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Impact of SARS-CoV-2 on incidence, treatment and outcome of very preterm born infants in Switzerland: a retrospective, population-based cohort study

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Summary

AIMS OF THE STUDY: To assess whether the COVID-19 pandemic caused by SARS-CoV-2 had an impact on incidence, treatment or major adverse short-term outcome of preterm-born infants in Switzerland.

METHODS: Retrospective cohort study of preterm infants born in 2020 based on two independent data sources from the Swiss Federal Statistics Office (FSO) and SwissNeoNet. Based on FSO data, we calculated the odds ratios for extremely preterm (22–27 weeks gestation), very preterm (28–31 weeks gestation), and late preterm (32–36 weeks gestation) births during the pandemic. Based on SwissNeoNet data of infants born between 22 and 31 weeks gestation, we compared infants born during the Swiss lockdown period in 2020 with infants born during the same period between 2015 and 2019, all infants of 2020 with all infants between 2015 and 2019 and infants born to mothers tested SARS-CoV-2 positive and negative. Possible associations with the pandemic were tested using logistic regression adjusted for case-mix. As a control, we compared births of 2019 with those of 2015–2018.

RESULTS: The FSO data revealed equivalent odds for extremely preterm births in 2020 (odds ratio [OR] 1.01, 95% confidence interval [CI] 0.89–1.14), as well as somewhat lower odds ratios for very preterm (OR 0.9, 95% CI 0.82–1.00) and late preterm (OR 0.91, 95% CI 0.88–0.93) births in 2020. A comparison between 2019 and 2015–2018, however, revealed matching odds ratios rendering an association to the pandemic unlikely. In the SwissNeoNet data, 137 infants were born during lockdown in 2020 compared with 134 births per year during 2015–2019. When including all infants, 744 infants were compared to 845 births, respectively. The only difference observed in treatments and short term outcomes between 2020 and the reference years were a higher odds for respiratory distress syndrome (OR 1.6, 95% CI 1.08–2.37) and provision of continuous positive airway pressure (CPAP) (OR 1.39, 95% CI 1.05–1.84).

CONCLUSIONS: Our Swiss population-based analysis did not identify the elsewhere reported association between the COVID-19 pandemic and a reduced preterm birth rate. However, we can confirm a possible link between the COVID-19 pandemic and higher odds of respiratory distress syndrome, possibly coupled with CPAP requirements. Further observation of potential effects of the pandemic on health and health care provision to newborns may however be indicated based on the literature available so far and that our data only covers the first 9 months of the current pandemic.

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Introduction

The COVID-19 pandemic, based on the uncontrolled proliferation of the novel SARS-CoV-2 virus, had a dramatic impact on many areas of public life and public health. In the field of neonatology, several reports evaluated the incidence of preterm births in relation to the pandemic. Most declared a reduced incidence of admissions, some as dramatic as 75% or more. To date, six reports have covered a large geographical region. They were published from Ireland, Denmark, the Netherlands, the UK, Japan and the

Lazio region in Italy, and all declared a substantial decrease in infants born between 22–27 weeks, 28–31 weeks, and 32–36 weeks or above, corresponding to extremely preterm, very preterm, late preterm or term born infants [1–6]. Most of the reports speculate that it was not the virus itself that contributed to the observed reduction, but instead the mitigating measures implemented by governments to limit the pandemic. Among those measures were reduced mobility leading to less pollution, physical activity and overall infection rates.

In Switzerland, the first strict mitigation measures in response to the COVID-19 pandemic were imposed on 16 March 2020, and were gradually relaxed 55 days later, from 11 May 2020 onwards. During this lockdown period, a reduction of around 60% in the average daily mobility was observed, with decreases of over 90% for public transport [7]. Schools were closed from 17 March to 3 April, air quality improved [8], and impaired mental well-being was associated with younger age, urban residential environment, health problems and not being able to go to work [9]. All of these issues have the potential to affect pregnancy and/or child-birth. The second wave of the pandemic took place in Europe during the autumn and winter of 2020. Switzerland was among the countries with the highest case numbers and deaths per capita [10]. During this period, Switzerland had a more liberal implementation of mitigation measures to slow down virus transmission, such as social distancing, testing and restricting mobility, than other European countries. The mitigating measures of Switzerland's immediate neighbours Germany, France and Italy, for instance, were classified as being considerably more stringent [10].

Based on the above mentioned large and predominantly European studies, and the effect the pandemic had on every-day life in Switzerland, SwissNeoNet monitored the development of the pandemic in the Swiss perinatal centres and continuously reported to their unit directors whether there was any discernible association between the COVID-19 pandemic and the incidence, treatment and outcome of Swiss preterm infants. In this study, we summarise these reports.

Methods

This was a population-based, retrospective cohort study including all live born infants between defined weeks of gestation in Switzerland from 2015 to 2020. We used two independent data sources: (1) the publicly available birth registry records of the Swiss Federal Statistical Office (FSO) that provide an annual number of births for infants born between 22+0–27+6 (extremely preterm), 28+0–31+6 (very preterm), 32+0–36+6 (late preterm) and all term born infants [11]; (2) the minimum neonatal dataset of the Swiss Neonatal Network and Follow-up Group (SwissNeoNet), which prospectively collects routine diagnoses and treatments electronically for infants born between 22+0–31+6 during their primary hospitalisation period. For this study, we were therefore able to use only accumulated numbers of infants in the three gestational age strata from FSO, whereas SwissNeoNet provided individual datasets with details on diagnoses and treatments for each newborn, but only of the two first gestational age strata.

ABBREVIATIONS

aOR	adjusted odds ratio
BWZ	birth weight z-score
CI	confidence interval
CPAP	continuous positive airway pressure
FSO	Swiss Federal Statistical Office
GA	gestational age
IVH	intraventricular haemorrhage
LOS	late onset sepsis
NEC	necrotising enterocolitis
OR	odds ratio
ROP	retinopathy of prematurity

Data collection and evaluation for this study was approved by the Swiss Association of Research Ethics Committees (BASEC PB_2016-02299 and 2021-00950). Participating centres were obliged to inform parents about the scientific use of anonymised data.

At SwissNeoNet, gestational age (GA) was collected as the best estimate available based on prenatal ultrasound examination during the first trimester of pregnancy. Birth weight z-scores (BWZ), intraventricular haemorrhage grades 3–4 (IVH), necrotising enterocolitis of Bell's stage ≥2 (NEC), late onset neonatal sepsis (LOS) and retinopathy of prematurity stages 3–4 (ROP) were defined as previously published [12, 13]. Respiratory distress syndrome was recorded when the child had either meconium aspiration syndrome, infectious pneumopathy, hyaline membrane disease, wet lung syndrome, spontaneous pneumothorax, or transient respiratory disease lasting longer than 2 hours. One day of mechanical ventilation, nasal continuous positive airway pressure (CPAP) or supplemental O_2 was defined as requiring ≥12 hours oxygen above room air concentration. Major morbidity was a composite outcome of either IVH, NEC, LOS, O_2 requirement ≥28 days, or ROP. Infants born during the lockdown period were identified either by their date of birth or, where missing, a Boolean marker (born during lockdown yes or no). The result of any SARS-CoV-2 polymerase chain reaction (PCR), serum or antigen test during the pregnancy of the mother or the hospitalisation period of the child was recorded. If any of them were positive, the patient was recorded as having SARS-CoV-2 in this study.

The SwissNeoNet patient population coverage was assessed by comparison with the FSO data and yielded 100% of all live births between 22 and 31 weeks of gestation. Nevertheless, from experience we assume that there may be differences in the pool of data as SwissNeoNet does not collect infants born in peripheral hospitals without neonatology units that are predominantly below 24 weeks gestation and receive a priori comfort care, and the publicly available FSO data does not include births of mothers without Swiss residency whereas SwissNeoNet does. Completeness and plausibility of SwissNeoNet records were checked upon electronic data entry. Missing data were requested until completed. Each SwissNeoNet member centre is subject to data audits every 3 years whereby SwissNeoNet verifies a random sample of 10% of the submitted datasets with the original patient file. Accuracy is high (>95% of items). Data on ROP was missing in 1.5%

of surviving infants, all other data were complete. The FSO data contain no information on mortality or morbidity.

For this study, we calculated the odds for extremely, very and late preterm birth in 2020 compared with 2015–2019 based on the FSO records. We next used the SwissNeoNet data to compare the number of infants per gestational week between the Swiss lockdown period in 2020 with the mean numbers of the matching gestational weeks and periods of 2015–2019. The Swiss lockdown period lasted for 55 days from 17 March to 10 May 2020. We repeated this analysis by comparing the number of infants per gestational week of the entire year 2020 with those of 2015–2019. We included also those infants who were born prior to the onset of the COVID-19 pandemic as we did not have the dates of births of all infants in our collective and could not exclude infants born before 17 March. Also, we wanted to keep the SwissNeoNet analysis compatible with the FSO analysis which also had to contain all infants in 2020.We next compared the median and interquartile range for metric variables and proportions for categorical variables for the same two periods. As control, we repeated the analysis for the entire year by comparing 2019 with the years 2015 to 2018. Next, we added a numerical comparison between infants born to mothers with a positive test for SARS-CoV-2 (either PCR, serum or antigen) and infants of mothers tested negatively for SARS-CoV-2. For this latter analysis, we excluded all infants born to mothers not tested for SARS-CoV-2. There was no universal testing regimen observed over all Swiss perinatal centres and we collected all test results regardless of whether they were performed before, during or after pregnancy.

Statistical analyses

For crude comparisons we used chi-square tests with Yates' correction for categorical and the Mann-Whitney U-test for metric variables. As we tested 17 hypotheses using the same SwissNeoNet collectives, we set the level for rejecting the null hypothesis to <0.003. Odds ratios using FSO data (table 1) were calculated by contingency table.

For adjusted odds ratios based on SwissNeoNet data, we performed multivariable adjusted logistic regression to compare outcome between periods (table 2), or between infants of mothers with or without SARS-CoV-2 infection (table 3). Adjustment was made for GA, BWZ, and male sex, i.e. those risk factors that usually have the strongest impact on outcome and that we assumed were not affected by the COVID-19 pandemic [14]. All statistical analyses were performed using R Version 4.1.1 [15].

Results

The FSO reported 297 live births from 22–27 weeks gestation, 479 from 28–31 weeks gestation, 4657 from 32–36 weeks gestation, and 85,593 for the entire year 2020 (table 1).

In comparison with the reference years 2015–2019, odds for being born extremely preterm were 1.01 (95% CI 0.89–1.14), 0.9 (95% CI 0.82–1.00) for very preterm, and 0.91 (95% CI 0.88–0.93) for late preterm. Comparison of 2019 with the years 2015–2018, however, also revealed lower odds for being born either very (OR 0.86, 95% CI 0.78–0.95) or late (OR 0.96, 95% CI 0.93–0.99) preterm.

During the Swiss COVID-19 lockdown period from 17 March to 10 May in 2020, 137 infants were born from 22+0 to 31+6 weeks gestation in the nine Swiss perinatal centres. During the same interval of dates within the years 2015–2019, 668 infants were born resulting in a mean 134 infants pear year, 2% less than in 2020. Over the entire year, 744 infants were born in 2020, compared with 4223 over the 5-year period from 2015 to 2019, yielding a mean of 845 infants per year, 12% more than in 2020. Figure 1 displays the distribution of number of infants per gestational week for the lockdown period (panel A) and the entire year (panel B), again for 2020 and as mean number of infants for the reference years 2015–2019.

During the lockdown period there were clearly fewer births at 22, 23, 27 and 28 weeks gestation and more births at 25, 28 and 31 weeks gestation, resulting in a slightly higher median gestational age for 2020 versus the reference years (Table 2A). Over the entire year, there were fewer births in most gestational age strata in 2020 than in the reference years, particularly from 27 to 30 weeks gestation but not at 24 or 31 weeks gestation, where there were more births in 2020. The median gestational age between 2020 and reference years only differs in the interquartile range but not the median of either (table 2B).

As control, we compared the number of births per gestational week in 2019 with those from 2015 to 2018 (fig. 1C). A total of 740 births in 2019 compared to 3483 during 2015–2018, a mean of 870 infants per year, 15% more than in 2019 (table 2C). The data from the FSO yields a mean 857 live-born infants from 2015 to 2018 versus 757 (–12%) for 2019 and 776 (–9%) for 2020, mirroring our observation.

Table 2 lists the baseline characteristics and the crude outcomes compared between the lockdown period of 2020 versus the same date range of the reference years (A), as well as the entire year 2020 versus the entire reference

Table 1:
Number of births per gestational age range, odds ratios for preterm birth based on FSO data.

Collective	Cases	Controls	Total cases	Total controls	OR	Lower CI	Upper CI
	2020	**2015–2019**	**2020**	**2015–2019**			
22–27 weeks GA (extremely preterm)	297	1491	85,593	434,015	1.01	0.89	1.14
28–31 weeks GA (very preterm)	479	2690	85,593	434,015	0.90	0.82	1.00
32–36 weeks GA (late preterm)	4657	26099	85,593	434,015	0.91	0.88	0.93
	2019	**2015–2018**	**2019**	**2015– 2018**			
22–27 weeks GA (extremely preterm)	288	1203	85,811	348,204	0.97	0.85	1.11
28–31 weeks GA (very preterm)	469	2221	85,811	348,204	0.86	0.78	0.95
32–36 weeks GA (late preterm)	4990	21109	85,811	348,204	0.96	0.93	0.99

CI: confidence interval, GA: gestational age; OR: odds ratio based on contingency tables (without adjustment)

years (B). None of the null hypotheses tested could be rejected as a result of the Bonferroni correction of the significance level. Those hypotheses closest to the significance level for the entire year comparison had an adjusted odds ratio with a 95% confidence interval (CI) outside the reference value 1: outborn (p = 0.01; OR 0.53, 95% CI 0.35–0.81), multiple births (p = 0.01; OR 0.79, 95% CI 0.67–0.94), respiratory distress syndrome (p = 0.04; OR 1.6, 95% CI 1.08–2.37), and any CPAP (p = 0.02; OR 1.39, 95% CI 1.05–1.84). The control analysis comparing

Figure 1: Number of births per gestational age between 22 and 31 weeks gestation in Switzerland.

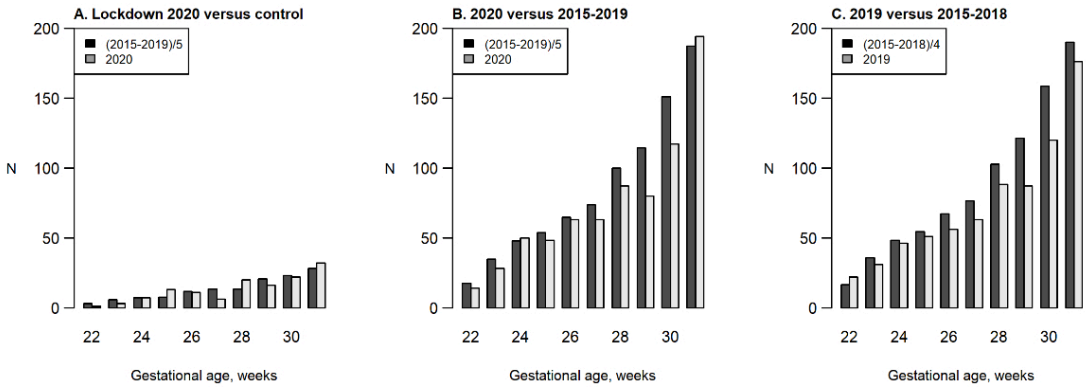

Table 2:
Incidence, treatment and outcome of infants born between 22 and 31 weeks gestation based on SwissNeoNet data.

	A) Lockdown period					B) Entire year					C) Control analysis				
	2015–2019	2020	p-value	aOR	95% CI	2015–2019	2020	p-value	aOR	95% CI	2015–2018	2019	p-value	aOR	95% CI
N	668	137				4223	744				3483	740			
Gestational age (IQR)	29.1 (26.9-30.7)	29.3 (26.6-30.9)	0.63			29.1 (26.9-30.7)	29.1 (26.6-31)	0.63			29.1 (26.9-30.7)	29.1 (26.5-30.9)	0.58		
Birth weight z-score (Voigt 2006) (IQR)	-0.1 (-0.6-0.4)	0 (-0.6-0.4)	0.46			-0.1 (-0.7-0.4)	-0.1 (-0.7-0.4)	0.52			-0.1 (-0.7-0.4)	-0.1 (-0.7-0.4)	0.18		
Sex male, n (%)	363 (54.8%)	69 (52.7%)	0.72			2239 (53%)	401 (53.9%)	0.69			1837 (52.7%)	402 (54.3%)	0.46		
Outborn, n (%)	32 (4.8%)	3 (2.3%)	0.29	0.43	0.13-1.44	257 (6.1%)	26 (3.5%)	0.01	0.53	0.35-0.81	234 (6.7%)	23 (3.1%)	0.00	0.45	0.29-0.69
Multiple births, n(%)	241 (36.4%)	43 (32.8%)	0.50	0.85	0.57-1.27	1499 (35.5%)	226 (30.4%)	0.01	0.79	0.67-0.94	1260 (36.2%)	239 (32.3%)	0.05	0.84	0.71-1
Any antenatal steroids, n (%)	582 (88.9%)	115 (87.8%)	0.84	0.85	0.47-1.54	3698 (88.3%)	650 (87.5%)	0.56	0.93	0.73-1.2	3042 (88.3%)	656 (88.6%)	0.81	1.12	0.86-1.45
Child died in delivery room, n (%)	44 (6.6%)	6 (4.6%)	0.49	1.02	0.31-3.36	266 (6.3%)	42 (5.6%)	0.55	1.21	0.79-1.85	216 (6.2%)	50 (6.8%)	0.63	1.18	0.78-1.79
Child died at any time, n (%)	71 (10.7%)	9 (6.9%)	0.24	0.63	0.27-1.47	545 (12.9%)	82 (11%)	0.17	0.74	0.55-1	444 (12.7%)	101 (13.6%)	0.55	0.9	0.67-1.21
Major morbidity*, n (%)	105 (19.4%)	28 (27.5%)	0.09	1.51	0.88-2.59	664 (20.1%)	123 (21.7%)	0.41	1	0.78-1.27	541 (19.8%)	123 (21.8%)	0.28	1	0.78-1.29
Respiratory distress syndrome, n (%)	574 (92.9%)	121 (96.8%)	0.15	2.35	0.82-6.72	3704 (93.6%)	672 (95.7%)	0.04	1.6	1.08-2.37	3061 (93.7%)	643 (93.2%)	0.68	0.92	0.66-1.29
Any ventilation, n(%)	324 (52.4%)	64 (52%)	>0.99	1.01	0.64-1.6	2045 (51.7%)	356 (50.9%)	0.73	0.96	0.79-1.16	1693 (51.9%)	352 (51%)	0.71	0.92	0.76-1.12
Any CPAP, n (%)	563 (91.1%)	117 (94.4%)	0.31	1.68	0.74-3.8	3483 (88.1%)	638 (91.1%)	0.02	1.39	1.05-1.84	2880 (88.2%)	603 (87.4%)	0.58	0.92	0.72-1.18
Supplemental O_2 at 36 weeks GA*, n (%)	67 (11.4%)	22 (18.2%)	0.06	1.92	1.03-3.57	446 (12.2%)	91 (13.8%)	0.28	1.1	0.83-1.45	369 (12.2%)	77 (12.1%)	0.99	0.82	0.61-1.11
Late onset sepsis, n(%)	57 (9.2%)	13 (10.4%)	0.81	1.16	0.59-2.3	343 (8.7%)	75 (10.7%)	0.10	1.24	0.93-1.65	280 (8.6%)	63 (9.1%)	0.69	0.97	0.72-1.32
Severe IVH, n(%)	32 (5.2%)	10 (8.1%)	0.30	1.61	0.75-3.45	238 (6%)	46 (6.6%)	0.65	1.06	0.75-1.48	193 (5.9%)	45 (6.6%)	0.58	1.07	0.75-1.51
NEC stage ≥2, n (%)	26 (4.2%)	2 (1.6%)	0.26	0.36	0.08-1.56	150 (3.8%)	24 (3.4%)	0.71	0.86	0.55-1.34	127 (3.9%)	23 (3.3%)	0.56	0.78	0.49-1.23
Severe ROP*, n(%)	13 (2.4%)	6 (5.9%)	0.11	2.55	0.88-7.39	103 (3.1%)	18 (3.2%)	>0.99	0.78	0.44-1.36	78 (2.9%)	25 (4.5%)	0.06	1.21	0.72-2.02

aOR: adjusted odds ratio based on logistic regression; CI: confidence interval; CPAP: continuous positive airway pressure; IQR: interquartile range; GA: gestational age; IVH: intraventricular haemorrhage; n: number of infants; NEC: necrotising enterocolitis; ROP: retinopathy of prematurity.

No aORs were calculated for gestational age, birth-weight z-score or male sex as they form part of the logistic regression model for case-mix adjustment.

* Survivors only

2019 to 2015–2018 revealed similar results, except that only the odds for being outborn were below 1 (p <0.001; OR 0.45, 95% CI 0.29–0.69), whereas multiple birth was at the threshold and having respiratory distress syndrome or receiving any CPAP were comparable to the previous years.

Mothers of 295 very preterm infants (38% of infants born in 2020) were tested for SARS-CoV-2, of whom mothers of 22 infants tested positive. Of the 744 infants born, 85 were tested of whom only one child tested positive for SARS-CoV-2. Table 3 displays the 22 infants of the mothers tested positive versus the 273 infants of mothers tested negative for SARS-CoV-2. None of the parameters revealed any difference between the two groups, including those that were different between infants of the entire year 2020 and the reference years 2015 to 2019 (as described above).

Discussion

We present a population-based, geographically defined cohort study using data from the Swiss Federal Statistical Office (FSO) and from SwissNeoNet. A Comparison between 2020 and 2015–2019 with the FSO data revealed somewhat lower odds ratios for very preterm and late preterm births in 2020. A comparison between 2019 with 2015–2018, however, revealed matching lower odds ratios for very preterm and late preterm births in 2019. The reduced incidence in 2020 is therefore unlikely to be associated to the COVID-19 pandemic. According to a report by the FSO, stillbirth rates per 1000 births had sunk steadily from 4.14 to 3.72 between 2015 and 2020 and thus also did not show any association with the pandemic [16]. Using SwissNeoNet data, we observed no noteworthy difference in the number of infants born per gestational age either during lockdown or during the entire year, except for some minor differences when the entire years in the gestational age range from 27+0 to 30+6 weeks were compared: there were fewer births during 2020 than during the reference years. Again, congruent differences occurred in the same gestational age strata in 2019 when compared with 2015 to 2018 (see fig. 1).

A recent rapid review on the impact of lockdown measures on perinatal outcomes found 17 publications including data from Denmark, UK, Ireland, Nepal, Italy, Israel, Botswana, Australia, China, Netherlands, Saudi Arabia, Austria, Zimbabwe, India and Spain [17]. The larger studies showed conflicting results, reporting both increases and decreases in selected perinatal outcomes. In the meta-analysis of this publication, they found that lockdown measures were associated with a significant relative risk of stillbirth of 1.33 (95% CI 1.04–1.69) during lockdown when compared with a prior period . However, they however found no association of lockdown measures with a significant risk of preterm birth compared with pre-pandemic periods. This finding is surprising, considering the reports from various geographically defined cohorts that showed a reduction during the lockdown period; For example, Ireland reported a 73% reduction for very low birth-weight infants, Denmark an approximate 90% reduction for extremely preterm singleton infants, Japan a 33% reduction for very preterm infants, Lazio (Italy) a 33% reduction for late preterm infants [1, 2, 5, 6]. Nevertheless, we can confirm neither a reduction in still births nor preterm birth that can be associated with COVID-19 in Switzerland.

For clinical practices and outcomes, the comparison between the lockdown periods of 2020 versus 2015–2019 in Switzerland revealed no difference. The entire 2020 compared with 2015–2019, however, revealed close to significant crude differences in proportions and significant lower adjusted odds ratios for outborn infants and multiple births, and higher adjusted odds ratios for respiratory distress syndrome and CPAP provision in 2020. Again, the compari-

Table 3:
Incidence, treatment and outcome of infants born with versus without confirmed maternal SARS-CoV-2 infection.

	Mother negative	Mother positive	p-value	aOR	95% CI
N	273 (92.5%)	22 (7.5%)			
Gestational age (IQR)	29 (26.6–30.7)	29.6 (26.4–31.1)	0.58		
Birth weight z-score (Voigt 2006) (IQR)	-0.2 (-0.7–0.4)	0 (-0.9–0.3)	0.86		
Sex male, n (%)	155 (56.8%)	12 (54.5%)	1.00		
Outborn, n (%)	4 (1.5%)	2 (9.1%)	0.10	7.04	1.19-41.55
Multiple births, n (%)	92 (33.7%)	4 (18.2%)	0.21	0.41	0.13-1.25
Any antenatal steroids, n (%)	249 (91.2%)	21 (95.5%)	0.77	1.96	0.25-15.62
Child died in delivery room, n (%)	7 (2.6%)	0 (0%)	0.97	NA	
Child died at any time, n (%)	21 (7.7%)	1 (4.5%)	0.91	0.62	0.07-5.34
Major morbidity*, n (%)	58 (26.4%)	5 (23.8%)	1.00	0.5	0.12-2.08
Respiratory distress syndrome, n (%)	256 (96.2%)	20 (90.9%)	0.52	0.42	0.08-2.15
Any ventilation, n (%)	129 (48.7%)	14 (63.6%)	0.26	2.44	0.84-7.08
Any CPAP, n (%)	250 (94.3%)	20 (90.9%)	0.85	0.61	0.13-2.9
Supplemental oxygen at 36 weeks GA*, N (%)	51 (20.3%)	4 (19%)	1.00	0.36	0.08-1.72
Late onset sepsis, n (%)	39 (14.7%)	6 (27.3%)	0.21	2.54	0.81-7.97
Severe IVH, n (%)	10 (3.8%)	2 (9.1%)	0.52	2.86	0.5-16.27
NEC stage ≥2, n (%)	10 (3.8%)	1 (4.5%)	>0.99	1.31	0.15-11.15
Severe ROP*, N (%)	9 (4.1%)	0 (0%)	0.73	NA	

aOR: adjusted odds ratio based on logistic regression; CI: confidence interval; CPAP: continuous positive airway pressure; iqr: interquartile range; GA: gestational age; IVH: intraventricular haemorrhage; N: number of infants; NEC: necrotizing enterocolitis; ROP: retinopathy of prematurity.

No aORs were calculated for gestational age, birth-weight z-score or male sex as they form part of the logistic regression model for case-mix adjustment.

* Survivors only

son between 2019 and 2015–2018 revealed matching odds for outborn infants and multiple births, and the steady decrease in multiple births was also reported by the Swiss FSO, confirming that this trend is without association to COVID-19 [18]. This decrease in multiple births in 2020 and 2019 versus 2015–2018 may even be one of the reasons for the reduced odds for very and late preterm birth in 2019 versus 2015–2018 mentioned above and for the congruent reduction in number of infants per gestational age weeks 27–30 in figure 1B and C. Since the revision of the Swiss law on assisted reproductive technology in September 2017, an increase in single embryo transfers rather than multiple embryo transfers may have reduced the incidence of multiple births and thereby simultaneously of preterm births as of 2019, as multiple births are at higher risk for being born preterm [19, 20]. As the lower adjusted odds ratios for outborn infants in the entire year analysis (B) is repeated in the control analysis (C), we assume that this effect is independent of the COVID-19 pandemic. Instead, it could be the effect of closer collaboration between Swiss centres using a web-accessible bed availability app in which centres reveal their free beds daily so that centres without capacity can transfer mothers [21]. The higher odds for respiratory distress syndrome and CPAP provision, however, occurred exclusively in 2020 when compared with 2015–2019. In a nationwide, prospective cohort study of all live-births between 11 March 2020 and 31 January 2021 in Sweden recently reported that maternal SARS-CoV-2 test positivity was significantly associated with respiratory distress syndrome (OR 2.4, 95% CI 1.50–3.84) but not with mortality [22]. Their analysis, however, included all 88,159 live births from 22 to 43 weeks gestational age of which 2323 (1.6%) were delivered by mothers who tested positive for SARS-CoV-2. In Switzerland, we only have records of 22 infants born from 22 to 31 weeks gestation to mothers who were tested positive for SARS-CoV-2, of whom only one infant also tested positive. None of the statistical tests for treatment or outcome comparisons between infants of mothers tested positive versus those tested negative for SARS-CoV-2 led to any significant result. However, it is possible that the low number of recorded maternal SARS-CoV-2 infections is insufficient for statistical testing. The somewhat higher odds for respiratory distress syndrome and the possibly associated higher need for CPAP seen when the whole of 2020 was compared with the reference years may be associated with the COVID-19 pandemic. As in Sweden, Swiss data show no association in any sub-cohort of the pandemic with mortality or any other major neonatal morbidity measured. The higher provision of CPAP may also be a representation of the general trend towards less invasive forms of respiratory treatment as previously observed in Switzerland [23].

A strength of our study was that we evaluated prospectively collected population-based data appraised for accuracy and derived from two independent sources. We added a control analysis in order to avoid premature conclusions. Limitations concern the FSO data, which are available for full years only and cannot be split up into birth date related periods, such as the lockdown period, to confirm this part of our analysis with the SwissNeoNet data. Based on the clear results largely confirmed by the analysis of the entire year, it is, however, unlikely that we have missed a possible association of birth incidence with the COVID-19 pandemic, even with the small sample size originating from the 55-day lockdown period. As some SwissNeoNet records have no date of birth we were also not able to exclude those births in 2020 that occurred prior to the pandemic, before 17 March. However, we do not believe that it would have revealed any other possible associations than the one found for respiratory distress syndrome as there were no tendencies observable other than those that were also apparent in the control analysis comparing 2019 and 2015–2018. Lastly, we have no means of knowing whether the confirmed maternal or infant SARS-CoV-2 infections were the only ones that occurred as several mothers and infants were not tested during the pandemic. It is therefore likely that mothers or infants positive for SARS-CoV-2 were missed.

In conclusion, neither our data from SwissNeoNet nor the data from the Swiss FSO showed any association between incidence, treatment or outcome with the COVID-19 pandemic other than a possible link towards higher odds for respiratory distress syndrome together with a possibly higher provision of CPAP. Continuous further observation of possible effects of the pandemic on the health and healthcare provision of newborns may be warranted based on the literature available so far and on the fact that our data only cover the first 9 months of the current pandemic.

Data sharing statement

The data that support the findings of this study are available from the corresponding author upon reasonable request. The data are not publicly available owing to ethical restrictions.

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Coi-Statement

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