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Disease severity, pregnancy outcomes, and maternal deaths among pregnant patients with severe acute respiratory syndrome coronavirus 2 infection in Washington State

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On behalf of the Washington State COVID-19 in Pregnancy Collaborative

BACKGROUND: Evidence is accumulating that coronavirus disease 2019 increases the risk of hospitalization and mechanical ventilation in pregnant patients and for preterm delivery. However, the impact on maternal mortality and whether morbidity is differentially affected by disease severity at delivery and trimester of infection are unknown.

OBJECTIVE: This study aimed to describe disease severity and outcomes of severe acute respiratory syndrome coronavirus 2 infections in pregnancy across the Washington State, including pregnancy complications and outcomes, hospitalization, and case fatality.

STUDY DESIGN: Pregnant patients with a polymerase chain reaction–confirmed severe acute respiratory syndrome coronavirus 2 infection between March 1, 2020, and June 30, 2020, were identified in a multicenter retrospective cohort study from 35 sites in Washington State. Sites captured 61% of annual state deliveries. Case-fatality rates in pregnancy were compared with coronavirus disease 2019 fatality rates in similarly aged adults in Washington State using rate ratios and rate differences. Maternal and neonatal outcomes were compared by trimester of infection and disease severity at the time of delivery.

RESULTS: The principal study findings were as follows: (1) among 240 pregnant patients in Washington State with severe acute respiratory syndrome coronavirus 2 infections, 1 in 11 developed severe or critical disease, 1 in 10 were hospitalized for coronavirus disease 2019, and 1 in 80 died; (2) the coronavirus disease 2019—associated hospitalization rate was 3.5-fold higher than in similarly aged adults in Washington State (10.0% vs 2.8%; rate ratio, 3.5; 95% confidence interval, 2.3–5.3); (3) pregnant patients hospitalized for a respiratory concern were more likely to have a comorbidity or underlying conditions including asthma, hypertension, type 2 diabetes mellitus, autoimmune disease, and class III obesity; (4) 3 maternal deaths (1.3%) were attributed to coronavirus disease 2019 for a maternal mortality rate of 1250 of 100,000 pregnancies (95% confidence interval, 257–3653); (5) the coronavirus disease 2019 case fatality in pregnancy was a significant 13.6-fold (95% confidence interval, 2.7–43.6) higher in pregnant patients than in similarly aged individuals in Washington State with an absolute difference in mortality rate of 1.2% (95% confidence interval, 0.3 to 2.6); and (6) preterm birth was significantly higher among women with severe or critical coronavirus disease 2019 at delivery than for women who had recovered from coronavirus disease 2019 (45.4% severe or critical coronavirus disease 2019 vs 5.2% mild coronavirus disease 2019; P<.001).

CONCLUSION: Coronavirus disease 2019 hospitalization and case-fatality rates in pregnant patients were significantly higher than in similarly aged adults in Washington State. These data indicate that pregnant patients are at risk of severe or critical disease and mortality compared to nonpregnant adults, and also at risk for preterm birth.

Key words: case fatality, coronavirus, COVID-19, fetus, maternal mortality, pneumonia, pregnancy, preterm birth, SARS-CoV-2

Introduction

In the early months of the coronavirus disease 2019 (COVID-19) pandemic, pregnant patients faced uncertain risks associated with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.1 SARS-CoV-2 infection in pregnancy is now known to result in a spectrum of asymptomatic to critical maternal disease.2–7 Evidence is accumulating that pregnant patients with SARS-CoV-2 infections are at a higher risk of hospitalization, mechanical ventilation, intensive care unit (ICU) admission, and preterm birth.2,7–11 In June of 2020, a United States population-based study by the Centers for Disease Control and Prevention (CDC) found that pregnant patients with SARS-CoV-2 infections were at a higher risk of hospitalization, mechanical ventilation, and ICU admission, but mortality rates were...
Why was this study conducted?
Whether coronavirus disease 2019 (COVID-19) poses a risk for pregnant women to develop severe or critical disease and the impact on maternal mortality and morbidity are poorly understood.

Key findings
In a multicenter retrospective cohort study of facilities covering 61% of annual births in Washington State, there were 240 pregnant patients with severe acute respiratory syndrome coronavirus 2 infections, 24 COVID-19—associated hospitalizations (10%), and 3 maternal deaths (1.25%). The COVID-19 case-fatality rate in pregnant patients was 13.6-fold higher than similarly aged individuals with COVID-19.

What does this add to what is known?
Our data suggest the impact of COVID-19 on pregnant patients is greater than currently appreciated, with an elevated risk of maternal death.

Methods
Washington State COVID-19 in Pregnancy Collaborative
The WA-CPC includes 35 large hospitals (n=22) and clinic systems providing prenatal care (n=13) in Washington State, encompassing 61% of the approximate 86,000 annual state deliveries (Supplemental Table). The majority of the participating hospitals had established universal screening for SARS-CoV-2 by nasopharyngeal swab before or at the time of the delivery admission by May 2020 (March, 14%; April, 64%; May, 76%), with the remaining hospitals initiating universal testing for scheduled delivery admissions only.

Eligible cases were pregnant patients (≥18 years old) with a polymerase chain reaction (PCR) test—confirmed SARS-CoV-2 infection during any trimester of pregnancy detected between March 1, 2020, and June 30, 2020. Pregnant women were tested for many reasons including exposure to a known SARS-CoV-2 case, symptoms, recent travel, personal requests, and universal screening at labor and delivery. Collaborating sites identified eligible patients using diagnostic codes and site-specific algorithms. Deidentified data were abstracted from electronic medical records, and each record was reviewed by a second abstractor for quality control.

Final disease and delivery outcome data were abstracted between July 7, 2020, and September 10, 2020, based on site capacity. COVID-19 disease severity was defined as1 (1) mild (asymptomatic, nonpneumonia, mild pneumonia), (2) severe (dyspnea, respiratory rate of ≥30 breaths per minute, percutaneous oxygen saturation of ≥93% on room air at rest, arterial oxygen tension over inspiratory oxygen fraction of <300 mm Hg, or lung infiltrates of >50% within 24-48 hours), and (3) critical (severe respiratory distress, respiratory failure requiring mechanical ventilation, shock, or multiple organ dysfunction or failure). Hospitalized participants were considered “hospitalized owing to COVID-19 concern” based on the reason for admission noted by the abstracting team, including respiratory concerns and “other” COVID-19 concerns. Patients admitted for concurrent obstetrical (eg, delivery) and COVID-19 concerns were considered hospitalized for COVID-19 concern.

This multisite medical records review was approved by institutional review boards (IRBs) at the University of Washington (STUDY# 00009701, approved March 6, 2020) and Swedish Medical Center (STUDY #2020000172, approved March 19, 2020). All other sites entered into reliance agreements with the University of Washington IRB.
Statistical analyses
Demographic and SARS-CoV-2 infection characteristics in pregnancy were summarized by proportions and medians (interquartile range [IQR]) overall and were compared across COVID-19 hospitalization status using chi-squared and Kruskal-Wallis tests. Maternal, delivery, and neonatal outcome characteristics were summarized for patients who had delivered by the time of delivery or their last positive test was >14 days before delivery in alignment with quarantine guidelines during the study period; this categorization was independent of disease severity. Women who were PCR positive for SARS-CoV-2 in the preceding 14 days of delivery or admitted with post–COVID-19 complications at the time of delivery (even in absence of continued PCR positivity) were considered to have “active COVID-19” and further classified by mild or severe or critical disease status. Delivery outcomes were compared among COVID-19 recovered, mild COVID-19, and severe or critical COVID at delivery and by trimester of infection, using the chi-squared and Kruskal-Wallis tests, where appropriate.

Collaborating sites captured the majority of pregnancies in Washington State with the highest coverage in regions most affected by COVID-19 (Supplemental Table). We calculated crude rate ratios (RRs) and rate differences (RDs) with Poisson exact 95% confidence interval (CI) to compare COVID-19–associated hospitalization and case-fatality rates in our study population with rates experienced by 20- to 39-year-old adults with SARS-CoV-2 in Washington State using publicly available data from the Washington State Department of Health; this comparison group served as the best publicly available proxy for rates in reproductive-aged women because data were only available by age group or gender, but not both. Notably, nonpregnant adults were tested for SARS-CoV-2 for the same reasons as pregnant people including universal screening before medical procedures. Hospitalization and case-fatality rates at the state level were estimated between March 1, 2020, and September 26, 2020, because outcomes were collected for some study participants through September and to account for the lag between infection detection and mortality outcomes. Both crude RR and RD were calculated given the small number of events in this study population to ascertain both relative and absolute risks.

Results
Severe acute respiratory syndrome coronavirus 2 infections in pregnancy
A total of 240 confirmed cases of SARS-CoV-2 infections in pregnancy were detected by WA-CPC sites including 24 (10.0%) who were hospitalized for a COVID-19 respiratory concern. Demographic and coexisting conditions are presented in Table 1. Of these, 46 cases were previously published including details on 8 deliveries. The median age was 28 years (IQR, 24–33.5). Nearly half were white (113 of 240) and half reported Hispanic ethnicity (126 of 240). Two-thirds were publicly insured (160 of 240). The most common underlying conditions were prepregnancy obesity (body mass index of $\geq 30.0$, 45.3% [102 of 225]), asthma (8.3%; 20 of 240), type 2 diabetes mellitus (5.4%; 13 of 240), and hypertension (4.6%; 11 of 240). Pregnant patients with SARS-CoV-2 infections who were hospitalized for a COVID-19 concern were slightly older (median, 32 vs 28 years old; $P=0.04$) and more likely than nonhospitalized pregnant patients with SARS-CoV-2 infection to have at least 1 comorbidity or underlying condition (45.8% vs 17.6%; $P=0.001$), such as asthma (20.8% vs 6.9%; $P=0.02$), hypertension (20.8% vs 2.8%; $P<0.001$), type 2 diabetes mellitus (12.5% vs 4.6%; $P=0.11$), autoimmune disease (8.3% vs 0.9%; $P<0.01$), and class III obesity (21.1% vs 6.3%; $P=0.01$) (Table 1).

Pregnant patients hospitalized for coronavirus disease 2019–associated respiratory concern
Notably, 24 cases (10.0%) were hospitalized specifically for COVID-19 symptoms, with 3 having concurrent delivery–related indications (Table 3). One-third of the hospitalized patients (8 of 24) were admitted to the ICU (3.3% of study population; 8 of 240); 1 pregnant patient was hospitalized and admitted to the ICU twice. Overall, the SARS-CoV-2 hospitalization rate in pregnant patients was 3.5-fold higher than the rate among individuals aged 20 to 39 years with confirmed SARS-CoV-2 in Washington State (10.0% [24 of 240] vs 2.8% [985 of 34,902]; RR, 3.5; 95% CI, 2.3–5.3) (Table 4).

Most pregnant patients hospitalized for COVID-19 had severe or critical disease (79.2%; 19 of 24), but 20.8% (5 of 24) who were admitted for a COVID-19 concern were ultimately considered to have mild disease by the disease severity criteria (Table 2). All 4 pregnant patients with critical COVID-19 disease developed confirmed or suspected acute respiratory distress syndrome; 3 of these patients ultimately died. Almost half of the hospitalized patients (40.9%; 9 of 22) delivered during their admission for COVID-19 (Table 3); 19 of the hospitalized patients (79.1%; 19 of 24) received some level of oxygen support,
with 16.7% of hospitalized patients (4 of 24) receiving mechanical ventilation. Laboratory testing in addition to a SARS-CoV-2 PCR was performed on a minority of patients, who typically had severe or critical COVID-19. Using pregnancy-specific norms for laboratory values,20 43.5% (10 of 23) had lymphopenia, 77.3% (17 of 22) had an elevated aspartate aminotransferase, 53.3% (8 of 15) had an elevated C-reactive protein, 29.4% (5 of 17) had an elevated D-dimer, and 4.4% (1 of 23) had an elevated creatinine during COVID-19–associated hospitalization (Table 3). The

| Characteristics                                      | All pregnant patients (N=240) | Not hospitalized for COVID-19 concern (n=216) | Hospitalized for COVID-19 concern (n=24) | P value |
|------------------------------------------------------|-------------------------------|-----------------------------------------------|------------------------------------------|---------|
| Demographics                                         |                               |                                               |                                          |         |
| Age (y)                                               | 28 (24–34)                    | 28 (24–33)                                    | 32 (26–35)                               | .04     |
| Race                                                  |                               |                                               |                                          | .14     |
| American Indian or Alaska Native                      | 10 (4.2)                      | 8 (3.7)                                       | 2 (8.3)                                  |         |
| Asian                                                 | 8 (3.3)                       | 8 (3.7)                                       | 0 (0)                                    |         |
| Native Hawaiian or other Pacific Islander             | 8 (3.3)                       | 5 (2.3)                                       | 3 (12.5)                                 |         |
| Black or African American                             | 20 (8.3)                      | 19 (8.8)                                      | 1 (4.2)                                  |         |
| White                                                 | 113 (47.1)                    | 104 (48.2)                                    | 9 (37.5)                                 |         |
| Multiracial                                          | 2 (0.8)                       | 2 (0.9)                                       | 0 (0)                                    |         |
| Other                                                 | 28 (11.7)                     | 26 (12.0)                                     | 2 (8.3)                                  |         |
| Unknown                                               | 51 (21.3)                     | 44 (20.4)                                     | 7 (29.2)                                 |         |
| Ethnicity                                             |                               |                                               |                                          | .29     |
| Hispanic or Latino                                    | 126 (52.5)                    | 117 (54.2)                                    | 9 (37.5)                                 |         |
| Not Hispanic or Latino                                | 108 (45.0)                    | 94 (43.5)                                     | 14 (58.3)                                |         |
| Unknown                                               | 6 (2.5)                       | 5 (2.3)                                       | 1 (4.2)                                  |         |
| Type of insurance at diagnosis                        |                               |                                               |                                          | .11     |
| Public                                                | 160 (66.7)                    | 146 (67.6)                                    | 14 (58.3)                                |         |
| Private                                               | 74 (30.8)                     | 66 (30.6)                                     | 8 (33.3)                                 |         |
| Other                                                 | 4 (1.7)                       | 2 (0.9)                                       | 2 (8.3)                                  |         |
| Uninsured                                             | 1 (0.4)                       | 1 (0.5)                                       | 0 (0)                                    |         |
| Unknown                                               | 1 (0.4)                       | 1 (0.5)                                       | 0 (0)                                    |         |
| Pregnancy history†                                     |                               |                                               |                                          | .08     |
| Parity                                                | 1 (1–3)                       | 1 (1–2)                                       | 1.5 (1–4)                                |         |
| History of preterm birth                              | 23 (9.6)                      | 21 (9.8)                                      | 2 (8.3)                                  | .82     |
| Prepregnancy comorbidities or underlying conditions   |                               |                                               |                                          |         |
| Any comorbidity or underlying condition (excluding obesity)† | 49 (20.4)                    | 38 (17.6)                                     | 11 (45.8)                                | .001    |
| Asthma                                                | 20 (8.3)                      | 15 (6.9)                                      | 5 (20.8)                                 | .02     |
| Type 2 diabetes mellitus                              | 13 (5.4)                      | 10 (4.6)                                      | 3 (12.5)                                 | .11     |
| Hypertension                                          | 11 (4.6)                      | 6 (2.8)                                       | 5 (20.8)                                 | <.001   |
| Cardiovascular disease                                | 6 (2.5)                       | 5 (2.3)                                       | 1 (4.2)                                  | .58     |
| Autoimmune disease                                    | 4 (1.7)                       | 2 (0.9)                                       | 2 (8.3)                                  | <.01    |
| Hypothyroidism                                        | 4 (1.7)                       | 3 (1.4)                                       | 1 (4.2)                                  | .31     |

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most common targeted treatments for COVID-19 disease among hospitalized pregnant patients were remdesivir (37.5%; 9 of 24), followed by dexamethasone (12.5%; 3 of 24), hydroxychloroquine (8.3%; 2 of 24), and convalescent plasma (8.3%; 2 of 24) with some patients receiving multiple therapies.

Maternal deaths in pregnant patients with severe acute respiratory syndrome coronavirus 2019 infection

There were 3 deaths among 240 pregnant patients with a SARS-CoV-2 infection for a maternal mortality rate of 1.2% (95% CI, 2.7 to 2.57) (Table 4). Overall, the SARS-CoV-2 case-fatality rate among included pregnant patients was a significant 13.6-fold higher in pregnant patients than the 91.7 of 100,000 rate in similarly aged 20- to 39-year-olds in Washington State (RR, 13.6; 95% CI, 2.7 to 43.6), equating to an absolute RD of 1.2% (95% CI, −0.26 to 2.57) (Table 4). The 3 deaths in pregnant patients constitute 9.4% of the total deaths (3 of 32) in this age group in Washington State assuming all 3 deaths were included in the state’s surveillance data.

The 3 pregnant patients who died owing to COVID-19 disease were all publicly insured, aged 35 to 39 years, and from minority racial-ethnic groups. Each had significant comorbidities that included obesity, hypertension, autoimmune disease, or congenital heart disease. Notably, 2 of the maternal deaths occurred during the early postpartum period and 1 in the first trimester; 1 patient died from respiratory failure before she could have benefited from COVID-19 therapeutics. One died from a postpartum pulmonary embolus after recovering from a prolonged COVID-19 hospitalization where she received venous thromboprophylaxis during and after her hospital stay. A third patient died of respiratory failure after a neonate was born to women, who died of respiratory failure before she recovered from COVID-19 (including congenital heart disease). Notably, 2 of the remaining 155 patients with infections in the second and third trimesters, nearly all patients had a live birth (98.7%; n=153) (Table 5). There were 2 stillbirths in this study; neither stillbirth was attributed to SARS-CoV-2 infection. An extensive investigation to determine the cause of death was performed in 1 case, as previously reported, and a genetic cause was attributed to the second death. Maternal and delivery characteristics were similar between women with SARS-CoV-2 infections in the second and third trimesters (Table 5).

At the time of delivery for pregnant patients with second- and third-trimester SARS-CoV-2 infections, 43.2% (67 of 155) were considered recovered from COVID-19 (including 11 women experiencing severe disease earlier in pregnancy); an additional 49.7% (77 of 155) had mild COVID-19, and 7.1% (11 of 155) had severe or critical COVID-19 at delivery (Table 6). Pregnant women with severe or critical COVID-19 at delivery were more likely to have a preterm birth (45.4% severe or...
### TABLE 2
COVID-19 severity, hospitalization, and outcomes by trimester of infection in pregnant patients

| Characteristic | All pregnant patients N=240<sup>a</sup> | Hospitalization status | Trimester of SARS-CoV-2 infection | Pvalue | First (n=38) | Second (n=67) | Third (n=135) | Pvalue |
|---------------|------------------------------------------|------------------------|-----------------------------------|--------|--------------|--------------|--------------|--------|
| Trimester of infection<sup>c</sup> |               |                       |                                   | <.001  |              |              |              |        |
| First         | 38 (15.8)    | 37 (17.1)             | 1 (4.2)                          |        |              |              |              |        |
| Second        | 67 (27.9)    | 62 (28.7)             | 5 (20.8)                         |        |              |              |              |        |
| Third         | 135 (56.3)   | 117 (54.2)            | 18 (75.0)                        |        |              |              |              |        |
| Symptomatic at first COVID-19 positive test<sup>c</sup> |               |                       |                                   | .02    |              |              |              | <.001  |
| Asymptomatic  | 55 (22.9)    | 54 (25.0)             | 1<sup>d</sup> (4.2)             |        |              |              |              |        |
| Symptomatic   | 185 (77.1)   | 162 (75.0)            | 23 (95.8)                        |        |              |              |              |        |
| Disease severity |                                  |                        |                                   | <.001  |              |              |              | .28    |
| Mild          | 218 (90.8)   | 213 (98.6)            | 5 (20.8)                         |        |              |              |              |        |
| Severe        | 18 (7.5)     | 3<sup>e</sup> (1.4)  | 15 (62.5)                        |        |              |              |              |        |
| Critical      | 4 (1.7)      | 0 (0)                 | 4 (16.7)                         |        |              |              |              |        |
| Outcomes      |               |                       |                                   |        |              |              |              |        |
| Hospitalized for COVID-19 concern | 24 (10.0) | 1 (2.6) | 5 (7.5) | 18 (13.3) | .11 |
| Admitted to ICU | 8 (3.3) | 0 (0.0) | 8 (33.3) | 0 (0) | 1 (1.5) | 7 (5.2) | .74 |
| Maternal death | 3 (1.3) | 0 (0.0) | 3 (12.5) | <.001 | 1 (2.6) | 1 (1.5) | 1 (0.7) | .64 |
| Final pregnancy outcome<sup>f</sup> | 158 (65.8) | 135 (62.5) | 23 (95.8) | .001 | 3 (7.9) | 27 (40.3) | 128 (94.8) | <.001 |
| COVID-19 at final outcome<sup>g</sup> | 90 (57.0) | 78 (57.8) | 12 (62.1) | .62 | 2 (66.7) | 2 (7.4) | 86 (67.2) | <.001 |
| Recovered from COVID-19 at final outcome | 68 (43.0) | 57 (42.2) | 11 (47.8) | .62 | 1 (33.3) | 25 (92.6) | 42 (32.8) | <.001 |

Gray shading indicates cells with no data.

COVID-19, coronavirus disease 2019; ICU, intensive care unit; SARS-COV-2, severe acute respiratory syndrome coronavirus 2.

<sup>a</sup> Summarized as number (percentage) or median (interquartile range); <sup>1</sup> One patient was hospitalized and admitted to ICU twice several months apart; <sup>2</sup> At the time of the first positive SARS-CoV-2 test; <sup>3</sup> This patient was tested owing to a known exposure to COVID-19 and became symptomatic before hospitalization; <sup>4</sup> All 3 patients had dyspnea but were not ultimately hospitalized; <sup>5</sup> Includes 1 maternal death and 2 spontaneous abortions in pregnant patients with first-trimester SARS-CoV-2 infections; <sup>6</sup> Includes pregnant patients with mild or severe or critical COVID-19 at the time of final pregnancy outcome.

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critical COVID-19 vs 5.2% mild COVID-19 vs 0.9% recovered; \(P<.001\) and to deliver owing to COVID-19 (63.6% severe or critical COVID-19 vs 2.6% mild COVID-19 vs 0% recovered; \(P<.001\)). The frequency of gestational diabetes mellitus and new-onset hypertensive disorders of pregnancy or postpartum, was similar by COVID-19 status at delivery (Table 6).

**Neonatal outcomes**

There were 3 sets of twins for a total of 156 live-born neonates. Neonates born to mothers with severe or critical COVID-19 at the time of delivery were more likely to have low birthweight (<2500 g) and more likely to be admitted to the NICU for fetal indications than those born to women with mild COVID-19 or recovered from COVID-19 at the time of delivery (Table 6). Of the 144 neonates with SARS-CoV-2 test results available, one-third were tested at least once (31.3%; 45 of 144) and none tested positive (Table 5). The remaining two-thirds were not tested for SARS-CoV-2. Neonatal testing was most common among pregnant patients with severe COVID-19 at delivery (77.9%; 7 of 9) but conducted only of half of patients with mild COVID-19 at delivery (44.9%; 35 of 77); SARS-CoV-2 testing was uncommon among women considered COVID-19 recovered at delivery (5.3%; 3 of 57). Neonates were generally healthy with the most common diagnoses of respiratory distress (n=6), hyperbilirubinemia (n=4), and possible sepsis (n=3). Other diagnoses included meconium aspiration syndrome, metabolic acidosis, hypoglycemia, supraventricular tachycardia, pneumonia, and hypotonia.

**Discussion**

**Principal findings**

Although most pregnant patients with SARS-CoV-2 in pregnancy experienced mild disease and recovered, 1 in 11 developed severe or critical disease, 1 in 10 were hospitalized specifically for a COVID-19 concern, 1 in 30 were admitted to the ICU for respiratory concerns, 1 in 60 were mechanically ventilated, and 1 in 80 died. Case-fatality rates in pregnant patients with SARS-CoV-2 infections were nearly 14-fold higher than that of similarly aged individuals in Washington State with COVID-19, making up nearly 10% of
SARS-CoV-2 deaths among 20- to 39-year-olds in Washington State. In addition, the case-fatality rate in pregnant and recently pregnant patients with SARS-CoV-2 infections of 1250 of 100,000 pregnancies is in stark contrast to the Washington State maternal mortality rate of 37.3 of 100,000 live births and pregnancy-related maternal mortality rate of 11.2 of 100,000 live births.\(^2\) Nearly half of the hospitalized patients delivered during a hospital admission for respiratory concerns, which raises the risk of preterm birth and associated complications of prematurity.\(^3\) Notably, these deaths occurred after the “first wave” in Washington State and at a time when remdesivir and other therapeutics (dexamethasone) were administered to many patients in our study. The case-fatality rate and morbidity associated with SARS-CoV-2 infections in pregnancy in Washington States provide additional evidence for enhanced COVID-19 disease in pregnancy.

### Results in the context of what is known

The CDC listed pregnant patients as a population at an increased risk of severe COVID-19 disease only recently after an expanded analysis of United States surveillance data of reproductive-aged women with SARS-CoV-2 infections.\(^9,12,23\) Pregnant patients with SARS-CoV-2 were at an increased risk of ICU admission, ventilation, and death; however, pregnancy status was missing for 64.5% of COVID-19 cases.\(^12\) Notably, in mid-October of 2020, the CDC reported only 45 maternal deaths in pregnant women with confirmed SARS-CoV-2 infections across the United States;\(^9\) if complete, this would mean that the 3 cases in our study population represented 7% of the total maternal deaths in pregnant women with SARS-CoV-2 across the United States despite annual births among our study sites making up an estimated 1.4% of the total nationwide.\(^24\) This is most likely caused by underreporting and not a higher death rate in Washington State. There is a long history of underreporting pregnancy status in important surveillance data including infectious disease reporting and in United States death records;\(^25\) although efforts are ongoing to rectify this, we are concerned that pregnant patients are at an increased risk of maternal mortality owing to COVID-19 and that deaths in this unique group may be significantly undercounted in the United States.

Our finding that deaths in pregnant patients contributed disproportionately to deaths from COVID-19 among 20- to 39-year-olds in Washington State is similar to what was observed during the influenza A virus (IAV) H1N1 2009 pandemic. Although approximately 1% of the United States population is pregnant at any point in time, deaths in pregnant women contributed 5.7% of all deaths from IAV H1N1 2009 in pooled data from a systematic review.\(^26\) Similar to deaths in pregnant patients from IAV H1N1 2009, all 3 pregnant patients with a SARS-CoV-2 infection in our study who died were obese or had other underlying conditions.\(^14,27,28\) Notably, 2 of 3 maternal deaths occurred after delivery after a prolonged or second hospitalization for COVID-19–associated complications highlighting the postpartum period as a high-risk period; this was also a high-risk time period for maternal mortality owing to IAV H1N1 2009.\(^29\)

However, unlike the IAV H1N1 2009 pandemic when pregnant women were...
quickly identified in the United States as a high-risk and vulnerable group, pregnancy was not identified as a high-risk condition for COVID-19 disease or mortality for the first critical 8 months of the pandemic. Given the similarity in clinical course between COVID-19 and IAV H1N1 2009 with an increased risk of mortality during pregnancy and the postpartum period, we strongly recommend that pregnant patients should be considered a high-risk population to novel highly pathogenic respiratory viruses until proven otherwise by population-based studies with good ascertainment of pregnancy status.

### TABLE 5
Maternal, delivery, and neonatal outcomes among pregnant patients with SARS-CoV-2 infections overall and by trimester of infection

| Characteristicsa | Overallb | Trimester of infection | Pvalue |
|------------------|----------|------------------------|--------|
|                  |          | Second                 | Third  |        |
| Pregnancy outcome|          |                        |        |        |
| Live birth       | n=155    | 153 (98.7)             | 26 (96.3) | 127 (99.2) | .0001 |
| Stillbirth       | n=155    | 2 (1.3)                | 1 (3.7)  | 1 (0.8)  | .32   |
| Delivery         | n=155    | 20 (2—58)              | 99 (85—105) | 8 (1—35) | .02   |
| Induction        | (n=121)  | 49 (40.5)              | 9 (39.1)  | 40 (40.8) | .88   |
| Cesarean delivery| n=155    | 55 (35.5)              | 9 (33.3)  | 46 (35.9) | .80   |
| Delivery induced | n=155    | 9 (5.8)                | 0 (0)    | 9 (7.0)  | .16   |
| Gastrointestinal| n=155    | 16 (10.3)              | 2 (7.4)   | 14 (10.9) | .58   |
| New-onset hypertensive disorder of pregnancy or postpartumb | n=155    | 19 (12.3)              | 3 (11.1)  | 16 (12.3) | .84   |
| Diagnosed at or after COVID-19 diagnosis | n=155    | 17 (89.5)              | 3 (100)   | 14 (87.5) | .52   |
| Nonreassuring fetal status/fetal distress | n=155    | 19 (12.3)              | 3 (11.1)  | 16 (12.5) | .84   |
| Neonatal outcomes | n=156c | 3261 (2905, 3640) | 3206 (2887—3510) | 3261 (2908, 3665) | .38 |
| Low birth weight (g) | n=155    | 7 (4.6)                | 0 (0)     | 7 (5.5)  | .22   |
| SARS-CoV-2 positive | n=155    | 45 (31.3)              | 1 (4.2)   | 44 (36.7) | .002  |
| NICU admissionl | n=155    | 11 (7.1)               | 1 (3.9)   | 10 (7.8) | .48   |

COVID-19, coronavirus disease 2019; HELLP, hemolysis, elevated liver enzymes, and a low platelet count; IQR, interquartile range; NICU, neonatal intensive care unit; PPROM, preterm premature rupture of membranes; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

a Presented as n (percentage) and median (IQR); b Excludes 3 cases of SARS-CoV-2 infection during the first trimester; 2 cases ended in spontaneous abortion and 1 led to a maternal death; c COVID-19 was either the singular indication or a contributory indication for delivery; d A new-onset hypertensive disorder of pregnancy or postpartum included any of the following diagnoses: new-onset gestational hypertension, preeclampsia, eclampsia, chronic hypertension with superimposed preeclampsia, and HELLP; e Live births only (n=156). There were 3 twin gestations; f Birthweight is missing for 2 neonates (n=154); g Testing data missing for 12 neonates, for a total of 24 neonates born to pregnant patients with second-trimester SARS-CoV-2 infections and 120 neonates born to pregnant patients with third-trimester SARS-CoV-2 infections; h NICU admission occurred for a neonatal health indication. Does not include NICU admission solely for COVID-19 precautions. N=155, data missing for 1 neonate.

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Research implications
The impact of COVID-19 on maternal and neonatal health is limited by the paucity of data sets that capture outcomes from hospitalized and nonhospitalized cases across all trimesters of pregnancy. In our study in Washington State, pregnant patients with severe or...
critical disease at the time of delivery had a higher likelihood of preterm birth, which can have important long-term adverse impacts on the lifelong health of the child (eg, brain and lung injury).32,33 When comparing outcomes by trimester of SARS-CoV-2 infection, pregnancy complications and delivery outcomes were similar; however, the number of delivery outcomes for second-trimester infections was small so this finding does not prove an absence of differential outcomes by trimester of infection. Further studies of pregnancy outcomes by trimester of infection will be important to determine whether there is an impact of pregnancy complications, fetal growth, and neonatal outcomes. Finally, it will be important to follow neonates for many years to determine the long-term sequelae of the spectrum of maternal COVID-19 disease; in particular, the risk of neuropsychiatric disease, such as autism spectrum disorder, is important to determine after a several maternal infection.34,35

Strengths and limitations
This study's major strength was its capture of confirmed SARS-CoV-2 cases from 35 sites across Washington State representing 61% of annual deliveries across the state. Including cases from all trimesters of pregnancy and regardless of symptoms status enabled a more thorough examination of spectrum of SARS-

### TABLE 6
Maternal, delivery, and neonatal outcomes among pregnant patients with SARS-CoV-2 infections by infection status at delivery

| Characteristics | COVID-19 status at delivery | Pvalue |
|-----------------|-----------------------------|--------|
|                 | Recovered at delivery | Mild COVID-19 at delivery | Severe or critical COVID-19 at delivery |
| Delivery characteristics | n=67 | n=77 | n=11 |
| Timing | | | |
| Time from first COVID-19 positive test to outcome (d) | 58 (34,092) | 3 (0−11) | 8 (3−14) | .0001 |
| Gestational age at delivery (wk) | 39 (37.7−40) | 39.3 (38.6−40.1) | 37 (33.9−39.1) | <.01 |
| Preterm birth | 6 (9.0) | 4 (5.2) | 5 (45.4) | <.001 |
| Owing to preterm labor or PPROM | 5 (83.3) | 1 (25.0) | 1 (20.0) | .07 |
| Mode of delivery | | | |
| Induction (n=121 with any labor) | 23 (39.7) | 24 (41.4) | 2 (40.0) | .98 |
| Cesarean delivery | 22 (32.8) | 26 (33.8) | 7 (63.6) | .13 |
| Delivery induced or performed owing to COVID-19 | 0 (0) | 2 (2.6) | 7 (63.6) | <.001 |
| Obstetrical or fetal complications | n=67 | n=77 | n=11 |
| Gestational diabetes | 8 (11.9) | 6 (7.8) | 2 (18.2) | .48 |
| New-onset hypertensive disorder of pregnancy or postpartum | 5 (7.5) | 14 (18.2) | 0 (0) | .07 |
| Diagnosed at or after COVID-19 diagnosis | 5 (100.0) | 12 (85.7) | 0 (0) | .37 |
| Nonreassuring fetal status or fetal distress | 4 (6.0) | 9 (11.7) | 6 (54.6) | <.001 |
| Neonatal outcomes | n=67 | n=78 | n=11 |
| Birthweight (g) | 3261 (2950−3560) | 3304 (2955, 3705) | 2690 (2490−3020) | <.001 |
| Low birthweight (<2500 g) | 2 (3.0) | 2 (2.6) | 3 (27.3) | .001 |
| SARS-CoV-2 testing performed | 3 (5.3) | 35 (44.9) | 7 (77.9) | <.001 |
| NICU admission | 2 (3.0) | 6 (7.7) | 3 (27.3) | .01 |

COVID-19, coronavirus disease 2019; HELLP, hemolysis, elevated liver enzymes, and a low platelet count; IQR, interquartile range; NICU, neonatal intensive care unit; PPROM, preterm premature rupture of membranes; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

a Presented as number (percentage) and median(IQR); b One patient was readmitted several months after a severe COVID-19 infection owing to a COVID-19−associated complication and was considered to have “active COVID-19” in this analysis although she had a negative polymerase chain reaction test result at the time; c n=155, excluding 2 spontaneous abortions; d COVID-19 was the singular indication or a contributing indication for delivery; e Data collection tools included new-onset gestational hypertension, preeclampsia, eclampsia, chronic hypertension with superimposed preeclampsia, and HELLP; f Live births only (n=156). There were 3 twin gestations; g Birthweight is missing for 2 neonates (n=154); h Testing data missing for 12 neonates, for a total of 57 neonates born to pregnant patients considered COVID-19 recovered at delivery, 78 neonates born to pregnant patients with mild COVID-19 at delivery, and 9 neonates born to pregnant patients with severe COVID-19 at delivery; i NICU admission occurred for a neonatal health indication. Does not include NICU admission solely for COVID-19 precautions. n=155, data missing for 1 neonate.

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Our outcome data for was completed before pregnancy wide rates. Moreover, data collection detection across sites. Therefore, the pregnancy, despite several methods for case ascertainment of asymptomatic and milder cases, particularly earlier in pregnancy. This study also had limitations, including the potential for under-ascertainment of asymptomatic and earlier pregnant patients. Therefore, the/undercounting of maternal deaths, which is likely given the missing pregnancy status in 65% of COVID-19 case reports. We also found a significantly higher likelihood of preterm birth in pregnant patients with severe or critical COVID-19 disease concerning given the long-term adverse outcomes on a child’s health through the life course. Greater attention to pregnant patients as a unique population at higher risk of SARS-CoV-2 infection sequelae is critical to preventing maternal and neonatal morbidity and mortality. These data strongly support the need to offer vaccination to pregnant women at risk of acquiring SARS-CoV-2 infection and include pregnant people in clinical trials and other observational evaluations of vaccines and COVID-19 therapies (Video 1).

Conclusions
Our finding of a markedly higher mortality rate among pregnant people with SARS-CoV-2 infection in a state-wide multicenter cohort study representing the majority of annual births in Washington State is compelling evidence that pregnant patients are a population at high risk of morbidity and mortality associated with SARS-CoV-2 infection. The overall 1 in 80 maternal mortality rate in pregnancy coupled with the potential over-representation of pregnant people in Washington State’s SARS-CoV-2 deaths in 20- to 39-year-olds is cause for concern. Furthermore, these maternal deaths represented 7% of those known to the CDC in mid-October, despite our population representing only 1.4% of the nation’s births; this suggests undercounting of maternal deaths, which is likely given the missing pregnancy status in 65% of COVID-19 case reports. We also found a significantly higher likelihood of preterm birth in pregnant patients with severe or critical COVID-19 disease concerning given the long-term adverse outcomes on a child’s health through the life course. Greater attention to pregnant patients as a unique population at higher risk of SARS-CoV-2 infection sequelae is critical to preventing maternal and neonatal morbidity and mortality. These data strongly support the need to offer vaccination to pregnant women at risk of acquiring SARS-CoV-2 infection and include pregnant people in clinical trials and other observational evaluations of vaccines and COVID-19 therapies (Video 1).

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| Participating site                                      | Type                          | Annual delivery volume  |
|--------------------------------------------------------|-------------------------------|-------------------------|
| 1 University of Washington Medical Center: Montlake     | Hospital                      | 1900                    |
| 2 University of Washington Medical Center: Northwest    | Hospital                      | 900                     |
| 3 Swedish: Issaquah                                     | Hospital                      | 12,000 system-wide b    |
| 4 Swedish: First Hill                                   | Hospital                      | b                       |
| 5 Swedish: Ballard                                      | Hospital                      | b                       |
| 6 Swedish: Edmonds                                      | Hospital                      | b                       |
| 7 University of Washington Valley Medical Center         | Hospital                      | 3200                    |
| 8 MultiCare: Covington Medical Center                   | Hospital                      | 250                     |
| 9 MultiCare: Auburn Medical Center                      | Hospital                      | 1108 b                  |
| 10 MultiCare: Tacoma General Hospital                   | Hospital                      | 2921                    |
| 11 MultiCare: Good Samaritan Hospital                   | Hospital                      | 2227                    |
| 12 MultiCare: Spokane Valley Hospital                   | Hospital                      | 604                     |
| 13 MultiCare: Deaconess Medical Center                  | Hospital                      | 1384                    |
| 14 EvergreenHealth Medical Center - Kirkland            | Hospital                      | 4600                    |
| 15 PeaceHealth St. Joseph Medical Center—Bellingham     | Hospital                      | 1875                    |
| 16 Providence Regional Medical Center—Everett           | Hospital                      | 4250                    |
| 17 Jefferson Medical Center                             | Hospital                      | 125                     |
| 18 Legacy Salmon Creek Medical Center                   | Hospital                      | 3600                    |
| 19 Virginia Mason Memorial Hospital                     | Hospital                      | 2385                    |
| 20 Central WA Hospital, Confluence                      | Hospital                      | 1300                    |
| 21 UW Medicine Maternal-Fetal Medicine Clinic at Yakima | Clinic                        | n/a                     |
| 22 Yakima Valley Farm Workers Clinics: Valley Vista     | Clinic                        | 119                     |
| 23 Yakima Valley Farm Workers Clinics: Pasco Miramar    | Clinic                        | 6                       |
| 24 Yakima Valley Farm Workers Clinics: Mission Avenue   | Clinic                        | 134                     |
| 25 Yakima Valley Farm Workers Clinics: West Central Community Center | Clinic | 48 |
| 26 Yakima Valley Farm Workers Clinics: Northeast Community Center | Clinic | 122 |
| 27 Yakima Valley Farm Workers Clinics: Grandview        | Clinic                        | 356                     |
| 28 Yakima Valley Farm Workers Clinics: Lincoln Avenue   | Clinic                        | 1809                    |
| 29 Yakima Valley Farm Workers Clinics: Yakima Medical Dental Clinic | Clinic | 1356 |
| 30 Yakima Valley Farm Workers Clinics: Mountain View Women’s Clinic | Clinic | 242 |
| 31 Yakima Valley Farm Workers Clinics: Toppenish        | Clinic                        | 1164                    |
| 32 Yakima Valley Farm Workers Clinics: Family Medical Center Walla Walla | Clinic | 283 |

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| Participating site                          | Type       | Annual delivery volume<sup>a</sup> |
|-------------------------------------------|------------|-----------------------------------|
| 33 The Vancouver Clinic                   | Clinic<sup>d</sup> | n/a<sup>d</sup>                   |
| 34 PeaceHealth Southwest Medical Center   | Hospital   | 2000                              |
| 35 Mid Valley Hospital                    | Hospital   | 240                               |

<sup>a</sup> Collaborating sites reported their approximate annual delivery number. The annual delivery numbers for MultiCare facilities are the 2019 actuals. The annual delivery numbers for the Yakima Valley Farm Workers Clinics are the number of women in their care who delivered in 2019; <sup>b</sup> Annual delivery volume is reported system-wide for Swedish Medical Center sites; <sup>c</sup> Deliveries occur across Greater Yakima region; <sup>d</sup> Vancouver Clinic patients deliver at PeaceHealth Southwest Medical Center and Legacy Salmon Creek Medical Center. The total number of deliveries at the Vancouver Clinic do not count toward the total number of annual deliveries captured by the Washington State COVID-19 in Pregnancy Collaborative because they are included with PeaceHealth Southwest Medical Center and Legacy Salmon Creek Medical Center numbers.

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