



The impact of the COVID-19 pandemic on gestational carriers

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Abstract

Reproductive medicine has been significantly impacted by the coronavirus (COVID-19) pandemic, and this includes the gestational carrier (GC) process. The objectives of this commentary are to evaluate the impact of COVID-19 on the GC process, as well to communicate Shady Grove Fertility's considerations of and response to COVID-19 on the GC process to the larger assisted reproductive technology (ART) community. We also gathered conclusions drawn from available data on the impact of COVID-19 infection on maternal and neonatal morbidity and mortality as well as on counseling patients on vaccination. We compiled proposals to mitigate risk and to maximize safe evaluation and treatment for GCs during the ongoing pandemic. Over 2 years after the onset of the pandemic, the multiple resurgences of cases in the USA have necessitated nimble strategies to provide ongoing and safe reproductive care and have posed unique challenges to the GC process. With the prospect of the virus continuing to spread globally well into the future, as healthcare professionals of the ART community, we will need to ensure effective collaboration and communication as we provide care during the ongoing pandemic.

Keywords COVID-19 · Gestational carrier · Pandemic · Vaccine

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Assisted reproduction utilizing a gestational carrier (GC) involves a carefully screened volunteer who is recruited or known to the intended parents (IP). The GC will carry a pregnancy from an embryo transferred after in vitro fertilization (of an egg that is not her own, with sperm). A GC is indicated for patients with a diagnosis of uterine factor infertility, in the setting of medical contraindications to pregnancy, or by patients unable to carry a pregnancy such as males with same sex partners. According to the recent data in the USA, approximately 2% of all assisted reproductive technology (ART) cycles occur with GCs [1]. While ART centers vary on the number of GC cycles completed annually, most practices participate in treatment cycles that require a GC. The coronavirus disease (COVID-19) pandemic acutely affected the delivery of care at all ART centers, especially GC-IP arrangements. Even as 2022 draws to a close, COVID-19 remains an ongoing challenge to the timely completion of these complex treatment cycles. Our paper details the challenges of navigating the pandemic while still trying to optimize ART treatment cycles involving a GC.

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Overview of the immediate impact of COVID-19 on GC cycles in the USA

The COVID-19 pandemic appeared as a rapid threat to the entire practice of reproductive medicine and was classified as a pandemic by the World Health Organization on March 11, 2020 [2]. COVID-19 is caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), a highly contagious RNA virus that is transmitted via respiratory droplets. At the onset of the pandemic, the impact of COVID-19 infection on pregnancy was unknown. The American Society for Reproductive Medicine (ASRM) issued guidance for its members on March 17, 2020. The multidisciplinary task force of physicians, embryologists, and mental health professionals recommended the immediate suspension of new, non-urgent treatment cycles, the cancelation of all pending embryo transfers, the suspension of all non-urgent diagnostic procedures, and a shift to the use of telemedicine [3].

In response to the ASRM guidance, Shady Grove Fertility (SGF) completed its last ongoing GC transfer cycle on March 26, 2020 (cycles in progress before the closure can take up to 1 month to complete). On this same day, all reproductive care involving a GC was suspended until further notice. Telemedicine consults were immediately available. Using state and local guidelines regarding safe reopening, we gradually resumed treatment for IPs in need of a GC in May 2020. The practice considered it safe to initiate transfer cycles when the GC resided locally. At the time, those traveling from states with high infection rates were required to quarantine upon arrival, thus delaying care. All in-cycle monitoring would be performed at one centralized location. All diagnostic testing resumed under safety precautions including the use of personal protective equipment, limited and spaced appointment times, and social distancing.

It is fair to assume that ASRM viewed the drastic reduction of all fertility treatments as a temporary measure, with the normal delivery of reproductive care resuming in reasonable time. However, more than 2 years after its onset, COVID-19 has presented as a series of infectious waves as new variants have emerged. The multiple resurgences of cases in the USA have necessitated nimble strategies to provide ongoing, safe reproductive care. The ART community must adapt to provide care with the effects of COVID-19 extending years in the future. The field must also be prepared for future epidemics and pandemics. In this article, we share insights from our response to COVID-19 on the GC process to the larger reproductive care community. We also gathered available data on COVID-19 infection and vaccination during pregnancy and suggested proposals to mitigate risk and to maximize safe evaluation and treatment for GCs during the ongoing pandemic.

Changes in the GC evaluation process in response to COVID-19

The medical and psychological evaluation process for a GC is complex. It often requires several months to complete. The GC uterine evaluation remains one of the most impacted steps by the pandemic. Previously, a GC would complete the mock embryo transfer (MET) and hysterosalpingogram (HSG) during one visit. The MET is a practice embryo transfer with an empty catheter and saline, completed prior to the actual embryo transfer. It provides information about the ease of passing through the endocervical canal and the length and shape of the uterine cavity. The HSG is an X-ray test to outline the internal shape of the uterine cavity and evaluate the patency of the fallopian tubes. Of note, while the HSG is considered a standard test by most practitioners, practices may utilize other anatomical tests such as a sonohysterogram to visualize the uterine cavity. The ability of a GC candidate to partially complete laboratory testing and/or the uterine evaluation remotely had become common prior to the pandemic. Many GCs do not live geographically near the fertility center where the IPs have cryopreserved embryos for future use. The utilization of remote testing is more important than ever in the GC process. The advantages of remote testing are numerous including minimizing inconvenience for potential GCs, mitigating travel costs, and reducing the travel-related risks of COVID-19 exposure. However, the process is dependent on outside ART centers being willing to conduct testing on patients who will complete a treatment cycle elsewhere.

The transition to complete remote testing of GCs comes with a loss of direct contact. Prior to COVID-19, all GCs were required to make at least one in-person visit to the ART center. The GC would receive in-person teaching regarding the medications necessary for uterine endometrial lining preparation for a frozen embryo transfer (FET) cycle. The GC would also leave with the ability to complete a mock estrogen cycle (MEEP) remotely if required. The MEEP is a practice hormonal stimulation of the endometrial lining to confirm its optimal development. This coordinated in-person visit also permitted the efficient scheduling of the final psychological evaluation. The GC (and partner if applicable) requires an individual counseling session followed by a group meeting that includes the IPs. This coordinated visit served as a decisive step to allow patients to meet the clinical team, complete testing, and have their questions answered. It provided the most efficient way to care for out-of-state and international IPs. Prior to the pandemic, after completion of this process, the IPs were instructed to proceed with the execution of legal contracts. Due to changing federal and state travel requirements and quarantines, a coordinated in-person visit has been difficult to arrange or impractical for

international IPs and out-of-state GCs. This resulted in a less efficient timeline to complete a match.

The urgency of the pandemic required innovation, and our practice has adapted new policies and procedures, including for the GC evaluation process. The psychological evaluation is now being completed via telemedicine. If possible, a GC can schedule the medical evaluation remotely. The pre-COVID-19 GC evaluation was intended to maximize the probability that the potential GC would be an appropriate candidate, minimize the cost and time requirements for all the participants, and reduce the potential for psychological harm to the IPs and GC from disappointment over a canceled match. Over the coming years, the impact of these changes regarding patient satisfaction and outcomes will need to be reassessed.

Psychological impact of COVID-19 on the GC process

The psychological impact of the pandemic on the GC process remains unstudied. The GC process often results in a special lifelong connection between all participants, who now need to cope with increased uncertainty regarding delays in testing, potential travel restrictions, financial implications, and the evolution of data on the risks of COVID-19 in pregnancy.

Psychological outcomes of the GC experience prior to the pandemic in the USA have not been rigorously studied, although qualitative interviews highlight that GCs consider their role meaningful and do not have adverse psychological outcomes from their participation in the arrangement. A 2018 qualitative study showed that bonding with the IPs and creating “fictive kin” ties is often the outcome of the intense and intimate process of collaborative pregnancy [4]. A cross-sectional study from early 2020 demonstrated that many GCs viewed this as a positive experience, involving deliberate efforts to establish a trustful GC-IP partnership, and having a meaningful impact on other people’s lives. Most IPs and GCs maintained ongoing contact after birth [5].

Until the pandemic ends, the physical interactions between the IPs and GC will be significantly reduced. It is now common for a GC previously unknown to the IP to have an ongoing pregnancy with no prior in-person meeting. Protocol modifications intended for safety will exacerbate stress for participants. SGF has intermittently limited those allowed in the transfer room (video is permitted). IPs also must manage intermittent restrictions regarding routine obstetrical appointments and the potential for hospitals to limit the number of support people in the delivery room. The reworked protocol of the GC selection process could lead to

a significant emotional fallout for the IPs and GC, making the overall experience far less intimate and rewarding.

ASRM has issued ethics and practice committee guidelines for GCs that include recommendations for the psychological consideration of a GC’s own family [6]. In a study investigating the impact of COVID-19 on family life, common themes reported by parents included concerns about the effect of COVID-19 on their children, health concerns for others, the stresses of the balancing act of parent life, assisting with children’s school work, and working from home [7]. The pandemic has placed extra stress on parenting, and psychological consideration of the GC and family is pertinent to ensure adequate psychological evaluation and preparation. Consideration of COVID-19 induced family stressors are likely important to minimize GC withdrawal during the prolonged screening process or even after a failed treatment cycle. Most IP-GC contracts will include up to three transfer cycles to achieve a successful delivery. The commitment of a GC to the process might diminish if not successful immediately.

Is it safe to get pregnant?

The COVID-19 pandemic is now part of the foreseeable future. No major medical organizations are advising patients to avoid pregnancy. In the USA, over 90 million cases and over 1 million deaths have been reported since 2020. Among pregnant patients, there have been over 200,000 cases and close to 300 deaths [8].

For logistic and clear chain of custody reasons pre-COVID-19, all GC transfer cycles at our practice were FETs. The IPs would proceed with an IVF cycle and embryo vitrification as soon as feasible, in most cases prior to starting the recruitment of a GC. Thus, it is possible for IPs who are not comfortable with the unknown risks of COVID-19 to delay recruiting a GC or scheduling a FET. However, after over 2 years of the pandemic, waiting for its conclusion seems impractical.

Our practice provides counseling to all patients undergoing treatment during the pandemic and requires the completion of an additional COVID-19 consent. Existing data indicates that COVID-19 in pregnancy increases the risk of maternal morbidity and mortality [9]. Available data suggests that those pregnant and symptomatic with COVID-19 are at increased risk of more severe illness compared with their non-pregnant counterparts [10, 11]. Additionally, the Centers for Disease Control and Prevention (CDC) includes pregnant individuals in the “increased risk” category for severe COVID-19 illness. Available data shows that pregnant women are at increased risk of intensive care unit admissions, need for ventilatory support, and death when compared with symptomatic non-pregnant women [11, 12].

Comorbidities can exacerbate the symptoms of COVID-19 infection. For example, current data suggests that pregnant women with COVID-19 who have gestational diabetes are at greater risk of severe illness and mortality when compared to pregnant women without such comorbidity [13–16]. Additional comorbidities to consider avoiding in GCs are obesity and asthma, as they are common in reproductive-age women and are also established risk factors for poorer outcomes of COVID-19 infection [17, 18]. The optimal GC candidate is a woman younger than 35 with at least one full-term uncomplicated pregnancy, no miscarriages, and no comorbidities. Some centers will be more flexible in considering candidates when the potential GC is known to the IPs. ART providers need to maintain strict selection criteria despite the significant decrease in available GCs. The priority must be safety for this special group of medical volunteers and the resulting pregnancies.

Emerging data has suggested an association between symptomatic and asymptomatic COVID-19 infection and preeclampsia [10, 19, 20]. Additionally, there have been rare reports of severe placentitis in pregnant individuals with SARS-CoV-2 [21]. However, these reports have several limitations, and more data regarding preeclampsia and placentitis in those with SARS-CoV-2 infection are needed to guide any potential changes in clinical management.

The incidence of low birth weight and neonatal intensive care unit admissions for neonates among women with COVID-19 appears higher than the general population [22], and COVID-19 infection has been shown to increase the rate of preterm birth [10]. Compared to asymptomatic pregnant individuals, severe to critical COVID-19 illness in pregnancy has been associated with adverse perinatal outcomes, while mild to moderate illness has not been associated with adverse perinatal outcomes [23]. A retrospective cohort study identified that offspring of mothers infected with SARS-CoV-2 during pregnancy were significantly more likely to have a neurodevelopmental diagnosis (such as motor or language developmental delay) in the first 12 months of life, particularly those with mothers with a third trimester infection, compared with offspring of mothers in the control group (who were not infected) [24].

Proposals to maximize the safe evaluation and treatment of GCs during the ongoing pandemic

Providers should counsel patients regarding precautions that reduce the risk of exposure to COVID-19. Beyond encouraging patients to wear a mask in public, practice hand washing frequently, implement physical distancing, and utilize outdoor venues [25], paramount strategies include employing vaccination and the use of antiviral medications if indicated.

To date, remdesivir is the only drug approved by the Food and Drug Administration (FDA) for the treatment of COVID-19. Paxlovid (ritonavir-boosted nirmatrelvir), molnupiravir, and some anti-SARS-CoV-2 monoclonal antibodies have received Emergency Use Authorizations (EUA) from the FDA for COVID-19 [26]. The FDA EUA states that molnupiravir is not recommended for pregnant patients as fetal toxicity has been observed in animal studies [27]. Of note, Paxlovid is an investigational medicine that can be used in mild to moderate COVID-19 patients who are at substantial risk of progression to severe COVID-19, including hospitalization or death. Pregnancy is considered a condition that puts individuals at high risk for clinical progression. The safety and efficacy of treating pregnant patients with Paxlovid has not been established. The concomitant use of Paxlovid and certain drugs utilized in obstetric settings (such as nifedipine, methylergonovine, fentanyl, midazolam, or betamethasone) may result in potentially significant drug interactions [28].

Additionally, routine testing of members of the household at risk of exposure can be used as a strategy to prevent infection. The CDC now suggests that fully vaccinated people can refrain from routine screening tests [29]. However, testing vaccinated individuals might continue to be useful in some situations, including in areas where there is wide community spread or low vaccination rates or among individuals at a higher risk of more severe infection, such as pregnant individuals.

Risk mitigation not elimination

Providers need to educate patients with accurate, unbiased, and current scientific information regarding risks of COVID-19 while pregnant, although this knowledge continues to evolve. The threshold for safety for a GC needs to be even higher than that of patients accepting the potential risks of their own.

The ART center in charge of the embryo transfer needs to establish a consistent SARS-CoV-2 testing strategy for GC cycles. The first consideration will be when to conduct viral testing. It is reasonable to recommend testing for all GCs prior to the start of medication and 1–3 days prior to the intended transfer. If a GC develops symptoms of COVID-19 after the start of a cycle or has a known positive exposure, testing should be completed as soon as possible within guidelines. A FET cycle can be canceled up to the day of the intended transfer if the lab is notified not to proceed with thawing the embryo. It will be particularly important to make sure that the GC will have access to timely, accurate testing.

The second consideration will be the type of viral test to utilize. This requires a nimble strategy that takes into

consideration the turnaround time for results, local availability and access to a testing laboratory, the sensitivity and specificity of the test, and the prevalence of COVID-19 in the community. The two primary types of tests available for diagnosis are nucleic acid amplification tests (NAATs, the reverse transcription-polymerase chain reaction or PCR) that detect viral nucleic acid genes, and immunoassays that detect specific viral antigens [30]. Antigen tests remain the most practical and rapid method to test the general public with the understanding that its sensitivity is less than the PCR test. Unfortunately, antigen tests are more likely to miss the asymptomatic GC or one with a low viral load. The antigen test is very specific; a positive result is highly accurate. We recommend utilizing PCR testing primarily and antigen testing if necessary.

If a GC becomes symptomatic prior to the embryo transfer, the most prudent approach is to cancel the cycle even if viral tests are negative. Rescheduling a transfer requires 1 month. If the pretest probability of infection is high due to symptoms, a positive exposure and/or high community spread, the likelihood of infection remains high even with a negative test.

The optimal testing strategy utilizes a PCR test, if feasible, to minimize false negatives prior to the initiation of medication by the GC and occurs as close as possible to the day of intended embryo transfer. The timing of the viral test relative to symptom onset also influences the false negative rate. Of course, an asymptomatic GC who tests negative in close proximity to the transfer can develop symptoms and a confirmed infection soon after. This risk is part of the counseling that IPs and GCs are given prior to transfer.

An additional precaution for risk mitigation includes avoiding cycles during times of anticipated or current surges of COVID-19 in areas where the gestational carrier resides. This includes winter months (where people spend more time indoors, in close quarters, and with less ventilated air) and when the climate is drier and colder (which has been shown to prolong the degradation of the virus) [31].

Another important consideration should be the occupation of the GC and her partner. Studies have documented an increased risk of COVID-19 in frontline healthcare workers who are predominantly women despite the proper use of PPE [32, 33]. Occupations that involve primarily telework would be preferable to minimize the risks of contracting COVID-19 in a pregnancy.

Vaccination status and variant risk remain important contributing factors to morbidity in COVID-19 infection during pregnancy. Variants have differed in their rate of breakthrough infection in people vaccinated, rate of transmission, and severity of symptoms [34]. Although mitigation factors are important, currently vaccination is the only non-pharmacological method proven to reduce morbidity and mortality in the GC and fetus. While a GC may become infected with

COVID-19 during the process, knowingly performing an FET in a COVID-19 positive patient should absolutely be avoided.

COVID vaccination counseling

Overall, the rate of vaccination for COVID-19 remains lower among pregnant individuals than the general population. The latest numbers show 67% of the US population, and 56% of pregnant persons are fully vaccinated against COVID-19 [35]. Providers should discuss vaccine safety and efficacy with GCs and IPs as part of the consent process. It is important to help GCs and IPs understand that seropositivity from vaccination or infection does not cause sterility and that COVID-19 vaccines are safe during pregnancy and breastfeeding. The antibodies produced from vaccination or infection are transferred to the fetus conferring immunity [36]. Vaccination continues to be recommended by the ASRM, the American College of Obstetricians and Gynecologists (ACOG), the Society for Maternal–Fetal Medicine (SMFM), and the CDC for all persons who are pregnant or considering pregnancy [36–38]. Existing data suggests that COVID-19 vaccination during pregnancy does not increase the risk of miscarriage [9]. At our practice, physicians initially required vaccination as a prerequisite for a GC match to proceed. However, the practice position changed over time to one of strongly encouraging vaccination for GCs. The change in policy was mediated by the refusal of the contracting pool of GC candidates to be vaccinated. Prior to the pandemic, an average match time would be 6–9 months for a GC. Now, IPs are routinely being told to expect a 12–24-month wait to find a suitable GC. This has created a logistical and ethical challenge for ART providers and IPs. The GCs who are hesitant to receive the vaccine are in great demand. The IPs are overwhelmed by an extended time period to find any GC at all and will often capitulate to the GC's refusal to be vaccinated. ART physicians find themselves in the uncomfortable position of facilitating treatment without minimizing risk to the GC and the pregnancy. Is it reasonable to proceed with treatment if the GC and IPs have been counseled and agree to the increased risks of pregnancy without vaccination?

Comprehensive demographic data regarding GCs and treatment cycles are not available in the USA; only the total number of cycles is reported annually to the Society for Assisted Reproductive Technology (SART). Most GCs are recruited by independent agencies that are contracted to work on behalf of IPs and facilitate GC identification, screening, and cycle coordination with the ART clinic. In general, agencies are not reporting an issue with GC withdrawal after a match is complete since the start of the pandemic. The agencies are primarily challenged by recruiting

from a smaller pool of GC candidates who remain highly vaccine resistant.

It is conjecture as to why the more limited pool of potential GCs appear more vaccine resistant. A recent paper by Aly et al. shows lack of trust could be the primary reason for vaccine hesitancy in reproductive-age women [39]. Additional research is needed to identify the factors that make a GC willing to use exogenous hormones to achieve a pregnancy and yet remain unwilling to be vaccinated despite a preponderance of data showing risk reduction to the pregnancy.

Our new reality

The potential risks of COVID-19 may deter both IPs and GC from proceeding with third-party assisted reproduction. Studies are needed to evaluate the psychosocial impact of the virus on the GC experience from multiple perspectives. It is plausible that all participants will experience increased stress and diminished satisfaction. The IP and GC need to contend with uncertainty of a GC acquiring a COVID-19 infection and the potential consequences for the GC, the IPs, and the IPs' child. The reworked protocol of the GC selection process could lead to a significant emotional fallout for the IPs and GC. The IPs and the GC will experience a loss of physical contact and in-person communication with each other and with medical providers, making the overall experience far less intimate. It is the intimacy of this incredibly special human relationship and the unique journey to parenthood that is highly rewarding for most IPs and GCs.

We will need to remain flexible to provide care during the ongoing pandemic. This is also a time to strengthen our professional relationships. The GC process involves an agency for recruitment, multiple clinical providers, (clinical coordinator, nurse, mental health provider, and physician) and legal counsel. We encourage institutions to establish and host interdisciplinary committees and meetings to allow better communication and coordination during this challenging time.

Declarations

Conflict of interest Micah J. Hill is involved in thread robotics. All other authors declare no competing interest.

References

- Murugappan G, Farland L, Missmer S, Correia KF, Anchan RM, Ginsburg E. Gestational carrier in assisted reproductive technology. *Fertil Steril*. 2018;3:420–8. <https://doi.org/10.1016/j.fertnstert.2017.11.011>.
- World Health Organization. WHO Director-General's opening remarks at the media briefing on COVID-19 - 11 March 2020. <https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020>. Accessed 22 Aug 2022.
- American Society for Reproductive Medicine (ASRM). Patient management and clinical recommendations during the coronavirus (COVID-19) pandemic Update No. 1. 2020. <https://www.asrm.org/globalassets/asrm/asrm-content/news-and-publications/covid-19/covidtaskforceupdate1.pdf>. Accessed 22 Aug 2022.
- Terman E, Berend Z. Surrogate non-motherhood: Israeli and US surrogates speak about kinship and parenthood. *Anthropol Med*. 2018;25:296–310. <https://doi.org/10.1080/13648470.2017.1401825>.
- Yee S, Hemalal S, Librach C. "Not my child to give away": a qualitative analysis of gestational surrogates' experiences. *Women Birth*. 2022;33:e256–65. <https://doi.org/10.1016/j.wombi.2019.02.003>.
- : Ethics Committee of the American Society for Reproductive Medicine. Consideration of the gestational carrier: an Ethics Committee opinion. *Fert Steril*. 2018;110:1017–21. <https://doi.org/10.1016/j.fertnstert.2018.08.029>.
- Chia K, Schwartz C, Towner E, Kasparianb NA, Callaghan B. Parenting under pressure: a mixed-methods investigation of the impact of COVID-19 on family life. *J Affect Disord Rep*. 2021;5:100161. <https://doi.org/10.1016/j.jadr.2021.100161>.
- Centers for Disease Control and Prevention. CDC Vaccine safety datalink-vaccination coverage in pregnancy. 2021a. <https://covid.cdc.gov/covid-data-tracker/#vaccinations-pregnant-women>. Accessed 22 Aug 2022.
- American Society for Reproductive Medicine (ASRM). Update No. 13 Variants, vaccines, and vaccination. 2021a. <https://www.asrm.org/news-and-publications/covid-19/statements/patient-management-and-clinical-recommendations-during-the-coronavirus-covid-19-pandemic/>. Accessed 22 Aug 2022.
- Ellington S, Strid P, Tong VT, Woodworth K, Galang RR, Zambrano LD, Nahabedian MS, Anderson K, Gilboa SM. Characteristics of women of reproductive age with laboratory-confirmed SARS-CoV-2 infection by pregnancy status United States, January 22–June 7, 2020. *MMWR Morb Mortal Wkly*. 2020;69:769–75. <https://doi.org/10.15585/mmwr.mm6925a1>.
- Khan DSA, Pirzada AN, Ali A, Salam RA, Das JK, Lassi ZS. The differences in clinical presentation, management, and prognosis of laboratory-confirmed COVID-19 between pregnant and non-pregnant women: a systematic review and meta-analysis. *Int J Environ Res Public Health*. 2021;18:5613. <https://doi.org/10.3390/ijerph18115613>.
- Zambrano LD, Ellington S, Strid P, Galang RR, Oduyebo T, Tong VT, Woodworth KR, Nahabedian JF, Azziz-Baumgartner E, Gilboa SM, Meaney-Delman D. Update: characteristics of symptomatic women of reproductive age with laboratory-confirmed SARS-CoV-2 infection by pregnancy status — United States, January 22–October 3, 2020. *MMWR Morb Mortal Wkly*. 2020;69:1641–7. <https://doi.org/10.15585/mmwr.mm6944e3>.
- Popkin BM, Du S, Green WD, Beck MA, Taghred A, Herbst CH, Alsukait RF, Alluhidan M, Nahar A, Shekar M. Individuals with obesity and COVID-19: a global perspective on the epidemiology and biological relationships. *Obes Rev*. 2020;11:e13128. <https://doi.org/10.1111/obr.13128>.
- Lima-Martínez M, Boada CC, Madera-Silva MD, Marín W, Contreras M. COVID-19 and diabetes mellitus: a bidirectional relationship. *Clin Investig Arterioscler*. 2021;33:151–7. <https://doi.org/10.1016/j.arteri.2020.10.001>.
- Lokken EM, Walker CL, Delaney S, Kachikis A, Kretzer NM, Erickson A, Resnick R, Vanderhoeven J, Hwang JK, Barnhart N, Rah J, McCartney SA, Ma KK, Huebner EM, Thomas C, Sheng

- JS, Paek BW, Retzlaff K, Kline CR, Munson J, Blain M, LaCourse SM, Deutsch G, Adams-Waldorf KM. Clinical characteristics of 46 pregnant women with a severe acute respiratory syndrome coronavirus 2 infection in Washington State. *Am J Obstet Gynecol*. 2020;6(911):e1-911.e14. <https://doi.org/10.1016/j.ajog.2020.05.031>.
16. Kleinwechter HJ, Weber KS, Mingers N, Ramsauer B, Schaefer-Graf UM, Groten T, Kuschel B, Backes C, Banz-Jansen C, Berghaeuser MA, Brotsack IA, Dressler-Steinbach I, Engelbrecht C, Engler-Hauschild S, Gruber TM, Hepp V, Hollatz-Galuschki E, Iannaccone A, Jebens A, von Kaisenberg CS, Kaup L, Keil C, Kladt C, Kolben T, Kraft K, Kunze M, Lastinger J, Luedemann K, Manz J, Morfeld CA, Parchmann O, Pfaff L, Reinhardt K, Runkel A, Schmidt M, Sourouni M, Stelbrink J, Stubert J, Stumpfe FM, Treptow A, Rüdiger M, Pecks U. COVID-19-Related Obstetric and Neonatal Outcome Study (CRONOS) Network. Gestational diabetes mellitus and COVID-19: results from the COVID-19-Related Obstetric and Neonatal Outcome Study (CRONOS). *Am J Obstet Gynecol*. 2022; 14: S0002-9378(22)00372-6. <https://doi.org/10.1016/j.ajog.2022.05.027>
 17. Aggarwal AN, Agarwal R, Dhooria S, Prasad KT, Sehgal IS, Muthu V. Impact of asthma on severity and outcomes in COVID-19. *Respir Care*. 2021;66:1912–23. <https://doi.org/10.4187/respcare.09113>.
 18. Huang Y, Lu Y, Huang YM, Wang M, Ling W, Sui Y, Zhao HL. Obesity in patients with COVID-19: a systematic review and meta-analysis. *Metabolism*. 2020;113:154378. <https://doi.org/10.1016/j.metabol.2020.154378>.
 19. Papageorgiou AT, Deruelle P, Gunier RB, Rauch S, García-May PK, Mhatre M, Usman MA, Abd-Elsalam S, Etuk S, Simmons LE, Napolitano R, Deantoni S, Liu B, Prefumo F, Savasi V, do Vale MS, Baafi E, Zainab G, Nieto R, Maiz N, Aminu MB, Cardona-Perez JA, Craik R, Winsey A, Tavchioska G, Bako B, Oros D, Rego A, Benski AC, Hassan-Hanga F, Savorani M, Giuliani F, Sentilhes L, Risso M, Takahashi K, Vecchiarelli C, Ikenoue S, Thiruvengadam R, Soto Conti CP, Ferrazzi E, Cetin I, Nachinab VB, Ernawati E, Duro EA, Kholin A, Firlit ML, Easter SR, Sichitiu J, Bowale A, Casale R, Cerbo RM, Cavoretto PI, Eskenazi B, Thornton JG, Bhutta ZA, Kennedy SH, Villar J. Preeclampsia and COVID-19: results from the INTERCOVID prospective longitudinal study. *Am J Obstet Gynecol*. 2021; 225: 289.e1-289.e17. <https://doi.org/10.1016/j.ajog.2021.05.014>
 20. Conde-Agudelo A, Romero R. SARS-CoV-2 infection during pregnancy and risk of preeclampsia: a systematic review and meta analysis. *Am J Obstet Gynecol*. 2021;2226:68–89. <https://doi.org/10.1016/j.ajog.2021.07.009>.
 21. Fitzgerald B, O'Donoghue K, McEntagart N, Gillan JE, Kelehan P, O'Leary J, Downey P, Dean J, De Gascun CF, Birmingham J, Armstrong F, Al Fathi A, Maher N, Murphy C, Burke L. Fetal deaths in Ireland due to SARS-CoV-2 placentitis caused by SARS-CoV-2 alpha. *Arch Pathol Lab Med*. 2022;146:529–37. <https://doi.org/10.5858/arpa.2021-0586-SA>.
 22. Villar J, Ariff S, Gunier RB, Thiruvengadam R, Rauch S, Kholin A, Roggero P, Prefumo F, Silva do Vale M, Cardona-Perez JA, Maiz N, Cetin I, Savasi V, Deruelle P, Easter SR, Sichitiu J, Soto Conti CP, Ernawati E, Mhatre M, Teji JS, Liu B, Capelli C, Oberto M, Salazar L, Gravett MG, Cavoretto PI, Nachinab VB, Galadanci H, Oros D, Ayede AI, Sentilhes L, Bako B, Savorani M, Cena H, García-May, PK, Etuk S, Casale R, Abd-Elsalam S, Ikenoue S, Aminu MB, Vecchiarelli C, Duro EA, Usman MA, John-Akinola, Y, Nieto R, Ferrazzi E, Bhutta ZA, Langer A, Kennedy SH, Papageorgiou AT. Maternal and neonatal morbidity and mortality among pregnant women with and without COVID-19 infection the INTERCOVID multinational cohort study. *JAMA Pediatr*. 2021; 8: 817 – 826. <https://doi.org/10.1001/jamapediatrics.2021.1050>
 23. Metz TD, Clifton RG, Hughes BL, Sandoval G, Saade GR, Grobman WA, Manuck TA, Miodovnik M, Sowles A, Clark K, Gyamfi-Bannerman C, Mendez-Figueroa H, Sehdev HM, Rouse DJ, Tita A, Bailit J, Costantine MM, Simhan HN, Macones GA. For the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) Maternal-Fetal Medicine Units (MFMU) Network: Disease severity and perinatal outcomes of pregnant patients with coronavirus disease 2019 (COVID-19). *Obstet & Gynecol*. 2021;137:571–80. <https://doi.org/10.1097/AOG.0000000000004339>.
 24. Edlow AG, Castro VM, Shook LL, Kaimal AJ, Perlis RH. Neurodevelopmental outcomes at 1 year in infants of mothers who tested positive for SARS-CoV-2 during pregnancy. *JAMA Netw Open*. 2022;5:e2215787. <https://doi.org/10.1001/jamanetworkopen.2022.15787>.
 25. American College of Obstetricians and Gynecologists (ACOG). COVID-19 FAQs for obstetrician-gynecologists. <https://www.acog.org/clinical-information/physician-faqs/covid-19-faqs-for-ob-gyns-obstetrics>. Accessed 22 Aug 2022.
 26. NIH COVID Treatment Guidelines. Antiviral drugs that are approved, authorized, or under evaluation for treatment of COVID-19. 2022a. www.covid19treatmentguidelines.nih.gov. Accessed 22 Aug 2022.
 27. NIH COVID Treatment Guidelines. Molnupiravir. 2022b. www.covid19treatmentguidelines.nih.gov. Accessed 22 Aug 2022.
 28. Pfizer Labs. Fact sheet for patients, parents, and caregivers emergency use authorization (EUA) of Paxlovid for coronavirus disease 2019 (COVID-19). 2022. <https://www.paxlovid.com/>. Accessed 22 Aug 2022.
 29. Centers for Disease Control and Prevention. Stay Up to Date with Your COVID-19 Vaccines. 2022a. https://www.cdc.gov/coronavirus/2019-ncov/vaccines/stay-up-to-date.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019-ncov%2Fvaccines%2Ffully-vaccinated-guidance.html. Accessed 22 Aug 2022.
 30. Centers for Disease Control and Prevention. Overview of testing for SARS-CoV-2, the virus that causes COVID-19. 2022c. <https://www.cdc.gov/coronavirus/2019-ncov/hcp/testing-overview.html>. Accessed 22 Aug 2022.
 31. Riddell S, Goldie S, Hill A, Eagles D, Drew TW. The effect of temperature on persistence of SARS-CoV-2 on common surfaces. *Viral J*. 2020;7:145. <https://doi.org/10.1186/s12985-020-01418-7>.
 32. Mutambudzi M, Niedwiedz C, Macdonald EB, Leyland A, Mair F, Anderson J, Celis-Morales C, Cleland J, Forbes J, Gill G, Hastie C, Ho F, Jani B, Mackay DF, Nicholl B, O'Donnell C, Sattar N, Welsh P, Pell J, Katikireddi SV, Demou E. Occupation and risk of severe COVID-19: prospective cohort study of 120 075 UK Biobank participants. *Occup Environ Med*. 2020;5:307–14. <https://doi.org/10.1101/2020.05.22.20109892>.
 33. Nguyen LH, Drew DA, Joshi AD, Guo C, Ma W, Mehta RS, Sikavi DR, Lo C, Kwon S, Song M, Mucci LA, Stampfer MJ, Willett WC, Eliassen AH, Hart JE, Chavarro JE, Rich-Edwards JW, Davies R, Capdevila J, Lee KA, Lochlainn MN, Varsavsky T, Graham MS, Sudre CH, Cardoso MJ, Wolf J, Ourselin S, Steves CJ, Spector TD, Chan AT. Risk of COVID-19 among frontline healthcare workers and the general community: a prospective cohort study. *The Lancet Public Health*. 2020;9:475–83. [https://doi.org/10.1016/S2468-2667\(20\)30164-X](https://doi.org/10.1016/S2468-2667(20)30164-X).
 34. Centers for Disease Control and Prevention. What you need to know about variants. 2022b. <https://www.cdc.gov/coronavirus/2019-ncov/variants/about-variants.html>. Accessed 22 Aug 2022.
 35. Centers for Disease Control and Prevention. CDC Updated COVID-19 vaccine recommendations. 2021b. https://covid.cdc.gov/covid-data-tracker/#vaccinations_vacc-people-additional-dose-totalpop. Accessed 22 Aug 2022.

36. Society for Maternal Female Medicine. Provider considerations for engaging in COVID-19 vaccine counseling with pregnant and lactating patients. 2021. <https://www.sfm.org/covidclinical>. Accessed 22 Aug 2022.
37. American Society for Reproductive Medicine. COVID-19 vaccination and vaccination hesitancy. Update No. 17. 2021b. <https://www.asrm.org/news-and-publications/news-and-research/press-releases-and-bulletins/update-no.-19--awareness-of-complexity-in-uncertain-times-covid-19/>. Accessed 22 Aug 2022.
38. American College of Obstetricians and Gynecologists. COVID-19 vaccination considerations for obstetric-gynecologic care. 2021b. <https://www.acog.org/clinical/clinical-guidance/practice-advisory/articles/2020/12/covid-19-vaccination-considerations-for-obstetric-gynecologic-care>. Accessed 22 Aug 2022.
39. Aly J, Choi L, Christy YA. The impact of coronavirus on reproduction: contraceptive access, pregnancy rates, pregnancy delay, and the role of vaccination. *F S Rev.* 2022;3:190–200. <https://doi.org/10.1016/j.xfnr.2022.05.002>.

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