

# Insights from a community-based survey on factors Influencing Acceptance and Uptake of Paxlovid (nirmatrelvir and ritonavir) as a COVID-19 Antiviral Medication in Singapore

**Sheng En Alexius Matthias Soh**

National Centre for Infectious Diseases

**Wei Ling Brenda Ong**

National Centre for Infectious Diseases

**Tun-Linn Thein**

National Centre for Infectious Diseases

**Konstadina Griva**

Nanyang Technological University

**I-Cheng Mark Chen**

[mark\\_ic\\_chen@ncid.sg](mailto:mark_ic_chen@ncid.sg)

National Centre for Infectious Diseases

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## Research Article

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# Abstract

## Introduction

Antiviral treatment can reduce the burden of COVID-19. But utilisation can be suboptimal, even in a setting like Singapore where it is fully subsidized for those with selected medical conditions and older adults ( $\geq 50$  years). We hence investigated the factors affecting awareness, acceptance, and initiative to request Paxlovid.

## Methods

We assessed the Paxlovid awareness, factors impacting its uptake in a survey conducted from August 2022 to September 2022 through the SOCRATES cohort. Multivariable logistic regression was used to investigate associations between sociodemographics, perceptions, and attitudes with the key study outcomes.

## Results

Among respondents to the Paxlovid survey, 54% were aware of Paxlovid. On being provided essential details about Paxlovid, 75% reported they would likely be receptive to taking it if prescribed, and 38% indicated the initiative to request for it if it was not suggested by their doctors. Factors associated with being aware of Paxlovid include aged 40 years old and above, higher education, citing websites as an information source, greater trust in healthcare providers (aOR: 1.65, 95% CI 1.26–2.15) and government communications (aOR: 0.69, 95% CI 0.55–0.86), and higher perceived risk of COVID-19 infection (aOR: 1.25, 95% CI 1.10–1.42). Factors associated with acceptance to take Paxlovid include male gender, citing trust in healthcare providers (aOR: 1.49, 95% CI 1.11–1.99) and government communications (aOR: 1.38, 95% CI 1.09–1.76), and higher perceived severity of COVID-19 (aOR: 1.23, 95% CI 1.07–1.42). Factors associated with initiative to request Paxlovid include male gender, having pre-existing diabetes and higher perceived severity of COVID-19 (aOR: 1.24, 95% CI 1.09–1.40). The most common reasons for why respondents might not take Paxlovid were concerns about side effects (64%), concerns about costs (29%), and the perception that COVID-19 is a mild (25%).

## Conclusion

The majority of our respondents would take Paxlovid if it was prescribed to them, but a much smaller proportion would have the initiative to request for this. Key factors that may influence uptake are COVID-19 threat perceptions, trust in healthcare and government, and perceptions of the drug's side effects and cost.

## 1. Introduction

The COVID-19 pandemic prompted the development of numerous tools to counter the newly emerged severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Amongst these were oral antiviral drugs,

including nirmatrelvir/ritonavir (Paxlovid). When administered early, Paxlovid can shorten recovery time, reduce the burden of long COVID-19, alleviate pressure on hospitals during epidemics, and save lives in high-risk groups and those with medical risk factors (1). In Singapore, Paxlovid is recommended for individuals aged 50 years (2) and older and those with underlying health conditions and is fully subsidised for eligible patients (3, 4). Should a new COVID-19 variant with both greater severity and enhanced immune escape properties emerge, it will likely be challenging to develop and deploy updated COVID-19 vaccines in time to mitigate the potential impact (5–7). In such a situation, Paxlovid may be a critical intervention not just for the groups currently considered vulnerable, but also the wider population.

However, despite its accessibility (8), the use of Paxlovid in Singapore remains reportedly low, even in vulnerable groups (4). A study conducted by Wee et al. (9) in 2022 showed that only 2.7% of notified cases aged 60 and above received Paxlovid. Underutilisation and missed opportunities for early treatment may arise due to patients' hesitancy to take COVID-19 antiviral medication as advised (10). Several articles have postulated that factors contributing to hesitancy towards a recommended intervention like antivirals includes lack of prior awareness, reduced perceptions of COVID-19 threat and severity, inadequate trust in the healthcare system or messaging about the drug, and perceptions about Paxlovid's efficacy, side effects and cost (8, 10–15). In addition, medical professionals may also be reluctant to prescribe Paxlovid (16), in which case it is also worthwhile to ascertain if these factors are important drivers of a patient's initiative to request Paxlovid from their doctors. However, there has been little empirical data examining how any of these factors specifically affects utilization of Paxlovid, and none in the context of COVID-19 in Singapore.

To better understand acceptance and use of Paxlovid as a COVID-19 antiviral treatment in Singapore, we conducted a survey using an ongoing community-based cohort (SOCRATES). We aimed to identify factors associated with participants' awareness of Paxlovid, their acceptance of Paxlovid should it be prescribed, and their initiative to request Paxlovid if it is not offered by their healthcare provider. We also document possible reasons as to why our participants would not take Paxlovid.

## **2. Methods**

### **2.1 Study design**

The SOCRATES (Strengthening Our Community's Resilience Against Threats from Emerging Infections) research study was initiated before the COVID-19 pandemic in February 2019, specifically to assess public perceptions and response to the threat from and our interventions against infectious diseases. The intent was to set up a pre-enrolled cohort recruited from the public that could be efficiently surveyed on issues pertinent to circulating infectious diseases and allow rapid and repeated surveys during a public health emergency caused by an emerging infection, as was the case with COVID-19.

The design and setting up of the SOCRATES study have previously been described (17). Briefly, we recruited participants aged 16 years and above into the SOCRATES cohort through various methods,

including invitations to participants of other research studies, door-to-door recruitment, and word-of-mouth referrals. Participants could complete the surveys in English or key local languages (Malay and Mandarin).

Enrolment was performed through interviews conducted in person or via video-conferencing. Sociodemographic characteristics and pre-existing chronic illness were also collected at the enrolment interview. Subsequent follow-up surveys were conducted via FormSG (<https://www.form.gov.sg>), an online platform managed by the Singapore Government. The use of online methods for interviews and follow-up surveys allowed us to continue study-related activities in the face of restrictions imposed to minimise the spread of COVID-19.

## 2.2 Survey on Paxlovid and factors influencing awareness and uptake

Following the government's announcement on 31st January 2022 (4) on the introduction of Paxlovid to Singapore through primary care providers, and that it would be fully subsidised for adults aged 60 years and older as well as those with selected medical conditions (those at risk of developing severe disease, have active cancer or serious heart, lung or kidney disorders, or are on ongoing immunosuppressive treatment)(4), we collected our data about Paxlovid between 29th August and 6th September 2022 as part of the 36th survey wave launched in our cohort.

A single questionnaire item each was used to quantify **awareness** of Paxlovid ("Have you heard about the use of Paxlovid medication to reduce COVID-19 severity?"), **acceptance** towards taking Paxlovid ("If you were infected with COVID-19 and the healthcare provider prescribes the Paxlovid medication to you, how likely are you to take these drugs?") and the **initiative** to request Paxlovid ("If you were infected with COVID-19, would you ask the healthcare provider whether you can be treated with Paxlovid medication?"). These three items were prefaced by a short preamble text (Table S1) taken from an online news article about Paxlovid rollout in Singapore (18). Responses were regrouped where needed into binary outcomes. Those answering "yes" to the first question were categorised as being "aware", while those answering "no" were considered "unaware" of Paxlovid. For the second question, those who reported being "very likely" or "likely" to take Paxlovid were considered as having higher acceptance of Paxlovid, with those who responded "very unlikely" or "unlikely" having lower acceptance. For the third question, those who replied that they would "ask about this medication" were classified as having initiative to request Paxlovid (versus those who would not ask, or would not want to take Paxlovid even if it were recommended).

To investigate factors potentially associated with uptake, we used data collected on enrolment into our cohort for respondent characteristics such as current age, ethnicity, gender, highest education level, employment status, household income, and presence of common chronic illnesses (specifically diabetes and hypertension). We also used our participant's previous survey responses (about 15 months before the survey on Paxlovid) to investigate the role of trust in the healthcare system ("*Our healthcare institutions, doctors, nurses and other healthcare professionals will be able to provide appropriate medical treatment to you if you contract the COVID-19 infection during the outbreak*") and trust in government

communications (*"The authorities will adequately communicate facts and information about COVID-19 to the public"*), with responses captured on a 4-point Likert scale, ranging from "Strongly agree" to "Strongly disagree". Additional questionnaire items for probing acceptance of Paxlovid were based on factors postulated by others (8, 10–15) and the conceptual framework of the Health Belief Model (19).

Participants were asked about their perceived susceptibility to being infected (*"I believe there is a strong likelihood I will contract COVID-19"*) and severe COVID-19 if infected (*"I believe that if I were to contract COVID-19 it would have serious consequences to my health"*) on a 5-point Likert scale ("Strongly agree" to "Strongly disagree"). In addition, respondents were asked to make multiple selections from a list of reasons why they may not take Paxlovid, including items representing perceived barriers (costs, side effects, inconvenience) and benefits (or lack thereof, such as perceived ineffectiveness of Paxlovid).

## 2.3 Data analysis

We explored in three separate analyses if demographic characteristics, as well as attitudes and perceptions, were associated with the three previously defined outcome variables representing awareness, acceptance and initiative. Univariate and multivariable logistic regression was used to identify factors associated with the above binary outcomes, with results presented as crude and adjusted odds ratios (ORs), and p-values of < 0.05 considered statistically significant. In the regression analyses, demographic factors were coded as categorical variables while the questions regarding perceptions of COVID-19 and trust were modelled as scores.

All statistical analysis was performed on STATA 15 for Windows.

## 3. Results

### Demographics of the Paxlovid survey respondents

Among the 2136 total participants in the SOCRATES cohort, there were 1432 respondents (60% female, mean age = 47.9 years, response rate = 68%) for the survey on Paxlovid (Table 1), of which 137 (10%) were from door-to-door recruitment, 580 (41%) from other cohorts, and 715 (50%) from referrals. The majority of respondents identified as Chinese (89%), held tertiary education (59%), and resided in 4-5 bedroom publicly owned flats (57%). About a third had a monthly household income of less than \$5,000 (33%). Those who responded to the Paxlovid survey were reasonably similar to the rest of the cohort. However, minority ethnic groups were under-represented relative to population data from the Singapore Department of Statistics, as were individuals with fewer years of education (14% with 'O' / 'N' level and below amongst respondents versus 47% in national data). Most of the respondents either strongly agreed or agreed that the healthcare system and communications by the authorities regarding COVID-19 could be trusted (97% and 89% respectively, see Table S2). Levels of trust decreased slightly over serial surveys, and we used the respondent's most recent response to this question in our multivariable analyses. In survey responses collected in August 2022, more than half (54%) either strongly agreed or agreed that they were likely to contract COVID-19, with 40% also believing contracting COVID-19 would have serious consequences on their health (Table S3).

More than half (54%) of respondents had heard about Paxlovid before our survey. Figure 1A indicates significant but subtle differences in acceptance towards Paxlovid by prior awareness ( $p=0.009$ ). Those with prior awareness had a higher proportion who were “very likely” to take Paxlovid if prescribed compared to those who had not previously heard of Paxlovid (23% vs 16%). However, when considering those who were “very likely” and “likely” to take Paxlovid as those with higher acceptance, then proportions were similar regardless of whether they were previously aware (75%) or not (74%). Overall, 38% would take the initiative to request Paxlovid if not suggested by their doctor, either by asking their doctor (25%) or even seeking a second opinion from another healthcare provider (13%). Figure 1B indicates that these proportions did not vary significantly by prior awareness of Paxlovid. However, if we assume that prior awareness of Paxlovid is needed for a patient to take the initiative to request Paxlovid from a doctor who did not offer it, then only 19.9% of all respondents would do so.

Table 2 gives the results from our multivariable regression models. The final model for awareness indicated significant association for age, education, trust in healthcare providers, trust in government communications and likely to get COVID-19 infection. As compared to respondents aged below 30, significant association for prior awareness were observed for respondents aged 40-49 (aOR: 2.03, 95% CI 1.28 – 3.23), 50-59 years old (aOR: 2.47, 95% CI 1.55 – 3.94) and 60 and above (aOR: 3.62, 95% CI 2.23 – 5.88), indicating successively higher Paxlovid awareness among older age groups. Those with more years of education also had significantly greater awareness of Paxlovid, as did respondents who predominantly relied on websites as their preferred information source (aOR: 1.65, 95% CI 1.27 – 2.14) relative to those who did not rely on websites. Those who strongly agreed that healthcare providers could be trusted were more likely to have prior awareness of Paxlovid. When modelled as a score, the level of trust in healthcare providers was significantly associated with having prior awareness (OR: 1.65, 95% CI 1.26 – 2.15). Conversely, increasing trust in government communications was associated with lower proportions with prior awareness (aOR: 0.69, 95% CI 0.55 – 0.86). Those who perceived a higher likelihood of COVID-19 infection were significantly more likely to have prior awareness of Paxlovid (aOR: 1.25, 95% CI 1.10 – 1.42).

Table 3 gives the results from our multivariable regression model to predict respondents’ acceptance of Paxlovid. The model showed significant association for gender, trust in healthcare providers, trust in government communications and serious consequences if infected. Female gender was significantly associated with lower acceptance (aOR: 0.42, 95% CI 0.31 – 0.57) when compared to males, but no significant associations were found for other socio-demographic factors. Higher levels of trust in healthcare providers (aOR: 1.49, 95% CI 1.11 – 1.99) and government communications (aOR: 1.38, 95% CI 1.09 – 1.76) were significantly associated with higher acceptance. Those who perceived more serious consequences from COVID-19 (aOR: 1.23, 95% CI 1.07 – 1.42) also had higher acceptance.

Regarding the initiative to request Paxlovid, Table S4 shows that females were less likely (aOR: 0.50, 95% CI 0.39 – 0.64), while those who perceived more serious consequences from COVID-19 (aOR: 1.24, 95% CI 1.09 – 1.40) were more likely to take the initiative to request Paxlovid.

Figure 2 ranks several concerns from our respondents about taking Paxlovid. The top three were potential side effects (64%), the cost of Paxlovid (29%), and perceptions that COVID-19 is not severe (25%). The proportions for all three differed significantly by acceptance but not prior awareness. In those with higher acceptance of Paxlovid, cost was more frequently (32% vs 21%,  $p < 0.001$ ), while side effects (60% vs 74%,  $p < 0.001$ ) and perceptions that COVID-19 was a mild disease (23% vs 30%,  $p = 0.008$ ) were less frequently reported than in those with lower acceptance. Amongst those with lower acceptance towards Paxlovid, a substantial proportion believed that Paxlovid was not effective (18% vs 5% in those with higher acceptance,  $p < 0.001$ ).

Supplementary table S5 shows that more women than men were concerned about side effects (aOR: 1.37, 95% CI 1.07 – 1.76), while those with higher trust in healthcare providers (aOR: 0.78, 95% CI 0.60 – 1.02) were less likely to be so. In table S6, individuals aged 60 and above were less likely to be concerned about costs (aOR: 0.55, 95% CI 0.33 – 0.91). Respondents with lower trust in government communications were more likely to be concerned that Paxlovid is not effective (aOR: 0.46, 95% CI 0.33 – 0.64).

## 4. Discussion

Our findings suggest that the delivery of Paxlovid in our setting is highly dependent on having primary care doctors diagnose COVID-19 and recommend it to their patients. Only a slim majority of respondents had previously heard of Paxlovid as an effective treatment for reducing COVID-19 severity, and less than 20% were both sufficiently informed and had the initiative to request it. On the other hand, about three-quarters would likely or very likely take Paxlovid if prescribed, and acceptance did not markedly differ by prior awareness. Older age groups and more years of education were associated with greater awareness; the former were the target group for messaging on the benefits of treatment, and the latter may have greater exposure and better understanding and recall of information about Paxlovid. As for acceptance towards Paxlovid, risk perceptions regarding COVID-19 and respondents' levels of trust towards government messaging and healthcare providers were important and potentially modifiable factors. We also found significant differences in the concerns about taking Paxlovid between respondents with higher and lower acceptance.

Although a substantial majority said they would accept Paxlovid if it was prescribed to them, it is still relevant to highlight factors that prime a population for greater uptake. The relationship between some of these factors and concerns about taking Paxlovid are possibly applicable to settings beyond Singapore. Of the demographic factors, the only significant association was that females had lower acceptance. Interestingly, women were also more likely to express concerns about unwanted side effects (supplementary Table S5). In general, women have been found to experience more medication side effects than men, and their being aware of this, possibly through experiences with other medications, may have caused them to adopt a more cautious view of new medications, including COVID-19 antivirals. Moreover, there are genuine concerns that molnupiravir, the other COVID-19 antiviral available in

Singapore, can cause DNA mutations and hence birth defects in a developing foetus (20), and this could have led to wider concerns amongst women about COVID-19 antiviral use in general.

The other notable factors significantly associated with acceptance arose from respondents' perceptions. Firstly, as with our previous work (17), greater trust in government communications was associated with higher acceptance and being less likely to cite the effectiveness of Paxlovid as a concern. Moreover, although trust in government communications was strongly correlated with trust in their healthcare providers (Spearman's  $r = 0.5735$ ,  $p < 0.001$ , for the two scores), the latter was also independently associated with higher acceptance. Those with greater trust in healthcare providers were also less likely to be concerned about side effects. The public often relies on guidance from government agencies and healthcare providers when making informed decisions about their health. Trust in government communications may reflect confidence in the overall public health response and the regulatory processes ensuring the safety and efficacy of medications such as Paxlovid (21, 22). Complementary to this, healthcare providers, acting as the primary point of contact for medical care, are positioned to recommend appropriate treatments based on individual patient needs while ensuring that prescribed medications are reasonably safe given each patient's medical history.

Kritzinger et al. (23) suggested that perceptions of the government's appropriateness in handling the crisis play an essential role in people's trust, and a consistent approach is needed to establish trust with the public over time. On the other hand, Amara et al. (24) discovered that respondents would already generally trust their healthcare providers, and we found that trust in healthcare providers was positively associated with awareness of Paxlovid. However, as healthcare encounters typically follow the advent of an illness episode, there is a potential limitation in relying on healthcare providers to inform their patients about Paxlovid. An earlier survey in our cohort (unpublished data) found that effective treatments can predispose individuals to seek medical care should they develop COVID-like symptoms. Therefore, while this survey found that prior awareness did not have a substantial effect on acceptance, awareness may still have an indirect effect on uptake by incentivising symptomatic individuals to seek care, particularly since Paxlovid should ideally be given early in the course of illness. However, those with higher trust in government communications had lower proportions with prior awareness. While somewhat unexpected, we speculate that that Paxlovid was not sufficiently promoted in government messaging platforms, so that those who were more dependent on such messaging may thus have been less aware. To fully leverage on the public's trust in healthcare providers and government communications, it would be necessary to firstly communicate messages that raise awareness so as to drive access to healthcare, then follow through by having healthcare providers recommend treatment to a receptive population.

Not unexpectedly, respondents who perceived that contracting COVID-19 could have severe consequences were more likely to have higher acceptance towards Paxlovid as well as have the initiative to request Paxlovid. Moreover, the perception that COVID-19 is a mild disease not needing such treatment was the third most frequent concern about Paxlovid, and significantly more common amongst those with lower acceptance towards Paxlovid. Perceptions of COVID-19 severity are not static. Over serial surveys, we observed a decrease in the proportion of people who strongly agreed or agreed that COVID-19



infection would have severe consequences (see Table S3). This may cause acceptance towards interventions like Paxlovid to decrease over time. Changing perceptions of COVID-19 severity are not unjustified since the omicron subvariants which have been dominant since early 2022, have been shown to be less severe than the preceding delta COVID-19 variant (25, 26). Also, after Singapore achieved high levels of vaccine coverage, there was an intentional pivot in messaging away from preventing infection to an emphasis on “living with COVID-19” (27–29). Such messaging could also have contributed to the shifts in perceptions. However, new COVID-19 variants continue to emerge, exhibiting varying degrees of resistance to immunity conferred by past infection and existing COVID-19 vaccines. One modelling study exploring vaccine allocation for facilitating an effective response to COVID-19 also highlighted how antiviral treatments might be necessary to supplement vaccination efforts, mainly when vaccine supply is limited or for COVID-19 variants that are partially resistant to current vaccines (30). Moreover, transmission models of SARS-CoV-2 also suggest that antiviral treatments may mitigate transmission of COVID-19 (31). Should a COVID-19 variant emerge with high levels of immune escape and more significant morbidity and mortality, antiviral treatments may need to be deployed more widely beyond older age groups and medically vulnerable individuals. If so, this would require an appropriately timed change of messaging about which groups should take Paxlovid, alongside an updated emphasis on imminent risks of infection and greater likelihood of severe disease to drive awareness of and acceptance towards antiviral use, respectively.

Some limitations apply when generalising our findings to the broader population. Firstly, it must be acknowledged that compared to the Singapore population, ethnic minorities, individuals with fewer years of education, and those living in smaller publicly owned residences are under-represented amongst our respondents. Some of these are underserved populations with poorer health literacy who also face more significant challenges in accessing health services and antiviral medications. Our study may hence be over-estimating awareness and acceptance of antiviral use for COVID-19. Secondly, by the time of our survey in the second half of 2022, a substantial proportion of our population (estimated in another survey of the cohort to be about 61%) might already have seen a doctor for COVID-19. If so, they may have learned of Paxlovid through their healthcare providers, and awareness of Paxlovid prior to diagnosis may be lower than we estimated. Moreover, this could also have contributed to the observed association that those with greater trust in healthcare providers were more likely to be aware of Paxlovid.

## 5. Conclusions

In summary, our study suggests that the levels of awareness of Paxlovid and the initiative to request this treatment from their doctors can be improved. Since most patients would accept Paxlovid if their doctors recommend it, increased uptake would largely depend on having our doctors recommend this to more of their patients. It will also be helpful to address common concerns about side effects, cost and effectiveness, but underpinning all such communications may be the level of trust in official channels and healthcare providers, which would need to be built over time. In addition, it is unsurprising but noteworthy that perceived severity was strongly associated with acceptance towards Paxlovid. Perceptions are likely influenced by both the epidemiology of circulating variants and how the risks

associated with COVID-19 are communicated and received. Therefore, when circumstances are rapidly evolving, trust can be particularly valuable for re-calibrating public perceptions of risk and benefit, so as to drive awareness of and acceptance towards antiviral agents and other interventions.

## Declarations

### Ethics approval and consent to participate

The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Institutional Review Board of the National Healthcare Group (Study reference number: 2018/01203 and Date of approval: 23 June 2021). Informed consent was obtained from all subjects involved in the study. This is not a clinical trial.

### Consent for publication

Not applicable

### Availability of data and materials

Please be advised that the information outlined in this article may be made available upon request from the designated corresponding author. However, we must emphasise that such disclosure is subject to the applicable legal and regulatory requirements, as well as at the sole discretion of the corresponding author.

### Competing interests

The authors declare no conflict of interest.

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### Authors' contributions

Conceptualisation, M.I.C., A.S.E.S. and B.W.L.O.;

methodology, M.I.C., A.S.E.S. and B.W.L.O.;

validation, M.I.C., A.S.E.S.;

formal analysis, M.I.C., A.S.E.S.;

investigation, M.I.C., A.S.E.S. and B.W.L.O.;

resources, M.I.C., A.S.E.S. and B.W.L.O.;

data curation, M.I.C., A.S.E.S.;

writing—original draft preparation, A.S.E.S.;

writing—review and editing, M.I.C., A.S.E.S., B.W.L.O., T.L.T and K.G;

visualisation, A.S.E.S.;

supervision, M.I.C.;

project administration, A.S.E.S. and B.W.L.O.;

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All authors have read and agreed to the published version of the manuscript.

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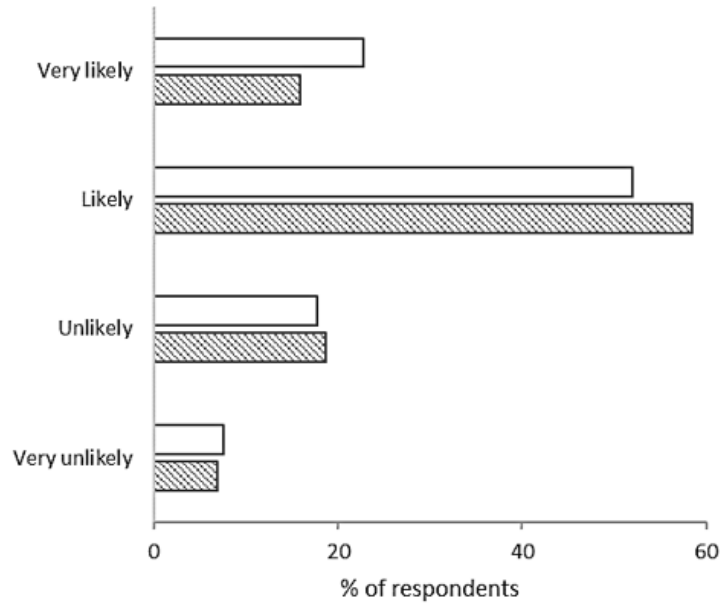
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## Tables

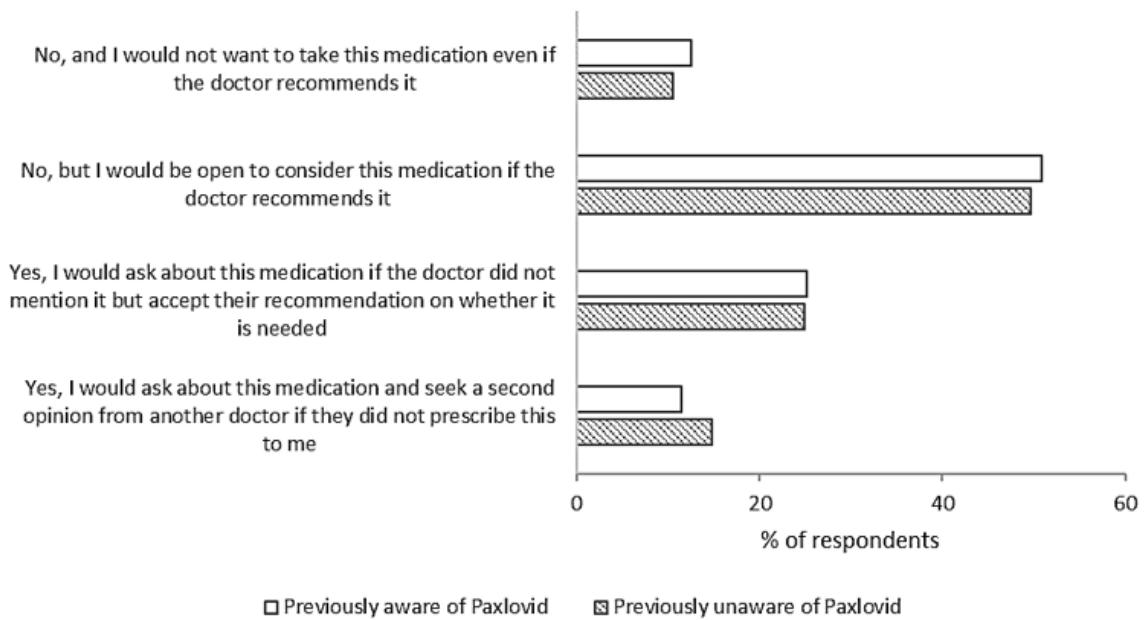
Tables 1-4 are available in the Supplementary Files section.

## Figures

A) Receptiveness to take Paxlovid (p=0.009)



B) Initiative to request Paxlovid (p=0.207)



**Figure 1**

Receptiveness to take Paxlovid if prescribed (A), and Initiative to request Paxlovid (B), stratified by whether the respondent was previously aware of Paxlovid. Pearson chi-square test was used to generate the p-values in the figure.

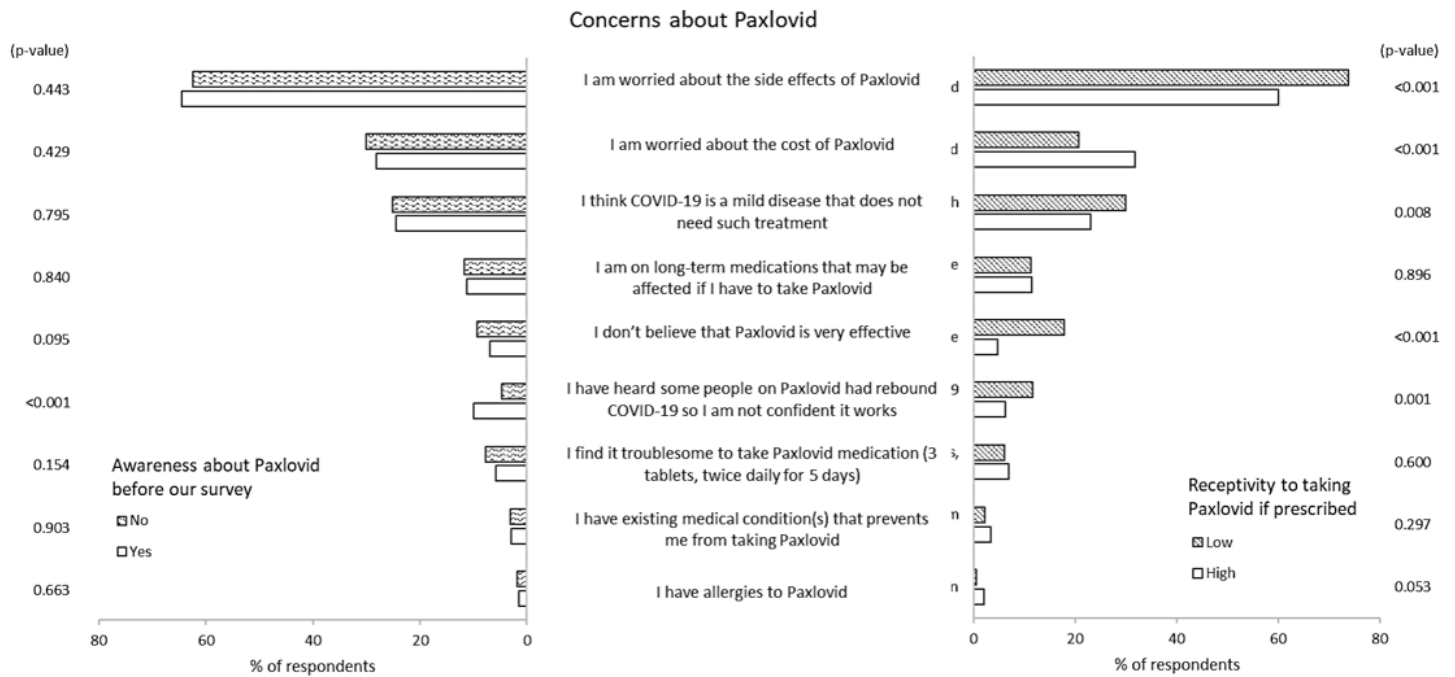


Figure 2

Concerns about taking Paxlovid

## Supplementary Files

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- [Manuscriptsupplementarymaterials.docx](#)
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