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ORIGINAL RESEARCH

Household Influenza Transmission and Healthcare Resource Utilization Among Patients Treated with Baloxavir vs Oseltamivir: A United States Outpatient Prospective Survey

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ABSTRACT

Introduction: Influenza is a common, seasonal infectious disease with broad medical, economic, and social consequences. Real-world evidence on the effect of influenza treatment on household transmission and healthcare resource utilization is limited in outpatient settings in the USA. This study examined the real-world effectiveness of baloxavir vs oseltamivir in reducing influenza household transmission and healthcare resource utilization.

Methods: This prospective electronic survey on patient-reported outcomes was conducted between October 2022 and May 2023 via CVS Pharmacy in the USA. Adult participants (≥18 years old) were eligible if they filled a prescription for baloxavir or oseltamivir at a CVS Pharmacy within 2 days of influenza symptom onset. Participant demographics, household transmission, and all-cause healthcare resource utilization were collected. Transmission and utilization outcomes were assessed using χ^2 and Fisher exact tests.

Results: Of 87,871 unique patients contacted, 1346 (1.5%) consented. Of 374 eligible patients, 286 (90 baloxavir- and 196 oseltamivir-treated patients) completed the survey and were included in the analysis. Mean age of participants was 45.4 years, 65.6% were female, and 86.7% were White. Lower household transmission was observed with baloxavir compared with oseltamivir therapy (17.8% vs 26.5%; relative risk = 0.67; 95% CI 0.41–1.11). Healthcare

Prior Presentation: A portion of these results were presented as a poster during Infectious Disease Week on October 12, 2023 in Boston, Massachusetts. In addition, a portion of these results were presented as an encore presentation at AMCP Nexus on October 18, 2023 in Orlando, Florida.

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resource utilization, particularly emergency department visits (0.0% vs 4.6%), was also numerically lower in the baloxavir-treated group; no hospitalizations were reported in either cohort.

Conclusions: The findings from this real-world study suggest that antiviral treatment of influenza with baloxavir may decrease household transmission and reduce healthcare resource utilization compared with oseltamivir.

Keywords: Baloxavir; Influenza; Oseltamivir; Real-world data; Transmission

Key Summary Points

Why carry out this study?
Baloxavir and oseltamivir are two US Food and Drug Administration-approved treatments for influenza, a common, seasonal infectious disease.
Real-world evidence on the effect of influenza treatment on household transmission and healthcare resource utilization are limited in US outpatient settings.
The hypothesis of the study was that lower household influenza transmission and reduced healthcare utilization would be observed for patients treated with baloxavir vs oseltamivir in a real-world setting.
What was learned from this study?
Patients who received baloxavir reported less household transmission compared with oseltamivir therapy.
Healthcare resource utilization was numerically lower in the baloxavir-treated group.
This study suggests that antiviral treatment of influenza with baloxavir may decrease household transmission and reduce healthcare resource utilization.

INTRODUCTION

Influenza is a common, seasonal infectious disease; 3–5 million patients experience severe illness and up to 650,000 deaths occur worldwide on an annual basis [1]. In the USA, influenza occurs annually from early fall through midspring and has a broad economic burden on the healthcare system [2]. An estimated 11.3–25.6 million healthcare encounters related to influenza occur on an annual basis, with costs ranging from $2.0 billion to $5.8 billion, including a large burden from office-based outpatient and emergency department visits [3, 4].

Seasonal influenza is easily transmitted through the respiratory system and spreads rapidly, particularly in households [5, 6]. Infectiousness is due to viral shedding in the respiratory system, which can occur before symptoms start and up to 1 week after becoming ill [7, 8]. Treating the primary infected patient with anti-influenza drugs may reduce symptoms as well as secondary infections between household members [5, 9–11]. Several antiviral medications, including neuraminidase inhibitors (i.e., oseltamivir, zanamivir, peramivir), are approved for treatment of influenza and can reduce the severity and duration of the disease; when given prophylactically, they can reduce the incidence of influenza infection and household transmission by up to 70–90% [12–14]. For example, a double-blind, randomized, placebo-controlled study in North America and Europe found that prophylactic use of oseltamivir reduced household transmission by 84% and was well tolerated [14]. Another option is baloxavir marboxil (baloxavir), a single-dose, oral, cap-dependent endonuclease inhibitor approved for influenza treatment and postexposure prophylaxis [15–18]. The BLOCKSTONE trial in Japan demonstrated that baloxavir markedly reduced the risk of developing influenza up to 86% vs placebo in prophylaxed households and was well tolerated [18]. Studies using large claims databases in Japan suggested that treatment with baloxavir reduced household transmission compared with oseltamivir [10, 11]; however, real-world data assessing the

effect of baloxavir on household transmission or healthcare resource utilization in the USA are limited.

Patient-reported outcomes are important tools in real-world studies to comprehensively capture a patient's disease experience and are useful in assessing the impact of the disease and subsequent therapeutic approaches [19, 20]. This prospective, noninterventional survey study aimed to describe household transmission and healthcare resource utilization among patients with influenza who filled a prescription for baloxavir vs oseltamivir in the USA.

METHODS

Study Design and Patient Eligibility

This was a prospective, real-world survey including participants with influenza and was conducted in the USA between October 2022 and May 2023. The study was conducted in accordance with legal and regulatory requirements, as well as with scientific purpose, value, and rigor, and followed generally accepted research practices described in Good Practices for Outcomes Research issued by the International Society for Pharmacoeconomics and Outcomes Research and Good Pharmacoepidemiology Practice guidelines. Primary staff for this study were certified by the Collaborative Institutional Training Initiative in Human Subjects Research and Good Clinical Practice. To uphold participant confidentiality, the study personnel implemented and complied with administrative, physical, and technical safeguards to reasonably and appropriately protect the confidentiality, integrity, and availability of protected health information collected during this study. Sponsor approval and continuing review was obtained through a central institutional review board (Sterling IRB), which evaluated this study and safeguarded the rights and welfare of participants. All patients provided informed consent.

Participant Population and Recruiting Process

Participants ≥ 18 years of age who filled a prescription for baloxavir or oseltamivir at any CVS Pharmacy site in the USA (index date, day 0) were recruited via email and/or call center to participate in the online survey. Eligible participants were able to independently fill out an English- or Spanish-language questionnaire and provide electronic consent. Influenza diagnosis and selection of treatment was based on the discretion of the participant's clinician and not a part of the study. Exclusion criteria included filling the prescription for baloxavir or oseltamivir > 2 days from influenza symptom onset consistent with their respective labels [17, 21], using the treatments for prophylaxis use, living alone, testing positive for COVID ≤ 30 days before index date, or not being the primary member of the household to experience influenza symptoms.

The study design is shown in Fig. 1. The day after a participant index date (day 1), the CVS Health recruitment team identified and generated a convenience sample using a 1:3 ratio of participants who filled a baloxavir or oseltamivir prescription on the same day in the same US state. The choice of a 1:3 ratio of baloxavir to oseltamivir was chosen in order to increase recruitment; oseltamivir is generic and prescribed more frequently than baloxavir. For participants with email addresses, an initial email invitation to the e-survey was sent from the CVS Health team on day 4, with subsequent follow-up reminders on days 6 and 8. Participants with phone numbers were called between days 6 and 8, informed about the study, and invited to participate on their own or with support from call center agents. Participants were required to complete the survey on days 6 to 8 to ensure that any members of their household who developed an influenza infection would be symptomatic.

Outcomes

The primary outcome of the study was household influenza transmission rate measured as proportion of household with any transmission (dichotomous) after the index person received baloxavir or oseltamivir. Secondary outcomes were patient-reported healthcare resource utilization (physician, urgent care, or telehealth visit), emergency department visit, or hospital inpatient admission by index patient from

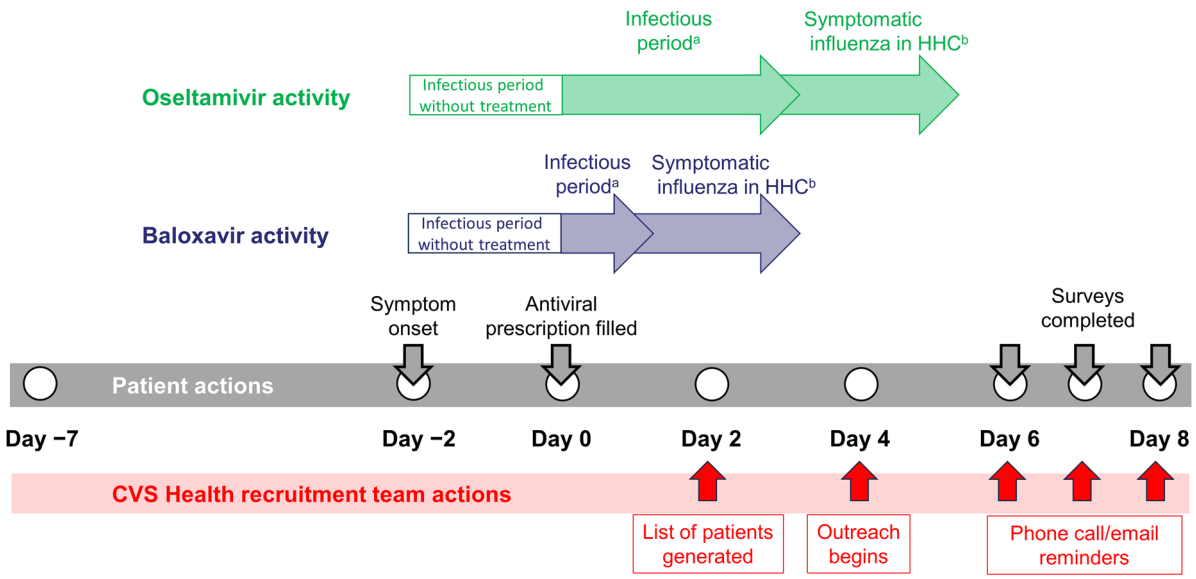

Fig. 1 Study design. *HHC* household contact. [a]Time of treatment start to cessation of viral shedding (assumed). [b]Time from infection to potential manifestation of symptoms in HHC (average, 2 days)

receipt of study drug to completion of survey; patients were not explicitly asked to report only influenza-related healthcare resource utilization. The survey questions are listed in the supplementary data.

Statistical Analysis

Analyses were performed for each patient cohort (all patients, baloxavir, and oseltamivir). To assess whether transmission was affected by household size, we conducted a subset analysis by household size = 2 and household size > 2. Patient demographics, clinical characteristics, household influenza transmission, and healthcare resource utilization were assessed using descriptive statistics. The presence or absence of any household transmission, emergency department visits, and hospital inpatient admission were summarized as categorical variables. Frequency counts and percentages were described for ordinal and categorical variables; mean and SD were used for continuous variables. Differences in the proportion of baloxavir- and oseltamivir-treated participants with household influenza transmission were assessed using χ^2 tests. The analysis did not adjust for potential confounders because of the small sample size. The Social Vulnerability Index (SVI) was calculated and reported descriptively. The SVI uses 15 US Census variables to determine the SVI of every census tract (tract range, 1200–8000 residents; optimal size, 4000 residents) in the USA and contains four themes: socioeconomic status, household composition, minority status, and housing type and transportation [22]. The zip code of the CVS store where the prescription was filled was used to generate the participant's SVI. SVI values range from 0 to 1 based on their percentile position among all census tracts in the USA; a higher SVI indicates higher vulnerability. All analyses were performed with SAS Version 9.4 (SAS Institute, Cary, NC, USA).

RESULTS

Patient Demographics

Of 87,871 unique participants contacted, 1346 (1.5%) consented, and 374 were eligible on the basis of inclusion and exclusion criteria (Fig. 2). Of the 286 participants who completed the

survey and were included in the analysis, 90 received baloxavir and 196 received oseltamivir.

Among the 286 participants, the mean (SD) age was 45.4 (15.3) years, 65.6% were female, and 86.7% were White (Table 1). There were no significant differences between the baloxavir- and oseltamivir-treated groups, except for Centers for Medicare & Medicaid Services regions ($P=0.02$). Over half of baloxavir-treated participants reported living in regions 4 (KY, TN, NC, SC, GA, MS, AL, and FL) and 6 (NM, OK, AR, TX, and LA) compared with oseltamivir-treated patients who were more evenly spread across the country. Participants in both treatment cohorts lived in communities with similar, medium social vulnerability (mean [SD], 0.63 [0.22]; $P=0.28$). A total of 136 participants (47.6%) reported comorbidities, and there were no significant differences in comorbid conditions between treatment groups (Table 2). The most common comorbidities reported by participants were obesity, asthma, and other chronic diseases (17.4%, 16.1%, and 11.9%, respectively). The most frequently reported measures to prevent transmission of influenza were frequent handwashing and not sharing utensils (80.1% and 73.8%, respectively). The most frequently reported over-the-counter medications for influenza symptoms were pain and fever medication (86.4%) and a combination of pain and fever medication and decongestants (52.8%).

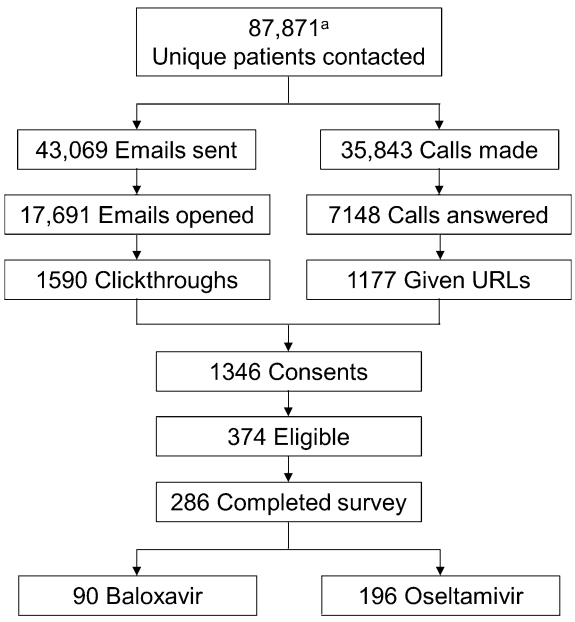

Fig. 2 Participant disposition flowchart. *URL* uniform resource locator. [a]Participants were recruited via email and/or call center

Incidence of Household Transmission

The proportion of families with household transmission was 17.8% (16/90) in the baloxavir-treated group and 26.5% (52/196) in the oseltamivir-treated group (Fig. 3). In a comparison between the two treatment groups, the relative risk (RR) was 0.67 (95% CI 0.41–1.11, $P=0.11$), which indicates that treatment with baloxavir was slightly favored with respect to decreasing household transmission.

Numerically, baloxavir-treated participants experienced less household transmission irrespective of household size (Fig. 4). Of the participants who reported living in a household of 2, a total of 16.7% of those treated with baloxavir reported influenza transmission compared with 23.2% of those treated with oseltamivir (RR = 0.72; 95% CI 0.32–1.62, $P=0.41$). Intrafamily transmission in households of >2 people was also numerically smaller with baloxavir than oseltamivir; 18.5% of baloxavir-treated participants reported transmission compared with 29.9% of oseltamivir-treated participants (RR = 0.62; 95% CI 0.33–1.17, $P=0.13$).

Healthcare Resource Utilization

Overall, healthcare resource utilization, particularly emergency department visits, between receipt of study drug and completion of the survey was lower in baloxavir-treated patients (Fig. 5). The proportion of participants who reported a visit to an urgent care clinic was similar in both treatment groups (14.4% baloxavir treated vs 15.8% oseltamivir treated; RR = 0.91; 95% CI 0.50–1.66, $P=0.77$). Of baloxavir-treated participants, 5.6% reported telehealth visits compared with 10.7% of oseltamivir-treated participants (RR = 0.52; 95% CI 0.20–1.33, $P=0.16$) and 2.2% vs 6.6% of baloxavir- and oseltamivir-treated participants, respectively, visited a doctor's office (RR = 0.33; 95% CI 0.08–1.45,

Table 1 Participant demographics

Characteristic	All ($N = 286$)	Baloxavir ($n = 90$)	Oseltamivir ($n = 196$)	*P* value
Age, mean (SD), years	45.4 (15.3)	46.3 (13.9)	45.0 (15.9)	0.50
Female, *n* (%)	187 (65.6)	55 (61.8)	132 (67.3)	0.36
Race, *n* (%)				
White	248 (86.7)	79 (87.8)	169 (86.2)	0.72
Black or African American	18 (6.3)	6 (6.7)	12 (6.1)	0.86
Asian	14 (4.9)	3 (3.3)	11 (5.6)	0.56
American Indian or Alaska Native	4 (1.4)	2 (2.2)	2 (1.0)	0.59
Native Hawaiian or other Pacific Islander	0	0	0	–
Other	9 (3.2)	1 (1.1)	8 (4.1)	0.28
Not provided	2 (0.7)	1 (1.1)	1 (0.5)	0.53
Hispanic				0.54
Yes	28 (9.8)	6 (6.7)	22 (11.2)	
No	254 (88.8)	83 (92.2)	171 (87.2)	
Not provided	4 (1.4)	1 (1.1)	3 (1.5)	
CMS region, *n* (%)				0.02
Region 1: ME, NH, VT, MA, CT, RI	12 (4.2)	1 (1.1)	11 (5.6)	
Region 2: NY, NJ, PR, VI	32 (11.2)	10 (11.1)	22 (11.2)	
Region 3: PA, DE, MD, DC, WV, VA	25 (8.8)	4 (4.4)	21 (10.7)	
Region 4: KY, TN, NC, SC, GA, MS, AL, FL	88 (30.8)	32 (35.6)	56 (28.6)	
Region 5: MN, WI, IL, MI, IN, OH	34 (11.9)	6 (6.7)	28 (14.3)	
Region 6: NM, OK, AR, TX, LA	50 (17.5)	22 (24.4)	28 (14.3)	
Region 7: NE, IA, KS, MO	4 (1.4)	3 (3.3)	1 (0.1)	
Region 8: MT, ND, SD, WY, UT, CO	3 (1.0)	1 (1.1)	2 (1.0)	
Region 9: CA, NV, AZ, GU	36 (12.6)	9 (10.0)	27 (13.8)	
Region 10: AK, WA, OR, ID	1 (0.4)	1 (1.1)	0	
Missing	1 (0.4)	1 (1.1)	0	
US Region, *n* (%)				0.06
Northeast	52 (18.2)	11 (12.2)	41 (20.9)	
South	154 (53.8)	58 (64.4)	96 (49.0)	
Midwest	38 (13.3)	9 (10.0)	29 (14.8)	
West	41 (14.3)	11 (12.2)	30 (15.3)	
Missing	1 (0.4)	1 (1.1)	0	
SVI, mean (SD)[a]	0.63 (0.22)	0.65 (0.23)	0.62 (0.21)	0.28

CMS Centers for Medicare & Medicaid Services, *SVI* Social Vulnerability Index

[a]The SVI score represents the proportion of census tracts that are equal to or lower than a census tract of interest in terms of social vulnerability. For example, an SVI score of 0.63 signifies that 63% of census tracts in the nation are less vulnerable than the census tract of interest and that 37% of census tracts in the nation are more vulnerable

Table 2 Participant comorbidities

Characteristic, *n* (%)	All (*N* = 286)	Baloxavir (*n* = 90)	Oseltamivir (*n* = 196)	*P* value
None	150 (52.4)	52 (57.8)	98 (50.0)	0.22
Obesity	50 (17.4)	14 (15.6)	36 (18.4)	0.56
Asthma	46 (16.1)	13 (14.4)	33 (16.8)	0.61
Other chronic diseases	34 (11.9)	9 (10.0)	25 (12.8)	0.50
Diabetes	19 (6.6)	4 (4.4)	15 (17.7)	0.31
Anemia	16 (5.6)	5 (5.6)	11 (5.6)	0.98
Cancer	7 (2.5)	3 (3.3)	4 (2.0)	0.51
Psoriasis	7 (2.5)	1 (1.1)	6 (3.1)	0.44
Inflammatory bowel disease	6 (2.1)	3 (3.3)	3 (1.5)	0.38
Kidney problems	6 (2.1)	1 (1.1)	5 (2.6)	0.67
Rheumatoid arthritis	6 (2.1)	1 (1.1)	5 (2.6)	0.67
Chronic obstructive pulmonary disease	4 (1.4)	1 (1.1)	3 (1.5)	1.0
Crohn disease	2 (0.7)	0	2 (1.0)	1.0
Pregnancy	2 (0.7)	0	2 (1.0)	1.0
Prior history of stroke	2 (0.7)	2 (2.2)	0	0.10
Epilepsy	1 (0.4)	0	1 (0.5)	1.0
HIV or AIDS	1 (0.4)	0	1 (0.5)	1.0
Neutropenia	1 (0.4)	1 (1.1)	0	0.14

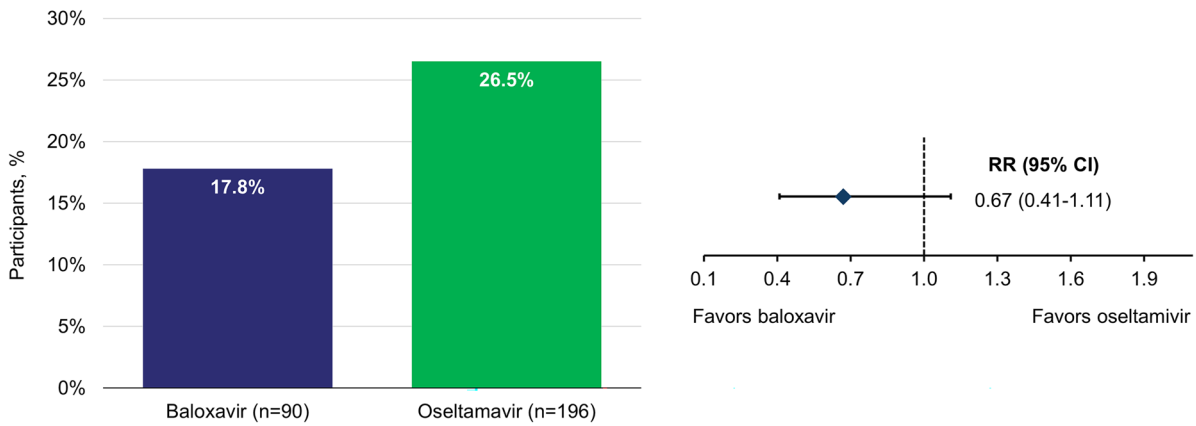

Fig. 3 Household influenza transmission reported by baloxavir- or oseltamivir-treated participants. *RR* relative risk

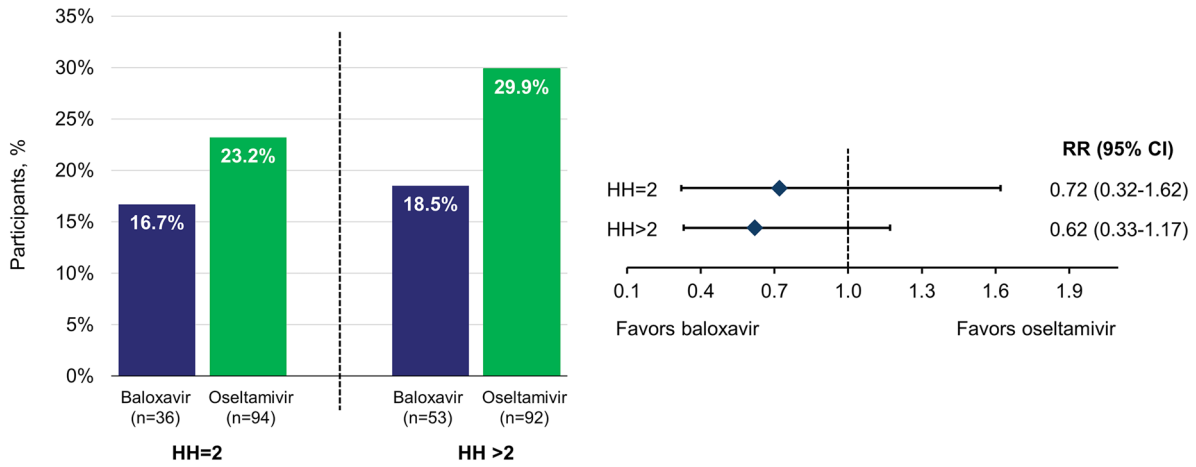

Fig. 4 Household transmission subgroup analyses by household size reported by baloxavir- or oseltamivir-treated patients. *HH* household, *RR* relative risk

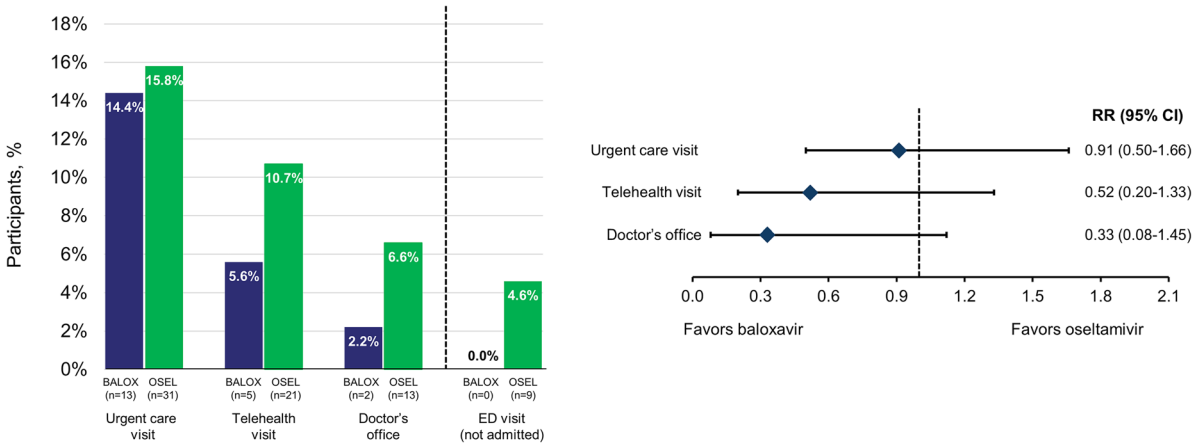

Fig. 5 Healthcare utilization reported by baloxavir- and oseltamivir-treated participants. *BALOX* baloxavir, *ED* emergency department, *OSEL* oseltamivir, *RR* relative risk

$P=0.16$). Nine oseltamivir-treated participants (4.6%) reported going to the emergency department but were not admitted to the hospital; no baloxavir-treated participants reported a visit to the emergency department or admission to hospital ($P=0.06$).

DISCUSSION

To our knowledge, this was the first comparative, real-world study describing patient-reported outcomes on the effect of baloxavir vs oseltamivir on influenza transmission and healthcare utilization in the USA. Numerically, smaller proportions of baloxavir-treated participants reported household transmission, irrespective of household size. Participants treated with baloxavir reported fewer outpatient and emergency department visits compared with participants treated with oseltamivir.

The data from this study are consistent with previously reported data from Japan, suggesting that baloxavir may be more effective than oseltamivir at preventing household

transmission of influenza [10, 11]. However, the Japanese data were limited in that their results were based on claims data, which required infected individuals to have had a formal interaction with a healthcare system, including disease coding or billing procedures, which may differ between Japan and the USA. Individuals who are infected by household members may not visit healthcare professionals for various reasons, including reduced incentive to seek care after one household member was diagnosed, and their data will not be captured in claims. This, and other claims data studies, may have underestimated actual household composition and subsequent influenza transmission [10, 11, 23]. In addition, claims data does not account for date of infection or symptom onset and can be less accurate. Despite these limitations, our study using patient-reported outcomes substantiates and expands those results by describing patient-reported transmission from households of a confirmed size and are in line with observational studies suggesting that treatment with antivirals is associated with lower infectivity [24–26]. Additional studies comparing the direct effect of baloxavir on transmission are warranted. A worldwide, phase 3 clinical trial assessing baloxavir for the reduction of direct transmission of influenza is in progress (NCT03969212) [27].

Household cohort studies have been a reliable tool in assessing the epidemiological impact of influenza and provide decisive data on estimating the transmission dynamics in households and the broader community [28–36]. Indeed, a substantial portion of viral transmission occurs in households [28, 29]; a prospective study estimated that as many as 50% of household contacts of patients with influenza were infected during the 2021–2022 influenza season [30]. However, until the 2009 H1N1 pandemic, direct information about seasonal influenza in the USA was based mostly on cohort studies conducted between 1948 and 1981 [31–33]. Cohort studies assessing influenza in the USA from 2009 on have focused on the transmission of the disease with little emphasis on the nonprophylactic role that antivirals may play in reducing transmission [34, 35]; one study that directly assessed the use of oseltamivir during the 2009 influenza pandemic suggested that early use of the antiviral was associated with reduced transmission [36]. Our study addresses these knowledge gaps by excluding participants who sought treatment for prophylactic use and comparing the effects of baloxavir and oseltamivir on secondary household transmission.

Limiting household transmission is a key goal of influenza prevention, as the health and wellness of residents can widely differ from member to member. Patients with severe influenza infections have more active and prolonged virus shedding, increasing the transmission risk and healthcare utilization [37]. Influenza often leads to severe infection in patients with comorbidities and can often exacerbate them, causing and complicating severe illness [1]. Our study included a population in which almost half of participants reported comorbidities; nonetheless, household transmission between the two treatment groups was less than 30%, demonstrating real-world effectiveness of antiviral therapies in reducing the impact of influenza on those with comorbidities. Controlling household transmission is a valuable tool in reducing the spread of influenza to vulnerable populations and overall healthcare utilization. Further real-world studies in high-risk populations are needed to fully understand the effects of antivirals on household transmission.

A unique strength of our study was the methodology and use of CVS Pharmacy in gathering participant survey information. CVS Pharmacy is among the largest pharmacies in the USA, with approximately 10,000 stores across all 50 states and territories. This large national reach allows researchers to connect with a wide variety of patients and other household members who may provide a more representative view of the population in the USA on how infectious diseases are managed in the public domain. Although the methodology of our study was payer agnostic, it was in line with a retrospective cohort study that used insurance claims to directly compare the healthcare utilization and costs between treatment with baloxavir and oseltamivir [38]. Both results suggested that treatment with baloxavir was generally associated with less healthcare resource utilization than treatment with oseltamivir.

Baloxavir is a novel anti-influenza molecule that inhibits viral cap-dependent endonuclease activity and is the first in this new antiviral class that inhibits the viral cycle at a very early stage [39]. Data from CAPSTONE-1 and CAPSTONE-2 showed baloxavir reduced viral titers and stopped the shedding of infectious virus from the body more rapidly than oseltamivir [15, 16]. Also, baloxavir is a single dose compared with oseltamivir, which is administered for 5 days. Patients are likely to be more adherent to a therapy that requires one dose than to a therapy that requires multiple doses over several days; higher adherence may potentially increase effectiveness. For the US 2019–2020 flu season, a real-world study observed 27% of patients did not complete their antiviral treatment, which was primarily neuraminidase inhibitors, including oseltamivir [40].

The findings of this study may provide guidance on future clinical implications surrounding influenza and its treatment. Our study suggests that baloxavir treatment reduces household transmission and healthcare utilization, which may decrease rates of additional hospitalizations and transmissions outside of the home. As baloxavir currently requires a prescription prior to use, the development and distribution of readily available, over-the-counter diagnostic tests for influenza may streamline and increase the use of antiviral treatment and have the potential to further reduce the transmission and healthcare use observed in this study.

Our study has several limitations. Participation in the survey was voluntary, and survey information was self-reported. Our study was limited in its sample size, partly from a low response rate, which may have been due to the short period that patients had to respond to the survey. There is potential for follow-up bias, e.g., the effectiveness estimate to be biased because of eligible patients not completing the survey. For example, if the proportion of those eligible patients differed in response (outcome) the relative risk for household transmission for baloxavir versus oseltamivir could either increase or decrease. Although most transmission and healthcare resource utilization outcomes favored treatment with baloxavir over oseltamivir, the comparisons were not statistically significant. Patients were not explicitly asked if the healthcare resource utilization they reported was influenza related, so it is possible that some of it was not influenza related; however, results are consistent with a published claims analysis that reported lower resource use and costs of treatment with baloxavir compared with oseltamivir [38]. Also, influenza-like illness was self-reported and, without testing, it was not confirmed that the additional family member(s) had influenza and whether they got it before or after the index patient began treatment; it is reasonable to assume that a family member had influenza if they became ill within the window of time allowed after the index patient picked up an antiviral prescription. Sensitivity analyses (data not shown) indicated that potential bias may have minimal or no effect on study findings. A power analysis revealed that approximately 750 survey participants would be needed to highlight significant differences in household transmission. As a result of the size of the study cohort, sensitivity analyses and other subgroup analyses were not conducted and, in general, larger studies are needed to confirm these findings.

CONCLUSIONS

In this real-world, USA-based study of survey participants with influenza, numerically smaller proportions of participants reported household transmission and healthcare utilization when treated with baloxavir compared with oseltamivir. Future research could be conducted in different settings or patient populations (i.e., elderly) to further enhance and validate the findings of this study.

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Data Availability. The datasets generated during and/or analyzed during the current study are not publicly available due to patients not providing consent to data being shared publicly.

Declarations

Conflict of Interest. J.H. Best, M. Sedeghi, and A. Seetasith are employees of Genentech, Inc., and hold shares in F. Hoffmann-La Roche Ltd. L. Albensi was formerly an employee of CVS at the time of this analysis. X. Sun is an employee and shareholder of CVS. S. Joshi has no disclosures. M. Zervos has received funding from ContraFect (consultant), GSK (grant/research support), Johnson & Johnson (grant/research support), and Pfizer (grant/research support).

Ethical Approval. The study was conducted in accordance with legal and regulatory requirements, as well as with scientific purpose, value, and rigor, and followed generally accepted research practices described in Good Practices for Outcomes Research issued by the International Society for Pharmacoeconomics and Outcomes Research and Good Pharmacoepidemiology Practice guidelines. Sponsor approval and continuing review was obtained through a central institutional review board (Sterling IRB), which evaluated this study and safeguarded the rights and welfare of participants. All patients provided informed consent.

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