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 Prevalence of SARS-CoV-2 Infection in Pregnant Women, by Sampling Strategy
 Allotey J et al. BMJ. 2020 Sep 1;370:m3320

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Are Pregnant Women More Likely to Acquire SARS-CoV-2?

- Most overall population studies **do not provide pregnancy status** for females.
- While initial data from CDC did not suggest higher prevalence in pregnant women (CDC COVID-19 Response Team. *MMWR*. 2020 Mar 31) some more recent data is of concern.
- In a study of universal pre-procedural SARS-CoV-2 rPCR tests before all surgeries or deliveries in 5,543 persons in St. Louis hospital May-July 2020, positivity rates were higher in Ob than Surgical unit patients (Kelly JC et al. *Am J Obstet Gynecol*. 2020 Sep 21:S0002-9378(20)31107-9).

	Ob Unit (N=552)	Surgical Unit (N=5,011)	Adjusted* OR
Sars SARS-CoV-2 +	25 (4.7%)	14 (0.3%)	4.7 (2.3-10.6)

*Adjusted for age, race

- CDC recently reported 9% of reproductive-aged women (8,207/91,412) with lab-proven SARS-CoV-2 between Jan-June were pregnant; this was higher than expected, as CDC estimates ~5% of women aged 15-44 years are pregnant at a given point in time (Ellington S et al. *MMWR* 2020 Jun;69:769-75).

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Prevalence of SARS-CoV-2 Infection in Pregnant Women, by Sampling Strategy

Allotey J et al. *BMJ*. 2020 Sep 1;370:m3320

- Systematic review; prevalence of positive SARS-CoV-2 rPCR in 26 studies including 11,432 pregnant women attending or admitted to hospital

Study	n	Prevalence (%)	Sampling Strategy
Overall	11,432	10%	Universal screening
Universal screening	11,432	7%	Prevalence 7% (95% CI 4-10%)
Symptom-based	11,432	18%	Prevalence 18% (95% CI 10-28%)

- Overall 10% prevalence SARS-CoV-2 infection in pregnant women hospitalized in pandemic locales
- Infection prevalence rates >15% were all from US, except 1 study from France.
- Universal screening: rPCR of all pregnant women presenting at labor/delivery.
- Symptom-based: rPCR only if symptoms of infection or history of close contact to individual with infection.

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Do Symptoms Differ in Pregnant vs Non-Pregnant Women with COVID-19?

Ellington S et al. MMWR. 2020 Jun;69:769-75

CDC compared COVID-19 disease among 8,207 pregnant and 83,205 non-pregnant women of reproductive age in US with positive SARS-CoV-2 rtPCR reported January 22-June 7 2020.



Symptomatic pregnant and nonpregnant women with COVID-19 reported similar frequencies cough (>50%) and dyspnea (30%), but pregnant women less frequently reported fever, muscle aches, chills, headache and diarrhea.

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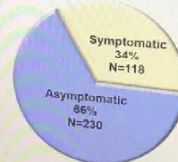
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Universal Screening for SARS-CoV-2: Majority of Infected Pregnant Women Are Asymptomatic

Author	Country	Total n	% + rtPCR	% Asymptomatic
Stilton	US (NY)	214	15.4% (n=33)	73.3% (n=23)
Vincibros	US (NY)	181	19.3% (n=32)	65.6% (n=21)
Campbell	US (CT)	770	3.9% (n=30)	73.3% (n=22)
Goldfield	US (Boston)	757	2.9% (n=21)	45% (n=9)
Lacourse	US (Seattle)	358	2.7% (n=10)	20% (n=5)
Baskley	US (NY)	100	17.9% (n=18)	100% (n=5)
Bliz	US (NY)	375	17.1% (n=64)	70.2% (n=45)
Fanzani	Italy (Milan)	1565	3.1% (n=49)	55.1% (n=27)
Miler	US (Chicago)	635	3.6% (n=23)	43.5% (n=10)
Bernaczek	US (Ohio)	492	2.0% (n=10)	70% (n=7)
Fassett	US (CA)	3023	0.4% (n=12)	100% (n=7)
Thane	UK (London)	120	7.5% (n=9)	83.3% (n=8)
Chen	Portugal (Aveiro)	102	11.7% (n=12)	91.5% (n=11)
Chen	Japan (Tokyo)	80	3.8% (n=3)	100% (n=2)
Chen	China (Suzhou)	582	6.4% (n=37)	43% (n=16)

15 papers reporting on universal nasopharyngeal SARS-CoV-2 rtPCR testing of 10,108 women presenting in labor in hospitals in midst of COVID-19 pandemic

348 (3.4%) were positive on SARS-CoV-2 rtPCR.



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Risk Factors for Hospitalization with COVID-19 in Pregnancy

The UK Obstetric Surveillance System SARS-CoV-2 Infection in Pregnancy Collaborative Group (UKOSS). *BMJ* 2020 Jun 8;369:m2107

- Population-based surveillance system, including all 194 maternity units in the UK.
- Between March 1 – April 14, 2020, 86,293 pregnant women admitted to maternity units; 427 (5%) had confirmed SARS-CoV-2 infection.

Estimated incidence hospitalization with SARS-CoV-2 in pregnancy in different population subgroups

Subgroup	Incidence/1000 pregnant women	Adjusted Odds Ratio (95% CI)
Black	28.4 black vs 3.5 white	8.1 (6.2-10.5)
Age ≥35 years	8.8 age ≥35 yr vs 3.9 age 20-34 yr	2.3 (1.8-2.7)
BMI 25-<30 - overweight	6.8 BMI 25-30 vs 3.5 BMI <25	2.0 (1.5-2.5)
BMI >30 - obese	8.7 BMI ≥30 vs 3.5 BMI <25	2.5 (2.0-3.2)

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More Severe COVID-19 in Pregnant vs Non-Pregnant Women of Reproductive Age: US

Ellington S et al. *MMWR*. 2020 Jun;69:769-75

- Compared severity of COVID-19 disease among 8,207 pregnant and 83,205 non-pregnant women of reproductive age with positive SARS-CoV-2 rtPCR reported to CDC in US January 22-June 7 2020.

Comparison of Outcomes, Pregnant vs Non-Pregnant Women with COVID-19

Outcome	Pregnant women (N=8,207)	Non-pregnant women (N=83,205)	Adjusted* Rate Ratio (95% CI)
Hospitalization	2,587 (31.5%)	4,840 (5.8%)	5.4 (5.1-5.6)
ICU admission	120 (1.5%)	757 (0.9%)	1.5 (1.2-1.8)
Mechanical ventilation	42 (0.5%)	225 (0.3%)	1.7 (0.1-2.4)
Death	16 (0.2%)	208 (0.2%)	0.9 (0.5-1.5)

*Adjusted for age as continuous variable, yes/no for underlying condition, and race/ethnicity; non-pregnant women are referent group.

- Older age risk factor for severity; when stratified by age, all outcomes more frequent among women aged 35-44 years than among those aged 15-34 years.

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More Severe COVID-19 in Pregnant vs Non-Pregnant Women of Reproductive Age: Living Systematic Review

Allotey J et al. *BMJ*. 2020. Sept;370:m3320

- Living systematic review University Birmingham UK – identified 77 papers including 13,118 pregnant women and 83,486 non-pregnant women of reproductive age hospitalized with COVID-19.

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Comparison of Outcomes, Pregnant vs Non-Pregnant Women with COVID-19

	No. Studies	Pregnant women	Non-pregnant women	Odds Ratio (95% CI)
ICU admission	4	121/8,276 (1.5%)	758/83,330 (0.9%)	1.6 (1.3-2.0)
Mechanical ventilation	4	43/8,276 (0.5%)	226/83,330 (0.3%)	1.9 (1.4-2.6)
Maternal death	4	16/8,282 (0.2%)	208/83,327 (0.2%)	0.81 (0.5-1.3)

- Older age (≥ 35 years), high body mass index and pre-existing co-morbidity (hypertension, diabetes) were risk factors for severity of COVID-19 in pregnancy.

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What are Requirements for *In Utero* Transmission?

- In utero* infection requires the pathogen to be able to **reach and cross the placenta and to infect the fetus**.
 - Is there **viremia** to enable the virus to reach placenta?
 - Rarely – 21/587 (3.6%) samples, 8 studies; \uparrow likelihood severe disease
 - Are there receptors for SARS-CoV-2 in the **placenta**?
 - ACE2 & TMPRSS2 found in placenta, late>early, but co-expression may be minimal (other proteases present and could substitute for TMPRSS2).
 - Are there receptors for SARS-CoV-2 in the **fetus** to enable infection of fetus?
 - ACE2 & TMPRSS2 in fetal lung (peak mid-gestation), heart, liver
 - Is there **placental disruption** to allow viral passage *without* placenta infection?
 - Possible due to coagulopathy – in one study, 10/20 placentas showed some evidence of vascular malperfusion or fetal vascular thrombosis.

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What Are Requirements for Breast Milk Transmission?

- If so, is the virus infectious?

- 2 cases of infants fed +PCR milk, uninfected (Chen et al. Pediatrics 2020 Aug 25 [247:2 samples])
- No replication-competent virus in 1 + PCR milk sample (Chen et al. Pediatrics 2020 Aug 25 [247:2 samples])
- 2 cases of infants fed +PCR milk, infected while breastfeeding, but mother infected postpartum, horizontal tx cannot be excluded (Chen et al. Pediatrics 2020 Aug 25 [247:2 samples])

- Has SARS-CoV-2 been detected by rPCR in breast milk?

- Rarely - 20/196 milk samples (10%) from 10/85 women (12%) positive by PCR, generally transiently, in 12 studies

- Postnatal transmission through breastfeeding requires infant exposure to infectious breast milk and infant infection via oral or gastrointestinal route.

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Living Systematic Review: Potential SARS-CoV-2 Vertical Transmission Cases

- Preliminary review (May 28) - 87 papers including 869 infants
- 52/869 with suspect infection (6.0%): 49 positive rtPCR on respiratory secretions, 3 infants reported with IgM found in neonatal blood.
- However, major issues in most of these papers - for example:
 - Timing of maternal infection (25% first diagnosed postpartum)
 - Type sample ("throat" vs nasopharyngeal vs not specified)
 - Timing of infant testing (many done several days after birth)
 - Lack of confirmatory testing
 - Lack of placental/amniotic fluid testing
 - Lack of serologic testing in the virologic-positive children