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BRIEF REPORT

Perceptions and Barriers to Outpatient Antiviral Therapy for COVID-19 and Influenza as Observed by Infectious Disease Specialists in North America: Results of an Emerging Infections Network (EIN) Survey, February 2024

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Antiviral therapy is underutilized for outpatients at increased risk for severe COVID-19 or influenza. Results from this survey offer insights into treatment barriers from the infectious disease specialist perspective. Further education is needed about the benefits of early antiviral therapy.

Keywords. antivirals; barriers; COVID-19; influenza; treatment.

Early antiviral treatment reduces the risk of severe disease among outpatients with COVID-19 or influenza who have elevated risk for severe disease and is recommended by the Infectious Diseases Society of America and the Centers for Disease Control and Prevention (CDC) [1–4]. For COVID-19, antivirals with demonstrated clinical efficacy and effectiveness include nirmatrelvir/ritonavir (Paxlovid), remdesivir (Veklury), and molnupiravir (Lagevrio) [5–8]. For influenza, treatment options include oseltamivir (generic or Tamiflu), baloxavir marboxil (Xofluza), zanamivir (Relenza), or peramivir (Rapivab) [9–15].

Recent studies suggest a substantial underuse of antiviral medications among outpatients at increased risk for severe illness from COVID-19 and/or influenza. For diagnosed COVID-19, outpatient antiviral usage ranged between 4.9% and 26% for various groups with higher risk [16–18]. For diagnosed influenza, outpatient antiviral usage ranged between 19% and 37% in similar groups with higher risk [19–22]. To better understand this underutilization, we conducted a survey to assess perspectives and barriers of antiviral usage for outpatients with COVID-19 and influenza as perceived by infectious disease specialists in North America.

METHODS

The Emerging Infections Network (EIN; https://ein.idsociety.org/) is a sentinel network composed of infectious disease specialists in North America and sponsored by the Infectious Diseases Society of America. We emailed an online survey 3 times to 1898 EIN members who were practicing clinicians during January and February 2024.

The survey (https://ein.idsociety.org/surveys/survey/174/) asked questions about the likelihood of using specific antivirals for COVID-19 or influenza, the indications providers considered for using antivirals, the barriers prevalent when prescribing antivirals, what resources would help increase antiviral treatment, and about a hypothetical monoclonal antibody product. Pemivibart (Pemgarda), a monoclonal antibody for COVID-19 preexposure prophylaxis, was not included because it did not receive Food and Drug Administration approval until after the survey had ended. Respondents had the option of providing free-text responses after each question and at the end of the survey.

We conducted descriptive analyses of all responses. Answers from Likert-scale questions were dichotomized into 2 options for analyses (eg, "likely to use" vs "unlikely to use"). We used chi-square tests ($\alpha = .05$) to conduct bivariate comparisons of respondents' likelihood to choose a particular antiviral and their practice type, geographic location, and years of experience. Free-text responses were organized into similar themes by qualitative analysis experts and themes were then described.

RESULTS

In total, 30% (565/1898) responded to the survey. Of these respondents, 109 (19%) did not complete the survey because they did not manage COVID-19 or influenza patients in the past 6 months. Of the remaining 81% (456/565) of respondents, all were infectious disease practitioners, 94% were physicians, 86% had 5 years or more of practicing since completing training, 86% managed adult patients, and 79% practiced at university or teaching hospitals. All 456 respondents were located within the United States and Puerto Rico with the South having the highest representation (30%) and the Northeast having the lowest (22%) (Supplementary Table 1).

For COVID-19 treatment, 74% of respondents reported that they or typical providers at their institution would regularly

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consider nirmatrelvir/ritonavir for eligible outpatients, whereas only 39% indicated the same for remdesivir. For influenza, 86% of respondents indicated that they or typical providers would regularly consider oseltamivir for eligible outpatients. In contrast, 7% or fewer of respondents reported that they or typical providers would likely consider molnupiravir for COVID-19 or baloxavir marboxil, zanamivir, or peramivir for influenza (Supplementary Table 1).

Adult infectious disease respondents were more likely to report using nirmatrelvir/ritonavir for treatment of COVID-19 compared to pediatric infectious disease respondents (79% vs 51%, respectively; $P < .0001$) and pediatric infectious disease respondents were more likely to report using peramivir for treatment of influenza compared to adult infectious disease respondents (4% vs 1%, respectively; $P = .021$). The likelihood of using oseltamivir varied with years of experience ($P < .019$). Practice type, geographic location, and years of experience did not show other associations with individual antiviral medications (Supplementary Table 1).

When prescribing COVID-19 and influenza antivirals, respondents identified immunosuppression (97% and 93%), underlying medical conditions (95% and 89%), and age (89% and 83%) as the most common factors that typical providers consider (Table 1). Additionally, most respondents (89%) noted they would offer preexposure prophylaxis to immunocompromised patients if an effective monoclonal antibody product became available against SARS-CoV-2.

The most common perceived provider barriers for COVID-19 antivirals were difficulty assessing drug interactions (58%), short treatment window (54%), and concerns about potential adverse effects (46%). The most common perceived patient barriers for COVID-19 antivirals were side effects (61%), perceived low risk of COVID-19 (54%), and not feeling sick (51%). For influenza, only short treatment window (59%) was indicated by more than 40% of respondents as a perceived barrier for either patients or providers (Table 1).

Free-text responses (n = 144) revealed additional themes. The most common theme was related to provider skepticism on the benefits of antiviral treatment (48% of free-text responses) with respondents offering several reasons for skepticism such as the benefits appearing too small, antivirals lacking evidence-based data, or feeling uncertain about the clinical indications. The second leading theme was related to accessibility (31% of free-text responses) with respondents showing concerns about the cost of the medications, limited hospital access to the antivirals, and difficulty administering some of the antivirals (Table 2).

When asked what resources would help increase the uptake of antivirals to eligible patients for both COVID-19 and influenza, 86% of respondents reported increased low-cost rapid multiplex testing would be somewhat or very helpful, followed by provider and patient education (85%) and expanding insurance or access (83%) (Supplementary Table 2).

Table 1. Factors Considered and Barriers to Outpatient Antiviral Treatment for COVID-19 and Influenza, United States, 2024

Factors Typical Providers Consider When Prescribing	COVID-19	Influenza
Immunosuppressive condition or medications	442 (97%)	424 (93%)
Other underlying medical conditions	431 (95%)	404 (89%)
Age (eg, young children, older adults)	404 (89%)	377 (83%)
Patient request	291 (64%)	267 (59%)
Prior immunization(s)	171 (38%)	104 (23%)
Prior infection(s)	111 (24%)	43 (9%)
(No factors selected)	6 (1%)	13 (3%)
Perceived patient barriers/hesitation		
Concerns about side effects (eg, metallic taste) or safety	277 (61%)	93 (20%)
Not at risk for severe disease because of prior infection and/or vaccination	246 (54%)	150 (33%)
Doesn't feel sick	233 (51%)	155 (34%)
Concerns about rebound after treatment	213 (47%)	6 (1%)
Affordability of treatment	152 (33%)	87 (19%)
(No barrier selected)	40 (9%)	160 (35%)
Perceived provider barriers/hesitation		
Difficulty assessing drug interactions	263 (58%)	13 (3%)
Short treatment window	244 (54%)	269 (59%)
Potential adverse effects from treatment	208 (46%)	84 (18%)
Unsure about eligibility criteria	168 (37%)	63 (14%)
Do not feel antiviral treatment is effective or no randomized controlled trial data to support use	118 (26%)	97 (21%)
Immunity from illness or vaccination	111 (24%)	43 (9%)
Unknown lab results (eg, renal function)	96 (21%)	23 (5%)
(No barrier selected)	53 (12%)	131 (29%)

N = 456. (Respondents selected all that applied; numbers add to >100%).

DISCUSSION

This nationwide survey of infectious disease specialists revealed important barriers to antiviral uptake for SARS CoV-2 infections and influenza. Although most respondents reported that they or their colleagues would consider using nirmatrelvir/ritonavir for COVID-19 or oseltamivir for influenza for eligible patients, many voiced concerns about initiating treatment given the limited timeframe for optimal effectiveness. These barriers could contribute to low antiviral usage in the United States in populations with higher risk, and our findings may help ongoing education efforts on antivirals for COVID-19 and influenza.

Respondents also indicated increased availability to low-cost, rapid multiplex testing would be the most helpful for increasing antiviral usage. This highlights the need to expand testing access for prompt diagnosis to capitalize on the short treatment window. Additionally, education about the benefits of early testing for persons at higher risk, even with initial mild

Table 2. Thematic Summary on Barriers to Outpatient Antiviral Treatment for COVID-19 and Influenza Patients, United States, 2024

Theme	Illustrative Quotation
Provider skepticism n = 69	(1) "Paxlovid was a homerun early on but in 2024 with most population either having been vaccinated, prior infection or a combination, it's unclear who this drug is for."
	(2) "…the use of Paxlovid to reduce hospitalization was studied during a time when risk of COVID-19 complications in the population was far higher, as was the rate of unvaccinated and/or never infected individuals in the population. In summary, the [number needed to treat] NNT for these drugs to prevent complications of COVID-19 has climbed substantially, and as such, many providers are less aggressive in prescribing them for many patients…"
	(3) "I think there is a general lack of knowledge of the change in guidance on when to initiate therapeutics. Candidacy has changed over time and due to a waning interest, many providers simply do not have a good knowledge of who is eligible, and even what drugs are currently available."
Accessibility n = 45	(4) "Major barriers for us are the short treatment window and limited access to testing (especially flu but COVID tests now $$ and less available). Most clinics not well equipped to appropriately triage, assess and prescribe same d and access to testing is a limitation…"
	(5) "Availability and accessibility of meds. Example IV peramivir is never available, and IV remdesivir for outpatient COVID is not logistically feasible/ accessible."
Drug limitations n = 27	(6) "Paxlovid is a useful drug in some patients. It has significant, sometimes insurmountable, issues with drug-drug interactions. The patients who could benefit most, those with transplants and cancer chemotherapy, often are completely unable to receive the drug because of drug safely…"
Timeliness n = 22	(7) "Need to get patients and primary care providers to understand how important early diagnosis is for starting therapy. Too often I have calls about a patient 5–7 d into illness when these drugs are no longer indicated."
Patient skepticism n = 19	(8) "I think we are all burnt out by families patients and misinformation. I think we have taken the position of, we have offered it, and are not spending another second overcoming resistance to treatment, document and moving on."
	(9) "… Concern for rebound is high amongst patients. Many patients do not believe COVID is an issue anymore, which leads to less testing and concern even if tested to talk to a provider about treatment options."
	(10) "Providers, especially primary care and nurses, PAs who regurgitate things they hear [from certain networks] are a major problem, and even mainstream media. I have seen immunosuppressed patients in the hospital who were actively discouraged from getting vaccine or Paxlovid by these people."

N = 144. (Some respondents provided answers with more than 1 theme; numbers add to >100%).

symptoms, could also facilitate early treatment to prevent severe outcomes.

For COVID-19, difficulty assessing drug interactions was reported as the most common perceived provider barrier. The complexity of checking for interactions and renal disease may dissuade some clinicians from routinely prescribing nirmatrelvir/ritonavir for suitable patients. However, online tools [21] and electronic medical record tools are available to examine potential drug–drug interactions and dose adjustments for nirmatrelvir/ritonavir. Also, prescribers can consult pharmacists to review patients' medication profiles to assess for harmful drug–drug interactions, renal dosing, and treatment alternatives.

Common perceived patient barriers noted by respondents were concerns about side effects and rebound from COVID-19 antivirals, along with perception of lower personal risk for severe illness. Knowing that serious side effects are uncommon with appropriate nirmatrelvir/ritonavir prescriptions [4] may enable patients to make informed decisions. Groups with higher risk for severe COVID-19 would also benefit from targeted messaging about risk factors for severe illness, the importance of early testing and treatment, and how antivirals prevent mild illness from progressing to severe disease. In our survey, respondents indicated education for providers and patients as the second most valuable intervention to increase the uptake of antivirals.

The CDC has developed online resources to assist clinicians with outpatient COVID-19 and flu treatment [3, 4]. These resources provide details on patient access programs, current research on effectiveness and rebound, guidelines on eligibility and treatment options, links to drug interaction and renal dosing tools, criteria for preexposure prophylaxis, Food and Drug Administration fact sheets, webinars on treatment, and more. Additionally, the CDC is working with several medical organizations to educate members about treatment of these respiratory pathogens.

This survey has some important limitations. First, it reflects perceptions of infectious disease specialists and not providers who manage most outpatients with COVID-19 and influenza. However, infectious disease physicians are often consulted by other clinicians on COVID-19 and influenza treatment and if they are misinformed, there is a risk that these myths will be perpetuated. Second, this convenience sample may not fully represent the views of all U.S. infectious disease specialists. Finally, although the response rate of our survey was comparable to recent EIN surveys focused on clinicians, the 30% participation rate introduces the potential for response bias.

In conclusion, this survey offers valuable insights into the perspectives and barriers related to antiviral usage for COVID-19 and influenza. To ensure optimal patient outcomes, clinicians and patients need easy access to up-to-date information on antiviral benefits and risks, alongside readily available testing and treatment options. However, more research is needed to further understand the barriers to antiviral usage, particularly among primary care providers. To reduce morbidity and mortality from COVID-19 and influenza in patients with

higher risk, clinicians should consider prioritizing early antiviral treatment for those who stand to benefit most.

Supplementary Data

Supplementary materials are available at *Open Forum 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 findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention (CDC). Emerging Infections Network queries are to gauge the current landscape of infectious disease practice. As such, these queries fall within the scope of nonresearch program evaluation, as described in current CDC policy.

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Patient consent. This study did not include factors necessitating patient consent.

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