Preterm birth during the COVID-19 pandemic: more, less or just the same?

Abstract

Objectives - Coronavirus disease (COVID-19) and its mitigations measures have been associated with changes in preterm birth (PTB) incidences. The objective is to summarize and comment on the literature on COVID-19 and PTB, and to compare PTB incidence between 2019 (pre-COVID-19) and 2020 (COVID-19) in three Belgian tertiary care hospitals.

Methods - A non-systematic review on COVID-19 and PTB was performed, literature was summarized in a table. Preterm birth rates in Ghent University Hospital, Ziekenhuis Oost-Limburg and University Hospital Leuven in 2019 and 2020 were compared. Chi-square and Fisher's exact tests were used to compare PTB rates between 2019 and 2020, and Kaplan Meier survival analysis was used to compare pregnancy duration. The mean outcome measure was PTB incidence in 2020 (COVID-19) compared with PTB incidence in 2019 (pre-COVID-19).

Results - Some (parts of) countries report decreases in PTB rates, others report no differences in incidence, and a minority of countries report an increased incidence of PTB. Almost all studies only consider live-births. In three tertiary care hospitals in Flanders, there were no differences in PTB rates before and during the COVID-19 pandemic.

Conclusion - The impact of the (mitigation measures during the) COVID-19 pandemic on PTB incidence is unclear and difficult to explore. To enable a correct interpretation, all conceptions before and during the pandemic should be taken into consideration, as well as all births, still or alive.

Keywords: COVID-19, SARS-CoV-2, preterm birth, prematurity, infectious disease

Introduction

In December 2019, a cluster of patients with pneumonia of unknown origin was identified in Wuhan, China. On January 7th, 2020, a new coronavirus, Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), was identified as the etiologic micro-organism and on March 11th, 2020 the World Health Organization declared a global pandemic [1]. Gradually it became clear that pregnant women are at risk of serious illness with a higher risk of admission to the intensive care unit, ventilation, extra-corporal membrane oxygenation, cesarean section, and maternal death [2,3]. Coronavirus disease-19 (COVID-19) during pregnancy is also associated with an up to 60% higher risk of preterm birth (PTB)[3]. However, the incidence of PTB during the pandemic seems to be lower in (regions of) some nations [4-20]. Other studies show no difference [21-30], and two studies reported a rise in PTB rates [31,32]. The mitigation measures, increased awareness of personal and environmental hygiene, reduction in air pollution and reduction in work related stress, are possible explanations for a reduction in PTB. On the other hand, psychosocial stress, less institutional deliveries and overcrowding in the hospitals, could instigate a higher risk [33].

The aims of this study were (1) to compare the results and methodologic approach of the articles that reported on PTB rates during the COVID-19 pandemic and (2) to provide additional data on PTB incidence before and during the COVID-19 pandemic in Flanders, Belgium.

Methodology

A first literature search was conducted on the PubMed database (by ID) on April 29th 2021 using the search terms “preterm birth” and “COVID-19”. This search was update (by KN) on December 19th 2021. Articles were screened on title and abstract. From the included articles,

data on the study populations, aim of the article, applied methodology, and results on PTB incidence were extracted and summarised in a table.

Preterm birth rates in Flanders (Belgium) of the year 2019 (before) and the year 2020 (during) were compared. Multiple databases were consulted: the preterm birth databases of the maternal intensive care units at Ghent University Hospital, Ghent, and Ziekenhuis Oost-Limburg (ZOL), Genk, and the hospital databases of the University Hospital of Leuven, ZOL, and Ghent University Hospital. The preterm birth databases collect data on admissions for threatened PTB at 24 to 34 weeks' gestational age, irrespective of the etiology. The hospital database of Ghent provided data on all pregnancies with a known end date of the pregnancy (including miscarriages, immature births, intra-uterine demises and terminations of pregnancy). The hospital database of Leuven provided data on all pregnancies which ended at a gestational age of 22 weeks or more (including immature births, intra-uterine demises and terminations of pregnancy). The hospital database of ZOL provided data on all liveborn children with a gestational age of 22 weeks or more, stillborn children with a birthweight of 500 grams or more, and stillborn children at a gestational age from 25^{+5} weeks onwards. Data from the three hospitals concerning pregnancies that ended at a gestational age of 22 weeks or more were also combined for analysis. A sensitivity analysis on the data of Ghent University Hospital was done, excluding terminations of pregnancy, stillbirths and the some cases in which neonatal intensive care was withheld at birth.

Women in the preterm birth databases gave informed consent for inclusion (ethical committee reference B670201732321). The data from the hospital databases were extracted anonymously. This study was approved by the Medical Ethics Committees of Ghent University Hospital (reference number BC-10150), Leuven University Hospital (S66280) and ZOL (Z-2021042).

The following data from the years 2019 (pre-COVID-19) and 2020 (COVID-19) were extracted: from the preterm birth databases, number of admissions, back-transfers to referral centers, and (preterm) births, as well as reason for admission; from the hospital birth databases, number of miscarriages (< 14 weeks)(Ghent), immature births (14 - 21^{+6} weeks)(Ghent), preterm births (22 - 36^{+6} weeks)(Ghent, Leuven, Genk), and term births (≥ 37 weeks)(Ghent, Leuven, Genk). The distribution of the number of miscarriages, immature, preterm and term births in 2019 and 2020 was checked and compared using the Chi-square or Fisher's exact test. Kaplan Meier survival analysis was used to compare pregnancy duration before and during the COVID-19 pandemic. Data analysis was done in R version 4.0.5 using the packages Tidyverse and Survminer. The R.project and datasets are available in the Supplementary files.

Results

Summary of the literature on PTB incidence during the COVID-19 pandemic

On December 19th, 2021, 337 articles were found, of which 28 articles, which reported on changes in incidence of PTB, were withheld (Table 1). The overall incidence of PTB seemed to be lower during the COVID-19 pandemic in (regions of) some nations: Australia (Melbourne; Brisbane), Ireland (Limerick, Clare, North Tipperary (less very and extremely low birth weights); Dublin), the Netherlands, centers in certain states of the United States (Pennsylvania; Philadelphia; and Tennessee), France, Argentina (Cordoba), and Iceland [4-14]. Others reported a lower incidence of PTB below certain gestational ages: Botswana (PTB < 32 weeks' gestational age), Denmark (PTB < 28 weeks), Israel (Tel Aviv, PTB < 34 and < 32 weeks), Saudi Arabia (PTB < 28 weeks and 32-36^{+6} weeks), Australia (Melbourne, PTB < 34 weeks), and the Netherlands (iatrogenic PTB < 32 and < 28 weeks)[15-20]. Yet other studies showed no difference in PTB rates below any gestational age cut-off: Spain (Castilla-y-Léon), Sweden, the United Kingdom (London), centers in certain states of the United States (Massachusetts,

Philadelphia), countries from a multinational study (Denmark, Austria, Ireland, Spain, India, Turkey, United States, Czech Republic, Germany, Switzerland, Poland, Greece, Norway, China, Belgium, Italy, and Greece), Austria (Vienna), Canada (Ontario), and Jordan [21-30]. Finally, two studies, conducted in Nepal and Uruguay (Montevideo), reported a rise in PTB during lockdown [31,32].

The population included in the studies varies significantly between the studies: different sources of data (hospital registry, nationwide registry-based,...), different background PTB incidences, different gestational ages, different compared timeframes of inclusion. In most studies only liveborn singletons were included. The statistical methodologies also differed. Most studies wanted to investigate the impact of lockdown on PTB. However, only two studies applied causal inference methods [7, 29]. Most studies compared PTB rates with Chi-square tests, t-tests or logistic regression, with or without adjustment for variables believed to be confounders. One study used survival analysis [19]. The outcomes are mainly comparisons of PTB rates during and before the SARS-CoV-2 pandemic and/or lockdown measures. In line with the methodologies, the results are mostly descriptive comparisons of PTB rates or associations between the pandemic and/or lockdown and PTB rates (Table 1).

[Table 1 near here]

Data from the preterm birth databases (admissions for threatening PTB)

In Ghent University Hospital, Ghent, 178 women were admitted for threatening PTB in 2019 and 179 in 2020. Of these admissions, in 2019, 37 women (20.9%) were transferred back to the referral center, and yet have an unknown date of delivery, 119 women (66.9%) delivered preterm, and 22 women delivered term (12.4%). In 2020, 40 women (22.3%) delivered in the referral center, 119 delivered preterm (66.5%), and 20 delivered term (11.2%). When born

preterm in Ghent University Hospital, the mean gestational age at birth was 31.3 (±4.0) weeks in 2019 and 31.1 (±4.0) weeks in 2020.

In Ziekenhuis Oost-Limburg (ZOL), Genk, 90 women were admitted for threatening PTB in 2019 and 64 in 2020. Of these admissions, in 2019, 20 women (22.2%) were transferred back to the referral center, and yet have an unknown date of delivery, 52 women (57.8%) delivered preterm, and 18 women delivered term (20.0%). In 2020, 10 women (15.6%) delivered in the referral center, 41 delivered preterm (64.0%), and 13 delivered term (20.3%). When born preterm in ZOL, the mean gestational age at birth was 31.6 (±3.0) weeks in 2019 and 31.5 (±2.3) weeks in 2020.

The reason for admission was categorised in 'spontaneous preterm labour' (SPL), 'preterm prelabour rupture of membranes' (PPROM), 'placental pathology' (being preeclampsia, hemolysis elevated liver enzymes and low platelets and/or fetal growth retardation), 'placenta praevia', a combination of the aforementioned (miscellaneous), or another reason, such as intrahepatic cholestasis or infectious pathology. The results are summarised in Table 2. In general, there is a different distribution between the centers. There are more admissions for SPL and PPROM (66.3% in 2019, 62.0% in 2020) and less admissions for placental pathology (19.1% in 2019, 22.9% in 2020) in Ghent University Hospital compared to ZOL (SPL/PPROM: 24.5% in 2019, 34.4% in 2020; placental: 28.9% in 2019, 21.9% in 2020). In both centers, there were no differences in reason for admission between 2019 and 2020.

[Table 2 near here]

For both centers, Kaplan Meier curves, depicting time from admission to birth in 2019 and 2020, show no differences in time to birth (Figure 1, A&B). The median duration of admission to birth in Ghent University Hospital was 11 days (95% confidence interval (CI) [7, 20 days]) in 2019 and 7 days (95%CI[5, 12]) in 2020. The median duration of admission to birth in ZOL was 20.5 days (95%CI[13, 28]) in 2019 and 15.5 days (95%CI[7, 34]) in 2020. Also, no differences were found between 2019 and 2020 in time from admission to birth for women who delivered in Ghent University Hospital and ZOL after being admitted for threatened PTB due to SPL, PPROM or placental insufficiency (Figure1, C&D).

Data from the hospital databases (pregnancy duration)(Figure 2)(Table 3)

The proportions of pregnancy endings and statistical comparisons between the pre-COVID (2019) and COVID-era (2020) are summarized in table 3.

In the three hospitals combined, in 2019, there were 5307 gestations of which the date of pregnancy ending was known and in 2020 there were 5282 pregnancies. Gestational age was categorised in preterm births (22 - 36^{+6} weeks) and term births (37 - 41^{+6} weeks). There were 901 preterm births (17.0%) in 2019 and 821 (15.5%) in 2020 (chi-square: 3.29, p-value: .07). Finally, 4406 women delivered at term (83.0%) in 2019 and 4461 (84.5%) in 2020 (chi-square: 4.00, p-value: .05).

No correlation was found between the year of birth and being born preterm (22 - 36^{+6} weeks) or term (≥ 37 weeks)(Ghent [chi-square: 1.51, p-value = .22], Leuven [chi-square: 1.92, p-value = .17], Genk [chi-square: 0.22, p-value = .64], all [chi-square: 4.00, p-value = .05]), the severity of PTB (extreme, very or moderate/late)(Ghent [chi-square: 1.65, p-value = .44], Leuven [chi-square: 3.29, p-value = .35], ZOL [chi-square: 1.06, p-value = .79], all [chi-square: 3.42, p-value = .18]), or the gestational age at the end of pregnancy (miscarriage, immature birth, PTB and term birth)(Ghent [chi-square: 2.48, p-value: .48]).

[Table 3 near here]

A sensitivity analysis on Ghent University data was done excluding terminations of pregnancy, stillbirths and the some cases in which neonatal intensive care was withheld at birth. Of all 2405 cases with a known end date of pregnancy in Ghent University Hospital, 1922 delivered from 24 weeks' gestation onward. Cases with Apgar score zero at five minutes after birth were excluded (60 cases, 3.1%; 33 in 2019 and 27 in 2020). There were 1862 cases in the sensitivity analysis, 974 births in 2019 and 888 births in 2020. Of these, 250 cases (25.7%) delivered preterm in 2019 and 212 (23.9%) in 2020. 724 cases (74.3%) delivered term in 2019 and 676 (76.1%) in 2020. No differences in gestational age distribution at birth were found between 2019 and 2020.

Discussion

We found no difference in PTB incidence before (2019) and during (2020) the SARS-CoV-2 pandemic in three Flemish tertiary care hospitals. Previous reports comparing PTB rates before and during the SARS-CoV-2 pandemic or before, during and/or after COVID-19 lockdowns show conflicting results. Several studies, conducted in several countries, reported reduced PTB rates during pandemic, compared to prepandemic, periods. Other studies, including the current one, reported no significant increase or decrease in PTB rates. Two countries, Nepal and Uruguay, reported higher PTB rates during the lockdown. Power analysis is lacking in all but two studies [19, 24]. A living systematic review and meta-analysis found that the COVID-19 pandemic is associated with reduced, be it very small, unadjusted odds for PTB (uaOR 0.94, 95%CI[0.91, 0.98])[34]. This finding was mainly driven by single-center studies and there was no difference in adjusted odds for PTB or within PTB subcategories. In our centers, we did not

see any differences in PTB rates between 2019 and 2020. A post-hoc power calculation shows that, for a type I error rate of 0.05%, the power of our study is 55.3%. This means that the risk of wrongfully accepting the null hypothesis, which states that there is no difference in PTB rate before and during the SARS-CoV-2 pandemic in the three included hospitals, is 44.7%, which is high. The Flemish Study Centre for Perinatal Epidemiology (SPE), which collects data on all births from 22 weeks onwards in Flanders and Brussels (Belgium), reported a decrease of 6.0% of premature born singletons during COVID (weeks 12 to 52 of 2020) compared to the same period in 2019. During summer (weeks 27 to 40), there even was a decrease of 8.6%. There were no differences in PTB rate before (weeks 12 to 18) and immediately after lockdown (weeks 19 to 26) between 2019 and 2020 [35].

Several hypotheses have been postulated to explain the association between lower PTB rates and COVID-19 mitigation measures [9,11,14]: reduced physical activity, lower work load and better work-life balance, reduced work-related physical and emotional stress, decreased air pollution due to less traffic, improved sleep quality, better nutrition, financial support from the government, better hygiene, lower incidence of infections in general, etc. Indeed, maternal infections, mainly ascending infections from the lower genital tract, play a key role in the pathophysiology of most spontaneous PTB cases [36]. It is plausible that social distance, hygiene measures and face masks reduced the risk for certain maternal infections, especially respiratory tract infections (e.g. common cold, flu, …). However, it is unlikely that changes in lifestyle and increased (mainly hand)hygiene alter the complex vaginal microbiome in a way that reduces the risk for ascending genital infections and spontaneous PTB. On the other hand, national lockdown in response to the pandemic might also have negative effects on daily life such as increased fear and emotional stress, financial problems, more intimate partner violence,

increased unemployment, malnutrition, reduced accessibility of health care facilities and reluctance to find in-hospital care [34].

Due to important clinical, methodological and statistical heterogeneity among previously published studies, the results should be interpreted with caution. The methodology of the studies was very diverse and mostly only briefly described. Some studies wanted to explore the impact of the mitigation measures, and others wanted to compare PTB rates before and during the COVID-19 pandemic and/or before, during and after lockdown. To explore the former, only two studies applied causal inference techniques [7,15]. The study performed in the Netherlands concluded that the national introduction of mitigation measures was associated with a considerable reduction in PTBs [7]. The study in Botswana examined a composite outcome that included PTB and concluded that there was a modest reduction in risk of the composite outcome mainly driven by reductions in PTB and small for gestational age fetuses. Most studies used the Chi-square test or regression analysis to compare pre-pandemic and pandemic PTB rates.

The nominators used to calculate the PTB rates differed strongly between studies. The populations included in studies conducted in low-, middle- as well as high-income countries also were very heterogenous, with prepandemic PTB rates varying between 5.2 and 19.6%. Preterm birth can be spontaneous, following PPROM, preterm contractions or cervical insufficiency, or can be medically-induced. The results from previous publications describing a positive effect of lockdown on PTB risk are inconsistent in, or do not report about whether this effect is due to reduced spontaneous or medically-induced PTBs. In some studies, the lower PTB rates during lockdown periods were driven by reduced spontaneous PTB rates [2,6], while other studies only found significantly lower medically-induced PTB rates [3,7–9].

Moreover, the timing, duration and stringency of lockdown or mitigation measures vary between countries and regions or states within countries. Some studies compared an era during the COVID-19 pandemic with the same era in the preceding year; others compared with several preceding years.

A major methodological issue is that all studies were retrospective and only included births, mostly of liveborn children. The descriptions of PTB rates and associations made, need to be viewed in that perspective. From a causal inference point of view, there is a high risk of selection bias, particularly collider stratification bias. Other factors might have an influence on both a pregnancy resulting in a (live)birth, as well as on PTB. When looking only at (live)births, a spurious path is created between for example COVID-19 mitigation measures, (live)births and PTB. Depending on how strongly the other factors weigh, the direction of the impact may be more or less biased [37, 38]. On the other hand, it is possible that not only PTB rates are affected but also miscarriages and immature births. A decrease in PTB rates might coincide with a significant increase in miscarriages and/or immature births, which are a serious adverse outcome of pregnancy.

Our study is purely descriptive and also has methodological flaws. Extraction of the hospital database of Ghent University Hospital allowed to include pregnancies which ended over the whole range of gestational ages. However, early miscarriages for which no pregnancy file was started, were not included. Patients who changed hospitals during their pregnancy or, for the patients included in the preterm birth database, who were admitted at the maternal intensive care unit and later on transferred back to the referral hospital were also not included, since the end date of the pregnancy was missing. These shortcomings make the results prone to selection bias. The three centers in the study are tertiary centers with patients with a higher risk profile

and intra-uterine transfers up to a gestational age of 34 weeks. The rate of preterm births in the surrounding hospitals is unknown. The back-transferals to the referring hospitals might also have been a source of informative censoring which could bias the Kaplan Meier graphs. Competing events, such as termination of pregnancies and stillbirths, were not accounted for. They were included in the datasets of Ghent and Leuven, and according to weight and gestational age in some cases in the ZOL dataset. A sensitivity analysis on the data of Ghent, which excluded children who were not born alive, also showed no differences in PTB rates before and during the pandemic.

Conclusion

The COVID-19 pandemic brought about an explosion of scientific publications. Unfortunately, a large proportion of these publications damaged evidence-based medicine's integrity and is characterized by methodological flaws. Obstetrical COVID-19 literature is also a victim of these flaws and should be read bearing in mind these issues. When we purely describe the data of three high-risk maternities in Flanders, Belgium, we do not see any changes in PTB rates before and during the pandemic. Preterm birth is a multicausal condition. COVID-19, on the one hand, is a serious disease which can be an indication for preterm delivery in order to optimize the condition of the mother. Hygienic and quarantine measures, on the other hand, could play a role in lowering the risk of PTB. Whether these measures had an impact on PTB rates, should be explored using causal inference techniques, rather than reporting descriptive analyses. When exploring the impact of the SARS-CoV-2 pandemic on PTB incidence, evolutions in the occurrence of miscarriages, immature births and term births should also be considered, as well as the incidence of stillbirths and terminations of pregnancies.

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Disclosures

The authors report there are no competing interests to declare.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee (Medical Ethics Committee of Ghent University Hospital, (reference number BC-10150), Leuven University Hospital (S66280) and ZOL (Z-2021042)) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent

Informed consent was obtained from all individual patients in the preterm birth databases. Data from the hospital registers were retrieved anonymously, no informed consent was retrieved from the patients included.

Clinical trials registry

The preterm birth database is registered at clinicaltrials.gov under the number NCT03405116. There was no trial registration for this particular study.

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Tables

Table 1

Location	Aim	Lockdown	Statistical analysis	Population	Outcome	Results	Conclusion
REDUCTION IN PRETERM BIRTH							
Australia[4] 3 centers in Melbourne	Investigate the effect of the lockdown on PTB rates	July 8 - Sep 28, 2020	(1) Interrupted time-series analysis with an auto-regressive integrated moving average model (2) Comparison (not further specified) of rates of PTB	Inclusion: (1) Women who gave birth at Monash Health's three maternity hospitals between Jan 1, 2018 and Sep 30, 2020 (2) Same population July-Sep 2020 and same period 2019 Exclusion: (1, 2) pregnancy terminations, stillbirths	(1) PTB < 28w (2) PTB < 28w, < 34w, < 37w	(1) Lower rate of overall PTB after July 2020, p = .007 *(result not available for the stipulated primary outcome PTB < 28 weeks)* (2) PTB < 28w: OR 0.46, 95%CI [0.21, 0.99] PTB < 34w: OR 0.71, 95%CI [0.51, 0.98] PTB< 37w: OR 0.81, 95%CI [0.67, 0.98]	Lower PTB rates. Confirmation of an association between lockdown and reduced PTB rates.
Ireland[5] 1 center covering counties Limerick, Clare, North Tipperary and nearby catchment areas	Investigate whether redefined social and behavioral boundaries have fostered an environment favorable to influence the VLBW and ELBW birth rates	March 12 - May 18, 2020	(1) Significance of temporal trends in VLBW and ELBW rates per 1000 births assessed using Poisson regression with time as continuous variable, annually and from Jan to April 2001-2019 (2) Poisson regression and rate ratio analysis to compare the observed VLBW rate for Jan to April 2020 to historical data (3) Estimates of the prevalence of VLBW and ELBW per 1000 births pre-2020 and the potential impact of Jan to April 2020 regional data on the national expectation of VLBW for 2020 in Ireland	Inclusion: VLBW and ELBW live births Jan 1, 2001 - April 30, 2020 Exclusion: None	VLBW and ELBW birth rates	(1) No temporal trends in VLBW and ELBW from 2001 to 2019 (2) VLBW rate per 1000 live births Jan-April: 8.18 (2001-2019) vs 2.17 (2020). Rate ratio: 3.77, 95%CI [1.21, 11.75] ELBW rate per 1000 live births Jan-April: 3.0 (2001-2019) vs 0.0 (2020). Rate ratio: 3.0, 95%CI [2.43, 3.70] (3) VLBW rate per 1000 live births: 8.41 (2001-2019). Regional expectation for 2020: 2.27. Estimate of a reduction of VLBW infants from 500-600 to 400 per 60,000 births	Reduction in births involving VLBW and ELBW infants during the Irish national lockdown.
Ireland[6] 1 center in Dublin	Explore any apparent trends in maternal or neonatal outcomes by comparing maternity outcomes before, during and after the pandemic	March 27 - ?, 2020	(1) Pearson correlation coefficient (2) Chi-square and Fisher's exact tests	Inclusion: Not specified Jan 1 - July 31, 2020 and same periods 2018-19 Exclusion: Not specified	(1) Correlation between covid deaths and birth statistics (2) PTB rates	(1) No correlation between covid deaths and PTB (r = 0.339) (2) Overall PTB 2020: 7.4% 2019: 9.0% 2018: 8.1% p = .03	Reduction in preterm deliveries in comparison to the same time period in the preceding two years. However, February 2020 was the only month individually to demonstrate a statistically significant difference.
Netherlands[7] Nationwide	Study the impact of the COVID-19 mitigation measures on the incidence of PTB	Mitigation measures on March 9, March	Difference-in-regression-discontinuity analysis	Inclusion: Singleton babies who had undergone neonatal blood spot screening	Overall incidence of PTB before and after start of mitigation measures (number of	Discontinuity in the regression lines for the initial set of mitigation measures (March 9).	The national introduction of COVID-19 mitigation measures in the Netherlands was associated with a

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		15 and March 23 (lockdown), 2020	4 time windows: 1, 2, 3 and 4 months before and after dates of implementation; comparison with same time periods in 2010-19	Oct 9, 2010 - July 16, 2020 Exclusion: Multiple births Gestational age < 24w or > 41w^{+6}	babies born at < 37 weeks, per 1000 babies that underwent neonatal blood spot screening) Stratified analyses according to degree of prematurity	Overall PTB: March 9, 2020 measures ± 1 month: OR = 0.91, 95%CI [0.68, 1.20]; ± 2 months: OR = 0.77, 95%CI [0.66, 0.91]; ± 3 months: OR = 0.85, 95%CI [0.73, 0.98]; ± 4 months: OR = 0.84, 95%CI [0.73, 0.97] Consistent across gestational age strata. No significant change in PTB for measures implemented on March 15 and 23	considerable reduction in PTBs.
United States, Pennsylvania[8] 1 center	Explore the cause of the decreased incidence of PTB	March 6 - ?, 2020	Chi-square and t-tests	Inclusion: Singleton births ≥ 20w Jan 1, 2018 - Oct 27, 2020 Exclusion: Missing gestational age, self-paying insurance, birth during "wash-out" period (Feb-March 2020)	Overall PTB PTB < 34w PTB < 28w	Overall PTB: 10.1 vs 11.1%, p = .04 PTB < 34w: 3.1 vs 3.6%, p = .09 PTB < 28w: 0.8 vs 1.0%, p = .29	The frequency of PTBs is decreasing during the COVID-19 pandemic. The decrease could be attributed to COVID-19 responses that differentially benefit women who reside in more advantaged neighborhoods.
United States, Philadelphia[9] 1 center	Evaluate the incidence of PTB during the COVID-19 pandemic in 2020 compared with a similar period in 2019	-	Chi-square analysis using ORs for categorical variables Logistic regression models. Adjusted for race/ethnicity.	Inclusion: Births ≥ 20w March 1 - July 31, 2020 and same period 2019 Exclusion: None	Incidence of PTB between 2 groups, before and during the COVID-19 pandemic PTB 34^{+0}-36^{+6}w PTB < 34w PTB < 28w	Overall PTB: 9.9 vs 12.6%; OR 0.76, 95%CI [0.58, 0.99]; aOR 0.75, 95%CI [0.57, 0.99] PTB 34^{+0}-36^{+6}w: 7.4 vs 7.9%, aOR 0.93, 95%CI [0.67, 1.28] PTB < 34w: 2.5 vs 4.7%, aOR 0.51, 95%CI [0.31, 0.92] PTB < 28w: 0.6 vs 1.5%, aOR 0.37, 95%CI [0.15, 0.93]	A significant (25%) decrease in the odds of PTB during the COVID-19 pandemic compared with a similar prepandemic period. A significant decrease in early PTB, which has the highest risk of neonatal morbidity and mortality.
United States, Tennessee[10] Statewide	Examine the association of stay-at-home orders with birth outcomes	March 22 - April 30, 2020	(1) Descriptive statistics (2) Logistic regression models. Adjusted for maternal age, education, race/ethnicity, diabetes, and hypertension	Inclusion: Birth records from 2015-2020 Exclusion: Gestational age < 17w or > 47w	Odds of PTB during the 2020 stay-at-home order compared with same periods in 2015 and 2019	(1) Overall PTB in 2020 vs 2015-2019: 10.2 vs 11.3%, p = .003 PTB < 32w: 1.8 vs 2.0%, p = .27 PTB 35-36w: 5.8 vs 6.5%, p = .03 (2) aOR for PTB: 0.86, 95%CI [0.79, 0.93]	Lower odds of PTB in 2020 during the Tennessee stay-at-home order compared with the 5 preceding years.
Australia[11] 1 center in Brisbane	Investigate PTB rates during lockdown in the largest single tertiary	Beginning restrictions	Multinomial logistic regressions. Adjusted for maternal age, BMI,	Inclusion: Singleton live births	PTB rate PTB 23^{+0}-27^{+6}w	"Early" period 2020 vs same period average 2013-2019:	The early restrictions in the COVID-19 pandemic were associated with lower

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	perinatal center in Queensland	"early": March 16 - Apr 17, 2020 Strictest "late": Mar 30 - May 1, 2020	parity, socioeconomic status, asthma, diabetes, hypertensive disorder	March 16 - May 1, 2013-2020 Exclusion: None	PTB 28^{+0}-31^{+6}w PTB 32^{+0}-36^{+6}w compared to livebirths > 37w	Overall PTB: aOR 0.62, 95% CI [0.43, 0.88] * planned: aOR 0.50, 95%CI [0.31, 0.83] * spontaneous: aOR 0.80, 95%CI [0.48, 1.36] PTB 32^{+0}-36^{+6}w: aOR 0.53, 95% CI [0.35, 0.80] * planned: aOR 0.39, 95%CI [0.22, 0.71] * spontaneous : aOR 0.77, 95%CI [0.43, 1.40] No differences for extreme and very PTB rates No differences in "late" period	planned (not spontaneous) moderate and late PTB rates.
France[12] Nationwide	Establish a decrease in risk of prematurity in France after the beginning of lockdown	March 17, 2020 - ?	Chi-square test and *"the variations"* (relative risk difference)	Inclusion: Newborns (not further specified), singletons and multiples April-May 2020 and same period 2017-19 Exclusion: Not specified	Comparison of PTB rates by month between two periods: Jan-Sept 2017-2019 (mean rate) and Jan-Sept 2020 PTB < 37w PTB 22-28w PTB 29-31w PTB 32-36w	April-May 2017-2019 vs April-May 2020, for singletons: * < 37w: decrease of 7.23%, p < .01 * 22-28w: decrease of 12.90%, p = .03 * 28-31w: increase of 1.96%, p = .69 * 32-36w: decrease of 8.24%, p <.01 * "decrease was still observed after the end of lockdown (June-Sep 2020)" Jan-Sep 2017-2019 vs Jan-Sep 2020, for multiples: no decrease in PTB	Large-scale socio-environmental modifications like the lockdown in spring 2020 may be associated with beneficial effects on perinatal morbidity
Argentina[13] 10 birth centers in Cordoba	Compare incidence of PTB of pregnancies conceived during lockdown compared to pregnancies conceived before lockdown, adjusted by potential confounders	August 13 - December 31, 2020	(1) Chi square test and student t-test. (2) Multivariate logistic regressions (crude and adjusted OR with 95%CI). Variables which were adjusted for not specified.	Inclusion: Singleton live births ≥ 22w August 13 - Dec 31, 2020 and same period 2019 Exclusion: Multiple pregnancies, major congenital malformations	(1) Rates of PTB PTB <37w (for PTB <34w and PTB <32w, see article) (2) Association lockdown and PTB	(1) PTB rate < 37w: 8.5 vs 9.6%, risk difference - 1.1%, 95%CI [-1.93, -0.18], p = 0.02; Medically indicated PTB < 37w: 4.3 vs 5.3%, risk difference -1.0%, 95%CI [-1.62, -0.33], p = 0.01; Spontaneous PTB < 37w: 4.2 vs 4.3%, risk difference -0.1%, 95%CI [-0.70, -0.53], p = 0.78 (2) PTB < 37w: crude OR 0.88, 95% CI [0.79, 0.98], aOR 0.89, 95% CI [0.80, 0.99]	Multivariate analysis shows that childbirth during the mandatory lockdown period was significantly associated with a decreased risk of PTB.
Iceland[14] Nationwide	Compare PTB rates during the lockdown periods in 2020 in Iceland with rates during the same periods in 2016-2019	March 13 - May 25, 2020 (lockdown 1) Oct 5 - Dec 31, 2020 (lockdown 2)	Generalized linear mixed models with binomial distribution and logit link to account for clustering. Adjusted for parity, age, country of origin, residential area, cohabitation, employment,	Inclusion: Singleton births ≥ 22w Lockdown periods 2020 vs same periods 2016-2019 Exclusion:	PTB rate Overall PTB PTB 22^{+0}-31^{+6}w PTB 32^{+0}-36^{+6}w	Lockdown 1, overall PTB rate: aOR 0.69, 95% [CI 0.49, 0.97] Jun-Sep, overall PTB rate: aOR 0.67, 95%CI [0.49, 0.89]	There was a reduction in overall PTB rate during and following the first lockdown.

Location	Aim	Lockdown	Statistical analysis	Population	Outcome	Results	Conclusion
			essential hypertension, and pre-existing diabetes	None		Lockdown 2, overall PTB rate: aOR 1.22, 95%CI [0.89, 1.67] PTB 22-32 and PTB 32-37w: see article Table 3	
Botswana[15] 8 centers covering 45% of all births	Estimate the risk of adverse birth outcomes before, during and after the COVID-19 national lockdown compared with the same 3 periods in 2017-19	April 2 - May 7, 2020	Differences-in-differences analysis, 95%CI obtained using a linear probability model with robust standard errors to account for clustering within delivery sites	Inclusion: Singleton births ≥ 24w Jan 1 - July 20 2020 and same periods 2017-19 Exclusion: Not specified	Adverse birth outcome (composite outcome including PTB) and severe adverse birth outcome	Lockdown period, 2020 vs 2017-19: Overall PTB: -1.27%, 95%CI [-2.71%, 0.17%]; vs prelockdown: -1.52%, 95%CI [-3.14%, 0.10%] PTB < 32w: -0.47%, 95%CI [-1.15%, 0.21%]; vs prelockdown: -0.26%, 95%CI [-0.80%, 0.27%] Postlockdown period, 2020 vs 2017-19: Overall PTB: -0.66%, 95%CI [-1.66%, 0.34%]; vs prelockdown: -0.91%, 95%CI [-2.57%, 0.75%] PTB < 32w: -1.09%, 95%CI [-1.54, -0.64%]; vs prelockdown: -0.88%, 95%CI [-1.46%, -0.31%]	Modest reduction in risk of any adverse outcome and any severe adverse outcome from the prelockdown to postlockdown periods, mostly driven by reductions in preterm birth, very preterm birth, and (very) small for gestational age fetuses.
Denmark[16] Nationwide	Investigate the impact of the lockdown on PTB rates	March 12- April 15, 2020	(1) Likelihood ratio-based tests, estimates and CIs regarding changes in composition of gestational age at birth categories between the lockdown period and consolidated reference period for 2015-2019 were obtained from a series of logistic regressions (2) Unspecified methodology	Inclusion: (1) Singleton births March 12 - April 14, 2020 and same periods 2015-19 (2) Singleton births Jan 20 - Feb 22, from 2015 to 2020 Exclusion: (1, 2) Not specified	The odds of being born during lockdown by gestational age category: PTB < 28w PTB 28-31^{+6}w PTB 32-36^{+6}w Birth 37-41^{+6}w Birth ≥ 42w	(1) PTB < 28w: OR 0.09, 95%CI [0.01, 0.40] PTB 28-31^{+6}w: OR 1.11, 95%CI[0.75, 1.61] PTB 32-36^{+6}w: OR 0.98, 95%CI[0.84, 1.13] Birth 37-41^{+6}w: OR 1.06, 95%CI[0.95, 1.20] Birth ≥ 42w: OR 0.92, 95%CI[0.74, 1.13] Gestational age distribution 2020 significantly different from 2015-19, p = .004 Proportion extremely and very PTB lockdown 2020 significantly	Potential effect of nationwide lockdown on extremely PTB rates.

Location	Aim	Lockdown	Statistical analysis	Population	Outcome	Results	Conclusion
						different from same period 2015-19 , p = .003 (2) No differences in birth rates in the Jan-Feb periods	
Israel[17] 1 center in Tel Aviv	Determine the change in PTB rate and neonatal outcomes during the pandemic compared with that in de prepandemic periods by evaluating multiple obstetrical characteristics during more than 3 pandemic months	March 20 - June 27, 2020	Comparison of maternal and pregnancy characteristics during the pandemic and corresponding prepandemic periods (OR are calculated only for significantly different categorical variables)	Inclusion: Singleton births March 20 - June 27, 2020 (group 1), parallel period in 2019 (group 2), annual periods in 2011-2019 (group 3) Exclusion: Not specified	Maternal, obstetrical and delivery characteristics, and neonatal outcomes	Overall PTB: OR not available, p = .07 PTB < 34w: OR 0.45, 95%CI [0.30, 0.68] PTB < 32w: OR 0.47, 95%CI [0.27, 0.79]	More than 50% reduction in PTB rate at < 34 weeks' gestation, possibly resulting in improved neonatal outcomes.
Saudi Arabia[18] 1 center in Riyad	Study the effects of lockdown in restoring the overall health of the intrauterine habitat and whether it would influence the continuation of fetal life	March 1- June 30, 2020	(1) Chi-square test (2) Poisson regression models	Inclusion: Live born infants March 1 - June 30, 2020 and same periods 2017-19 Exclusion: Abortions, stillbirths, intrauterine fetal death	(1) Differences in PTB rates (2) PTB rates' temporal trends per 1000 live births over 16 months	(1) 2020 vs 2017-2019 PTB < 28w: p = .05 PTB 28-31^{+6}w: p = .94 PTB 32-36^{+6}w: p < .001 (2) Overall PTB 2020: 151/1000 Overall PTB 2017: 198/1000, p = .14 Overall PTB 2018: 185/1000, p = .27 Overall PTB 2019: 196/1000, p = .14	Significant reduction in PTB rates during quarantine in extremely premature and late preterm. No statistically significant reduction in overall PTB rate.
Australia[19] 3 centers in Melbourne	Investigate the effect of restriction measures to mitigate COVID-19 transmission on pregnancy duration and outcome	First restrictions (less stringent) March 16– May 31, 2020 Stricter restrictions July 8 - Sep 28, 2020 From August 2, 2020 curfew 8pm-5am	(1) Generalized linear models with Poisson family, log link function and robust variance. Adjusted for maternal age, BMI, smoking, parity, fetal sex and other baseline characteristics that differed significantly between the groups. (2) *a.* Kaplan–Meier survival estimates and Cox regression model *b.* Competing-risk regression (iatrogenic PTB as competing event)	Inclusion: Births with estimated conception date Nov 1, 2019 – Feb 29, 2020 (exposed) or Nov 1, 2018 – Feb 28, 2019 (control) and delivery > 20w Exclusion: Major structural or chromosomal fetal anomaly	(1) Effect of restriction measures on PTB < 34w (2)*(a, b)* Effect of restriction measures on the duration of pregnancy	(1) PTB < 34w: 2.4 vs 3.4%, RR 0.71, 95%CI [0.53, 0.95], p = 0.022; spontaneous: 1.2% vs 1.9%, RR 0.64, 95%CI [0.43, 0.96], p = 0.029; iatrogenic: 1.2% vs 1.4%, RR 0.78, 95%CI [0.38, 1.25], p = 0.0332) (2) *a.* PTB exposed vs controls: HR 0.81, 95%CI [0.69, 0.95], p = 0.008 *b.* Effect of exposure on spontaneous PTB was stronger and started earlier (HR 0.81, 95%CI [0.64, 1.03], p = 0.087) than effect on medically indicated PTB (HR 0.89, 95% CI [0.70, 1.12], p = 0.305)	Lower rate of PTB < 34w due to reduced spontaneous PTB rate in women exposed to strict mitigation measures.
Netherlands[20]	Assess the association between the initial	March 15 - May 15, 2020	Logistic regression models	Inclusion:	PTB < 32w PTB < 28w	Singletons:	During lockdown there was a significant decrease in

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Data from all 10 perinatal centers	COVID-19 lockdown in the Netherlands and the incidence of PTB < 32w, taking onset of delivery and composition of pregnancy into account			Singleton and multiple live births March 15 - May 15, 2020 and same periods 15, 2015-18 Exclusion: Antepartum and intrapartum fetal death		PTB <32w: 6.1 vs 6.5‰, OR 0.94, 95%CI [0.79, 1.12] PTB <28w: 2.2 vs 2.2‰, OR 1.01, 95%CI [0.75, 1.34] Multiples: PTB <32w: 90.5 vs 76.5‰, OR 1.20, 95%CI [0.82, 1.75] PTB <28w: 42.9 vs 18.1‰, OR 2.43, 95%CI [1.35, 4.39] Iatrogenic/spontaneous: see Table 3	iatrogenic PTB < 32w and < 28w.
NO DIFFERENCE IN PTB RATES							
Spain[21] 13 centers in Castilla-y-Léon region	Explore the potential link between national lockdown measures and changes in preterm births	March 15 - May 3, 2020	(1) Joinpoint regression analysis (2) Proportions with 95%CI (3) Logistic regression models. Adjusted for hospital, sex, type of delivery, and multiple pregnancies	Inclusion: Births ≥ 23w Jan 1, 2015 - June 21, 2020 Exclusion: None	(1) Trends (2) PTB rates (3) PTB proportions (lockdown vs previous years)	(1) No time point at which the declining trend of births significantly changed (2) Overall PTB: 6.17%, 95%CI [4.96, 7.39] vs 6.23%, 95%CI [5.73, 6.74] PTB 32^{+0}-36^{6}w: 5.24%, 95%CI [4.12, 6.37] vs 5.41%, 95%CI [4.93, 5.88] PTB 28^{+0}-$31+^{6}$w: 0.40%, 95%CI [0.08, 0.72] vs 0.50%, 95%CI [0.35, 0.65] PTB 23^{+0}-27^{+6}w: 0.53%, 95%CI [0.16, 0.90] vs 0.34%, 95%CI [0.22, 0.46]; OR 2.09, 95%CI [1.02, 4.28] (3) aOR 0.97, 95%CI [0.77, 1.22]	The association between the decreased number of PTBs and nationwide lockdown remains a subject of debate.
Sweden[22] Nationwide	Investigate associations between being born during a period when many public health interventions aimed at mitigating the spread of COVID-19 were enforced and the risk of PTB	April 1 - May 31, 2020	Multinomial logistic regression models. Adjusted for maternal age, birth country, body mass index, smoking status, and parity	Inclusion: Singleton births April 1 - May 31, 2020 and same periods 2015-19 Exclusion: Not specified	Risk of PTB	Overall PTB: 45.4‰ live births in 2020 vs 47.6‰ in 2015-19; OR 0.95, 95%CI [0.88, 1.03]; aOR 0.96, 95%CI [0.89, 1.04], adj risk difference -1.9, 95%CI [-5.2, 1.9] PTB < 28^{+0}w: 2.4‰ vs 2.8‰; OR 0.88, 95%CI [0.64, 1.22]; aOR 0.92, 95%CI [0.66, 1.28], adj risk difference -0.2, 95%CI [-1.0, 0.8] PTB 28^{+0}-31^{+6}w: 4.4‰ vs 4.2‰; OR 1.05, 95%CI [0.82, 1.33]; aOR 1.09,	No association between being born in the period April to May 2020, compared with April to May 2015-19.

Location	Aim	Lockdown	Statistical analysis	Population	Outcome	Results	Conclusion
						95%CI [0.85, 1.40]; adj risk difference 0.4, 95%CI [-0.6, 1.7] PTB 32^{+0}- 36^{+6}w: 38.5‰ vs 40.7‰; OR 0.94, 95%CI [0.87, 1.03]; aOR 0.95, 95%CI [0.87, 1.03]; adj risk difference -2.0, 95%CI [-5.3, 1.2]	
United Kingdom[23] 1 center in London	Investigate the change in PTB rates during the pandemic	-	Group comparisons using Mann-Whitney U and Fisher's exact tests	Inclusion: Not specified 2 epochs: Oct 1, 2019 - Jan 31, 2020 and Feb 1 - June 14, 2020 Exclusion: Not specified	PTB < 37w PTB < 34w	Overall PTB: difference -0.68, 95%CI[-2.43, 1.07] PTB < 34w: difference 1.13, 95%CI[-0.05, 2.30]	No significant differences over time in births before 37 and 34 weeks' gestation.
United States, Massachusetts[24] 4 centers	Investigate the change in PTB rate during the peak COVID-19 pandemic era compared with the pre-COVID-19 era	-	(1) Overall gestational age distribution during and before COVID-19 era (2) Rate of PTB using various thresholds	Inclusion: Singleton live births ≥ 20w April to July 2020 and same period 2019 Exclusion: ≥ 37 weeks	PTB rates	(1) Identical distribution of gestational ages (p = .8) (2) No differences in PTB rate PTB < 37w: p = .4 PTB < 34w: p = .3 PTB < 32w: p = .1 PTB < 28w: p = .3	No reduction in preterm birth rate. Findings do not support the theory that quarantine or health care delivery changes decrease the rates of PTB.
United States, Philadelphia[25] 2 centers	Determine if preterm birth rates have changed during the SARS-CoV-2 pandemic	-	(1) Fisher's exact test (2) Marginal effects models. Adjusted for birth month, age, parity, body mass index, race/ethnicity, marital status, smoking, and insurance status	Inclusion: Singleton live births March-June 2020 and same periods 2018-19 Exclusion: Not specified	Overall PTB	Overall PTB: (1) 9.5 vs 10.5%, p = .12 (2) adj risk difference: -1.1%, 95%CI[-2.4%, 0.2%]	No significant changes in preterm rates during the SARS-CoV-2 pandemic in a racially diverse urban cohort from 2 Philadelphia hospitals.
Multicountry[26] - not peer reviewed	To evaluate if the number of admitted extremely preterm (EP) born infants changed in NICUs within the SafeBoosC-III consortium during the global lockdown	-	E-mail survey to principal investigators of all 79 NICUs within the SafeBoosC-III consortium (1) Chi-square test, α = 5% (2) Chi-square test, α = 1% (3) Linear regression, α = 1%	Inclusion: EP infants admitted to NICU during the 3 months of rigorous lockdown restrictions in 2020 and same period 2019 Exclusion: Not specified	(1) Difference in total number of EP infants admitted to NICU within three months with most rigorous lockdown restrictions and EP infants admitted in corresponding three months in 2019 (2) Differences in admissions between regions (3) Correlations between level of local	(1) 428 EP infants in 2020 vs 457 in 2019 (p = .33) (2) No significant differences within geographical regions (3) No correlation between level of lockdown and change in number of admissions of EP infants (p = .3)	No confirmation of major reduction in the number of extremely preterm births during the first phase of the COVID-19 pandemic.

Location	Aim	Lockdown	Statistical analysis	Population	Outcome	Results	Conclusion
					lockdown restrictions and change in number of EP infants admissions		
Austria[27] 1 center in Vienna	To evaluate whether the national lockdown has a negative effect on PTB rate	March 15 - June 15, 2020	Logistic regression	Inclusion: Singleton live births March-July 2020 and pre-lockdown months Jan-Feb 2020 Exclusion: Maternal COVID-19 infection	PTB 32-36w PTB < 32w	PTB 32-36w 54.2/1000 vs 63/1000; OR 1.01, 95%CI [0.97, 1.05] PTB rate <32w 28.9/1000 vs 14.9/1000; OR 1.92, 95%CI [0.76, 4.79]	The stressful lockdown phase in Austria seems to have no negative effect on gestational length among non-infected mothers.
Canada[28] Province of Ontario	Evaluate rates of PTB during the first 6 months of the pandemic	Not specified	Generalized estimating equations models (clustering at the level of birth institution) Adjusted for maternal age, parity, singleton vs multiple birth, income, rural residence, hypertension, diabetes, assisted reproductive technology, short interbirth interval, and history of PTB	Inclusion: In-hospital births ≥ 20w March 15 - Sep 30, 2020, corresponding calendar periods 2015-2019	Live PTB < 37w	7.5 vs 7.5%, aOR 0.99, 95%CI [0.97, 1.03]	There were no differences in the overall risk of PTB during the first 6 months of the COVID-19 pandemic
Canada[29] Province of Ontario	Evaluate whether the COVID-19 pandemic affected PTB rates in Ontario by comparing rates of early pandemic time period with rates from the previous 17.5 years	March 18 –?, 2020	(1) Special cause variation: Laney control P′ charts to describe and detect common cause (usual) and special cause (unusual) variations in 6-months periods (2) Change in slope: interrupted time-series analysis method to evaluate sudden change at the start of the pandemic and difference in rates of change of PTB over time (slopes)	Inclusion: Resident pregnant people who delivered in any hospital in Ontario, aged 13-59 years, matched to their live offspring, born between 21^{+0} and 36^{+6}w "pandemic period" = Jan-Dec 2020, "free from pandemic effects" = July 2002 – Dec 2019 Exclusion: Live births at 21 weeks	(1) Special cause variation in PTB rates (2) Difference in rates of change (slope) of PTB	(1) No special cause variation in PTB rate during 12 months pandemic period (2) No significant change in slope, trends or cut-off between pre-pandemic and pandemic periods for PTB	No special cause variation (unusual change) in PTB, overall or by subgroups, during the first 12 months of the COVID-19 pandemic compared with the previous 17.5 years. Interrupted time-series analysis did not identify statistically significant differences in slopes of rates of change for preterm birth and its subgroups.
Jordan[30] Nationwide	Assess the alterations in PTB rate trends during COVID-19 national lockdown	March 17 - April 30, 2020	Multinomial and binary logistic regression models. Adjusted for age, income, education, occupation, nationality, health sector, and multiplicity	Inclusion: Births between 24 and 42w 2 study periods: 11 months before (May 2019 - Mar 2020) vs 9 months during (April - Dec, 2020) the pandemic	Prematurity (< 28w, 28-32w, 32-37w)	No significant between-period difference in the proportion of preterm babies *(no numerical results provided)*	No difference in PTB rates between the 2 periods.

Location	Aim	Lockdown	Statistical analysis	Population	Outcome	Results	Conclusion
				Exclusion: None			
INCREASE IN PRETERM BIRTH							
Nepal[31] 9 centers across all 7 provinces	To assess the indirect impact of the lockdown on use of public health facilities for childbirth, quality of intrapartum care, institutional stillbirth rate and neonatal mortality	March 21- May 30, 2020	Generalized linear model with Poisson distribution and log-link function. Adjusted for ethnicity, maternal age, and obstetric characteristics	Inclusion: Women ≥ 22 weeks' gestation admitted in the labor room with positive fetal heart beat at admission 12.5 weeks before (Jan 1-March 20, 2020) and 9.5 weeks during (March 21-May 30, 2020) lockdown Exclusion: Multiple births	Institutional PTB (< 37w) before and during lockdown	Increase in overall PTB: 20.0 during vs 16.7% before lockdown, p = .0016. Unadjusted risk ratio: 1.20, 95%CI [1.11, 1.30] Adjusted risk ratio: 1.30, 95%CI [1.20, 1.40]	Institutional births reduced by approximately half. The decrease in the number of institutional births and increase in adverse outcomes are concerning.
Uruguay[32] 1 center in Montevideo	Determine the effect of the mitigation measures of the COVID-19 pandemic on perinatal results	-	Not specified	Inclusion: Not specified March 15 - Sep 30, 2020 and corresponding months in 2019 Exclusion: Not specified	PTB rates	Overall PTB 14.5 vs 12.2%, p = .005, RR 1.19, 95%CI [1.05, 1.35]	Mitigation measures of the COVID-19 pandemic aggravate the effects of the global syndemic on the reproductive process of the social sectors most violated in their rights.

Abbreviations: aOR = adjusted odds ratio, COVID = coronavirus disease, CI = confidence interval, ELBW = extremely low birth weight, HR = hazard ratio, OR = odds ratio, PTB = preterm birth, RR = relative risk, VLBW = very low birth weight, w = weeks,

Table 2

Hospital	Year	SPL	PPROM	Placental pathology	Placenta praevia	Miscellaneous	Other	Preterm birth (24-36^{+6} weeks)	Total
Ghent University Hospital	2019	82 (46.1)	36 (20.2)	34 (19.1)	5 (2.8)	2 (1.1)	19 (10.7)	119 (66.9)	178
	2020	66 (36.9)	45 (25.1)	41 (22.9)	6 (3.4)	4 (2.2)	17 (9.5)	119 (66.5)	179
	Chi square/ Fisher's exact 2019 vs 2020	3.11 p = .08	1.23 p = .27	0.78 p = .38	0.09 p = .77	0.35 p = 1.00	0.14 0.71	0.006 p = .94	-
Ziekenhuis Oost-Limburg	2019	14 (15.6)	8 (8.9)	26 (28.9)	6 (6.7)	8 (8.9)	28 (31.1)	52 (57.8)	90
	2020	13 (20.3)	9 (14.1)	14 (21.9)	5 (7.8)	9 (14.1)	14 (21.9)	41 (64.0)	64
	Chi square/ Fisher's exact 2019 vs 2020	0.59 p = .44	1.02 p = .31	0.96 p = .33	0.07 p = .79	1.02 p = .31	1.61 p = .20	0.62 p = .43	-

Abbreviations: SPL = spontaneous preterm labour, PPROM = preterm prelabour rupture of membranes

Table 3

Hospital	Year		Miscarriage (<14 weeks)	Immature birth (14-21^{+6} weeks)	Preterm birth (22-36^{+6} weeks)		Term birth (37-41^{+6} weeks)		Total	
Ghent University Hospital	2019	Proportion	169/1251 13.5%	58/1251 4.6%	299/1251 23.9%	299/1024 29.2%	725/1251 58.0%	725/929 78.0%	1251	1024
	2020		172/1154 14.9%	53/1154 4.6%	248/1154 21.5%	248/929 26.7%	681/1154 59.0%	681/929 73.3%	1154	929
	2019 vs 2020	Chi square	0.96 p = .33	0.10 p = .75	0.10 p = .75	0.07 p = .79	0.28 p = .60	1.51 p = .22	-	-
University Hospital Leuven	2019	Proportion	-	-	-	371/2239 16.6%	-	1868/2239 83.4%	-	2239
	2020		-	-	-	360/2387 15.1%	-	2027/2387 84.9%	-	2387
	2019 vs 2020	Chi square	-	-	-	1.29 p = .26	-	1.92 p = .17	-	-
Ziekenhuis Oost-Limburg	2019	Proportion	-	-	-	231/2044 11.3%	-	1813/2044 88.7%	-	2044*
	2020		-	-	-	248/1966 12.6%	-	1753/1966 89.2%	-	1966*
	2019 vs 2020	Chi square	-	-	-	0.28 p = .60	-	0.22 p = .64	-	-
All 3 hospitals	2019	Proportion	-	-	-	901/5307 17.0%	-	4406/5307 83.0%	-	5307*
	2020		-	-	-	821/5282 15.5%	-	4461/5282 84.5%	-	5282*
	2019 vs 2020	Chi square	-	-	-	3.29 p = .07	-	4.00 p = .05	-	
	proportions denominator		number of pregnancies	number of pregnancies	number of pregnancies	number of births (≥22w)	number of pregnancies	number of births (≥22w)	number of pregnancies	number of births (≥22w)

Abbreviations: CI = confidence interval, w = weeks

* for Ziekenhuis Oost-Limburg: liveborn > 22 weeks or stillborn at 500 grams or more or stillborn at a gestational age of 25^{+5} weeks or more

Figures

Figure 1. Kaplan Meier graphs comparing admissions for threatened preterm birth between 2019 and 2020 in Ghent University Hospital and Ziekenhuis Oost-Limburg, Genk.

Figure 2. Kaplan Meier graphs comparing births between 2019 and 2020 in Ghent University Hospital, University Hospital Leuven and Ziekenhuis Oost-Limburg, Genk.