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COVID-19 Antiviral Medication Use Among Pregnant and Recently Pregnant US Outpatients

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Background. Pregnant people are at risk of severe coronavirus disease 2019 (COVID-19) and associated complications. While withholding treatment from pregnant patients is not recommended, little is known about the frequency of antiviral medication use during pregnancy.

Methods. Using Medicaid and commercial insurance databases, we constructed a national claims-based cohort study of pregnant, recently pregnant, and nonpregnant female patients 18–49 years old with an outpatient diagnosis of COVID-19 between 21 December 2021 and 30 September 2022. Outpatient treatment with a recommended antiviral medication was identified within 5 days of diagnosis, using national drug codes in outpatient prescription drug claims. Propensity score–matched prevalence ratios (PRs) were used to compare antiviral treatment by pregnancy status.

Results. A total of 412 755 publicly and privately insured patients with COVID-19 were identified, including 33 855 currently pregnant, 2460 recently pregnant, and 376 440 nonpregnant female patients; 6.8% had a record of antiviral medication use, including 1.3% of pregnant, 5.4% of recently pregnant, and 7.3% of nonpregnant women. Most commonly ritonavir-boosted nirmatrelvir was administered. The prevalence of antiviral medication use was 67% lower among pregnant patients compared with nonpregnant patients (PR, 0.33 [95% confidence interval, .30–.36]), even among patients with ≥1 high-risk medical condition (0.29 [.25–.33]). Antiviral medication use was slightly lower among recently pregnant women with ≥1 high-risk medical condition than among nonpregnant women with similar conditions (PR, 0.57; [95% confidence interval, .44–.72]).

Conclusions. Despite US clinical guidelines, we observed low rates of outpatient treatment for COVID-19 among pregnant patients, indicating possible missed opportunities to treat COVID-19 illness during pregnancy and lactation.

Keywords. COVID-19; SARS-CoV-2; pregnancy; antiviral medication; treatment.

Pregnant people are at risk of severe coronavirus disease 2019 (COVID-19) illness, which has been shown to result in fetal and neonatal health complications [1, 2]. The odds of admission to an intensive care unit and the need for invasive ventilation following COVID-19 illness are 2-fold higher in pregnant and recently pregnant people compared with nonpregnant women of reproductive age [1]. Severe COVID-19 illness during pregnancy has been linked to increased risks of preterm birth, cesarean delivery, and fetal growth restriction [1].

As COVID-19 can be severe during pregnancy, timely, appropriate treatment could reduce the risk of severe disease and subsequent adverse maternal, fetal, and neonatal outcomes. The COVID-19 Treatment Guidelines Panel of the National Institutes for Health (NIH) have recommended against withholding treatment from pregnant or lactating individuals [3]. The panel recommended ritonavir-boosted nirmatrelvir (NMV/r) for treatment in nonhospitalized pregnant patients with mild-to-moderate COVID-19 at risk for progression to severe illness [3]. Remdesivir could be used to treat nonhospitalized adults with mild to moderate COVID-19, including pregnant patients [3]. Although not used as frontline medications, molnupiravir, and bebtelovimab were also made available to treat pregnant patients where other therapeutic options are unavailable (see Supplementary Table 1) [3, 4].

These US-based treatment guidelines stand in contrast with those from other national health authorities. Historically, the National Health Service in the United Kingdom, the

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Department of Health and Aged Care in Australia, and the government of Canada have not explicitly recommended COVID-19 antiviral medication use during pregnancy [5]. More recently the Canadian government has recommended that COVID-19 treatment decisions be made using shared decision making [6]. The European Medicine Agency recommends against the use of antiviral medication during pregnancy and among women of reproductive potential who are not using contraception [7]. Furthermore, as with COVID-19 vaccine trials [8, 9], pregnant people have been excluded from clinical trials evaluating COVID-19 therapeutics [10]. One review demonstrated that 80% of clinical trials for COVID-19 treatments specifically excluded pregnant participants [11]. The evidence supporting the safety and effectiveness of COVID-19 treatments during pregnancy is therefore limited, which may influence hesitancy to prescribe and/or use antiviral medications during pregnancy and lactation. Here, we quantify and compare patients with COVID-19 treated with antiviral medication overall and among pregnant, recently pregnant, and nonpregnant patients in the United States.

METHODS

Data Collection

We conducted a national US claims-based cohort study of pregnant, recently pregnant, and nonpregnant female patients aged 18–49 years with an outpatient diagnosis of COVID-19 using the Merative MarketScan commercial claims and multistate Medicaid database (2017–2022). MarketScan databases are among the largest and longest running proprietary US claims databases, providing deidentified, longitudinal, patient-level claims data for >273 million unique patients [12]. Data are sourced from employers, states, health plans, hospitals, and electronic medical records and include information on health insurance, Medicaid and Medicare eligibility, medical claims and encounters, prescription drug claims, benefit plan information, hospital discharge information, and mortality data [12]. The study period began after the first date of emergency use authorization for an outpatient therapeutic (NMV/r, authorized on 21 December 2021) and ended on the last date of available data (30 September 2022).

Study Sample and Eligibility Criteria

The study cohort was restricted to pregnant patients who were (1) aged 18–49 years, (2) had an outpatient record of a COVID-19 diagnosis, and (3) had pharmaceutical benefits coverage. We identified COVID-19 diagnoses from outpatient claims data using *International Classification of Diseases, Tenth Revision, Clinical Modification* codes (U07.1, J12.82). We used a previously validated algorithm [13] to identify pregnancies within the cohort, using inpatient and outpatient claims data. The algorithm uses inpatient and outpatient medical encounters to estimate gestational age and assign a pregnancy start and end date [13]. For comparison, a random sample of nonpregnant women of reproductive age (18–49 years) were selected from the MarketScan data with no indication of a pregnancy during their enrollment.

Participants were categorized as (1) pregnant, (2) recently pregnant, or (3) nonpregnant. Pregnant patients had a date of diagnosis on or after the date of pregnancy start and on or before the date of pregnancy end. Recently pregnant patients with a record of live birth were selected as a proxy for "lactating" people, since identification of breastfeeding is challenging in administrative health data. Recently pregnant patients had a date of diagnosis during the 3 months following a live birth, a period when >80% of infants are still breastfed [14]. Nonpregnant patients were nonpregnant women of reproductive age who had a date of COVID-19 diagnosis during the study period. For those with multiple COVID-19 diagnoses during the study period, we restricted analyses to the first COVID-19 diagnosis identified.

Identification of COVID-19 Antiviral Medication

We identified recommended and available COVID-19 antiviral medications using national drug codes in pharmaceutical claims records (Supplementary Table 1). Consistent with National Institutes of Health treatment guidelines for COVID-19 [3] and antiviral medications for consideration during pregnancy [4], medications extracted for this analysis included remdesivir, NMV/r, molnupiravir, and bebtelovimab. We considered a patient "treated" if there was a record of a medication dispensed within 3 days of the date of COVID-19 diagnosis.

Covariate Information

Participants' ages were derived from health plan enrollment information. Medical conditions placing patients at high-risk of progression to severe COVID-19 were extracted from all available outpatient and inpatient claims records during the year preceding the COVID-19 diagnosis [15]. High-risk medical conditions included asthma, diabetes, chronic heart conditions, obesity, chronic kidney disease, liver disease, pulmonary fibrosis, cystic fibrosis, cancer, immunocompromising conditions, tuberculosis, organ transplantation, disability, neurological conditions, mental health conditions, and cigarette smoking. For pregnant patients, we also identified the gestational age at infection based on the estimated date of pregnancy start and the date of COVID-19 diagnosis.

Statistical Analysis

We estimated the proportion of COVID-19 patients who received treatment with a recommended antiviral medication, overall and by pregnancy status. Descriptive analyses examined the characteristics of patients with treated and untreated COVID-19 by pregnancy status. To compare the rate of treatment among pregnant or recently pregnant versus nonpregnant patients, we fit a log-binomial regression model with pregnancy status as an independent variable and treatment status as the

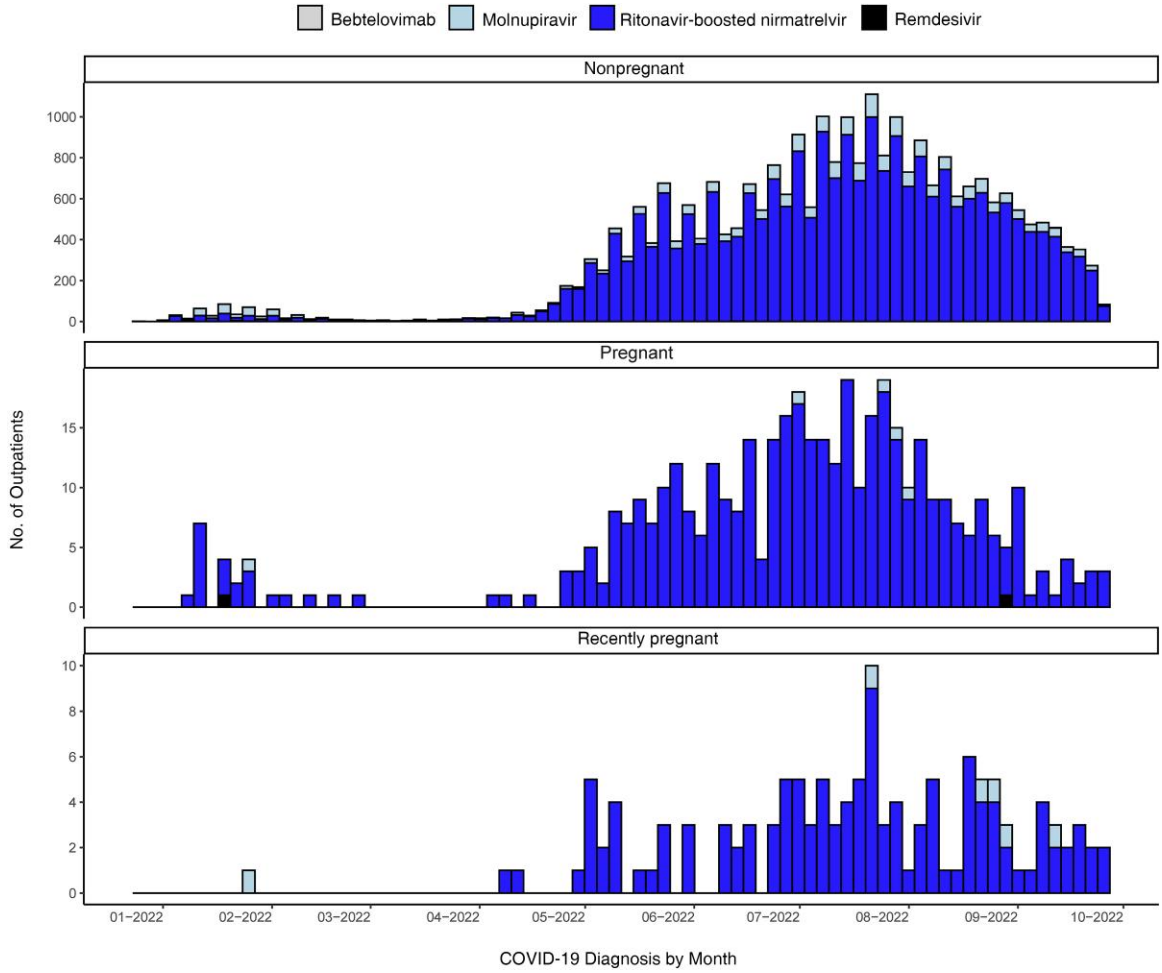

Figure 1. Distribution of antiviral medications used to treat coronavirus disease 2019 (COVID-19) among outpatients, by pregnancy status.

outcome variable. We adjusted for age group (18–24, 24–29, 30–34, 35–39, or ≥40 years), month and year of COVID-19 diagnosis, insurance health plan (commercial insurance, Medicaid), and the presence of a high-risk medical condition.

We also fit propensity score (PS)–matched models, matching pregnant to nonpregnant patients (1:4) and recently pregnant to nonpregnant patients (1:4), using nearest-neighbor matching (0.05 caliper) with replacement. Matching was performed using the MatchIt package in R software (version 4.3.2). Covariate balance was checked after matching by plotting and comparing standardized mean differences in covariates between matched and unmatched samples. We considered a standardized mean difference <0.1 to indicate covariate balance. PSs were calculated using logistic regression, with pregnancy status as the dependent variable and age group, presence of a high-risk medical condition, month and year of COVID-19 diagnosis, and insurance health plan as independent variables. Log-binomial regression models were used to estimate prevalence ratios (PRs), comparing the prevalence of treatment after PS matching.

Ethics Statement

This research used deidentified existing health records and was deemed human subjects review exempt by the National Institutes of Health and the institutional review board of the University of San Francisco

RESULTS

Among 412 755 outpatients with COVID-19 (see Supplementary Figure 1), we identified 376 440 COVID-19 cases in nonpregnant, 33 855 in pregnant, and 2460 in recently pregnant patients. In total, 27 978 of the 412 755 outpatients (6.8% [95% confidence interval (CI), 6.7%–6.9%]) were treated with an antiviral medication, including 27 422 nonpregnant (7.3% [7.2%–7.4%]), 424 pregnant (1.3% [1.1%–1.4%]), and 132 recently pregnant patients (5.4% [4.5%–6.3%]). Most commonly, patients were dispensed NMV/r (25 432 of 27 978 [90.9%]), and the rest were treated with molnupiravir (2535 of 27 978 [9.1%]) or intravenous remdesivir (10 of 27 978 [<0.1%]) (Figure 1); 1 nonpregnant

Table 1. Characteristics of Nonpregnant, Pregnant, and Recently Pregnant Outpatients With Coronavirus Disease 2019 (N = 412 755) by Treatment Status

Characteristic	Nonpregnant Patients, No. (%) (n = 376 440)		Pregnant Patients, No. (%) (n = 33 855)		Recently Pregnant Patients, No. (%) (n = 2460)	
	Treatment[a] (n = 27 422)	No Treatment (n = 349 018)	Treatment[a] (n = 424)	No Treatment (n = 33 431)	Treatment[a] (n = 132)	No Treatment (n = 2328)
Antiviral medication dispensed						
NMV/r	24 889 (90.8)	NA	417 (98.3)	NA	126 (95.5)	NA
Molnupiravir	2524 (9.2)	NA	5 (1.2)	NA	6 (4.5)	NA
Remdesivir	8 (<0.1)	NA	2 (0.5)	NA	0 (0)	NA
Bebtelovimab	1 (<0.1)	NA	0 (0)	NA	0 (0)	NA
Patient age						
18–24 y	3069 (11.2)	82 245 (23.6)	90 (21.1)	7437 (22.2)	16 (12.1)	524 (22.5)
25–29 y	2718 (9.9)	48 903 (14.0)	93 (21.5)	9584 (28.7)	22 (16.7)	609 (26.2)
30–34 y	3813 (13.9)	54 953 (15.7)	135 (31.8)	10 128 (30.3)	45 (34.1)	698 (30.0)
35–39 y	5212 (19.0)	59 501 (17.0)	83 (19.6)	5143 (15.4)	39 (29.5)	394 (16.9)
>39 y	12 610 (46.0)	103 416 (29.6)	23 (5.4)	1139 (3.4)	10 (7.6)	103 (4.4)
Insurance type						
Public	4114 (15.0)	93 055 (26.7)	192 (45.3)	15 509 (46.4)	47 (35.6)	1105 (47.5)
Private	23 308 (85.0)	255 963 (73.3)	232 (54.7)	17 922 (53.6)	85 (64.4)	1223 (52.5)
High-risk conditions						
≥1 condition	19 398 (70.7)	199 621 (57.2)	199 (46.9)	13 108 (39.2)	58 (43.9)	932 (40.0)
Asthma	5719 (20.9)	50 545 (14.5)	43 (10.1)	3373 (10.1)	21 (15.9)	235 (10.1)
Diabetes	3062 (11.8)	22 870 (6.6)	15 (3.5)	779 (2.3)	5 (3.8)	52 (2.2)
Heart condition	1406 (5.1)	12 196 (3.5)	4 (0.9)	466 (1.4)	2 (1.5)	31 (1.3)
Obesity	8588 (31.3)	75 452 (21.6)	65 (15.3)	4496 (13.4)	27 (20.5)	365 (15.7)
CKD	243 (0.9)	2700 (0.8)	1 (0.2)	68 (0.2)	0 (0)	6 (0.3)
Liver disease	2277 (8.3)	19 302 (5.5)	6 (1.4)	781 (2.3)	6 (4.5)	70 (3.0)
Pulmonary fibrosis	90 (0.3)	819 (0.2)	3 (0.7)	29 (0.1)	0 (0)	3 (0.1)
Cystic fibrosis	14 (0.1)	142 (<0.1)	0 (0)	15 (<0.1)	0 (0)	0 (0)
Cancer	1078 (3.9)	7355 (2.1)	3 (0.7)	229 (0.7)	4 (3.0)	17 (0.7)
Immunocompromise	1562 (5.7)	11 057 (3.2)	11 (2.6)	485 (1.5)	8 (6.1)	39 (1.7)
Tuberculosis	19 (0.1)	259 (0.1)	1 (0.2)	19 (0.1)	0 (0)	1 (<0.1)
Organ transplant	51 (0.2)	725 (0.2)	0 (0)	19 (0.1)	0 (0)	0 (0)
Disability	2673 (9.7)	28 698 (8.2)	27 (6.4)	1430 (4.3)	10 (7.6)	105 (4.5)
Neurological condition	4549 (16.6)	40 807 (11.7)	27 (6.4)	1647 (4.9)	10 (7.6)	106 (4.5)
Mental health condition	9063 (33.1)	98 507 (28.2)	105 (24.8)	6243 (18.7)	18 (13.6)	450 (19.3)
Smoking	3424 (12.5)	48 197 (13.8)	62 (14.6)	4269 (12.8)	15 (11.4)	306 (13.1)
No high-risk conditions	8024 (29.3)	149 397 (42.8)	225 (53.1)	20 323 (60.8)	74 (56.1)	1396 (60.0)
Gestational age at infection						
0–13 wk	NA	NA	38 (9.0)	7037 (21.1)	NA	NA
14–27 wk	NA	NA	154 (36.3)	12 114 (36.2)	NA	NA
≥28 wk	NA	NA	232 (54.7)	14 280 (42.7)	NA	NA

Abbreviations: CKD, chronic kidney disease; NA, not applicable; NMV/r, ritonavir-boosted nirmatrelvir.

[a]Treatment was defined as a record of a coronavirus disease 2019 antiviral medication within 3 days of the date of diagnosis, as recorded in the patient's outpatient drug claims.

patient had a record of treatment with bebtelovimab. Most treated patients had COVID-19 diagnosed between May and September 2022.

Compared with pregnant patients, proportionally more treated nonpregnant and recently pregnant patients were aged 35–49 years and had private health insurance (Table 1). While treatment rates increased with age for nonpregnant and recently pregnant patients, we observed no such trend for pregnant patients (Table 1); 85% of nonpregnant and 64% of recently pregnant patients who received treatment had private health insurance, compared with 55% of pregnant patients who received treatment. Treatment rates were also higher for nonpregnant and recently pregnant patients with private health insurance (8.3% and 6.5%, respectively) compared with nonpregnant and recently pregnant patients with Medicaid (4.2% and 4.1%, respectively). No such difference was observed for pregnant patients (1.3% for those with commercial insurance and 1.2% for those with Medicaid).

Among pregnant patients who received antiviral treatment, 9% were in the first trimester, 36% in the second trimester, and 55% in the third trimester of pregnancy. A higher proportion of untreated pregnant patients were in the first trimester of pregnancy (21%) and fewer were in the third (43%) (Table 1). PS matching showed good balance between pregnant and

nonpregnant patients (Supplementary Figure 2) and recently pregnant and nonpregnant patients (Supplementary Figure 3). PS-matched models indicated that pregnant patients were treated 67% less frequently compared with nonpregnant patients (PR, 0.33 [95% CI, .30–.36]). The prevalence of treatment was also slightly lower among recently pregnant people (PR 0.72 [95% CI, .61–.85]).

Fifty-eight percent of nonpregnant, 39% of pregnant, and 40% of recently pregnant patients had a high-risk medical condition (Table 1). The percentage of patients identified with a high-risk medical condition was higher among the treated group, with 71% of treated nonpregnant, 47% of treated pregnant, and 44% of treated recently pregnant patients having evidence of a high-risk medical condition. The most common high-risk medical conditions among treated nonpregnant patients were mental health conditions (33%), obesity (31%), asthma (21%), neurological conditions (17%), and diabetes (12%). The prevalence of these conditions was lower among pregnant and recently pregnant patients who received antiviral treatment.

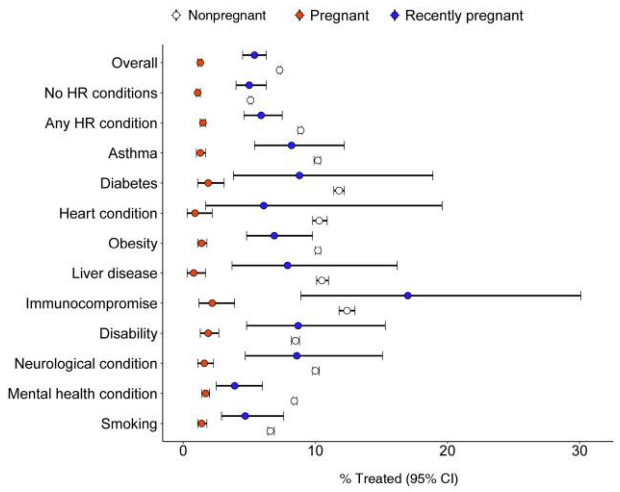

Figure 2. Percentage of outpatients with a clinical diagnosis of coronavirus disease 2019 who received a recommended antiviral treatment, by pregnancy status. Abbreviations: CI, confidence interval; HR, high-risk.

Correspondingly, we observed a higher prevalence of antiviral treatment for nonpregnant and recently pregnant patients with a high-risk medical condition (8.9% [95% CI 8.7%–5.2%] and 5.9% [4.6%–7.5%], respectively) compared with pregnant patients (1.5% [1.3%–1.7%]) (Figure 2). PS-matched models indicated that pregnant patients with a high-risk medical condition were 71% less likely to receive treatment than their nonpregnant counterparts (PR 0.29 [95% CI, .25–.33]) (Table 2). Recently pregnant patients similarly had lower rates of treatment than nonpregnant patients (PR 0.57 [95% CI, .44–.72]).

Compared with those with a high-risk medical condition, proportionally fewer patients without a high-risk medical condition were treated. A similar proportion of nonpregnant (5.1% [95% CI, 5.0%–5.2%] and recently pregnant (5.0% [4.0%–6.3%]) patients without a high-risk medical condition who received antiviral treatment were observed (PR, 0.93 [.74–1.16]) (Table 2). In contrast, 1.1% (95% CI, 1.0%, 1.3%) of pregnant patients with no high-risk medical condition received antiviral treatment, which was 63% lower than their nonpregnant counterparts (PR, 0.37 [.33–.42]).

DISCUSSION

In our study, treatment of COVID-19 was low among eligible pregnant, recently pregnant, and nonpregnant US outpatients.

Table 2. Prevalence Ratios Comparing Rates of Treatment for Coronavirus Disease 2019 in Pregnant and Recently Pregnant Patients Versus Nonpregnant Female Patients of Reproductive Age

Patient Category	No. of Patients	Proportion Treated (95% CI), %	PR (95% CI)		
			Unadjusted	Adjusted[a]	PS Matched[a]
Among all patients					
Nonpregnant	376 440	7.3 (7.2–7.4)	Reference	Reference	Reference
Pregnant	33 855	1.3 (1.1–1.4)	0.17 (.16–.19)	0.35 (.32–.38)	0.33 (.30–.36)
Recently pregnant	2460	5.4 (4.5–6.3)	0.74 (.62–.87)	0.62 (.52–.72)	0.72 (.61–.85)
Among patients with health conditions					
Nonpregnant	219 019	8.9 (8.7–9.0)	Reference	Reference	Reference
Pregnant	13 307	1.5 (1.3–1.7)	0.17 (.15–.19)	0.35 (.31–.40)	0.29 (.25–.33)
Recently pregnant	990	5.9 (4.6–7.5)	0.66 (.51–.84)	0.55 (.42–.69)	0.57 (.44–.72)
Among patients with no health conditions					
Nonpregnant	157 421	5.1 (5.0–5.2)	Reference	Reference	Reference
Pregnant	20 548	1.1 (1.0–1.3)	0.21 (.19–.24)	0.41 (.35–.46)	0.37 (.33–.42)
Recently pregnant	1470	5.0 (4.0–6.3)	0.98 (.78–1.22)	0.79 (.63–.97)	0.93 (.74–1.16)

Abbreviations: CI, confidence interval; PR, prevalence ratio; PS, propensity score.

[a]Adjusted PRs were estimated using log-binomial regression models accounting for age group, month and year of coronavirus disease 2019 diagnosis, and presence of ≥1 high-risk medical condition and were clustered by insurance provider; PS-matched PRs were estimated from log-binomial regression models with pregnant or recently pregnant patients matched to nonpregnant patients (1:4) by means of PS.

We observed disparities in COVID-19 treatment by pregnancy status, with lower prevalence of antiviral medication use among pregnant patients compared with nonpregnant and recently pregnant patients. Although our study was not designed to identify the cause of this disparity, possible reasons could include clinician hesitancy to prescribe COVID-19 antiviral medications and/or patient hesitancy to use them. Irrespective of the underlying reason, our results show that <2% of pregnant patients with COVID-19 received antiviral medications. Furthermore, <2% of pregnant patients with an additional high-risk medical condition received recommended antiviral medications to reduce their risk of progression to severe disease. Our observation of higher rates of treatment among nonpregnant and recently pregnant patients suggests that pregnant patients in the United States are currently not receiving equitable recommended treatment for COVID-19 compared with their nonpregnant peers. Given the evidence in support of the effectiveness of NMV/r in preventing hospitalization and death in nonpregnant adults, this likely represents missed opportunities to prevent progression to more severe illness and health consequences in pregnant patient groups [16, 17].

The low treatment rates identified in our study align with other studies, including a recent US study showing that only 12% of eligible outpatients were treated with NMV/r [18]. Fewer studies have evaluated COVID-19 treatment among pregnant and recently pregnant patients. In a previous cross-sectional study of 35 pregnant and 5 recently pregnant vaccinated individuals with breakthrough severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections, the authors found that 18 of the 35 pregnant patients and 3 of the 5 recently pregnant patients were prescribed NMV/r, and 12 of 18 pregnant patients and 2 of 3 recently pregnant patients who were prescribed NMV/r reported taking the medication [19]. This corresponds to 34% and 40% treatment rates, respectively, among pregnant recently pregnant patients. While this is a single study with a small, selective sample, it suggests that low treatment rates are the result of a combination of provider hesitancy to prescribe and patient hesitancy to accept antiviral medication during pregnancy. Results from our larger, national investigation of treatment rates imply that treatment rates may be lower than previously reported.

Further investigation into the causes of these lower COVID-19 treatment rates is needed. Given the consistent evidence documenting safety concerns as a reason for vaccine hesitancy during pregnancy [20–22], it is possible that limited evidence on the safety and effectiveness of COVID-19 antiviral medications during pregnancy is a contributing factor. The majority of research supporting the safety of NMV/r has focused on experiences with ritonavir as part of antiretroviral therapy, mostly showing no adverse effects among human immunodeficiency virus (HIV)–infected pregnancies [5, 23] However, some studies have shown an increase in the rate of preterm birth among HIV-infected pregnant patients receiving ritonavir as part of antiretroviral therapy [24, 25]. The evidence on nirmatrelvir is more limited, but animal studies indicate no concerning developmental toxicity in rabbits or rats [26].

While no clinical trial has evaluated the safety or effectiveness of antiviral medications to treat COVID-19 among pregnant people, several small case series of NMV/r use during pregnancy have been conducted. A clinical case review involving 47 pregnant patients revealed no significant increase in serious adverse events following NMV/r treatment but did reveal an unexpectedly high rate of cesarean deliveries [27]. Fewer comparative studies have been conducted. A study in Taiwan of 85 pregnant patients, 30 of whom were treated with NMV/r, reported a higher rate of cesarean deliveries and small size for gestational age among NMV/r-treated patients [28]. A recent US study including 437 pregnant patients with COVID-19 who were counseled on NMV/r observed higher rates of preeclampsia among the 114 patients who took NMV/r [29]. The largest study to date included 2209 pregnant patients with COVID-19 in Hong Kong, 221 of whom received NMV/r [30]. Using a target trial emulation, the authors showed that NMV/r treatment during pregnancy was associated with lower maternal morbidity and mortality rates and reduced risks of cesarean delivery and preterm birth [30]. Given the limited evidence documenting the maternal, fetal, and neonatal health effects of NMV/r use during pregnancy, additional research on the safety and effectiveness of antiviral medications for treatment of COVID-19 is needed to support informed decision making among pregnant patients with COVID-19.

These limited data stand in contrast to the extensive evidence supporting the safety and effectiveness of antiviral medications to treat influenza during pregnancy. Pregnant people are also at higher risk of severe influenza, and oseltamivir is the frontline treatment for influenza in pregnancy [31]. Compared with the treatment rates observed here, higher treatment rates have been reported for oseltamivir, a medication with extensive data to support the safety of oseltamivir administration during pregnancy [32, 33]. Antiviral treatment among pregnant patients increased during the 2009 H1N1 pandemic [34], with treatment rates as high as 87% [35]. A more recent post–H1N1 pandemic study of 2786 patients presenting for outpatient care with an acute respiratory illness during the 2013–2014 influenza season found that treatment rates were high among pregnant people presenting for care early (3 of 7 patients [43%]) [36]; however, this study was restricted to an incredibly small sample of pregnant participants. Nevertheless, prior experience from oseltamivir treatment during pregnancy indicates that higher treatment rates among pregnant patients are possible.

Our study has several strengths and limitations. First, this was the largest study of antiviral medication used to treat COVID-19 during and around the time of pregnancy in the United States. Using comprehensive outpatient medical information for publicly and privately insured patients, we were able

to capture antiviral medication use throughout pregnancy and during the first few months postpartum. Medications like NMV/r are available by prescription only, with some exceptions. In March 2022, the Biden administration introduced the "Test to Treat" initiative [37], which allowed access to NMV/r to those tested for SARS-CoV-2 at pharmacies and health centers for on-site clinics. In July 2022, the Federal Drug Administration updated the emergency use authorization for NMV/r to allow pharmacists to prescribe the medication directly for those with mild to moderate COVID-19 [38]. Since these additional mechanisms to access antiviral medications for the treatment of COVID-19 would have resulted in billing private or public insurance providers, it is unlikely that antiviral medications for the treatment of COVID-19 were dispensed in this cohort and not captured in the MarketScan databases.

Despite these strengths, we note several limitations to our approach. Outpatient prescription records provide information only on payments for medications prescribed and dispensed, but not if a pregnant patient was prescribed the medication and did not fill the prescription. Prescribing rates may therefore have been higher among pregnant patients than observed in outpatient pharmacy claim records, and our results should not be interpreted as such. Although we used PS matching to restrict differences between pregnant and nonpregnant patients, this was an observational study, and it is possible that some residual confounding by factors differing between groups exists. Furthermore, we used a previously validated algorithm for identifying pregnancies and estimating pregnancy start date [13]; however, these algorithms are not perfect, and some pregnant patients may have been misclassified as nonpregnant, particularly in the earlier stages of pregnancy. Finally, our analyses were restricted to US outpatients and are reflective of US policies on antiviral medications. The results are not necessarily generalizable to other countries or contexts.

In conclusion, treatment rates observed among currently pregnant patients with a COVID-19 diagnosis were lower than those in their recently pregnant or nonpregnant counterparts, including pregnant patients with ≥1 high-risk medical condition. Because pregnant patients are at higher risk for progression to severe illness, further research on the reason for low treatment is needed.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

Disclaimer. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Data sharing. The authors are not permitted to disclose the study data beyond the research team. However, the data can be accessed through direct request to Merative, and R scripts used to analyze the data can be made available on reasonable request.

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Potential conflicts of interest. A. K. R. reports membership on a data safety monitoring board (DSMB) for matters unrelated to the presented research. S. G. S. reports consulting for Pfizer, Moderna, CSL Seqirus, Novavax, and Evo Health on work unrelated to the presented research. F. M. M. is an investigator in pediatric studies of coronavirus disease 2019 vaccines for Pfizer and Moderna and for a pediatric remdesivir study conducted by Gilead Sciences; serves as investigator on projects supported by a National Institutes of Health (NIH) contract for a Vaccine Treatment and Evaluation Unit; serves as a member of the DSMB for clinical trials conducted by Pfizer, Moderna, Meissa Vaccines, Virometix, and the NIH; and is a member of the American Academy of Pediatrics Committee of Infectious Diseases and the Immunization Expert Group of the American College of Obstetrics and Gynecology and cochair of the COVAX Maternal Immunization Working Group. All other authors report no potential conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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