Use of rapid tests and antiviral medications for influenza among primary care providers in the United States

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Abstract

Limited data are available about how physicians diagnose and treat influenza. We conducted an internet-based survey of primary care and emergency physicians to evaluate the use of influenza testing and antiviral medications for diagnosis and treatment of influenza. In April 2005, an electronic link to a 33-question, web-based survey was emailed to members of the American College of Physicians, American Academy of Pediatrics, American Academy of Family Physicians, and American College of Emergency Physicians. Of the 157,674 physician members of the four medical societies, 2,649 surveys were completed (1.7%). The majority of participants were internists (59%). Sixty percent of respondents reported using rapid tests to diagnose influenza. Factors associated with using rapid influenza tests included physician specialty, type of patient insurance, and practice setting. After controlling for insurance and community setting, emergency physicians and pediatricians were more likely to use rapid influenza tests than internists [odds ratio (OR) 3.7, confidence interval (CI): 2.3–6.1; and OR 1.7, CI: 1.4–2.1, respectively]. Eighty-six percent of respondents reported prescribing influenza antiviral medications. Reasons for not prescribing antivirals included: patients do not usually present for clinical care within 48 hours of symptom onset (53.0%), cost of antivirals (42.6%) and skepticism about antiviral drug effectiveness (21.7%). The use of rapid tests and antiviral medications for influenza varied by medical specialty. Educating physicians about the utility and limitations of rapid influenza tests and antivirals, and educating patients about seeking prompt medical care for influenza-like illness during influenza season could lead to more rapid diagnosis and improved management of influenza.

Keywords Antivirals, influenza, primary care, rapid tests.

Introduction

Influenza is a contagious, acute febrile respiratory illness associated with an estimated annual average of >200,000 hospitalizations and 36,000 deaths in the United States.1,2 Despite this considerable burden of disease, limited data are available concerning how healthcare providers diagnose and treat influenza in clinical practice.

The accuracy of diagnosing influenza on clinical grounds alone is complicated by the co-circulation of other respiratory pathogens during influenza season that cause symptoms similar to those observed with influenza virus infection.3,4 Rapid influenza diagnostic tests allow physicians to obtain prompt results on which to base their treatment decisions.5 Few guidelines concerning the use of rapid influenza tests are available,5,6 while the number of commercially available rapid tests has increased, little is known about how often and when these tests are used by primary care physicians.

In the United States, four prescription antivirals in two medication classes are available for treatment of influenza:5 the adamantanes (amantadine and rimantadine), and the neuraminidase inhibitors (oseltamivir and zanamivir). However, the Advisory Committee on Immunization Practices has recommended against the use of adamantanes beginning with the 2005–2006 influenza season because of high levels of adamantane resistance among circulating influenza A viruses.7,8 Oseltamivir and zanamivir are

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approved for treatment of influenza A and B in persons aged ≥1 year old and ≥7 years old, and for chemoprophylaxis of influenza in persons ≥1 year old and ≥5 years old, respectively. The efficacy of antivirals for treatment and chemoprophylaxis of influenza has been evaluated in published studies. However, limited data exist regarding primary care physicians’ use of antiviral medications for influenza. A cross-sectional study of 336 physicians in Texas and Massachusetts conducted during 2004 found that 61% of doctors had prescribed antivirals within the previous year, and a study of 738 primary care physicians in four states during the 2006–2007 influenza seasons found that 53.8% had prescribed antiviral agents. We conducted an internet-based survey to evaluate influenza testing practices, including the use of rapid diagnostic tests, and antiviral prescription use for treatment and chemoprophylaxis of influenza among a large group of US primary care and emergency physicians.

Methods

The Centers for Disease Control and Prevention’s Influenza Division partnered with four major medical professional organizations to assess utilization of influenza testing and influenza antiviral medication prescribing practices during the 2004–2005 influenza season. The American College of Physicians (ACP), the American Academy of Pediatrics (AAP), the American Academy of Family Physicians (AAFP), and the American College of Emergency Physicians (ACEP), all agreed to electronically send information about our web-based survey to their physician members. In April 2005, each society requested that their members with email addresses on file complete our survey. Recruitment strategies differed among the four medical associations. The ACP sent out a description of the survey along with a hyperlink to the survey website in an electronic mail to its non-student, non-resident members. The AAP sent out a description of the survey with a hyperlink to the web survey as part of an electronic, breaking-news summary that is periodically distributed to members. The ACEP included a description of the survey with a uniform resource locator (URL) to the survey in its biweekly electronic newsletter. The AAFP described the survey and placed the link in the weekly electronic newsletter and posted the URL on its members-only website. Invitation letters informed potential respondents that their names and other identifying information would remain confidential and that their response would only be reported in aggregate form.

The web-based survey instrument was developed and deployed using the mrInterview V2.2 software (SPSS Inc., Chicago, IL, USA). The survey website was deployed on a CDC web server running Windows Internet Information Service 5.0 (Microsoft, Redmond, WA, USA). Respondents accessed the website via a URL provided in their email invitation or from a referring URL on one of the partner organization’s websites. Upon clicking the URL, users were connected to the survey over a 128-bit Secure Sockets Layer connection. All data collected via the web-based survey were stored in a secure relational SQL Server 2000 database at CDC (Microsoft).

The instrument asked respondents to answer 33 questions across several screens about demographics, use of rapid influenza tests, and use of antiviral medications. Survey respondents could answer all questions in total; however, some respondents could have answered fewer questions because the survey contained conditional skip patterns or ‘routing’ that directed respondents only to relevant questions based upon answers to previous questions.

Upon closing the survey, respondent data were exported to an analytical dataset, transformed, and analyzed using SAS 9.13 (SAS Institute Inc., Cary, NC, USA, 2005) and Epi-Info 6 (Centers for Disease Control, Atlanta, GA, USA, 2000). Data analysis was performed using descriptive statistics, categorical data analysis techniques, and multivariable logistic regression. A chi-squared test was used to generate two-sided P-values; P-values of 0.05 or less were considered statistically significant. Partially completed surveys were excluded from the analyses.

The study was determined to be exempt from CDC institutional review board review because no personal identifiers were collected. All four participating medical professional societies approved the study.

Results

Of the 157 674 members of the professional medical organizations who were informed electronically about the survey, 3573 (2.3%) completed at least part of the survey. Of those, 924 (26%) began the survey, but failed to complete it entirely, and were excluded from further analysis. Seventy-four percent (2649) of respondents (or 17% of the total number of physicians who were informed about the survey) completed the survey. Demographic information was similar among physicians who completed any portion of the survey compared with physicians who completed the entire survey. Survey participation by specialty was as follows: internists, 6.5% (1563/23 960); pediatricians, 1.5% (888/60 000); emergency physicians, 0.7% (116/17 000); and family practitioners, 0.1% (80/56 000). Thirty-six respondents identified ‘medicine/pediatrics’ as their primary specialty, and 27 respondents did not identify a primary specialty. Because the survey was voluntary and anonymous, no information was available about non-respondents. However, the mean age (48 years) of participating internists, a group that comprised the majority of respondents, was relatively similar to those of all eligible
ACP members (mean age = 52 years) (American College of Physicians, unpublished data). Of internists that completed the survey, 65% were male, compared to 73% of all ACP members. Respondents included physicians practicing in all 50 states as well as the District of Columbia, Puerto Rico, Guam and the US Virgin Islands. Fifty-nine percent were male (Table 1). The median age was 47 years (range: 26–90 years). The majority of the respondents were internists (59%). Only six respondents (0.2%) indicated that they were not currently practicing medicine. Most respondents practiced in an outpatient primary care setting (87.2%), and 37.6% treated patients with private insurance, while 36.2% cared for patients covered by Medicaid and Medicare. Nearly half (44%) of those who completed the survey were affiliated with an academic institution.

Physicians reported ordering rapid influenza tests much more often than other tests for influenza. Eighty-four percent (84%) of those who completed the survey were affiliated with an academic institution. Nearly half (44%) of those who completed the survey were affiliated with an academic institution. Most respondents reported ordering rapid influenza tests much more often than other tests for influenza. Eighty-four percent (84%) of those who completed the survey were affiliated with an academic institution.

| Gender | Number of respondents (percentage) |
|--------|-----------------------------------|
| Male   | 1554 (59.4)                       |
| Age    | Mean = 47.1; median = 47; mode = 48 |
| Medical specialty | Number of respondents (percentage) |
| Internal medicine | 1563 (59.0) |
| Pediatrics | 888 (33.5) |
| Family practice | 80 (3.0) |
| Medicine/Pediatrics | 36 (1.4) |
| Emergency medicine | 116 (4.4) |
| Primary practice site | Number of respondents (percentage) |
| Outpatient office or clinic | 2297 (87.2) |
| Inpatient hospital setting | 172 (6.5) |
| Emergency room | 127 (4.8) |
| Nursing home or other residential institution | 39 (1.5) |
| Affiliation with an academic institution | 1156 (43.9) |
| Community type | Number of respondents (percentage) |
| Urban | 1044 (39.7) |
| Suburban | 1175 (44.6) |
| Rural | 413 (15.7) |
| Most common insurance plan among patients | Number of respondents (percentage) |
| Private insurance | 987 (37.6) |
| HMO | 466 (17.8) |
| Medicaid and medicare | 950 (36.2) |
| Uninsured | 116 (4.4) |

Table 1. Characteristics of survey respondents

Table 2. Use of rapid tests and antiviral medications for influenza by specialty

| Specialty | Number answering 'yes' (%) | Odds ratio | 95% Confidence intervals |
|-----------|----------------------------|------------|--------------------------|
| Internal medicine | 821 (53.5) | Reference group |
| Pediatrics | 597 (69.2) | 1.7 | 1.4–2.1 |
| Family practice | 48 (66.7) | 1.2 | 0.7–2.1 |
| Medicine/Pediatrics | 24 (68.6) | 1.9 | 0.9–4.0 |
| Emergency medicine | 93 (80.2) | 3.7 | 2.3–6.1 |

When you suspect a patient has influenza, do you ever prescribe antiviral medications?**

| Specialty | Number | Odds ratio | 95% Confidence intervals |
|-----------|--------|------------|--------------------------|
| Internal medicine | 1359 (88.9) | Reference group |
| Pediatrics | 668 (77.5) | 0.3 | 0.2–0.3 |
| Family practice | 70 (98.6) | 6.8 | 0.9–49.9 |
| Medicine/Pediatrics | 33 (94.3) | 1.7 | 0.4–7.5 |
| Emergency medicine | 105 (91.3) | 1.0 | 0.5–2.1 |

*Predominant type of patient insurance and community included in logistic regression models.

**Predominant type of patient insurance, community, and use of rapid tests for influenza were included in the logistic regression model.

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cians and pediatricians remained more likely to use rapid tests than internists (Table 2).

Overall 85–6% of participants reported having prescribed antiviral medications when they suspected that a patient has influenza. The percentage varied by specialty, from a low among pediatricians (77–5%) to a high among family practitioners (98–6%) (P < 0.001). After controlling for predominant type of patient insurance, practice community, and use of rapid tests, pediatricians remained less likely than internists to use antivirals (Table 2). There were no statistically significant differences in antiviral use between internists and family practitioners, emergency physicians, or medicine/pediatrics physicians.

Physicians who reported using rapid influenza tests were more likely to report prescribing antivirals than those who did not use rapid tests (OR 2.9, 95% CI: 2.3–3.6). Among those who reported using antivirals for treatment, oseltamivir was prescribed most often (69–9%), followed by amantadine (21–2%), rimantadine (80%), and zanamivir (9%). Overall, 46–0% percent of physicians said they ‘always’ prescribed antiviral medications for treatment of influenza when a patient presents with influenza symptoms within 48 hours from illness onset, compared to 41–8% of physicians who reported doing so ‘sometimes’, and 12–2% who reported prescribing antivirals ‘rarely’ in this setting. Physicians cited the fact that patients do not usually present for clinical care within 48 hours of symptom onset (53–0%), the high cost of antivirals (42–6%), and skepticism about the effectiveness of antivirals (21–7%) as the most common reasons they did not prescribe these medications.

Over half of physicians (57–5%) said they had prescribed antivirals for chemoprophylaxis of influenza. Among these respondents, oseltamivir was prescribed most often (55–3%) followed by amantadine (30–8%), rimantadine (13–1%), and zanamivir (0–8%). Physicians who used rapid tests were more likely to prescribe antivirals for influenza chemoprophylaxis than non-rapid test users (OR 2.58, 95% CI: 2.2–3.1).

Discussion

Our survey is the first to address testing and prescribing patterns for influenza among a nationwide cohort of primary care physicians from four specialties (internal medicine, pediatrics, family practice, and emergency medicine). While only a small percentage of physicians eligible to participate completed the survey, the absolute number of responses was high, especially among internists.

Sixty percent of primary care physicians reported ordering rapid influenza tests. These findings are similar to results from a cross-sectional study conducted at the end of the 2003–2004 influenza season, in which 62% of 336 physicians from Texas and Massachusetts reported using rapid influenza tests, and a more recent study of 730 primary care physicians in four states during the 2006–2007 influenza season, in which 61% of physicians reported ordering rapid influenza antigen tests. Thirty percent of participants reported not using rapid influenza tests because clinical diagnosis of influenza was considered adequate and because rapid tests were viewed as not helpful for clinical management. Several studies suggest that rapid tests can be a useful aid in diagnosing influenza virus infection, especially when the prevalence of influenza in a community is moderate, although the use of these tests appears to be of limited use when the prevalence of influenza is <10%. The positive predictive value of rapid tests is lowest during periods of low influenza activity, and the World Health Organization recommends that during these periods of low influenza activity positive results be interpreted with caution and confirmed by immunofluorescence, viral culture or RT-PCR. Additionally, during periods of high influenza activity, the negative predictive value of rapid tests is relatively low, and therefore specimens that test negative by rapid test should be retested by confirmatory tests such as viral culture or RT-PCR.

Thirty-four percent of respondents cited high costs as a reason for not ordering rapid influenza tests. Rapid diagnostic tests have been shown to reduce additional diagnostic testing, inappropriate prescribing of antibiotics, and overall hospital costs. Thus, ultimately increased use of rapid influenza tests to diagnose influenza could lead to increased cost savings.

In our survey, 4-8% of physicians reported ordering serology to diagnose influenza. Reliable influenza serological testing is not widely available, and requires collection of paired acute and convalescent sera. Therefore, serological testing results cannot inform clinical management of the acutely ill patient.

We found that 86% of respondents reported prescribing antiviral medications for influenza treatment. This proportion is substantially higher than the reported 61% of physicians that prescribed antivirals during the 2003–2004 influenza season and the reported 54% of physicians that prescribed antivirals during the 2006–2007 seasons in two smaller studies. The differences between the studies may reflect the fact that our survey was conducted at the end of an influenza season characterized by a highly publicized influenza vaccine shortage. It may also reflect a volunteer bias; clinicians who had a high interest in influenza management may have been more likely to use rapid influenza tests and antiviral medications and to participate in the on-line survey than those who did not respond to the survey, or those who participated in other studies.

In addition, because of the anticipated influenza vaccine shortage for the 2004–2005 season, CDC issued specific guidelines on the use of antivirals in October 2004, encour-
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Among H1N1 isolates. Despite CDC recommendations for the 2005–2006 influenza season, a recommendation that recommending against using amantadine or rimantidine for influenza during the 2006–2007 influenza season described nearly universal resistance to amantadine among H3N2 viruses and 15.5% resistance among H1N1 isolates.30 Despite CDC recommendations and these recent surveillance data showing high adamantane resistance among influenza viruses, a recent study found that 26% of primary care physicians prescribed adamantanes for influenza during the 2006–2007 influenza season.17 Although a low prevalence of influenza virus resistance to oseltamivir in recent seasons has been reported, influenza surveillance in Europe from November 2007 to January 2008 showed 14% of H1N1 viruses were resistant to oseltamivir.31 Continued global virological surveillance for emergence of resistant influenza virus strains and better physician education about surveillance data and treatment guidelines are therefore critical.

We used mInterview software to design a questionnaire and distribute it electronically to a large number of clinicians, all in a short amount of time. This software allowed us to collect and analyze data rapidly. Such an approach could be helpful during future influenza seasons if events occur such as the unexpectedly high prevalence of influenza A resistance to adamantanes in the 2005–2006 season; the effect of sudden changes in practice guidelines due to unforeseen events could be evaluated in a timely way to facilitate rapid development and issuance of revised guidelines.

Real-time, web-based data collection eliminates the need for entering data into computer databases as well as the costs associated with distribution of the survey (e.g., postal costs, paper, envelopes, copying, etc.). Quality of collected data is also improved as web-based forms can perform data validation as survey responses are entered. Unlike the traditional paper-based surveys, web-based surveys can make use of validation rules that provide error messages to respondents in real-time if data entry errors are made, allowing correction prior to survey submission, and thereby improving data quality.

Our study has a number of limitations. The survey was limited to physicians who were members of the four medical professional societies with email addresses on file. Therefore, the responses may not be representative of the views of all members or the clinical practice of non-member physicians and may not be generalizable to all members of the four participating organizations. For example, the percentage of physicians who reported having an academic affiliation in our survey (44%) was substantially higher than the percentage of physician members of the ACP and the ACEP who report academic affiliations (9% and 23%, respectively) (American College of Physicians, American College of Emergency Physicians, Unpublished Data); no data were available from the AAFP or AAP. Due in part to differences in recruitment of survey respondents by each of the organizations, response varied by specialty. The overall proportion of survey respondents among eligible physician members was <2%, and the absolute numbers of participating emergency physicians and family practitioners was quite low. This may reflect the fact that many physicians are very busy and overburdened with electronic communication. Additionally, despite the large absolute number of survey respondents, it is likely that some volunteer bias was present. For example, only physicians who had internet access and actively checked their email accounts could have completed our survey. Due to privacy concerns, we were unable to obtain demographic data on non-respondents and therefore, a true non-response bias analysis could not be completed. However, despite the low frequency of eligible participants, the absolute number of respondents was high among internists and pediatricians, and our survey is the largest to date to address the use of testing and antivirals for influenza among physicians, and the only one to do so in a nationwide cohort.

Rapid influenza tests can be a useful tool for prompt diagnosis of influenza9,14–17 and early antiviral treatment can effectively reduce the duration of illness and may reduce complications from infection with susceptible viruses.5,23,24,26 Our results show considerable variation in the use of these two tools by physicians. These findings are consistent with a previous cross-sectional study that demonstrated considerable variability in prescribing of antiviral medications.33 Focused investigation of these differences in practice patterns among primary care physicians could help
identify ways in which primary care specialties could be better informed about the use of rapid testing and antivirals for influenza. Educating physicians about the utility (as well as limitations) of rapid influenza tests and the effectiveness and efficacy of antiviral medications could improve the diagnosis and treatment of influenza and might reduce unnecessary antibiotic use and other diagnostic tests.\(^3\)–\(^6\)

Guidelines for use of rapid influenza tests, and wider circulation of current guidelines for use of antiviral medications for influenza,\(^6\)\(^,\)\(^3\)\(^7\)\(^,\)\(^3\)\(^8\) – especially in light of the current high prevalence of adamantane-resistant influenza A virus strains and oseltamivir-resistant influenza A(H1N1) virus strains – could offer important direction for primary care physicians in their approach to clinical management of suspected influenza patients.

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