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Research Letter | Infectious Diseases

Antibiotic Prescription for Outpatients With COVID-19 in Primary Care Settings in Japan

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Introduction

Although antibiotics are ineffective for viral infections, including COVID-19, physicians often prescribe antibiotics for COVID-19.[1,2] However, little is known about characteristics of patients and physicians associated with antibiotic prescription for COVID-19.

Methods

We analyzed the Japan Medical Data Survey (JAMDAS) database collected by M3 Inc,[3] an outpatient health care database of nationwide primary care physician clinics in Japan. The Nihonbashi-Sakura Clinic Ethics Committee approved this study and waived informed consent because we used deidentified data. Per the STROBE reporting guidelines, we analyzed outpatient visits for COVID-19 (defined using *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision*, code U07.1) in 843 clinics continuously observed from April 1, 2020, to February 28, 2023. We excluded visits with codiagnoses for which antibiotics may be appropriate. We reported national estimates by weighting all analyses using the inverse of the estimated probability of inclusion in JAMDAS (inclusion probability), which was calculated using clinic-level logistic regression with inclusion in JAMDAS as the outcome and clinic characteristics as variables in the sample of all Japanese medical institutions (eMethods in Supplement 1).

We described trends of antibiotic prescription rates. We examined associations of patient (sex, age, and presence of comorbidities [Charlson Comorbidity Index scores ≥1[4]]) and physician characteristics (sex and age) with antibiotic prescribing using a logistic regression model that adjusted for months and prefectures. Practices were attributed to the clinic owner physician because most Japanese clinics are solo practices.[5] We adjusted *P* values for multiple comparisons using Benjamini-Hochberg method. We considered a 2-sided $P < .05$ as statistically significant and used Stata, version 17 (StataCorp LLC).

Results

Among 528 676 patients with COVID-19 (median age, 33 years [IQR, 15-49 years]; 272 965 females [51.6%]), 47 329 (9.0%) received antibiotic prescriptions. Clarithromycin was most commonly prescribed (25.1% of total antibiotic prescriptions), followed by cefcapene (19.9%), cefditoren (10.2%), levofloxacin (9.9%), and amoxicillin (9.4%). Monthly antibiotic prescription rates decreased sharply in January 2022 (mean, 24.8% before vs 7.5% after January 2022) (**Figure 1**). This decrease was similarly observed when restricted to 554 clinics that had treated COVID-19 before January 2022 (24.8% before vs 6.1% after January 2022). Patients seen after January 2022 were older (mean [SD], 31.8 [21.6] vs 34.1 [21.9] years) and less likely to have comorbidities (18.2% vs 10.7%) compared with those seen before January 2022.

Antibiotic prescription rates varied by clinic; the top 10% of clinics with the highest absolute number of antibiotic prescriptions accounted for 85.2% of all antibiotic prescriptions, with a mean antibiotic prescription rate of 29.0% (95% CI, 28.7%-29.3%) (45.4% [95% CI, 44.6%-46.1%] before

+ Supplemental content

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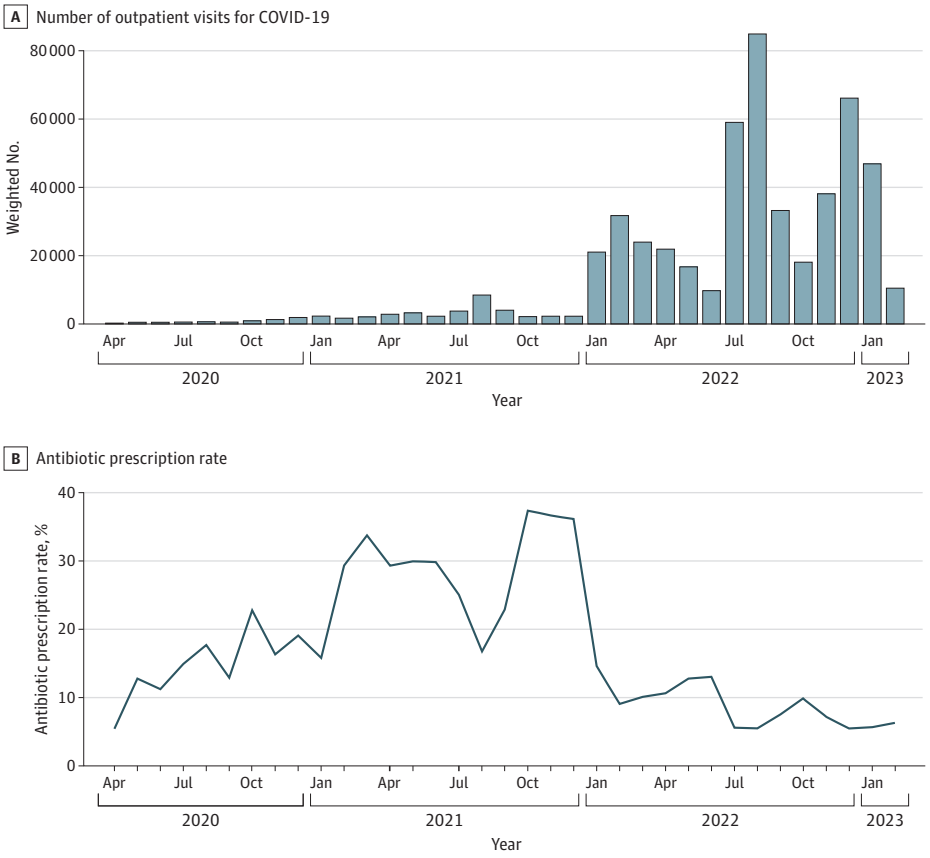
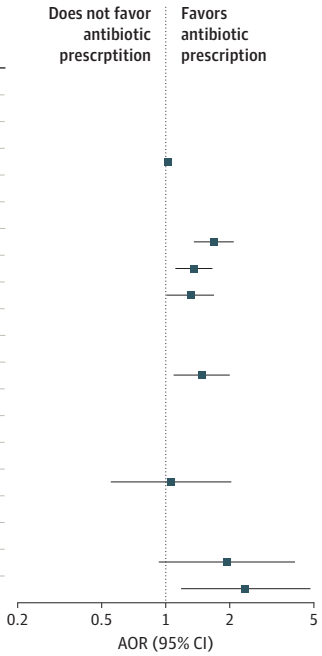
Figure 1. Outpatient Visits for COVID-19 and Rates of Antibiotic Prescription



A, Number of outpatient visits for COVID-19. B, Monthly trend of antibiotic prescription rates. The figures showed nationally representative estimates, which were calculated by using clinic-level weights (inverse of the inclusion probabilities). Data are from patients with COVID-19 who visited 843 primary care physicians' clinics in the Japan Medical Data Survey database.

Figure 2. Antibiotic Prescription by Patient and Primary Care Physician Clinic

Characteristic	Weighted No. of visits	AOR (95% CI)	*P* value	Adjusted *P* value
Patient				
Sex				
Male	255 711	1 [Reference]		
Female	272 965	1.02 (0.98-1.06)	.39	.45
Age, y				
≤17	147 103	1 [Reference]		
18-39	176 272	1.69 (1.37-2.09)	<.001	<.001
40-64	152 678	1.36 (1.11-1.66)	.003	.01
≥65	52 622	1.31 (1.01-1.69)	.04	.06
Comorbidities				
No	468 180	1 [Reference]		
Yes	60 496	1.48 (1.09-2.00)	.01	.03
Physician				
Sex				
Male	480 717	1 [Reference]		
Female	47 959	1.05 (0.55-2.01)	.87	.87
Age, y				
≤44	67 421	1 [Reference]		
45-59	209 795	1.94 (0.92-4.07)	.08	.11
≥60	251 460	2.38 (1.19-4.77)	.01	.03



We examined the associations of patient characteristics (sex, age, and comorbidities [no indicates Charlson Comorbidity Index of 0; yes indicates Charlson Comorbidity Index of ≥1]) and physician characteristics (sex and age) with antibiotic prescribing using a logistic regression model that adjusted for indicators of months and prefectures where clinics were located. Clinic-level weights were applied; therefore, numbers of patients in each category may not add up to the total number of patients. Standard errors were clustered at the clinic level. To account for multiple comparisons (8 comparisons), we adjusted *P* values using the Benjamini–Hochberg method at a threshold of $P < .05$. AOR indicates adjusted odds ratio.

vs 26.0% [95% CI, 25.7%-26.3%] after January 2022). The remaining 90% of clinics had a mean antibiotic prescription rate of 1.9% (95% CI, 1.9%-2.0%) (7.0% [95% CI, 6.6%-7.5%] before vs 1.6% [95% CI, 1.5%-1.6%] after January 2022).

Antibiotic prescription rates were higher among adults aged 18-39 years (adjusted odds ratio [AOR], 1.69; 95% CI, 1.37-2.09; $P < .001$) and 40-64 (AOR, 1.36; 95% CI, 1.11-1.66; $P = .01$) than among children younger than 18 years (**Figure 2**). The presence of comorbidities was associated with higher antibiotic prescription rates (AOR, 1.48; 95% CI, 1.09-2.00; $P = .03$). Patient sex was not associated with antibiotic prescribing. Physicians aged 60 years or older were more likely to prescribe antibiotics than those aged 44 years or younger (AOR, 2.38; 95% CI, 1.19-4.47; $P = .03$); physician sex was not associated with antibiotic prescribing.

Discussion

In primary care for COVID-19 in Japan, antibiotic prescriptions were clustered among a small proportion of clinicians. Physician age was a significant factor, comparable with patient age and presence of comorbidities. This variation may be due to differences in clinical training on appropriate antibiotic use.[6] Results suggest the decrease in antibiotic prescriptions with the emergence of the Omicron variant around January 2022 might be associated with decreased patient severity and comorbidities, rather than clinic-level factors.

Study limitations included the inability to fully account for unmeasured confounders (eg, severity of illness) and potentially limited generalizability to clinics not included in JAMDAS or to other contexts. Our findings may be helpful for policy makers to develop interventions to encourage appropriate antibiotic use.

ARTICLE INFORMATION

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Conflict of Interest Disclosures: Dr Miyawaki reported receiving personal fees from M3 Inc during the conduct of the study; and personal fees from Mitsubishi Tanabe Pharma outside the submitted work. Mr Kitajima reported receiving personal fees from M3 Inc, which provides the JAMDAS database used in this article, as an employee during the conduct of the study; and personal fees from M3 Inc as an employee outside the submitted work. Mr Iwata reported receiving personal fees from M3 Inc as an employee during the conduct of the study; and personal

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SUPPLEMENT 1.

eMethods
eReferences

SUPPLEMENT 2.

Data Sharing Statement