

Pregnancy and outcomes in Covid-19 patients

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Game plan

- ▶ Review a recent set of articles on pregnancy and newborn outcomes among Covid-19 patients —primary focus on one case series from one hospital system
- ▶ Review a newer article on antibody transmission from mothers to infants post vaccination in 3rd trimester

Objectives

- ▶ List main risk factors for moderate-severe Covid-19 among all pregnant women reporting to a single hospital system (Yale)
- ▶ List alternative study designs to more thoroughly evaluate risks for Covid-19 transmission to newborns
- ▶ Suggest ways to further evaluate vaccine production of antibodies and evidence of protection of infants
- ▶ Pass a quiz at the end

Take home messages

- ▶ Vaccination during 3rd trimester results in IgG antibodies in cord blood, with levels correlating with timing of mothers' vaccination
- ▶ Obesity is a strong risk factor for moderate-severe Covid-19 among pregnant women in the Yale study
- ▶ Hispanic ethnicity in the Yale study was a strong risk factor for moderate to severe Covid-19 in pregnancy
- ▶ Among SARS-CoV-2 infected mothers, risk of vertical transmission at birth appears to be low, based on most studies (not all studies)
- ▶ Considering that Covid-19 is on the increase in reproductive-age women, our knowing more about the disease in this group would be helpful/important for the public health

Efficient transplacental transfer of SARS-CoV-2 antibodies to newborns –Israel study (Rottenstreich et al, Medrxiv, 2021)

- ▶ 20 mother-infant dyads, single hospital in Israel
- ▶ Mean age of moms: 32 years
- ▶ On median, deliveries occurred 11 days post vaccination of moms
- ▶ Antibodies found in maternal sera, and cord blood
- ▶ Antibody levels correlated with time lapsed since vaccination
- ▶ Antibody transmission efficiency was not as favorable as with other vaccines

Limitations of this report

- ▶ Single hospital
- ▶ Small sample size
- ▶ All participants in 3rd trimester...what happens if vaccine is given earlier?
- ▶ Side effects of vaccine not discussed
- ▶ Not a RCT

Introduction of Covid-19 concerns in pregnant mothers and offspring

- ▶ Early reports indicated that pregnant women and their offspring were not at increased risk for Covid-19 (many of those reports)
- ▶ More recent articles suggested that they are at increased risk, probably due to physiologic changes of pregnancy and virus ability to cross 'barriers' (many of these, too!)
- ▶ Isolated reports of vertical transmission that are well-characterized
- ▶ Covid-19 is increasing in incidence in childbearing age group in past several months, at least in the US
- ▶ Many unanswered questions about vertical transmission, timing of mothers' infections, treatment of babies and of moms (during pregnancy), etc.

Study design, Yale study , Grechukina et al, Am J Ob Gyn

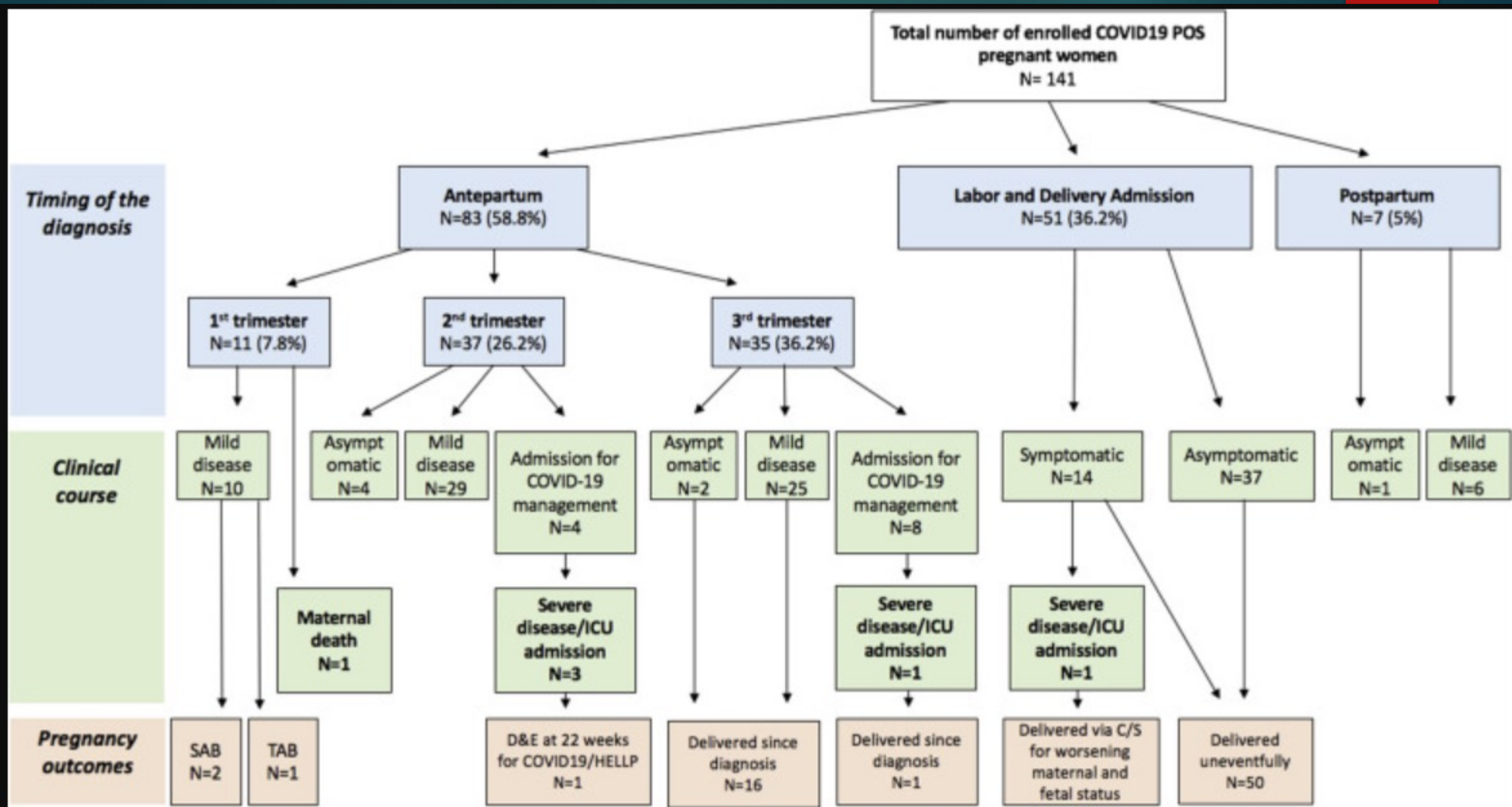
- ▶ Case series
- ▶ Chart review of all pregnant women over specific time period
- ▶ All tested for SARS-CoV-2 per hospital protocol*
- ▶ Disease severity classified according to WHO criteria: asymptomatic, mild, moderate, severe
- ▶ Self-reported demographic info collected; ob history and BMI data also
- ▶ Babies swabbed for SARS-CoV-2 (60 were swabbed/141 babies) within 48 hours of birth
- ▶ Chi-squares and unadjusted OR's presented associating certain risk factors with moderate/severe disease outcomes (combined)

Key findings, Yale study , Grechukina et al, Am J Ob Gyn

- ▶ 141 positive pregnant patients, representing 9% of total deliveries
- ▶ Overall % with mod to severe disease: 4.3%
- ▶ Hispanic women over-represented in Covid cases
- ▶ Hispanic ethnicity assoc with 5.5 fold increase in mod-severe disease
- ▶ Obesity associated with 5.0 fold increase in mod-severe disease (BMI>30 pre-pregnancy)
- ▶ 31% of Covid-19 mothers asymptomatic
- ▶ Most common symptoms reported for mildly asymptomatic patients were cough, muscle aches, sore throat

Neonatal outcomes, Yale study, Grechukina et al, Am J Ob Gyn

- ▶ 60/60 babies tested were swab negative before 48 hours of life
- ▶ None of the newborns were admitted for Covid-19

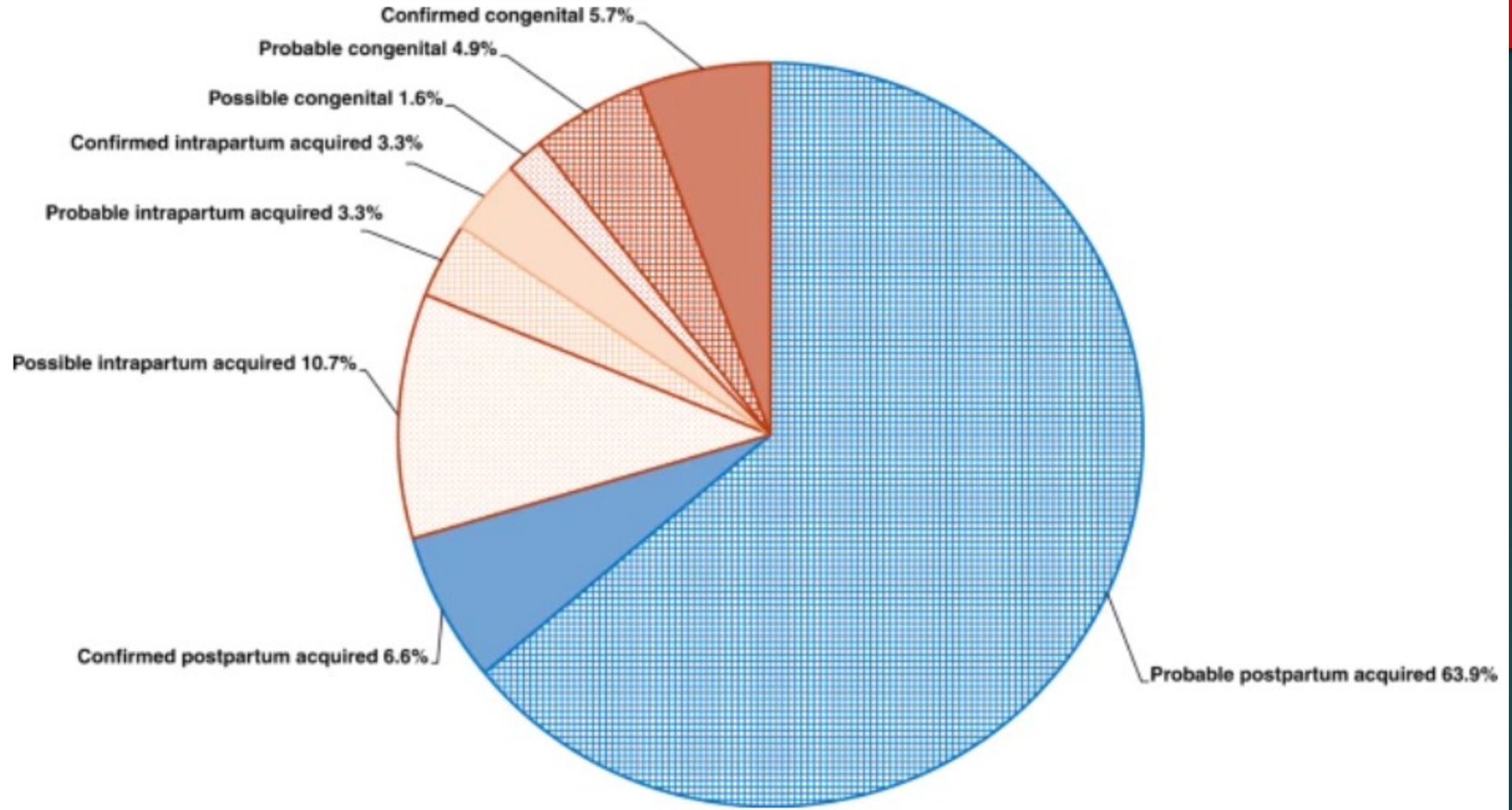


Related studies—Fenitizia et al

- ▶ Case series: 2 positive babies of 31 (6.5%) Covid-19 pregnancies...investigators performed tests at multiple sites and did antibody studies
- ▶ They concluded vertical (in utero) transmission is rare but possible.
- ▶ One positive breastmilk sample
- ▶ One asymptomatic baby, one baby moderately ill (not dependent upon degree of severity in the mother)

Neonatal Covid-19 acquisition— Raschetti et al

- ▶ Systematic review of 176 published cases from around the planet
- ▶ 30% of all cases thought to be vertical transmission (they were indefinite about their level of certainty about all of these cases, see next pie chart)
- ▶ They conclude that environmental acquisition from later exposure is responsible for most cases in neonates
- ▶ In my humble view, some of the findings from this review are questionable (or at least, very unclear)



Classification of neonatal meningitis by etiology and timing of acquisition

Outcomes of neonates born to mothers with severe Covid-19 in NY. Dumetriu et al, JAMApediatrics

- ▶ 100 mothers positive or suspected Covid-19, 101 babies
- ▶ 141 tests performed on babies days 0-25 of life
- ▶ 2 newborn babies 'presumptive positive' PCR test but clinically asymptomatic
- ▶ 55 babies followed in special clinic negative 3-10 days of life
- ▶ 23 additional babies in other clinics negative at 3-25 days of life
- ▶ Newborns mostly roomed in with moms and mostly breastfed
- ▶ Authors' conclusions: no clinical evidence of vertical transmission in this case series

Table 3. Characteristics of Neonates Born to Mothers With Asymptomatic/Mild Illness vs Severe/Critical COVID-19

Variable	Maternal severity of COVID-19			Difference (95% CI)	P value
	All	Asymptomatic/mild ^a	Severe/critical ^a		
SARS-CoV-2 transmission					
Testing-based transmission, No./total No. (%) [95% CI]					
Total newborns	2/101 (2.0) [0.2 to 7.0]	2/91 (2.2)	0/10	NA	>.99
Total tests given	2/141 (1.4) [0.2 to 5.0]	2/123 (1.6)	0/18	NA	>.99
Vertical transmission					
Tested ≤ HOL-23	1/15 (7.0) [0.2 to 32.0]	1/14 (7.1)	0/1	NA	>.99
Tested ≥ HOL-24	1/86 (1.2) [0.03 to 6.3]	1/77 (1.3)	0/9	NA	>.99
Perinatal transmission, retesting	0/31 [0.0 to 11.2]	0/26	0/5	NA	NA ^b
Clinical-based transmission, No./total No. (%) [95% CI]					
Vertical transmission	0/101 [0.0 to 3.6]	0/91	0/10	NA	NA ^b
Perinatal transmission	0/55 [0.0 to 6.5]	0/49	0/6	NA	NA ^b

limitations

- ▶ Each of the studies presented has clear limitations—mostly due to the lack of study protocol before the studies began (chart reviews ‘after the fact’)
- ▶ More sophisticated study designs (besides case series) can better unravel the exposure-outcome relation between Covid-19 pregnant mothers and transmission before or during childbirth
- ▶ As in many other Covid-19 research thrusts, the likelihood of infected mothers passing on SARS-CoV-2 before or at time of birth...remains incompletely evaluated (at this time)

Quiz

- ▶ What study design/s would you choose to evaluate risks for moderate to severe Covid-19 among pregnant women? Why? Assume no limitations on funding or time.
- ▶ What prevention messages would you design and 'market' to concerned pregnant women re: Covid-19 in a marketing or prevention-related campaign? Would you promote vaccination?
- ▶ In the Yale study, what were the strongest risk factors for mod-severe Covid-19 among mothers?
- ▶ How would you counsel concerned pregnant patients with Covid-19, about transmission risk to newborns?

references

- ▶ Grechukhina O, Greenberg V, Lundsberg LS, Deshmukh U, Cate J, Lipkind HS, Campbell KH, Pettker CM, Kohari KS, Reddy UM. Coronavirus Disease 2019 (COVID-19) pregnancy outcomes in a racially and ethnically diverse population. *Am J Obstet Gynecol MFM*. 2020 Oct 7:100246. doi: [10.1016/j.ajogmf.2020.100246](https://doi.org/10.1016/j.ajogmf.2020.100246). Epub ahead of print. PMID: 33047100; PMCID: PMC7539936.
- ▶ **Vertical Transmission**
 1. <https://www.cidrap.umn.edu/news-perspective/2020/10/study-finds-low-risk-infants-moms-covid-19>
- ▶ Dumitriu D, Emeruwa UN, Hanft E, et al. Outcomes of Neonates Born to Mothers With Severe Acute Respiratory Syndrome Coronavirus 2 Infection at a Large Medical Center in New York City. *JAMA Pediatr*. Published online October 12, 2020. doi:[10.1001/jamapediatrics.2020.4298](https://doi.org/10.1001/jamapediatrics.2020.4298)
- ▶ Fenizia C, Biasin M, Cetin I, Vergani P, Mileto D, Spinillo A, Gismondo MR, Perotti F, Callegari C, Mancon A, Cammarata S, Beretta I, Nebuloni M, Trabattoni D, Clerici M, Savasi V. Analysis of SARS-CoV-2 vertical transmission during pregnancy. *Nat Commun*. 2020 Oct 12;11(1):5128. doi: [10.1038/s41467-020-18933-4](https://doi.org/10.1038/s41467-020-18933-4). PMID: 33046695.

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