

EVIDENCE SYNTHESIS BRIEFING NOTE

TOPIC: INCIDENCE, SEVERITY AND MANAGEMENT OF COVID-19 ACROSS ACUTELY ILL COVID-19 OBSTETRICAL PATIENTS

Literature search completed as of May 6, 2021.^a This Briefing Note was completed by the Evidence Synthesis Unit (Research, Analysis and Evaluation Branch, Ministry of Health).

Purpose: To examine the incidence, severity, and management of COVID-19 in pregnant COVID-19 patients.

Key Findings:

- **Incidence:** The prevalence of COVID-19 among pregnant women is difficult to estimate given geographic and temporal variability in the prevalence of COVID-19 and differing thresholds for testing pregnant women. There seems to be a higher risk of COVID-19 in the third trimester in pregnant women compared to the first and second trimesters. The symptomatic infection in pregnant women generally seems to be of lower incidence compared to the general population, and there are high rates of asymptomatic infection in pregnant women.
- **Severity:** There is mixed evidence on the severity of COVID-19 in pregnant women: some studies report that pregnant status raises the morbidity of COVID-19 (e.g., ICU admission, mechanical ventilation), while others indicate that the clinical presentation of COVID-19 in pregnant women resembles that of non-pregnant women. Jurisdictional guidance/reports note that there is an increased risk of ICU admission and mechanical ventilation in pregnant women with COVID-19 compared to symptomatic non-pregnant women. Some studies and jurisdictional reports suggest that certain factors (e.g., increased age, obesity, pre-existing comorbidities, pre-eclampsia) are associated with severe COVID-19 in pregnancy.
- **Outcomes:** Most research evidence and jurisdictional reports indicate that pregnant women with COVID-19 may be at a higher risk of maternal mortality and maternal/neonatal morbidities than non-infected women, including preeclampsia, preterm birth, prelabour rupture of membranes, caesarean delivery, low birth weight infants, or neonatal intensive care admission. However, it is unclear if these outcomes are directly due to SARS-CoV-2 infection or an indirect effect that results from severe maternal illness or iatrogenic intervention.
- **Management:** Research evidence and guidance from Canada, US, UK, Italy, Australia, and the World Health Organization (WHO) suggest one or more of the following recommendations for managing pregnant patients with suspected/confirmed COVID-19: appropriate screening, triaging, and isolation; individualized delivery planning dependent on the patient's clinical status, gestational age, fetal condition, and shared decision-making; designated multispecialty care teams; and appropriate infection prevention and control measures.
- **Prone Positioning:** Successful prone positioning of pregnant patients with COVID-19 have been described in three case reports, and guidance/reports from Alberta, US, Australia, and WHO suggest prone positioning is feasible in some types of pregnant/postpartum patients with COVID-19 with the help of support devices (e.g., pillows, padding).
- **Medications:** Certain antibiotics, antivirals, corticosteroids, and immunosuppressants have been used for the management of COVID-19-infected pregnant women. Data is scarce regarding the efficacy and safety of remdesivir, tocilizumab, and sarilumab in pregnant women with COVID-19 and some studies suggest avoiding their use. However, remdesivir may be offered to pregnant patients with COVID-19 that meet certain criteria (e.g., compassionate use, moderate-to-severe COVID-19 not requiring ventilation) according to guidelines from the US, UK, and Australia. UK and Australian guidelines also suggest considering tocilizumab in specific cases, but not sarilumab.

Implementation Implications: There is limited high-quality evidence due to the relatively recent emergence of COVID-19 and the rapidly evolving nature of the pandemic but reports thus far suggest pregnant women with acute COVID-19 illness are at high risk of morbidities and mortality. Information, counseling, and adequate monitoring are essential to prevent and manage adverse effects of SARS-CoV-2 infection during pregnancy. Further studies on women from all trimesters are warranted, and a long-term follow-up plan for the offspring of pregnant women affected by COVID-19 should be established.

^a This briefing note includes current available evidence as of the noted date. It is not intended to be an exhaustive analysis, and other relevant findings may have been reported since completion.

Supporting Evidence

[Table 1](#) describes scientific evidence and jurisdictional guidance/experiences regarding COVID-19 in obstetrical patients, including incidence, severity, outcomes, and management. In the Appendix, [Table 2](#) and [Table 3](#) provide detailed summaries of the scientific evidence and Canadian/international guidance, respectively. The majority of the information presented is taken directly from the identified sources. In particular, the following topics are reviewed:

- **Incidence:** Rates of SARS-CoV-2 infection among pregnant women across trimesters, and how this compares to the general population and to non-pregnant women of reproductive age.
- **Severity:** Rates of hospital admission, intensive care unit (ICU) admission, and mechanical ventilation amongst pregnant women with SARS-CoV-2 infection and how it compares to the general population and to non-pregnant women of reproductive age.
- **Outcomes:** Outcomes of hospitalized and critically ill pregnant patients with SARS-CoV-2 infection, including ICU mortality, hospital mortality, ICU length of stay, hospital length of stay, pre-term delivery, emergent delivery, and admission of baby to neonatal intensive care (NICU).
- **Management:** The unique management considerations for pregnant women hospitalized with COVID-19 respiratory failure compared to the general hospitalized COVID-19 population, including ward or critical care, use of prone positioning, safety profile of medications (particularly remdesivir, tocilizumab, and sarilumab), delivery protocols, and organizational considerations.

The following limitations should be noted:

- Because of the extensive amount of literature available on these topics, the scientific evidence searches were limited to systematic reviews, meta-analyses, and reviews. However, some individual studies were included if identified and relevant.
- The majority of the information presented contains clinical outcomes and guidance; these recommendations are those of the authors of the original studies and the Research, Analysis, and Evaluation Branch does not have the expertise to evaluate such recommendations.
- The methodological quality of all the sources identified are unclear as they have not been assessed.
- No information was identified on how the emergence of COVID-19 variants of concern have impacted the incidence, severity, outcomes, and management of pregnant patients with COVID-19.

Table 1: Summary of Scientific Evidence and Jurisdictional Guidance and Experiences regarding Incidence, Severity, and Management of COVID-19 Obstetrical Patients

<p>Scientific Evidence</p>	<ul style="list-style-type: none"> • Incidence: Findings from 13 sources suggest that the population prevalence of COVID-19 among pregnant women is difficult to estimate given geographic and temporal variability in the prevalence of COVID-19 and differing thresholds for testing pregnant women. There seems to be a higher risk of COVID-19 in the third trimester in pregnant women compared to the first and second trimesters. The symptomatic infection in pregnant women generally seems to be of lower incidence compared to the general population, and there are high rates of asymptomatic infection in pregnant women. Similar to data from the general population internationally, SARS-CoV-2 infection may be higher in pregnant women who are racial/ethnic minorities, uninsured, low income, or from neighborhoods with low income, high crowding, or increased density. For example: <ul style="list-style-type: none"> ○ The PregCOV-19 living systematic review and meta-analysis (Sept 1, 2020) of 73 international studies with 67,271 women found that 10% of pregnant and recently pregnant women attending or admitted to hospital for any reason were diagnosed as having suspected or confirmed COVID-19.¹ ○ A US Centers for Disease Control and Prevention (CDC) study (Nov 6, 2020) assessed data from the National Notifiable Diseases Surveillance System of 1,300,938 women aged 15-44 years with laboratory results indicative of acute infection with SARS-CoV-2. Data on pregnancy status were available for 461,825 (35.5%) women with laboratory-confirmed infection, 409,462 (88.7%) of whom were symptomatic. Among symptomatic women, 23,434 (5.7%) were reported to be pregnant.² ○ A review (May 2021) of 196 studies noted that, in Europe, estimates of COVID-19 prevalence differed based on region and time period, ranging from 0.6% in Lombardy (Italy) in early March 2020 to 7.0% in London during the same period. Multiple studies on universal screening programs have also confirmed high rates of asymptomatic or pre-symptomatic disease, ranging from 61.5% of women with a positive test in Belgium to 85-90% in areas of London and New York City.³ • Severity: There is mixed evidence from 40 sources on the severity of COVID-19 in pregnant women: some studies report that pregnant status raises the morbidity of COVID-19 (e.g., ICU admission, mechanical ventilation), while others indicate that the clinical presentation of COVID-19 in pregnant women resembles that of non-pregnant women, which generally includes mild cough, breathlessness, and fever. Some studies suggest that certain factors (e.g., increased maternal age, obesity, pre-existing comorbidities, pre-eclampsia) are associated with severe COVID-19 in pregnancy. For example: <ul style="list-style-type: none"> ○ A systematic review and meta-analysis (Jan 2021) noted that the pooled prevalence of ICU admission and death among pregnant women with COVID-19 were comparable with those reported in non-pregnant women.⁴ ○ A systematic review and meta-analysis (Jan 2, 2021) found pregnant patients present with similar clinical characteristics of COVID-19 when compared with the general population, but they may be more asymptomatic.⁵ ○ A review of systematic reviews (Jan 2021) estimated that maternal ICU admission and mechanical ventilation rates of pregnant women with COVID-19 were 3–10% and 1.4–5.5%, respectively, after accounting for the quality of studies. Reported maternal ICU admission, mechanical ventilation, and mortality rates of pregnant women with COVID-19 were high
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	<p>when compared with non-pregnant women. A possible interpretation of this finding was the existence of other comorbidities accompanying pregnancy, compared with non-pregnant women at a similar age.^{6,b}</p> <ul style="list-style-type: none"> ○ A study (Feb 20, 2021) by the World Association of Perinatal Medicine Working Group on COVID-19 examined high- and low-risk pregnancies complicated by severe COVID-19 infection from 76 centres from 25 countries. The risk of composite adverse maternal outcomes (i.e., maternal mortality and morbidity, including ICU admission, use of mechanical ventilation, or death) was higher in high-risk pregnancies than in low-risk pregnancies. Pregnancies were considered high-risk in case of either pre-existing chronic medical conditions in pregnancy (i.e., pregestational diabetes mellitus, chronic hypertension, or autoimmune disease) or obstetrical disorders occurring in pregnancy (i.e., preeclampsia, gestational hypertension, or gestational diabetes mellitus).⁷ ○ The INTERCOVID^c multinational study (Apr 22, 2021) involving 43 institutions across 18 countries found pregnant women with a COVID-19 diagnosis were associated with a greater risk of admission to ICU and referral to a higher level of care. Among all ICU admissions, women with COVID-19 diagnosis stayed 3.73 days longer than pregnant women without COVID-19.⁸ ○ A systematic review and meta-analysis (Mar 24, 2021) found that the proportions of mechanical ventilation support (2%, 4%, and 6%) and ICU admission (6%, 5%, and 7%) for COVID-19-infected pregnant women were similar across the US, Asia, and Europe, respectively.⁹ ● Outcomes: The majority of findings from 42 sources indicates that pregnant women with COVID-19 may be at a higher risk of maternal mortality and maternal and neonatal morbidities than non-pregnant or non-infected women, including: preeclampsia, preterm birth, prelabour rupture of membranes (PROM), caesarean delivery, low birth weight infants, and neonates requiring NICU admission. For example: <ul style="list-style-type: none"> ○ A systematic review and meta-analysis (Sept 2020) estimated the rates of caesarean section (72%), premature birth (23%), low birth weight (7%), and adverse pregnancy events (27%) across 61 studies. The rate of caesarean section was substantially higher in Chinese studies (91%) compared to the US (40%) or European (38%) studies. The rates of preterm birth and adverse pregnancy events were also lowest in the US studies (12%, 15%) compared to Chinese (17%, 21%) and European studies (19%, 19%). Adverse pregnancy outcomes were associated with infection acquired at early gestational ages, more symptomatic presentation, myalgia symptom at presentation, and use of oxygen support therapy.¹⁰
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^b The review noted that assessment of the existing systematic reviews, using the AMSTAR 2 tool, classified 59% of them as “critically low quality” to “low quality”. However, it should be taken into account that currently available systematic reviews based their results on a large number of preliminary studies conducted due to the urgent need for quick answers. For these reasons, further original studies with women from all pregnancy trimesters and longer follow-up periods, and, consequently, further systematic reviews synthesizing their results, are required to provide clinical practice with more definite answers regarding the effects of SARS-CoV-2 infection on such a sensitive group of patients as pregnant women and their fetuses/neonates. So far, data are not robust enough to lead to definite points and regulations ([Papapanou et al., Jan 2021](#)).

^c The International Fetal and Newborn Growth Consortium for the 21st Century, or INTERGROWTH-21st, is a global, multidisciplinary network of more than 300 researchers and clinicians from 27 institutions in 18 countries worldwide and coordinated from the University of Oxford ([INTERGROWTH-21st, 2021](#)). INTERCOVID is a large, multi-national, prospective cohort study with the aim of assessing the effect of COVID-19 in pregnancy on maternal, fetal, and neonatal outcomes worldwide ([INTERGROWTH-21st, 2021](#)).

	<ul style="list-style-type: none"> ○ A review of systematic reviews (Jan 2021) reported the following rates regarding both preterm and term gestations: 52.3–95.8% for caesarean sections; 4.2–44.7% for vaginal deliveries; 14.3–63.8% for preterm deliveries and 22.7–32.2% for preterm labour; and 5.3–12.7% for PROM and 6.4–16.1% for preterm PROM. Maternal mortality rate was <2%, while stillbirth, NICU admission (which may be attributed to precaution or severe maternal infection), and mortality rates were <2.5%, 3.1–76.9%, and <3%, respectively. Available data were more contradictory for mortality rates, and the increased rates, when reported, have been also attributed to the specific health care provision of the participants' countries.¹¹ ○ A systematic review and meta-analysis (Apr 19, 2021) found that SARS-CoV-2 infection in pregnancy, compared with no infection, was associated with preeclampsia, preterm birth, stillbirth, ICU admission, lower birth weight, and NICU admission; COVID-19 was not associated with caesarean delivery, postpartum hemorrhage, or neonatal death compared with no COVID-19. Compared with asymptomatic COVID-19, symptomatic COVID-19 in pregnancy was associated with increased risk of preterm birth and caesarean delivery. Compared with mild COVID-19, severe COVID-19 was strongly associated with preeclampsia, preterm birth, caesarean delivery, low birth weight, and NICU admission.¹² ● Management: Ten studies and four guidelines for the management of pregnant women with COVID-19 generally discussed screening protocols, place of care, staffing models, infection prevention and control measures, delivery timing, medications, and neonatal care. In particular: <ul style="list-style-type: none"> ○ These women should be cared for in isolation (ideally negative-pressure isolation rooms), where there is limited human traffic and appropriate personal protective equipment and infection control measures are followed. ○ Care should be provided by a multidisciplinary team (e.g., obstetricians, maternal-fetal medicine subspecialists, obstetric anesthetists, midwives). ○ The timing and mode of delivery should be individualized, dependent mainly on the clinical status of the patient, gestational age, and fetal condition. ○ Temporary separation of a mother with known/suspected COVID-19 from her newborn should be decided on a case-by-case basis: 1) if temporary separation is chosen, mothers who intend to breastfeed should practice hand and breast hygiene and express their milk, which can be fed to the newborn by a healthy caregiver; or 2) if separation is not chosen, other measures can be used to reduce risk of infection (e.g., face mask use and hand/breast hygiene by mothers before each feeding). ○ Isolating newborns born to COVID-19 mothers from those born to non-infected mothers may be considered. Newborns born to mothers with confirmed/suspected COVID-19 may be tested 24 hours after birth for SARS-CoV-2 and, if negative, again at approximately 48 hours, if testing capacity is available. ○ A study (Nov 9, 2020) examined 11 obstetrics guidelines, published from December 2019 to April 2020, from China, Italy, Spain, the UK, and US to compare their recommendations and to assess how useful they could be to maternal health workers. Six guidelines covered more than 80% of the 30 foundational topics the study identified. The study highlighted the existence of 10 points of conflict among the recommendations (i.e., mask wearing, personal and social hygiene, antenatal care visits, partner/companion, antenatal corticosteroids, respiratory analgesia, cord clamping, skin-to-skin practice, mother/child separation, and breastfeeding). The present research revealed a lack of uniformity and consistency, resulting in potentially challenging decisions for health care providers.¹³
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	<ul style="list-style-type: none"> • Prone Positioning: Three case reports described successful prone positioning for pregnant patients with COVID-19. For example, a study (Mar 16, 2021) reported that a 31-year-old pregnant woman with symptomatic COVID-19, which was complicated by progressive hypoxemia requiring intensive care and emergent delivery by caesarean section, was successfully supported with mechanical ventilation and prone positioning and ultimately recovered. Prone positioning was implemented in an effort to improve oxygenation.¹⁴ <ul style="list-style-type: none"> ○ To address the need for low-cost, low-harm interventions during the COVID-19 pandemic wherein hypoxemia predominates, a study (Aug 2020) presented an algorithm for prone positioning of both intubated and non-intubated pregnant women with COVID-19, including indications, contraindications, and a step-by-step guide.¹⁵ • Medications: Eleven studies were identified on therapeutics for the management of COVID-19-infected pregnant women, including antibiotics, antivirals, glucocorticoids, and immunosuppressants. Recommendations are currently based on limited available data, and more studies are needed to establish evidence-based protocols of care. In particular, data are scarce regarding the efficacy and safety of remdesivir, tocilizumab, and sarilumab in pregnant women with COVID-19; thus, they should be avoided. For example: <ul style="list-style-type: none"> ○ A review (Aug 2020) found management of pregnant women with COVID-19 varied according to health institution, with most being treated with medications considered to be relatively safe during pregnancy: antibiotics (e.g., cefoperazone, sulbactam, ceftriaxone, cefazolin, azithromycin), antiviral therapy (e.g., lopinavir, ritonavir, oseltamivir, ganciclovir), and a few were treated with corticosteroids (e.g., dexamethasone, methylprednisolone).¹⁶ ○ A systematic review and meta-analysis (Mar 24, 2021) reported that the proportion of oxygen support, antibiotics, antivirals, and plasma therapy administration, except for hydroxychloroquine, was substantially higher in Asian studies (55%, 78%, 80%, 6%, and 0%) compared to the US (7%, 1%, 12%, 0%, and 7%) or European (33%, 12%, 14%, 1%, and 26%) studies, respectively.^d Even in case reports reflecting severe cases, the use of antivirals and antibiotics was higher in Asian studies compared to the US, Latin American, and European studies. The review concluded that minimizing the use of some therapeutics particularly antibiotics, antivirals, oxygen therapy, immunosuppressants, and hydroxychloroquine by risk stratification and careful consideration may further improve maternal and clinical outcomes.¹⁷ ○ A US study (Apr 21, 2021) described the use of remdesivir in hospitalized pregnant women with confirmed COVID-19 infection and O2 saturation <94% who met the criteria to be enrolled in a compassionate use program. Of the 86 patients enrolled in the study, 19 delivered before their first course of remdesivir and were included in the immediate post-partum group. The remaining patients, whose median gestational age was 28 weeks, were started on remdesivir with follow-up after 28 days. After the 28-day follow-up, the oxygen requirement in 96% of the pregnant patients decreased, and 93% of those requiring mechanical ventilation were extubated, 93% recovered, and 90% were discharged. Adverse events (e.g., anemia, constipation, dysphagia, worsening hypoxia) were experienced in 29% (22/67) of the cohort. Other side effects shown included increasing liver function tests
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^d Given the lack of efficacy data for most therapeutics of COVID-19, the practice in the US and European countries might have been to minimally expose any therapeutics to average-risk pregnant patients. The highest use of antibiotics in Asian studies may be due to local guidelines for managing COVID-19 patients, suspicion of bacterial or fungal coinfections due to unavailability of rapid and affordable testing to differentiate viral and bacterial infections, and health-care-associated infections due to prolonged hospitalization ([Dubey et al., Mar 24, 2021](#)).

	<p>and serum creatinine levels with seven pregnant women discontinuing the study drug due to adverse events.¹⁸</p>
<p>International Scan</p>	<ul style="list-style-type: none"> • Incidence: The Royal College of Midwives (RCM) and Royal College of Obstetricians and Gynaecologists (RCOG) in the UK notes that pregnant women do not appear more likely to contract COVID-19 than the general population, and the National Institute of Health (NIH) in Italy states that the prevalence of COVID-19 disease in pregnancy appears to be substantially similar to those of the general population. • Severity: Guidance and reports from the US (CDC, American College of Obstetricians and Gynecologists [ACOG], NYC Health, and UpToDate),^e UK (RCM/RCOG), and Italy (NIH) state that there is an increased risk of ICU admission^f, need for mechanical ventilation and ventilatory support for pregnant women with symptomatic COVID-19 infection, when compared with symptomatic non-pregnant women. Risk factors for severe disease may include age ≥ 30–35 years, obesity, hypertension, pre-existing diabetes, and immigrant status. • Outcomes: Guidance and reports from the US (CDC, ACOG, NYC Health, and UpToDate), UK (RCM/RCOG), and Italy (NIH) indicate that there may be an increased rate of preterm delivery, stillbirth, caesarean delivery, or death in pregnant women with COVID-19 compared to the general pregnant population. It is, however, unclear if these outcomes are directly due to SARS-CoV-2 infection or an indirect effect that results from severe maternal illness or iatrogenic intervention. For example: <ul style="list-style-type: none"> ○ A NIH report (Feb 5, 2021) described the results of the Italian Obstetric Surveillance System study, which showed that the average preterm birth rate was 14.4% during the first wave of the pandemic, with a decrease during the observation period. In February and March 2020, the rate was 17.5%; however, the rate fell to 11% in July and August 2020, largely due to increased identification of asymptomatic women at the time of hospitalization. Overall, the majority of preterm births (7.7%) were due to iatrogenic causes, 3.5% to PROM, and 3.2% to spontaneous onset. Moreover, during the first wave of the pandemic, the rate of caesarean section was 33.7% (in line with national rates), and infants who were not separated from their mothers at birth, roomed-in, and received breastmilk had outcomes as good as the infants who were separated from their mothers after birth.¹⁹ ○ A RCM/RCOG report (Feb 19, 2021) noted that, compared to pregnant women without COVID-19, pregnant women with symptomatic COVID-19 requiring hospitalization have overall worse maternal outcomes, including an increased risk of death, although the risk remains very low (the UK maternal mortality rate from COVID-19 is 2.2 per 100,000 maternities). Aside from preterm birth, the report indicated there is no evidence that COVID-19 infection has an adverse effect on the fetus or on neonatal outcomes.²⁰ • Management: Guidance and reports from the US (National Institute of Health, CDC, ACOG, Society for Maternal Fetal Medicine [SMFM], UpToDate, and NYC Health), UK (RCM/RCOG), Italy (NIH), Australia (National COVID-19 Clinical Evidence Taskforce), and the World Health Organization (WHO) suggest one or more of the following recommendations for managing pregnant patients with suspected/confirmed COVID-19: appropriate screening, triaging, and isolation; individualized delivery planning; designated multispecialty care teams; and

^e UpToDate Inc is a company in the Wolters Kluwer Health division of Wolters Kluwer whose main product is UpToDate, a software system that is a point-of-care medical resource for health care professionals ([UpToDate, 2021](#)).

^f According to the Royal College of Midwives/Royal College of Obstetricians and Gynaecologists, higher rates of ICU admission may reflect a lower threshold for admission to ICU, rather than more severe disease ([RCM/RCOG, Feb 19, 2021](#)).

	<p>appropriate infection prevention and control measures. In addition, the ACOG has developed an algorithm to evaluate and manage pregnant outpatients with suspected or confirmed SARS-CoV-2 infection.²¹</p> <ul style="list-style-type: none"> • Prone Positioning: Guidance and reports from the US (SMFM and UpToDate), Australia (National COVID-19 Clinical Evidence Taskforce), and the WHO suggest prone positioning is feasible in pregnant/postpartum patients with COVID-19 with the help of support devices (e.g., pillows, padding). <ul style="list-style-type: none"> ○ The RCM/RCOG report (Feb 19, 2021) from the UK noted that there is little evidence on the use of prone positioning in pregnancy. Guidance from the Intensive Care Society in the UK advises that it is relatively contraindicated in the second and third trimesters of pregnancy, but acknowledges that there is other published guidance available on how this can be undertaken successfully.²² • Medications: In the US, the NIH states that potentially effective treatment for COVID-19 should not be withheld from pregnant women because of theoretical concerns related to the safety of therapeutic agents in pregnancy, and the SMFM recommends that remdesivir be offered to pregnant patients with COVID-19 meeting criteria for compassionate use, based on positive results from the Adaptive COVID-19 Treatment Trial (ACTT-1). The UK (RCM/RCOG) and Australia (National COVID-19 Clinical Evidence Taskforce) offered the following recommendations for remdesivir and tocilizumab: <ul style="list-style-type: none"> ○ The RCM/RCOG noted that remdesivir should be avoided in pregnant women with COVID-19 unless clinicians believe the benefits of treatment outweigh the risks to the individual. Although data for the use of tocilizumab in pregnancy are limited, there is currently no compelling evidence that tocilizumab is teratogenic or fetotoxic, and so it may be considered in specific cases.²³ ○ The National COVID-19 Clinical Evidence Taskforce recommends considering the use of the following medications for pregnant or breastfeeding women: 1) remdesivir for those hospitalized with moderate to severe COVID-19 who do not require ventilation; and 2) tocilizumab for those who require supplemental oxygen, particularly where there is evidence of systemic inflammation. Sarilumab is not recommended for the treatment of COVID-19 outside of randomized trials with appropriate ethical approval.²⁴ • Registries: Registries are being developed to collect data on how COVID-19 affects pregnancy and newborns. For example: <ul style="list-style-type: none"> ○ Pregnancy CoRonavirus Outcomes RegIsTrY (PRIORITY) is the official US registry led by the University of California, San Francisco. ○ International Registry of Coronavirus Exposure in Pregnancy (IRCEP) is led by an international group of investigators.²⁵
<p>Canadian Scan</p>	<ul style="list-style-type: none"> • Incidence: A report (Feb 25, 2021) from the Canadian Surveillance of COVID-19 in Pregnancy (CANCOVID-Preg) examined the epidemiology of 1,880 COVID-19-positive pregnant cases from March 1 to December 31, 2020 across five Canadian provinces (British Columbia, Alberta, Ontario, Quebec, and Manitoba). Although the risk of COVID-19 acquisition among pregnant women cannot be determined from the data, compared to the general population, infection rates appear to be lower among pregnant women in every province with the exception of British Columbia. Among pregnant positive cases, 44.6% were between 30–35 years of age. Most cases were diagnosed between 14–27 weeks’ gestation (38.7%), with infection most often acquired via the community-at-large (50.6%). Obesity was the most common underlying condition (11.9%). The most common symptoms associated with a positive COVID-19

	<p>diagnosis during pregnancy were cough (47.0%), headache (31.0%), fever (29.8%) and rhinitis (25.6%).²⁶</p> <ul style="list-style-type: none"> • Severity: Two Canadian reports suggest that pregnant women with COVID-19 may be at increased risk for hospital or ICU admission compared to non-pregnant women with COVID-19: <ul style="list-style-type: none"> ○ The CANCOVID-Preg report (Feb 25, 2021) indicated that although the absolute risk is low, compared to their non-pregnant counterparts, COVID-19-infected pregnant women remain at increased risk of being hospitalized and admitted to the ICU across five Canadian provinces (British Columbia, Alberta, Ontario, Quebec, and Manitoba). Among the 1,839 women with complete information about any COVID-19 related hospitalization or ICU admission from March to December 2020, 8.1% were hospitalized and 1.6% were admitted to the ICU.²⁷ ○ According to a report (Feb 15, 2021) by the Society of Obstetricians and Gynaecologists of Canada (SOGC), interim Canadian data from a three-province (Ontario, British Columbia, and Alberta) analysis of population outcomes in pregnancy from March 1 to September 20, 2020 reveals that hospitalization and ICU admission are both increased in pregnant women over non-pregnant women by a wider margin. The rate of hospitalization was 11% and the rate of ICU admission was 2.3%.²⁸ • Outcomes: Two Canadian reports suggest that pregnant women with COVID-19 may be at risk for some morbidities (e.g., preterm birth): <ul style="list-style-type: none"> ○ The CANCOVID-Preg report (Feb 25, 2021) found that among the 738 cases with delivery and gestational age data from March to December 2020, 82.0% occurred at term and 12.3% at preterm gestation across five Canadian provinces (British Columbia, Alberta, Ontario, Quebec, and Manitoba). Preterm birth etiology showed 40.2% were medically indicated and 45.1% were spontaneous. The majority of infants (82.1%) were in the normal range for birth weight (i.e., 2,500–4,000 grams) and were not admitted to the NICU (83.3%).²⁹ ○ The SOGC report (Feb 15, 2021) noted that the rate of preterm birth was 15% which is approximately twice the background rate in the population across Ontario, British Columbia, and Alberta from March 1 to September 20, 2020. Caesarean section was 33% and neonatal intensive care was 15%.³⁰ • Management: Guidance from SOGC, Manitoba, and British Columbia suggest isolating pregnant patients with suspected/confirmed COVID-19 into single-occupancy rooms, minimizing movements between rooms and hospital sites, having designated multidisciplinary care teams, and using droplet and contact precautions. • Prone Positioning: A report (Feb 3, 2021) by Alberta Health Services COVID-19 Scientific Advisory Group on prone positioning for awake, non-intubated COVID-19 patients states that if being considered for awake prone positioning outside of a clinical trial, patients should be assessed to determine their risk for escalating care. Low-risk COVID-19 patients, where prone positioning may be implemented with caution on a medical ward, include pregnant women in the second or third trimester.³¹ • Medications: Guidance from SOGC, Manitoba, and British Columbia recommend that certain antibiotics (e.g., amoxicillin, ceftriaxone) and corticosteroids (e.g., dexamethasone) may be administered depending on the patient profile.^{32,33,34}
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<p>Ontario Scan</p>	<ul style="list-style-type: none"> • <u>Incidence:</u> <ul style="list-style-type: none"> ○ A report (Apr 26, 2021) by the Better Outcomes Registry & Network (BORN) Ontario reported that the approximate number of currently pregnant individuals in Ontario with a due date after April 1, 2021 is 84,500. There has been a cumulative total of 1,403 laboratory-confirmed positive cases of SARS-CoV-2 infection in pregnant individuals reported between March 1, 2020 and March 31, 2021.³⁵ • <u>Severity:</u> <ul style="list-style-type: none"> ○ The BORN Ontario report (Apr 26, 2021) found that pregnant individuals in Ontario had higher rates of hospitalization and ICU admission relative to non-pregnant individuals of similar age during the first and second waves of the pandemic.³⁶ ○ According to SOGC members (Apr 15, 2021), there was a daily wave of pregnant women coming into Ontario ICUs, many requiring ventilators, during April 2021. Pregnant women who have COVID-19 appear more likely to develop respiratory complications requiring intensive care than women and individuals who are not pregnant.³⁷ • <u>Outcomes:</u> The BORN Ontario report (Apr 26, 2021) observed a higher rate of preterm birth among infected versus non-infected pregnant individuals in Ontario. Of 1,403 confirmed cases, 792 gave birth at ≥ 20 weeks of gestational age: <ul style="list-style-type: none"> ○ 99.1% of these births were live births; ○ 11.2% of live births to individuals who had SARS-CoV-2 infection prior to 37 weeks' gestation were born preterm (for comparison, the incidence of preterm birth in Ontario was 8.3% in 2018/19); ○ The incidence of stillbirth among these births was 8.8 per 1,000 births (for comparison, the incidence of stillbirth in Ontario was 4.7 per 1,000 births in 2018/19; however, the absolute number of stillbirth events reported in SARS-CoV-2-infected individuals is very low [seven stillbirths] and the incidence should be interpreted cautiously); and ○ 15.9% of newborns born to mothers with SARS-CoV-2 infection were admitted to a NICU (for comparison, the rate of NICU admission in Ontario was 13.2% in 2018/19).³⁸
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Appendix

Table 2: Summary of Research Evidence on Incidence, Severity, and Management of COVID-19 Obstetrical Patients (ordered from most recent date of publication)

Reference	Abstract Summary
Incidence (e.g., rate of COVID-19 among pregnant women compared to the general population and non-pregnant women)	
<p>Mark, E. G., McAleese, S., Golden, W. C., Gilmore, M. M., Sick-Samuels, A., Curless, M. S., Nogee, L. M., Milstone, A. M., & Johnson, J. (May 2021). Coronavirus Disease 2019 in Pregnancy and Outcomes Among Pregnant Women and Neonates: A Literature Review. <i>The Pediatric infectious disease journal</i>, 40(5), 473–478.</p>	<ul style="list-style-type: none"> • 196 studies published February 1, 2020 through August 15, 2020 reported 1,922 women with COVID-19 during pregnancy and 1,361 neonates with perinatal exposure. • Population prevalence of COVID-19 among pregnant women is difficult to estimate given geographic and temporal variability in the prevalence of COVID-19 and differing thresholds for testing pregnant women. However, some studies provide local estimates: <ul style="list-style-type: none"> ○ Data from New York City in late March to early April 2020 report the highest prevalence of COVID-19 in pregnant women undergoing universal screening at the time of delivery, with results ranging from 15.4% to 19.9% of all women admitted. ○ Prevalence estimates in the US were lower over April, ranging from 0.0% (in Los Angeles) to 3.9% (in Connecticut). ○ The prevalence among women admitted for delivery at the same three academic centers in Connecticut rose from 0.5% prevalence in the first two weeks of April 2020 to 5% in the second two weeks of April 2020. ○ In Europe, prevalence estimates (based on universal screening data) differed based on region and time period, ranging from 0.6% in the Lombardy region of Italy in early March to 7.0% in March in London. • Multiple studies on universal screening programs have confirmed high rates of asymptomatic or presymptomatic disease, ranging from 61.5% of women with a positive test in Belgium to 85-90% in areas of London and New York City. • Most reported cases of COVID-19 in pregnancy to date have been third trimester infections; among women for whom trimester was reported, 89% had third trimester infections
<p>Joseph, N. T., Rasmussen, S. A., & Jamieson, D. J. (Apr 2021). The effects of COVID-19 on pregnancy and implications for reproductive medicine. <i>Fertility and sterility</i>, 115(4), 824–830.</p>	<ul style="list-style-type: none"> • Studies of pregnant people presenting for delivery have shown rates of SARS-CoV-2 infection in the United States to range from ~2% to 20%, depending on the level of disease in the community studied. • COVID-19 has the potential to worsen existing disparities in maternal and infant mortality. Similar to data from the general population, SARS-CoV-2 infection has been higher in pregnant women who were racial/ethnic minorities, uninsured, low income, or from neighborhoods with low income, high crowding, or increased density. These findings have been seen in different US locations and internationally.
<p>Soheili, M., Moradi, G., Baradaran, H. R., Soheili, M., Mokhtari, M. M., & Moradi, Y. (Feb 18, 2021). Clinical manifestation and maternal complications and neonatal outcomes in pregnant women with COVID-19: a comprehensive evidence synthesis and meta-analysis. <i>The journal of maternal-fetal & neonatal medicine: the official journal of the European Association of Perinatal Medicine</i>, the</p>	<ul style="list-style-type: none"> • 74 studies with total 5,560 pregnant women included in this systematic review. • There may be a higher risk of COVID-19 in the third trimester in pregnant women comparing to the first and second trimester. It can be due to higher BMI in the third trimester causing the likelihood of disease deterioration to increase, which can trigger a cascade of side effects starting with coagulation, pneumonia, hypoxemia affecting the placenta leading to ICU admission, fetal distress, premature birth and higher rates of C-section.

<p><i>Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstetricians, 1–14. Advance online publication.</i></p>	
<p>Cavalcante, M. B., Cavalcante, C., Sarno, M., Barini, R., & Kwak-Kim, J. (Feb 2021). Maternal immune responses and obstetrical outcomes of pregnant women with COVID-19 and possible health risks of offspring. <i>Journal of reproductive immunology</i>, 143, 103250.</p>	<ul style="list-style-type: none"> • Few studies have evaluated the prevalence of COVID-19 in pregnant women. <ul style="list-style-type: none"> ○ A study from a maternity hospital in New York reported a 15.4 % prevalence of SARS-CoV-2 infection in pregnant women admitted for delivery, including 1.9 % symptomatic and 13.5 % asymptomatic cases. ○ Another study reported a 12.2 % prevalence of SARS-CoV-2 infection among pregnant women without specifying each trimester. • With the emerging SARS-CoV-2 antibody testing, 6.2 % (80/1,293) of parturient women in Philadelphia (from April 4 to June 3, 2020) was reported to have IgG and/or IgM SARS-CoV-2-specific antibodies.
<p>Novoa, R. H., Quintana, W., Llancarí, P., Urbina-Quispe, K., Guevara-Ríos, E., & Ventura, W. (Jan-Feb 2021). Maternal clinical characteristics and perinatal outcomes among pregnant women with coronavirus disease 2019. A systematic review. <i>Travel medicine and infectious disease</i>, 39, 101919.</p>	<ul style="list-style-type: none"> • 143 articles were selected for full-text assessment; 33 for descriptive analyses, and 4 case-controls for meta-analysis. For the descriptive analysis, the study included a total of 322 pregnant women, 111 (34.5%) patients from Netherlands, 80 (24.8%) from US, 76 (23.6%) from China, 43 (13.3%) from Italy, 2 (0.6%) from Canada, and one each from Honduras, South Korea, Sweden, Germany, Turkey, Iran, Australia, Spain, Peru, and India. • Data regarding time to diagnosis of COVID-19 by trimester in 179 women were collected. Five (2.8%) were in the first trimester, nine (5.0%) in the second, and 165 (92.2%) in the third. • Among 169 pregnant women, 42 (28.4%) were asymptomatic at admission but qRT-PCR tested SARS-CoV-2-positive.
<p>Di Toro, F., Gjoka, M., Di Lorenzo, G., De Santo, D., De Seta, F., Maso, G., Risso, F. M., Romano, F., Wiesenfeld, U., Levi-D'Ancona, R., Ronfani, L., & Ricci, G. (Jan 2021). Impact of COVID-19 on maternal and neonatal outcomes: a systematic review and meta-analysis. <i>Clinical microbiology and infection: the official publication of the European Society of Clinical Microbiology and Infectious Diseases</i>, 27(1), 36–46.</p>	<ul style="list-style-type: none"> • Twenty-four articles, including 1,100 pregnancies, were selected. The study population was composed of 511 Chinese women, 482 European women, and 107 North American women. • Five hundred eighty-eight women were registered as COVID-19 cases on clinical evaluation. • The pooled prevalence of pneumonia was 89% (95% CI 70–100).
<p>Papapanou, M., Papaioannou, M., Petta, A., Routsis, E., Farmaki, M., Vlahos, N., & Siristatidis, C. (Jan 2021). Maternal and Neonatal Characteristics and Outcomes of COVID-19 in Pregnancy: An Overview of Systematic Reviews.</p>	<ul style="list-style-type: none"> • Thirty-nine reviews were analyzed. • Evidence on participants' trimester of SARS-CoV-2 infection could be extracted by 16 reviews. <ul style="list-style-type: none"> ○ Only two reviews (12.5%) clearly stated the inclusion of first-trimester pregnancies with SARS-CoV-2 infection, with rates of women that were infected during their first trimester of pregnancy in these two reviews being 5% and 6%. ○ Seven reviews (46.7%) clearly stated the inclusion of second trimester pregnancies with SARS-CoV-2 infection, with rates of women that were infected during their second trimester varying between 1% and 10%. ○ Five reviews (31.25%) clearly included only second and third trimester pregnancies.

<p><i>International journal of environmental research and public health</i>, 18(2), 596.</p>	<ul style="list-style-type: none"> ○ Three reviews (18.75%) stated including mostly third trimester pregnancies, without further clarifying the number of pregnancies in first or second trimester. ○ Six reviews (37.5%) analyzed exclusively third trimester pregnancies. ● In general, the symptomatic infection in pregnant women seems to be of lower incidence compared to the general population. Nonetheless, in cases of pregnant women with symptoms like fever and cough, negative outcomes may be expected especially after hospitalization due to the severity of the symptoms required. ● Asymptomatic women ranged between 7.5% and 32.6%; of note, this percentage might be higher, given that pregnant women undergo a larger number of tests than the general population. ● It should not be overseen that assessment of the existing systematic reviews, using the AMSTAR 2 tool, classified 59% of them as “critically low quality” to “low quality”. However, it should be taken into account that currently available systematic reviews based their results on a large number of preliminary studies conducted due to the urgent need for quick answers. For these reasons, further original studies with women from all pregnancy trimesters and longer follow-up periods, and, consequently, further systematic reviews synthesizing their results, are required to provide clinical practice with more definite answers regarding the effects of SARS-CoV-2 infection on such a sensitive group of patients as pregnant women and their fetuses/neonates. So far, data are not robust enough to lead to definite points and regulations.
<p>Amaral, W., Moraes, C. L., Rodrigues, A., Noll, M., Arruda, J. T., & Mendonça, C. R. (Dec 2020). Maternal Coronavirus Infections and Neonates Born to Mothers with SARS-CoV-2: A Systematic Review. <i>Healthcare</i> (Basel, Switzerland), 8(4), 511.</p>	<ul style="list-style-type: none"> ● The 70 selected studies included a total of 1,457 pregnant women diagnosed with COVID-19 in the first, second, and third trimesters of pregnancy, as well as 1,042 newborns from infected mothers. Twenty-one (1.4%) of the pregnant women were in the first trimester, 97 (6.6%) in the second trimester, and 1,339 (91.9%) in the third trimester of pregnancy. <ul style="list-style-type: none"> ○ Of the 70 studies included, 34 were carried out in China, 10 in the United States, eight in Italy, three in Iran, one in Korea, one in Turkey, one in Peru, one in Switzerland, two in France, four in Spain, one in Australia, one in the Netherlands and Ireland, one in Canada, one in the United Kingdom, and one in Sweden.
<p>University of Birmingham. (Nov 29, 2020). PregCOV-19 Living Systematic Review: Prevalence of COVID-19 in pregnant and postnatal women.</p> <p>University of Birmingham. (Nov 29, 2020). PregCOV-19 Living Systematic Review: COVID-19 and maternal outcomes.</p> <p>*The findings are to be published shortly and is currently undergoing peer review.</p>	<ul style="list-style-type: none"> ● The PregCOV-19 project conducts a series of living systematic reviews involving pregnant and postnatal women at risk, suspected, and diagnosed to have COVID-19. ● As of November 29, 2020, based on data from 75 cohort studies across 20 countries that included 67,271 pregnant women: <ul style="list-style-type: none"> ○ The prevalence of COVID-19 in pregnant women admitted to the hospitals appears to be similar or lower than the general population based on available data. ○ 10% of all pregnant women admitted to hospital were diagnosed to have COVID-19 (73 studies; ranged from 7-12%). ○ 73% of pregnant women with COVID-19 were asymptomatic.
<p>Zambrano, L. D., Ellington, S., Strid, P., Galang, R. R., Oduyebo, T., Tong, V. T., Woodworth, K. R., Nahabedian, J. F., 3rd, Azziz-Baumgartner, E.,</p>	<ul style="list-style-type: none"> ● The CDC received reports through national COVID-19 case surveillance or through the National Notifiable Diseases Surveillance System (NNDSS) of 1,300,938 women aged 15-44 years with laboratory results indicative of acute infection with SARS-CoV-2. Data on pregnancy status were available for 461,825 (35.5%) women with laboratory-confirmed infection, 409,462 (88.7%) of whom were symptomatic. Among symptomatic women, 23,434 (5.7%) were reported to be pregnant.

<p>Gilboa, S. M., Meaney-Delman, D., & CDC COVID-19 Response Pregnancy and Infant Linked Outcomes Team. (Nov 6, 2020). 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. <i>MMWR. Morbidity and mortality weekly report</i>, 69(44), 1641-1647.</p>	
<p>Allotey, J., Stallings, E., Bonet, M., Yap, M., Chatterjee, S., Kew, T., Debenham, L., Llavall, A. C., Dixit, A., Zhou, D., Balaji, R., Lee, S. I., Qiu, X., Yuan, M., Coomar, D., van Wely, M., van Leeuwen, E., Kostova, E., Kunst, H., Khalil, A., ... for PregCOV-19 Living Systematic Review Consortium (Sept 1, 2020). Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. <i>BMJ (Clinical research ed.)</i>, 370, m3320.</p>	<ul style="list-style-type: none"> • This living systematic review and meta-analysis included 192 studies. • Overall, 10% (95% confidence interval 7% to 12%; 73 studies with 67,271 women) of pregnant and recently pregnant women attending or admitted to hospital for any reason were diagnosed as having suspected or confirmed COVID-19.
<p>Pettirosso, E., Giles, M., Cole, S., & Rees, M. (Aug 10, 2020). COVID-19 and pregnancy: A review of clinical characteristics, obstetric outcomes and vertical transmission. <i>The Australian & New Zealand journal of obstetrics & gynaecology</i>, 60(5), 640-659.</p>	<ul style="list-style-type: none"> • Sixty articles were included in this review. Some pregnant participants may have been included in multiple publications, as admission dates overlap for reports from the same hospital. However, a total of 1,287 confirmed SARS-CoV-2 positive pregnant cases are reported. • Where universal testing was undertaken, asymptomatic infection occurred in 43.5-92% of cases. • In symptomatic patients, fever was the most common sign, occurring in 10-100% of cases both at admission and postpartum. Only one study compared clinical symptoms between COVID-19 positive pregnant and non-pregnant groups: fever was less prevalent in pregnant than non-pregnant patients (44% vs 100%, P < 0.05), while there was no significant difference in cough, dyspnoea, or fatigue incidence.
<p>Pierce-Williams, R., Burd, J., Felder, L., Khoury, R., Bernstein, P. S., Avila, K., Penfield, C. A., Roman, A. S., DeBolt, C. A., Stone, J. L., Bianco, A., Kern-Goldberger, A. R., Hirshberg,</p>	<ul style="list-style-type: none"> • This cohort study of 64 pregnant women with severe or critical COVID-19 hospitalized at 12 US institutions between March 5, 2020, and April 20, 2020 found 44 (69%) had severe disease, and 20 (31%) had critical disease. • The average gestational age at symptom onset of COVID-19 was 29.9±5.8 weeks (range 16.6–39.1 weeks), with hospital admission at 30.7±5.7 weeks. No patients included in this study were postpartum at the onset of symptoms or hospitalization. Only 23% of women with

<p>A., Srinivas, S. K., Jayakumar, J. S., Brandt, J. S., Anastasio, H., Birsner, M., O'Brien, D. S., Sedev, H. M., ... Berghella, V. (Aug 2020). Clinical course of severe and critical coronavirus disease 2019 in hospitalized pregnancies: a United States cohort study. <i>American journal of obstetrics & gynecology MFM</i>, 2(3), 100134.</p>	<p>severe disease experienced symptom onset at <24 weeks, whereas all women with critical disease experienced symptom onset at >24 weeks ($P=.024$). Sixty-nine percent of women developed symptoms at <34 weeks, and 86% of women developed symptoms at <37 weeks.</p>
<p>Severity (e.g., rate of hospital/ICU admission, rate of mechanical ventilation)</p>	
<p>D'Antonio, F., Sen, C., Mascio, D. D., Galindo, A., Villalain, C., Herraiz, I., Arisoy, R., Ovayolu, A., Eroğlu, H., Canales, M. G., Ladella, S., Cojocar, L., Turan, O., Turan, S., Hadar, E., Brzezinski-Sinai, N. A., Dollinger, S., Uyaniklar, O., Ocakoglu, S. R., Atak, Z., ... On the behalf of the World Association of Perinatal Medicine working group on coronavirus disease 2019 (Jul 2021). Maternal and perinatal outcomes in high compared to low risk pregnancies complicated by severe acute respiratory syndrome coronavirus 2 infection (phase 2): the World Association of Perinatal Medicine working group on coronavirus disease 2019. <i>American journal of obstetrics & gynecology MFM</i>, 3(4), 100329. Advance online publication.</p>	<ul style="list-style-type: none"> • This was a multinational retrospective cohort study involving women with laboratory-confirmed severe acute respiratory syndrome coronavirus 2 infection from 76 centers from 25 countries in Europe, the United States, South America, Asia, and Australia from April 4, 2020 to October 28, 2020. • The risk of composite adverse maternal outcomes (maternal mortality and morbidity, including admission to the intensive care unit, use of mechanical ventilation, or death) was higher in high-risk pregnancies than in low-risk pregnancies. Women carrying high-risk pregnancies were at higher risk of hospital admission, presence of severe respiratory symptoms, admission to the intensive care unit, and invasive mechanical ventilation. • Pregnancies were considered high risk in case of either pre-existing chronic medical conditions in pregnancy (pregestational diabetes mellitus, chronic hypertension, or autoimmune disease) or obstetrical disorders occurring in pregnancy (preeclampsia, gestational hypertension, or gestational diabetes mellitus).

<p>Mark, E. G., McAleese, S., Golden, W. C., Gilmore, M. M., Sick-Samuels, A., Curless, M. S., Noguee, L. M., Milstone, A. M., & Johnson, J. (May 2021). Coronavirus Disease 2019 in Pregnancy and Outcomes Among Pregnant Women and Neonates: A Literature Review. <i>The Pediatric infectious disease journal</i>, 40(5), 473–478.</p>	<ul style="list-style-type: none"> • 196 studies published February 1, 2020 through August 15, 2020 reported 1,922 women with COVID-19 during pregnancy and 1,361 neonates with perinatal exposure: • Among pregnant women with COVID-19, 181 (11%) were admitted to the ICU and 123 (8%) required mechanical ventilation.
<p>Granja M, G, Oliveira A, C, R, de Figueiredo C, S, Gomes A, P, Ferreira E, C, Giestal-de-Araujo E, de Castro-Faria-Neto H, C. (Apr 28, 2021). SARS-CoV-2 Infection in Pregnant Women: Neuroimmune-Endocrine Changes at the Maternal-Fetal Interface. <i>Neuroimmunomodulation</i>.</p>	<ul style="list-style-type: none"> • There is no evidence showing significant differences in the pathophysiology or severity of the disease between pregnant and non-pregnant women. In fact, pregnant women generally showed mild to moderate degrees of infection.
<p>Villar, J., Ariff, S., Gunier, R. B., Thiruvengadam, R., Rauch, S., Kholin, A., Roggero, P., Prefumo, F., do Vale, M. S., Cardona-Perez, J. A., Maiz, N., Cetin, I., Savasi, V., Deruelle, P., Easter, S. R., Sichitiu, J., Soto Conti, C. P., Ernawati, E., Mhatre, M., Teji, J. S., ... Papageorghiou, A. T. (Apr 22, 2021). Maternal and Neonatal Morbidity and Mortality Among Pregnant Women With and Without COVID-19 Infection: The INTERCOVID Multinational Cohort Study. <i>JAMA pediatrics</i>, e211050. Advance online publication.</p>	<ul style="list-style-type: none"> • A total of 706 pregnant women with COVID-19 diagnosis and 1,424 pregnant women without COVID-19 diagnosis were enrolled in this cohort study that took place from March to October 2020, involving 43 institutions in 18 countries. • COVID-19 in pregnancy was associated with consistent and substantial increases in severe maternal morbidity and mortality when pregnant women with and without COVID-19 diagnosis were compared. <ul style="list-style-type: none"> ○ Women with COVID-19 diagnosis were at higher risk for severe infections and intensive care unit admission. ○ There was an association with a greater risk of admission to ICU/high-dependency unit (RR, 5.04; 95% CI, 3.13-8.10) and referral to a higher level of care (RR, 6.07; 95% CI, 1.23-30.01). Among all ICU admissions, women with COVID-19 diagnosis stayed 3.73 (95% CI, 2.37-5.86) days longer than women without COVID-19 diagnosis.
<p>Hapshy, V., Aziz, D., Kahar, P., Khanna, D., Johnson, K. E., & Parmar, M. S. (Apr 21, 2021). COVID-19 and Pregnancy: Risk, Symptoms, Diagnosis, and</p>	<ul style="list-style-type: none"> • The mortality rate in pregnant and non-pregnant patients is relatively equal. For example, in two systematic reviews in New York and of selected widespread databases, the mortality rate of over 250 and 350 patients, respectively, was 0.0%. • There is an increased hospitalization and ICU admissions rate with mechanical ventilation compared to a matched non-pregnant cohort. However, this is not associated with any increased rate of mortality in pregnant patients.

<p>Treatment. <i>SN comprehensive clinical medicine</i>, 1–7. Advance online publication.</p>	
<p>Aghaamoo, S., Ghods, K., & Rahmadian, M. (Apr 19, 2021). Pregnant women with COVID-19: the placental involvement and consequences. <i>Journal of molecular histology</i>, 1–9.</p>	<ul style="list-style-type: none"> • Pregnancy may increase the risk of ICU admission and mechanical ventilation requirement.
<p>Wei, S. Q., Bilodeau-Bertrand, M., Liu, S., & Auger, N. (Apr 19, 2021). The impact of COVID-19 on pregnancy outcomes: a systematic review and meta-analysis. <i>CMAJ</i>, 193(16), E540–E548.</p>	<ul style="list-style-type: none"> • 42 studies involving 438,548 people who were pregnant were included in the review. • Compared with mild COVID-19, severe COVID-19 was strongly associated with ICU admission (OR 15.46, 95% CI 5.79 to 41.23; I2 = 0%; 5 studies) and mechanical ventilation (OR 19.31, 95% CI 9.38 to 39.72; I2 = 0%; 5 studies).
<p>Mirbeyk, M., Saghazadeh, A., & Rezaei, N. (Apr 2, 2021). A systematic review of pregnant women with COVID-19 and their neonates. <i>Archives of gynecology and obstetrics</i>, 1–34.</p>	<ul style="list-style-type: none"> • 37 articles involving 364 pregnant women with COVID-19 and 302 neonates were included in this review. The vast majority of pregnant patients were in their third trimester of pregnancy, and only 45 cases were in the first or second trimester (12.4%). • The course of COVID-19 in pregnant women resembles that of other populations. However, there is not sufficient evidence to establish that COVID-19 would not complicate pregnancy. • Most mothers described mild to moderate manifestations of COVID-19. Of 364 pregnant women, 25 were asymptomatic at the time of admission. The most common symptoms were fever (62.4%) and cough (45.3%). • Twenty-two (6.0%) pregnant patients developed severe pneumonia. Among them, 10 cases (2.8%) required mechanical ventilation and therefore were admitted to the ICU. Two of these 10 patients died from severe pneumonia and multiple organ dysfunction.
<p>Joseph, N. T., Rasmussen, S. A., & Jamieson, D. J. (Apr 2021). The effects of COVID-19 on pregnancy and implications for reproductive medicine. <i>Fertility and sterility</i>, 115(4), 824–830.</p>	<ul style="list-style-type: none"> • Emerging surveillance data and large cohort studies suggest that pregnancy is associated with an increased risk of intensive care unit hospitalization, invasive ventilation, and death. • Similar to data from the general population, SARS-CoV-2 disease severity has been higher in pregnant women who were racial/ethnic minorities, uninsured, low income, or from neighborhoods with low income, high crowding, or increased density. These findings have been seen in different U.S. locations and internationally. COVID-19 has the potential to worsen existing disparities in maternal and infant mortality.
<p>Dubey, P., Thakur, B., Reddy, S., Martinez, C. A., Nurunnabi, M., Manuel, S. L., Chheda, S., Bracamontes, C., & Dwivedi, A. K. (Mar 24, 2021). Current trends and geographical differences in therapeutic profile and outcomes of COVID-19 among pregnant women - a systematic review and meta-analysis. <i>BMC pregnancy and childbirth</i>, 21(1), 247.</p>	<ul style="list-style-type: none"> • 1,239 pregnant women with COVID-19 from 66 studies were analyzed. • The proportion of mechanical ventilation was estimated to be 3% with a 6% ICU admission rate (95%CI: 2, 10%). The proportions of mechanical ventilation support (2, 4, and 6%) and ICU admission (6, 5, and 7%) were found to be similar across the US, Asia, and Europe, respectively.

<p>Elsaddig, M., & Khalil, A. (Mar 18, 2021). Effects of the COVID pandemic on pregnancy outcomes. <i>Best practice & research. Clinical obstetrics & gynaecology</i>, S1521-6934(21)00043-2.</p>	<ul style="list-style-type: none"> • Current research indicates that the clinical presentation of COVID-19 in pregnant women resembles that of non-pregnant women, which generally includes a mild cough, breathlessness, and fever. • Risk factors for severe disease mirror those in the general population and include diabetes, chronic hypertension, obesity, and Black, Asian and minority ethnic background.
<p>Karimi, L., Makvandi, S., Vahedian-Azimi, A., Sathyapalan, T., & Sahebkar, A. (Mar 5, 2021). Effect of COVID-19 on Mortality of Pregnant and Postpartum Women: A Systematic Review and Meta-Analysis. <i>Journal of pregnancy</i>, 2021, 8870129.</p>	<ul style="list-style-type: none"> • 117 studies with a total of 11,758 pregnant women were included in this review. • The rate of severe pneumonia was reported from 0 to 14%. • The majority of the patients were admitted to the ICU. • Duration from admission to death was between two and 22 days. The most common complication during treatment of COVID-19 in pregnant and postpartum women was acute respiratory distress syndrome (ARDS).
<p>Oltean, I., Tran, J., Lawrence, S., Ruschkowski, B. A., Zeng, N., Bardwell, C., Nasr, Y., de Nanassy, J., & El Demellawy, D. (Mar 2, 2021). Impact of SARS-CoV-2 on the clinical outcomes and placental pathology of pregnant women and their infants: A systematic review. <i>Heliyon</i>, 7(3), e06393.</p>	<ul style="list-style-type: none"> • Forty-one studies and case reports from 315 women confirmed to have SARS-CoV-2 and 262 neonates who underwent PCR testing were included in the review. • Results suggest elevated rates of ICU admission in comparison to pregnant women without SARS-CoV-2. • Six cases of maternal ICU admission, representing 1.9% of total SARS-CoV-2 laboratory confirmed pregnancies. In contrast, the ICU admission rate for pregnant or postpartum women admitted to Canadian hospitals in 2019 was 0.32 per 100 pregnancies. Therefore, the rate of ICU admission in this systematic review is six times higher than in healthy pregnant women from the general population.
<p>Salem D, Katranji F, Bakdash T. (Mar 2021). COVID-19 infection in pregnant women: Review of maternal and fetal outcomes. <i>Int J Gynaecol Obstet</i>. 152(3):291-298.</p>	<ul style="list-style-type: none"> • Pregnant women who become COVID-19-positive are usually either asymptomatic or mild-to-moderately symptomatic, similar to non-pregnant women. • Pneumonia is one of the most common outcomes in pregnant women with COVID-19. • The third trimester seems to be the most vulnerable period of infection.
<p>Hudak M. L. (Feb 23, 2021). Consequences of the SARS-CoV-2 pandemic in the perinatal period. <i>Current opinion in pediatrics</i>, 33(2), 181–187.</p>	<ul style="list-style-type: none"> • Large population-based studies have conclusively demonstrated that pregnant women with a history of SARS-CoV-2 infection develop more severe disease than non-pregnant women. For example: <ul style="list-style-type: none"> ○ Among 1.3 million US women of reproductive age (aged 15-44 years) who tested positive for SARS-CoV-2 between January 22 and October 3, 2020, pregnancy status was known for 409,462 symptomatic women among which 23,434 were pregnant (5.7%). After adjustments for underlying medical conditions, age, and race/ethnicity, pregnant women compared to non-pregnant women had significantly higher adjusted risk ratios (RRs) of ICU admission, invasive ventilation, utilization of extracorporeal membrane oxygenation, and death. Although black women comprised 14% of the total cohort, they experienced 37% of all deaths and 27% of deaths in pregnant women. The RRs for death and ICU admission were highest in Hispanic or Latina women and in non-Hispanic Asian and Native Hawaiian/Pacific Islander women, respectively. COVID-19 has amplified health inequities in minority populations. ○ Data over an eight-month period from the Premier Healthcare Database (encompassing all-payer information for 20% of US hospitalizations) was used to construct a propensity model that compared the outcomes of pregnant women with and without COVID-19 infection. Among 406,446 women who gave birth, 6,380 (1.6%) had a diagnosis of COVID-19. The adjusted odds ratios (aOR) for death, ICU admission, and

	<p>use of mechanical ventilation for pregnant women with COVID-19 infection were 26.1, 6.5, and 23.7, respectively. Underlining findings in the general population, COVID-19 in pregnant women increased the odds of serious extrapulmonary complications including myocardial infarction, venous thromboembolism, and any thrombotic event.</p>
<p>Cavalcante, M. B., Cavalcante, C., Sarno, M., Barini, R., & Kwak-Kim, J. (Feb 2021). Maternal immune responses and obstetrical outcomes of pregnant women with COVID-19 and possible health risks of offspring. <i>Journal of reproductive immunology</i>, 143, 103250.</p>	<ul style="list-style-type: none"> • The risk of adverse clinical outcomes in pregnant women with COVID-19 is still unclear. <ul style="list-style-type: none"> ○ Some authors have observed that pregnant women with COVID-19 had a clinical course of the disease similar to that of non-pregnant women. • In contrast, others suggest that the pregnant status raises the morbidity of COVID-19, especially in the presence of risk factors such as black and Hispanic race, obesity, advanced maternal, age, and medical comorbidities.
<p>Novoa, R. H., Quintana, W., Llancari, P., Urbina-Quispe, K., Guevara-Ríos, E., & Ventura, W. (Jan-Feb 2021). Maternal clinical characteristics and perinatal outcomes among pregnant women with coronavirus disease 2019. A systematic review. <i>Travel medicine and infectious disease</i>, 39, 101919.</p>	<ul style="list-style-type: none"> • 143 articles were selected for full-text assessment; 33 for descriptive analyses, and four case-controls for meta-analysis. For the descriptive analysis, the study included a total of 322 pregnant women, 111 (34.5%) patients from Netherlands, 80 (24.8%) from US, 76 (23.6%) from China, 43 (13.3%) from Italy, 2 (0.6%) from Canada, and one each from Honduras, South Korea, Sweden, Germany, Turkey, Iran, Australia, Spain, Peru, and India. • The maternal clinical characteristics of COVID-19-positive pregnant women frequently include fever and cough, though significantly less frequently than non-pregnant women with COVID-19. • Maternal mortality is rare. However, there is a considerable proportion of women that required ICU due to complication of COVID-19 infection. <ul style="list-style-type: none"> ○ Thirty patients (10.3%) with COVID-19-related complications required ICU and one (0.3%) died. Nine patients had data on the risk factors for admission to ICU, with the most frequent being obesity (3/9; 30%). All nine patients were admitted after 29 weeks of gestation (i.e., third trimester). Eight patients (8/9) underwent delivery by caesarean section. One patient had a preterm vaginal delivery spontaneously in the ICU. • Fifty-two (17.9%) patients reported the need for oxygen support. Eleven (3.8%) patients needed mechanical ventilation and one needed extracorporeal membrane oxygenation (0.3%).
<p>Jafari, M., Pormohammad, A., Sheikh Neshin, S. A., Ghorbani, S., Bose, D., Alimohammadi, S., Basirjafari, S., Mohammadi, M., Rasmussen-Ivey, C., Razizadeh, M. H., Nouri-Vaskeh, M., & Zarei, M. (Jan 2, 2021). Clinical characteristics and outcomes of pregnant women with COVID-19 and comparison with control patients: A systematic review and meta-analysis. <i>Reviews in medical virology</i>, e2208.</p>	<ul style="list-style-type: none"> • In this large-scale study, 128,176 non-pregnant patients (228 studies) and 10,000 pregnant patients (121 studies) with confirmed COVID-19 cases were included in a meta-analysis. The mean of age and gestational age of admission in pregnant women was 33 years old and 36 weeks, respectively. • Overall, pregnant patients present with similar clinical characteristics of COVID-19 when compared with the general population, but they may be more asymptomatic. • Pregnant women show the same manifestations of COVID-19 as non-pregnant adult patients. Fever and cough are the most common symptoms in both groups, followed by myalgia and chill in pregnant and dysgeusia and fatigue in non-pregnant patients.

<p>Wang, C. L., Liu, Y. Y., Wu, C. H., Wang, C. Y., Wang, C. H., & Long, C. Y. (Jan 1, 2021). Impact of COVID-19 on Pregnancy. <i>International journal of medical sciences</i>, 18(3), 763–767.</p>	<ul style="list-style-type: none"> • In pregnant women who develop COVID-19 pneumonia, early data have shown a similar rate of ICU admission to nonpregnant women. • The clinical course of COVID-19 pneumonia in pregnant women has been reported to be similar to that in non-pregnant women. In addition, pregnant women do not appear to be at a higher risk of being infected with COVID-19 or suffering from more severe disease than other adults of similar age. • All studies included in this review were case reports or series of low quality.
<p>Papapanou, M., Papaioannou, M., Petta, A., Routsis, E., Farmaki, M., Vlahos, N., & Siristatidis, C. (Jan 2021). Maternal and Neonatal Characteristics and Outcomes of COVID-19 in Pregnancy: An Overview of Systematic Reviews. <i>International journal of environmental research and public health</i>, 18(2), 596.</p>	<ul style="list-style-type: none"> • Thirty-nine reviews were analyzed. • Maternal ICU admission and mechanical ventilation rates were 3-28.5% and 1.4-12%, respectively. After accounting for the quality of the studies, among secondary outcomes the ranges of maternal ICU admission (3-10%) and mechanical ventilation rates (1.4-5.5%) were found to be relatively lower. • Reported maternal ICU admission, mechanical ventilation, and mortality rates were high, when compared with non-pregnant women. A possible interpretation to this finding was the existence of other comorbidities accompanying pregnancy, compared with non-pregnant women at a similar age. Concerning mortality rates, available data were more contradictory. The increased rates, when reported, have been also attributed to the specific health care provision of the participants' countries. • It should not be overseen that assessment of the existing systematic reviews, using the AMSTAR 2 tool, classified 59% of them as “critically low quality” to “low quality”. However, it should be taken into account that currently available systematic reviews based their results on a large number of preliminary studies conducted due to the urgent need for quick answers. For these reasons, further original studies with women from all pregnancy trimesters and longer follow-up periods, and, consequently, further systematic reviews synthesizing their results, are required to provide clinical practice with more definite answers regarding the effects of SARS-CoV-2 infection on such a sensitive group of patients as pregnant women and their fetuses/neonates. So far, data are not robust enough to lead to definite points and regulations.
<p>Di Toro, F., Gjoka, M., Di Lorenzo, G., De Santo, D., De Seta, F., Maso, G., Risso, F. M., Romano, F., Wiesenfeld, U., Levi-D'Ancona, R., Ronfani, L., & Ricci, G. (Jan 2021). Impact of COVID-19 on maternal and neonatal outcomes: a systematic review and meta-analysis. <i>Clinical microbiology and infection: the official publication of the European Society of Clinical Microbiology and Infectious Diseases</i>, 27(1), 36–46.</p>	<ul style="list-style-type: none"> • Twenty-four articles, including 1,100 pregnancies, were selected. The study population was composed of 511 Chinese women, 482 European women, and 107 North American women. • Although adverse outcomes, such as ICU admission or patient death, can occur, the clinical course of COVID-19 in most women is not severe, and the infection does not significantly influence the pregnancy. • The pooled prevalences of ICU admission and maternal death were comparable with those reported in non-pregnant women. <ul style="list-style-type: none"> ○ The pooled prevalence of women admitted to the intensive care unit was 8% (95% CI 1–20). • The pooled prevalence of women undergoing mechanical ventilation was 13% (95% CI 2–30%).
<p>Islam, M. M., Poly, T. N., Walther, B. A., Yang, H. C., Wang, C. W., Hsieh, W. S., Atique, S., Salmani, H., Alsinglawi, B., Lin, M. C., Jian, W. S., & Jack Li, Y. C. (Dec 3, 2020). Clinical Characteristics and Neonatal Outcomes of Pregnant Patients With COVID-19: A Systematic Review. <i>Frontiers in medicine</i>, 7, 573468.</p>	<ul style="list-style-type: none"> • Based on data for 235 pregnant women with COVID-19 (age range of 25-40 years and the gestational age range of eight to 40 weeks plus six days) across 13 studies, the clinical, laboratory, and radiological characteristics of pregnant women with COVID-19 were similar to those of the non-pregnant or general populations.

<p>Chi, J., Gong, W., & Gao, Q. (Dec 1, 2020). Clinical characteristics and outcomes of pregnant women with COVID-19 and the risk of vertical transmission: a systematic review. <i>Archives of gynecology and obstetrics</i>, 303(2), 337–345.</p>	<ul style="list-style-type: none"> • This systematic review summarizes the clinical features and maternal-infant outcomes of 230 women with COVID-19 (154 deliveries, 66 ongoing pregnancies, and 10 abortions) and 156 newborns from 20 eligible studies. • The results of this systematic review showed that the clinical manifestations of pregnant women with COVID-19 were similar to those of general COVID-19 patients, including fever, cough, myalgia, shortness of breath, and diarrhea. <ul style="list-style-type: none"> ◦ Most pregnant patients were mildly ill. Only seven (4.00%) pregnant women were critically ill, 14 (8.00%) women had severe cases, and 144 (82.29%) women had moderate disease. Ten (5.71%) pregnant women were asymptomatic. • The mortality of pregnant women with COVID-19 was lower than that of overall COVID-19 patients. • In terms of treatment, seven (5.19%) pregnant women received mechanical ventilation, and 67 (59.82%) pregnant women received oxygen support through a nasal catheter.
<p>Hassanipour, S., Faradonbeh, S. B., Momeni, K., Heidarifard, Z., Khosousi, M. J., Khosousi, L., Ameri, H., & Arab-Zozani, M. (Dec 2020). A systematic review and meta-analysis of pregnancy and COVID-19: Signs and symptoms, laboratory tests, and perinatal outcomes. <i>International journal of reproductive biomedicine</i>, 18(12), 1005–1018.</p>	<ul style="list-style-type: none"> • A total of 10 articles were reviewed in this study, which analyzed 135 pregnant women, all of whom were in the third trimester of pregnancy. • The common clinical manifestations of pregnant women with COVID-19 include fever and cough, and the less common symptoms are sore throat and diarrhea.
<p>Amaral, W., Moraes, C. L., Rodrigues, A., Noll, M., Arruda, J. T., & Mendonça, C. R. (Dec 2020). Maternal Coronavirus Infections and Neonates Born to Mothers with SARS-CoV-2: A Systematic Review. <i>Healthcare (Basel, Switzerland)</i>, 8(4), 511.</p>	<ul style="list-style-type: none"> • The 70 selected studies included a total of 1,457 pregnant women diagnosed with COVID-19 in the first, second, and third trimesters of pregnancy, as well as 1,042 newborns from infected mothers. <ul style="list-style-type: none"> ◦ Of the 70 studies included, 34 were carried out in China, 10 in the United States, eight in Italy, three in Iran, one in Korea, one in Turkey, one in Peru, one in Switzerland, two in France, four in Spain, one in Australia, one in the Netherlands and Ireland, one in Canada, one in the United Kingdom, and one in Sweden. • Among pregnant women diagnosed with COVID-19, 68 (4.6%) were admitted in ICU.
<p>University of Birmingham. (Nov 29, 2020). PregCOV-19 Living Systematic Review: Prevalence of COVID-19 in pregnant and postnatal women.</p> <p>University of Birmingham. (Nov 29, 2020). PregCOV-19 Living Systematic Review: COVID-19 and maternal outcomes.</p>	<ul style="list-style-type: none"> • As of November 29, 2020, based on data from 192 studies across 30 countries that included 64,676 pregnant women suspected or confirmed with COVID-19: <ul style="list-style-type: none"> ◦ 4% of pregnant and recently pregnant women diagnosed with COVID-19 were admitted to the ICU and 3% needed invasive ventilation (92 studies). ◦ Pregnant or recently pregnant women with COVID-19 appear to be at increased risk of needing admission to an ICU compared with non-pregnant reproductive aged women with COVID-19 (92 studies). • Pregnant women with COVID-19 are also at increased risk of death (92 studies).

<p>*The findings are to be published shortly and is currently undergoing peer review.</p>	
<p>University of Birmingham. (Nov 29, 2020). PregCOV-19 Living Systematic Review: Presentation of COVID-19 in pregnant and postnatal women.</p> <p>*The findings are to be published shortly and is currently undergoing peer review.</p>	<ul style="list-style-type: none"> • The PregCOV-19 project conducts a series of living systematic reviews involving pregnant and postnatal women at risk, suspected, and diagnosed to have COVID-19. • As of November 29, 2020, based on data from 192 studies across 30 countries that included 64,676 pregnant women suspected or confirmed with COVID-19, the clinical manifestations of COVID-19 in pregnancy and postpartum appears to be broadly similar to the general population (studies included pregnant women admitted to the hospitals and not all pregnant women): <ul style="list-style-type: none"> ○ The common symptoms of COVID-19 in pregnancy and postpartum were cough (41%) and fever (40%). ○ Breathlessness and muscle ache were reported in approximately 20% of women. • The common laboratory findings were lymphopenia (33%), raised white cell count (26%), and raised C reactive protein levels (49%).
<p>Rodrigues, C., Baía, I., Domingues, R., & Barros, H. (Nov 23, 2020). Pregnancy and Breastfeeding During COVID-19 Pandemic: A Systematic Review of Published Pregnancy Cases. <i>Frontiers in public health</i>, 8, 558144.</p>	<ul style="list-style-type: none"> • The review identified 161 original studies (published until June 26th, 2020) reporting 3,985 cases of pregnant women with COVID-19 (1,007 discharged while pregnant). The majority of cases occurred in the USA ($n = 1,206$, 30%), China ($n = 823$, 21%), France ($n = 672$, 17%), UK ($n = 440$, 11%), Mexico ($n = 308$, 8%), Spain ($n = 241$, 6%), and Italy ($n = 202$, 5%). Maternal age ranged from 15 to 49 years. • The clinical characteristics of COVID-19 were similar to those described in non-pregnant women, presenting mild or moderate symptoms. • Pregnant women do not appear to be at increased risk of severe illness of SARS-CoV-2 infection compared with non-pregnant women in the general population. • Two hundred and fifteen pregnant women required admission to an intensive care unit (6.4%), 5.4% were mechanically ventilated ($n = 160$), and 0.5% required ECMO ($n = 15$).
<p>Zambrano, L. D., Ellington, S., Strid, P., Galang, R. R., Oduyebo, T., Tong, V. T., Woodworth, K. R., Nahabedian, J. F., 3rd, Azziz-Baumgartner, E., Gilboa, S. M., Meaney-Delman, D., & CDC COVID-19 Response Pregnancy and Infant Linked Outcomes Team. (Nov 6, 2020). 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. <i>MMWR. Morbidity and mortality weekly report</i>, 69(44), 1641-1647.</p>	<ul style="list-style-type: none"> • CDC received reports through national COVID-19 case surveillance or through the National Notifiable Diseases Surveillance System (NNDSS) of 1,300,938 women aged 15-44 years with laboratory results indicative of acute infection with SARS-CoV-2. Data on pregnancy status were available for 461,825 (35.5%) women with laboratory-confirmed infection, 409,462 (88.7%) of whom were symptomatic. Among symptomatic women, 23,434 (5.7%) were reported to be pregnant. • After adjusting for age, race/ethnicity, and underlying medical conditions, pregnant women were significantly more likely than nonpregnant women to be admitted to an intensive care unit (ICU) (10.5 versus 3.9 per 1,000 cases; adjusted risk ratio [aRR] = 3.0; 95% confidence interval [CI] = 2.6–3.4), receive invasive ventilation (2.9 versus 1.1 per 1,000 cases; aRR = 2.9; 95% CI = 2.2–3.8), receive extracorporeal membrane oxygenation (ECMO) (0.7 versus 0.3 per 1,000 cases; aRR = 2.4; 95% CI = 1.5–4.0), and die (1.5 versus 1.2 per 1,000 cases; aRR = 1.7; 95% CI = 1.2–2.4). Stratifying these analyses by age and race/ethnicity highlighted disparities in risk by subgroup. • Although the absolute risks for severe outcomes for women were low, pregnant women were at increased risk for severe COVID-19–associated illness.

<p>Yee J, Kim W, Han JM, et al. (Oct 22, 2020). Clinical manifestations and perinatal outcomes of pregnant women with COVID-19: a systematic review and meta-analysis. <i>Sci Rep.</i>;10(1):18126.</p>	<ul style="list-style-type: none"> • Based on 11 Chinese studies involving with 9,032 pregnant women with COVID-19 and 338 infants included in a meta-analysis, pregnant women with COVID-19 have relatively mild symptoms (e.g., fatigue, cough, fever, dyspnea, sore throat). However, abnormal proportions of laboratory parameters were similar or even increased, compared to general population. • Milder symptoms in pregnant COVID-19 patients may be explained by the younger average age compared to the general COVID-19 patient population; additionally, as there were much fewer comorbidities, symptoms might have appeared to be less profound in the pregnant population.
<p>Figueiro-Filho, E. A., Yudin, M., & Farine, D. (Oct 2, 2020). COVID-19 during pregnancy: an overview of maternal characteristics, clinical symptoms, maternal and neonatal outcomes of 10,996 cases described in 15 countries. <i>Journal of perinatal medicine</i>, 48(9), 900–911.</p>	<ul style="list-style-type: none"> • Based on eight studies representing 10,966 cases distributed in 15 countries around the world (Canada, US, Honduras, Brazil, Peru, Spain, Italy, France, Netherlands, Sweden, Turkey, Iran, China, Korea, and Australia) until July 20, 2020, the maternal characteristics and clinical symptoms are not worse or different from the general population. • Pregnant women are not more affected by the respiratory complications of COVID-19, when compared to the outcomes described in the general population. <ul style="list-style-type: none"> ○ Maternal ICU admission was described in 3.7% of cases, with respiratory support necessary in 5.25% of cases. ○ Maternal hospitalization occurred in 35% of cases and 84% of pregnant women recovered from COVID-19 (1,340/1,595). • Maternal death was described in 1.13% of cases (144/10,987) with special attention to the Brazilian report that described an alarming rate of 12.7% (124/978).
<p>Diriba, K., Awulachew, E., & Getu, E. (Sept 4, 2020). The effect of coronavirus infection (SARS-CoV-2, MERS-CoV, and SARS-CoV) during pregnancy and the possibility of vertical maternal-fetal transmission: a systematic review and meta-analysis. <i>European journal of medical research</i>, 25(1), 39.</p>	<ul style="list-style-type: none"> • 39 studies involving 1,316 pregnant women (1,271 with SARS-CoV-2, 12 with MERS-CoV, and 33 with SARS-CoV) were included in this systematic review and meta-analysis. 25 studies reported information on infections caused by SARS-CoV-2 among a total of 1,271 pregnancies. <ul style="list-style-type: none"> ○ 28.5% of pregnant women were admitted to ICU.
<p>Allotey, J., Stallings, E., Bonet, M., Yap, M., Chatterjee, S., Kew, T., Debenham, L., Llavall, A. C., Dixit, A., Zhou, D., Balaji, R., Lee, S. I., Qiu, X., Yuan, M., Coomar, D., van Wely, M., van Leeuwen, E., Kostova, E., Kunst, H., Khalil, A., ... for PregCOV-19 Living Systematic Review Consortium (Sept 1, 2020). Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. <i>BMJ (Clinical research ed.)</i>, 370, m3320.</p>	<ul style="list-style-type: none"> • This living systematic review and meta-analysis included 192 studies. • The most common clinical manifestations of COVID-19 in pregnancy were fever (40%) and cough (41%). • Compared with non-pregnant women of reproductive age, pregnant and recently pregnant women with covid-19 were less likely to have symptoms or report symptoms of fever, dyspnoea, and myalgia. • The odds of admission to an intensive care unit, invasive ventilation, and need for extra corporeal membrane oxygenation were higher in pregnant and recently pregnant than non-pregnant reproductive aged women. • Increased maternal age, high body mass index, any pre-existing maternal comorbidity, chronic hypertension, pre-existing diabetes, and pre-eclampsia were associated with severe covid-19 in pregnancy. • In pregnant women with covid-19, increased maternal age, high body mass index, non-white ethnicity, any pre-existing maternal comorbidity including chronic hypertension and diabetes, and pre-eclampsia were associated with serious complications such as admission to an intensive care unit, invasive ventilation, and maternal death.

<p>Pettirosso, E., Giles, M., Cole, S., & Rees, M. (Aug 10, 2020). COVID-19 and pregnancy: A review of clinical characteristics, obstetric outcomes and vertical transmission. <i>The Australian & New Zealand journal of obstetrics & gynaecology</i>, 60(5), 640–659.</p>	<ul style="list-style-type: none"> • Sixty articles were included in this review. Some pregnant participants may have been included in multiple publications, as admission dates overlap for reports from the same hospital. However, a total of 1,287 confirmed SARS-CoV-2 positive pregnant cases are reported. • Unlike for SARS, MERS, or influenza, pregnancy does not appear to be associated with an elevated risk of serious maternal COVID-19 illness compared with the non-pregnant population. In almost all cohort studies describing disease severity, rates of severe and critical disease approximated those of the general population. • A total of 111 severe and 40 critical cases were reported across 13 cohort studies. Of these studies, severe COVID-19 illness (pneumonia requiring oxygen support or non-invasive ventilation) occurred in 0-18% of patients. Critical disease (defined as progression to acute respiratory distress syndrome, sepsis, or acute organ dysfunction) was reported in 0-5% of cases. • Extrapulmonary complications occurred in some severe and critical patients, including cardiac impairment, renal failure, and coagulopathy.
<p>Gao, Y. J., Ye, L., Zhang, J. S., Yin, Y. X., Liu, M., Yu, H. B., & Zhou, R. (Aug 3, 2020). Clinical features and outcomes of pregnant women with COVID-19: a systematic review and meta-analysis. <i>BMC infectious diseases</i>, 20(1), 564.</p>	<ul style="list-style-type: none"> • The meta-analysis included 236 pregnant women with COVID-19 (160 pregnant women with COVID-19 in China and 76 pregnant women with COVID-19 in America). The incidences of fever, cough, and positive CT findings in pregnant women with COVID-19 are less than those in the normal population with COVID-19. • The subgroup analysis showed that compared with non-pregnant patients, pregnant women with COVID-19 had significantly lower incidences of fever (pregnant women, 51%; non-pregnant patients, 91%; $P < 0.00001$) and cough (pregnant women, 31%; non-pregnant patients, 67%; $P < 0.0001$).
<p>Pierce-Williams, R., Burd, J., Felder, L., Khoury, R., Bernstein, P. S., Avila, K., Penfield, C. A., Roman, A. S., DeBolt, C. A., Stone, J. L., Bianco, A., Kern-Goldberger, A. R., Hirshberg, A., Srinivas, S. K., Jayakumar, J. S., Brandt, J. S., Anastasio, H., Birsner, M., O'Brien, D. S., Sedev, H. M., ... Berghella, V. (Aug 2020). Clinical course of severe and critical coronavirus disease 2019 in hospitalized pregnancies: a United States cohort study. <i>American journal of obstetrics & gynecology MFM</i>, 2(3), 100134.</p>	<ul style="list-style-type: none"> • This cohort study of 64 pregnant women with severe or critical COVID-19 hospitalized at 12 US institutions between March 5, 2020, and April 20, 2020 found 44 (69%) had severe disease, and 20 (31%) had critical disease. Data suggest that the clinical course of severe or critical COVID-19 in hospitalized pregnant women may be shorter than in hospitalized nonpregnant patients. • In pregnant women with severe or critical COVID-19, admission into the hospital typically occurred about seven days after symptom onset, and the duration of hospitalization was six days (six [severe group] vs 12 [critical group]). • Women with critical disease had a high rate of acute respiratory distress syndrome, and there was one case of cardiac arrest, but there were no cases of cardiomyopathy or maternal mortality. • Hospitalization of pregnant women with severe or critical COVID-19 resulted in delivery during the clinical course of the disease in 50% of this cohort, usually in the third trimester. • There were no perinatal deaths in this cohort.

<p>Narang, K., Enninga, E., Gunaratne, M., Ibirogbu, E. R., Trad, A., Elrefaei, A., Theiler, R. N., Ruano, R., Szymanski, L. M., Chakraborty, R., & Garovic, V. D. (Aug 2020). SARS-CoV-2 Infection and COVID-19 During Pregnancy: A Multidisciplinary Review. <i>Mayo Clinic proceedings</i>, 95(8), 1750–1765.</p>	<ul style="list-style-type: none"> • This review summarizes nine guidelines (updated as of April 22, 2020) from six societies⁹ for medical/obstetric care and outlines future directions for optimization of treatment and preventive strategies for pregnant patients with COVID-19 with the understanding that relevant data are limited and rapidly changing. • Pregnant women with SARS-CoV-2 infection may experience more severe symptoms compared with non-pregnant women. • Existing limited data have reported on rapid deterioration in women who had no symptoms on arrival and were subsequently diagnosed as having severe COVID-19. In some, but not all, patients, maternal comorbidities were present (hypertension, diabetes, cholestasis of pregnancy). Case reports have also described cases of quickly worsening maternal status with the ultimate diagnosis of cardiomyopathy.
<p>Ashraf, M. A., Keshavarz, P., Hosseinpour, P., Erfani, A., Roshanshad, A., Pourdast, A., Nowrouzi-Sohrabi, P., Chaichian, S., & Poordast, T. (Jul-Sept 2020). Coronavirus Disease 2019 (COVID-19): A Systematic Review of Pregnancy and the Possibility of Vertical Transmission. <i>Journal of reproduction & infertility</i>, 21(3), 157–168.</p>	<ul style="list-style-type: none"> • 21 articles were reviewed, and clinical characteristics of 90 pregnant patients and 92 neonates born to mothers infected with COVID-19 were reviewed. There were no differences in the clinical characteristics of pregnant women and non-pregnant COVID-19 patients. <ul style="list-style-type: none"> ○ Three mothers were admitted to ICU and required mechanical ventilation; among them, one died, and one was on extracorporeal membrane oxygenation.
<p>Matar, R., Arahmani, L., Monzer, N., Debiante, L. G., Berbari, E., Fares, J., Fitzpatrick, F., & Murad, M. H. (Jun 23, 2020). Clinical Presentation and Outcomes of Pregnant Women With Coronavirus Disease 2019: A Systematic Review and Meta-analysis. <i>Clinical infectious diseases: an official publication of the Infectious Diseases Society of America</i>, 72(3), 521–533.</p>	<ul style="list-style-type: none"> • Based on 24 studies (136 women), the clinical picture in pregnant women with COVID-19 did not differ from the nonpregnant population. The most common symptoms were fever (62.9%) and cough (36.8%).

⁹ The six societies are: Society for Maternal-Fetal Medicine (SMFM), the American College of Obstetricians and Gynecologists (ACOG) from the United States, the Royal College of Obstetricians and Gynaecologists (RCOG) from the United Kingdom, the International Society of Ultrasound in Obstetrics and Gynecology (ISUOG), the Centers for Disease Control and Prevention (CDC), and the World Health Organization (WHO). The recommendations from the SMFM focus on high-risk pregnancies, and those from the ACOG and the RCOG focus on all pregnancies. The WHO and the CDC focus on recommendations that can be generalized across all patient populations, and ISUOG focuses on sonography and care of ultrasound equipment.

<p>Smith, V., Seo, D., Warty, R., Payne, O., Salih, M., Chin, K. L., Ofori-Asenso, R., Krishnan, S., da Silva Costa, F., Vollenhoven, B., & Wallace, E. (June 4, 2020). Maternal and neonatal outcomes associated with COVID-19 infection: A systematic review. <i>PloS one</i>, 15(6), e0234187.</p>	<ul style="list-style-type: none"> Based on data from nine studies (n=92), 67.4% (62/92) of women were symptomatic at presentation. COVID-19-positive pregnant women seem to present with fewer symptoms than the general population and may be RT-PCR negative despite having signs of viral pneumonia.
<p>Outcomes (e.g., hospital/ICU length of stay, hospital/ICU mortality, pre-term/emergent delivery, NICU admission)</p>	
<p>D'Antonio, F., Sen, C., Mascio, D. D., Galindo, A., Villalain, C., Herraiz, I., Arisoy, R., Ovayolu, A., Eroğlu, H., Canales, M. G., Ladella, S., Cojocar, L., Turan, O., Turan, S., Hadar, E., Brzezinski-Sinai, N. A., Dollinger, S., Uyaniklar, O., Ocakouglu, S. R., Atak, Z., ... On the behalf of the World Association of Perinatal Medicine working group on coronavirus disease 2019 (Jul 2021). Maternal and perinatal outcomes in high compared to low risk pregnancies complicated by severe acute respiratory syndrome coronavirus 2 infection (phase 2): the World Association of Perinatal Medicine working group on coronavirus disease 2019. <i>American journal of obstetrics & gynecology MFM</i>, 3(4), 100329. Advance online publication.</p>	<ul style="list-style-type: none"> This was a multinational retrospective cohort study involving women with laboratory-confirmed severe acute respiratory syndrome coronavirus 2 infection from 76 centers from 25 countries in Europe, the United States, South America, Asia, and Australia from April 4, 2020 to October 28, 2020. High-risk pregnancies were at high risk of adverse perinatal outcomes. However, such association was mainly because of the higher incidence of miscarriage in high-risk pregnancies compared with that in low-risk pregnancies. <ul style="list-style-type: none"> Pregnancies were considered high-risk in case of either pre-existing chronic medical conditions in pregnancy (pregestational diabetes mellitus, chronic hypertension, or autoimmune disease) or obstetrical disorders occurring in pregnancy (preeclampsia, gestational hypertension, or gestational diabetes mellitus). There was no difference found when assessing for fetal outcomes in high-risk pregnancies compared with that in low-risk pregnancies.
<p>Mark, E. G., McAleese, S., Golden, W. C., Gilmore, M. M., Sick-Samuels, A., Curless, M. S., Noguee, L. M., Milstone, A. M., & Johnson, J. (May 2021). Coronavirus Disease 2019 in Pregnancy and Outcomes Among Pregnant Women and Neonates: A Literature Review. <i>The Pediatric</i></p>	<ul style="list-style-type: none"> 196 studies published February 1, 2020 through August 15, 2020 reported 1,922 women with COVID-19 during pregnancy and 1,361 neonates with perinatal exposure. Most studies did not report final delivery outcome among women who were infected in the first or second trimester and remained pregnant at the time of infection, although there have been a few case reports of uncomplicated deliveries at term in convalesced mothers. <ul style="list-style-type: none"> There were 22 maternal deaths. Among women who delivered, 28% had a preterm birth and 57% had a Caesarean section. 68% of neonates with known disposition were separated from mother immediately after delivery and cared for in an isolation room in the nursery or NICU. Respiratory distress was the most common symptom among neonates with perinatal COVID-19 exposure.

<p><i>infectious disease journal</i>, 40(5), 473–478.</p>	<ul style="list-style-type: none"> • Neonatal length of stay was highly variable, with some case reports describing prolonged admission for isolation and observation despite lack of symptoms or positive testing.
<p>Karimi, L., Makvandi, S., Vahedian-Azimi, A., Sathyapalan, T., & Sahebkar, A. (Mar 5, 2021). Effect of COVID-19 on Mortality of Pregnant and Postpartum Women: A Systematic Review and Meta-Analysis. <i>Journal of pregnancy</i>, 2021, 8870129.</p>	<ul style="list-style-type: none"> • 117 studies with a total of 11,758 pregnant women were included in this review. • COVID-19 infection in pregnant women was associated with higher rates (and pooled proportions) of Caesarean section and mortality. <ul style="list-style-type: none"> ○ There were 153 deaths out of 11,758 pregnant and postpartum women affected by COVID-19 (1.30%), of which 19 deceased patients were in high-income countries including the United Kingdom, United States, Italy, Switzerland, France, Sweden, Portugal, Netherlands, Ireland, Spain, Canada, and Australia (mortality rate = 0.19%) and 134 women were in middle-income countries including China, Iran, Iraq, Jordan, Peru, Turkey, India, Venezuela, Thailand, Brazil, and Honduras (mortality rate = 8.51%). ○ The mode of delivery in deceased cases with sufficient data (n = 12) was as follows: 58.3% had Caesarean section, 25% had vaginal delivery, and 16.7% were not full term. • Duration from admission to death was between two and 22 days. The most common complication during treatment of COVID-19 in pregnant and postpartum women was acute respiratory distress syndrome (ARDS).
<p>La Verde, M., Riemma, G., Torella, M., Cianci, S., Savoia, F., Licciardi, F., Scida, S., Morlando, M., Colacurci, N., & De Franciscis, P. (Apr 30, 2021). Maternal death related to COVID-19: A systematic review and meta-analysis focused on maternal co-morbidities and clinical characteristics. <i>International journal of gynaecology and obstetrics</i>, 10.1002/ijgo.13726. Advance online publication.</p>	<ul style="list-style-type: none"> • Thirteen studies with 154 deceased patients were included. COVID-19 with at least one co-morbidity increases risk of intensive care and mortality. • Obesity doubled the risk of death. • No differences were found for gestational diabetes or asthma. • Overall, at least one severe co-morbidity showed a twofold increased risk of death. • Admission to intensive care was related to a fivefold increased risk of death, with no difference in need for respiratory support or mechanical ventilation.
<p>Villar, J., Ariff, S., Gunier, R. B., Thiruvengadam, R., Rauch, S., Kholin, A., Roggero, P., Prefumo, F., do Vale, M. S., Cardona-Perez, J. A., Maiz, N., Cetin, I., Savasi, V., Deruelle, P., Easter, S. R., Sichitiu, J., Soto Conti, C. P., Ernawati, E., Mhatre, M., Teji, J. S., ... Papageorghiou, A. T. (Apr 22, 2021). Maternal and Neonatal Morbidity and Mortality Among Pregnant Women With and Without COVID-19 Infection: The INTERCOVID Multinational Cohort Study. <i>JAMA pediatrics</i>, e211050. Advance online publication.</p>	<ul style="list-style-type: none"> • A total of 706 pregnant women with COVID-19 diagnosis and 1,424 pregnant women without COVID-19 diagnosis were enrolled in this cohort study that took place from March to October 2020, involving 43 institutions in 18 countries. • COVID-19 in pregnancy was associated with consistent and substantial increases in severe maternal morbidity and mortality and neonatal complications when pregnant women with and without COVID-19 diagnosis were compared. <ul style="list-style-type: none"> ○ Women with COVID-19 diagnosis were at higher risk for preeclampsia/eclampsia, severe infections, maternal mortality, preterm birth, medically indicated preterm birth, severe neonatal morbidity index, and severe perinatal morbidity and mortality index. ○ Fever and shortness of breath for any duration was associated with increased risk of severe maternal complications and neonatal complications. • Asymptomatic women with COVID-19 diagnosis remained at higher risk only for maternal morbidity and preeclampsia.

<p>Hapshy, V., Aziz, D., Kahar, P., Khanna, D., Johnson, K. E., & Parmar, M. S. (Apr 21, 2021). COVID-19 and Pregnancy: Risk, Symptoms, Diagnosis, and Treatment. <i>SN comprehensive clinical medicine</i>, 1–7. Advance online publication.</p>	<ul style="list-style-type: none"> Findings regarding maternal morbidity included an increased risk of acquiring severe COVID-19 infection requiring a higher level of inpatient hospital care along with an increased risk of preterm labour and Caesarean delivery.
<p>Wei, S. Q., Bilodeau-Bertrand, M., Liu, S., & Auger, N. (Apr 19, 2021). The impact of COVID-19 on pregnancy outcomes: a systematic review and meta-analysis. <i>CMAJ</i>, 193(16), E540–E548.</p>	<ul style="list-style-type: none"> 42 studies involving 438,548 people who were pregnant were included in the review. Compared with no infection, SARS-CoV-2 infection in pregnancy was associated with preeclampsia (OR 1.33, 95% CI 1.03 to 1.73; I2 = 31%; based on 13 studies), preterm birth (OR 1.82, 95% CI 1.38 to 2.39; I2 = 64%; 18 studies), stillbirth (OR 2.11, 95% CI 1.14 to 3.90; I2 = 24%; 6 studies), ICU admission (OR 4.78, 95% CI 2.03 to 11.25; I2 = 76%; 5 studies), lower birth weight (grams; mean difference -68.96, 95% CI -130.22 to -7.69; I2 = 29%; 13 studies) and NICU admission (OR 3.69, 95% CI 1.39 to 9.82; I2 = 94%; 10 studies). COVID-19 was not associated with gestational diabetes, Caesarean delivery, postpartum hemorrhage, or neonatal death compared with no COVID-19. Compared with asymptomatic COVID-19, symptomatic COVID-19 in pregnancy was associated with increased risk of preterm birth (OR 2.29, 95% CI 1.49 to 3.53; I2 = 57%; based on 9 studies) and Caesarean delivery (OR 1.57, 95% CI 1.32 to 1.85; I2 = 1%; 9 studies). Compared with mild COVID-19, severe COVID-19 was strongly associated with preeclampsia (OR 4.16, 95% CI 1.55 to 11.15; I2 = 0%; based on 5 studies), preterm birth (OR 4.29, 95% CI 2.41 to 7.63; I2 = 61%; 10 studies), gestational diabetes (OR 1.99, 95% CI 1.09 to 3.64; I2 = 14%; 5 studies), ICU admission (OR 15.46, 95% CI 5.79 to 41.23; I2 = 0%; 5 studies), mechanical ventilation (OR 19.31, 95% CI 9.38 to 39.72; I2 = 0%; 5 studies), Caesarean delivery (OR 2.58, 95% CI 1.64 to 4.06; I2 = 43%; 8 studies), low birth weight (OR 1.89, 95% CI 1.14 to 3.12; I2 = 0%; 2 studies) and NICU admission (OR 3.95, 95% CI 1.43 to 10.95; I2 = 79%; 5 studies).
<p>Aghaamoo, S., Ghods, K., & Rahmanian, M. (Apr 19, 2021). Pregnant women with COVID-19: the placental involvement and consequences. <i>Journal of molecular histology</i>, 1–9.</p>	<ul style="list-style-type: none"> COVID-19 may increase the frequency of abruption, preterm premature rupture of the membranes, preterm labour, and maternal death, stillbirth, intrauterine growth restriction, and newborns with fetal distress or admitted to the ICU. The adverse fetoneonatal consequences of COVID-19 might be associated with placental dysfunctions.
<p>Mirbeyk, M., Saghazadeh, A., & Rezaei, N. (Apr 2, 2021). A systematic review of pregnant women with COVID-19 and their neonates. <i>Archives of gynecology and obstetrics</i>, 1–34.</p>	<ul style="list-style-type: none"> 37 articles involving 364 pregnant women with COVID-19 and 302 neonates were included in this review. The vast majority of pregnant patients were in their third trimester of pregnancy, and only 45 cases were in the first or second trimester (12.4%). The course of COVID-19 in pregnant women resembles that of other populations. However, there is not sufficient evidence to establish that COVID-19 would not complicate pregnancy. Studies included a total of 302 neonates from mothers with COVID-19. Of the studies that provided data, there were 210 full-term and 65 preterm neonates. One baby was born dead from a mother who also died from COVID-19. Of the babies born alive from mothers with COVID-19, five newborns faced critical conditions, and two later died. There were 257 Caesarean sections and 42 vaginal delivery. This relatively higher rate of Caesarean sections would reflect the existence of indications for a Caesarean section as well as the role of fear of vertical transmission.

<p>Huntley, B., Mulder, I. A., Di Mascio, D., Vintzileos, W. S., Vintzileos, A. M., Berghella, V., & Chauhan, S. P. (Apr 2021). Adverse Pregnancy Outcomes Among Individuals With and Without Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2): A Systematic Review and Meta-analysis. <i>Obstetrics and gynecology</i>, 137(4), 585–596.</p>	<ul style="list-style-type: none"> • Six studies were included in this review, including 728 deliveries to patients who tested positive for SARS-CoV-2 and 3,836 contemporaneous deliveries to patients who tested negative. • The incidences of intrauterine fetal death and neonatal death were similar among individuals who tested positive compared with negative for SARS-CoV-2 when admitted to labour and delivery. Other immediate outcomes of the newborns were also similar among those born to individuals who tested positive compared with negative for SARS-CoV-2. <ul style="list-style-type: none"> ○ Intrauterine fetal death occurred in eight of 728 (1.1%) patients who tested positive and 44 of 3,836 (1.1%) who tested negative ($P=.60$). ○ Neonatal death occurred in zero of 432 (0.0%) patients who tested positive and five of 2,400 (0.2%) who tested negative ($P=.90$). ○ Preterm birth occurred in 95 of 714 (13.3%) patients who tested positive and 446 of 3,759 (11.9%) who tested negative ($P=.31$). ○ Maternal death occurred in three of 559 (0.5%) patients who tested positive and eight of 3,155 (0.3%) who tested negative ($P=.23$).
<p>Joseph, N. T., Rasmussen, S. A., & Jamieson, D. J. (Apr 2021). The effects of COVID-19 on pregnancy and implications for reproductive medicine. <i>Fertility and sterility</i>, 115(4), 824–830.</p>	<ul style="list-style-type: none"> • Adverse maternal and obstetrical outcomes appear to occur more often among pregnancies complicated by COVID-19 than among unaffected pregnancies. • Data from late second- and third-trimester pregnancies suggest an increased risk of adverse obstetrical outcomes associated with SARS-CoV-2 infection. • Pregnancies complicated by SARS-CoV-2 infection are associated with increased likelihood of Caesarean delivery (but it is unclear whether the indication for the Caesarean delivery was for worsening maternal status, other obstetrical indications, or concern for perinatal transmission) and preterm birth. Intrauterine transmission occurs, but seems to be rare.
<p>Chmielewska, B., Barratt, I., Townsend, R., Kalafat, E., van der Meulen, J., Gurol-Urganci, I., O'Brien, P., Morris, E., Draycott, T., Thangaratinam, S., Le Doare, K., Ladhani, S., von Dadelszen, P., Magee, L., & Khalil, A. (Mar 31, 2021). Effects of the COVID-19 pandemic on maternal and perinatal outcomes: a systematic review and meta-analysis. <i>The Lancet. Global health</i>, S2214-109X(21)00079-6. Advance online publication.</p>	<ul style="list-style-type: none"> • 40 studies were included in this analysis. Global maternal and fetal outcomes have worsened during the COVID-19 pandemic, with an increase in maternal deaths, stillbirth, ruptured ectopic pregnancies, and maternal depression. Some outcomes show considerable disparity between high-resource and low-resource settings. • There were significant increases in stillbirth (pooled OR 1.28 [95% CI 1.07–1.54]; $I^2=63%$; 12 studies, 168,295 pregnancies during and 198,993 before the pandemic) and maternal death (1.37 [1.22–1.53]; $I^2=0%$, two studies [both from low-income and middle-income countries], 1,237,018 and 2,224,859 pregnancies) during versus before the pandemic. • Preterm births before 37 weeks' gestation were not significantly changed overall (0.94 [0.87–1.02]; $I^2=75%$; 15 studies, 170,640 and 656,423 pregnancies), but were decreased in high-income countries (0.91 [0.84–0.99]; $I^2=63%$; 12 studies, 159,987 and 635,118 pregnancies), where spontaneous preterm birth was also decreased (0.81 [0.67–0.97]; two studies, 4,204 and 6,818 pregnancies). • Surgically managed ectopic pregnancies were increased during the pandemic (OR 5.81 [2.16–15.6]; $I^2=26%$; three studies, 37 and 272 pregnancies). • No overall significant effects were identified for other outcomes included in the quantitative analysis: maternal gestational diabetes; hypertensive disorders of pregnancy; preterm birth before 34 weeks', 32 weeks', or 28 weeks' gestation; iatrogenic preterm birth; labour induction; modes of delivery (spontaneous vaginal delivery, caesarean section, or instrumental delivery); post-partum haemorrhage; neonatal death; low birthweight (<2,500 g); or neonatal intensive care unit admission.
<p>Dubey, P., Thakur, B., Reddy, S., Martinez, C. A., Nurunnabi, M., Manuel, S. L., Chheda, S., Bracamontes, C., & Dwivedi, A. K. (Mar 24, 2021). Current trends and geographical differences in therapeutic profile and outcomes of COVID-19 among pregnant women -</p>	<ul style="list-style-type: none"> • 1,239 pregnant women with COVID-19 from 66 studies were analyzed. • The highest preterm birth and the average length of hospital stay (35%, 11.9 days) were estimated in Asian studies compared to the US studies (13%, 9.4 days) and European studies (29%, 7.3 days), respectively.

<p>a systematic review and meta-analysis. <i>BMC pregnancy and childbirth</i>, 21(1), 247.</p>	
<p>Elsaddig, M., & Khalil, A. (Mar 18, 2021). Effects of the COVID pandemic on pregnancy outcomes. <i>Best practice & research. Clinical obstetrics & gynaecology</i>, S1521-6934(21)00043-2.</p>	<ul style="list-style-type: none"> • Compared with pregnant women without COVID-19, pregnant women with symptomatic COVID-19 requiring admission to hospital have worse maternal outcomes, including death, although the absolute risk remains very low. • Caesarean section rates among pregnant women with COVID-19 are higher than in those without COVID-19. Studies also demonstrate a higher frequency of preterm births among women with COVID-19; the majority are iatrogenic, most likely related to the deterioration in maternal disease.
<p>Oltean, I., Tran, J., Lawrence, S., Ruschkowski, B. A., Zeng, N., Bardwell, C., Nasr, Y., de Nanassy, J., & El Demellawy, D. (Mar 2, 2021). Impact of SARS-CoV-2 on the clinical outcomes and placental pathology of pregnant women and their infants: A systematic review. <i>Heliyon</i>, 7(3), e06393.</p>	<ul style="list-style-type: none"> • Forty-one studies and case reports from 315 women confirmed to have SARS-CoV-2 and 262 neonates who underwent PCR testing were included in the review. Results suggest elevated rates of gestational diabetes, preeclampsia, C-sections, pre-term birth, and C-reactive protein (CRP) in comparison to pregnant women without SARS-CoV-2.
<p>Hudak M. L. (Feb 23, 2021). Consequences of the SARS-CoV-2 pandemic in the perinatal period. <i>Current opinion in pediatrics</i>, 33(2), 181–187.</p>	<ul style="list-style-type: none"> • Large population-based studies have conclusively demonstrated that pregnant women with a history of SARS-CoV-2 infection develop more severe disease than non-pregnant women and experience worse perinatal outcomes. • The severity of SARS-CoV-2 infection is greater in pregnant compared to non-pregnant women as measured by mortality and morbidities, including myocardial infarction, venous thromboembolic and other thrombotic events, preeclampsia, preterm labour, and preterm birth. • Despite lack of rigorous case definitions for perinatal transmission, cumulative transmission of SARS-CoV-2 infection from mother to infant by transplacental, perinatal, and postnatal routes appears to be low. • Infants appear to be at higher risk of testing positive for SARS-CoV-2 if the mother has tested positive within one week of delivery or is herself symptomatic at the time of maternity admission. • Infants who test positive in the hospital almost always have no or mild signs of disease, most of which may be attributable to prematurity, and rarely require readmission for clinical signs consistent with COVID-19.
<p>Soheili, M., Moradi, G., Baradaran, H. R., Soheili, M., Mokhtari, M. M., & Moradi, Y. (Feb 18, 2021). Clinical manifestation and maternal complications and neonatal outcomes in pregnant women with COVID-19: a comprehensive evidence synthesis and meta-analysis. <i>The journal of maternal-fetal & neonatal medicine: the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania</i></p>	<ul style="list-style-type: none"> • 74 studies with total 5,560 pregnant women included in this systematic review. • Pregnant women with COVID-19 with or without pneumonia are at a higher risk of preeclampsia, preterm birth, miscarriage, and Caesarean delivery. • The risk of LBW and intrauterine fetal distress seems to be increased in neonates.

<p><i>Perinatal Societies, the International Society of Perinatal Obstetricians, 1–14. Advance online publication.</i></p>	
<p>Cavalcante, M. B., Cavalcante, C., Sarno, M., Barini, R., & Kwak-Kim, J. (Feb 2021). Maternal immune responses and obstetrical outcomes of pregnant women with COVID-19 and possible health risks of offspring. <i>Journal of reproductive immunology</i>, 143, 103250.</p>	<ul style="list-style-type: none"> • Mortality in pregnant women with COVID-19 appears to be similar to that observed among pregnant women without COVID-19 and the general population. <ul style="list-style-type: none"> ○ The COVID-19 related maternal mortality ratio (MMR) in 194 obstetric units in the UK was 1% (5/427 pregnant women) and in 33 French maternity units was 0.2 % (1/617 pregnant women). ○ An epidemiological study of reproductive age women with COVID-19, performed in the period January 22 - June 7, 2020 in the US revealed that pregnant women have the same MR as non-pregnant women [16/8,207 (0.2 %) vs. 208/83,205 (0.2 %), adjusted Relative Risk (aRR) 0.9, 95 % confidence interval (CI) 0.5–1.5]. However, pregnant women with COVID-19 were more likely to be admitted to the ICU (aRR 1.5, 95 % CI 1.2–1.8) and receive mechanical ventilation (aRR 1.7, 95 % CI 1.2–2.4). ○ Contrarily, a study reported a significantly higher MMR among Brazilian pregnant women with COVID-19 (12.7 %) than that of the general population (overall 5%). • Initial studies demonstrate a possible association between COVID-19 and preterm birth, intrauterine growth restriction, and low birth weight, which have been reported to increase risks for long-term non-communicable diseases in adulthood. The association between COVID-19 and long-term sequelae is uncertain and hypothetical at this point. Therefore, the establishment of a long-term follow-up plan for the offspring of pregnant women affected by COVID-19 should be carefully established.
<p>Novoa, R. H., Quintana, W., Llancarí, P., Urbina-Quispe, K., Guevara-Ríos, E., & Ventura, W. (Jan-Feb 2021). Maternal clinical characteristics and perinatal outcomes among pregnant women with coronavirus disease 2019. A systematic review. <i>Travel medicine and infectious disease</i>, 39, 101919.</p>	<ul style="list-style-type: none"> • 143 articles were selected for full-text assessment; 33 for descriptive analyses, and 4 case-controls for meta-analysis. For the descriptive analysis, the study included a total of 322 pregnant women, 111 (34.5%) patients from Netherlands, 80 (24.8%) from US, 76 (23.6%) from China, 43 (13.3%) from Italy, 2 (0.6%) from Canada, and one each from Honduras, South Korea, Sweden, Germany, Turkey, Iran, Australia, Spain, Peru, and India. • 195 (60.6%) delivered, and 125 (38.8%) remained pregnant during the study. • Caesarean was reported in 99 (50.8%) women and vaginal delivery in 64 (32.8%). • The main adverse obstetric outcome found is iatrogenic preterm delivery (i.e. Caesarean or induction delivery due to worsening of the medical or obstetric condition). • There was a considerable proportion of low birth weight infants and neonates requiring admission to the NICU. Twenty-four (27.9%) newborns were severely ill, requiring NICU admission, but only two (5.6%) required mechanical ventilation.
<p>Jafari, M., Pormohammad, A., Sheikh Neshin, S. A., Ghorbani, S., Bose, D., Alimohammadi, S., Basirjafari, S., Mohammadi, M., Rasmussen-Ivey, C., Razizadeh, M. H., Nouri-Vaskeh, M., & Zarei, M. (Jan 2, 2021). Clinical characteristics and outcomes of pregnant women with COVID-19 and comparison with control patients: A systematic review and meta-analysis. <i>Reviews in medical virology</i>, e2208.</p>	<ul style="list-style-type: none"> • In this large-scale study, 128,176 non-pregnant patients (228 studies) and 10,000 pregnant patients (121 studies) with confirmed COVID-19 cases were included in a meta-analysis. The mean of age and gestational age of admission in pregnant women was 33 years old and 36 weeks, respectively. • Case fatality rate (CFR) of non-pregnant hospitalized patients is 6.4% (4.4-8.5), and mortality due to all-cause for pregnant patients with COVID-19 is 11.3% (9.6-13.3). • Regarding the complications of pregnancy, postpartum hemorrhage, caesarean delivery, preterm labour, and preterm birth are in turn the most prevalent complications. • Caesarean delivery, low birth weight (LBW), and preterm birth are more probable in pregnant woman with COVID-19 than pregnant women without COVID-19. • The most prevalent neonatal complications are neonatal intensive care unit admission, fetal distress, and LBW. • Interpretations of these results should be done cautiously due to the heterogeneity between studies.

<p>Papapanou, M., Papaioannou, M., Petta, A., Routsis, E., Farmaki, M., Vlahos, N., & Siristatidis, C. (Jan 2021). Maternal and Neonatal Characteristics and Outcomes of COVID-19 in Pregnancy: An Overview of Systematic Reviews. <i>International journal of environmental research and public health</i>, 18(2), 596.</p>	<ul style="list-style-type: none"> • Thirty-nine reviews were analyzed. Increased rates of Caesarean sections and preterm birth rates were found, with iatrogenic reasons potentially involved. <ul style="list-style-type: none"> ○ Reported rates, regarding both preterm and term gestations, varied between 52.3-95.8% for Caesarean sections; 4.2-44.7% for vaginal deliveries; 14.3-63.8% specifically for preterm deliveries and 22.7-32.2% for preterm labour; and 5.3-12.7% for PROM and 6.4-16.1% for pPROM. ○ Maternal mortality rate was <2%, while stillbirth, neonatal ICU admission, and mortality rates were <2.5%, 3.1–76.9%, and <3%, respectively. Concerning mortality rates, available data were more contradictory. The increased rates, when reported, have been also attributed to the specific health care provision of the participants' countries. Neonates were more frequently admitted to NICU, which may be attributed to precaution or severe maternal infection. ○ After accounting for the quality of the studies, ranges of the primary outcomes remained almost unchanged. • It should not be overseen that assessment of the existing systematic reviews, using the AMSTAR 2 tool, classified 59% of them as “critically low quality” to “low quality”. However, it should be taken into account that currently available systematic reviews based their results on a large number of preliminary studies conducted due to the urgent need for quick answers. For these reasons, further original studies with women from all pregnancy trimesters and longer follow-up periods, and, consequently, further systematic reviews synthesizing their results, are required to provide clinical practice with more definite answers regarding the effects of SARS-CoV-2 infection on such a sensitive group of patients as pregnant women and their fetuses/neonates. So far, data are not robust enough to lead to definite points and regulations.
<p>Bellos, I., Pandita, A., & Panza, R. (Jan 2021). Maternal and perinatal outcomes in pregnant women infected by SARS-CoV-2: A meta-analysis. <i>European journal of obstetrics, gynecology, and reproductive biology</i>, 256: 194–204.</p>	<ul style="list-style-type: none"> • This meta-analysis of 16 observational studies and 44 case reports/series found that the maternal and neonatal clinical course for COVID-19 is typically mild, presenting low mortality rates. <ul style="list-style-type: none"> ○ The rate of neonatal transmission did not differ between women with and without severe disease. ○ Caesarean section rates were high, mainly due to concerns about perinatal transmission. • The incidence of preterm birth was remarkable, although the risk of preeclampsia and placental previa were estimated to be low.
<p>Di Toro, F., Gjoka, M., Di Lorenzo, G., De Santo, D., De Seta, F., Maso, G., Riso, F. M., Romano, F., Wiesenfeld, U., Levi-D'Ancona, R., Ronfani, L., & Ricci, G. (Jan 2021). Impact of COVID-19 on maternal and neonatal outcomes: a systematic review and meta-analysis. <i>Clinical microbiology and infection: the official publication of the European Society of Clinical Microbiology and Infectious Diseases</i>, 27(1), 36–46.</p>	<ul style="list-style-type: none"> • Twenty-four articles, including 1,100 pregnancies, were selected. The study population was composed of 511 Chinese women, 482 European women, 107 North American women. • Although adverse outcomes such as ICU admission or patient death can occur, the clinical course of COVID-19 in most women is not severe, and the infection does not significantly influence the pregnancy. This meta-analysis shows a high frequency of preterm births and caesarean deliveries and a low rate of breastfeeding, not fully explained by the severity of maternal disease or fetal compromise. <ul style="list-style-type: none"> ○ Three stillbirths and five maternal deaths were reported. ○ A pooled prevalence of 85% (95% CI 72–94) was observed for caesarean deliveries. ○ There were three neonatal deaths. ○ The prevalence of COVID-19-related admission to the neonatal intensive care unit was 2% (95% CI 0–6). • The pooled prevalence of preterm delivery was 23%. This rate seems to be higher than that observed in the general obstetric population, where it ranges from about 5% in several European countries to 18% in some African countries. The data show that higher frequency was due to worsening maternal and fetal conditions with the need to deliver prematurely, but also to rupture of membranes and spontaneous delivery. It is unclear, however, whether COVID-19 might be the direct cause of preterm delivery; viral infection during pregnancy can induce an abnormal response to an opportunistic bacterial infection that might lead to preterm labour and delivery.
<p>Wang, C. L., Liu, Y. Y., Wu, C. H., Wang, C. Y., Wang, C. H., & Long, C. Y. (Jan 1, 2021). Impact of COVID-19</p>	<ul style="list-style-type: none"> • In pregnant women who develop COVID-19 pneumonia, early data have shown higher rates of preterm and Caesarean delivery compared to non-pregnant women. • All studies included in this review were case reports or series of low quality.

<p>on Pregnancy. <i>International journal of medical sciences</i>, 18(3), 763–767.</p>	
<p>Chi, J., Gong, W., & Gao, Q. (Dec 1, 2020). Clinical characteristics and outcomes of pregnant women with COVID-19 and the risk of vertical transmission: a systematic review. <i>Archives of gynecology and obstetrics</i>, 303(2), 337–345.</p>	<ul style="list-style-type: none"> • This systematic review summarizes the clinical features and maternal–infant outcomes of 230 women with COVID-19 (154 deliveries, 66 ongoing pregnancies, and 10 abortions) and 156 newborns from 20 eligible studies. A total of 34.62% of the pregnant patients had obstetric complications. • Common obstetric complications, such as gestational hypertension, preeclampsia, and gestational diabetes mellitus, may affect the outcomes. • Caesarean section was more common than vaginal delivery for pregnant women with COVID-19. Premature delivery was the main adverse event for newborns. • The most common adverse pregnancy outcome, premature delivery, occurred in up to 24.74% of pregnant women. Premature rupture of membranes, fetal distress, and even fetal death were also reported. One mother and two newborns died (the maternal mortality rate was 0.43%, and the neonatal mortality rate was 1.28%).
<p>Hassanipour, S., Faradonbeh, S. B., Momeni, K., Heidarifard, Z., Khosousi, M. J., Khosousi, L., Ameri, H., & Arab-Zozani, M. (Dec 2020). A systematic review and meta-analysis of pregnancy and COVID-19: Signs and symptoms, laboratory tests, and perinatal outcomes. <i>International journal of reproductive biomedicine</i>, 18(12), 1005–1018.</p>	<ul style="list-style-type: none"> • A total of 10 articles were reviewed in this study, which analyzed 135 pregnant women, all of whom were in the third trimester of pregnancy. • The majority of pregnancies ended up with Caesarean section, which is much higher than the WHO's recommendation for vaginal route delivery.
<p>Amaral, W., Moraes, C. L., Rodrigues, A., Noll, M., Arruda, J. T., & Mendonça, C. R. (Dec 2020). Maternal Coronavirus Infections and Neonates Born to Mothers with SARS-CoV-2: A Systematic Review. <i>Healthcare</i> (Basel, Switzerland), 8(4), 511.</p>	<ul style="list-style-type: none"> • The 70 selected studies included a total of 1,457 pregnant women diagnosed with COVID-19 in the first, second, and third trimesters of pregnancy, as well as 1,042 newborns from infected mothers. <ul style="list-style-type: none"> ○ Of the 70 studies included, 34 were carried out in China, 10 in the United States, eight in Italy, three in Iran, one in Korea, one in Turkey, one in Peru, one in Switzerland, two in France, four in Spain, one in Australia, one in the Netherlands and Ireland, one in Canada, one in the United Kingdom, and one in Sweden. • This review indicates that COVID-19 during pregnancy can result in maternal, fetal, and neonatal complications. Among maternal and fetal outcomes, premature birth ($n = 64$), maternal death ($n = 15$), intrauterine fetal death or neonatal death ($n = 16$), cases of intrauterine fetal distress ($n = 28$), miscarriage ($n = 7$), decreased fetal movements ($n = 19$), and severe neonatal asphyxia ($n = 5$) were the most frequent. • Among neonates born to infected mothers, 187 (17.9%) required admission to neonatal ICUs. • There were 15 (1.0%) cases of maternal death, mostly from United Kingdom ($n = 5$) and Iran ($n = 7$).
<p>University of Birmingham. (Nov 29, 2020). PregCOV-19 Living Systematic Review: COVID-19 and maternal outcomes.</p> <p>*The findings are to be published shortly and is currently undergoing peer review.</p>	<ul style="list-style-type: none"> • The PregCOV-19 project conducts a series of living systematic reviews involving pregnant and postnatal women at risk, suspected, and diagnosed to have COVID-19. • As of November 29, 2020, based on data from 192 studies across 30 countries that included 64,676 pregnant women suspected or confirmed with COVID-19: <ul style="list-style-type: none"> ○ 17% delivered preterm before 37 weeks, and 6% had spontaneous preterm birth. ○ Pregnant women with COVID-19 are also at increased risk of delivering preterm, and their babies being admitted to the neonatal unit compared to pregnant women without COVID-19. The estimates for preterm birth are likely to be influenced by iatrogenic indications. • Some women were still pregnant at the end of the study period and outcomes were not known.

<p>Rodrigues, C., Baía, I., Domingues, R., & Barros, H. (Nov 23, 2020). Pregnancy and Breastfeeding During COVID-19 Pandemic: A Systematic Review of Published Pregnancy Cases. <i>Frontiers in public health</i>, 8, 558144.</p>	<ul style="list-style-type: none"> • The review identified 161 original studies reporting 3,985 cases of pregnant women with COVID-19 (1,007 discharged while pregnant). The majority of cases occurred in the USA (n = 1,206, 30%), China (n = 823, 21%), France (n = 672, 17%), UK (n = 440, 11%), Mexico (n = 308, 8%), Spain (n = 241, 6%), and Italy (n = 202, 5%). Maternal age ranged from 15 to 49 years. • Although the complications appear to be similar to those of non-pregnant women, services must be prepared to attend to complications, especially in pregnant women with comorbidities. <ul style="list-style-type: none"> ○ The 2,059 published cases with pregnancy outcomes resulted in 42 abortions, 21 stillbirths, and 2,015 live births. ○ Preterm birth occurred in 23% of cases. Most of preterm births were iatrogenic for maternal and/or fetal compromise. ○ There were 10 neonatal deaths. • Twenty-eight maternal deaths with COVID-19 were reported (0.7%).
<p>Abou Ghayda, R., Li, H., Lee, K. H., Lee, H. W., Hong, S. H., Kwak, M., Lee, M., Kwon, M., Koyanagi, A., Kronbichler, A., Jacob, L., Smith, L., & Shin, J. I. (Nov 2020). COVID-19 and Adverse Pregnancy Outcome: A Systematic Review of 104 Cases. <i>Journal of clinical medicine</i>, 9(11), 3441.</p>	<ul style="list-style-type: none"> • 11 case series studies comprising 104 pregnant women with COVID-19 were included in the review. Ninety-one cases originated from China, and nine cases from Iran and four cases from Italy. • Although the review found that pregnancy with COVID-19 has significantly higher maternal mortality ratio compared to that of pregnancy without the disease, the authors concluded that evidence is too weak to state that COVID-19 results in poorer maternal outcome due to multiple factors. The number of COVID-19 pregnancy outcomes was not large enough to draw a conclusion and long-term outcomes are yet to be determined as the pandemic is still unfolding. • Caesarean section was the mode of delivery for half of the women (50.0%), although no information was available for 28.8% of the cases. • Regarding obstetrical and neonatal outcomes, fetal distress (13.5%), pre-labour rupture of membranes (9.6%), prematurity (8.7%), fetal death (4.8%), and abortion (2.9%) were reported.
<p>Yee J, Kim W, Han JM, et al. (Oct 22, 2020). Clinical manifestations and perinatal outcomes of pregnant women with COVID-19: a systematic review and meta-analysis. <i>Sci Rep.</i>;10(1):18126.</p>	<ul style="list-style-type: none"> • Based on 11 Chinese studies involving with 9,032 pregnant women with COVID-19 and 338 infants in a meta-analysis, around 30% of pregnant women with COVID-19 experienced preterm delivery, whereas the mean birth weight was 2,855.9 g. Fetal death and detection of SARS-CoV-2 were observed in about 2%, whereas neonatal death was found to be 0.4%
<p>Figueiro-Filho, E. A., Yudin, M., & Farine, D. (Oct 2, 2020). COVID-19 during pregnancy: an overview of maternal characteristics, clinical symptoms, maternal and neonatal outcomes of 10,996 cases described in 15 countries. <i>Journal of perinatal medicine</i>, 48(9), 900–911.</p>	<ul style="list-style-type: none"> • Based on eight studies representing 10,966 cases distributed in 15 countries around the world (Canada, US, Honduras, Brazil, Peru, Spain, Italy, France, Netherlands, Sweden, Turkey, Iran, China, Korea, and Australia) until July 20, 2020, the maternal and neonatal outcomes are not worse or different from the general population. • Live birth was present in 98% of reports, with 78% term deliveries. • Preterm birth <37 weeks was seen in 21% of cases. • The majority of cases had no newborn complications, although admission to NICU was reported in almost 20% of cases. • Fetal demise/stillbirth rates were 1.7% (19/11,130), neonatal death described in 0.8% (9/1,137), and SARS-COV2-Negative tests were found in 98.4% of neonates (1,098/1,116). • Of note is that the neonatal information was not retrieved from all studies and some of them had no information on babies' outcomes.
<p>Diriba, K., Awulachew, E., & Getu, E. (Sept 4, 2020). The effect of coronavirus infection (SARS-CoV-2, MERS-CoV, and SARS-CoV) during pregnancy and the possibility of vertical maternal-fetal transmission: a</p>	<ul style="list-style-type: none"> • 39 studies involving 1,316 pregnant women (1,271 with SARS-CoV-2, 12 with MERS-CoV, and 33 with SARS-CoV) were included in this systematic review and meta-analysis. The study found that pregnant women infected with coronaviruses are at increased risk of adverse obstetrical outcomes, compared with the general population. • 25 studies reported information on infections caused by SARS-CoV-2 among a total of 1,271 pregnancies. <ul style="list-style-type: none"> ○ The rate of maternal death was reported in 1.5% of cases.

<p>systematic review and meta-analysis. <i>European journal of medical research</i>, 25(1), 39.</p>	<ul style="list-style-type: none"> ○ The prevalence of SARS-CoV-2 among preterm birth at <37 and 34 weeks of gestation was 14.3% and 8.9%, respectively, while 46.2% of pregnant women give birth at >37 weeks of gestation. ○ Preeclampsia was reported among 5.7% of pregnant women with COVID-19. ○ pPROM was reported in 8.9%, while the rate of fetal growth restriction was reported in 1.2%. ○ Miscarriage was rated 2.4%. ○ The prevalence of Caesarean delivery was 57%. ○ Fetal distress was reported among 25%, while the rate of neonatal asphyxia was 1.6%. ● The rate of newborns admitted to NICU was 11.6%, with perinatal death reported in 2.9% of cases.
<p>Allotey, J., Stallings, E., Bonet, M., Yap, M., Chatterjee, S., Kew, T., Debenham, L., Llavall, A. C., Dixit, A., Zhou, D., Balaji, R., Lee, S. I., Qiu, X., Yuan, M., Coomar, D., van Wely, M., van Leeuwen, E., Kostova, E., Kunst, H., Khalil, A., ... for PregCOV-19 Living Systematic Review Consortium (Sept 1, 2020). Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. <i>BMJ</i> (Clinical research ed.), 370, m3320.</p>	<ul style="list-style-type: none"> ● This living systematic review and meta-analysis of 192 studies. Compared to pregnant women without COVID-19, those with the disease had increased odds of maternal death, of needing admission to the intensive care unit, and of preterm birth. ● Overall, 339 pregnant women with confirmed COVID-19 died from any cause. ● The odds of admission to the neonatal intensive care unit were higher in babies born to mothers with COVID-19 versus those without COVID-19.
<p>Dubey, P., Reddy, S. Y., Manuel, S., & Dwivedi, A. K. (Sept 2020). Maternal and neonatal characteristics and outcomes among COVID-19 infected women: An updated systematic review and meta-analysis. <i>European journal of obstetrics, gynecology, and reproductive biology</i>, 252, 490–501.</p>	<ul style="list-style-type: none"> ● A total of 790 COVID-19 positive females and 548 neonates from 61 studies were analyzed. Adverse pregnancy outcomes were prevalent in COVID-19 infected females and varied by location, type, and size of the studies. ● The rates of C-section, premature birth, low birth weight, and adverse pregnancy events were estimated as 72%, 23%, 7%, and 27% respectively. ● In the heterogeneity analysis, the rate of C-section was substantially higher in Chinese studies (91%) compared to the US (40%) or European (38%) studies. The rates of preterm birth and adverse pregnancy events were also lowest in the US studies (12%, 15%) compared to Chinese (17%, 21%), and European studies (19%, 19%). ● In case reports, the rates of C-section, preterm birth, and low birth weight were estimated as 69%, 56%, and 35%, respectively. ● Adverse pregnancy outcomes were associated with infection acquired at early gestational ages, more symptomatic presentation, myalgia symptom at presentation, and use of oxygen support therapy.
<p>Pettiroso, E., Giles, M., Cole, S., & Rees, M. (Aug 10, 2020). COVID-19 and pregnancy: A review of clinical characteristics, obstetric outcomes and vertical transmission. <i>The Australian & New Zealand journal of</i></p>	<ul style="list-style-type: none"> ● Sixty articles were included in this review. Some pregnant participants may have been included in multiple publications, as admission dates overlap for reports from the same hospital. However, a total of 1,287 confirmed SARS-CoV-2 positive pregnant cases are reported. ● Of the 22 studies that identified and reported outcomes for women diagnosed with COVID-19 at less than 37 weeks gestation, preterm birth was reported in 10% to 100% of cases. <ul style="list-style-type: none"> ○ Prevalence of preterm birth was elevated in numerous studies; however, those with the highest rates tended to have the smallest participant numbers.

<p><i>obstetrics & gynaecology</i>, 60(5), 640–659.</p>	<ul style="list-style-type: none"> ○ Preterm delivery occurred due to: an obstetric indication (preterm labour, preterm prelabour rupture of membranes, fetal distress), worsening COVID-19, for no reported indication, or a combination of these causes. ○ Three studies compared the rates of preterm birth between rtPCR-confirmed SARS-CoV-2 positive and negative pregnant women. Two studies identified no significant difference between groups, while one study noted an increased incidence of preterm birth in the SARS-CoV-2 positive group. ● Caesarean section was commonly performed for patients with COVID-19. As such, the incidence of caesarean section in most studies ranged from 40% to 100%.
<p>Narang, K., Enninga, E., Gunaratne, M., Ibirogba, E. R., Trad, A., Elrefaei, A., Theiler, R. N., Ruano, R., Szymanski, L. M., Chakraborty, R., & Garovic, V. D. (Aug 2020). SARS-CoV-2 Infection and COVID-19 During Pregnancy: A Multidisciplinary Review. <i>Mayo Clinic proceedings</i>, 95(8), 1750–1765.</p>	<ul style="list-style-type: none"> ● This review summarizes nine guidelines (updated as of April 22, 2020) from six societies^h for medical/obstetric care and outlines future directions for optimization of treatment and preventive strategies for pregnant patients with COVID-19 with the understanding that relevant data are limited and rapidly changing. ● Studies to date have reported higher risks of pregnancy complications, including preterm birth and preeclampsia, as well as higher rates of Caesarean delivery.
<p>Pierce-Williams, R., Burd, J., Felder, L., Khoury, R., Bernstein, P. S., Avila, K., Penfield, C. A., Roman, A. S., DeBolt, C. A., Stone, J. L., Bianco, A., Kern-Goldberger, A. R., Hirshberg, A., Srinivas, S. K., Jayakumar, J. S., Brandt, J. S., Anastasio, H., Birsner, M., O'Brien, D. S., Sedev, H. M., ... Berghella, V. (Aug 2020). Clinical course of severe and critical coronavirus disease 2019 in hospitalized pregnancies: a United States cohort study. <i>American journal of obstetrics & gynecology MF</i>, 2(3), 100134.</p>	<ul style="list-style-type: none"> ● This cohort study of 64 pregnant women with severe or critical COVID-19 hospitalized at 12 US institutions between March 5, 2020, and April 20, 2020 found 44 (69%) had severe disease, and 20 (31%) had critical disease. Data suggest that the clinical course of severe or critical COVID-19 in hospitalized pregnant women may be shorter than in hospitalized nonpregnant patients. ● In pregnant women with severe or critical COVID-19, admission into the hospital typically occurred about seven days after symptom onset, and the duration of hospitalization was six days (six [severe group] vs 12 [critical group]). ● Women with critical disease had a high rate of acute respiratory distress syndrome, and there was one case of cardiac arrest, but there were no cases of cardiomyopathy or maternal mortality. ● Hospitalization of pregnant women with severe or critical COVID-19 resulted in delivery during the clinical course of the disease in 50% of this cohort, usually in the third trimester. ● There were no perinatal deaths in this cohort.
<p>Gao, Y. J., Ye, L., Zhang, J. S., Yin, Y. X., Liu, M., Yu, H. B., & Zhou, R. (Aug 3, 2020). Clinical features and</p>	<ul style="list-style-type: none"> ● The meta-analysis included 236 pregnant women with COVID-19 (160 pregnant women with COVID-19 in China and 76 pregnant women with COVID-19 in America).

^h The six societies are: Society for Maternal-Fetal Medicine (SMFM), the American College of Obstetricians and Gynecologists (ACOG) from the United States, the Royal College of Obstetricians and Gynaecologists (RCOG) from the United Kingdom, the International Society of Ultrasound in Obstetrics and Gynecology (ISUOG), the Centers for Disease Control and Prevention (CDC), and the World Health Organization (WHO). The recommendations from the SMFM focus on high-risk pregnancies, and those from the ACOG and the RCOG focus on all pregnancies. The WHO and the CDC focus on recommendations that can be generalized across all patient populations, and ISUOG focuses on sonography and care of ultrasound equipment.

<p>outcomes of pregnant women with COVID-19: a systematic review and meta-analysis. <i>BMC infectious diseases</i>, 20(1), 564.</p>	<ul style="list-style-type: none"> ○ The results were as follows: caesarean section (65%; 95% CI, 0.42–0.87), fetal distress (29%; 95% CI, 0.08–0.49), preterm labour (23%; 95% CI, 0.14–0.32), and severe case or death (12%; 95% CI, 0.03–0.20). ● The rate of preterm labour is higher among pregnant with COVID-19 than among normal pregnant women. The rate of preterm labour in normal pregnant women who are healthy and not infected with any virus worldwide is approximately 11%, which is lower than the result in this article (23%). The possible reason for the higher rate is that women in the third trimester of pregnancy induce delivery early after becoming ill with COVID-19 to proceed with further treatment. Most of these women choose early delivery by caesarean section to avoid a prolonged labour, which may worsen COVID-19 for pregnant women and increase the risk of infection for the medical staff.
<p>Ashraf, M. A., Keshavarz, P., Hosseinpour, P., Erfani, A., Roshanshad, A., Pourdast, A., Nowrouzi-Sohrabi, P., Chaichian, S., & Poordast, T. (Jul-Sept 2020). Coronavirus Disease 2019 (COVID-19): A Systematic Review of Pregnancy and the Possibility of Vertical Transmission. <i>Journal of reproduction & infertility</i>, 21(3), 157–168.</p>	<ul style="list-style-type: none"> ● 21 articles were reviewed, and clinical characteristics of 90 pregnant patients and 92 neonates born to mothers infected with COVID-19 were reviewed. <ul style="list-style-type: none"> ○ The most commonly reported complications were preterm labour and fetal distress. ● Out of 92 neonates, one died, and one was born dead. Breathing problems and pneumonia were reported as the most common neonatal complications.
<p>Matar, R., Alrahmani, L., Monzer, N., Debiane, L. G., Berbari, E., Fares, J., Fitzpatrick, F., & Murad, M. H. (Jun 23, 2020). Clinical Presentation and Outcomes of Pregnant Women With Coronavirus Disease 2019: A Systematic Review and Meta-analysis. <i>Clinical infectious diseases: an official publication of the Infectious Diseases Society of America</i>, 72(3), 521–533.</p>	<ul style="list-style-type: none"> ● Based on 24 studies (136 women), the rate of preterm birth and Caesarean delivery are considerably higher than international averages: <ul style="list-style-type: none"> ○ The preterm birth rate was 37.7% and Caesarean delivery rate was 76%. ○ There was one maternal death. ● There were two fetal COVID-19 cases.
<p>Smith, V., Seo, D., Warty, R., Payne, O., Salih, M., Chin, K. L., Ofori-Asenso, R., Krishnan, S., da Silva Costa, F., Vollenhoven, B., & Wallace, E. (June 4, 2020). Maternal and neonatal outcomes associated with COVID-19 infection: A systematic review. <i>PloS one</i>, 15(6), e0234187.</p>	<ul style="list-style-type: none"> ● Based on data from nine studies (n=92), 67.4% (62/92) of women were symptomatic at presentation. The incidence of preterm births, low birth weight, C-section, and NICU admission appear higher than the general population: <ul style="list-style-type: none"> ○ Maternal mortality rate was 0% and only one patient required intensive care and ventilation. ○ 63.8% (30/47) had preterm births, 61.1% (11/18) fetal distress, and 80% (40/50) a Caesarean section. ● 76.92% (11/13) of neonates required NICU admission and 42.8% (40/50) had a low birth weight.

Management (e.g., organization/care considerations, delivery)	
<p>Mark, E. G., McAleese, S., Golden, W. C., Gilmore, M. M., Sick-Samuels, A., Curless, M. S., Noguee, L. M., Milstone, A. M., & Johnson, J. (May 2021). Coronavirus Disease 2019 in Pregnancy and Outcomes Among Pregnant Women and Neonates: A Literature Review. <i>The Pediatric infectious disease journal</i>, 40(5), 473–478.</p>	<ul style="list-style-type: none"> Recommended infection control measures in the home after hospital discharge of mother and baby include physical distancing when possible and use of a mask and hand hygiene during breast-feeding and other newborn care. Similarly, infection control measures must be implemented in health care facilities to reduce risk of postnatal acquisition from an infected caregiver, especially given high rates of asymptomatic infection.
<p>Aghaamoo, S., Ghods, K., & Rahmadian, M. (Apr 19, 2021). Pregnant women with COVID-19: the placental involvement and consequences. <i>Journal of molecular histology</i>, 1–9.</p>	<ul style="list-style-type: none"> Close coordination and collaboration between midwifery and neonatal unit are needed to manage the maternal and fetoneonatal outcomes following infection. Accordingly, a program should be developed in hospitals to implement strict infection control measures and screen pregnant women, quarantine infected women, and monitor neonates closely at the risk of COVID-19.
<p>Joseph, N. T., Rasmussen, S. A., & Jamieson, D. J. (Apr 2021). The effects of COVID-19 on pregnancy and implications for reproductive medicine. <i>Fertility and sterility</i>, 115(4), 824–830.</p>	<ul style="list-style-type: none"> The response to COVID-19 has brought about innovations around health system delivery, including the widespread rapid implementation of telehealth. For example, during the pandemic, the CDC recommended optimizing use of telehealth services and the federal government improved access to telehealth services in the US. In addition, the American College of Obstetricians and Gynecologists published recommendations for telehealth use in February 2020. Models of prenatal care that reduce in-person visits and increase telehealth visits were rapidly integrated into many health care systems. In addition to potentially reducing the risk of exposure in the health care setting, models such as this found high patient satisfaction. In addition, this has the capacity to improve access, attendance, and utilization of pregnancy services to those previously unable to access care. In this way, health systems are capitalizing on health information technologies and mobile health platforms to improve access, especially to those in remote or resource-limited settings.
<p>Pountoukidou, A., Potamiti-Komi, M., Sarri, V., Papapanou, M., Routsis, E., Tsiatsiani, A. M., Vlahos, N., & Siristatidis, C. (Apr 2021). Management and Prevention of COVID-19 in Pregnancy and Pandemic Obstetric Care: A Review of Current Practices. <i>Healthcare (Basel, Switzerland)</i>, 9(4), 467.</p>	<ul style="list-style-type: none"> This review aimed to summarize the up-to-date information about the prevention and management of suspected/confirmed SARS-CoV-2 infection in obstetric patients and obstetric care during prenatal, intrapartum, and postpartum periods. Recommendations are currently based on limited available data. More original studies on infected pregnant women are needed to establish totally evidence-based protocols of care for these patients. Some of the main recommendations are listed below: <ul style="list-style-type: none"> Women with a low risk for infection and uncomplicated pregnancy: Elective and non-urgent appointments should be postponed or completed through telehealth. Vaccination should be discussed and distance and personal hygiene preventive measures should be recommended. Routine ultrasound examinations should be adjusted in order to minimize exposure to the virus. Standardized criteria should evaluate the need for admission. Women with moderate/high-risk for infection: Women should be isolated and tested with RT-PCR. The mode and timing of delivery should follow routine obstetric indications. In case of infection, glucocorticoids are recommended in critically ill pregnant women, after individualized evaluation. Place of care: All potential/confirmed COVID-19 women should be placed in single isolation rooms or negative pressure rooms, if available, based on screening results (e.g., fever of ≥ 38 °C which persists even after paracetamol use, findings associated with pneumonia in chest X-ray). Pregnant women with other co-morbidities, such as chronic hypertension, immune system disorders, pulmonary diseases, use of

	<p>immunosuppressive drugs, or diabetes are considered high-risk. Additional factors associated with ethnicity minorities and socioeconomic status may increase the disease's burden and should therefore not be overseen.</p> <ul style="list-style-type: none"> ○ A pregnant woman needs admission to the intensive care unit if she needs vasopressors or mechanical ventilation. ○ All pregnant women with a contact history with a COVID-19 positive person or temperature of ≥ 37.3 °C and respiratory symptoms should be admitted to an emergency internal medicine or specialist outpatient department fever clinic. ● During labour and concomitant infection, the duration of the first two stages should be reduced as possible to decrease aerosolization, while minimization of hemorrhage is essential during the third stage. ● Close maternal monitoring and adequate oxygenation when necessary always remain a prerequisite. ● Discharge should be considered on the first or second day postpartum, also depending on delivery mode. ● Breastfeeding with protective equipment is recommended, as its benefits outweigh the risks of neonatal infection.
<p>Dubey, P., Thakur, B., Reddy, S., Martinez, C. A., Nurunnabi, M., Manuel, S. L., Chheda, S., Bracamontes, C., & Dwivedi, A. K. (Mar 24, 2021). Current trends and geographical differences in therapeutic profile and outcomes of COVID-19 among pregnant women - a systematic review and meta-analysis. <i>BMC pregnancy and childbirth</i>, 21(1), 247.</p>	<ul style="list-style-type: none"> ● 1,239 pregnant women with COVID-19 from 66 studies were analyzed. ● Overall, avoiding unnecessary treatments and early screening of asymptomatic pregnant women particularly in their 30s may minimize adverse consequences of COVID-19.
<p>Hudak M. L. (Feb 23, 2021). Consequences of the SARS-CoV-2 pandemic in the perinatal period. <i>Current opinion in pediatrics</i>, 33(2), 181–187.</p>	<ul style="list-style-type: none"> ● The rate of positivity is not higher in infants who room in with the mother compared to infants who are initially separated and cared for in a SARS-CoV-2-free environment.
<p>Islam, M. M., Poly, T. N., Walther, B. A., Yang, H. C., Wang, C. W., Hsieh, W. S., Atique, S., Salmani, H., Alsinglawi, B., Lin, M. C., Jian, W. S., & Jack Li, Y. C. (Dec 3, 2020). Clinical Characteristics and Neonatal Outcomes of Pregnant Patients With COVID-19: A Systematic Review. <i>Frontiers in medicine</i>, 7, 573468.</p>	<ul style="list-style-type: none"> ● Based on data for 235 pregnant women with COVID-19 (age range of 25-40 years and the gestational age range of eight to 40 weeks plus six days) across 13 studies: <ul style="list-style-type: none"> ○ CT scan imaging is found to be an effective strategy to identify asymptomatic pregnant women with COVID-19 early as it shows the abnormality in patients. ○ Timely identification and intervention of patients can reduce obstetrical complications such as miscarriage, intrauterine growth restriction, and pre-term delivery, and improve pregnancy outcomes. ○ Symptomatic patients need to be admitted to a hospital quickly and isolated in the intensive care unit with a negative pressure room. ○ In the process of fetal monitoring, regular fetal heart rate should be monitored electronically to assess the fetal status dependent upon the gestational age. ● The study findings also show that there is no association between COVID-19 and pregnancy termination; therefore, a decision regarding the delivery process must be individualized.
<p>Dubey, P., Reddy, S. Y., Manuel, S., & Dwivedi, A. K. (Sept 2020). Maternal and neonatal characteristics</p>	<ul style="list-style-type: none"> ● Regular screening for coronavirus infection, early identification of infection in asymptomatic pregnant women, and safe practice to avoid acquiring an infection during early gestational ages may be associated with more favorable pregnancy outcomes.

<p>and outcomes among COVID-19 infected women: An updated systematic review and meta-analysis. <i>European journal of obstetrics, gynecology, and reproductive biology</i>, 252, 490–501.</p>	
<p>Narang, K., Enninga, E., Gunaratne, M., Ibirogba, E. R., Trad, A., Elrefaei, A., Theiler, R. N., Ruano, R., Szymanski, L. M., Chakraborty, R., & Garovic, V. D. (Aug 2020). SARS-CoV-2 Infection and COVID-19 During Pregnancy: A Multidisciplinary Review. <i>Mayo Clinic proceedings</i>, 95(8), 1750–1765.</p>	<ul style="list-style-type: none"> • This review summarizes nine guidelines (updated as of April 22, 2020) from six societies¹ for medical/obstetric care and outlines future directions for optimization of treatment and preventive strategies for pregnant patients with COVID-19 with the understanding that relevant data are limited and rapidly changing. • Prenatal/Antepartum Care: The consensus among all societies recommends the use of telehealth for prenatal visits. Ultrasound and antenatal surveillance should be combined with visits for laboratory tests or prenatal care. Patients should be screened for symptoms, travel history, and contact history before any face-to-face visits; those who are symptomatic or meet the criteria should undergo testing for SARS-CoV-2 using qRT-PCR. Appropriate PPE should be worn by patients and health care workers. Administration of antenatal corticosteroids for fetal lung maturation should still be considered if a pregnancy is between 24 0/7 and 33 6/7 weeks' gestation, but the risk/benefit balance needs to be discussed by the multidisciplinary team. Data on the use of corticosteroids during late preterm (34 0/7 to 36 6/7 weeks) are still controversial, but routine administration is not advised. • Intrapartum Care: Institutions should have a designated area for triaging, screening, and admitting SARS-CoV-2–positive patients. The mode and timing of delivery should follow routine obstetric indications, keeping in mind that COVID-19 alone is not an indication for CD, unless there is fetal distress or deteriorating maternal clinical status. Societies recommend that only 1 consistent healthy asymptomatic individual providing support should be present during labour and delivery. Aerosol-generating procedures, including forceful pushing during the second stage of labour and oxygen supplementation for intrauterine resuscitation, should be limited and appropriate PPE (N95) worn. Water births are contraindicated due to the limited ability to monitor mother and baby, and the risk of fecal transmission. • Postpartum Care: Breastfeeding should not be discouraged, and mother and baby separation is not advised, unless the mother is acutely ill. Mothers are advised to follow appropriate respiratory hygiene by wearing masks during skin-to-skin contact and breastfeeding. Mothers should wash hands before handling their babies or touching pumps or bottles and should avoid coughing while their babies are feeding. All surfaces and breast pumps should be sanitized after each use. In an effort to limit infection exposure, hospital length of stay should be decreased to one day for vaginal deliveries and two days for Caesarean deliveries. Postpartum visits should be performed through telehealth and patients advised to continue compliance with social distancing after discharge. The method of telehealth should be individualized based on institution resources and availability.
<p>Rasmussen, S. A., & Jamieson, D. J. (Jul 2020). Caring for Women Who Are Planning a Pregnancy, Pregnant, or Postpartum During the COVID-19 Pandemic. <i>JAMA</i>, 324(2), 190–191.</p>	<p>Guideline recommendations (American Academy of Pediatrics, American College of Obstetricians and Gynecologists, Centers for Disease Control and Prevention, Society for Maternal-Fetal Medicine, and Society for Obstetric Anesthesia and Perinatology) for the care of pregnant women known or suspected to have COVID-19 admitted for delivery include:</p> <ul style="list-style-type: none"> • Place a mask on the patient on presentation and isolate in a single-person room with the door closed. Airborne isolation rooms should be used for aerosolizing procedures (ACOG, CDC, SMFM, SOAP).

¹ The six societies are: Society for Maternal-Fetal Medicine (SMFM), the American College of Obstetricians and Gynecologists (ACOG) from the United States, the Royal College of Obstetricians and Gynaecologists (RCOG) from the United Kingdom, the International Society of Ultrasound in Obstetrics and Gynecology (ISUOG), the Centers for Disease Control and Prevention (CDC), and the World Health Organization (WHO). The recommendations from the SMFM focus on high-risk pregnancies, and those from the ACOG and the RCOG focus on all pregnancies. The WHO and the CDC focus on recommendations that can be generalized across all patient populations, and ISUOG focuses on sonography and care of ultrasound equipment.

	<ul style="list-style-type: none"> • Consider separating patients with COVID-19 in one area of the obstetric unit and using a designated team of trained clinicians in these areas (SMFM, SOAP). • Weigh benefits and risks of magnesium sulfate for fetal neuroprotection or for preeclampsia/intrapartum seizure prophylaxis given potential maternal respiratory depression (SMFM, SOAP). • Consider adjusting antenatal corticosteroid use for fetal maturation, given the risk of worsening patient outcomes with corticosteroid use in patients with COVID-19 (e.g., offer antenatal steroids for patients <34 weeks' gestation, weigh risks and benefits and individualize decisions for ≥34 weeks' gestation) (ACOG, SMFM, SOAP). • Consider early epidural analgesia to mitigate the risks associated with general anesthesia in the setting of an urgent Caesarean delivery (SMFM, SOAP). • Do not alter delivery timing or mode (e.g., Caesarean delivery, operative vaginal delivery) due to patients' COVID-19 infection status. However, for women with COVID-19 in the third trimester, it may be reasonable to attempt to postpone delivery to decrease risk of neonatal transmission (ACOG). • Consider temporary separation of mothers with confirmed COVID-19 from their newborns (ACOG, AAP, CDC). • Determination of whether to temporarily separate a mother with known or suspected COVID-19 should be made on a case-by-case basis, using shared decision-making (ACOG, CDC). • If temporary separation is chosen, mothers who intend to breastfeed should practice hand and breast hygiene and express their milk. Expressed milk can be fed to the newborn by a healthy caregiver (ACOG, AAP, CDC, SMFM, SOAP). • If separation is not chosen, use other measures to reduce risk of infection, such as physical barriers and face mask use by the mother (AAP, CDC). • Mothers who choose to feed at the breast should wear a face mask and practice hand and breast hygiene before each feeding (AAP, ACOG, CDC, SMFM, SOAP). • Newborns born to mothers with confirmed COVID-19 at the time of delivery should be considered to have suspected COVID-19 and be isolated from healthy newborns (AAP, ACOG, CDC). • Newborns born to mothers with confirmed or suspected COVID-19 at the time of delivery should be tested 24 hours after birth for SARS-CoV-2 and, if negative, again at approximately 48 hours if testing capacity is available (AAP, CDC).
<p>Prone Positioning</p>	
<p>Roddy, J. T., Collier, W. S., & Kurman, J. S. (Mar 16, 2021). Prone positioning for severe ARDS in a postpartum COVID-19 patient following caesarean section. <i>BMJ case reports</i>, 14(3), e240385.</p>	<ul style="list-style-type: none"> • A 31-year-old pregnant woman presented with symptomatic COVID-19, which was complicated by progressive hypoxaemia requiring intensive care and emergent delivery by caesarean section. Afterward, she was successfully supported with mechanical ventilation and prone positioning and ultimately recovered. Prone positioning was implemented in an effort to improve oxygenation. • The patient's presentation with respiratory failure due to COVID-19 complicating pregnancy falls into several higher prevalence demographics previously reported for requiring hospitalization: she was from a minority group, of elevated body mass index (BMI), and in the third trimester of pregnancy. Her course was complicated by respiratory failure requiring high flow oxygen, delivery by C-section, and ultimately intubation and postpartum prone positioning due to COVID-19 related ARDS. • Previously studied regimens for prone positioning have consisted of intermittent prone positioning during a majority of the day with several hours spent supine. This patient was unable to tolerate supination for the first several days following intubation due to hypoxaemia, so she remained prone for the first 72 hours, following which she successfully had a more standard intermittent regimen for the remainder of her intubation. Prolonged pronation has been studied in limited sample size feasibility studies and proposed as a possible alternative to established intermittent prone positioning. Several factors must be considered, however, including frequent repositioning to avoid facial pressure sores and facial oedema.

<p>Venus, K., Munshi, L., & Fralick, M. (Nov 23, 2020). Prone positioning for patients with hypoxic respiratory failure related to COVID-19. <i>CMAJ</i>, 192(47), E1532–E1537.</p>	<ul style="list-style-type: none"> • Little is known about the effects of prone positioning during pregnancy on the fetus, as pregnant patients are frequently excluded from trials (a practice recently challenged during the COVID-19 pandemic), although a previous case report described successful prone positioning for a pregnant patient who was critically ill with viral pneumonia. • Successful use of prone positioning for a pregnant patient with COVID-19 has been documented in a case report.
<p>Tolcher, M. C., McKinney, J. R., Eppes, C. S., Muigai, D., Shamsirsaz, A., Guntupalli, K. K., & Nates, J. L. (Aug 2020). Prone Positioning for Pregnant Women With Hypoxemia Due to Coronavirus Disease 2019 (COVID-19). <i>Obstetrics and gynecology</i>, 136(2), 259–261.</p>	<ul style="list-style-type: none"> • The COVID-19 pandemic has prompted expanded use of prone positioning for refractory hypoxemia. • Clinical trials have demonstrated beneficial effects of early prone positioning for acute respiratory distress syndrome (ARDS), including decreased mortality. However, pregnant women were excluded from these trials. • To address the need for low-cost, low-harm interventions in the face of a widespread viral syndrome wherein hypoxemia predominates, the study authors developed an algorithm for prone positioning of both intubated and non-intubated pregnant women, including indications, contraindications, and a step-by-step guide. This algorithm may be appropriate for a wide spectrum of hypoxemia severity among pregnant women. Among the populations who can benefit from prone positioning are pregnant women experiencing severe respiratory distress, as long as the physiologic changes and risks of pregnancy are taken into account. • To develop this algorithm, the study authors extracted and combined information from separate institutional protocols developed for prone positioning of nonpregnant patients in the medical intensive care unit and from one developed specifically for pregnant patients anticipated to be admitted to a dedicated obstetric intensive care unit. This algorithm is the amalgamation of the clinical expertise and proning experiences of medical and obstetrics intensivists, which was further honed using early experience gained from prone positioning of pregnant women with hypoxemia related to COVID-19. • Simulation training that includes both obstetric and critical care staff is essential for optimizing outcomes by familiarizing staff with this uncommon procedure in pregnancy. Multidisciplinary collaboration and care planning discussions between the obstetrics, intensive care, anesthesiology, and neonatology teams should be carried out at the time of admission of a pregnant patient to the intensive care unit and should be ongoing during the course of care to capitalize on varying areas of expertise and to optimize patient outcomes. • Prone positioning may not be successful in all cases. Oxygen saturation or arterial blood gas level should be closely monitored to assess responsiveness. If the patient is unable to tolerate the position, right or left lateral positions may be attempted. In addition, shorter prone position sessions may be considered for patients with mild or moderate ARDS (e.g., two hours in awake pregnant women). Prone positioning for intubated patients with severe ARDS is typically performed for at least 16 hours per day. • Potential complications of prone positioning include facial edema and skin breakdown; pressure ulcers; dislodgement of the endotracheal tube, lines, or drains; and worsening oxygenation or hemodynamic instability.
<p>Guidelines</p>	
<p>DiLorenzo, M. A., O'Connor, S. K., Ezekwesili, C., Sampath, S., Zhao, M., Yarrington, C., & Pierre, C. (Mar 4, 2021). COVID-19 guidelines for pregnant women and new mothers: A systematic evidence review. <i>International journal of gynaecology and obstetrics</i>, 10. Advance online publication.</p>	<ul style="list-style-type: none"> • A total of 74 articles were included in the review. In general, there was a focus on shared decision making when approaching topics such as breastfeeding and post-partum social distancing. Guidelines for decontamination were fairly uniform. • Most articles recommended direct breastfeeding with enhanced precaution measures. • Recommendations regarding post-partum social distancing varied, although articles published more recently often recommended keeping the mother and newborn in the same room when possible. • Decontamination recommendations emphasized mask wearing, good hand hygiene, and proper cleaning of surfaces.
<p>Benski, C., Di Filippo, D., Taraschi, G., & Reich, M. R. (Nov 9, 2020).</p>	<ul style="list-style-type: none"> • This study examined the obstetrics guidelines released from December 2019 to April 2020 to compare their recommendations and to assess how useful they could be to maternal health workers. The study reviewed 11 guidelines on obstetrics management, assessing four domains:

<p>Guidelines for Pregnancy Management During the COVID-19 Pandemic: A Public Health Conundrum. <i>International journal of environmental research and public health</i>, 17(21), 8277.</p>	<p>(1) timeliness: the time between the declaration of pandemics by WHO and a guideline release and update; (2) accessibility: the readiness to access a guideline by searching it on a common browser; (3) completeness: the amount of foundational topics covered; and (4) consistency: the agreement among different guidelines.</p> <ul style="list-style-type: none"> • The guidelines were from China, Italy, Spain, the UK, US: guidelines published by the Italian and Spanish Ministries of Health, the Italian Association of Hospital Gynecologists and Obstetricians (AOGOI) and the Italian Society of Gynecology and Obstetrics (SIGO), the Society for Maternal Fetal Medicine (SMFM), a Chinese expert consensus, and the Royal College of Obstetricians and Gynaecologists (RCOG), International Federation of Gynaecology and Obstetrics (FIGO), the American College of Obstetrics and Gynecology (ACOG), the International Society of Ultrasound of Obstetrics and Gynecology (ISUOG), World Health Organization (WHO), and the Centers for Disease Control and Prevention (CDC). • In terms of timeliness, the Royal College of Obstetricians and Gynaecologists (RCOG) was the first organization to release their recommendation. Only four guidelines were accessible with one click, while only 6/11 guidelines covered more than 80% of the 30 foundational topics the study identified. For consistency, the study highlights the existence of 10 points of conflict among the recommendations (i.e., mask wearing, personal and social hygiene, antenatal care visits, partner/companion, antenatal corticosteroids, respiratory analgesia, cord clamping, skin-to-skin practice, mother/child separation, and breastfeeding). The present research revealed a lack of uniformity and consistency, resulting in potentially challenging decisions for health care providers.
<p>Favre, G., Pomar, L., Qi, X., Nielsen-Saines, K., Musso, D., & Baud, D. (Jun 2020). Guidelines for pregnant women with suspected SARS-CoV-2 infection. <i>The Lancet. Infectious diseases</i>, 20(6), 652–653.</p>	<ul style="list-style-type: none"> • This study proposed a detailed management algorithm for health care providers regarding recommendations for management of pregnant women at risk of SARS-CoV-2 infection. • Pregnant women with laboratory-confirmed SARS-CoV-2 infection who are asymptomatic should be self-monitored at home for clinical features of COVID-19 for at least 14 days. These patients and those recovering from mild illness should be monitored with bimonthly fetal growth ultrasounds and Doppler assessments because of the potential risk for intrauterine growth restriction. • Pregnant women with COVID-19 pneumonia should be managed by a multidisciplinary team at a tertiary care centre. • When quick Sepsis-related Organ Failure Assessment criteria are met, the patient should be transferred to an intensive care unit. • For pregnant women with confirmed infection, the choice of delivery timing should be individualized depending on the week of gestation and maternal, fetal, and delivery conditions. • Whenever possible, vaginal delivery via induction of labour, with eventual instrumental delivery to avoid maternal exhaustion, should be favoured to avoid unnecessary surgical complications in an already sick patient. Septic shock, acute organ failure, or fetal distress should prompt emergency Caesarean delivery (or termination if legal before fetal viability). • Newborns of mothers positive for SARS-CoV-2 should be isolated for at least 14 days or until viral shedding clears, during which time direct breastfeeding is not recommended.
<p>Poon, L. C., Yang, H., Lee, J., Copel, J. A., Leung, T. Y., Zhang, Y., Chen, D., & Prefumo, F. (Mar 20, 2020). ISUOG Interim Guidance on 2019 novel coronavirus infection during pregnancy and puerperium: information for healthcare professionals. <i>Ultrasound in obstetrics & gynecology: the official journal of the International Society of</i></p>	<ul style="list-style-type: none"> • The International Society of Ultrasound in Obstetrics and Gynecology (ISUOG) issued guidance on management during pregnancy and puerperium. • Place of Care: Suspected, probable, and confirmed cases of COVID-19 infection should be managed initially by designated tertiary hospitals with effective isolation facilities and protection equipment. Suspected/probable cases should be treated in isolation and confirmed cases should be managed in a negative-pressure isolation room. A confirmed case that is critically ill should be admitted to a negative-pressure isolation room in an ICU. Designated hospitals should set up a dedicated negative-pressure operating room and a neonatal isolation ward. All attending medical staff should don PPE (respirator, goggle, face protective shield, surgical gown and gloves) when providing care for confirmed cases of COVID-19 infection.

<p><i>Ultrasound in Obstetrics and Gynecology</i>, 55(5), 700–708.</p>	<ul style="list-style-type: none"> ○ In areas with widespread local transmission of the disease, health services may be unable to provide such levels of care to all suspected, probable or confirmed cases. Pregnant women with a mild clinical presentation may not initially require hospital admission and home confinement can be considered, provided that this is possible logistically and that monitoring of the woman's condition can be ensured. ○ If negative-pressure isolation rooms are not available, patients should be isolated in single rooms, or grouped together once COVID-19 infection has been confirmed. ● Confirmed Cases (severe and critical disease): Aggressive treatment is required, including supporting measures with hydration, oxygen therapy and chest physiotherapy. The case should be managed in a negative-pressure isolation room in the ICU, preferably with the woman in a left lateral position, with the support of a multidisciplinary team (obstetricians, maternal-fetal-medicine subspecialists, intensivists, obstetric anesthetists, midwives, virologists, microbiologists, neonatologists, infectious-disease specialists). <ul style="list-style-type: none"> ○ Appropriate antibiotic treatment in combination with antiviral treatment should be used promptly when there is suspected or confirmed secondary bacterial infection, following discussion with microbiologists. ○ Blood-pressure monitoring and fluid-balance management: in patients without septic shock, conservative fluid management measures should be undertaken; in patients with septic shock, fluid resuscitation and inotropes are required to maintain an average arterial pressure ≥ 60 mmHg (1 mmHg = 0.133 kPa) and a lactate level <2 mmol/L. ○ Oxygen therapy: supplemental oxygen should be used to maintain oxygen saturation $\geq 95\%$; oxygen should be given promptly to patients with hypoxemia and/or shock, and method of ventilation should be according to the patient's condition and following guidance from the intensivists and obstetric anesthetists. ○ Fetal monitoring: If appropriate, cardiotocography for fetal heart rate monitoring should be undertaken when pregnancy is ≥ 26-28 weeks of gestation, and ultrasound assessment of fetal growth and amniotic fluid volume with umbilical artery Doppler should be performed, if necessary, once the patient is stabilized. ○ Medically indicated preterm delivery should be considered by the multidisciplinary team on a case-by-case basis. ● Childbirth: For suspected, probable and confirmed cases of COVID-19 infection, delivery should be conducted in a negative-pressure isolation room. The timing and mode of delivery should be individualized, dependent mainly on the clinical status of the patient, gestational age and fetal condition. <ul style="list-style-type: none"> ○ In the event that an infected woman has spontaneous onset of labor with optimal progress, she can be allowed to deliver vaginally. Shortening the second stage by operative vaginal delivery can be considered, as active pushing while wearing a surgical mask may be difficult for the woman to achieve. ○ Induction of labor can be considered when the cervix is favorable, but there should be a low threshold to expedite the delivery when there is fetal distress, poor progress in labor and/or deterioration in maternal condition. ○ For preterm cases requiring delivery, caution is urged regarding the use of antenatal steroids (dexamethasone or betamethasone) for fetal lung maturation in a critically ill patient, because this can potentially worsen the clinical condition and the administration of antenatal steroids would delay the delivery that is necessary for management of the patient. ○ Regarding neonatal management of suspected, probable and confirmed cases of maternal COVID-19 infection, the umbilical cord should be clamped promptly and the neonate should be transferred to the resuscitation area for assessment by the attending pediatric team
<p>Liang, H., & Acharya, G. (Mar 5, 2020). Novel corona virus disease (COVID-19) in pregnancy: What clinical recommendations to follow?. <i>Acta obstetrica et</i></p>	<ul style="list-style-type: none"> ● A computed tomography (CT) scan of the chest without contrast is the most useful investigation to confirm or rule out viral pneumonia, and should be performed in suspected cases as the risk of radiation exposure to the fetus is very small. ● Viral nucleic acid detection using real-time polymerase chain reaction (RT-PCR) is considered the reference standard for the diagnosis. Specimens should be obtained from saliva, upper respiratory tract (nasopharyngeal and oropharyngeal swabs), lower respiratory tract (sputum, endotracheal aspirate, or bronchoalveolar lavage), urine and stool if possible. Repeated testing may be required to confirm the diagnosis. If the

<p><i>gynecologica Scandinavica</i>, 99(4), 439–442.</p>	<p>SARS-COV-2 nucleic acid is not detected in respiratory tract samples taken on two consecutive occasions at least 24 hours apart, COVID-19 can be ruled out. Serology as a diagnostic procedure should be used only if RT-PCR is not available.</p> <ul style="list-style-type: none"> • Pregnant women suspected of COVID-19 should be isolated and investigated. Those diagnosed with infection should be promptly admitted to a negative pressure isolation ward, preferably in a designated hospital with adequate facilities and multi-disciplinary expertise to manage critically ill obstetric patients. <ul style="list-style-type: none"> ○ They should be triaged and stratified into mild (symptomatic patient with stable vital signs), severe (respiration rate ≥ 30/min, resting SaO₂ $\leq 93\%$, arterial blood oxygen partial pressure (PaO₂)/ oxygen concentration (FiO₂) ≤ 300 mmHg) or critical (shock with organ failure, respiratory failure requiring mechanical ventilation or refractory hypoxemia requiring extra-corporal membrane oxygenation) categories based on clinical evaluation, and managed by a multidisciplinary team of midwife, obstetrician, specialist in intensive care medicine, microbiologist, anesthetist and neonatologist. ○ All medical staff caring for COVID-19 patients should use personal protective equipment including gown, N95 masks, goggles, and gloves. ○ Special consideration should be given to physiological adaptations in pregnancy when treating pregnant women with COVID-19 infection. • Timing of delivery should be individualized based on disease severity, existing comorbidities such as preeclampsia, diabetes, cardiac disease etc, obstetric history, and gestational age and fetal condition.
<p>Medications</p>	
<p>Hapshy, V., Aziz, D., Kahar, P., Khanna, D., Johnson, K. E., & Parmar, M. S. (Apr 21, 2021). COVID-19 and Pregnancy: Risk, Symptoms, Diagnosis, and Treatment. <i>SN comprehensive clinical medicine</i>, 1–7. Advance online publication.</p>	<ul style="list-style-type: none"> • Recently accepted manuscript data spanning from March 21 to June 16, 2020 described the use of remdesivir in hospitalized pregnant women with confirmed COVID-19 infection and O₂ saturation $< 94\%$ who met the criteria to be enrolled in the compassionate use program. Of the 86 patients enrolled in this study, 19 were delivered before their first course of remdesivir and were included in the immediate post-partum group. The remaining patients, whose median gestational age was 28 weeks, were started on remdesivir with follow-up after 28 days. <ul style="list-style-type: none"> ○ After the 28-day follow-up, the oxygen requirement in 96% of the pregnant patients decreased. ○ Furthermore, 93% of those requiring mechanical ventilation were extubated, 93% recovered, and 90% were discharged. ○ Adverse events were experienced in 29% (22/67) of the cohort. These adverse events were described as anemia, constipation, dysphagia, worsening hypoxia, and deep vein thrombosis, among others. Other side effects shown included increasing liver function tests and serum creatinine levels with seven pregnant women discontinuing the study drug due to adverse events. ○ Currently, remdesivir is classified as a pregnancy category B2 pharmaceutical drug - epitomizing the limited data of remdesivir in the pregnant cohort. There is little data regarding the fetal effects of remdesivir from its current usage in the treatment of COVID-19 infections or during prior clinical trials to treat Ebola. With consideration of the low molecular weight and avid protein binding, it is hypothesized that remdesivir may cross the placenta, although more clinical studies are needed to determine any adverse neonatal effects. • Corticosteroids, such as dexamethasone, are currently indicated in the treatment of severely ill non-pregnant patients who require oxygen or ventilatory support. Corticosteroids are often indicated in pregnant patients who are in or at high risk for preterm labour to promote fetal lung maturity. Dexamethasone or betamethasone is the preferred agents used to induce fetal pulmonary maturation in patients between 24 and 34 weeks of gestation at increased risk for preterm labour. <ul style="list-style-type: none"> ○ More recently, there has been data supporting the use of dexamethasone in patients with severe COVID-19 infection. This controlled trial demonstrated that in patients either requiring oxygen support or on mechanical ventilation, there was a decrease in 28-day mortality rates. ○ Potential side effects of dexamethasone on the developing fetus include theoretical distortions of osteogenesis in the fetus and fetal malformations such as oral clefts and intrauterine fetal growth restriction. ○ Despite these possible adverse outcomes, the American College of Obstetricians and Gynecologists (ACOG) recommends that treatment with dexamethasone should not be withheld in pregnant patients when indicated. Thus, it is recommended to use dexamethasone in pregnant patients in the ICU or mechanically ventilated patients due to the benefits shown in the treatment of COVID-19 and for the maturing neonate.

<p>Pountoukidou, A., Potamiti-Komi, M., Sarri, V., Papapanou, M., Routsis, E., Tsiatsiani, A. M., Vlahos, N., & Siristatidis, C. (Apr 2021). Management and Prevention of COVID-19 in Pregnancy and Pandemic Obstetric Care: A Review of Current Practices. <i>Healthcare (Basel, Switzerland)</i>, 9(4), 467.</p>	<ul style="list-style-type: none"> • This review aimed to summarize the up-to-date information about the prevention and management of suspected/confirmed SARS-CoV-2 infection in obstetric patients and obstetric care during prenatal, intrapartum, and postpartum periods. Recommendations are currently based on limited available data. More original studies on infected pregnant women are needed to establish totally evidence-based protocols of care for these patients. • Lopinavir–ritonavir and chloroquine/hydroxychloroquine were considered as candidate options for treatment of SARS-CoV-2 infection and could be applied in pregnancy as well, as they have not been associated with significant adverse neonatal outcomes. However, new available data indicate doubt that there is a clear therapeutic benefit from their use in COVID-19 patients or support that the benefit is outweighed by their toxicity. • Remdesivir is an antiviral agent, being initially proven to control in vitro viral replication and therefore forming the rationale to be tested for clinical use. On 1 May 2020, the drug was approved for hospitalized children ≥ 12 years and adults with COVID-19. However, there is insufficient evidence for its safety during pregnancy, mainly due to its unknown risk of transplacental transfer. Most relevant trials have excluded pregnant and breastfeeding women, although high recovery rates were observed in pregnant women who received compassionate use of remdesivir. Therefore, standard-of-care administration of remdesivir in pregnant women with COVID-19 should be currently avoided. • Tocilizumab is an interleukin-6 receptor antagonist, which may counteract the inflammatory response in patients with severe COVID-19. Studies have demonstrated that tocilizumab is safe and efficacious in reducing mortality among critically ill patients. However, due to the limited number of observational studies with considerable heterogeneity, its effectiveness needs to be further investigated through adequately conducted randomized clinical trials. There is also currently no compelling evidence that it is linked to fetal malformations, but further investigation is required to confirm the benefit–risk and safety profile of tocilizumab in pregnant women. • The use of glucocorticoids was initially discouraged, as it was associated with unfavorable outcomes in COVID-19 positive patients. Until recently, WHO recommended against the routine use of systematic corticosteroids, as it appeared that they delay viral clearance without important survival benefits. <ul style="list-style-type: none"> ○ In contrast, new evidence supported that dexamethasone can provide significant reduction in mortality for individuals with COVID-19 requiring mechanical ventilation or supplemental oxygen; thus, pregnant women meeting these criteria could be considered for corticosteroid use. Unfortunately, dexamethasone has exhibited a higher rate of placental transfer than other glucocorticoids, so that its extended administration may lead to adverse neonatal effects. ○ In contrast, other glucocorticoids, such as methylprednisolone and hydrocortisone, have resulted in less fetal steroid exposure, so that they could be administered as an alternative option for maternal treatment. ○ According to the UK Royal College of Obstetricians and Gynaecologists guidelines, oral prednisolone or intravenous hydrocortisone for 10 days or until hospital discharge can be used. If steroids are indicated for the enhancement of fetal lung maturity, dexamethasone is recommended in the usual doses and then replaced with oral prednisolone or hydrocortisone to complete a total of 10 days in the cases of severe maternal disease. • Venous thromboembolism prophylaxis should be considered in hospitalized patients with COVID-19 due to the associated risk of excessive inflammation, hypoxia, immobilization, and diffuse intravascular coagulation. As pregnancy per se is linked to a hypercoagulable state, obstetric patients that are admitted to hospital should be given anticoagulation treatment. Low-molecular-weight heparin is recommended in prophylactic doses after an individual-based decision according to relevant risk factors and meticulous evaluation of possible contraindications. • Antibiotics, such as amoxicillin, azithromycin, and ceftriaxone, which are commonly used in pregnancy, are recommended in cases in which there is a clinical suspicion of coexistent bacterial infection or sepsis. • Supportive therapy is an important part of the management of every infection with balanced nutrition, hydration, adequate levels of electrolytes, and rest. According to the severity of infection, supplement oxygen inhalation in 60-100% concentration is recommended to be given at a rate
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	<p>of 40L/min. It is also necessary to check vital signs and oxygenation closely so that there is the ability to promptly react to any disorder or imbalance.</p>
<p>Dubey, P., Thakur, B., Reddy, S., Martinez, C. A., Nurunnabi, M., Manuel, S. L., Chheda, S., Bracamontes, C., & Dwivedi, A. K. (Mar 24, 2021). Current trends and geographical differences in therapeutic profile and outcomes of COVID-19 among pregnant women - a systematic review and meta-analysis. <i>BMC pregnancy and childbirth</i>, 21(1), 247.</p>	<ul style="list-style-type: none"> • 1,239 pregnant women with COVID-19 from 66 studies were analyzed. Minimizing the use of some therapeutics particularly antibiotics, antivirals, oxygen therapy, immunosuppressants, and hydroxychloroquine by risk stratification and careful consideration may further improve maternal and clinical outcomes. • In case series analysis reflecting average-risk patients, the proportion of oxygen support, antibiotics, antivirals, and plasma therapy administration except for hydroxychloroquine was substantially higher in Asian studies (55, 78, 80, 6, and 0%) compared to the US (7, 1, 12, 0, and 7%) or European (33, 12, 14, 1, and 26%) studies, respectively. • Even in case reports reflecting severe cases, the use of antivirals and antibiotics was higher in Asian studies compared to the US, Latin American, and European studies. • A significant decline in the use of most therapeutics along with adverse outcomes of COVID-19 in pregnant women was observed. • Given the lack of efficacy data for most therapeutics of COVID-19, the practice in the US and European countries might have been to minimally expose any therapeutics to average-risk pregnant patients. The highest use of antibiotics in Asian studies may be due to local guidelines for managing COVID-19 patients, suspicion of bacterial or fungal coinfections due to unavailability of rapid and affordable testing to differentiate viral and bacterial infections, and health-care-associated infections due to prolonged hospitalization.
<p>Martínez-Sánchez, N., De la Calle Fernández-Miranda, M., & Bartha, J. L. (Feb 25, 2021). Safety profile of treatments administered in covid 19 infection in pregnant women. <i>Clinica e investigacion en ginecologia y obstetricia</i>, 100663. Advance online publication.</p>	<ul style="list-style-type: none"> • There has been a wide experience with the use of hydroxychloroquine and lopinavir/ritonavir in pregnant women. • Tocilizumab and interferon beta could be used if benefits exceed risks. • There is no experience using remdesivir in pregnancy.
<p>Novoa, R. H., Quintana, W., Llancari, P., Urbina-Quispe, K., Guevara-Ríos, E., & Ventura, W. (Jan-Feb 2021). Maternal clinical characteristics and perinatal outcomes among pregnant women with coronavirus disease 2019. A systematic review. <i>Travel medicine and infectious disease</i>, 39, 101919.</p>	<ul style="list-style-type: none"> • 143 articles were selected for full-text assessment; 33 for descriptive analyses, and 4 case-controls for meta-analysis. For the descriptive analysis, the study included a total of 322 pregnant women, 111 (34.5%) patients from Netherlands, 80 (24.8%) from US, 76 (23.6%) from China, 43 (13.3%) from Italy, 2 (0.6%) from Canada, and one each from Honduras, South Korea, Sweden, Germany, Turkey, Iran, Australia, Spain, Peru, and India. • 67(27.0%) patients received some antiviral treatment such as oseltamivir, lopinavir, ritonavir and ganciclovir. Antibiotics were given to 97(39.1%) patients (moxifloxacin, cephalosporin, azithromycin, penicillin). Corticosteroids were given to 41(16.5%) patients. Other treatments reported were hydroxychloroquine (n = 13,5.2%) and immune gamma globulin (n = 2,0.8%).
<p>Taylor, M. M., Kobeissi, L., Kim, C., Amin, A., Thorson, A. E., Bellare, N. B., Brizuela, V., Bonet, M., Kara, E., Thwin, S. S., Kuganatham, H., Ali, M., Oladapo, O. T., & Broutet, N. (Dec 16, 2020). Inclusion of pregnant women in COVID-19 treatment trials: a review and global call to action. <i>The</i></p>	<ul style="list-style-type: none"> • This study explored the inclusion of pregnant women in treatment trials of COVID-19 by reviewing 10 international clinical trial registries at two timepoints in 2020. Despite the surge in treatment studies for COVID-19, the proportion excluding pregnant women remains consistent. Exclusion was not well justified as many of the treatments being evaluated have no or low safety concerns during pregnancy. Inclusion of pregnant women in clinical treatment trials is urgently needed to identify effective COVID-19 treatment for this population. • The study identified 155 COVID-19 treatment studies of non-biological drugs for the April 7-10, 2020 timepoint, of which 124 (80%) specifically excluded pregnant women. The same registry search for the July 10-15, 2020 timepoint, yielded 722 treatment studies, of which 538 (75%) specifically excluded pregnant women.

<p><i>Lancet. Global health</i>, 9(3), e366–e371.</p>	<ul style="list-style-type: none"> • The study then focused on studies that included at least one of six drugs (remdesivir, lopinavir–ritonavir, interferon beta, corticosteroids, chloroquine and hydroxychloroquine, and ivermectin) under evaluation for COVID-19. Of 176 such studies, 130 (74%) listed pregnancy as an exclusion criterion. Of 35 studies that evaluated high-dose vitamin treatment for COVID-19, 27 (77%) excluded pregnant women. • The available data on the use of remdesivir in pregnant women remain scarce.
<p>Abou Ghayda, R., Li, H., Lee, K. H., Lee, H. W., Hong, S. H., Kwak, M., Lee, M., Kwon, M., Koyanagi, A., Kronbichler, A., Jacob, L., Smith, L., & Shin, J. I. (Nov 2020). COVID-19 and Adverse Pregnancy Outcome: A Systematic Review of 104 Cases. <i>Journal of clinical medicine</i>, 9(11), 3441.</p>	<ul style="list-style-type: none"> • 11 case series studies comprising 104 pregnant women with COVID-19 were included in the review. Ninety-one cases originated from China, and nine cases from Iran and four cases from Italy. • Although the review found that pregnancy with COVID-19 has significantly higher maternal mortality ratio compared to that of pregnancy without the disease, the authors concluded that the evidence is too weak to state that COVID-19 results in poorer maternal outcome due to multiple factors. The number of COVID-19 pregnancy outcomes was not large enough to draw a conclusion and long-term outcomes are yet to be determined as the pandemic is still unfolding. • The most common treatment for COVID-19 was administration of antibiotics (25.9%) followed by antivirals (17.3%) and hydroxychloroquine (9.6%). Common antibiotics included ceftriaxone, vancomycin, and azithromycin. Common antivirals included oseltamivir and lopinavir/ritonavir. • Twenty women received one or two types of treatment, such as antibiotics combined with antivirals, and eleven women received three or more types of treatment.
<p>D'Souza, R., Ashraf, R., Rowe, H., Zipursky, J., Clarfield, L., Maxwell, C., Arzola, C., Lapinsky, S., Paquette, K., Murthy, S., Cheng, M. P., & Malhamé, I. (Sept 21, 2020). Pregnancy and COVID-19: pharmacologic considerations. <i>Ultrasound in obstetrics & gynecology: the official journal of the International Society of Ultrasound in Obstetrics and Gynecology</i>, 57(2), 195–203.</p>	<ul style="list-style-type: none"> • Antenatal corticosteroids may be used routinely for fetal lung maturation between 24 and 34 weeks' gestation, but decisions in those with critical illness and those <24 or >34 weeks' gestation should be made on a case-by-case basis. • Magnesium sulfate may be used for seizure prophylaxis and fetal neuroprotection, albeit cautiously in those with hypoxia and renal compromise. • There are no contraindications to using low-dose aspirin to prevent placenta-mediated pregnancy complications when indicated. • An algorithm for thromboprophylaxis in pregnant patients with COVID-19 is presented, which considers disease severity, timing of delivery in relation to disease onset, inpatient vs outpatient status, underlying comorbidities and contraindications to the use of anticoagulation. • Nitrous oxide may be administered for labor analgesia while using appropriate personal protective equipment. • Intravenous remifentanyl patient-controlled analgesia should be used with caution in patients with respiratory depression. Liberal use of neuraxial labor analgesia may reduce the need for emergency general anesthesia which results in aerosolization. • Short courses of non-steroidal anti-inflammatory drugs can be administered for postpartum analgesia, but opioids should be used with caution due to the risk of respiratory depression. • For mechanically ventilated pregnant patients, neuromuscular blockade should be used for the shortest duration possible and reversal agents should be available on hand if delivery is imminent. • To date, dexamethasone is the only proven and recommended experimental treatment for pregnant patients with COVID-19 who are mechanically ventilated or who require supplemental oxygen. • Although hydroxychloroquine, lopinavir/ritonavir, and remdesivir may be used during pregnancy and lactation within the context of clinical trials, data from non-pregnant populations have not shown benefit. • The role of monoclonal antibodies (tocilizumab), immunomodulators (tacrolimus), interferon, inhaled nitric oxide, and convalescent plasma in pregnancy and lactation needs further evaluation.

<p>Narang, K., Enninga, E., Gunaratne, M., Ibiroga, E. R., Trad, A., Elrefaei, A., Theiler, R. N., Ruano, R., Szymanski, L. M., Chakraborty, R., & Garovic, V. D. (Aug 2020). SARS-CoV-2 Infection and COVID-19 During Pregnancy: A Multidisciplinary Review. <i>Mayo Clinic proceedings</i>, 95(8), 1750–1765.</p>	<ul style="list-style-type: none"> • This review summarizes nine guidelines (updated as of April 22, 2020) from six societies^j for medical/obstetric care and outlines future directions for optimization of treatment and preventive strategies for pregnant patients with COVID-19 with the understanding that relevant data are limited and rapidly changing. • Pharmacologic therapy is limited to medications with proven safety during pregnancy and lactation; safety data are often unavailable for medications in the early stages of clinical trials (e.g., remdesivir, sarilumab, tocilizumab). • Based on 23 studies, spanning January 1 to April 22, 2020 and including 185 patients, addressed obstetrical and neonatal outcomes of SARS-CoV-2 infection in pregnancy. Management of these patients varied according to institution. Most were treated with medications that are considered to be relatively safe during pregnancy: antibiotics (cefoperazone, sulbactam, ceftriaxone, cefazolin, and azithromycin), antiviral therapy (lopinavir, ritonavir, oseltamivir, and ganciclovir), and a few were treated with corticosteroids (dexamethasone, methylprednisolone).
<p>Pierce-Williams, R., Burd, J., Felder, L., Khoury, R., Bernstein, P. S., Avila, K., Penfield, C. A., Roman, A. S., DeBolt, C. A., Stone, J. L., Bianco, A., Kern-Goldberger, A. R., Hirshberg, A., Srinivas, S. K., Jayakumar, J. S., Brandt, J. S., Anastasio, H., Birsner, M., O'Brien, D. S., Sedev, H. M., ... Berghella, V. (Aug 2020). Clinical course of severe and critical coronavirus disease 2019 in hospitalized pregnancies: a United States cohort study. <i>American journal of obstetrics & gynecology MFM</i>, 2(3), 100134.</p>	<ul style="list-style-type: none"> • This cohort study of 64 pregnant women with severe or critical COVID-19 hospitalized at 12 US institutions between March 5, 2020, and April 20, 2020 found 44 (69%) had severe disease, and 20 (31%) had critical disease. • Most women (81%) were treated with hydroxychloroquine; 7% of women with severe disease and 65% of women with critical disease received remdesivir. All women with critical disease received either prophylactic or therapeutic anticoagulation during their admission. • Pregnant women with severe or critical COVID-19 were admitted to the hospital about seven days after the onset of symptoms and stayed in the hospital for six days (median, six days [severe group] and 10.5 days [critical group]; P=.01). Intubation was usually performed around day nine on patients who required it; peak respiratory support for women with severe conditions was performed on day eight. Hospitalization of pregnant women with severe or critical COVID-19 resulted in delivery during the course of the disease in 50% of this cohort. Furthermore, 75% of all women with critical COVID-19 had mostly iatrogenic preterm delivery. • Data suggest that the clinical course of severe or critical COVID-19 in hospitalized pregnant women may be shorter than in hospitalized nonpregnant patients.
<p>Liang, H., & Acharya, G. (Mar 5, 2020). Novel corona virus disease (COVID-19) in pregnancy: What clinical recommendations to follow?. <i>Acta obstetrica et gynecologica Scandinavica</i>, 99(4), 439–442.</p>	<ul style="list-style-type: none"> • Supportive Therapy: Adequate rest, hydration, nutritional support, and water and electrolyte balance should be ensured. It is essential to monitor vital signs and oxygen saturation closely. Depending on the severity of the disease, supplemental oxygen inhalation (60%-100% concentration at a rate of 40 L/min) should be given via high-flow nasal cannula depending on the severity of hypoxemia. Intubation and mechanical ventilation or even extra-corporal membrane oxygenation (ECMO) may be required to maintain oxygenation. Other complications may include septic shock, acute kidney injury, and virus-induced cardiac injury. Therefore, it is important to check arterial blood gases, lactate, renal function, liver function and cardiac enzymes as indicated by the clinical situation. • Antiviral Treatment: This has been routinely used to treat COVID-19 infection in China, and is also recommended for pregnant patients. Combination therapy with antiproteases Lopinavir/Ritonavir has been the preferred drug regimen as it is known to be relatively safe in

^j The six societies are: Society for Maternal-Fetal Medicine (SMFM), the American College of Obstetricians and Gynecologists (ACOG) from the United States, the Royal College of Obstetricians and Gynaecologists (RCOG) from the United Kingdom, the International Society of Ultrasound in Obstetrics and Gynecology (ISUOG), the Centers for Disease Control and Prevention (CDC), and the World Health Organization (WHO). The recommendations from the SMFM focus on high-risk pregnancies, and those from the ACOG and the RCOG focus on all pregnancies. The WHO and the CDC focus on recommendations that can be generalized across all patient populations, and ISUOG focuses on sonography and care of ultrasound equipment.

	<p>pregnancy. The recommended dose is two capsules of Lopinavir/Ritonavir (200 mg/50 mg per capsule) orally together with nebulized α-interferon inhalation (5 million IU in 2 mL of sterile water for injection) twice a day.</p> <ul style="list-style-type: none"> ○ WHO advises caution and careful risk-benefit analysis before using investigational therapeutic agents in pregnant women outside clinical trials. Remdesivir, a nucleotide analog, and chloroquine, an antimalarial drug, are promising drugs against COVID-19 as they are known to inhibit SARS-COV-2 virus in vitro.¹⁴ Clinical trials have already started in China and are planned elsewhere. ● Antibacterial Treatment: The extensive lung damage by the virus substantially increases the risk of secondary bacterial pneumonia. Antibiotics are indicated only if there is evidence of secondary bacterial infection. Intravenous Ceftriaxone can be administered initially while awaiting culture and sensitivity results. ● Corticosteroid Therapy: In general, use of corticosteroids in the treatment of COVID-19 pneumonia is not recommended as it may delay the virus clearance from the body. However, short-term (three to five days) administration of methylprednisolone (1-2 mg/Kg bodyweight per day) has been used frequently in China, especially when dyspnea and hypoxemia are severe, in an attempt to ameliorate lung inflammation and prevent acute respiratory distress syndrome. This regimen is also recommended for pregnant women with COVID-19, although data on its effectiveness and safety need further evaluation. Administration of Betamethasone 12mg intramuscularly followed by another dose 24 hours later should be considered to promote fetal lung maturity when preterm delivery is anticipated.
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Table 3: Summary of Jurisdictional Guidance and Experiences regarding Incidence, Severity, and Management of COVID-19 Obstetrical Patients

Jurisdiction/Organization	Summary of Findings
<p>Canada</p> <p>Canadian Surveillance of COVID-19 in Pregnancy: Epidemiology, Maternal and Infant Outcomes (CANCOVID-Preg)</p> <p>(Feb 25, 2021)</p>	<ul style="list-style-type: none"> Maternal and infant outcomes (n=1,880 pregnant positive cases; March 1, 2020 to December 31, 2020) from five Canadian provinces (British Columbia, Alberta, Ontario, Quebec, and Manitoba) were analyzed. <p>Incidence</p> <ul style="list-style-type: none"> Although the risk of COVID-19 acquisition among pregnant women cannot be determined from the data, compared to the general population, infection rates appear to be lower among pregnant women in every province noted below with the exception of BC. Among pregnant positive cases, 44.6% were between 30 and 35 years of age. Most cases were diagnosed between 14 and 27 weeks' gestation (38.7%), with infection most often acquired via the community-at-large (50.6%). Obesity was the most common underlying condition (11.9%). The most common symptoms associated with a positive COVID-19 diagnosis during pregnancy were cough (47.0%), headache (31.0%), fever (29.8%) and rhinitis (25.6%). <p>Severity</p> <ul style="list-style-type: none"> These data show that although the absolute risk is low, compared to their non-pregnant counterparts, COVID-19 infected pregnant women remain at increased risk of being hospitalized (RR = 5.33, 95% CI: 4.51 to 6.20) and admitted to the ICU (RR=5.88, 95% CI: 3.80 to 8.22). Among the 1,839 women with complete information about any COVID-19 related hospitalization or ICU admission, 8.1% were hospitalized and 1.6% were admitted to the ICU. Two previous reports by CANCOVID-Preg described increased risk of hospitalization (Report #1: (RR = 6.57, 95% CI: 4.82 to 8.95; Report # 2: RR = 4.18, 95% CI: 3.34 to 5.09) and ICU admission (Report #1: RR=8.49, 95% CI: 4.13 to 17.46; Report #2: RR=4.07, 95% CI: 2.13 to 6.43) in Canada. <p>Outcomes</p> <ul style="list-style-type: none"> Among the 738 cases with delivery and gestational age data, 82.0% occurred at term and 12.3% at preterm gestation. Preterm birth etiology showed 40.2% were medically indicated and 45.1% were spontaneous. The majority of infants (82.1%) were in the normal range for birth weight (i.e., 2,500-4,000 grams) and were not admitted to the NICU (83.3%). CANCOVID-Preg previously found increased preterm birth rates (Report #1: 15.0%, Report #2: 12.2%) and NICU admission (Report #1: 15.4%, Report #2: 14.0%).³⁹
<p>Society of Obstetricians and Gynaecologists of Canada (SOGC)</p> <p>(Feb 15, 2021; May 4, 2021)</p>	<p>Severity</p> <ul style="list-style-type: none"> Interim Canadian data from a three province (Ontario, British Columbia, and Alberta) analysis of population outcomes in pregnancy from March 1 – September 20, 2020 reveal that hospitalization and ICU admission are both increased in pregnant women over non-pregnant women by a wider margin. The rate of hospitalization was 11% and the rate of ICU admission was 2.3%.⁴⁰ <p>Outcomes</p> <ul style="list-style-type: none"> Interim Canadian data from a three province (Ontario, British Columbia, and Alberta) analysis of population outcomes in pregnancy from March 1 – September 20, 2020 reveals that the rate of preterm birth was 15% which is approximately two-fold the background rate in the population. Caesarean section was 33% and neonatal intensive care was 15%.⁴¹ <p>Management</p> <ul style="list-style-type: none"> Pregnant patients suspected of having or having been exposed to COVID-19 should be triaged quickly, given a mask to wear, and transferred to a single-occupancy room as quickly as possible.

	<ul style="list-style-type: none"> • Testing should be performed as per local guidelines and recommendations. Pregnancy does not appear to alter test performance. • Expectant management at home may be appropriate for many pregnant patients, however given the increase in adverse outcomes, close virtual follow-up should be instituted to permit rapid admission should clinical condition worsen. For those requiring admission, droplet and contact infection precautions are adequate. • Droplet and contact precautions should be used, including wearing a surgical mask with eye protection, a gown, and gloves. • If breastfeeding is chosen, it should be encouraged within the first hour of life after appropriate hand hygiene, while the mother is wearing a mask. Cleansing the chest/breast could be considered.⁴² <p>Medications</p> <ul style="list-style-type: none"> • Vaccination: Consensus statements include: <ul style="list-style-type: none"> ○ Pregnant individuals should be offered vaccination at any time during pregnancy or while breastfeeding if no contraindications exist. ○ The SOGC supports the use of all available COVID-19 vaccines approved in Canada in any trimester of pregnancy and during breastfeeding in accordance with regional eligibility. ○ The decision to be vaccinated is based on the individual's personal values, as well as an understanding that the risk of infection and/or morbidity from COVID-19 outweighs the theorized and undescribed risk of being vaccinated during pregnancy or while breastfeeding. Individuals should not be precluded from vaccination based on pregnancy status or breastfeeding. ○ Given that pregnant people are at increased risk of morbidity from COVID-19 infection, all pregnant persons should be eligible to receive a COVID-19 vaccination.⁴³ • Antibiotics: Health care providers can consider empiric antibiotic therapy for superimposed bacterial pneumonia in pregnant patients with confirmed COVID-19 infection or severe respiratory disease. First-line antibiotics are oral amoxicillin for stable patients and ceftriaxone for severe disease, based on general recommendations for the management of pneumonia.⁴⁴ • Corticosteroids: Initiation of antepartum corticosteroids for fetal maturation is recommended as per current guideline if preterm delivery is anticipated based on maternal condition. Initiation of corticosteroid therapy for maternal benefit should be initiated in cases of severe infection to reduce the risk of COVID-19 associated mortality. Standard of care for adults severely affected by COVID-19 would be dexamethasone 6 mg daily for up to 10 days.⁴⁵
Ontario	
<p>Society of Obstetricians and Gynaecologists of Canada (SOGC)</p> <p>(Apr 15, 2021)</p>	<p>Severity</p> <ul style="list-style-type: none"> • According to SOGC members, there is currently a daily wave of pregnant women and individuals coming into Ontario ICUs, many requiring ventilators. • Pregnant women and individuals who have COVID-19 appear more likely to develop respiratory complications requiring intensive care than women and individuals who are not pregnant. Providing ventilator support in pregnancy is more challenging, and the risks are greater to both mother and child.⁴⁶
<p>Better Outcomes Registry & Network (BORN) Ontario</p> <p>(Apr 26, 2021)</p>	<p>Incidence and Severity</p> <ul style="list-style-type: none"> • The approximate number of currently pregnant individuals in Ontario with a due date after April 1, 2021 is 84,500. • There has been a cumulative total of 1,403 laboratory-confirmed positive cases of SARS-CoV-2 infection in pregnant individuals reported in Ontario between March 1, 2020 and March 31, 2021. Seventy-three had a COVID-19 related hospitalization and 13 were admitted to ICU. • In the first and second waves of the COVID-19 pandemic, pregnant individuals in Ontario and across Canada had higher rates of hospitalization and intensive care unit (ICU) admission relative to non-pregnant individuals of similar age. • BORN started a special data collection in March of 2020 to capture COVID-19 information submitted by hospitals and midwifery practice groups. This information is linked with the pregnancy and birth records in the BORN Information System. To date, BORN has received 514 case reports. It

	<p>is not surprising that this number is different from the 1,403 laboratory confirmed cases – many of these pregnant individuals are early in pregnancy and may not have presented to a hospital yet for care or birth. These data are also shared with the national network (CANCOVID-Preg).</p> <ul style="list-style-type: none"> Nationally, 4,631 cases of SARS-CoV-2 infection have been reported in pregnant individuals. However, this is known to be underreported due to some provinces not fully participating in the CANCOVID-Preg Network. Additional clinical data on 2,824 cases (including cases from Ontario) from March 1, 2020 to December 31, 2020 are also available. <p>Outcomes</p> <ul style="list-style-type: none"> A higher rate of preterm birth was observed among infected versus non-infected pregnant individuals in Ontario and Canada. Of the 1,403 confirmed cases, 792 have given birth at ≥ 20 weeks of gestational age: <ul style="list-style-type: none"> 785 (99.1%) of these births were live births. 11.2% of live births to individuals who had SARS-CoV-2 infection prior to 37 weeks' gestation were born preterm (before 37 weeks of gestation); for comparison, the incidence of preterm birth in Ontario was 8.3% in fiscal year 2018/2019. The incidence of stillbirth among these births was 8.8 per 1,000 births; for comparison, the incidence of stillbirth in Ontario was 4.7 per 1,000 births in fiscal year 2018/19. Note, however, that the absolute number of stillbirth events reported in SARS-CoV-2 infected individuals is very low (seven stillbirths) and the incidence should be interpreted cautiously. 15.9% of newborns born to mothers with SARS-CoV-2 infection were admitted to a neonatal intensive care unit (NICU); for comparison, the rate of NICU admission in Ontario was 13.2% in fiscal year 2018/19.⁴⁷
<p>British Columbia</p>	
<p>BC Centre for Disease Control / BC Ministry of Health – Guideline for the Admission and Hospital Management of Pregnant Women</p> <p>(Sept 4, 2020)</p>	<p>Severity</p> <ul style="list-style-type: none"> Pregnant women/individuals are not at more risk of acquiring SARS CoV-2, nor at more risk of getting severe disease than adults of comparable age. <p>Outcomes</p> <ul style="list-style-type: none"> To date, information is available for about 60 cases of pregnant women with confirmed COVID-19 in China. The pregnancy outcomes have been reported to be good overall, with spontaneous and iatrogenic preterm labour being the most reported adverse pregnancy outcomes. Within this cohort of ~60 cases there is no strong evidence of vertical transmission at this point. There is currently no reported increased risk of congenital anomaly for teratogenicity, though the number of reported cases is small. <p>Management</p> <ul style="list-style-type: none"> Do not move patient between sites if at all possible. Minimize room transfers and in-hospital movement. Only essential staff should enter patient's room. Ideally, care should be done by a multidisciplinary team, this team may include Internal Medicine, Infectious diseases, Critical Care, Anesthesia and Obstetrics and Gynecology. For sites with an onsite ICU, mother-baby dyads will be cared for at the local site assuming the onsite NICU can manage the gestational age of the newborn. Do not transfer unless the local site cannot meet both mother and neonate requirements. <p>Medications</p> <ul style="list-style-type: none"> Consider empiric antibiotic therapy for superimposed bacterial pneumonia or severe respiratory disease. Note, as data is gathered, this recommendation may change. First-line antibiotics are oral amoxicillin for stable patients and ceftriaxone for severe disease, based on general recommendations for the management of pneumonia. Initiation of antepartum corticosteroids for fetal maturation could be considered as per current guidelines if preterm delivery is indicated or anticipated based on maternal condition.⁴⁸

Manitoba	
<p>Shared Health – COVID-19 Provincial Guidance on the Management of COVID-suspect and COVID-positive Obstetrical Patients and their Newborns</p> <p>(Feb 4, 2021)</p>	<p>Management</p> <ul style="list-style-type: none"> • Suspect or positive cases of COVID-19 should be cared for in a private room. The patient is not required to be in an Airborne Infection Isolation Room (AIIR) room. The patient should wear a procedure mask wherever possible.⁴⁹ <p>Medications</p> <ul style="list-style-type: none"> • For a patient requiring enhanced care for respiratory deterioration, steroid therapy is indicated once supplemental oxygenation is required.⁵⁰
Alberta	
<p>Alberta Health Services – COVID-19 Scientific Advisory Group</p> <p>(Feb 3, 2021)</p>	<p>Prone Positioning</p> <ul style="list-style-type: none"> • This evidence report on prone positioning for awake, non-intubated patients with SARS-COV-2 pneumonia states that if being considered for awake prone positioning outside of a clinical trial, COVID-19 patients should be assessed to determine their risk for escalating care. Low-risk patients, where prone positioning may be implemented with caution on a medical ward, include pregnancy (2nd/3rd trimesters).⁵¹
United States (US)	
<p>National Institute of Health – COVID-19 Treatment Guidelines</p> <p>(Aug 27, 2020)</p>	<p>Management</p> <ul style="list-style-type: none"> • Management of COVID-19 in the pregnant patient should include: <ul style="list-style-type: none"> ○ Fetal and uterine contraction monitoring, when appropriate, based on gestational age. ○ Individualized delivery planning. ○ A multispecialty, team-based approach that may include consultation with obstetric, maternal-fetal medicine, infectious disease, pulmonary and critical care, and pediatric specialists, as appropriate. <p>Medications</p> <ul style="list-style-type: none"> • Potentially effective treatment for COVID-19 should not be withheld from pregnant women because of theoretical concerns related to the safety of therapeutic agents in pregnancy. • Decisions regarding the use of drugs approved for other indications or investigational drugs for the treatment of COVID-19 in pregnant patients must be made with shared decision-making between the patient and the clinical team, considering the safety of the medication for the pregnant woman and the fetus and the severity of maternal disease.⁵²
<p>Centers for Disease Control and Prevention – Considerations for Inpatient Obstetric Healthcare Settings</p> <p>(Dec 1, 2020)</p>	<p>Severity</p> <ul style="list-style-type: none"> • Pregnant people are at an increased risk for severe illness from COVID-19 compared to non-pregnant people. <p>Outcomes</p> <ul style="list-style-type: none"> • There might be an increased risk of adverse pregnancy outcomes, such as preterm birth, among pregnant people with COVID-19. <p>Management</p> <ul style="list-style-type: none"> • Appropriate isolation of pregnant patients who have suspected or confirmed COVID-19. • All health care facilities that provide obstetric care must ensure that their personnel are correctly trained and capable of implementing recommended infection control interventions, including the use of personal protective equipment.⁵³

<p>American College of Obstetricians and Gynecologists</p> <p>(2020)</p>	<p><u>Severity</u></p> <ul style="list-style-type: none"> • Available data suggest that symptomatic pregnant women with COVID-19 are at increased risk of more severe illness compared with nonpregnant peers. • Although the absolute risk for severe COVID-19 is low, available data indicate an increased risk of ICU admission, need for mechanical ventilation and ventilatory support (ECMO), and death reported in pregnant women with symptomatic COVID-19 infection, when compared with symptomatic non-pregnant women. • Data are emerging that pregnant individuals over the age of 30 years are at an increased risk of moderate-to-severe or critical illness compared to pregnant patients who are less than 20 years of age. • Although data presented above suggest an increase in risk of severe outcomes in pregnant women with symptomatic SARS-CoV-2 infection, the absolute risk is still substantially lower than that of pandemic H1N1 influenza infection during pregnancy. <p><u>Outcomes</u></p> <ul style="list-style-type: none"> • Although there are cases of reported vertical transmission of SARS-CoV-2, currently available data indicate that vertical transmission appears to be uncommon. • Some studies have suggested that there may be an increased rate of preterm delivery and stillbirth in pregnant women with active SARS-CoV-2 infection compared with the background rate of these outcomes in the general pregnant population. It is unclear if these outcomes are directly due to SARS-CoV-2 infection or an indirect effect that results from severe maternal illness or iatrogenic intervention.⁵⁴ <p><u>Management</u></p> <ul style="list-style-type: none"> • Timing of delivery, in most cases, should not be dictated by maternal COVID-19 infection. For women with suspected or confirmed COVID-19 early in pregnancy who recover, no alteration to the usual timing of delivery is indicated. For women with suspected or confirmed COVID-19 in the third trimester who recover, it is reasonable to attempt to postpone delivery (if no other medical indications arise) until a negative testing result is obtained or quarantine status is lifted in an attempt to avoid transmission to the neonate. In general, COVID-19 infection itself is not an indication for delivery.⁵⁵ • ACOG has developed an algorithm to evaluate and manage pregnant outpatients with suspected or confirmed SARS-CoV-2 infection.⁵⁶
<p>Society for Maternal Fetal Medicine – Management Considerations for Pregnant Patients With COVID-19</p> <p>(Feb 2, 2021)</p>	<p><u>Severity</u></p> <ul style="list-style-type: none"> • Scoring systems may be utilized to aid in the assessment of severe disease, such as modifications of the Sequential Organ Failure Assessment (SOFA) score, the "quick" qSOFA, and the modified Early Warning Signs score. However, data are limited or inconclusive on the effectiveness of early warning signs in pregnancy, and these scoring systems may not consistently reflect who will become the most critically ill with COVID-19. • An algorithm can be used when considering the admission of a COVID-19 patient to intensive care (Fig 1 in report). <p><u>Management</u></p> <ul style="list-style-type: none"> • It is recommended that COVID-19 positive patients wear masks at all times and remain isolated, whether outpatient or inpatient, until convalesced, unless not feasible due to clinical care needs. • Inpatient monitoring may be needed for the following categories of patients: pregnant COVID-19 patients with moderate to severe signs and symptoms or oxygen saturation less than 95%; pregnant COVID-19 patients with comorbid conditions (e.g., hypertension, diabetes); and pregnant COVID-19 patients with fevers greater than 39 °C despite acetaminophen. • Intubation timing for severe disease patients should be individualized. • Timing of delivery in critically ill pregnant women should be individualized. Decisions should be based on maternal status, concurrent pulmonary disease (e.g., cystic fibrosis, asthma, sarcoidosis), critical illness, ability to wean off the ventilator and ventilator mechanics, gestational age at time of delivery, and shared decision-making with the patient or healthcare proxy.

	<p><u>Prone Positioning</u></p> <ul style="list-style-type: none"> • Prone positioning is feasible in pregnant as well as postpartum patients, including the recently delivered. Padding and/or support devices (e.g., pillows, padding from the operating room, etc.) may need to be utilized to position the patient properly. The most important aspect of this maneuver is to ensure that the endotracheal tube remains in place throughout rotation and positioning and that it is secured afterward. • "Passive prone positioning," in which the patient is not intubated and positions herself in either the lateral decubitus (typically for ~2 hours in each position) or fully prone position, may aid in patient comfort and theoretically help avoid intubation. <p><u>Medications</u></p> <ul style="list-style-type: none"> • <u>Remdesivir</u>: SMFM recommends that remdesivir be offered to pregnant patients with COVID-19 meeting criteria for compassionate use. <ul style="list-style-type: none"> ○ The Adaptive COVID-19 Treatment Trial (ACTT-1) investigated the use of the antiviral agent remdesivir among patients requiring oxygen therapy due to COVID-19 infection and demonstrated a decreased duration of disease in treated patients. Because of these promising results, the National Institutes of Health (NIH) COVID-19 Treatment Guidelines Panel recommends remdesivir for treatment of COVID-19 in hospitalized patients with SpO2 ≤94% on ambient air (at sea level) or those who require supplemental oxygen (AI). The Panel recommends remdesivir for treatment of COVID-19 in patients who are on mechanical ventilation or extracorporeal membrane oxygenation (ECMO) (BI). There is no known fetal toxicity associated with remdesivir. • <u>Dexamethasone</u>: Since the benefit of mortality reduction outweighs the risk of fetal steroid exposure for this short course of treatment, SMFM recommends that this treatment should also be offered to pregnant patients with COVID-19 requiring oxygen or mechanical ventilation: <ul style="list-style-type: none"> ○ If glucocorticoids are indicated for fetal lung maturity, dexamethasone 6 mg IM every 12 hours for 48 hours (4 doses) followed by up to a total of 10 days of 6 mg dexamethasone PO/IV daily. ○ If glucocorticoids are not indicated for fetal lung maturity, 6 mg dexamethasone daily (PO/IV) for up to 10 days should be utilized as in nonpregnant patients. • <u>Monoclonal Antibodies</u>: As Bamlanivimab and Casirivimab are used in mild to moderate COVID-19 patients, risks and benefits to the pregnant patient and fetus should be assessed by providers. The NIH COVID guidelines state that there is inadequate evidence for or against use of these agents in general. However, there is no absolute contraindication to their use in appropriate pregnant patients. • <u>Antibiotics</u>: If clinicians suspect community-acquired pneumonia coinfection, the use of antibiotics is reasonable. <ul style="list-style-type: none"> ○ Ceftriaxone plus azithromycin or ceftriaxone alone are commonly used to treat community-acquired pneumonia and are not contraindicated in pregnancy. ○ For patients with severe disease or who have risk factors for hospital-acquired, ventilator-acquired, and/or drug-resistant types of pneumonia, broad-spectrum agents should be employed, such as cefepime, meropenem, piperacillin-tazobactam, linezolid, and vancomycin, all of which are acceptable in pregnancy.⁵⁷
<p>Society for Maternal Fetal Medicine – Labor and Delivery COVID-19 Considerations</p> <p>(Oct 9, 2020)</p>	<p><u>Management</u></p> <ul style="list-style-type: none"> • One strategy to reduce exposure risk is to co-locate patients who are persons under investigation and women who test positive for SARS-CoV2 into a restricted area of the hospital. While not all facilities are able to create an independent obstetrics COVID-19 unit, attempts should be made to designate specific locations for the purposes of containment, which will limit the exposure of unaffected patients and staff. For hospitals that have the staffing capacity, consider using a designated team of trained clinicians to care for women in these cohorted rooms. • Women who test positive for SARS-CoV2 or PUIs should ideally be placed in an isolation room with droplet and contact precautions. Airborne infection isolation rooms (single-patient negative-pressure rooms with a minimum of 6 air changes per hour), if available, can be used if performance of aerosolizing procedures is anticipated. Hospital facilities can inform whether specific rooms, such as operating rooms (ORs) or rooms in which higher acuity evaluations are performed (eg, when intubation may be required), can be safely converted to negative-pressure rooms. These rooms can be designated for Caesarean deliveries for women who test positive for SARS-CoV2 or PUIs. Conversion may not be

	<p>possible in all facilities and, with proper PPE and patient transfer protocols, Caesarean deliveries can still be safely performed in a positive-pressure OR.</p> <ul style="list-style-type: none"> • See guidance for other recommendations related to PPE, triage and testing procedures, labour and delivery, and postpartum care.⁵⁸
<p>UpToDate – COVID-19 Pregnancy Issues and Antenatal Care (May 5, 2021)</p>	<p><u>Severity</u></p> <ul style="list-style-type: none"> • Clinical manifestations of COVID-19 in pregnant people are generally similar to those in nonpregnant individuals. • Pregnancy does not appear to increase susceptibility to acquiring SARS-CoV-2 infection, and most infected mothers recover without undergoing delivery. However, pregnant people with the infection appear to be at increased risk for developing severe disease necessitating maternal intensive care unit admission and mechanical ventilation, and in rare cases, extracorporeal membrane oxygenation may be needed. Risk factors for severe disease include age ≥ 35 years, obesity, hypertension, and pre-existing diabetes. <p><u>Outcomes</u></p> <ul style="list-style-type: none"> • Maternal deaths are in excess of those in nonpregnant females of reproductive age with COVID-19. • Infected pregnant people, especially those who develop pneumonia, also appear to have a small increase in frequency of preterm birth and possibly Caesarean delivery. These complications are likely related to severe maternal illness. Whether intrauterine infection occurs is still under investigation. A few early newborn infections and placental infections have been reported, suggesting possible but uncommon vertical transmission. <p><u>Management</u></p> <ul style="list-style-type: none"> • Timing of delivery should be individualized based on maternal status, concurrent disorders, gestational age, and shared decision-making with the patient or health care proxy. • Whether the mother's respiratory disease will be improved by delivery and the risk of postnatal transmission in the delivery room when maternal symptoms are acute are both unclear. • For the hospitalized patient with COVID-19 with pneumonia but not intubated, some authorities have advocated consideration of delivery in pregnancies >32 to 34 weeks in the setting of worsening status. The rationale is that delivery is performed before the pulmonary situation worsens and ongoing maternal hypoxemia places the fetus at risk of compromise. Most authorities do not advocate delivery prior to 32 weeks, even though the maternal situation may worsen in the second week, given the known morbidity and mortality of very preterm infants. • Timing of delivery of the hospitalized pregnant patient intubated and critically ill with COVID-19 is challenging. After 32 to 34 weeks, some have advocated delivery if the patient is stable to avoid any pregnancy-related problems if the maternal condition subsequently deteriorates, but this could exacerbate the maternal condition. Others consider delivery only for patients with refractory hypoxemic respiratory failure or worsening critical illness. <p><u>Prone Positioning</u></p> <ul style="list-style-type: none"> • In the ICU, severely ill patients with COVID-19 are often managed in the prone position; the left lateral position is an alternative but may not be as effective. Some ICUs have extended this approach to pregnant patients, although even a semi-prone position can be a difficult position in which to place a pregnant woman in the last half of pregnancy. Padding above and below the gravid uterus >24 weeks is desirable to offload the uterus and avoid aortocaval compression. <p><u>Medications</u></p> <ul style="list-style-type: none"> • For pregnant patients who would otherwise qualify for remdesivir (and for whom it is available), remdesivir is recommended. • Drugs that may be considered for use in pregnant patients include: Baricitinib and Bamlanivimab-etesevimab, and casirivimab-imdevimab. • COVID-19 vaccination is recommended for pregnant people rather than deferring vaccination until after delivery or after breastfeeding. • In pregnant patients who meet criteria for use of glucocorticoids for maternal treatment of COVID-19 and also meet criteria for use of antenatal corticosteroids for fetal maturity, we suggest administering the usual doses of dexamethasone (four doses of 6 mg given intravenously 12 hours

	<p>apart) to induce fetal maturation and continue dexamethasone to complete the course of maternal treatment for COVID-19 (6 mg orally or intravenously daily for 10 days or until discharge, whichever is shorter).</p> <ul style="list-style-type: none"> For pregnant patients hospitalized for severe COVID-19, prophylactic-dose anticoagulation is recommended, if there are no contraindications to its use, and generally discontinued when the patient is discharged to home.⁵⁹
<p>NYC Health – COVID-19: Recommendations for Providers Serving People Who Are Pregnant, Breastfeeding or Chest feeding, or Caring for Newborns</p> <p>(Mar 13, 2021)</p>	<ul style="list-style-type: none"> Based on the American College of Obstetrics and Gynecology (ACOG)’s algorithm for the assessment and management of pregnant people with suspected or confirmed COVID-19, this guidance sets forth recommendations for health care providers serving people who are pregnant, breastfeeding or chest feeding, or caring for newborns during the COVID-19 public health emergency. <p>Severity</p> <ul style="list-style-type: none"> Based on what is currently known, people who are pregnant are at a higher risk for severe illness from COVID-19 than people who are not pregnant. <p>Outcomes</p> <ul style="list-style-type: none"> People who are pregnant and who have COVID-19 may also have a higher risk for preterm birth and other adverse pregnancy outcomes. <p>Management</p> <ul style="list-style-type: none"> To date, some studies have suggested an increased rate of preterm delivery and stillbirth in people who are pregnant and have active SARS-CoV-2 (the virus that causes COVID-19) infection compared with those in the general population. It is unclear whether these outcomes are directly due to SARS-CoV-2 infection or an indirect effect resulting from severe maternal illness or iatrogenic intervention. As such, there is currently no recommendation to change counseling on risks of fetal anomalies or other outcomes. Risk assessments for pregnancy care and delivery planning should be based on maternal risk factors as per routine. Management of intrapartum (while giving birth) status should not change unless the pregnant person or fetus displays symptoms. <ul style="list-style-type: none"> Pulmonary imaging should not be withheld due to pregnancy status. Caesarean delivery should be based on obstetric (fetal or maternal) indications and not on COVID-19 status alone. Presence of a patient’s support team (even virtually) should not be withheld. Practitioners should follow the usual clinical indications for operative vaginal delivery.⁶⁰
<p>United Kingdom (UK) and Europe</p>	
<p>The Royal College of Midwives / Royal College of Obstetricians and Gynaecologists</p> <p>(Feb 19, 2021)</p>	<p>Incidence</p> <ul style="list-style-type: none"> Pregnant women do not appear more likely to contract the infection than the general population. The majority of pregnant women who are infected with SARS-CoV-2 will be asymptomatic. <p>Severity</p> <ul style="list-style-type: none"> Compared to non-pregnant women with COVID-19, pregnant women with COVID-19: <ul style="list-style-type: none"> Have higher rates of intensive care unit (ICU) admission; this may reflect a lower threshold for admission to ICU, rather than more severe disease. Are not at increased risk of death from COVID-19, according to the largest systematic review. Were however found in more recent data from the USA and Mexico to have a slightly higher risk of death in these specific national health care settings. <p>Outcomes</p> <ul style="list-style-type: none"> Compared to pregnant women without COVID-19, pregnant women with symptomatic COVID-19 requiring hospitalization have overall worse maternal outcomes, including an increased risk of death, although that risk remains very low (the UK maternal mortality rate from COVID-19 is 2.2 per 100,000 maternities). Aside from preterm birth, there is no evidence that COVID-19 infection has an adverse effect on the fetus or on neonatal outcomes.

	<p>Management</p> <ul style="list-style-type: none"> • Service modifications are required to enable social distancing measures, to reduce the risk of transmission between women, staff, and other clinic/hospital visitors, and to provide care to women who are self-isolating for suspected or confirmed COVID-19 for whom a hospital attendance is essential. • Maternity units should develop triage tools to assess the severity of illness for women who telephone with suspected or confirmed COVID-19. This should include an assessment of symptoms, clinical and social risk factors, and escalation pathways. This should include ‘safety netting advice’ about the risks of deterioration and when to seek urgent medical attention. • For women with possible or confirmed COVID-19, for whom hospital attendance is required or who self-present (this includes women who live with an individual who has possible or confirmed COVID-19): <ul style="list-style-type: none"> ○ Women should be cared for within isolation rooms from which all non-essential items have been removed prior to the woman’s arrival (this includes other rooms in which the woman spends time during her hospital attendance [e.g. scan rooms when bedside scans are not appropriate]). ○ Women should immediately be escorted to an isolation room or cohort bay/ward, suitable for the majority of care during their hospital visit or stay. • For asymptomatic women who test positive for SARS-CoV-2 on admission, continuous electronic fetal monitoring (CEFM) during labour using cardiotocography (CTG) is not recommended solely due to a positive test. • The number of staff members entering the room should be minimised, and units should develop a local policy specifying essential personnel for emergency scenarios. • Women with symptomatic suspected or confirmed COVID-19 should be offered delayed cord clamping and skin-to-skin contact with their baby if the condition of the woman and infant allows. <p>Prone Positioning</p> <ul style="list-style-type: none"> • For pregnant women in the third trimester who are unwell, an individualized assessment should be undertaken by the MDT to decide whether emergency caesarean birth or IOL should be prioritized, either to facilitate maternal resuscitation (including the need for prone positioning) or because of concerns regarding fetal health. • Prone positioning of patients with moderate to severe acute respiratory distress syndrome (ARDS) can improve respiratory function and has been recommended for the care of patients with COVID-19. There is little evidence on the use of prone positioning in pregnancy and guidance from the Intensive Care Society in the UK advises that it is relatively contraindicated in the second and third trimesters of pregnancy. However, a review article on prone positioning for pregnant women who are unwell with COVID-19 provides advice, guidance, and an algorithm on how this can be undertaken successfully in the second and early third trimesters. <p>Medications</p> <ul style="list-style-type: none"> • Remdesivir: It should be avoided in pregnant women with COVID-19 unless clinicians believe the benefits of treatment outweigh the risks to the individual. Any decision to treat with remdesivir should be taken by an MDT that includes obstetric and infection specialists. Clinicians should be aware that the fetal risk profile of remdesivir is largely unknown. <ul style="list-style-type: none"> ○ When considering the use of remdesivir in women with COVID-19 who are breastfeeding, clinicians should consider the benefits and risks of treatment, and use only in women where benefit has been reported (hospitalized patients requiring oxygen therapy, especially early in disease course, and not in patients who are mechanically ventilated). Any decision to treat with remdesivir should be taken by an MDT that includes obstetric and infection specialists. • Tocilizumab: Although data for the use of tocilizumab in pregnancy in this situation are limited, there is currently no compelling evidence that tocilizumab is teratogenic or fetotoxic. For women meeting the criteria above (hypoxic with systemic inflammation), the use of tocilizumab should be considered. It is recommended that any decision to treat with anti-IL6 agents should be taken by an MDT to include obstetric and infection specialists, and given if the benefits outweigh the risks.⁶¹
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<p>The National Institute of Health in Italy – Interim guidance on pregnancy, childbirth, breastfeeding and care of infants (0-2 years) in response to the COVID-19 emergency</p> <p>(Feb 5, 2021)</p>	<p><u>Incidence</u></p> <ul style="list-style-type: none"> • The prevalence and clinical manifestations of COVID-19 disease in pregnancy appear to be substantially similar to those of the general population. • The Italian Obstetric Surveillance System (ItOSS) study showed that, during the first wave of the pandemic, women with previous comorbidities (e.g., hypertension), obese women, and women of non-Italian citizenship had a significantly higher risk of developing COVID-19 pneumonia. <p><u>Severity</u></p> <ul style="list-style-type: none"> • Pregnant women do not appear to be at any greater risk than non-pregnant women for severe COVID-19 infection requiring hospitalization. <p><u>Outcomes</u></p> <ul style="list-style-type: none"> • Currently, there is no evidence of an increased risk of abortion, stillbirth, or neonatal death related to maternal COVID-19 infection. • There is currently no evidence of teratogenic effects on the fetus. • The evidence supporting an increased risk of fetal underdevelopment is not conclusive; it is currently considered a possible event. • The pregnancies of women infected with SARS-CoV-2 appear to be associated with a higher frequency of preterm delivery. <ul style="list-style-type: none"> ○ The ItOSS study showed that, during the first wave of the pandemic, the average preterm birth rate was 14.4%, with a decrease during the observation period. In the months of February-March, the rate was 17.5%. In July-August, thanks to the identification of asymptomatic women at the time of hospitalisation, the rate fell to 11%. Overall, the majority of preterm births (7.7%) were due to iatrogenic causes, 3.5% to premature rupture of the membranes, and 3.2% to spontaneous onset. • The ItOSS study found that, during the first wave of the pandemic, between February 25 and July 31, 2020, infants who were not separated from their mothers at birth, roomed-in and received breastmilk had as good outcomes as the infants who were separated from their mothers after birth. • The ItOSS study showed that, during the first wave of the pandemic, the rate of caesarean section was 33.7%, in line with national rates. <p><u>Management</u></p> <ul style="list-style-type: none"> • Pregnant women with a mild, suspected or confirmed COVID-19 infection should receive care at home in coordination with the Local Health Authorities (LHA) services. Hospitalization should be reserved for cases of rapidly-worsening clinical conditions or when a hospital cannot be promptly reached. It is always advisable to go to the COVID birth facilities that have been set up in each Region. • Routine, in-person pre-natal and post-natal visits in hospitals should be postponed if possible, using alternative means of communication for receiving guidance to reduce access to hospitals. Once the isolation period is over, visits can be rescheduled following national and international guidelines and recommendations. • Although at present there is no evidence of a causal relationship between COVID-19 and the risk of fetal underdevelopment, a follow-up ultrasound 14 days after recovery from the acute disease diagnosed during pregnancy is recommended. • When an in-person check-up and/or hospitalization is required, local protocols need to be in place to ensure that pregnant women with confirmed or suspected COVID-19 infection are identified as soon as possible and isolated upon arrival at the health facility before proceeding with the pregnancy check-up. These protocols must include detailed instructions for providing separate spaces, clean and protected pathways, physical distancing, and a limited number of patients in the emergency room waiting room. They must also provide instructions for sanitizing the settings and equipment, for using of PPE, both for the pregnant woman and for the staff, and instructions for hospitalization in the ward, if necessary, and finally provide procedures to be followed in case of complications and/or development of critical conditions. • In the event of a suspected or confirmed infection, a multidisciplinary team should be available to provide care for the pregnant woman, including a gynaecologist, an anaesthetist, a midwife, a neonatologist, a paediatric nurse, and an infectious disease specialist. • COVID-19 positive mothers and their babies should be enabled to stay together, practice skin-to-skin contact and rooming-in day and night, especially after childbirth and during breastfeeding, except when the mother's or infant's clinical conditions are severe. • Based on international recommendations, delivery of care in the second and third stages of labour is not currently considered a procedure at risk of generating aerosols.
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	<p><u>Medications</u></p> <ul style="list-style-type: none"> • In cases of lymphocytosis, consider the possibility of a bacterial rather than a viral infection, and make sure antibiotics are used appropriately. • In unstable clinical conditions, pregnant women requiring steroid therapy should be given 40 mg of oral prednisolone once daily or 80 mg of intravenous hydrocortisone twice daily. • Prescribing thromboprophylaxis treatment during pregnancy should be assessed on a case-by-case basis. All COVID-19 positive women hospitalized during pregnancy should be offered low-molecular-weight heparin prophylaxis unless delivery is expected within 12 hours.⁶²
<p>Australasia</p>	
<p>National COVID-19 Clinical Evidence Taskforce – Australian guidelines for the clinical care of people with COVID-19</p> <p>(2021)</p>	<p><u>Management</u></p> <ul style="list-style-type: none"> • For pregnant women with COVID-19, mode of birth should remain as per usual care. Respiratory deterioration due to COVID-19 may prompt urgent delivery on an individual basis. • Delayed umbilical cord clamping is supported as part of standard care, independent of the presence of COVID-19. • Early skin-to-skin contact after birth and during the postnatal period is supported, irrespective of the presence of COVID-19. However, parents with COVID-19 should use infection prevention and control measures (mask and hand hygiene). • Breastfeeding is supported irrespective of the presence of COVID-19. However, women with COVID-19 who are breastfeeding should use infection prevention and control measures (mask and hand hygiene) while infectious. • For women with COVID-19 who have given birth, support rooming-in of mother and newborn in the birth suite and on the postnatal ward when both mother and baby are well. However, women with COVID-19 should use infection prevention and control measures (mask and hand hygiene). <p><u>Prone Positioning</u></p> <ul style="list-style-type: none"> • For mechanically ventilated pregnant women with COVID-19 and hypoxaemia despite optimizing ventilation, consider prone positioning for more than 12 hours a day. Proning of a pregnant woman should avoid abdominal compression and ensure a woman's hips and chest are supported. In the absence of specialised equipment, proning can be performed using pillows and blankets. Proning can be challenging in late gestation and delivery of the baby may be warranted. • For pregnant and postpartum women with COVID-19 and respiratory symptoms who are receiving any form of supplemental oxygen therapy and have not yet been intubated, consider prone positioning. When positioning a pregnant woman in prone, care should be taken to support the gravid uterus to reduce aorta-caval compression. Women who are deteriorating should be considered for early endotracheal intubation and invasive mechanical ventilation. Birth of the baby should be considered when it may enhance maternal resuscitation or be beneficial to the fetus. <p><u>Medications</u></p> <ul style="list-style-type: none"> • The use of antenatal corticosteroids for women at risk of preterm birth is supported as part of standard care, independent of the presence of COVID-19. • Use dexamethasone 6 mg daily intravenously or orally for up to 10 days in pregnant or breastfeeding women with COVID-19 who are receiving oxygen (including mechanically ventilated patients). Do not routinely use dexamethasone (or other corticosteroids) to treat COVID-19 in pregnant or breastfeeding women who do not require oxygen. • Consider using remdesivir for pregnant or breastfeeding women hospitalized with moderate to severe COVID-19 who do not require ventilation. • Consider using tocilizumab for the treatment of COVID-19 for pregnant or breastfeeding women who require supplemental oxygen, particularly where there is evidence of systemic inflammation. For the babies of women who received tocilizumab during pregnancy (after 20 weeks of gestation), live vaccines (rotavirus and BCG) should be avoided in the first six months of life. • Do not use lopinavir-ritonavir for the treatment of COVID-19. • Do not use sarilumab for the treatment of COVID-19 outside of randomized trials with appropriate ethical approval.⁶³

International Organizations	
<p>World Health Organization – COVID-19 Clinical management: living guidance</p> <p>(Jan 25, 2021)</p>	<p><u>Management</u></p> <ul style="list-style-type: none"> • Pregnant or recently pregnant women with suspected or confirmed mild COVID-19 may not require acute care in hospital, unless there is concern for rapid deterioration or an inability to promptly return to hospital. Isolation to contain virus transmission is recommended, and can be done at a health facility, community facility or at home, according to established COVID-19 care pathways. • Supplemental oxygen therapy should be administered immediately to any patient with emergency signs during resuscitation to target SpO₂ ≥ 94% and to any patient without emergency signs and hypoxaemia (i.e. stable hypoxemic patient) to target SpO₂ > 90% or ≥ 92–95% in pregnant women. • Mode of birth should be individualized, based on obstetric indications and the woman’s preferences. WHO recommends that induction of labour and caesarean section should only be undertaken when medically justified and based on maternal and fetal condition. COVID-19 positive status alone is not an indication for caesarean section. <p><u>Prone Positioning</u></p> <ul style="list-style-type: none"> • There is little evidence on prone positioning in pregnant women with ARDS; this could be considered in early pregnancy. Pregnant women in the third trimester may benefit from being placed in the lateral decubitus position.⁶⁴

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