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Research Article
General obstetrics

SARS-CoV-2 and pregnancy outcomes under universal and non-universal testing in Sweden: register-based nationwide cohort study

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Objective To assess associations of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and pregnancy outcomes considering testing policy and test-positivity-to-delivery interval.

Design Nationwide cohort study.

Setting Sweden.

Population From the Pregnancy-Register we identified 88 593 singleton births, 11 March 2020–31 January 2021, linked to data on SARS-CoV-2-positivity from the Public Health Agency, and information on neonatal care admission from the Neonatal Quality Register. Adjusted odds ratios (aORs) were estimated stratified by testing-policy and test-positivity-to-delivery interval.

Main outcome measures Five-minute Apgar score, neonatal care admission, stillbirth and preterm birth.

Results During pregnancy, SARS-CoV-2 test-positivity was 5.4% (794/14 665) under universal testing and 1.9% (1402/73 928) under non-universal testing. There were generally lower risks associated with SARS-CoV-2 under universal than non-universal testing. In women testing positive >10 days from delivery, generally no significant differences in risk were observed under either testing policy. Neonatal care admission was more common (15.3% versus 8.0%; aOR 2.24, 95% CI 1.62–3.11) in women testing positive ≤10 days before delivery under universal testing. There was no significant association with 5-minute Apgar score below 7 (1.0% versus 1.7%; aOR 0.64, 95% CI 0.24–1.72) or stillbirth (0.3% versus 0.4%; aOR 0.72, 95% CI 0.10–5.20). Compared with term births (2.1%), test-positivity was higher in medically indicated preterm birth (5.7%; aOR 2.70, 95% CI 1.60–4.58) but not significantly increased in spontaneous preterm birth (2.3%; aOR 1.12, 95% CI 0.62–2.02).

Conclusions Testing policy and timing of test-positivity impact associations between SARS-CoV-2-positivity and pregnancy outcomes. Under non-universal testing, women with complications near delivery are more likely to be tested than women without complications, thereby inflating any association with adverse pregnancy outcomes compared with findings under universal testing.

Keywords Apgar, coronavirus disease 2019, neonatal care, preterm birth, severe acute respiratory syndrome coronavirus 2, stillbirth, universal.

Tweetable abstract Testing policy and time from SARS-CoV-2 infection to delivery influence the association with pregnancy outcomes.

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Introduction

Pregnant women are considered a high-risk group compared with non-pregnant women for intensive care admission with invasive ventilation for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.[1,2] The infection has a wide variation in symptoms and where universal testing upon admission for delivery has been conducted, infection is often asymptomatic (New York City: 79%; Stockholm: 65%; Dallas: 42%).[3–5] Studies based on non-universal testing generally report SARS-CoV-2 test-positivity to be associated with higher risks of preterm birth, caesarean delivery and neonatal intensive care admission,[1,3,6] whereas studies on stillbirth risk have been inconclusive.[1,5–7]

However, variation in criteria for SARS-CoV-2 testing may influence study results.[1] It is plausible that reported risks associated with SARS-CoV-2 infection may be overestimated because non-universal testing probably results in pregnancies with complications near delivery being tested to a greater extent than uncomplicated pregnancies. Supporting this hypothesis, studies of maternity units with universal testing have reported lower risks or even lack of associations with adverse pregnancy outcomes including preterm birth.[5,7–9] Irrespective of testing policy, women who test positive may also be followed more closely for complications and the threshold for medical interventions may be lowered.

We hypothesised that under non-universal testing, women with complications near delivery were more often tested than women without complications, thereby inflating any association with adverse pregnancy outcomes compared with findings under universal testing. Furthermore, we hypothesised that timing of test-positivity was associated with the outcomes under study, with greater risks for women testing positive closer to delivery because ongoing infection would more likely affect the woman and infant. We therefore conducted a nationwide cohort study of pregnant women identified from the Swedish Pregnancy Register linked with national SARS-CoV-2 testing data. The aim of the study was to investigate low 5-minute Apgar score, neonatal care admission and stillbirth by testing policy and by time from testing positive for SARS-CoV-2 to delivery in test-positive women compared with women without positive tests. We also aimed to compare the risk of adverse pregnancy outcomes during the first 11 months of the pandemic with historical comparators from the previous 5 years.

Methods

Setting and data sources

In Sweden, the participation in the prenatal care programme is almost 100% and both prenatal care and delivery care are tax funded for all residents. With the use of the unique personal identity number or coordination number assigned to each Swedish resident at birth or immigration,[10] we linked information from the National Register for Communicable Diseases (SmiNet) at the Public Health Agency of Sweden and the Swedish Pregnancy and Neonatal Quality Registers.

SARS-CoV-2 is a notifiable pathogen according to the Swedish Communicable Disease Act, and it is mandatory to report every positive finding in a laboratory specimen (polymerase chain reaction test) along with the date. The registration of a positive finding is linked from the microbiology laboratory to SmiNet the same day. We did not have specific information on symptoms, onset of infection, negative tests or antibody test results. In Sweden, testing was initially (during spring 2020) restricted to persons needing hospital care for coronavirus disease 2019 (COVID-19) because of limited testing capacity. However, some regions have from the start of the pandemic, or during certain periods, tested all women admitted for antenatal or delivery care. From early June 2020, testing was offered and available also outside hospitals.

The population-based Swedish Pregnancy Register includes comprehensive information on each individual pregnancy and birth with prospectively collected information from the first antenatal healthcare visit to the postpartum visit for 92% of all births in Sweden since 2014.[11] After birth, information is automatically forwarded from the standardised electronic medical record to the register, which is updated twice daily. From the register we retrieved information on maternal, delivery and postpartum characteristics and outcomes. By linkage to the Swedish Neonatal Quality Register we retrieved information on neonatal care admissions.[12]

Study design

In Sweden, the first SARS-CoV-2 test-positive pregnant woman was admitted for delivery on 11 March 2020. We conducted a nationwide cohort study of singleton pregnancies based on women admitted for delivery between 11 March 2020 and 31 January 2021, as captured from the Swedish Pregnancy Register. Gestational age estimation was based on an algorithm including: (1) embryo transfer (4.4%), (2) ultrasound (94.1%), (3) last menstrual period (1.4%) and (4) postnatal assessment (0.1%). Women were included in the exposed group if they had a positive SARS-CoV-2 test between estimated conception date and delivery, and divided into two groups depending on the test-to-delivery-interval (≤10 days or >10 days). The comparator group consisted of pregnant women without a positive SARS-CoV-2 test in SmiNet during the study period. If a woman tested positive early in pregnancy and then was found to be negative at delivery, she would still be placed in the universal testing group but with test-positivity more than 10 days from delivery and would be analysed

separately. The cohort was further divided into periods for when delivery units used universal or non-universal testing, as testing policy influences exposure classification. Calendar periods for universal and non-universal testing policy for the included delivery units were obtained by telephone interviews and are provided in the supplementary appendix (Table S1).

To assess the public health impact of SARS-CoV-2 on adverse pregnancy outcomes, a historical comparison was also made comparing outcomes between the pandemic period (March 2020–January 2021) versus the same months during previous 5 years (March 2015–January 2020; excluding February for all years).

Outcomes

From the Swedish Pregnancy and Neonatal Quality Registers, we retrieved data on 5-minute Apgar score, neonatal care admission, stillbirth (death before birth from 22^{+0} weeks of gestational age) and spontaneous and medically indicated preterm birth (<37^{+0} weeks of gestation).

Statistical analysis

We compared risks in test-positive and non-positive women by estimating adjusted odds ratios (aORs) using logistic regression for 5-minute Apgar score less than 7, neonatal care admission and stillbirth controlling for parity (nulliparous/parous), age, body mass index (BMI), birth country (Nordic/non-Nordic) and healthcare region (Stockholm, West, South, Southeast, Central, North). If the number of outcome events was less than five, exact logistic regression was used (adjusted for birth country). Missing data for BMI (3–4%) and birth country (8–10%) were handled by coding them as separate missing categories. We calculated standardised difference between the groups, and a difference of less than −0.10 or more than 0.10 was considered to indicate significant group differences.

For preterm birth, we estimated adjusted odds ratios for test-positivity within the groups spontaneous preterm, medically indicated preterm, term and post-term birth with the same adjustment variables as above. This case–control analysis approach was chosen because women were often tested at time of delivery and those giving birth at 37^{+0} weeks of gestation or later were no longer at risk of delivering preterm (in contrast to low Apgar score, neonatal care and stillbirth, which could occur at any time after 22^{+0} weeks of gestation).

For assessment of the public health impact of SARS-CoV-2 infection, as well as the effects of pandemic measures including anxiety, travel disruption and behavioural changes, unadjusted risk differences were estimated for study outcomes for all pregnancies during the pandemic period versus historical comparators.

In a sensitivity analysis, data were re-analysed using test-to-delivery intervals of up to 20 days and more than 20 days instead of up to 10 days and more than 10 days as in the main analysis.

Data were analysed using SAS software, version 9.4 (SAS Institute, Cary, NC, USA). The study did not include any patient or public involvement and no core outcome set was used.

Results

Test-positivity and participant characteristics

Between 11 March 2020 and 31 January 2021, 89 988 births were recorded in the Swedish Pregnancy Register. We excluded 1228 multiple births and those with missing information on gestational age ($n = 74$), parity ($n = 56$) and births to women ($n = 37$) with a positive SARS-CoV-2 test after birth but before discharge (Figure S1). The study cohort included 88 593 women with singleton births. Of these, 14 665 delivered at units with a universal testing policy (794 test-positive; 5.4%) and 73 928 at units with non-universal testing (1402 test-positive; 1.9%). The proportion of test-positivity varied by testing policy during the study period (Figure S2); the proportion was higher at hospitals with universal testing during spring 2020, whereas differences were smaller but in the same direction during the autumn and winter (regional variations described in Figure S3).

The distributions of maternal and pregnancy characteristics were similar for most variables between test-positive and non-positive groups (Table 1). Test-positive women were less often of Nordic origin (55% versus 60% [standardised difference: −0.11] under universal testing and 60% versus 66% [standardised difference: −0.13] under non-universal testing), and there were also standardised differences greater than 0.10 for distribution across healthcare regions. Under non-universal testing, test-positive women were also more often obese than non-positive women (20% versus 15%; standardised difference: 0.12).

Median time from positive test to delivery was 26 days (interquartile range 1–65 days) for universal testing and 46 days (interquartile range 13–100 days) for non-universal testing (Figure S4).

Outcomes in women testing positive within 10 days from delivery

In women testing positive 10 days or less before delivery under universal testing, there was no significant difference compared with non-positive women in their infants' 5-minute Apgar score less than 7 (1.0% versus 1.7%; aOR 0.64, 95% CI 0.24–1.72) or stillbirth (0.3% versus 0.4%; aOR 0.72, 95% CI 0.10–5.20), but neonatal care admission was more common (15.3% versus 8.0%; aOR 2.24, 95% CI

Table 1. Characteristics of pregnant women in Sweden between 11 March 2020 and 31 January 2021 by SARS-CoV-2 testing policy at the delivery hospital and test-positivity

	Universal testing			Non-universal testing		
	Test-positive (*n* = 794)	**Non-positive (*n* = 13 871)**	**Standardised difference**	**Test-positive (*n* = 1 402)**	**Non-positive (*n* = 72 526)**	**Standardised difference**
Nulliparous, *n* (%)	328 (41.3)	6141 (44.3)	−0.060	614 (43.8)	31 185 (43.0)	0.016
Age (years), mean (SD)	31.5 ± 4.8	31.6 ± 5.0	−0.035	31.5 ± 5.0	31.4 ± 4.9	0.024
13–24 y, *n* (%)	68 (8.6)	1285 (9.3)	−0.025	127 (9.1)	6481 (8.9)	0.004
25–29 y, *n* (%)	234 (29.5)	3877 (28.0)	0.034	432 (30.8)	22 221 (30.6)	0.004
30–34 y, *n* (%)	307 (38.7)	5267 (38.0)	0.014	508 (36.2)	27 283 (37.6)	−0.029
≥35 y, *n* (%)	185 (23.3)	3442 (24.8)	−0.035	335 (23.9)	16 541 (22.8)	0.026
BMI (kg/m^2), mean (SD)	25.9 ± 5.0	25.5 ± 5.1	0.091	26.0 ± 5.2	25.3 ± 5.0	0.143
<18.5, *n* (%)	9 (1.1)	329 (2.4)	−0.094	23 (1.6)	1643 (2.3)	−0.045
18.5–<25, *n* (%)	384 (48.4)	7042 (50.8)	−0.048	648 (46.2)	37 817 (52.1)	−0.119
25–<30, *n* (%)	226 (28.5)	3667 (26.4)	0.045	400 (28.5)	18 960 (26.1)	0.054
≥30, *n* (%)	149 (18.8)	2262 (16.3)	0.065	277 (19.8)	11 033 (15.2)	0.120
Missing	*26 (3.3)*	*571 (4.1)*	−0.045	*54 (3.9)*	*3073 (4.2)*	−0.020
Education level, *n* (%)						
<10 y	84 (10.6)	1092 (7.9)	0.094	105 (7.5)	4585 (6.3)	0.046
10–12 y	245 (30.9)	4053 (29.2)	0.036	387 (27.6)	21 150 (29.2)	−0.035
>12 y	322 (40.6)	6233 (44.9)	−0.089	673 (48.0)	34 206 (47.2)	0.017
Missing	*143 (18.0)*	*2493 (18.0)*	0.001	*237 (16.9)*	*12 585 (17.4)*	−0.012
Smoker, *n* (%)	28 (3.5)	455 (3.3)	0.014	24 (1.7)	2606 (3.6)	−0.117
Missing	*16 (2.0)*	*320 (2.3)*	−0.020	*49 (3.5)*	*2672 (3.7)*	−0.010
Birth country, *n* (%)						
Nordic	435 (54.8)	8 349 (60.2)	−0.109	838 (59.8)	48 004 (66.2)	−0.133
Europe	40 (5.0)	888 (6.4)	−0.059	100 (7.1)	4678 (6.5)	0.027
Asia	18 (2.3)	521 (3.8)	−0.087	26 (1.9)	1934 (2.7)	−0.055
North Africa & Middle East	153 (19.3)	1814 (13.1)	0.169	226 (16.1)	7813 (10.8)	0.157
Sub-Saharan Africa	55 (6.9)	634 (4.6)	0.101	61 (4.4)	2262 (3.1)	0.065
Other	11 (1.4)	223 (1.6)	−0.018	36 (2.6)	1314 (1.8)	0.052
Missing	*82 (10.3)*	*1442 (10.4)*	−0.002	*115 (8.2)*	*6521 (9.0)*	−0.028
Not living with partner	66 (8.3)	1264 (9.1)	−0.028	101 (7.2)	5737 (7.9)	−0.027
Missing	6 (0.8)	201 (1.4)	−0.066	25 (1.8)	1368 (1.9)	−0.008
Any comorbidity, *n* (%)	292 (36.8)	5233 (37.7)	−0.020	528 (37.7)	26 237 (36.2)	0.031
Diabetes	16 (2.0)	208 (1.5)	0.039	18 (1.3)	827 (1.1)	0.013
Psychiatric disorder	145 (18.3)	2719 (19.6)	−0.034	266 (19.0)	13 095 (18.1)	0.024
Cardiovascular disease	12 (1.5)	303 (2.2)	−0.050	17 (1.2)	1103 (1.5)	−0.027
Healthcare region, *n* (%)						
Stockholm	292 (36.8)	5666 (40.8)	−0.084	515 (36.7)	18 712 (25.8)	0.237
West	117 (14.7)	1727 (12.5)	0.067	325 (23.2)	17 971 (24.8)	−0.037
South	144 (18.1)	1287 (9.3)	0.260	117 (8.3)	13 102 (18.1)	−0.290
Southeast	9 (1.1)	75 (0.5)	0.065	211 (15.0)	9779 (13.5)	0.045
Central	189 (23.8)	4195 (30.2)	−0.145	166 (11.8)	8394 (11.6)	0.008
North	43 (5.4)	921 (6.6)	−0.051	68 (4.9)	4568 (6.3)	−0.063

Standardised difference ≥0.10 (shaded grey) interpreted as indicating a meaningful difference.

1.62–3.11; Figure 1). The proportion of test-positivity in term births was 2.1%: 2.3% in spontaneous preterm births (aOR [versus term births] 1.12, 95% CI 0.62–2.02), 5.7% in medically indicated preterm births (aOR [versus term births] 2.70, 95% CI 1.60–4.58), and 1.8% in postterm births (aOR [versus term births] 0.86, 95% CI 0.63–1.17; Figure 2).

Under non-universal testing, infants of women testing positive 10 days or less before delivery compared with those of non-positive women had a higher risk for a 5-minute Apgar score less than 7 (3.3% versus 1.4%; aOR 2.05, 95% CI 1.09–3.85), stillbirth (1.3% versus 0.3%; aOR 4.06, 95% CI 1.50–11.0) and neonatal care admission (21.5% versus 8.3%; aOR 3.16, 95% CI 2.39–4.16; Figure 1). The

proportion of test-positivity in term births was 0.4%: 0.8% in spontaneous preterm births (aOR [versus term births] 2.02, 95% CI 1.23–3.31), 3.2% in medically indicated preterm births (aOR [versus term births] 8.79, 95% CI 6.03–12.82), and 0.3% in postterm births (aOR [versus term births] 0.80, 95% CI 0.58–1.09; Figure 2).

Outcomes in women testing positive more than 10 days from delivery

In women testing positive more than 10 days from delivery, no significant differences in 5-minute Apgar score below 7, neonatal care admission, or stillbirth were observed under either testing policy (Figure 1). Higher proportion of test-positivity was observed in the group with medically indicated preterm birth under non-universal testing (aOR 1.56, 95% CI 1.03–2.35; Figure 2).

Sensitivity analysis

Re-analysing the data using test-to-delivery-intervals of up to 20 and more than 20 days resulted in the same pattern with higher risks for test-positive versus non-positive women observed under non-universal than universal testing, and with no significant differences in either low Apgar scores or stillbirth in test-positive versus non-positive women under universal testing (Figure S5 and Figure S6).

Public health impact

Comparing outcomes during the pandemic period (births March 2020–January 2021) with historical comparators (births March 2015–January 2020 [excluding births in February all years]), lower risk of spontaneous preterm birth (3.2% versus 3.5%; risk difference −0.3%, 95% CI −0.4 to −0.2) and higher risk of medically indicated preterm birth (1.5% versus 1.4%; risk difference 0.1%, 95% CI 0.04–0.2) were observed, as well as for neonatal care (8.3% versus 8.1%; risk difference 0.2%, 95% CI 0.01–0.4). No significant differences were found for 5-minute Apgar score less than 7 and stillbirth (Figure 3 and Figure S7).

Discussion

Main findings

In this nationwide study from Sweden, under universal testing and compared with non-positive women, SARS-CoV-2 test-positivity 10 days or less from delivery was not significantly associated with spontaneous preterm birth, low 5-minute Apgar score, or stillbirth, but was significantly associated with higher risks for medically indicated preterm birth and neonatal care admission. Under non-universal testing, women testing positive 10 days or less before delivery had higher risks for all outcomes investigated, indicating bias potentially caused by women with pregnancy complications near delivery being tested more often under this policy.

Strengths and limitations

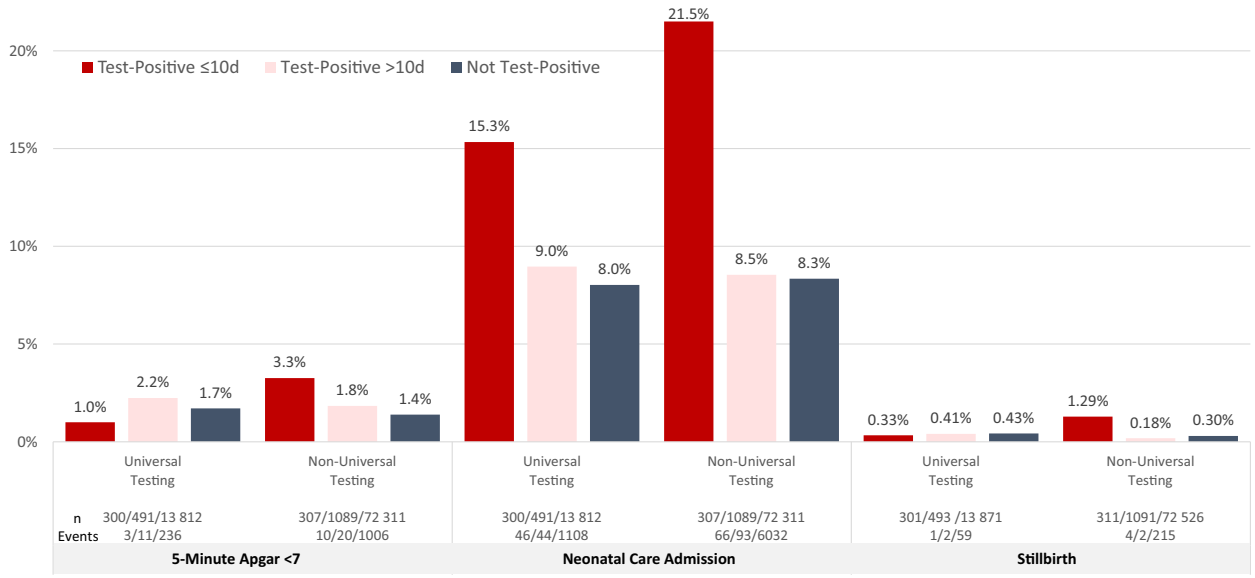
Strengths of this study include the nationwide design with linkage between the Swedish Pregnancy and Neonatal Quality Registers with the SmiNet Register, to which reporting of positive SARS-CoV-2 tests is mandatory.

A limitation is the lack of data on COVID-19 symptoms, precluding analyses by infection severity. It is reasonable to assume that the adverse effects of asymptomatic infection are limited, whereas severe infection may have strong effects on the risk for both mother and infant, which represents an avenue for future studies. Because the status of SARS-CoV-2-positivity was not known during the whole pregnancy the proportion of exposure more than 10 days before delivery may have been underestimated. We used data from hospitalisation during delivery and it is possible that women with obstetric complications could have been infected during their hospital stay, leading to a spurious association between SARS-CoV-2-positivity, preterm birth and neonatal care admission.[13]

As a result of the relatively low proportion of test-positive women, we had limited statistical power for rare outcomes such as stillbirth and low 5-minute Apgar score. There is also a risk of false-negative and false-positive results in tests for SARS-CoV-2;[14] but given the relatively low proportion, the impact of misclassification on estimates is likely to be low. Furthermore, we only had access to polymerase chain reaction test results and not to antibody test results for SARS-CoV-2. Finally, access to testing in the non-hospital setting was limited to non-existent during spring 2020, whereas test access was improved during the second wave of infections in the autumn and winter. Hence, the spectrum of infected women varied over time within the non-universal testing group.

Interpretation

In a meta-analysis[1] based on 35 studies (with approximately one-third of studies using universal testing), the risk of any preterm birth was increased three-fold for women with SARS-CoV-2 infection. The meta-analysis did not separate studies by testing policy and their findings contrast with consistent findings from single centre studies using universal testing, where relative risk estimates of preterm birth have ranged between 1.0 and 1.7.[5,7,8] A meta-analysis by Huntley et al., based on six studies comparing test-positive women with test-negative women under universal testing, found no association with preterm birth (13.3% versus 11.9%).[9] In the current study, testing policy and time from test-positivity to delivery strongly influenced findings: in women delivering within 10 days of testing positive, the proportion of SARS-CoV-2 test-positivity was



Adjusted[a] Odds Ratio (95%CI); Reference: Not Test-Positive						
Test+ ≤10 Days	0.64 (0.24–1.72)	2.05 (1.09–3.85)	2.24 (1.62–3.11)	3.16 (2.39–4.16)	0.72 (0.10–5.20)	4.06 (1.50–11.0)
Test+ >10 Days	1.36 (0.73–2.52)	1.29 (0.82–2.02)	1.13 (0.82–1.55)	1.03 (0.83–1.28)	0.97 (0.24–3.97)	0.60 (0.15–2.41)
Crude Odds Ratio (95%CI)						
Test+ ≤10 Days	0.64 (0.24–1.74)	2.10 (1.12–3.96)	2.08 (1.51–2.86)	3.01 (2.29–3.96)	0.78 (0.11–5.65)	4.39 (1.62–11.86)
Test+ >10 Days	1.32 (0.72–2.43)	1.33 (0.85–2.07)	1.13 (0.82–1.55)	1.03 (0.83–1.27)	0.96 (0.23–3.92)	0.62 (0.15–2.49)

[a]Adjusted for parity, BMI, age, birth country, and healthcare region (odds ratios estimated using logistic regression)
[b]If events <5, exact logistic regression was used with adjustment only for birth country

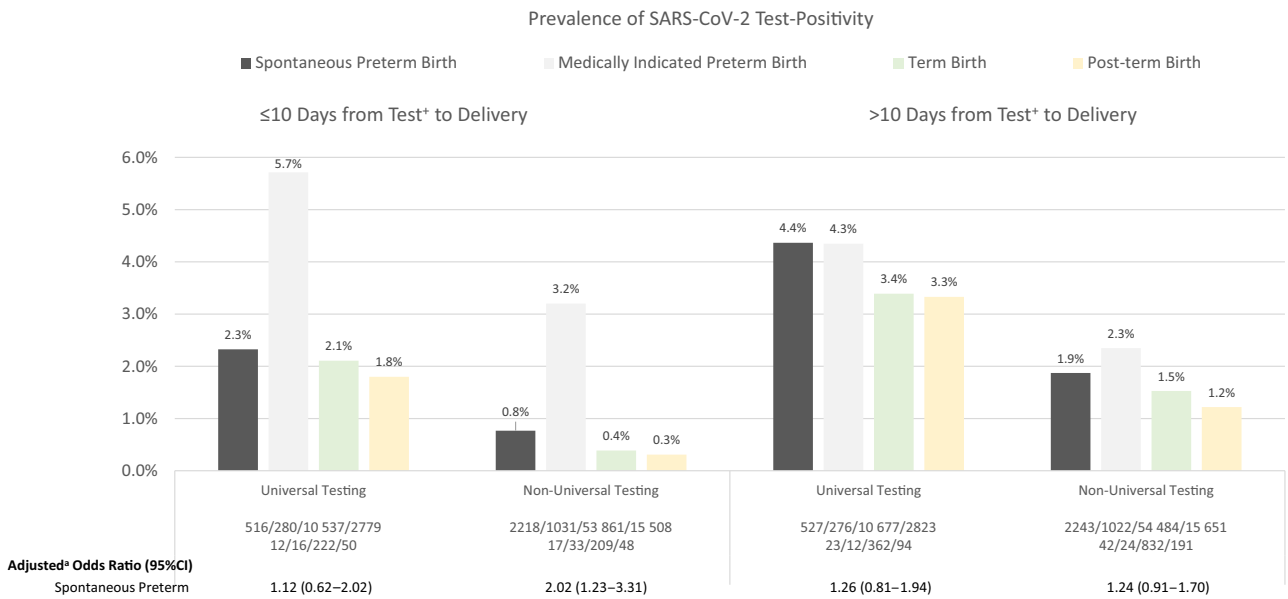
Figure 1. Pregnancy outcomes by SARS-CoV-2 test-positivity under universal and non-universal testing in women testing positive within 10 and more than 10 days from delivery compared with women not testing positive during pregnancy.

similar in spontaneous preterm births and term births under universal testing, contrasting with the more than two-fold higher proportion under non-universal testing in spontaneous preterm versus term births. For medically indicated preterm birth, a higher test-positivity proportion was observed under both testing policies but the magnitude differed markedly with a 2.7-fold higher odds under universal and 8.8-fold higher odds under non-universal testing. The proportion of spontaneous preterm birth was lower whereas that of medically indicated preterm birth was marginally higher during the pandemic period; however, this may not be clinically significant.

Previous studies have reported conflicting results regarding stillbirth.[1,5–7,15] We found no indication of increased stillbirth risk under universal testing (0.3% versus 0.4%) but a four-fold, statistically significantly higher risk under non-universal testing in women testing positive within 10 days from delivery, which can be compared with an odds ratio of 1.30 (95% CI 0.49–3.42) comparing test-positive with test-negative women under universal testing in the meta-analysis by Huntley et al.[9] We observed no change in the proportion of stillbirth during the pandemic compared with the previous 5 years, which is in line with findings from the first wave of COVID-19 in Sweden during spring 2020,[16] suggesting that the increased risk observed in non-universal testing is the result of selection bias.

Regarding infants of test-positive women, most reviews report high proportions of neonatal care admission (25% according to a meta-analysis),[1] but comparators are mostly lacking.[1,3,17,18] The present study also found an association between maternal SARS-CoV-2 infection and infant neonatal care admission, although the absolute risks varied by testing policy (15.3% under universal and 21.5% under non-universal testing). Despite the two-fold higher risk of neonatal care admission under universal testing, there was no difference in 5-minute Apgar score below 7 between infants of test-positive and non-positive women. The proportion of low 5-minute Apgar scores was higher for test-positive more than 10 days before delivery compared with 10 days or less, which was a discrepancy from the study hypothesis. In contrast, under non-universal testing a more than two-fold higher risk of 5-minute Apgar score below 7 was observed for infants of test-positive women. These findings probably reflect a lower threshold for admitting infants born from SARS-CoV-2-positive mothers for neonatal care.

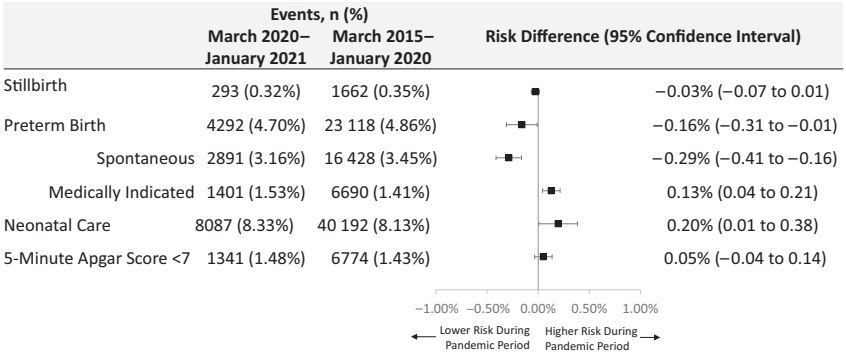
Under universal testing no difference in proportion of test-positivity was observed in spontaneous preterm versus term births. Similarly, no differences were found for low 5-minute Apgar score and stillbirth, outcomes that are also



Adjusted[a] Odds Ratio (95%CI)				
Spontaneous Preterm	1.12 (0.62–2.02)	2.02 (1.23–3.31)	1.26 (0.81–1.94)	1.24 (0.91–1.70)
Medically Indicated Preterm	2.70 (1.60–4.58)	8.79 (6.03–12.82)	1.34 (0.74–2.42)	1.56 (1.03–2.35)
Term Birth	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Post-term Birth	0.86 (0.63–1.17)	0.80 (0.58–1.09)	0.94 (0.75–1.19)	0.80 (0.68–0.94)
Crude Odds Ratio (95%CI)				
Spontaneous Preterm	1.11 (0.62–1.99)	1.98 (1.21–3.26)	1.30 (0.85–2.00)	1.23 (0.90–1.68)
Medically Indicated Preterm	2.82 (1.67–4.75)	8.49 (5.85–12.32)	1.30 (0.72–2.33)	1.55 (1.03–2.34
Term Birth	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Post-term Birth	0.85 (0.63–1.16)	0.80 (0.58–1.09)	0.98 (0.78–1.24)	0.80 (0.68–0.93)

[a]Adjusted for parity, BMI, age, birth country, and healthcare region

Figure 2. Proportion of SARS-CoV-2-positivity by gestational age at delivery under universal and non-universal testing.



	Events, n (%) March 2020–January 2021	Events, n (%) March 2015–January 2020	Risk Difference (95% Confidence Interval)
Stillbirth	293 (0.32%)	1662 (0.35%)	−0.03% (−0.07 to 0.01)
Preterm Birth	4292 (4.70%)	23 118 (4.86%)	−0.16% (−0.31 to −0.01)
Spontaneous	2891 (3.16%)	16 428 (3.45%)	−0.29% (−0.41 to −0.16)
Medically Indicated	1401 (1.53%)	6690 (1.41%)	0.13% (0.04 to 0.21)
Neonatal Care	8087 (8.33%)	40 192 (8.13%)	0.20% (0.01 to 0.38)
5-Minute Apgar Score <7	1341 (1.48%)	6774 (1.43%)	0.05% (−0.04 to 0.14)

Figure 3. Forest plot comparing outcomes during March 2020 and January 2021 (pandemic period) versus between March 2015 and January 2020 (pre-pandemic period; excluding February for all years). Live births with 5-minute Apgar data: $n = 91\,407/90\,632/91\,672$; total births: $n = 476\,166/473\,929/477\,788$.

generally regarded as insensitive to clinical management policies, although these outcomes were more rare, resulting in estimates being less precise. The null findings for spontaneous preterm birth, low 5-minute Apgar score and stillbirth under universal testing contrast with the findings under non-universal testing. Non-universal testing revealed a higher proportion of test-positivity in medically indicated preterm versus term births, and higher risk in test-positive than non-positive women of neonatal care admission. These outcomes may be influenced both by severe COVID-19 and by clinical management after receiving information of test-positivity. For example, because of limited experience of caring for infants born to test-positive women, the threshold for neonatal care admission may have been lowered. The proportion of 5-minute Apgar score less than 7 did not differ between the pandemic and pre-pandemic periods.

We hypothesised that non-universal testing would result in inflated risk estimates in women tested near delivery, as women with pregnancy complications may be more likely

to be tested for SARS-CoV-2. This is important because a majority of test-positive women have been asymptomatic in studies using universal testing at admission for delivery.[5,8] Supporting this hypothesis, we found consistently higher risks under non-universal testing compared with non-positive women for stillbirth (more than four-fold), neonatal care admission (three-fold) and low 5-minute Apgar score (two-fold). This is further supported by the meta-analysis by Huntley et al., in which studies comparing test-positive women with test-negative women did not find any association between SARS-CoV-2 infection and preterm birth, stillbirth or neonatal death.[9] Irrespective of testing policy, we observed no association between test-positivity more than 10 days before delivery and 5-minute Apgar score less than 7, stillbirth or neonatal admission. In addition, a sensitivity analysis for test-positivity 20 days before delivery revealed similar findings.

Conclusion

Testing policy and timing of test-positivity in relation to delivery impact associations between SARS-CoV-2-positivity and pregnancy outcomes. Under non-universal testing, women with complications near delivery are more likely to be tested than women without complications, thereby inflating any association with adverse pregnancy outcomes compared with findings under universal testing.

Disclosure of interests

JFL coordinates a study on behalf of the Swedish inflammatory bowel disease quality register (SWIBREG) which has received funding from Janssen corporation. All other authors declare no competing interests. Completed disclosure of interests form available to view online as supporting information.

Contribution to authorship

OS and MNeo conceived the study and drafted the first version of the manuscript. MNeo performed the statistical analysis. All authors contributed to the interpretation of data and read and approved the final manuscript.

Details of ethics approval

The study was approved by the Swedish Ethical Review Authority (Nos 202001499, 2020-04-23 and 2020-02468, 2020-06-18).

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Transparency statement

The corresponding author (OS) affirms that the manuscript is an honest, accurate and transparent account of the study being reported; that no important aspects of the study have been omitted and that any discrepancies from the study as planned have been disclosed.

Data availability

Individual data from the Swedish Pregnancy Register may not be shared according to Swedish law. Data on an aggregated level may be found at the register website (www.graviditetsregistret.se).

Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.■

Figure S1. Flow chart of the study population.

Figure S2. Proportion of women with SARS-CoV-2 positive test ever during pregnancy in Sweden from March 11, 2020, to January 31, 2021.

Figure S3. Proportion of test-positivity during pregnancy under universal and non-universal testing by month and healthcare region.

Figure S4. Distribution of days between test-positivity and birth.

Figure S5. Pregnancy outcomes by SARS-CoV-2 test-positivity under universal and non-universal testing in women testing positive ≤20 and >20 days from delivery compared with women not testing positive during pregnancy.

Figure S6. Proportion of SARS-CoV-2 positivity by gestational age at delivery under universal and non-universal testing split by women testing positive ≤20 and >20 days before delivery.

Figure S7. Comparison of outcomes during March 2020 to January 2021 versus March 2015-January 2020 (excluding February for all years).

Table S1. Dates for universal testing by delivery clinic.

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