## Title

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# Physician characteristics associated with antiviral prescriptions for older adults with COVID-19 in Japan: an observational study

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## ABSTRACT

**Objectives** Although guidelines recommend antiviral therapy for outpatients with COVID-19 who are at high risk of progressing to severe conditions, such as older adults, many patients do not receive appropriate treatment. Little is known, however, about the physician factors associated with the prescription of guideline-recommended antiviral therapy for patients with COVID-19.

**Design** A cross-sectional study.

**Setting** Data including outpatient visits in primary care clinics in Japan from April to August 2023.

**Participants** We analysed 30 953 outpatients aged ≥65 years treated with COVID-19 (mean (SD) age, 75.0 (7.6) years; 17 652 women (57.0%)) in 1394 primary care clinics.

**Outcome measures** The primary outcome was the prescription of guideline-recommended antivirals (ie, nirmatrelvir–ritonavir or molnupiravir), adjusted for patient characteristics, months of visits and regions.

**Results** Antiviral prescriptions were concentrated among a small proportion of physicians; for example, the top 10% of physicians that had the largest number of nirmatrelvir–ritonavir prescriptions accounted for 92.4% of all nirmatrelvir–ritonavir prescriptions. After adjusting for potential confounders, physicians with higher patient volumes were more likely to prescribe guideline-recommended antivirals to their patients (adjusted OR (aOR) for high vs low volume, 1.76; 95% CI 1.31 to 2.38; adjusted p<0.001). We found no evidence that the likelihood of guideline-recommended antiviral prescription differed based on physicians' gender (aOR for women vs men, 1.24; 95% CI 0.88 to 1.74; adjusted p=0.48) or age (aOR for 45–59 vs <45 years, 1.16; 95% CI 0.87 to 1.54; adjusted p=0.48; aOR for ≥60 vs <45 years, 0.88; 95% CI 0.66 to 1.16; adjusted p=0.48). These patterns were similar when examining nirmatrelvir–ritonavir and molnupiravir separately.

**Conclusions** Our findings suggest that provider-level factors, such as the clinical experience of treating the patients with COVID-19, play an important role in the appropriate prescription of antiviral medications for COVID-19 in the primary care setting.

## STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ To examine physician characteristics associated with antiviral prescriptions for older adults with COVID-19, we analysed nationwide primary care clinic database in Japan.
⇒ We could not fully account for unmeasured confounders that might be related to both the patients' choice of physicians and the likelihood of antiviral therapy use, such as the severity of COVID-19 symptoms.
⇒ Our findings might not be generalisable to other contexts, including hospital inpatient care and emergency department care and other countries.

## INTRODUCTION

Ensuring access to effective COVID-19 medications in primary care is essential to reduce hospitalisations due to COVID-19 and the burden on the healthcare system from its surge. Nirmatrelvir/ritonavir (Paxlovid) and molnupiravir (Lagevrio) are oral antiviral agents effective at preventing hospitalisation and death in patients with COVID-19 who are at high risk of progressing to severe conditions when initiated within 5 days of symptom onset.[1 2] Nirmatrelvir/ritonavir has been shown in multiple studies to be effective in preventing hospitalisation even after the emergence of the Omicron variant and the widespread use of COVID-19 vaccination.[3–8] Although guidelines recommend these oral antiviral agents for outpatients with COVID-19 who are at high risk of progressing to severe conditions, such as older adults,[1 2] studies have shown that substantial number of patients do not receive such treatment.[3 5 6 9 10]

Research has shown that variation in the receipt of antiviral therapy for COVID-19 according to patient characteristics, including older age, socioeconomic status, race, greater COVID-19 symptom severity and mobility difficulties.[9 10] However, although individual physicians play an important role in determining the healthcare services patients receive, to our knowledge, no study to date

has investigated physician characteristics associated with the prescription of antiviral therapy for patients with COVID-19. Given that the COVID-19 is one of the most common infections seen in primary care, understanding how prescribing antiviral therapy for recommended groups, such as older adults, differs between types of physicians is imperative to ensure that patients have appropriate access to antiviral therapy.

To address this important knowledge gap, using a nationwide primary care clinic database in Japan, we aimed to examine the physician-level variation in prescribing antivirals for older adults with COVID-19 and physician characteristics associated with antiviral prescriptions.

## METHODS

### Data

This cross-sectional study analysed the *Japan Medical Data Survey* (JAMDAS), a nationwide database of primary care clinics providing outpatient healthcare in Japan. The JAMDAS database is collected and compiled by M3, Inc (Tokyo, Japan)[11] and includes all outpatient visits to the analytic clinics and patient-level information on patients' diagnoses, prescriptions, medical practices provided, vital data and laboratory data. It also includes the characteristics of clinics and physicians working in the clinic (eg, regions where clinics are located and owner physicians' gender and age). All the physicians in our database were primary care physicians providing basic diagnosis and treatment of common illnesses and medical condition in their clinics. This database has been used in prior research, and details are described there.[12]

### Patient population

We analysed outpatients aged ≥65 years diagnosed with COVID-19 (defined using the *International Classification of Diseases, Tenth Edition* (ICD-10) code U07.1) in clinics continuously observed in the JAMDAS database from 1 April to 31 August 2023. We chose outpatients aged ≥65 years because this age group accounted for a majority of all COVID-19 deaths.[9] We analysed visits for which the COVID-19 diagnosis date corresponded with the date of the visit (ie, we excluded revisits after the initial visit).[12] We excluded patients with any steroid prescription or oxygen saturation <94% (1.5% of the total visits) to restrict to patients with mild-to-moderate COVID-19 who did not require supplemental oxygen. We also excluded patients who received intravenous antiviral treatment (<0.1%). To improve the generalisability of our findings, all analyses were weighted using the inverse of the inclusion probability of clinics being included in the JAMDAS database, an approach used in our prior study.[12]

### Physician characteristics

Physician characteristics examined were physicians' gender, age (<45, 45–59 or ≥60 years) and patient volume (defined as the terciles of the clinic's average number of older patients with COVID-19 per month). In identifying physician characteristics, we attributed each clinic to its owner physician because most Japanese clinics are solo-practices.[12 13] Although it should be noted that in the Japanese primary care system, some primary care physicians are also qualified as specialists, most of such physicians provide primary care for a wide range of conditions, including COVID-19, regardless of their specialty. Therefore, coupled with the lack of reliable information on specialist qualifications in our data, we did not include physician specialty in our analysis.

### Outcomes

The primary outcome was the prescription of oral antiviral therapy recommended in the guidelines in Japan and the USA (ie, nirmatrelvir–ritonavir or molnupiravir).[1 2] The prescription of guideline-recommended oral antiviral therapy is one of the most important process indicators in the care of COVID-19 because it has been proven to improve important clinical outcomes, such as patient hospitalisation and mortality.[1–8] Secondary outcomes were prescriptions of each antiviral agent. We also examined prescription of ensitrelvir, an antiviral agent developed in Japan that is not currently recommended in the US guidelines due to limited efficacy information.[1]

Nirmatrelvir–ritonavir, molnupiravir and ensitrelvir received emergency use approval from the Ministry of Health, Labour and Welfare in February 2022, December 2021 and November 2022, respectively and were subsequently became covered under the public health insurance systems in March 2023, September 2022 and March 2023, respectively. This indicates that, during the study period (April to August 2023), all available oral antivirals were covered by public health insurance systems and government subsidies, with no out-of-pocket cost for patients; furthermore, all physicians were authorised to prescribe the three oral viral agents studied, and all pharmacies were authorised to dispense them. Unlike the Test to Treat programme in the USA, only physicians could prescribe antivirals in Japan, not pharmacists.

### Adjustment variables

We adjusted for patient characteristics, months of visits and regions where clinics were located (Hokkaido, Tohoku, Kanto, Chubu, Kinki, Chugoku, Shikoku or Kyusyu/Okinawa). Patient characteristics included gender, age (65–74, 75–84 or ≥85 years), number of comorbidities (0, 1, or ≥2),[1] and use of drugs contraindicated with nirmatrelvir–ritonavir.[14] Comorbidities included 11 underlying conditions according to codiagnoses,[15] including cancer (ICD-10 code C00-C43 and C45-C97), chronic kidney disease (N18 and N19), chronic liver disease (B18, I85, I864, I982, K70–K76 and Z944), chronic lung disease (J40–J47, I26, I270, I272, J84), cerebrovascular disease (I60–I69), diabetes (E10–E14), dementia (F00–F03, F051 and G30), heart conditions (I20–I25 and I50), mental health conditions (F20–F33 and F43), obesity (body mass index ≥30 (calculated from body height and body weight recorded in electronic health record)) and the use of

immunosuppressive drugs (defined using the first-level Anatomical Therapeutic Chemical classification code L). Drugs contraindicated with nirmatrelvir–ritonavir coadministration were identified according to a list developed by the Japan Pharmaceutical and Medical Devices Agency.[16]

### Statistical analysis

First, we described patient characteristics and the treatment they received. Second, to examine clinic-level variation in antiviral prescribing, we aggregated the numbers of prescriptions of guideline-recommended oral antiviral therapy (nirmatrelvir–ritonavir and molnupiravir separately) for each clinic and examined their cumulative distributions.

Third, we examined associations of physician characteristics with antiviral prescribing patterns using logistic regression models that adjusted for patient characteristics (described in the Adjustment variables section), months and regions. We used generalised equation estimation to account for within-clinic correlation adjusting p values for multiple comparisons using the Benjamini-Hochberg method;[17] we used Stata, V.17 (StataCorp LLC).

### Patient and public involvement

Data were derived from administrative records; no patients were involved in setting the research question or the outcome measures, nor were they involved in developing plans or implementation of the study. No patients were asked to advise on interpretation or writing up of results.

## RESULTS

We analysed 30 953 outpatients (mean (SD) age, 75.0 (7.6) years; 17 652 women (57.0%)) aged 65 years or older treated with COVID-19 in 1394 primary care clinics. Among them, 11 055 (35.8%) received guideline-recommended antiviral prescriptions (table 1). Molnupiravir was more commonly prescribed than nirmatrelvir–ritonavir (9735 (31.5%) vs 1320 (4.3%)). Ensitrelvir was prescribed for 2016 (6.5%) patients. Patients who did not receive any oral antiviral agents accounted for more than half of the patients. The number of patients using drugs contraindicated with nirmatrelvir–ritonavir was small, 854 (2.8%). The proportion in each treatment category is shown in online supplemental table 1.

The distribution of volume of older patients with COVID-19 per physician was skewed to the right (online supplemental figure 1). The average number of older patients with COVID-19 per month of low, medium and high patient volume physicians was <1.8 (physician-level mean 0.8), 1.8 to 4.8 (physician-level mean 3.1) and 4.9–50.8 (physician-level mean 9.0), respectively.

We identified substantial physician-level variation in prescribing antivirals (figure 1). The 10% of physicians that had the largest number of nirmatrelvir–ritonavir prescriptions accounted for 92.4% of all nirmatrelvir–ritonavir prescriptions, and the 10% of physicians who had the largest number of molnupiravir prescriptions accounted for 52.8% of all molnupiravir prescriptions.

In logistic regression analyses (table 2), we found no evidence that the likelihood of guideline-recommended antiviral prescription differed based on physicians' gender (adjusted OR (aOR) for women vs men, 1.24; 95% CI 0.88 to 1.74; adjusted p=0.48) or age (aOR for 45–59 vs <45 years, 1.16; 95% CI 0.87 to 1.54; adjusted p=0.48; aOR for ≥60 vs <45 years, 0.88; 95% CI 0.66 to 1.16; adjusted p=0.48). However, physicians with higher patient volumes were more likely to prescribe guideline-recommended antivirals to their patients (aOR for high vs low volume, 1.76; 95% CI 1.31 to 2.38; adjusted p<0.001).

These patterns of the associations between physician characteristic and guideline-recommended antiviral prescriptions were similar when examining nirmatrelvir–ritonavir and molnupiravir separately (table 2), though the association between patient volume and nirmatrelvir–ritonavir prescribing did not reach statistical significance due to the low prescription rate of the nirmatrelvir–ritonavir. For ensitrelvir, we found no evidence that the prescription rates for older patients with COVID-19 differed based on physicians' gender (aOR for female vs male, 0.90; 95% CI 0.50 to 1.61; adjusted p=0.72), age (aOR for ≥60 vs <45 years, 1.24; 95% CI 0.72 to 2.13; adjusted p=0.55; and aOR for 45–59 vs <45 years, 1.35; 95% CI 0.79 to 2.29; adjusted p=0.55) or patient volume (aOR for high vs low volume, 0.81; 95% CI 0.51 to 1.28; adjusted p=0.55; and aOR for medium versus low volume, 0.64; 95% CI 0.40 to 1.04; adjusted p=0.36).

## DISCUSSION

Using a nationwide database of primary care clinics in Japan, we found that physicians with higher volumes of older patients with COVID-19 were more likely to prescribe guideline-recommended antivirals to their patients, suggesting that provider-level factors may play a role in the appropriate prescription of antiviral medications for COVID-19 in primary care settings. On the contrary, the likelihood of antiviral prescriptions for COVID-19 did not differ based on physicians' age or gender. Taken together, our findings indicate the importance of continued efforts, such as disseminating the information on the up-to-date clinical guidelines[18] and providing the education programme, peer support or enhanced specialty–primary care interactions for primary care physicians with limited experience of treating patients with COVID-19,[19] to improve access to antiviral therapy in populations at high risk of progressing to severe COVID-19.

We found that physicians' volume of patients with COVID-19 was associated with a higher rate of prescription of guideline-recommended antivirals. One explanation for this association is that accumulation of clinical experience in COVID-19 care associated with treating a larger number of patients with COVID-19 may improve physicians' antiviral prescribing patterns.[20] For example,

**Table 1** Characteristics and treatment received by older adults diagnosed with COVID-19 in Japanese primary care settings between April and August 2023

| | | By medication type, n (%) | | | |
|---|---|---|---|---|---|
| | **All, n (%)** | **Nirmatrelvir–ritonavir** | **Molnupiravir** | **Ensitrelvir** | **No treatment** |
| Number of visits | 30 953 | 1320 | 9735 | 2016 | 17 883 |
| Patient characteristics | | | | | |
| Gender | | | | | |
| Male | 13 301 (43.0) | 513 (38.9) | 4224 (43.4) | 940 (46.6) | 7625 (42.6) |
| Female | 17 652 (57.0) | 807 (61.1) | 5511 (56.6) | 1076 (53.4) | 10 258 (57.4) |
| Age, year | | | | | |
| 65–74 | 16 913 (54.6) | 684 (51.8) | 4441 (45.6) | 1251 (62.1) | 10 537 (58.9) |
| 75–84 | 6043 (19.5) | 222 (16.8) | 1977 (20.3) | 383 (19.0) | 3461 (19.4) |
| ≥ 85 | 7997 (25.8) | 415 (31.4) | 3316 (34.1) | 381 (18.9) | 3884 (21.7) |
| Number of comorbidities * | | | | | |
| 0 | 20 121 (65.0) | 826 (62.6) | 6134 (63.0) | 1450 (71.9) | 11 712 (65.5) |
| 1 | 5622 (18.2) | 238 (18.0) | 1714 (17.6) | 330 (16.4) | 3340 (18.7) |
| ≥ 2 | 5210 (16.8) | 256 (19.4) | 1887 (19.4) | 236 (11.7) | 2830 (15.8) |
| Use of drugs contraindicated with nirmatrelvir–ritonavir † | | | | | |
| No | 30 099 (97.2) | 1303 (98.7) | 9389 (96.4) | 1991 (98.8) | 17 416 (97.4) |
| Yes | 854 (2.8) | 17 (1.3) | 346 (3.6) | 24 (1.2) | 467 (2.6) |
| Month of 2023 | | | | | |
| April | 1338 (4.3) | 10 (0.8) | 275 (2.8) | 31 (1.5) | 1021 (5.7) |
| May | 2456 (7.9) | 54 (4.1) | 699 (7.2) | 82 (4.1) | 1620 (9.1) |
| June | 4215 (13.6) | 124 (9.4) | 1347 (13.8) | 283 (14.0) | 2461 (13.8) |
| July | 8737 (28.2) | 349 (26.4) | 2750 (28.2) | 689 (34.2) | 4950 (27.7) |
| August | 14 208 (45.9) | 783 (59.3) | 4665 (47.9) | 931 (46.2) | 7830 (43.8) |
| Physician characteristics | | | | | |
| Gender | | | | | |
| Male | 28 926 (93.5) | 1200 (90.9) | 9073 (93.2) | 1925 (95.5) | 16 728 (93.5) |
| Female | 2027 (6.5) | 120 (9.1) | 662 (6.8) | 90 (4.5) | 1155 (6.5) |
| Age, years | | | | | |
| <45 | 2357 (7.6) | 132 (10.0) | 714 (7.3) | 136 (6.7) | 1374 (7.7) |
| 45–59 | 9193 (29.7) | 420 (31.8) | 3608 (37.1) | 530 (26.3) | 4635 (25.9) |
| ≥ 60 | 19 403 (62.7) | 768 (58.2) | 5413 (55.6) | 1349 (66.9) | 11 873 (66.4) |
| Patient volume ‡ | | | | | |
| Low | 1602 (5.2) | 49 (3.7) | 401 (4.1) | 117 (5.8) | 1034 (5.8) |
| Medium | 7738 (25.0) | 272 (20.6) | 2016 (20.7) | 395 (19.6) | 5055 (28.3) |
| High | 21 613 (69.8) | 998 (75.6) | 7318 (75.2) | 1503 (74.6) | 11 794 (66.0) |

Data are from outpatients aged≥65 years with COVID-19 who visited 1394 primary care physicians' clinics as reported in the Japan Medical Data Survey database. To improve the generalisability of our findings, analyses were weighted using the inverse of the inclusion probability of each clinic to be included in the JAMDAS database; therefore, number of patients in each category may not add up to the total number of patients. The proportion in each treatment category is shown in online supplemental table 1.
*Comorbidities consisted of 11 underlying conditions, including cancer, chronic kidney disease, chronic liver disease, chronic lung disease, cerebrovascular disease, diabetes, dementia, heart conditions, mental health conditions, obesity and the use of immunosuppressive drugs.
†Defined based on past prescriptions at the clinic where the patient was seen.
‡Defined as the terciles of the clinic's average number of COVID-19 visits per month.

physicians providing care to more outpatients with COVID-19 may be more compliant with the latest guidelines and more accustomed to clinical process when prescribing antivirals (explaining to patients, assessing concomitant medications, arranging for pharmacies that can dispense them).[21] If this was the case, future

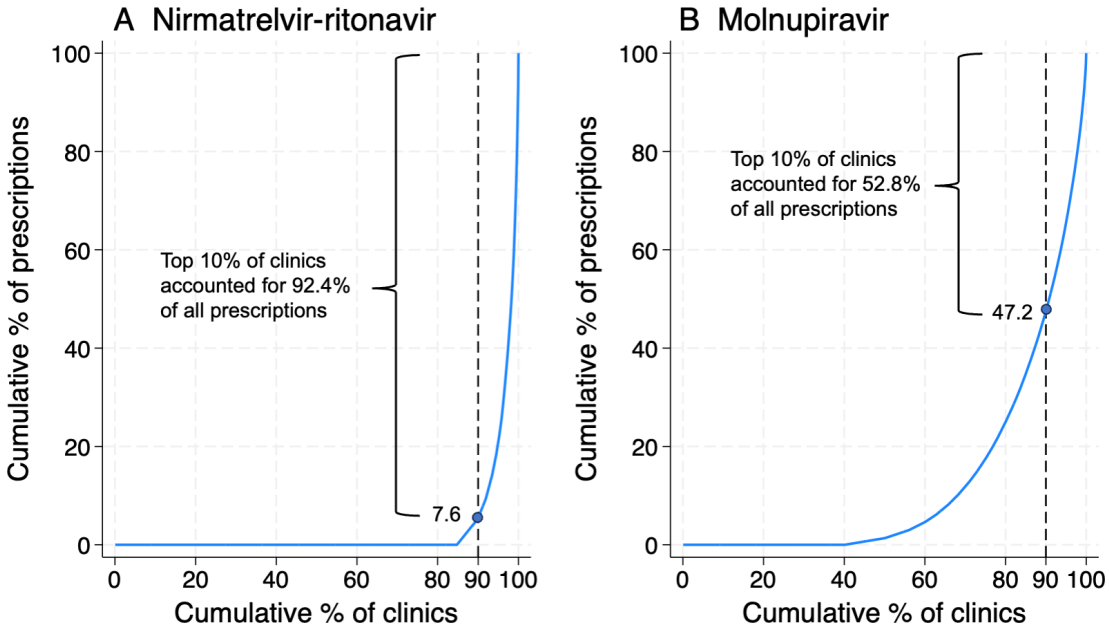


**Figure 1** Distribution of prescriptions of nirmatrelvir–ritonavir and molnupiravir in primary care clinics, April to August 2023. Data are from outpatients aged≥65 years with COVID-19 who visited 1394 primary care clinics as reported in the Japan Medical Data Survey database. We aggregated the number of prescriptions of nirmatrelvir–ritonavir (A) and molnupiravir (B) separately for each clinic and examined their cumulative distributions.

policies can encourage physicians with limited experience with treating patient with COVID-19 to see more patients through the promotion of telemedicine and the introduction of infection control measures for patients with COVID-19. A large number of Japanese primary care physicians were reportedly reluctant to provide care for COVID-19 due to the difficulties in physically separating patients with COVID-19 from other patients in their clinics,[22] combined with the limited expansion of telemedicine services.[23] When compared with physicians with low volumes of older patients with COVID-19, guideline-recommended antiviral prescribing rates were higher for high-volume physicians but did not differ for medium-volume physicians. In our study, the distribution of volume of older patients with COVID-19 per physician was right-skewed: physician-level averages of the count of these patients were 0.8, 3.1 and 9.0 per month for low, medium and high-volume physicians, respectively. Therefore, it was possible that the patient numbers in low and medium-volume clinics were too small to provide adequate clinical experience. Another possibility could be that the older patients with COVID-19 opted for clinics that frequently prescribed antivirals for COVID-19. If this is the case, patients might cluster in clinics with high rates of guideline-recommended antiviral prescribing, resulting in high volumes.

To our knowledge, this is the first study that investigated physician characteristics associated with the outpatient prescription of oral antiviral therapy for the COVID-19. In primary care settings, the associations between the number of patients with a particular condition and process measures of quality care at physician level have been investigated in conditions other than COVID-19, including diabetes,[24 25] chronic obstructive pulmonary disease[26] and upper respiratory tract infections,[27] with mixed results. In these studies, the number of patients is supposed to affect care quality in primary care in two conflicting ways.[25] While a physician responsible for a large number of patients with a specific condition may develop expertise in the condition, leading to more efficient and higher quality care, a high number of outpatients may place greater constraints on consultation time and physicians may have difficulty in providing quality care, particularly for patients with multiple complex and competing chronic conditions. In our study, unlike the conditions examined in previous studies, COVID-19 is relatively new conditions for primary care physicians, and, therefore, the impact of expertise acquisition on practice quality due to the increased number of patients with COVID-19 may have been more prominent, leading to a positive association between patient volume and quality of care.

In contrast, we found that the prescription rates of antivirals did not differ by physicians' gender or age. Prior studies have reported variations in practice patterns according to physician age, and it has been suggested that one possible contributing factor to this variation is the difference in medical training by physicians' age cohort.[28–30] However, COVID-19 is an emerging infectious disease for which there had been no treatment, and it is unlikely that physicians' knowledge of its treatment would differ by physician age.

There are several possible reasons for suboptimal antiviral prescribing, especially nirmatrelvir–ritonavir. First, physicians may have concerns about drug interactions with nirmatrelvir–ritonavir,[18] and this may be

**Table 2** Physician characteristics associated with antiviral prescribing for COVID-19

| Physician characteristics | Guideline-recommended antivirals (nirmatrelvir–ritonavir or molnupiravir) | | Nirmatrelvir–ritonavir | | Molnupiravir | | Ensitrelvir | |
|---|---|---|---|---|---|---|---|---|
| | aOR (95% CI) | Adjusted P | aOR (95% CI) | Adjusted P | aOR (95% CI) | Adjusted P | aOR (95% CI) | Adjusted P |
| Gender | | | | | | | | |
| Male | Reference | | Reference | | Reference | | Reference | |
| Female | 1.24 (0.88 to 1.74) | 0.48 | 2.72 (1.04 to 7.16) | 0.21 | 1.18 (0.83 to 1.68) | 0.61 | 0.90 (0.50 to 1.61) | 0.72 |
| Age, years | | | | | | | | |
| < 45 | Reference | | Reference | | Reference | | Reference | |
| 45–59 | 1.16 (0.87 to 1.54) | 0.48 | 0.82 (0.43 to 1.58) | 0.89 | 1.18 (0.88 to 1.59) | 0.61 | 1.35 (0.79 to 2.29) | 0.55 |
| ≥ 60 | 0.88 (0.66 to 1.16) | 0.48 | 0.91 (0.48 to 1.73) | 0.89 | 0.90 (0.67 to 1.22) | 0.63 | 1.24 (0.72 to 2.13) | 0.55 |
| Patient volume | | | | | | | | |
| Low | Reference | | Reference | | Reference | | Reference | |
| Medium | 1.04 (0.78 to 1.40) | 0.76 | 0.95 (0.49 to 1.85) | 0.89 | 1.04 (0.77 to 1.40) | 0.81 | 0.64 (0.40 to 1.04) | 0.36 |
| High | 1.76 (1.31 to 2.38) | <0.001 | 1.80 (0.996 to 3.35) | 0.16 | 1.65 (1.23 to 2.21) | 0.004 | 0.81 (0.51 to 1.28) | 0.55 |

We examined the associations of physician characteristics (gender, age and patient volume) with prescription of guideline-recommended antivirals using a logistic regression model that adjusted for patient characteristics (gender, age, number of comorbidities [0, 1 and≥2], and use of drugs contraindicated with nirmatrelvir–ritonavir) and indicators of months and regions. Clinic-level weights were applied. To account for multiple comparisons (five pairs for the analysis of each outcome), we adjusted P values for multiple comparisons using the Benjamini–Hochberg method. We considered a two-sided p<0.05 as statistically significant.
aOR, adjusted OR.

exacerbated by the limited pharmacist involvement in COVID-19 primary care in Japan. In our study, the proportion of patients using drugs contraindicated with nirmatrelvir–ritonavir was small (as shown in table 1), suggesting that the time and psychological barriers for healthcare providers in investigating the possibility of drug interactions, rather than the actual use of drugs with drug interactions, may be the primary factor hindering nirmatrelvir–ritonavir prescription. Second, physicians may also have concerns about 'rebound' with nirmatrelvir–ritonavir and molnupiravir, in which symptoms reappeared after the patient had responded to 5 days of treatment.[31–33] Third, molnupiravir was the only oral antiviral drug that could be prescribed in Japan between December 2021 and February 2022. That prescribing pattern might have persisted beyond February 2022, when nirmatrelvir–ritonavir was launched, which might lead to physicians' tendency to prescribe molnupiravir over nirmatrelvir–ritonavir.

Our study has limitations. First, as with any observational study, we could not fully account for unmeasured confounders. Patients may choose to see a physician with more experience treating COVID-19 when their COVID-19 symptoms are more severe or when they have risk factors for severe illness (eg, smoking and no vaccination), which were not fully measurable due to the lack of data on such information. Second, we were unable to examine how physician characteristics were associated with health outcomes, such as patient hospitalisation and mortality rates, because the primary care database we used did not include such information. Further research investigating the physician characteristics associated with the outcomes of patients with COVID-19 would be warranted. Third, although our analyses were weighted using the inverse of the inclusion probability of clinics in the JAMDAS database to improve the generalisability of our findings, our findings could have potentially limited generalisability to clinics not included in JAMDAS. Finally, our findings might not be generalisable to other contexts, including hospital inpatient care and emergency department care and other countries.

## CONCLUSION

We found that a substantial number of older outpatients in Japan did not receive antiviral prescriptions for COVID-19 in primary care, and antiviral prescriptions were concentrated among a small proportion of physicians. While the prescription rates of antivirals did not differ by physicians' gender or age, physicians' volume of patients with COVID-19 was associated with a higher rate of prescription of guideline-recommended antivirals, suggesting that provider-level factors play an important role in the appropriate prescription of antiviral medications for COVID-19 in primary care settings. Our findings may help policymakers develop interventions to improve access to antiviral therapy in populations at high risk of progressing to severe COVID-19.

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**Contributors** AM is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: AM and YT. Acquisition, analysis or interpretation of data: all authors. Drafting of the manuscript: AM. Critical revision of the manuscript for important intellectual content: YT, KK, AI and DS. Statistical analysis: AM, KK and YT. Administrative, technical or material support: KK, AI and DS. Supervision: YT.

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**Competing interests** AM reported receiving consulting fees from M3, Inc., which provides the JAMDAS database used in this article, during the conduct of the study. KK, AI and DS reported receiving personal fees from M3, Inc. as employees during the conduct of the study; and personal fees from M3, Inc. as employees outside the submitted work. YT reported receiving grants from the National Institutes of Health (NIH)/National Institute on Aging (R01AG068633 & R01AG082991), NIH/National Institute on Minority Health and Health Disparities (R01MD013913) and Gregory Annenberg Weingarten GRoW @Annenberg outside the submitted work; and serving on the board of directors for M3, Inc.

**Patient and public involvement** Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

**Patient consent for publication** Not applicable.

**Ethics approval** The study was approved by the Nihonbashi-Sakura Clinic Ethics Committee (approval date: 28 March 2023). The requirement for written informed consent was waived because all data were blinded.

**Provenance and peer review** Not commissioned; externally peer-reviewed.

**Data availability statement** Data may be obtained from a third party and are not publicly available. Due to a contract between the authors and M3, Inc., the data set used in this study cannot be shared, but the original database (JAMDAS) is available from M3, Inc. upon reasonable request.



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