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## ABSTRACT

Introduction: In December 2008, new interim guidelines on the use of influenza antiviral agents were released in response to a high prevalence of circulating oseltamivir-resistant A(H1N1) and adamantane-resistant A(H3N2) viruses. Zanamivir, oseltamivir +/- an adamantane, or oseltamivir was recommended, depending on virus type and local surveillance data.

Methods: Two web-based questionnaires were sent in 2009 to IDSA Emerging Infections Network (EIN) members about antiviral prescribing practices: in January about the 2007-2008 influenza season and in April, about the 2008-2009 season.

**Results:** In January, 646 (52%) of 1249 EIN members responded and in April, 350 (27%) of 1281 responded. Comparing responses from 2007-2008 and 2008-2009: 69% prescribed or recommended antivirals for treatment compared with 59%; for treatment, 80% prescribed oseltamivir and 10% zanamivir, compared with 48% and 39%, respectively (p = <.001). Overall, 28% reported treating a smaller proportion of patients during 2008-2009 compared with 2007-2008; 42% reported this was because they felt antivirals were less effective and 40% felt patients had less severe illness. In both seasons, 38-42% reported difficulty providing zanamivir to patients and 5% reported the same for oseltamivir. In January, 90% reported being able to test for viral type, but only 11% for subtype. During both seasons, ~55% used local surveillance data to make treatment decisions.

**Discussion:** A mild influenza season, difficulty obtaining recommended agents, and lack of access to subtype diagnosis and surveillance data may have contributed to reduced antiviral use during 2008-2009. The emergence of a new adamantaneresistant subtype, 2009 H1N1, could further complicate recommendations. Clinicians can obtain latest guidance at: (http://www.cdc.gov/h1n1flu/ recommendations.htm).

## INTRODUCTION

- Influenza antiviral agents
- » Adamantanes: amantadine and rimantadine
- » Neuraminidase Inhibitors (NAI): oseltamivir and zanamivir
- Resistance to antiviral agents
- » 2005-2006: 90% of A(H3N2) viruses resistant to adamantanes, all sensitive to NAI
- Adamantanes no longer recommended for use
- > 2007-2008: resistance to oseltamivir first detected among 12% of A(H1N1) viruses tested
- No change in treatment guidelines

### **INTRODUCTION** cont'd

- 2008-2009: >95% A(H1N1) resistant to oseltamivir, all susceptible to adamantanes
- 100% A(H3N2) resistant to adamantanes
- Large proportion of all circulating viruses were A(H1N1)
- December 19, 2008: new interim guidelines for the use of influenza antiviral agents: Use local surveillance data and influenza diagnostic testing to guide treatment decisions Infection with type A virus likely: zanamivir or
- oseltamivir and adamantane
- Infection with type B virus likely: oseltamivir or zanamivir
- Objectives:
- Describe physician antiviral prescribing practices before and after release of new interim guidance
- » Determine whether the guidelines were effectively communicated and easy to implement

### METHODS

- Emerging Infections Network (EIN) » Provider-based sentinel network established in 1995
- Surveys physicians on topics of clinical importance
- Web-based survey distributed two times January: 1,249 members surveyed on antiviral prescribing practices during 2007-2008 influenza season
- April: 1,281 members surveyed on antiviral prescribing practices during 2008-2009 influenza season
- » Reminders to encourage survey completion January survey re-sent twice • April survey not re-sent due to the 2009 pandemic influenza A(H1N1) outbreak

- Data collected and tabulated by EIN
- Proportions compared using Chi-square
- » P values <.05 considered statistically significant

# Influenza Antiviral Use in the Setting of Increased Resistance to Oseltamivir: A National Survey of the IDSA Emerging Infections Network, 2007-2009

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## RESULTS

#### Table 1: Use of influenza antiviral agents, 2007-2008 and 2008-2009

	2007-2008 Influenza Season # (%)	2008-2009 Influenza Season # (%)	р
Respondents	N=646	N=350	
Number taking care of patients with influenza	513 (79)	294 (84)	.08
Prescribed/recommended antiviral medications	N=509	N=350	
Treatment Yes No Prophylaxis	351 (69) 156 (31)	172 (59) 122 (42)	<.0001
Yes	174 (34)	67 (23) 227 (77)	<.0001
Proportion of patients with influenza that were treated with antiviral medications	N=371	N=228	
None 1-24% 25-49% 50-74% 75-99% All	20 (5) 131 (35) 50 (13) 57 (15) 55 (15) 33 (9)	55 (24) 65 (29) 23 (10) 26 (11) 27 (12) 22 (10)	<.0001 .05 .18 .14 .26 .82
Agents prescribed/recommended for treatment	N=347	N=171	
Oseltamivir Zanamivir Amantadine Rimantadine Combination therapy, not specified Combination therapy with oseltamivir and amantadine Combination therapy with oseltamivir and rimantadine	278 (80) 34 (10) 13 (4) 23 (7) 22 (6) Not asked Not asked	81 (48) 66 (39) 16 (9) 20 (12) Not asked 41 (24) 72 (42)	<.0001 <.0001 .0091 .05

- January: 646 (52%) of 1249 members responded
- » 58% reported that the majority or all of the patients they treated were inpatients April: 350 (27%) of 1281 members responded
- 2008-2009, compared with 2007-2008
- » A smaller proportion reported prescribing or recommending antivirals
- Smaller proportion prescribed oseltamivir for treatment, compared with zanamivir
- 66% prescribed combination therapy for treatment and prophylaxis, respectively, compared with 6%

### Factors considered when deciding whether to treat with antiviral agents

### 2007-2008

- Laboratory confirmation by diagnostic test (80%)
- Time from illness onset to presentation (79%)
- Underlying medical conditions of the patient (79%)
- Severity of symptoms (74%)
- Local influenza surveillance data (56%)
- Efficacy data from published studies (43%)
- Whether it was "flu season" (40%)
- National surveillance data (21%)

### 2008-2009

- Rapid test results that distinguish influenza type A from type B (62%)
- Local surveillance data on influenza viruses (54%)
- Did not have enough information (15%)
- Other sources (19%)
- National data/ recommendations
- CDC data/ recommendations
- Patient's clinical severity
- Statewide data

#### Table 2: Reasons for not treating patients with influenza with antiviral agents during the 2007-2008 influenza season

	2007-2008 Influenza Season N=501 %
Patient presented >2 days after onset of illness	73
Patient had mild illness	46
Did not see patients with influenza	19
Patient did not want to take medication	13
Patient too young to take antiviral	13
Contraindications	9
Patient could not afford the medication	9
Concern for side effects of antivirals	8
Patient could not take PO or inhaled	3
Patients had received influenza vaccination	3
Did not feel influenza antiviral agents are effective	2

 Circulation of antiviral resistant influenza viruses changed prescribing practices during the 2008-2009 influenza season

- » 58 (28%) reported treating a smaller proportion
- > 21 (42%) felt antivirals were less effective
- > 20 (40%) saw more patients with mild illness
- > 11 (22%) were concerned about side effects of antivirals
- 95% reported testing for influenza during the 2007-2008 influenza
- » 90% able to test for viral type
- > 79% results available <24 hours
- » 11% able to test for A virus subtype
- > 9% results available <24 hours, 49% 1-3 days, 23% 4-7 days, 12% >1 week
- Sources of information on influenza
- » MMWR including Influenza Updates: 70-86%
- » CDC influenza website (FluView): 45-68%
- » State health departments: 62%
- » 2008-2009: 85% reported interim guidelines were one of the most useful sources of information
- 4-7 weeks after the new recommendations were released
- > 90% were aware of interim recommendations
- > 87% felt they were easy to understand
- > 87% felt they provided enough information

### Figure 1: Level of difficulty reported by their patients, 2007-2008



#### Figure 2: Level of difficulty reported by physicians in providing antiviral agents to their patients, 2008-2009



obtaining zanamivir than oseltamivir

- » 2007-2008: 38% difficult or very difficult to provide zanamivir vs. 5% for oseltamivir (p=<.0001)
- » 2008-2009: 42% difficult or very difficult to provide zanamivir vs. 5% for oseltamivir (p = <.0001)
- 53% reported not available from outpatient pharmacy • 67% reported not available from inpatient pharmacy > 48% reported not available from both inpatient and

- outpatient pharmacies
- 2008-2009 vs. 2007-2008: despite new recommendations. there was no difference between proportion reporting difficult or very difficult to provide zanamivir (42% vs. 38%, p=.57)
- 2008-2009 vs. 2007-2008: more respondents prescribed amantadine and rimantadine
- » Similar proportion reported difficult or very difficult to provide adamantanes during both seasons amantadine: 10% vs. 14%, p=.5
- rimantadine: 19% vs. 30%, p=.14







Antiviral drug by level of difficulty

Antiviral drug by level of difficulty

During both seasons, respondents reported more difficulty

### LIMITATIONS

- Responses likely not generalizable to all physicians, especially those in primary care
- Majority with subspecialty training in Infectious Diseases
- Only half of EIN members responded to January survey
- Repeat mailings of April survey limited due to the 2009 pandemic influenza A (H1N1) outbreak
- Responses about 2008-2009 season may have been biased

### CONCLUSIONS

- Physicians reported prescribing fewer antiviral agents during the 2008-2009 influenza season
- » Lack of perceived effectiveness
- Milder illness during the 2008-2009 season
- Interim guidelines difficult to implement
- Difficulty providing zanamivir and adamantanes
- Agents less available from inpatient pharmacies
- Laboratory testing results on subtype not available
- Limited access to local influenza surveillance data
- 2009 pandemic influenza A (H1N1) virus further complicates antiviral agent
- <1% pandemic A(H1N1) viruses resistant to oseltamivir
- » 0% resistant to zanamivir
- Note that the second second
- Antiviral use guidelines can be obtained at: http://www.cdc.gov/h1n1flu/ recommendations.htmt