Working Groups. More detailed findings are highlighted in the following sections.

## KEY FINDINGS: BIOMEDICAL WORKING GROUP

The Biomedical PASC/Vaccine Working Group set out to create a set of CDEs that would collectively help researchers understand the clinical course of PASC, as well as vaccine hesitancy and outcomes and its effects on pregnant/postpartum individuals and their neonates (e.g., maternal and neonatal outcomes). This aims to build on PASC CDEs once developed and focuses specifically on the pregnant/postpartum population.

### Summary of Biomedical Recommendations

The Biomedical Working Group prioritized four total domains (bolded below) to guide recommendations. Each domain is made up of between one and three individual CDEs. The summaries below describe why each domain was chosen and why their underlying CDEs are important to better understanding the effects of PASC and vaccination for COVID-19 on pregnant and lactating individuals and their neonates.

- ✓ **COVID-19 Vaccination History:** This domain, which collects information on current and past COVID-19 vaccination, gives researchers an opportunity to understand details about the administered vaccine and reasons and/or factors that contributed to vaccine hesitancy.
- ✓ **Vaccine Attitudes:** This domain aims to understand the vaccine attitudes of pregnant/postpartum/lactating people who, especially due to limited data on the safety of COVID-19 vaccines in pregnant people from clinical trials, may have different attitudes towards vaccination than the rest of the population.
- ✓ **Pregnant/Postpartum:** This section includes elements related to PASC, menstruation, and sexual activity to help researchers to understand the long-term effects of infection or vaccination.
- ✓ **Family Planning:** This domain aims to provide a set of elements that can help researchers understand potential changes to menstruation and fertility.

The recommended measures associated with each of these domains can be found in the [Appendix : COVID-19 Pregnancy PASC/Vaccine Research report | Biomedical Recommended Measures](#).



# KEY FINDINGS

## KEY FINDINGS: PSYCHOSOCIAL WORKING GROUP

The Psychosocial Working Group aimed to create a set of CDEs that would collectively help researchers understand the psychological, behavioral, and socioeconomic effects of PASC on pregnant and postpartum people. Pregnant and postpartum people are uniquely and acutely affected by many of the changes caused by the pandemic, like impact on postpartum function and infant care, loss of health care coverage, decreased social supports, and more. The recommendations herein focus specifically on this intersection of pandemic effects and post-acute sequelae of SARS-CoV-2 infection.

### Summary of Psychosocial Recommendations

The Psychosocial Working Group prioritized six total domains to guide recommendations. The summaries below describe why each domain was chosen and why their underlying CDEs are important to better understanding the effects of COVID-19 and PASC on pregnant and lactating individuals and their neonates.

**Postpartum Outcomes:** These are screening questions intended to guide usage of postpartum CDEs. If a research participant experienced fetal or infant death or is not in custody of the infant, certain subsequent questions should not be asked out of sensitivity to the person's loss.

- ✓ **Pregnancy and Postpartum Function:** Taken from non-COVID specific questionnaires, this domain aims to understand pregnancy and postpartum-specific functional status, both physically and psychologically.
- ✓ **Infant Care Practices:** This domain includes the infant care practices of health care/well-baby visits, breastfeeding, infant sleeping habits, and mother-baby bonding to understand the possible correlation between PASC outcomes and infant care.
- ✓ **Childcare and Education:** Questions on childcare and educational changes of children in the household are included to understand the household childcare situation and potential demands on birthing individuals during the pandemic.
- ✓ **Attribution of Symptoms:** This domain aims to disentangle PASC symptoms from pregnancy and postpartum symptoms and/or the effects of living in a pandemic by obtaining self-reported attribution of symptoms.
- ✓ **Domestic Violence:** This domain, also included with the original set of CDEs, is highlighted due to its importance for pregnant and postpartum people, and its importance during the pandemic.
- ✓ **Access to Care:** This domain aims to understand maternal prenatal and postpartum health care, and possible disruptions.

The recommended measures associated with each of these domains can be found in the [Appendix : COVID-19 Pregnancy PASC/Vaccine Research report | Psychosocial Recommended Measures](#).

# APPENDIX

## Appendix

### Key Research Questions

#### **Post-Acute Sequelae of SARS-CoV-2 infection (PASC)**

- How can we differentiate the contributions of being pregnant/postpartum from recovering from acute COVID or having Long-COVID/PASC?
- Among people with Long-COVID/PASC, what is their functional status specific to taking care of baby?
- How are infant care practices affected (e.g., infant sleeping, breastfeeding, health care visits)?
- What are the neonatal outcomes of pregnancy with Long-COVID/PASC?

#### **Vaccine**

- Identify the reasons and attitudes for and against vaccination during pregnancy and postpartum.
- What are the biomedical outcomes of vaccination (e.g., side effects, including menstrual changes) during pregnancy and postpartum?
- Document neonatal outcomes after maternal vaccination.

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## Recommended Biomedical CDEs: Post-Acute Sequelae of SARS-CoV-2 in Pregnancy and Postpartum

A subset of measures included here are designated as “Tier 2.” Those without this designation—i.e., “Tier 1” measures—are recommended for all studies that may include participants of reproductive age and pregnant individuals. Tier 2 measures are suggested additional measures for studies focused exclusively on COVID-19 in pregnancy and/or for any study interested in taking a “deeper dive” in certain domains.

### COVID-19 Vaccination History

- Have [you/the participant] received a vaccination for COVID-19?
  - No (*If no, skip to... “if not vaccinated, why?”*)
  - Yes
- Have [you/the participant] completed the vaccination for COVID-19 (dose or doses)?
  - No (*If no, skip to... “if not vaccinated, why?”*)
  - Yes
    - **If yes**, on what date did the patient receive the first dose of vaccine?
      - Month/Day/Year
    - **If yes**, on what date did the patient receive the second dose of vaccine?
      - Month/Day/Year
      - N/A
    - Enter the name of the vaccine (if known)?<sup>1</sup>
      - AstraZeneca’s COVID-19 vaccine
      - Janssen’s (Johnson & Johnson) COVID-19 vaccine
      - Moderna’s COVID-19 vaccine
      - Novavax’s COVID-19 vaccine
      - Pfizer’s COVID-19 vaccine
      - Other, Specify
    - [Tier 2] Did [you/the participant] receive a COVID-19 vaccine 90 days after treatment with monoclonal antibodies or 30 days after an active COVID-19 infection?
      - No
      - Yes
      - Unknown
      - Prefer not to answer
- Did you experience any side effects within 2 weeks after the **FIRST** vaccine dose?<sup>2</sup>
  - No
  - Yes
  - I do not know
  - If yes, what side effect(s) did you experience? Select all that apply.
    - Pain where shot was given
    - Fever  $\geq 100.4^{\circ}\text{F}$
    - Fatigue/tiredness
    - Headache
    - Muscle pain in parts of your body beyond where shot was given

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<sup>1</sup> Project 5 Draft CDEs/FDA

<sup>2</sup> DR2 Vaccine Questions

- Immediate, severe allergic reaction (including difficulty breathing and feeling faint, nausea and/or vomiting)
  - Skin rash
  - Facial swelling
  - Other (please describe)
- Did you experience any side effects within 2 weeks after the **SECOND** vaccine dose [if applicable]?
  - No
  - Yes
  - I do not know
- If yes, what side effect(s) did you experience? Select all that apply.
  - Pain where shot was given
  - Fever  $\geq 100.4^{\circ}\text{F}$
  - Fatigue/tiredness
  - Headache
  - Muscle pain in parts of your body beyond where shot was given
  - Immediate, severe allergic reaction (including difficulty breathing and feeling faint, nausea and/or vomiting)
  - Skin rash
  - Facial swelling
  - Other (please describe)
- [Tier 2] Medications to treat symptoms post-vaccine
  - Ibuprofen
  - Acetaminophen
  - Aspirin
  - Antihistamines
  - Other, specify: \_\_\_\_\_
- If not vaccinated, Why? (Select ONE best reason)
  - The vaccine is not available to me
  - Doctor did not recommend it
  - My family did not want me to take it
  - It was not well tested in ethnically diverse people
  - It was not well tested among pregnant individuals
  - I cannot afford the vaccine
  - I have not had time to get it
  - I'm at low risk and do not need it
  - It is riskier to go get the vaccine than staying at home
  - Worried about side effects
  - The vaccine's technology hasn't been tested enough
  - Vaccine was approved too fast
  - No long-term safety data available
  - Concerned about vaccine storage
  - Already had COVID-19
  - Other, specify: \_\_\_\_\_



- Do you intend to receive a coronavirus (COVID-19) vaccine?<sup>3</sup>
  - I intend to get it as soon as possible
  - I intend to wait to see how it affects others in the community before I get it
  - I do not intend on getting it soon, but might sometime in the future
  - I do not intend to ever get the vaccine
- [Tier 2] Is there anything that might convince you to change your mind about getting vaccinated? (Based on those who would definitely not get the COVID-19 vaccine)<sup>4</sup>
  - No/Nothing
  - More research
  - If it were mandatory/required
  - Other
  - Don't know

## Vaccine Attitudes

[Tier 2] Please select how much you agree or disagree with the following statements about vaccines in general<sup>5</sup>

### START Vaccination Attitudes Examination (VAX) Scale

		<b>Strongly Agree</b>	<b>Agree</b>	<b>Slightly Agree</b>	<b>Slightly disagree</b>	<b>Disagree</b>	<b>Strongly disagree</b>
<b>1.</b>	I feel safe after being vaccinated.						
<b>2.</b>	Natural immunity lasts longer than a vaccination.						
<b>3.</b>	Vaccines can cause unforeseen problems.						
<b>4.</b>	Vaccines make a lot of money for pharmaceutical companies, but do not do much for regular people.						
<b>5.</b>	I worry about the unknown effects of vaccines in the future.						
<b>6.</b>	I feel protected after getting vaccinated.						
<b>7.</b>	Natural exposure to viruses and germs gives the safest protection.						
<b>8.</b>	Although most vaccines appear to be safe, there may be problems that we have not yet discovered.						
<b>9.</b>	Being exposed to diseases naturally is safer for the immune system than being exposed through vaccination.						
<b>10.</b>	Vaccination programs are a big con.						

<sup>3</sup> DR2 Vaccine Questions

<sup>4</sup> Kaiser Family Foundation COVID-19 Vaccine Monitor April 2021

<sup>5</sup> Vaccination Attitudes Examination (VAX) Scale

<b>11.</b>	I can rely on vaccines to stop serious infectious diseases.						
<b>12.</b>	Authorities promote vaccination for financial gain, not for people's health.						

*END Vaccination Attitudes Examination (VAX) Scale*

- Do you personally know someone who has been vaccinated for COVID-19?
  - No
  - Yes
  - Don't know
  
- [Tier 2] How much of a threat, if any, is the coronavirus outbreak for...<sup>6</sup>
  - The United States economy?
    - A major threat
    - A minor threat
    - Not a threat
  - Your personal health?
    - A major threat
    - A minor threat
    - Not a threat
  - Your personal financial situation?
    - A major threat
    - A minor threat
    - Not a threat
  
- [Tier 2] How concerned are you that you might spread the virus without knowing you have it?<sup>7</sup>
  - Very concerned
  - Somewhat concerned
  - Not too concerned
  - Not at all concerned
  
- [Tier 2] Do you personally know someone who has been hospitalized or died as a result of having COVID-19 (coronavirus)?<sup>8</sup>
  - No
  - Yes
  
- [Tier 2] Given the current situation with the coronavirus outbreak, would you feel comfortable or uncomfortable doing each of the following?<sup>9</sup>
  - Visiting with a close friend or family member inside their home
    - Totally comfortable
    - Mostly comfortable
    - Slightly uncomfortable
    - Very uncomfortable

<sup>6</sup> [Pew Research COVID-19 Vaccine Intent](#)

<sup>7</sup> [Pew Research COVID-19 Vaccine Intent](#)

<sup>8</sup> [Pew Research COVID-19 Vaccine Intent](#)

<sup>9</sup> [Pew Research COVID-19 Vaccine Intent](#)

- Going to the grocery store
  - Totally comfortable
  - Mostly comfortable
  - Slightly uncomfortable
  - Very uncomfortable
- Eating out in a restaurant
  - Totally comfortable
  - Mostly comfortable
  - Slightly uncomfortable
  - Very uncomfortable
- Taking a flight
  - Totally comfortable
  - Mostly comfortable
  - Slightly uncomfortable
  - Very uncomfortable
- Attending an indoor sporting event or concert
  - Totally comfortable
  - Mostly comfortable
  - Slightly uncomfortable
  - Very uncomfortable
- Attending a crowded party
  - Totally comfortable
  - Mostly comfortable
  - Slightly uncomfortable
  - Very uncomfortable
- Going to a hair salon
  - Totally comfortable
  - Mostly comfortable
  - Slightly uncomfortable
  - Very uncomfortable
- Going to the gym or indoor recreation?
  - Totally comfortable
  - Mostly comfortable
  - Slightly uncomfortable
  - Very uncomfortable
- [Tier 2] How often do you wear a mask in public buildings? <sup>10</sup>
  - All or most of the time
  - Some of the time
  - Hardly ever
  - Never
- [Tier 2] Have you asked your health care provider about the vaccine? <sup>11</sup>
  - No
  - Yes
  - Don't know

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<sup>10</sup> [Pew Research COVID-19 Vaccine Intent](#)

<sup>11</sup> [Kaiser Family Foundation COVID-19 Vaccine Monitor January 2021](#)

- Having gotten your COVID-19 vaccine, do you think you will now.....? (Based on those who have gotten at least one dose of the COVID-19 vaccine)<sup>12</sup>
  - Strictly follow social distancing guidelines
  - Probably follow most social distancing guidelines
  - No longer follow social distancing guidelines
  - Don't know
- [Tier 2] Which of the following applies to your plans about the COVID-19 vaccine for your child(ren)?<sup>13</sup>
  - I plan on getting the COVID-19 vaccine for my child(ren) as soon as it is available
  - I plan on getting the COVID-19 vaccine for my child(ren) eventually
  - I do not plan on getting the COVID-19 vaccine for my child(ren)
  - I am unsure
- How concerned are you, if at all, that...<sup>14</sup>
  - The COVID-19 vaccines are not as safe as they are said to be
    - Very concerned
    - Somewhat concerned
    - Not too concerned
    - Not at all concerned
    - Don't know
  - You might experience serious side effects from the COVID-19 vaccine
    - Very concerned
    - Somewhat concerned
    - Not too concerned
    - Not at all concerned
    - Don't know
- Do you feel you have enough information about...<sup>15</sup>
  - The potential side effects of the COVID-19 vaccine
    - Have enough information
    - Do not have enough information
    - Don't know
  - Where you will be able to get a COVID-19 vaccine
    - Have enough information
    - Do not have enough information
    - Don't know
  - When you will be able to get the COVID-19 vaccine
    - Have enough information
    - Do not have enough information
    - Don't know

## Pregnant/Postpartum

Note: for researchers studying COVID-19 in pregnancy or any study enrolling participants of reproductive age, please note the elements below should be considered in addition to the biomedical and psychosocial elements for pregnant individuals which can be found here: [Promoting Data Harmonization to Accelerate COVID - 19 Pregnancy Research report](#).

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<sup>12</sup> Adapted from DR2 Vaccine Questions

<sup>13</sup> DR2 Vaccine Questions

<sup>14</sup> [Kaiser Family Foundation COVID-19 Vaccine Monitor April 2021](#)

<sup>15</sup> [Kaiser Family Foundation COVID-19 Vaccine Monitor January 2021](#)

## Long COVID

### *Post-acute readmission*

Note: If the following questions are included in the PASC Adult Questionnaire, please skip the following two questions.

- Were [you/the participant] admitted to the hospital for a possible complication of COVID-19 after the acute illness?
  - No
  - Yes
    - If yes, date of (re)admission [\_D][\_D]/[\_M][\_M]/[\_Y][\_Y][\_Y][\_Y]
  - Unknown

### *New diagnosis of illness or complication related to COVID-19*

- Were [you/the participant] newly diagnosed with any illness or complication related to COVID-19?
  - Cardiovascular
  - Dermatological
  - Endocrine
  - Gastro-intestinal
  - Other Generic
  - Musculoskeletal
  - Mental Health
  - Neurological
  - Pulmonary
  - Renal

## Menses/Menstruation Changes<sup>16</sup>

- Have you had any periods (menstrual cycles) in the last 3 months? (We mean bleeding for which you needed a tampon or sanitary pad, NOT discharge (spotting) for which you needed a panty liner only)
  - No
  - Yes

### **If you have NOT had periods in the last 3 months:**

- What was the reason for not having periods?
  - Taking hormones continuously (e.g. the Pill, injections, Mirena, HRT)
  - Pregnant/breastfeeding
  - Unsure
  - Other (Please describe) \_\_\_\_\_
- The figure below shows examples of the amount of bleeding you can experience **every four hours** during your period (menstrual cycle). Please describe the amount of bleeding you typically experience **at its heaviest**, and **on average**.

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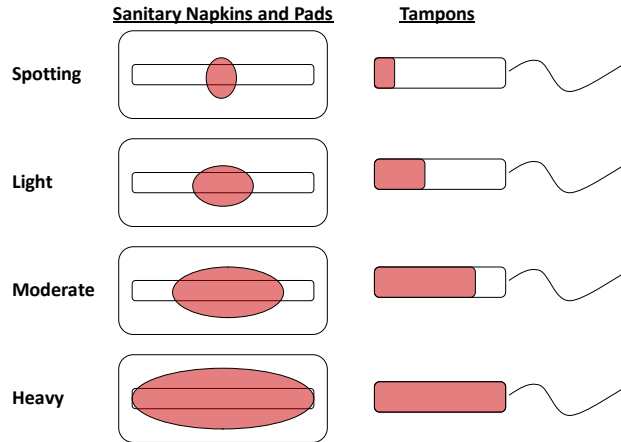
<sup>16</sup> Adapted from <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4252538/#SD1>

**At its heaviest?**

- ☐ Spotting  
☐ Light  
☐ Moderate  
☐ Heavy

**On average?**

- ☐ Spotting  
☐ Light  
☐ Moderate  
☐ Heavy



We are interested in what your period (menstrual cycle) was like when you were **NOT using hormonal contraception** (the Pill, patch, ring, injection or hormonal IUD). For each time period, please tell us if you had periods and what they were like. If you did not have periods or were using hormonal contraception the whole time, please enter the code for “no” or “used hormonal contraception” in the first row and then skip the rest of the column.

Please add the Code number in the appropriate column	[3 months] Pre- COVID diagnosis (skip if you have not been diagnosed)	Post-COVID diagnosis (skip if you have not been diagnosed)	[3 months] Pre- Vaccine (skip if you have not been vaccinated)	Post-Vaccine (skip if you have not been vaccinated)
<b>Did you have natural periods during this time period? (not on hormonal contraception)</b> 1=Yes 2=No 3=Used hormonal contraception for entire time frame	_____ If 1 entered above, please complete questions below	_____ If 1 entered above, please complete questions below	_____ If 1 entered above, please complete questions below	_____ If 1 entered above, please complete questions below
<b>Were your periods regular when not using hormonal contraception?</b> 1=extremely regular (period starts 1-2 days before or after it is expected) 2=very regular (period starts 3-4 days before or after it is expected) 3=regular (period starts 5-7 days before or after it is expected) 4=somewhat irregular (period starts 8-20 days before or after it is expected) 5=irregular (period starts more than 20 days before or after it is expected)	_____	_____	_____	_____
<b>How many days of bleeding did you usually have each period when not using hormonal contraception? (Not counting discharge or spotting for which you needed a panty liner only)</b>	_____ days or <input type="checkbox"/> Too irregular to say	_____ days or <input type="checkbox"/> Too irregular to say	_____ days or <input type="checkbox"/> Too irregular to say	_____ days or <input type="checkbox"/> Too irregular to say

<b>How heavy was your menstrual flow at its heaviest and on average, when not using hormonal contraception? Please use the figure on the previous page to describe the amount of bleeding that you typically experienced every four hours.</b> 1=Spotting 2=Light 3=Moderate 4=Heavy (clots/flooding)	At its heaviest: _____  On average: _____	At its heaviest: _____  On average: _____	At its heaviest: _____  On average: _____	At its heaviest: _____  On average: _____
<b>On average, how many days were there between the start of one period and the start of the next, when not using hormonal contraception?</b> 1=<24 days 2=24-31 days 3=32-38 days 4=39-50 days 5=51+ days 6=Too irregular to estimate	_____	_____	_____	_____

- Has there been a time in your life pre-COVID 19 vaccine or COVID-19 diagnosis when you typically had pelvic pain during your periods?
  - No pain
  - Mild cramps (medication never or rarely needed)
  - Moderate cramps (medication usually needed)
  - Severe cramps (medication and bed rest needed)
  - At what age did you start having period pain? \_\_\_\_ years
- Has there been a time in your life post-COVID 19 vaccine when you typically had pelvic pain during your periods?
  - No pain
  - Mild cramps (medication never or rarely needed)
  - Moderate cramps (medication usually needed)
  - Severe cramps (medication and bed rest needed)

## Family Planning<sup>17</sup>

Please think about the following questions...	[3 months] Pre- COVID diagnosis (skip if you have not been diagnosed)	Post-COVID diagnosis (skip if you have not been diagnosed)	[3 months] Pre-Vaccine (skip if you have not been vaccinated)	Post-Vaccine (skip if you have not been vaccinated)
Have you had vaginal sex, even once?	No/Yes	No/Yes	No/Yes	No/Yes

<sup>17</sup> Adapted from the NORC Teen Sexual Health Survey

How many times have you had vaginal sex? Your best guess is okay	_____ # times Not sure	_____ # times Not sure	_____ # times Not sure	_____ # times Not sure
In the past 3 months, have you had vaginal sex without you or your partner using any methods of birth control?  Types of birth control listed in drop-down below.	No/Yes	No/Yes	No/Yes	No/Yes
How many times have you had vaginal sex without you or your partner using any of these methods of birth control?	_____ # times Not sure	_____ # times Not sure	_____ # times Not sure	_____ # times Not sure

**Types of birth control [Drop-down]**

- Birth control pills
- Condom
- Partner's vasectomy
- Female sterilizing operation, such as tubal sterilization and hysterectomy
- Withdrawal, pulling out
- Depo-Provera™, injectables
- Hormonal implant (Norplant™, Implanon™, or Nexplanon™)
- Calendar rhythm, Standard Days, or Cycle Beads method
- Safe period by temperature or cervical mucus test (Two Day, Billings Ovulation, or Sympto-thermal Method)
- Diaphragm
- Female condom, vaginal pouch
- Foam
- Jelly or cream
- Cervical cap
- Suppository, insert
- Today™ sponge
- Intrauterine device (IUD), coil, loop (Mirena, Paraguard)
- Emergency Contraception
- Respondent was sterile
- Respondent's partner was sterile
- Lunelle™ injectable (monthly shot)
- Contraceptive patch
- Vaginal contraceptive ring
- Other method (please specify) : \_\_\_\_\_

*START Time to Pregnancy Assessment*

**Think about the 12 months *before* you were diagnosed with COVID-19:**

1. Were you pregnant during that time?
  - a. No: → go to question 2
  - b. Yes: → go to question 3
2. Were you *trying* to become pregnant during that time?
  - a. No: → go to question 5
  - b. Yes: → go to question 4
3. How many months of trying did it take you to get pregnant?



- a. \_\_\_\_\_ months; → go to question 5
- 4. How many months did you try but not get pregnant?
  - a. \_\_\_\_\_ months; → go to question 5

**Now think about the 12 months *after* you were diagnosed with COVID-19:**

- 5. Were you pregnant during that time?
  - a. No: → go to question 6
  - b. Yes: → go to question 7
- 6. Were you trying to become pregnant?
  - a. No: → go to question 9
  - b. Yes: → go to question 8
- 7. How many months of trying did it take you to get pregnant?
  - a. \_\_\_\_\_ months; → go to question 9
- 8. How many months did you try but not get pregnant?
  - a. \_\_\_\_\_ months; → go to question 9

**Think about the 12 months *before* you received the COVID-19 vaccine:**

- 9. Were you pregnant during that time?
  - a. No: → go to question 10
  - b. Yes: → go to question 11
- 10. Were you *trying* to become pregnant during that time?
  - a. No: → go to question 13
  - b. Yes: → go to question 12
- 11. How many months of trying did it take you to get pregnant?
  - a. \_\_\_\_\_ months; → go to question 13
- 12. How many months did you try but not get pregnant?
  - a. \_\_\_\_\_ months; → go to question 13

**Now think about the 12 months *after* you received the COVID-19 vaccine:**

- 13. Were you pregnant during that time?
  - a. No: → go to question 14
  - b. Yes: → go to question 15
- 14. Were you *trying* to become pregnant during that time?
  - a. No: *end of questionnaire*
  - b. Yes: → go to question 16
- 15. how many months of trying did it take you to get pregnant?
  - a. \_\_\_\_\_ months; *end of questionnaire*
- 16. How many months did you try but not get pregnant?
  - a. \_\_\_\_\_ months; *end of questionnaire*

*END Time to Pregnancy Assessment*

## PASC in Pregnancy and Postpartum Registry | Biospecimens Recommended Measures

Tier 1 Biospecimens (Neonate)				
Specimen	Collection	Timing	Storage	Sample Analyses
Neonate/Cord Blood	<ul style="list-style-type: none"> <li>• <b>Plasma / Buffy Coat:</b> EDTA tubes (at least 10mL total)</li> <li>• <b>Serum:</b> Serum separator (5mL)</li> </ul>	<ul style="list-style-type: none"> <li>• Date of Draw</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Plasma:</b> Freeze in 200 µL (max 1 mL) aliquots, store at -80°C</li> <li>• <b>Serum:</b> Freeze in 200 µL (max 1 mL) aliquots, store at -80°C</li> <li>• <b>Buffy coat:</b> Freeze, store at -80°C</li> </ul>	<p><b>Plasma / Serum:</b></p> <ul style="list-style-type: none"> <li>• SARS-CoV-2 RNA viral load</li> <li>• SARS-CoV-2 antibodies (IgG, IgA, neutralizing antibody evaluation)</li> <li>• Cytokine analysis</li> </ul> <p><b>Buffy coat:</b> Analysis of cellular fraction (Evaluation of properties of specific cellular fractions such as T-cells, monocytes)</p>
Neonatal Respiratory Specimens	<ul style="list-style-type: none"> <li>• Nasopharyngeal swab (preferred)</li> <li>• Nasal swab</li> <li>• Oropharyngeal swab (RTq-PCR)</li> <li>• Saliva vial / cup</li> </ul>	<ul style="list-style-type: none"> <li>• Delivery</li> <li>• At time of acute illness (if applicable)<sup>18</sup></li> </ul>	<ul style="list-style-type: none"> <li>• <b>Swab:</b> Swirl in PBS, aliquot PBS and freeze at -80°C</li> <li>• <i>If diagnostic swab can be retrieved from clinical lab, it can be used for quantitative (viral load) and other assays</i></li> <li>• <b>Saliva:</b> Process with DTT, store at -80C</li> </ul>	<ul style="list-style-type: none"> <li>• Use to confirm SARS-CoV-2 negative status in control group</li> <li>• SARS-CoV-2 RNA viral load</li> </ul>

Tier 1 Biospecimens (Maternal)				
Specimen	Collection	Timing	Storage	Sample Analyses
Maternal Blood <sup>19</sup>	<ul style="list-style-type: none"> <li><b>Plasma / Buffy Coat:</b> EDTA tubes (at least 10mL total)</li> <li><b>Serum:</b> Serum separator (5mL)</li> </ul>	<ul style="list-style-type: none"> <li>At time of acute illness <i>and / or</i></li> <li>At delivery</li> </ul>	<ul style="list-style-type: none"> <li><b>Plasma:</b> Freeze in 200 µL (max 1 mL) aliquots, store at -80°C</li> <li><b>Serum:</b> Freeze in 200 µL (max 1 mL) aliquots, store at -80°C</li> <li><b>Buffy coat:</b> Freeze, store at -80°C</li> </ul>	<b>Plasma / Serum:</b> <ul style="list-style-type: none"> <li>SARS-CoV-2 RNA viral load</li> <li>SARS-CoV-2 antibodies (IgG, IgA, neutralizing antibody evaluation)</li> <li>Cytokine analysis</li> </ul> <b>Buffy coat:</b> <ul style="list-style-type: none"> <li>Analysis of cellular fraction (Evaluation of properties of specific cellular fractions such as T-cells, monocytes)</li> </ul>
Cord Blood	<ul style="list-style-type: none"> <li><b>Plasma / Buffy Coat:</b> EDTA tubes (at least 10-15 mL total, may be less for pre-term deliveries)</li> <li><b>Serum:</b> Serum separator (7.5mL)</li> </ul>	<ul style="list-style-type: none"> <li>At delivery</li> </ul>	<ul style="list-style-type: none"> <li><b>Plasma:</b> Freeze in 200 µL (max 1 mL) aliquots, store at -80°C</li> <li><b>Serum:</b> Freeze in 200 µL (max 1 mL) aliquots, store at -80°C</li> <li><b>Buffy coat:</b> Freeze, store at -80°C</li> </ul>	<b>Plasma / Serum:</b> <ul style="list-style-type: none"> <li>SARS-CoV-2 RNA viral load</li> <li>SARS-CoV-2 antibodies (IgG, IgA, neutralizing antibody evaluation)</li> <li>Cytokine analysis</li> </ul> <b>Buffy coat:</b> <ul style="list-style-type: none"> <li>Analysis of cellular fraction (Evaluation of properties of specific cellular fractions such as T-cells, monocytes)</li> </ul>
Placenta	<ul style="list-style-type: none"> <li>Fixed tissue</li> </ul>	<ul style="list-style-type: none"> <li>At delivery</li> </ul>	<ul style="list-style-type: none"> <li>Store at 4°C until fixation</li> <li>Once fixed, can be stored as formalin-fixed paraffin embedded blocks</li> </ul>	<ul style="list-style-type: none"> <li>RNA <i>in situ</i> hybridization (RNA-ISH)</li> </ul>
	<ul style="list-style-type: none"> <li>Maternal side biopsy <i>and</i></li> <li>Fetal side biopsy</li> </ul>	<ul style="list-style-type: none"> <li>As soon as possible; within 1-2 hours of delivery maximum (RNA will degrade)</li> </ul>	<ul style="list-style-type: none"> <li>Process in RNA later, following manufacturer instructions</li> <li>Store preserved tissue at -80°C (or -20°C if 80°C not available)</li> </ul>	<ul style="list-style-type: none"> <li>SARS-CoV-2 RNA analyses<sup>20</sup></li> </ul>
Colostrum and/or mature milk	<ul style="list-style-type: none"> <li>Pump into colostrum cup <i>or</i></li> <li>Hand expression into colostrum cup</li> </ul> <p>For larger volume:</p> <ul style="list-style-type: none"> <li>Pump into pumping containers or storage containers</li> </ul>	<ul style="list-style-type: none"> <li>During delivery admission <i>or</i></li> <li>At postpartum visit</li> </ul>	<ul style="list-style-type: none"> <li><b>Small volume:</b> Aliquot (e.g. 1 mL aliquots) and store at -80°C</li> <li><b>Large volume</b> (e.g. 10 mL or above): Spin and separate cellular fraction and supernatant. Aliquot (e.g. 1 mL aliquots) and store at -80°C</li> </ul>	<ul style="list-style-type: none"> <li>SARS-CoV-2 RNA viral load<sup>21</sup></li> <li>SARS-CoV-2 antibodies (IgG, IgA, neutralizing antibody evaluation)</li> </ul>

Tier 2 Expanded Specimen Collection (Maternal)				
Specimen	Collection	Timing	Storage	Sample Analyses
Maternal Respiratory Specimens <sup>22</sup>	<ul style="list-style-type: none"> <li>Nasopharyngeal swab (preferred)</li> <li>Nasal swab</li> </ul>	<ul style="list-style-type: none"> <li>11-14 weeks<sup>23</sup></li> <li>18-22 weeks<sup>5</sup></li> <li>28-32 weeks<sup>5</sup></li> </ul>	<ul style="list-style-type: none"> <li><b>Swab:</b> Swirl in PBS, aliquot PBS and freeze at -80°C</li> </ul>	<ul style="list-style-type: none"> <li>Use to confirm SARS-CoV-2 negative status in control group</li> </ul>

	<ul style="list-style-type: none"> <li>Oropharyngeal swab (RTq-PCR)</li> <li>Saliva vial / cup</li> </ul>	<ul style="list-style-type: none"> <li>Delivery</li> <li>At time of acute illness (if applicable)<sup>24</sup></li> </ul>	<ul style="list-style-type: none"> <li><i>If diagnostic swab can be retrieved from clinical lab, it can be used for quantitative (viral load) and other assays</i></li> <li><b>Saliva:</b> Process with DTT, store at -80°C</li> </ul>	<ul style="list-style-type: none"> <li>SARS-CoV-2 RNA viral load</li> </ul>
Maternal Blood	<ul style="list-style-type: none"> <li><b>Plasma, Buffy Coat, and/or PBMC:</b> EDTA tubes (at least 10mL total)</li> <li><b>Serum:</b> Serum separator (5mL)</li> </ul>	<ul style="list-style-type: none"> <li>11-14 weeks<sup>5</sup></li> <li>18-22 weeks<sup>5</sup></li> <li>28-32 weeks<sup>5</sup></li> <li>Delivery</li> <li>At time of acute illness</li> </ul>	<ul style="list-style-type: none"> <li><b>Plasma:</b> Freeze in 200 µL (max 1 mL) aliquots, store at -80°C</li> <li><b>Serum:</b> Freeze in 200 µL (max 1 mL) aliquots, store at -80°C</li> <li><b>Buffy coat:</b> Freeze, store at -80°C</li> <li><b>PBMC:</b> Store in freezing media in liquid nitrogen (LN<sub>2</sub>)</li> </ul>	<ul style="list-style-type: none"> <li>Inflammatory markers (e.g. IL-6, TNF-α, IL-1B, IFN-γ, IL-10, CRP/ESR)</li> <li>T-cell, monocyte, other specific cell fraction experiments (EDTA only)</li> <li>AM cortisol or CRH</li> </ul>
	<ul style="list-style-type: none"> <li>PaxGene tube (2.5 or 5 mL)</li> </ul>	<ul style="list-style-type: none"> <li>11-14 weeks<sup>5</sup></li> <li>18-22 weeks<sup>5</sup></li> <li>28-32 weeks<sup>5</sup></li> <li>Delivery</li> <li>At time of acute illness</li> </ul>	<ul style="list-style-type: none"> <li>Shake vigorously</li> <li>May keep at room temp for 2-24 hrs</li> <li>Freeze whole tube, store at -80°C</li> </ul>	<ul style="list-style-type: none"> <li>Transcriptomic/global gene expression analyses</li> </ul>
Cord Blood	<ul style="list-style-type: none"> <li><b>For PBMC:</b> EDTA tubes (at least 10-15 mL total)</li> </ul>	<ul style="list-style-type: none"> <li>At delivery</li> </ul>	<ul style="list-style-type: none"> <li><b>Isolated PBMC:</b> Store in liquid nitrogen (LN<sub>2</sub>)</li> </ul>	<ul style="list-style-type: none"> <li><b>PBMC:</b></li> <li>Analysis of cellular fraction (scRNA-Seq, evaluation of properties of specific cellular fractions such as T-cells, monocytes)</li> <li>Genotyping (array-based)</li> </ul>
	<ul style="list-style-type: none"> <li>PaxGene tube (2.5 or 5 mL)</li> </ul>	<ul style="list-style-type: none"> <li>At delivery</li> </ul>	<ul style="list-style-type: none"> <li>Shake vigorously</li> <li>Keep at room temp for 2-24 hrs</li> <li>Freeze whole, store at -80°C</li> </ul>	<ul style="list-style-type: none"> <li>Transcriptomic/global gene expression analyses</li> </ul>
Placenta	<ul style="list-style-type: none"> <li>Maternal side placental biopsy <i>and</i></li> <li>Fetal side placental biopsy</li> </ul>	<ul style="list-style-type: none"> <li>As soon as possible; within 1-2 hours of delivery maximum (RNA will degrade)</li> </ul>	<ul style="list-style-type: none"> <li>Process in RNA later, following manufacturer instructions</li> <li>Store preserved tissue at -80°C</li> </ul>	<ul style="list-style-type: none"> <li>SARS-CoV-2 RNA viral load</li> <li>RNA RTq-PCR for specific genes of interest</li> <li>DNA methylation analyses</li> <li>Genotyping (array-based)</li> </ul>
	<ul style="list-style-type: none"> <li>Full thickness biopsies <i>or</i></li> <li>Remaining whole placenta</li> </ul>	<ul style="list-style-type: none"> <li>Take biopsies in pathology lab</li> </ul>	<ul style="list-style-type: none"> <li>Formalin-fixed, paraffin-embedded blocks</li> </ul>	<ul style="list-style-type: none"> <li>RNA <i>in situ</i> hybridization (RNA-ISH) to define placental infection</li> </ul>

<sup>1</sup> If a participant that was previously designated as a control becomes ill with COVID-19, specimens collected after that point can no longer be used as a control

<sup>19</sup> Blood draws for research in pregnancy should not exceed 50 mL in 8 weeks. Those with Hct < 24 should not provide blood for research

<sup>20</sup> Preservation in RNA later permits both RNA and DNA analyses

<sup>21</sup> Specific guidance to participants and adherence to breast cleaning protocols is critically important if breastmilk viral load quantification is planned

<sup>22</sup> Respiratory specimens only necessary to be collected to document COVID-19 negative status at the time of collection if the participant provides other samples for study

<sup>23</sup> Can alternatively collect at 1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup> trimester appointments. Ideally, align maternal respiratory specimens collection with maternal blood draw

<sup>24</sup> If a participant that was previously designated as a control becomes ill with COVID-19, specimens collected after that point can no longer be used as a control

			<ul style="list-style-type: none"> <li>Fixed tissue can be sectioned and stored on slides and in in paraffin-embedded blocks</li> </ul>	<ul style="list-style-type: none"> <li>ACE2/TMPRSS2 protein expression patterns</li> <li>Cd68/CD163 for Hofbauer cell hyperplasia and chronic histiocytic intervillitis</li> </ul>
Breastmilk	<b>Large volume:</b> <ul style="list-style-type: none"> <li>Pump into pumping containers or storage containers</li> </ul>	<ul style="list-style-type: none"> <li>At delivery <i>and/or</i></li> <li>Post-partum</li> </ul>	<ul style="list-style-type: none"> <li><b>Large volume</b> (e.g. 10 mL or above): Spin and separate cellular fraction and supernatant</li> </ul>	<b>Cellular fraction of breastmilk:</b> <ul style="list-style-type: none"> <li>Sequencing</li> <li>Isolation of T-cells, NK cells, and antibody-producing B cells</li> </ul>

Tier 3 (Maternal)				
Specimen	Collection Method	Timing	Storage	Sample Analyses
Saliva (Tier 3)	<ul style="list-style-type: none"> <li>Oragene</li> </ul>	<ul style="list-style-type: none"> <li>Follow time restrictions included in instructions</li> </ul>	<ul style="list-style-type: none"> <li>Process with DTT</li> <li>Store at -80°C</li> </ul>	<ul style="list-style-type: none"> <li>Genotyping</li> </ul>
Placenta	<ul style="list-style-type: none"> <li>Maternal biopsy <i>and</i></li> <li>Fetal side biopsy</li> </ul>	<ul style="list-style-type: none"> <li>As soon as possible; within 1-2 hours of delivery maximum (RNA will degrade)</li> </ul>	<ul style="list-style-type: none"> <li>Snap freeze tissue in liquid nitrogen (preferred) or on dry ice</li> <li>Store at -80°C</li> </ul>	<ul style="list-style-type: none"> <li>Protein isolation</li> <li>Single-cell RNA-seq</li> <li>DNA/RNA extraction</li> </ul>
	<ul style="list-style-type: none"> <li>Full thickness biopsies <i>or</i></li> <li>Remaining whole placenta</li> </ul>	<ul style="list-style-type: none"> <li>Take biopsies in pathology lab</li> </ul>	<ul style="list-style-type: none"> <li>Formalin-fixed, paraffin-embedded blocks</li> <li>Fixed tissue can be sectioned and stored on slides and in in paraffin-embedded blocks</li> </ul>	<ul style="list-style-type: none"> <li>CD147 &amp; CD26 protein expression patterns</li> </ul>
	<ul style="list-style-type: none"> <li>Membrane or decidua basalis</li> </ul>	<ul style="list-style-type: none"> <li>As soon as possible</li> <li>Within 1-2 hours of delivery maximum (RNA will degrade)</li> </ul>	<ul style="list-style-type: none"> <li>Process fresh for cell isolation per protocol</li> </ul>	<ul style="list-style-type: none"> <li>Inflammatory/immune analyses (e.g., FACS, flow cytometry, transcriptomics, pro-inflammatory cytokine quantification)</li> </ul>

## Recommended Psychosocial CDEs: Post-Acute Sequelae of SARS-CoV-2 in Pregnancy and Postpartum

Important Postpartum Pre-Questions: Many of the recommended elements below are specific to the postpartum period and are framed in a way that assumes there is a surviving newborn living with the birthing person.

**If either or both of the two questions below is answered “No” the items marked with “\*\*\*\*” below *should not be asked* out of sensitivity to the participant.**

- Is your baby alive now?
  - No- *We are very sorry for your loss.*
  - Yes
- Is your baby living with you now?
  - No
  - Yes

### Pregnancy and Postpartum Function

#### Pregnancy – Physical Function<sup>25</sup>

- The following questions ask about how much you have experienced some feelings about your current pregnancy. **During the last two weeks:**
  - To what extent have you felt that your physical changes associated with this pregnancy do not allow you to do what you need?
  - How worried have you been about not being able to perform activities around the house?
  - How worried have you been about carrying out the pregnancy successfully?
  - How worried have you been about not being able to handle labor and delivery?
  - Have you been forced to cut down on your physical activity?

#### **Response options:**

- Not at all
- A little
- A moderate amount
- Very much
- An extreme amount

#### Pregnancy – Psychological Function<sup>26</sup>

- The following questions focus on your feelings about some areas of life **in the last two weeks.**
  - To what extent have you felt that your psychological changes associated with this pregnancy do not allow you to do what you need?
    - Not at all
    - A little
    - A moderate amount
    - Very much
    - An extreme amount

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<sup>25</sup> Adapted from [QoL-Grav Questionnaire](#)

<sup>26</sup> Adapted from [QoL-Grav Questionnaire](#)

- How satisfied are you with how you have managed to adapt to this pregnancy ?
  - Very dissatisfied
  - Dissatisfied
  - Neither satisfied nor dissatisfied
  - Satisfied
  - Very satisfied

#### Postpartum Function - Infant Care Responsibilities<sup>27\*\*\*</sup>

- Please select the item that indicates to what extent you can perform the following aspects of your new baby's care:

	Not at all	Some days	Most days	All the time
Daytime feedings				
Night feedings				
Bathe the baby				
Change diapers				
Change the baby's clothes				
Play with the baby				

- During the past 2 weeks, have you had any health conditions that made it hard or impossible to take care of your baby?<sup>28 \*\*\*</sup>
  - No
  - Yes

#### Postpartum Function - Household Activities<sup>29</sup>

- Please select the item that indicates to what extent you can perform the following household activities even if you don't routinely do them:

	Not at all	Some days	Most days	All the time
Care of family/household members				
Cleaning the house				
Tidying the house (making beds, picking up things, etc.)				
Laundry				

<sup>27</sup> [Adapted from the Inventory of Functional Status After Childbirth \(IFSAC\)](#)

<sup>28</sup> [Adapted from the Inventory of Functional Status After Childbirth \(IFSAC\)](#)

<sup>29</sup> [Inventory of Functional Status After Childbirth \(IFSAC\)](#)

Doing dishes				
Cooking				
Household business (paying bills, banking, etc.)				
Grocery shopping				
Shopping, other than groceries				
Doing errands				
Heavy housework and maintenance work (seasonal cleaning, painting, etc.)				

### Infant Care Practices \*\*\*

#### Healthcare (infant) <sup>30</sup>

- Do you have health insurance or Medicaid for your new baby? \*\*\*
  - No
  - Yes
- Has your new baby gone as many times as you wanted for a well-baby checkup? \*\*\*
  - No
  - Yes
- Did any of these things keep your baby from having a well-baby checkup? Check ALL that apply. \*\*\*
  - I didn't have enough money or health insurance to pay for the visit(s)
  - I had no way to get my baby to the clinic or doctor's office
  - I didn't have anyone to take care of my other children
  - I couldn't get an appointment
  - My baby was too sick to go for a well-baby checkup
  - I was too sick to take my baby for a well-baby checkup
  - I was too tired to take my baby for a well-baby checkup
  - Other. Please tell us: [free text]
- How many times has your new baby gone for care when he or she was sick (not including well-baby checkups)? \*\*\*
  - Enter number \_[            ] times
    - None
    - My baby has not been sick
    - My baby is still in the hospital
- Has your new baby gone for care as many times as you wanted when he or she was sick? \*\*\*
  - No
  - Yes
- Did any of these things keep you from taking your baby for care when he or she was sick? Check ALL that apply. \*\*\*
  - I didn't have enough money or health insurance to pay for the visit

<sup>30</sup> Adapted from [PRAMS 8 Standard Questionnaire](#)



- I couldn't get an appointment
- I didn't have a regular doctor for my baby
- I had no way to get my baby to the clinic or doctor's office
- I didn't have anyone to take care of my other children
- I was too sick to take my baby for care
- I was too tired to take my baby for care
- Other – please tell us \_\_\_\_\_

### Breastfeeding \*\*\*

- Did you ever breastfeed or pump breast milk to feed your new baby, even for a short period of time?<sup>31</sup> \*\*\*
  - No [skip remaining breastfeeding questions]
  - Yes
- Are you currently breastfeeding or feeding pumped milk to your new baby?<sup>32</sup> \*\*\*
  - No
  - Yes [skip remaining breastfeeding questions]
- Did you breastfeed as long as you wanted to?<sup>33</sup> \*\*\*
  - No
  - Yes
- What were your reasons for stopping breastfeeding? Check ALL that apply.<sup>34</sup> \*\*\*
  - My baby had difficulty latching or nursing
  - Breast milk alone did not satisfy my baby
  - I thought my baby was not gaining enough weight
  - My nipples were sore, cracked, or bleeding or it was too painful
  - I thought I was not producing enough milk, or my milk dried up
  - I had too many other household duties
  - I felt it was the right time to stop breastfeeding
  - I got sick or I had to stop for medical reasons
  - I was too tired
  - I did not want to breastfeed anymore
  - I went back to work
  - I went back to school
  - My husband or partner did not support breastfeeding
  - My baby was jaundiced (yellowing of the skin or whites of the eyes)
  - Other→ Please tell us: [free text]

### Infant Sleeping Habits \*\*\*

- In the last 2 weeks, what is the typical amount of time your baby sleeps at night without waking up?<sup>35</sup> \*\*\*
  - 2 hours or less
  - 3 – 4 hours
  - 5 – 6 hours
  - 7 – 8 hours
  - 8 hours or more

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<sup>31</sup> Adapted from [PRAMS Phase 8 Core Questionnaire](#)

<sup>32</sup> Adapted from [PRAMS Phase 8 Core Questionnaire](#)

<sup>33</sup> [Infant Feeding Practices Survey \(IFPS – 3 Months\)](#)

<sup>34</sup> Adapted from [PRAMS Phase 8 Core Questionnaire](#)

<sup>35</sup> [Infant Feeding Practices Survey \(IFPS – 3 Months\)](#) | WG Modifications

*START Brief Infant Sleep Questionnaire (BISQ)*

- [Tier 2] The following questions relate to how your baby [youngest child] sleeps.<sup>36</sup> \*\*\*
  - Infant/child DOB: MM / DD / YYYY
  - Biological Sex at Birth: M / F / Don't know
- Sleeping arrangement: \*\*\*
  - Infant crib in a separate room
  - Infant crib in parents' room
  - In parents' bed
  - Infant crib in room with sibling
  - Other, Specify: \_\_\_\_\_
- In what position does your baby sleep most of the time? \*\*\*
  - On his/her belly
  - On his/her side
  - On his/her back
- How much time does your baby spend in sleep during the NIGHT (between 7 in the evening and 7 in the morning)? \*\*\*
  - Hours: \_\_\_\_\_ Minutes: \_\_\_\_\_
- How much time does your baby spend in sleep during the DAY (between 7 in the morning and 7 in the evening)? \*\*\*
  - Hours: \_\_\_\_\_ Minutes: \_\_\_\_\_
- Average number of night wakings per night: \_\_\_\_\_
- How much time during the night does your baby spend in wakefulness (from 10 in the evening to 6 in the morning)? \*\*\*
  - Hours: \_\_\_\_\_ Minutes: \_\_\_\_\_
- How long does it take to put your baby to sleep in the evening? \*\*\*
  - Hours: \_\_\_\_\_ Minutes: \_\_\_\_\_
- How does your baby fall asleep? \*\*\*
  - While feeding
  - Being rocked
  - Being held
  - In bed alone
  - In bed near parent
- When does your baby usually fall asleep for the night? \*\*\*
  - Hours: \_\_\_\_\_ Minutes: \_\_\_\_\_
- Do you consider your baby's sleep as a problem? \*\*\*
  - A very serious problem
  - A moderate problem
  - A small problem
  - A very small problem
  - Not a problem at all

*END Brief Infant Sleep Questionnaire (BISQ)*

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<sup>36</sup> [Brief Infant Sleep Questionnaire \(BISQ\)](#)

## [Tier 2] Feelings of Attachment to Newborn \*\*\*

### **Postpartum Only** \*\*\*

- This is the Impaired Bonding subscale (Factor/Scale 1) of the full Postpartum Bonding Questionnaire (PBQ). Please indicate how often the following are true for you. There are no 'right' or 'wrong' answers. Choose the answer which seems right in your recent experience<sup>37</sup>: \*\*\*

	Always	Very often	Quite often	Sometimes	Rarely	Never
I feel close to my baby						
I wish the old days when I had no baby would come back						
The baby doesn't seem to be mine						
My baby winds me up						
I love my baby to bits						
I feel happy when my baby smiles or laughs						
My baby irritates me						
My baby cries too much						
I feel trapped as a mother						
I resent my baby						
My baby is the most beautiful baby in the world						
I wish my baby would somehow go away						

## Childcare and Education

### Number of household members<sup>38</sup>

- How many total people live in your household now including yourself?
  - Please indicate the number of people living in your household: \_\_\_\_\_
  - Please indicate the number of people under 18 years-old living in your household: \_\_\_\_\_

### Impact of Pandemic on Childcare

- How has the COVID-19 outbreak affected your regular childcare? (Mark all that apply)<sup>39</sup>
  - I had difficulty arranging for childcare
  - I had to pay more for childcare
  - My spouse/partner or I had to change our work schedule to care for our children ourselves
  - My regular childcare has not been affected by the COVID-19 outbreak
  - I do not have a child in childcare

## [Tier 2] Impact of Pandemic on Children's Education<sup>40</sup>

- What is your household's current situation for childcare and/or schooling? (select all that apply)

<sup>37</sup> Adapted from the Postpartum Bonding Questionnaire

<sup>38</sup> 2020 COVID-19 Household Pulse Survey

<sup>39</sup> Environmental Influences on Child Health Outcomes (ECHO) COVID-19 Questionnaire

<sup>40</sup> Study of Pregnancy and Neonatal Health (SPAN) – Attained measures via personal communication

- I or someone in my household care for my child(ren) full-time
- I or someone in my household care for my child(ren) part-time
- I or someone in my household try to balance childcare/home schooling and work/telework responsibilities at home
- Someone from outside my household (friend, family, nanny) cares for my child(ren) in my home
- My child(ren) goes to a childcare center or someone else's home for childcare
- My child(ren) does not need childcare; they take care of themselves
- My child(ren) goes to school in-person
- My child(ren) goes to school virtually (online)

### Attribution of Symptoms<sup>41</sup>

Listed below are conditions you may or may not have ever experienced. For each condition, please circle the letter next to each reason or group of reasons that *corresponds to how much that might explain your condition*. Please check every item for each question. Also, answer whether you have had the condition in the last [3 months] by circling A (YES) or B (NO). Please answer all questions.

A (Not at all)    B (Somewhat)    C (Quite a bit)    D (A great deal)

	Not at all	Somewhat	Quite a bit	A great deal
<b>If I had a prolonged headache, I would probably think that it is because:</b>				
I am emotionally upset				
There is something wrong with muscles nerves or brain				
A loud noise, bright light or something else has irritated me				
It's an effect of living during a pandemic				
It's part of being pregnant				
It's part of being postpartum				
I have acute COVID-19				
I have "long COVID"				
Have you had a prolonged headache in the last 3 months? N/Y	N		Y	
<b>If I was sweating a lot, I would probably think that it is because:</b>				
I must have a fever or infection				
I'm anxious or nervous				
The room is too warm, I'm overdressed or working too hard				
It's an effect of living during a pandemic				
It's part of being pregnant				
It's part of being postpartum				
I have acute COVID-19				
I have "long COVID"				
Have you noticed yourself sweating a lot in the last 3 months? N/Y	N		Y	
<b>If I got dizzy all of a sudden, I would probably think it is because:</b>				
There is something wrong with my heart or blood pressure				
I am not eating enough or I got up too quickly				
I must be under a lot of stress				
It's an effect of living during a pandemic				
It's part of being pregnant				
It's part of being postpartum				

<sup>41</sup> Adapted from [Symptom Interpretation Questionnaire](#)

I have acute COVID-19				
I have "long COVID"				
Have you felt dizzy in the last 3 months? N/Y	N		Y	
<b>If I noticed my mouth was dry, I would probably think that it is because:</b>				
I must be scared or anxious about something				
I need to drink more liquids				
There is something wrong with my salivary glands				
It's an effect of living during a pandemic				
It's part of being pregnant				
It's part of being postpartum				
I have acute COVID-19				
I have "long COVID"				
Have you had a dry mouth in the last 3 months? N/Y	N		Y	
<b>If I felt my heart pounding in my chest, I would probably think that it is because:</b>				
I've exerted myself or drunk a lot of coffee				
I must be excited or afraid				
There must be something wrong with my heart				
It's an effect of living during a pandemic				
It's part of being pregnant				
It's part of being postpartum				
I have acute COVID-19				
I have "long COVID"				
Have you noticed your heart pounding in the last 3 months? N/Y	N		Y	
<b>If I feel fatigued, I would probably think that it is because:</b>				
I'm emotionally exhausted or discouraged				
I've been over-exerted myself or not exercising enough				
I'm anemic or my blood is weak				
It's an effect of living during a pandemic				
It's part of being pregnant				
It's part of being postpartum				
I have acute COVID-19				
I have "long COVID"				
Have you felt fatigued in the last 3 months? N/Y	N		Y	
<b>If I noticed my hand trembling, I would probably think that it is because:</b>				
I must have some sort of neurological problem				
I'm very nervous				
The muscles in my hand are tired				
It's an effect of living during a pandemic				
It's part of being pregnant				
It's part of being postpartum				
I have acute COVID-19				
I have "long COVID"				
Have you noticed your hands trembling in the last 3 months? N/Y	N		Y	
<b>If I had trouble sleeping, I would probably think that it is because:</b>				
Some kind of pain or physical discomfort is keeping me awake				
I'm not tired or I had too much coffee				
I'm worrying too much or I must be nervous about something				

It's an effect of living during a pandemic				
It's part of being pregnant				
It's part of being postpartum				
I have acute COVID-19				
I have "long COVID"				
Have you had trouble sleeping in the last 3 months? N/Y	N		Y	
<b>If my stomach was upset, I would probably think that it is because:</b>				
I've worried myself sick				
I have the flu or stomach irritation				
I've had something to eat that did not agree with me				
It's an effect of living during a pandemic				
It's part of being pregnant				
It's part of being postpartum				
I have acute COVID-19				
I have "long COVID"				
Have you had an upset stomach in the last 3 months? N/Y	N		Y	
<b>If I lost my appetite, I would probably think that it is because:</b>				
I've been eating too much or my body doesn't need as much food as before				
I'm worrying so much that food doesn't taste good any more				
I have some stomach or intestinal problem				
It's an effect of living during a pandemic				
It's part of being pregnant				
It's part of being postpartum				
I have acute COVID-19				
I have "long COVID"				
Have you lost your appetite in the last 3 months? N/Y	N		Y	
<b>If I had a hard time catching my breath, I would probably think that it is because:</b>				
My lungs are congested from infection, irritation, or heart trouble				
The room is stuffy or there is too much pollution in the air				
I'm over excited or anxious				
It's an effect of living during a pandemic				
It's part of being pregnant				
It's part of being postpartum				
I have acute COVID-19				
I have "long COVID"				
Have you had a hard time catching your breath in the last 3 months? N/Y	N		Y	
<b>If I noticed numbness or tingling in my hands or feet, I would probably think that it is because:</b>				
I'm under emotional stress				
There is something wrong with my nerves or blood circulation				
I am cold or my hand or foot went to sleep				
It's an effect of living during a pandemic				
It's part of being pregnant				
It's part of being postpartum				
I have acute COVID-19				
I have "long COVID"				

Have you had numbness or tingling in your hands or feet in the last 3 months? N/Y	N		Y	
<b>If I was constipated or irregular, I would probably think that it is because:</b>				
There is not enough fruit or fiber in my diet				
Nervous tension is keeping me from being regular				
There is something wrong with my bowels or intestines				
It's an effect of living during a pandemic				
It's part of being pregnant				
It's part of being postpartum				
I have acute COVID-19				
I have "long COVID"				
Have you been constipated or irregular in the last 3 months? N/Y	N		Y	

## Domestic Violence

### ***In the last 12 months, how often has a partner or spouse...***

- Yelled at you or said things to you that made you feel bad about yourself, embarrassed you in front of others, or frightened you?
  - Never
  - Almost never
  - Sometimes
  - Fairly often
  - Very often
- Done things like push, grab, hit, slap, kick, or throw things at you during an argument or because they were angry with you?
  - Never
  - Almost never
  - Sometimes
  - Fairly often
  - Very often

## Access to Care

### Prenatal Care<sup>43</sup>

- Did you get prenatal care as early in your pregnancy as you wanted?
  - No
  - Yes
- Did any of these things keep you from getting prenatal care when you wanted it? For each item, check No or Yes

	No	Yes
a. I couldn't get an appointment when I wanted one		
b. I didn't have enough money or insurance to pay for my visits		
c. I didn't have any transportation to get to the clinic or doctor's office		
d. The doctor or my health plan would not start care as early as I wanted		
e. I had too many other things going on		
f. I couldn't take time off from work or school		
g. I didn't have my Medicaid <or state Medicaid name> card		

<sup>43</sup> Adapted by [PRAMS Phase 8 Standard Questionnaire](#)

h. I didn't have anyone to take care of my children		
i. I didn't know that I was pregnant		
j. I didn't want anyone else to know I was pregnant		
k. I didn't want prenatal care		
l. I did not feel well enough to go to the appointment		
m. I was too tired to keep the appointment		

### Postpartum Care

- Since your pregnancy ended, have you had a postpartum checkup for yourself? A postpartum checkup is the regular checkup a person has about 4-6 weeks after giving birth<sup>44</sup>
  - No
  - Yes
- Did any of these things keep you from having a postpartum checkup? Check ALL that apply.<sup>45</sup>
  - I didn't have health insurance to cover the cost of the visit
  - I felt fine and did not think I needed to have a visit
  - I couldn't get an appointment when I wanted one
  - I didn't have any transportation to get to the clinic or doctor's office
  - I had too many things going on
  - I couldn't take time off from work
  - I arrived late at my appointment and they cancelled it
  - I was too sick to go for a checkup
  - I was too tired to go for a checkup
  - My baby was too sick to go for a checkup
  - Other - Please tell us:

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<sup>44</sup> PRAMS Phase 8 Core Questionnaire

<sup>45</sup> PRAMS Phase 8 Core Questionnaire