COVID-19 Outcomes in Pregnant Women by Trimester

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Our data show an increased risk of hospitalization with oxygen support for pregnant women with COVID-19. While there is no evidence of increased risk during the first trimester of pregnancy, pregnant women in their second and third trimesters face an elevated risk of hospitalization requiring oxygen support and, often, an elevated risk of ventilation or ICU care.

Ellington et al[1] found that, in women of reproductive age who tested positive for COVID-19, pregnancy was associated with an increased risk of ICU admission and need for mechanical ventilation but was not associated with an increased risk of mortality. Their analysis did not include trimester or delivery information.

This study looks at pregnant women diagnosed with COVID-19 and their likelihood of needing oxygen support and ventilation or ICU admission during different trimesters. Pregnancy trimester data, shown in Figure 1, reveals that more pregnant women were diagnosed with COVID-19 during the later stages of pregnancy. We speculate this is because many health systems have begun universal testing for COVID-19 in pregnant women, especially during the later stages of pregnancy and when patients are admitted to labor and delivery.[2,3]

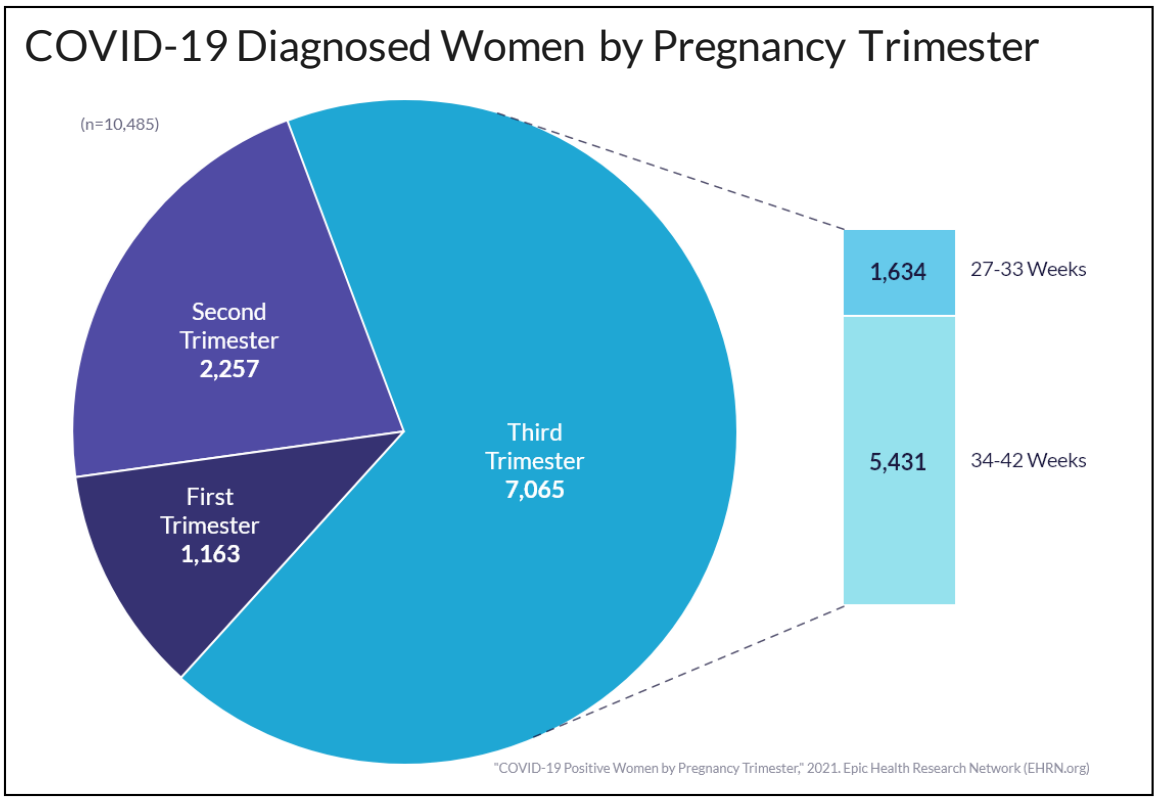

Figure 1: Number of women diagnosed with COVID-19 during pregnancy, by pregnancy trimester. Women who were diagnosed with COVID-19 during their third trimester are broken down further into early and late third trimester.

Our data show 39.1% of pregnant women with COVID-19 were admitted to the hospital within six weeks of COVID-19 positivity, compared to an admission rate of 5.1% in non-pregnant women of reproductive age. Our standard definition for a COVID-19 related admission identifies patients admitted for active COVID-19 disease and those admitted for other reasons where COVID-19 is documented for incidental reasons (e.g. recent diagnosis or positive test during admission). With many potential pregnancy-related reasons for admission, we used oxygen support during the admission as a proxy for active COVID-19 disease. These rates were 5.5% and 3.0% for pregnant and non-pregnant women, respectively. The number of deaths did not reach a level that would allow meaningful comparison (6 deaths in pregnant women), so we analyzed the ICU admission rate or need for mechanical ventilation as a measure of disease severity.

Pregnant women between the ages of 19 and 34 who are in their second or third trimesters have an elevated risk of hospitalization requiring oxygen, as well as ventilation and ICU admission, as shown in Figure 2. This elevated risk is not seen during the first trimester. This remains true even when women who delivered* while COVID-19 positive are removed from the dataset.

* "Deliveries" include deliveries, miscarriages, and fetal demise.

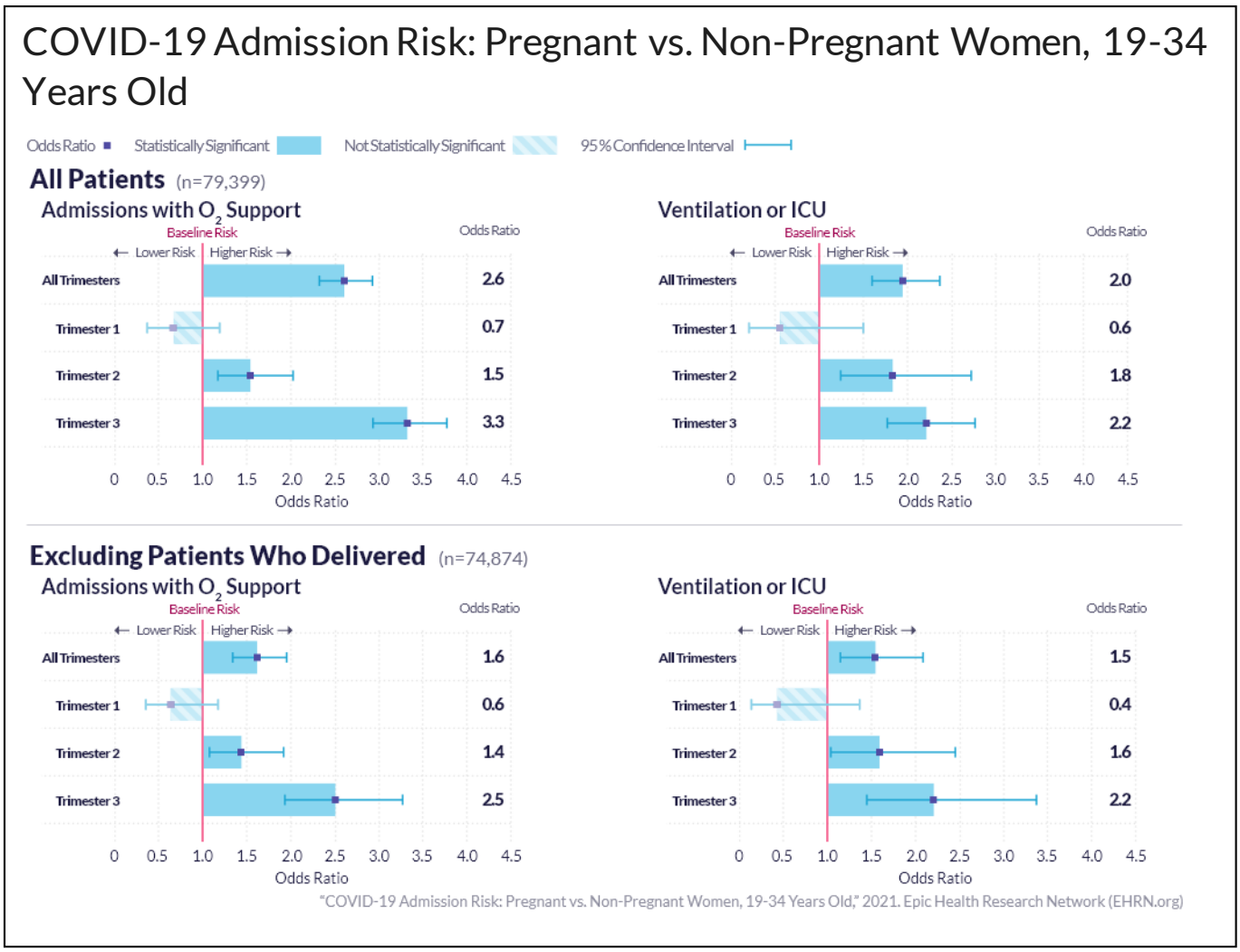

Figure 2: The light blue bars show risk of hospitalization requiring oxygen support and ventilation or ICU care (using odds ratios) in pregnancy overall and for each trimester compared to non-pregnant women, controlling for race, ethnicity, and comorbidities. For example, all pregnant women ages 19-34 have a risk of hospitalization for COVID-19 requiring oxygen support 2.6 times higher than non-pregnant women. The dark blue lines indicate 95% confidence intervals.

We see similar results in older pregnant women (ages 35 to 44), with no statistically significant differences for pregnant women in their first trimester, both for hospitalizations requiring oxygen and for ventilation or ICU care, as shown in Figure 3. There is a large decrease in the risk of ventilation or ICU care in the third trimester when women who deliver are removed from the population. This may be due in part to a smaller sample size or it may suggest some of the need for ventilation or ICU care is pregnancy related rather than COVID-19 related. Further study is needed to identify the specific aspects of pregnancy that influence the course of illness of COVID-19, as well how COVID-19 may affect pregnancy.

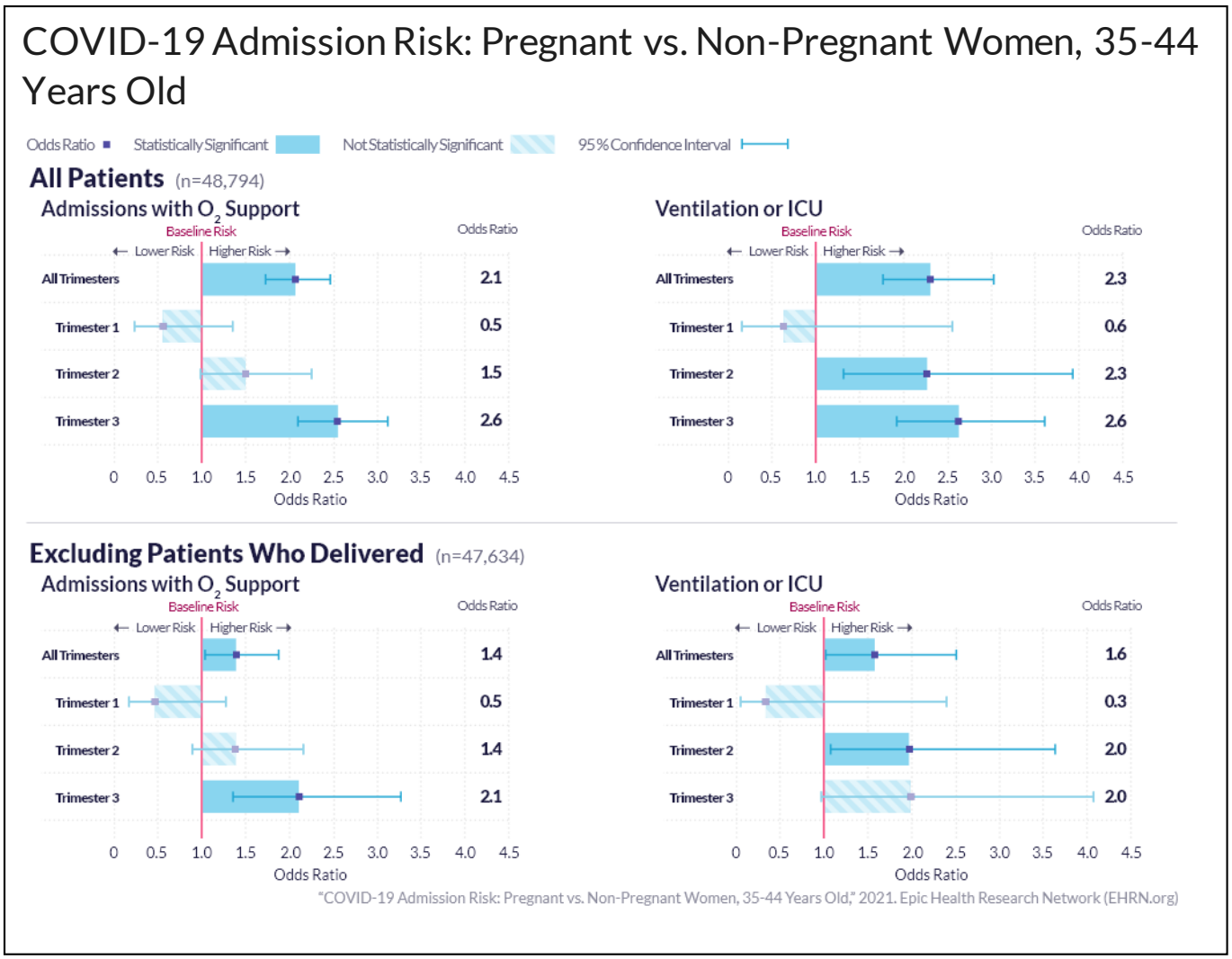

Figure 3: The light blue bars show risk of hospitalization requiring oxygen support and ventilation or ICU care (using odds ratios) in pregnancy overall and for each trimester compared to non-pregnant women, controlling for race, ethnicity, and comorbidities. For example, all pregnant women ages 35-44 have a risk of hospitalization for COVID-19 requiring oxygen support 2.1 times higher than non-pregnant women. The dark blue lines indicate 95% confidence intervals.

This study was completed by two teams (1: DW, MG, DB; 2: CA, AB, KG), each comprised of a clinician and two data scientists, who independently acquired and analyzed data. Both teams were involved in the interpretation of results and drafting of this brief. Overall, the two teams came to similar conclusions. Data are pooled EHR data from 128,193 women of reproductive age (19-44 years old) who were COVID-19 positive by November 30, 2020. At the time of COVID-19 positivity, 10,485 women were pregnant.

Term	Definition
Positive SARS-CoV-2 Lab Result	A final result for one of the lab components identified by individual health systems for SARS-CoV-2 with a "positive" value, as identified by the health systems.
COVID-19 Diagnosis	One of the following codes in one of the listed diagnosis settings. **Diagnosis Code**: U07.1 (ICD-10-CM), 840539006 (SNOMED) **Diagnosis Setting**: Encounter Diagnosis, Billing Diagnosis, Problem List, Hospital Problem, Discharge Diagnosis **Start Date**: Diagnosis noted date
COVID-19 Positive Patient	Patient with a positive SARS-CoV-2 lab result or a COVID-19 diagnosis. Start Date: The earlier of the earliest positive SARS-CoV-2 lab result collection date or earliest diagnosis noted date. If an inpatient admission began in the 7 days prior to this date, the admission date is used instead.
COVID-19 Related Admission	A hospital admission during which the patient has a positive SARS-CoV-2 lab test or COVID-19 diagnosis, OR a hospital admission with any respiratory diagnosis which happens within 14 days of the patient's COVID-19 "start date." **Respiratory Diagnosis Codes**: J00-J99 (ICD-10-CM)
Pregnant at COVID-19 Positive	A patient whose COVID-19 start date falls between her estimated conception date (estimated delivery date – 280) and her delivery date, or prior to 28 days after her estimated delivery date if no delivery is documented.
Pregnancy Trimester	The trimester a patient became COVID-19 positive. **First Trimester**: 0-12 weeks gestation **Second Trimester**: 13-26 weeks gestation **Third Trimester**: 27-42 weeks gestation
Basic Respiratory Support	A patient on supplementary oxygen with a flow rate under 30 lpm, or using any oxygen delivery device that is not a ventilator or high-flow oxygen device (e.g., ETT, LMA, CPAP, BiPAP, high-flow nasal cannula, T-piece, or blow-by).
Advanced Respiratory Support	A patient with an oxygen flow rate at or above 30 lpm or using a non-invasive ventilator mode or high flow oxygen delivery device (regardless of flow rate) that includes BiPAP, high-flow nasal cannula, T-piece, blow-by, or CPAP if administered between 8am-9pm (to exclude patients who were on nightly CPAP for apnea).

Ventilator Usage	A patient is considered to be on a ventilator if there is documentation other than "Off" or a non-invasive mode (e.g., CPAP, BiPAP) in a Vent Mode flowsheet row, or an oxygen delivery device of ventilator. Alternatively, a patient is considered to be on a ventilator if they have a procedure with one of the following CPT codes during their COVID-19 related admissions and are not indicated to have received oxygen with a flow rate at or above 30 lpm or using a non-invasive ventilator mode or high flow oxygen delivery device (regardless of flow rate) that includes BiPAP, high-flow nasal cannula, T-piece, blow-by, or CPAP if administered between 8 AM and 9 PM (to exclude patients who were on nightly CPAP for apnea). **CPT Codes**: 94002, 94003
Admission Requiring Oxygen Support	An admission in which the patient received either Basic Respiratory Support, Advanced Respiratory Support, or was placed on a Ventilator.
ICU Admission	An admission where the patient was billed with an ICU bed charge (revenue code 0200, 0201, 0202, 0203, or 0209) or admitted to a department marked as an ICU.

References

1. Ellington S, Strid P, Tong VT, et al. Characteristics of Women of Reproductive Age with Laboratory-Confirmed SARS-CoV-2 Infection by Pregnancy Status — United States, January 22–June 7, 2020. *MMWR Morb Mortal Wkly Rep*. 2020;69(25):769-775. doi:10.15585/mmwr.mm6925a1
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3. General Information Regarding Pregnant Individuals and COVID-19. Accessed May 9, 2020. https://www.acog.org/clinical/clinical-guidance/practice-advisory/articles/2020/03/novel-coronavirus-2019