ORIGINAL RESEARCH ARTICLE

Early suppression policies protected pregnant women from COVID-19 in 2020: A population-based surveillance from the Nordic countries

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Abstract

Introduction: The Coronavirus 2019 Disease (COVID-19) pandemic reached the Nordic countries in March 2020. Public health interventions to limit viral transmission varied across different countries both in timing and in magnitude. Interventions indicated by an Oxford Stringency Index ≥50 were implemented early (March 13–17, 2020) in Denmark, Finland, Norway and Iceland, and on March 26, 2020 in Sweden. The aim of the current study was to assess the incidence of COVID-19-related admissions of pregnant women in the Nordic countries in relation to the different national public health strategies during the first year of the pandemic.

Material and methods: This is a meta-analysis of population-based cohort studies in the five Nordic countries with national or regional surveillance in the Nordic Obstetric Surveillance System (NOSS) collaboration: national data from Denmark, Finland, Iceland and Norway, and regional data covering 31% of births in Sweden. The source population consisted of women giving birth in the included areas March 1–December 31, 2020. Pregnant women with a positive SARS-CoV-2 PCR test ≤14 days before hospital admission were included, and admissions were stratified as either COVID-19-related or non-COVID (other obstetric healthcare). Information about public health policies was retrieved retrospectively.

Results: In total, 392 382 maternities were considered. Of these, 600 women were diagnosed with SARS-CoV-2 infection and 137 (22.8%) were admitted for COVID-19 symptoms. The pooled incidence of COVID-19 admissions per 1000 maternities was

0.5 (95% confidence interval [CI] 0.2 to 1.2, $I^2=77.6$, $tau^2=0.68$, $P=0.0$), ranging from no admissions in Iceland to 1.9 admissions in the Swedish regions. Interventions to restrict viral transmission were less stringent in Sweden than in the other Nordic countries.

Conclusions: There was a clear variation in pregnant women's risk of COVID-19 admission across countries with similar healthcare systems but different public health interventions to limit viral transmission. The meta-analysis indicates that early suppression policies protected pregnant women from severe COVID-19 disease prior to the availability of individual protection with vaccines.

KEYWORDS
COVID-19, incidence, Nordic countries, pregnancy outcome, risk factor, SARS-CoV-2

1 | INTRODUCTION

The Coronavirus 2019 Disease (COVID-19) pandemic has presented a health challenge globally for 3 years.[1] During the first year of the pandemic many countries adopted strict restriction policies with social distancing and lockdowns (suppression) to limit viral transmission, whereas other countries opted for milder restrictive measures (mitigation).[2] Evaluation of these public health interventions is needed to ensure preparedness for future pandemics and to facilitate evidence-based policies and recommendations.

Two waves of the pandemic were seen in the Nordic countries during 2020. The countries adapted different restriction strategies at different time points of the pandemic.[3,4] The Oxford Stringency Index (SI) aimed to standardize and describe the government implementation of public health measures.[5] Denmark,[6] Finland,[7] Iceland[8] and Norway[9] all adopted early suppression strategies and surpassed the SI level of 50 for government response between March 13 and March 17, 2020. Sweden opted for a mitigation strategy and crossed the SI >50 on March 26.[5] Compared with the other Nordic countries, Sweden had less reduction in population mobility and a higher cumulative test positivity rate during the first wave.[10] The dominating virus variant was the wild type or Wuhan variant during 2020, and vaccines were not yet available. The Nordic countries have similar free-of-charge maternal and delivery care, and similar maternal and perinatal outcomes.[11]

Previous studies have examined pregnancies affected by the Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) disease and the clinical manifestations, risk factors and maternal and perinatal outcomes as summarized in a systemic review and meta-analysis.[12] Most of the studies were hospital-based with limited information on the source population, thus restricting incidence analyses and comparison between countries. They also lacked clear discrimination between admissions due to COVID-19 and admissions for other causes, such as pregnancy-related healthcare.[12]

The aim of the current study is to assess the incidence of COVID-19-related admissions in the Nordic countries and discuss this in the context of the national public health interventions. The secondary

> **Key message**
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> National restriction policies protected the pregnant population: COVID-19-related admissions were more frequent in the Swedish regions than in the other Nordic countries. Rapid, robust population-based surveillance is vital to monitor risk and could guide policies during societal emergencies.

objective is to describe risk factors for COVID-19-related admissions and maternal and perinatal outcomes after COVID-19-related hospital admission of pregnant women in the Nordic countries.

2 | MATERIAL AND METHODS

2.1 | Study population

The source population consisted of pregnant women giving birth at a gestational age of ≥22 weeks (maternities) in the Nordic countries between March 1, 2020 and December 31, 2020. The population-based surveillance was implemented nationally in all countries except Sweden, where three regional university hospitals and three regions represented 31% of the national maternities (University Hospitals at Karolinska (KUH), Sahlgrenska (SaUH) and Lund-Malmö (SkUH) and the regions of Halland, Dalarna and Vestmannland). These University Hospitals are tertiary national and regional referral hospitals and thus acquire patients from broader regions than just the specific geographic areas. The total number of births in the Swedish hospitals was 36 636, and this was used as the Swedish source population.

Pregnant women with a positive SARS-CoV-2 PCR test ≤14 days before or during hospital admission, and up to 2 days postpartum, were included. Hospital admissions were further categorized based on the clinical information as either COVID-19-related or
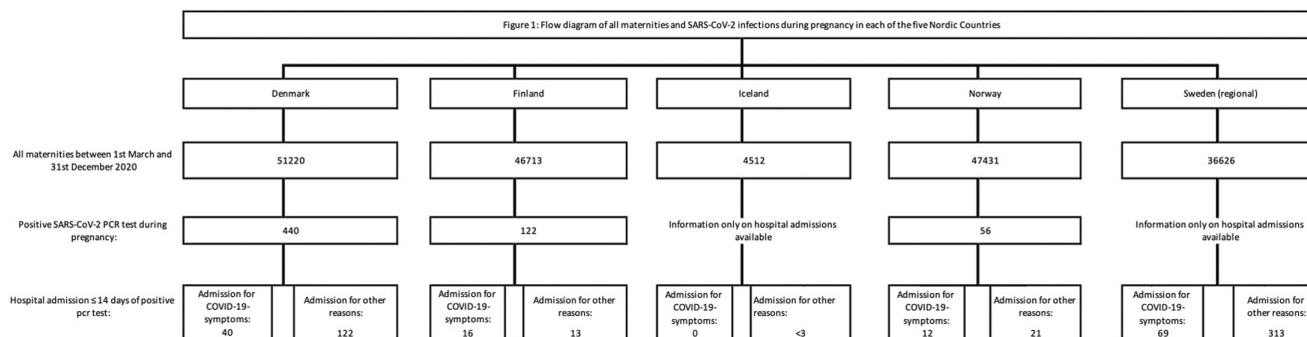
Figure 1: Flow diagram of all maternities and SARS-CoV-2 infections during pregnancy in each of the five Nordic Countries

FIGURE 1 Flow diagram of all maternal cases and SARS-CoV-2 infections during pregnancy in each of the five Nordic Countries.

non-COVID related (women admitted for other reasons, such as pregnancy-related healthcare, with a concurrent viral infection).

Despite somewhat differing national testing strategies in the different countries, pregnant women with severe symptoms possibly related to SARS-CoV-2 were tested in every country during the whole study period.

2.2 | Data collection

Prospectively recorded clinical information from medical records was collected in a uniform case report form. However, the surveillance modalities varied; Iceland and Norway based the surveillance at the national Medical Birth Registries, Denmark established a national database,[13] Finland combined clinical reporting and national registry linkages, and Sweden established a database for the participating hospitals and regions with data retrieved from the Hospital Discharge database and clinical records. Denmark, Finland, Iceland and Norway had systems to ensure complete reporting, including national registry linkages when possible. Further details about the data collection and surveillance have been described in a previous publication,[14] and is described in detail in Appendix S1.

Comparison data for all maternities in 2020 were obtained from The Association for Nordic Medical Birth Registers (NOMBIR)[11] and from the national Medical Birth Registries.

2.3 | Outcomes

The primary outcome was the incidence of COVID-19-related admission to hospital per 1000 maternities stratified according to reason for admission – COVID-19 or other obstetric reasons.

Secondary maternal outcomes were COVID-19-related admission to intensive care, mode of delivery (vaginal or cesarean) and preterm birth <37+0weeks. Secondary perinatal outcomes were stillbirth, infant admission to a neonatal unit and neonatal death prior to discharge after birth. Clinical information was reviewed for maternal intensive care admission and stillbirth to ascertain the role of COVID-19.

The following descriptive characteristics were included as covariates: maternal age at admission, obesity (body mass index ≥30kg/m^2), migrant background, parity (previous births with gestational age [GA] of 22weeks or more), gestational age at infection and at birth, chronic disease prior to pregnancy (asthma, diabetes, hypertension) and other diseases in pregnancy (gestational diabetes, preeclampsia). Migrant background was defined by the mother's country of birth outside the Nordic countries, with Nordic-born as a reference.

In addition to the published Oxford Stringency Index,[5] the following public health interventions were obtained for each country from government sources; lockdown of schools, universities, restaurants, public institutions, small businesses, gyms and venues, and public gathering restrictions.

2.4 | Statistical analyses

The national incidence results were stratified by admission group and aggregated national frequencies were pooled using meta-analysis of proportions.[15] Because of small proportions and large variations in the size of the study populations, we used both the new proposed package for STATA with logistic regression for meta-analysis of binomial data and the proportional meta-analysis with Freeman–Tukey double arcsine transformation.[12,13] The 95% confidence intervals (95% CI) were computed using Wilson's method.[16]

Among pregnant women admitted with SARS-CoV-2 infection, the risk factors associated with COVID-19 admission were assessed using non-COVID admissions as the reference group. Aggregate data from each country were used to estimate pooled relative risks for risk factors identified in the literature using a random effect maximum likelihood model (REML) with Hartung–Knapp–Sidik–Jonkman (HKSJ) variance estimator.[17]

Heterogeneity across national studies were described using the I^2-statistic[18] and tau^2. Although potential confounders or risk factors were identified in the literature and by using directed acyclic graphs, the small national datasets with few or no observations in subgroups limited adjustment of analyses.

The national teams chose their preferred statistical analysis program, and we have consequently described the study as a

conventional meta-analysis and not an individual participant data meta-analysis (IPD).

3 | RESULTS

There were 392 382 women giving birth during the study period. Of them, 600 had SARS-CoV-2-infection and 137 (22.8%) required hospital admission for COVID-19 symptoms (Figure 1).

The estimated pooled incidence of COVID-19-related admission was 0.5 per 1000 maternities (95% CI 0.56–1.41, I^2=87.55% and tau^2=0.44), with no admissions in Iceland (Figure 2). The incidence of COVID-19-related admission per 1000 maternities ranged from 0.3 (95% CI 0.1–0.4) and 0.4 (95% CI 0.2–0.7), in Finland and Norway, respectively, to 0.8 (95% CI 0.6–to 1.1) in Denmark and 1.9 (95% CI 1.5–2.4) in Sweden. The estimated pooled incidence of non-COVID admissions with concurrent SARS-CoV-2 infection per 1000 maternities was 1.1 (95% CI 0.4–3.5; I^2=91.7, tau^2=1.6, P=0.00), ranging from 0.3 (95% CI 0.2–0.6) in Finland to 2.4 (95% CI 2.0–2.8) in Denmark and 8.5 (95% CI 7.7 to 9.5) in Sweden.

The incidence of COVID-19-related admissions varied over time in each country; Figure 3 shows the incidence per average number of maternities by month, together with the main public health interventions by country.

3.1 | Risk factors

The characteristics of the women by admission group are described in Table 1. In the meta-analysis comparing characteristics among women with COVID-19-related admission with non-COVID admissions, obesity and asthma were risk factors for COVID-19 admission (crude relative risk [RR] 2.04, 95% CI 1.08–3.83, I^2=32.4%, P=0.218) and crude RR 2.02 (95% CI 1.14–3.55, I^2=0%, P=0.474), respectively (Figure 4).

3.2 | Secondary maternal and perinatal outcomes

In 2020, a total of 21 women needed treatment in an intensive care unit due to COVID-19, 14 of them (66.7%) in Sweden. Women with COVID-19-related admission delivered more frequently by cesarean section (RR 1.6, 95% CI 1.02–2.41, I^2=45.8%, P=0.041).

There were 21 preterm deliveries (15.3%) in the group of women admitted for COVID-19 symptoms vs 46 (9.7%) in the group admitted for non-COVID-19 reasons (pooled RR 1.5; 95% CI 0.6–3.9, P=0.265, I^2=22%; 95% CI 0%–75%, Cochran's Q=3.85, df=3, P=0.279).

There were fewer than three maternal deaths in the group admitted for COVID-19 symptoms and no maternal deaths in the group with admissions for other reasons. There were no stillbirths or neonatal deaths among births to women in the COVID-19 admission group during the study period. Women in the non-COVID group experienced four stillbirths due to primary causes other than COVID-19.

4 | DISCUSSION

This study shows considerable variation in the incidence of COVID-19-related admissions among pregnant women in the Nordic countries, ranging from no admissions (Iceland) to almost 2/1000 maternities (Sweden) during 2020. In the setting of similar obstetric healthcare services and background populations,[11] this indicates that suppression policies aimed to reduce viral transmission also protected pregnant women.

Two waves of infections were observed during 2020, and all countries tested symptomatic pregnant women and also identified contacts after the first initial weeks of the pandemic.[19] The incidence of COVID-19-related admission among pregnant women mirrors previous publications describing the incidence of SARS-CoV-2 infection among the general population in the Nordic countries; the
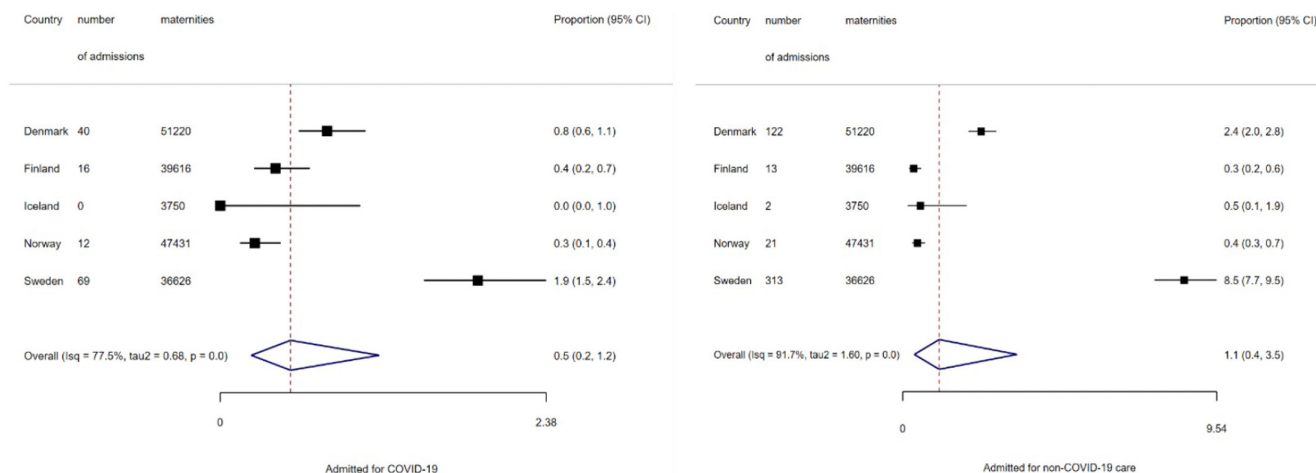

FIGURE 2 Incidence of admission with SARS-CoV-2 infection within 14 days of a positive PCR test per 1000 maternities, by admission group and country, March 1 to December 31, 2020.
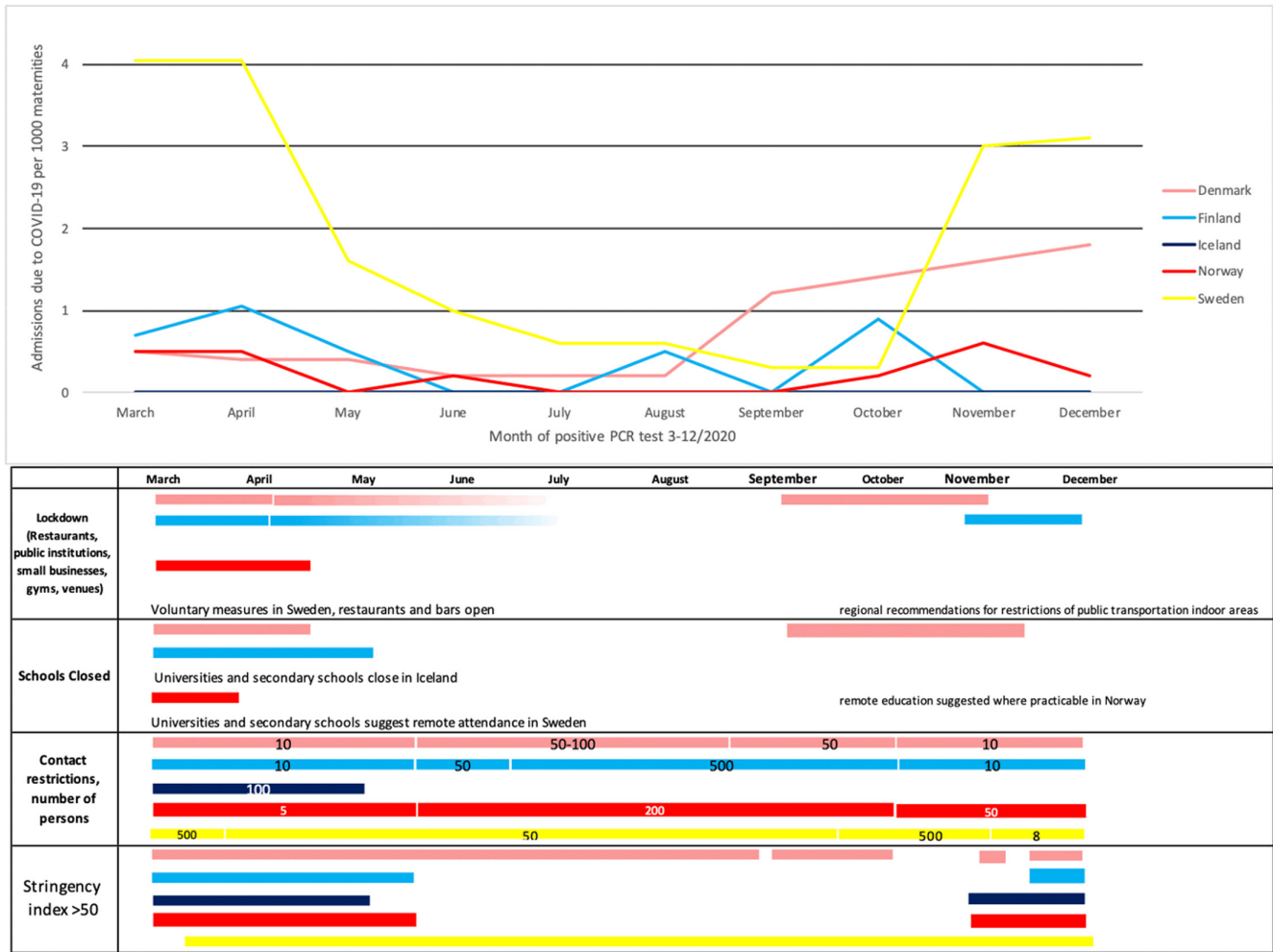
FIGURE 3 Upper panel, incidence of COVID-19-related admissions per 1000 maternal cases (average number of maternal cases per month), by month of positive PCR test and country. Lower panel, interventions implemented in each country, by month and the timing of Oxford Stringency Index >50 for each country.

peaks in incidence and hospital admissions were highest in Denmark and Sweden.[10] Norway had no pregnant patients that required intensive care treatment in 2020, and intensive care admission rates for COVID-19 were low overall.[20] Sweden had less stringent public health measures, and the implementation of such measures happened later than in the other countries.[10,21–23] It has been shown that early implementation of interventions and a higher Oxford SI was associated with a reduction in deaths.[5] In the current study, countries with an early SI >50 had a lower incidence of COVID-19-related admissions for pregnant women.

Although some maternal characteristics and pre-pregnancy medical conditions were risk factors for COVID-19 admissions, differences in these factors across countries are not likely to explain the differences in incidence of COVID-19-related admissions.[11] Women with COVID-19-related admission were more often obese and asthmatic and were more likely to deliver by cesarean than were other pregnant women admitted for other healthcare with a concurrent SARS-CoV-2 infection. These findings are in line with previous studies.[12,24] However, cesarean sections for any indication were included and not limited to COVID-19. In countries with fewer cases,

chance variation in other indications could impact the proportion estimate.[18] The number of women with either hypertension or diabetes prior to pregnancy, or gestational diabetes or preeclampsia was low. However, there were differences in the comorbidity rates between Sweden and the other Nordic countries, which may be due to underreporting. Sweden did not have register linkages and thus some comorbidities may have gone undetected.[25]

Maternal mortality increased in the UK and the USA during the pandemic, which was attributed to both COVID-19 disease and indirect effects of the pandemic, such as reduced contact with healthcare, reduction in quality of care due to health system workload and adverse mental health.[25,26] Similar surveillance in India showed that suppression of public health strategies and strict lock-downs were associated with reduced access to pregnancy-related healthcare and increase in adverse outcomes.[27] Maternal deaths are very rare in the Nordic countries,[28] with an overall estimate of six maternal deaths per 100 000 live births in 2005–2017. Maternal mortality reviews for 2020 have not yet been completed in all Nordic countries.

During the initial 4 months of the pandemic, a slight overall reduction in preterm births in addition to an increase in stillbirths

TABLE 1 Characteristics of pregnant women admitted to hospital because of COVID-19 infection in the Nordic countries between March 1 and December 31, 2020, by admission group and country (Denmark, Finland and Norway combined).

	COVID-19-related admission		Non-COVID admissions	
	Denmark, Finland, Iceland and Norway	Sweden	Denmark, Finland, Iceland and Norway	Sweden
	n = 68	*n* = 69	*n* = 158	*n* = 313
Age				
Mean age (SD)	Denmark 30.8 (4.8)	32.6 (5.0)	Denmark 31.4 (4.3)	31.9 (5.0)
	Finland 31.2 (4.8)		Finland 28.7 (6.0)	
			Iceland 28 (1.4)	
	Norway 32.2 (4.7)		Norway 32.7 (4.6)	
<35 years, *n* (%)	51 (75.0%)	39 (56.5%)	122 (77.2%)	212 (67.7%)
≥35 years	17 (25.0%)	27 (39.1%)	34 (21.5%)	92 (29.4%)
Missing	0	3 (4.3%)	0	9 (2.9%)
Body mass index				
Mean BMI (SD)	Denmark 27.8 (6.8)	29.2 (6.3)	Denmark 23.7 (4.2)	26.5 (5.0)
	Finland 30.8 (7.2)		Finland 27.7 (6.5)	
			Iceland 35.3 (8.8)	
	Norway 25.9 (2.8)		Norway 25.1 (4.7)	
<25, *n* (%)	24 (35.3%)	19 (27.5%)	90 (57.0%)	139 (44.4%)
25–29	22 (32.4%)	20 (29.0%)	51 (32.3%)	89 (28.4%)
30–34	16 (23.5%)	17 (24.6%)	12 (7.6%)	60 (19.2%)
≥35	10 (14.7%)	9 (13.0%)	7 (4.4%)	15 (4.8%)
Obese BMI ≥30				
N (%)	26 (38.2%)	28 (40.6%)	19 (12.0%)	75 (24.0%)
Missing	0	4 (5.8%)	0	10 (3.2%)
Parity				
Nulliparous	34 (50.0%)	16 (23.2%)	82 (51.9%)	117 (37.4%)
Parity missing	0	2 (2.9%)	0	2 (0.6%)
Multiple pregnancy				
Singleton pregnancy, *N* (%)	68 (100%)	66 (95.7%)	153 (96.8%)	308 (98.4%)
Migrant background, *N* (%)				
Country of birth missing, *n* (%)	58 (73.5%)	35 (68.6%)	63 (39.9%)	97 (53.3%)
	4 (5.9%)	6 (11.8%)	8 (5.1%)	34 (18.6%)
Comorbidities				
Pre-pregnancy medical problem	17 (25.0%)	4 (5.8%)	21 (13.3%)	21 (16.0%)
Hypertension	<3	<3	0	4 (1.3%)
Diabetes	3 (4.4%)	<3	<3	6 (1.9%)
Asthma	14 (20.6%)	<3	10 (6.3%)	11 (3.5%)
Missing information for preexisting disease	0		0	
Gestational diabetes	11 (16.2%)	10 (14.5%)	12 (7.6%)	22 (7.0%)
Gestational hypertension	<3	0	3 (1.9%)	11 (3.5%)
Gestational disease missing	0		0	

TABLE 1 (Continued)

	COVID-19-related admission		Non-COVID admissions	
	Denmark, Finland, Iceland and Norway	Sweden	Denmark, Finland, Iceland and Norway	Sweden
	$n = 68$	$n = 69$	$n = 158$	$n = 313$
Gestational age when testing Covid-positive, gestational week+days				
Median (IQR)	Denmark 27+5 (23+5 to 31+6)	33+2 (28+6 – 36+4)	Denmark 39+1 (22+5 – 40+1)	38+6 (36+2 to 40+1)
	Finland 31+4 (26+0 to 33+5)		Finland 39+1 (38+0 to 40+1)	
			Iceland 38+6 (IQR not available)	
	Norway 28+0 (23+6 to 35+4)		Norway 38+4 (34+6 to 39+4)	

Abbreviations: BMI, body mass index (kg/m^2); IQR, interquartile range; SD, standard deviation.
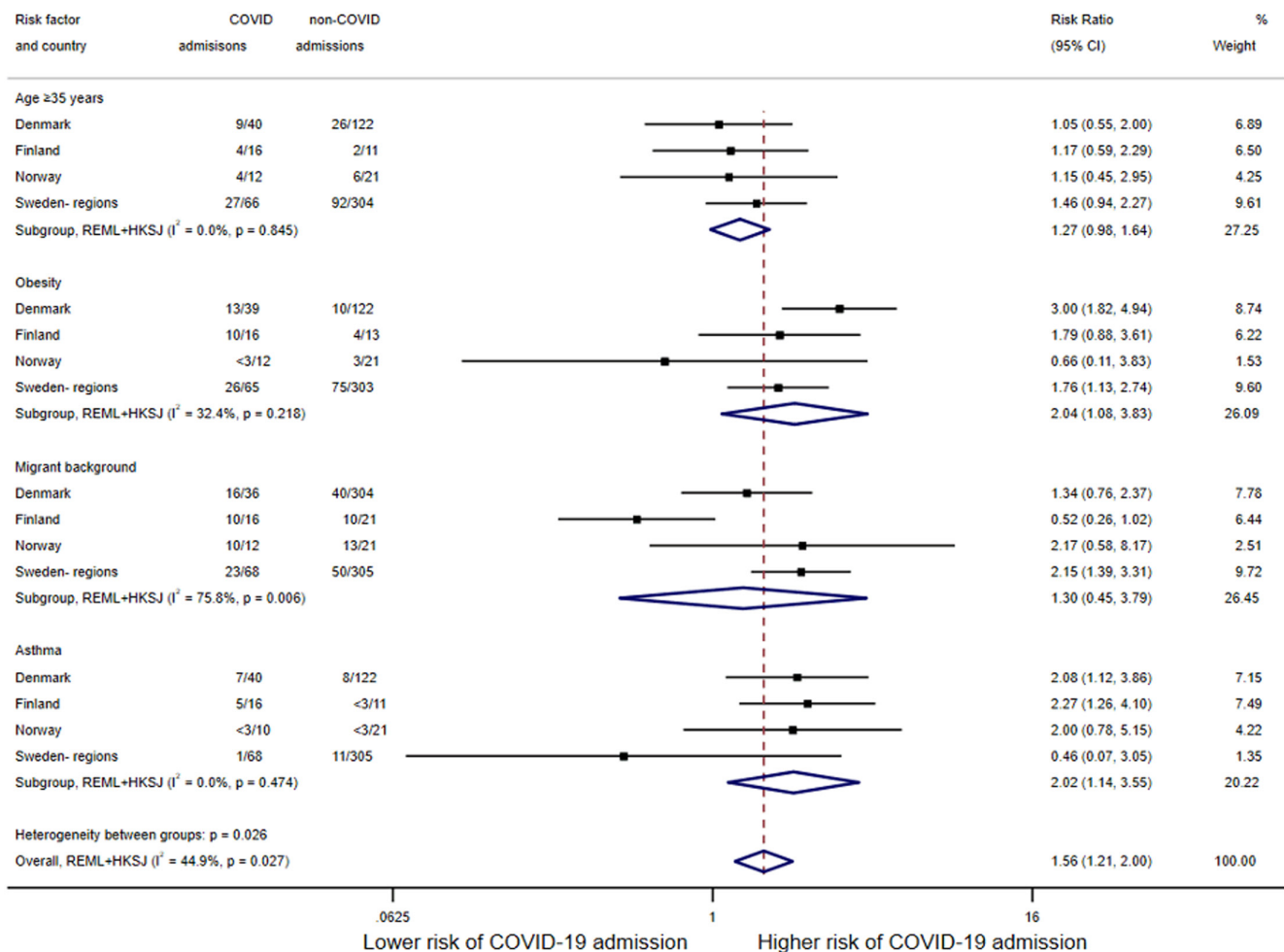
FIGURE 4 Risk ratio for COVID-19-related admissions in the Nordic countries stratified by age, obesity, migrant background and asthma, March 1 to December 21 2020, by country.

was noted in a large international study.[29] In our study, we found that women with COVID-19 during pregnancy had a higher risk of pre-term birth. However, there was no change in the overall rates of preterm birth or stillbirth in the Nordic countries in 2020.[11] A comprehensive and robust assessment of perinatal outcomes would require a longer study period than 10 months to reduce risk of bias,

such as selection of pregnancies ending at earlier gestation and with more severe outcomes.

The group of women admitted for non-COVID-19 healthcare was heterogeneous and does not represent the average pregnant population.[13] Some of the women had low obstetric risk and presented with coincidental mild or asymptomatic SARS-CoV-2 infection at the time of normal labor, whereas others were admitted for high-risk pregnancy complications. Denmark and some of the Swedish regions implemented screening of all pregnant women admitted to hospital during the study period; this strategy impacts identification of asymptomatic infection and might also explain the relatively higher rate of test-positives in Denmark.[19] Thus, the results of the non-COVID admissions have to be interpreted with caution, as the group of women admitted for COVID-19 symptoms is likely to present the real incidence of pregnant women with relatively severe COVID-19 symptoms.

The past experiences and ongoing activities of the NOSS study group enabled rapid planning and implementation of aligned case report forms. The availability of clinical information about the cause of admission was essential to avoid incorrect attribution of severe pregnancy outcomes among asymptomatic women with obstetric complications, to complications caused by the viral infection itself.[30]

The current study had several strengths. We obtained source population information and access to clinical data, which enabled incidence analyses and comparisons across countries. As the study population was mostly national, the population denominator was clearly defined. In addition, we discriminated between admissions due to COVID-19 and for non-COVID-19 reasons (such as admissions for pregnancy-related healthcare). As pregnant women are more likely to receive hospital care (related to the pregnancy and childbirth) than their non-pregnant peers, the achieved reduction of potential misclassification bias is particularly important. The current results give insight into the admissions, as previous studies with only registry-based codes for hospitalizations could not differentiate between the causes for admission.[31]

The population-based design also reduced the risk of selection bias in hospital admissions. However, the study also has limitations. Caution is required in the interpretation of the Swedish results, as data was available only from specific areas (31% of all births). The three participating university hospitals are referral institutions regionally and nationally and were located in geographic areas with high viral transmission early in the pandemic.[32] This may have led to selection bias regarding severe maternal morbidity, such as intensive care unit admission, as well as hospital admission in general.

The study cannot assess the incidence of infection and outcomes for pregnant women who were not hospitalized during infection. The chosen testing interval has been shown to identify all cases of acute infection.[33]

We encountered several barriers affecting both the study implementation and analysis of the results. Strict national interpretation of the General Data Protection Regulation (GDPR) prevented sharing of individual health information, even in anonymous format. Federated analysis of aggregate data rather than collection of individual data in one dataset, and the small national datasets with few or no observations in subgroups, limited adjusted analyses.

Linkage of national health registries and official statistics have been shown to be very important for data quality on severe outcomes such as maternal deaths.[34] Registry linkages may also reduce the reporting burden for clinicians. However, previous experience in the NOSS collaboration has shown that additional quality control is necessary when studying rare, severe outcomes.[35] In our study, high data costs and linkage fees along with delays in linkage approval and obtaining registry data were considerable barriers while facing a societal emergency.

Public health policies play a significant and often unacknowledged role in disease prevention, whereas individual risk factors and characteristics are more straightforward to assess. This meta-analysis indicates that public health interventions aiming to reduce deaths and limit viral transmission also protected pregnant women from severe health and pregnancy outcomes. The differences in the incidence of COVID-19 admission between countries were clear. Risk factors for hospital admission were similar to previous studies, but different distribution of risk factors across the countries was not a reasonable explanation for the observed differences.

5 | CONCLUSION

The current study indicates that national suppression policies played a substantial role in reducing risk of COVID-19-related admission among pregnant women in Denmark, Finland, Iceland and Norway.

Improved preparedness for future timely monitoring of maternal and perinatal health in the Nordic countries during outbreaks, epidemics or pandemics can be facilitated by hibernated, approved protocols with available funding for study infrastructure and analysis.

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CONFLICT OF INTEREST STATEMENT

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

ETHICS STATEMENT

National ethical approval was obtained from the following authorities:

Denmark: Danish Patient Safety Authority (reg. no. 31–1521–252: April 24, 2020) and the regional Data Protection Agency in Region Zealand (reg. no. REG-022–2020: March 23, 2020).

Finland: Helsinki University Hospital. (reg. no. HUS1624/2020: May 13, 2020) and the Finnish Institute for Health and Welfare (THL/5451/14.02.00/2020).

Iceland: Landspitali University Hospital, the National Bioethics Committee (reg. no. VSNb2020050016/03.0I: June 25, 2020) and the Icelandic Data Protection Authority (reg. no. 20–106: June 9, 2020).

Norway: Norwegian Institute of Public Health, Data Protection Officer (reg. no. 20_11054: April 3, 2020) and the Western Regional Ethics Committee (reg. no. 125890: March 26, 2020).

Sweden: The Swedish Ethical Review Authority (reg. no. 2020–03012: August 11, 2020 for SaUH and SkUH and reg. no. 2020–01499: April 22, 2020 for KUH).

In Denmark, Iceland, Norway and KUH, ethical approval exempted the studies from obtaining individual consent. In Finland, ethical approval is not required in register-based studies. In SaUH and SkUH, women received written information about the study, including an opt-out possibility. Data was managed and stored in accordance with national regulations and the General Data Protection Regulation (GDPR). National numbers of three or less are not presented to avoid identification.

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SUPPORTING INFORMATION

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