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## Stockpiling Drugs for an Avian Influenza Outbreak: Examining the Surge in Oseltamivir Prescriptions During Heightened Media Coverage of the Potential for a Worldwide Pandemic

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### Abstract

**OBJECTIVE**—During fall 2005, personal stockpiling of oseltamivir for use during an outbreak of H5N1 influenza virus infection was widely reported. The present study aimed to identify indications for oseltamivir prescriptions to determine whether oseltamivir that was not intended for seasonal influenza was inappropriately consumed and to compare persons who were likely to have stockpiled oseltamivir and those who did not with respect to their knowledge, understanding, concerns, and expectations regarding avian influenza.

**DESIGN**—Survey to evaluate usage patterns for oseltamivir and assess views about avian influenza.

**SUBJECTS**—A total of 109 outpatients who received a prescription for oseltamivir between September 1, 2005, and December 31, 2005, and 825 matched control subjects.

**RESULTS**—Of 109 prescriptions, 36 (33.0%) were prescribed for patients with appropriate indications. Sixty-eight (62.4%) of 109 patients identified as having received oseltamivir and 440 (53.3%) of 825 individuals identified as not having received it responded to the questionnaire. Only 2 prescription recipients whose oseltamivir was not intended for immediate consumption reported that they had consumed the oseltamivir. Persons who probably intended to stockpile oseltamivir were older and more often white than those unlikely to stockpile it. They also reported greater worry about avian influenza and more often expected avian influenza to spread to the United States than those unlikely to stockpile, but there were no significant differences in responses to other questionnaire items.

**CONCLUSIONS**—A large proportion of the oseltamivir prescriptions written in fall 2005 were probably intended for personal stockpiling. Similarities in participants' responses to questionnaire items suggest that educational campaigns may not be an effective method to curtail stockpiling of antimicrobial medications during an infectious threat. Promoting appropriate prescribing practices among providers may be a better means by which to minimize personal stockpiling.

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During the fall of 2005, reports of personal stockpiling of oseltamivir for use during a future outbreak of H5N1 influenza virus infection were widespread, coincident with increased media coverage of the potential for a worldwide pandemic. So much oseltamivir had been prescribed prior to the start of influenza season that the drug's manufacturer suspended shipments to the United States at the end of October 2005.<sup>1</sup> Subsequently, despite the fact that human cases of H5N1 influenza virus infection continue to occur, public awareness has diminished, and the demand for oseltamivir has markedly decreased. In light of emerging infectious diseases and the ongoing threat of bioterrorism, personal stockpiling of other drugs in response to public health threats is likely to occur in the future. Therefore, a clearer elucidation of the issues surrounding personal stockpiling is warranted.

Although stockpiling may be useful in specific contexts and certain situations, haphazard and panicked personal stockpiling of antimicrobials could decrease the availability of drugs for persons with active infection and prevent the strategic use of a limited drug supply when it is needed. Antimicrobials dispensed in anticipation of an outbreak may also be used inappropriately to treat illnesses other than those for which the drugs were intended.<sup>1</sup> The potential ramifications of self-medication with antimicrobial drugs include the propagation of antimicrobial resistance, unwarranted risk of adverse events, and suboptimal care for individuals who should receive more extensive clinical evaluation.

To our knowledge, no studies have examined patient-level prescribing and/or usage patterns for oseltamivir; in particular, there has apparently been no examination of prescribing practices and usage patterns for the oseltamivir that was prescribed out of proportion to influenza activity during periods of heightened media coverage of avian influenza. Furthermore, as far as we know, researchers have not examined the knowledge, beliefs, concerns, and/or expectations regarding avian influenza of patients who stockpiled oseltamivir. Elucidation of these issues may help illuminate the impact of personal stockpiling and develop public health responses or strategies aimed at minimizing this practice, if necessary, during future threats of pandemic illness and/or bioterrorism. Given this context, our study aimed to do the following: (1) assess individuals' reasons for receipt of an oseltamivir prescription between September and December 2005, (2) determine the extent to which oseltamivir prescribed during this period was later used inappropriately by patients, and (3) compare knowledge, understanding, concerns, and expectations regarding avian influenza among persons who obtained oseltamivir for probable stockpiling and persons who did not obtain this drug.

## METHODS

A cross-sectional study was performed involving patients who received care in the outpatient Clinical Practices of the University of Pennsylvania Health System. We identified individuals who received prescriptions for oseltamivir by use of an electronic medical record and order system during the period from September 1, 2005, to December 31, 2005. This period correlates with a period of intense media coverage of avian influenza, a marked increase in the number of oseltamivir prescriptions written nationally, and an absence of influenza in the surrounding geographic area.<sup>2</sup> We thus identified a period when there was a high probability that a prescription for oseltamivir was intended for stockpiling and not for treatment of a true influenza infection.

To determine the indication for the oseltamivir prescription, electronic medical records were reviewed. We defined the appropriate indications for an oseltamivir prescription as suspected influenza infection, suspected exposure to someone with influenza, or anticipation of travel to countries where avian influenza infection had previously been reported in humans and/or birds. If no indication for oseltamivir could be determined from review of the medical record,

responses to a questionnaire were used to clarify the indication. This questionnaire also assessed the drug usage patterns of patients with prescriptions for oseltamivir.

The answers to additional questionnaire items were used to compare knowledge, understanding, concerns, and expectations regarding avian influenza among persons who obtained oseltamivir for probable stockpiling and those who did not obtain the drug. For this comparison, case patients were defined as individuals who received a prescription for oseltamivir but did not have appropriate indications for such a prescription. Because it is unlikely that persons who obtained oseltamivir for appropriate reasons (as defined above) intended to stockpile the drug for a future pandemic, they were excluded from this comparison. Patients who did not receive oseltamivir prescriptions during the study period were randomly selected as control subjects; they were matched to each case patient with respect to their healthcare provider and received mailed questionnaires that contained only the survey items aimed at eliciting their beliefs about avian influenza. To be selected as control subjects, individuals must have had at least 1 interaction (eg, office visit or telephone call) with their healthcare provider in the 12 months before study enrollment. By limiting control subjects to those who satisfied this criterion, we hoped to minimize the number of patients enrolled in the study who could not have received oseltamivir because they were not active members of the providers' practices (eg, those who died, moved, or changed healthcare providers) without excluding those who had the opportunity to obtain a prescription (eg, by telephone), even if no office visit had occurred.

To ensure that patients whose indications for oseltamivir prescription could not be determined through record review were not routinely prescribed oseltamivir prior to influenza season, we determined whether oseltamivir was provided during the prior year (ie, the period from September 1 to December 31, 2004). Finally, individuals who did not receive oseltamivir but reported that they had asked a provider for or received medication for avian influenza over the past year were excluded from the study.

For each case patient (ie, each individual who received a prescription for oseltamivir but did not have appropriate indications for it), 8 control subjects were identified to ensure adequate sample size. Responses to questions were compared statistically by using the Fisher exact test or  $\chi^2$  for proportions and the Student *t* test or the Wilcoxon signed rank test for continuous data, depending on the distribution of the data.

Questionnaires were mailed between October 11 and 16, 2006. Individuals who did not respond received an additional 2 mailings, 3–4 weeks apart. To encourage participation, \$3.00 was sent in the initial mailing that included the letter and questionnaire. The study was approved by the University of Pennsylvania institutional review board.

## RESULTS

One hundred nine individuals received oseltamivir prescriptions from 45 providers during the study period. Internal medicine and family medicine specialists provided the most prescriptions (52 [47.7%] and 43 [39.4%] of 109, respectively), followed by gerontologists (6 [5.5%]), endocrinologists (5 [4.6%]), cardiologists (2 [1.8%]), and gynecologists (1 [0.9%]).

### Indications for Oseltamivir

Questionnaires were returned by 68 (62.4%) of 109 persons who received an oseltamivir prescription (24 [66.7%] of the 36 participants who had appropriate indications and 44 [60.3%] of 73 participants who had inappropriate indications). There was no statistically significant difference between those who responded and those who did not with respect to race, sex or age. When the medical record review and patient questionnaire responses were compared, 3

individuals whose indication for oseltamivir was not apparent from the medical record were reclassified as having had appropriate indications. Of 109 individuals who received oseltamivir prescriptions, 36 (33.0%) received a prescription for an appropriate indication (13 [36.1%] had suspected influenza, 5 [13.9%] had potentially been exposed to an individual with influenza, and 18 [50.0%] traveled to countries with known cases of avian influenza). Of the 73 (67.0%) individuals who received a prescription for an inappropriate reason, 11 (15.1%) specifically requested oseltamivir for avian influenza stockpiling, and 18 (24.7%) specifically requested oseltamivir without providing a specific reason. Other inappropriate indications included 5 individuals (6.8%) who planned to travel to countries where avian influenza had not been reported and 2 individuals (2.7%) who were involved in professional work with children. For 37 (50.7%) of 109 prescriptions, no indication was documented. Of the 33 survey respondents who specifically asked for oseltamivir but did not provide a reason and who had no indication documented in the medical record, 17 (51.5%) listed “concerns about bird flu” as a reason for obtaining the oseltamivir prescription. Other reasons included “concerns about flu in the upcoming season,” which was listed by 19 (57.5%) of 33 respondents, and “the prescription was for a friend or family member,” which was listed by 3 (9.1%) of 33 respondents.

### Use of Oseltamivir Among Those Who Received Prescriptions

All 16 respondents who received a prescription for oseltamivir because of suspected influenza or potential exposure consumed it appropriately, rather than saving it (usage patterns were unknown for 2 individuals who received prescriptions but did not respond to these questions). Two individuals who received a prescription for oseltamivir for other reasons reported that they had consumed the oseltamivir at a later date because of symptoms that included fever, rhinorrhea, and cough. One did so without direction from a physician or nurse.

### Comparison of Knowledge, Understanding, Concerns, and Expectations Regarding Avian Influenza

Questionnaires were successfully mailed to 825 individuals (of 872 selected) who did not obtain oseltamivir prescriptions (ie, control subjects), and 440 (53.3%) responded. There were no statistically significant differences with respect to race, sex, or age between control subjects who responded and those who did not. Eleven control subjects reported that they had either asked for or received medication for avian influenza and were therefore excluded from the study. The control subjects' ( $n = 429$ ) responses to questionnaire items were compared with case patients' ( $n = 44$ ) responses.

Compared with control subjects, case patients were older (median age [interquartile range], 67 years [55–74 years] vs 54 years [41–64 years];  $P < .001$ ) and more often Caucasian (33 [75.0%] vs 236 [55.0%];  $P = .01$ ). A similar proportion of case patients and control subjects had completed high school or a General Educational Development equivalent (39 [88.6%] of 44 vs 405 [94.4%] of 429;  $P = .13$ ), and there was no statistically significant difference between the 2 groups with respect to the number of hospitalizations reported during the prior year.

When asked whether they were worried about avian influenza, case patients and control subjects responded as follows: 4 case patients (9.1%) and 160 control subjects (37.3%) reported that they were “not at all worried” ( $P < .001$ ), 17 case patients (38.6%) and 163 control subjects (38.0%) reported that they were “a little worried” ( $P = .93$ ), 18 case patients (40.9%) and 77 control subjects (17.9%) reported that they were “moderately worried” ( $P < .001$ ), 3 case patients (6.8%) and 20 control subjects (4.7%) reported that they were “very worried” ( $P = .53$ ), and 2 case patients (4.5%) and 8 control subjects (1.9%) reported that they were “extremely worried” ( $P = .24$ ).

There were no statistically significant differences between case patients and control subjects with respect to the distribution of responses to questions aimed at assessing patients' knowledge and understanding of avian influenza (Tables 1, 2, and 3). The response to questions aimed at assessing patients' expectations and concerns regarding avian influenza was most often "don't know" for both case patients and control subjects (Tables 4 and 5). For this reason, the statistical comparison of responses from individuals who did not choose the response "don't know" was limited. However, analysis of these responses showed that case patients were more likely than control subjects to think that avian influenza would probably or definitely spread to the United States (20 [87.0%] of 23 vs 151 [61.9%] of 244;  $P = .02$ ). Six (40%) of 15 case patients and 47 (21.9%) of 215 control subjects believed that someone they care about would probably or definitely become infected ( $P = .11$ ), and 5 (22.7%) of 22 case patients and 30 (13.5%) of 222 control subjects believed that someone they cared about would die ( $P = .24$ ) during an outbreak in the United States. Both case patients and control subjects indicated that the United States was probably or definitely not prepared to deal with an outbreak (39 [92.9%] of 42 vs 310 [85.9%] of 361;  $P = .21$ ) and that medicine would probably or definitely not be obtainable in an outbreak situation (30 [81.1%] of 37 vs 227 [67.0%] of 339;  $P = .08$ ).

## DISCUSSION

Similar to the results described in other reports, our health system saw an unexpected increase in the number of oseltamivir prescriptions during fall 2005, which suggested personal stockpiling.<sup>2</sup> Review of electronic medical records in conjunction with questionnaire responses confirmed that the majority of prescriptions were provided to persons concerned about avian influenza. This is not surprising, given the reported 300% increase from 2004 to 2005 in national sales of oseltamivir during the fall months<sup>2</sup> and the fact that nearly half of all infectious diseases specialists surveyed reported that they had been asked for an oseltamivir prescription for personal stockpiling.<sup>3</sup> In recent history, there has been a similar public response to biological threats. Following the events of September 11, 2001, and the ensuing anthrax attacks, ciprofloxacin was widely prescribed and the number of prescriptions was out of proportion to the number of individuals potentially exposed; this was true even in geographic regions of the United States where anthrax cases and/or exposures had not occurred.<sup>4-6</sup>

One concern related to personal stockpiling is the inappropriate use of stockpiled drugs for self-diagnosed ailments.<sup>7</sup> Several groups have documented high rates of self-medication with antibacterial drugs for apparent viral upper respiratory tract infections, without physician consultation.<sup>8-10</sup> Drugs that are originally prescribed for a presumed bacterial illness are commonly not completely consumed, and the remaining pills are then consumed later when the patient has a cough or sore throat.<sup>8-10</sup> Very little of the oseltamivir not intended for immediate use was taken later by our study cohort. Ongoing concerns about an outbreak might have resulted in preservation of the oseltamivir for future use, or perhaps patients are less familiar with antiviral drugs and were reluctant to consume oseltamivir. Alternatively, the prescriptions for oseltamivir may not have been filled. Although we did not intend to determine the rate at which prescriptions were filled and did not address this issue in our questionnaire, several healthcare providers documented that their patients would not fill the oseltamivir prescription unless needed, and several questionnaire respondents specifically indicated that they did not fill their prescription. Regardless, inappropriate and unsupervised use of "leftover" drugs may not be as problematic for oseltamivir as it has been documented to be for antibacterial medications.

Not surprisingly, individuals likely to stockpile oseltamivir reported greater worry about avian influenza than did control subjects, and more of them reported the expectation that avian influenza would spread to the United States. Among those likely to stockpile, we also found a nonstatistical trend toward greater pessimism regarding the probability of being affected by



the disease. However, there were few statistically significant differences in the responses to other questionnaire items, particularly those relating to individuals' knowledge and understanding of avian influenza. Both groups were unable to answer a large proportion of the questions, either because of a lack of knowledge or because of uncertainty about their estimations and opinions. It is worth noting that there was a substantially lower number of "don't know" responses to questions pertaining to the United States' pandemic preparedness, with both case patients and control subjects demonstrating a clear lack of confidence in the government's readiness. Surprisingly, answers to several questions actually reflected underestimation of the potential ramifications of a human pandemic. For example, both case patients and control subjects most often reported that the human case-fatality rate associated with avian (ie, H5N1) influenza virus infection was less than 25% when, in fact, the mortality rate is greater than 60%.<sup>11</sup> Similarly, after "don't know," both groups most often responded that people they knew or cared about would not become infected or die during an outbreak. In contrast, an estimated one-third of the world's population was infected during the 1918 influenza pandemic. With a case-fatality rate of more than 2.5%, at least 50 million people died.<sup>12</sup>

Taken together, these findings suggest that the differences between case patients and control subjects that may have led to personal stockpiling reflect differences in individuals' personalities and their degree of apprehension about avian influenza, rather than differences in their basic knowledge. Differences in the number of interactions with their healthcare providers and access to, familiarity with, and/or level of comfort with their physician and/or the healthcare system may have also played a role in determining who stockpiled the drug and who did not. These results suggest that patient education and/or increased communication from public health officials may not have been effective in curtailing demand from persons who wished to stockpile oseltamivir for their personal use. This is especially true given that the case-fatality rate for H5N1 influenza virus infection and the potential for widespread infection were underestimated by respondents and the fact that public officials are not able to guarantee an adequate supply of antiviral medication. Thus, education of healthcare providers, in concert with the development of national and local guidelines and official recommendations regarding personal stockpiling, may be more effective by decreasing the number of providers willing to prescribe medication in situations in which stockpiling is considered an inappropriate use of a scarce resource. A recent report supports the need for such guidance.<sup>3</sup> Suggestions about how to counsel and advise concerned and demanding patients may also be beneficial. Because a large proportion of both case patients and control subjects responded "don't know" to many questions, however, open dialogue with patients about the current status of infectious threats may also be worthwhile.

Our study had several limitations. As in all surveys, our data may be subject to nonresponse bias, although there were no significant differences between those who responded and those who did not with respect to basic demographic characteristics. In addition, recall bias cannot be excluded, and patient responses most certainly reflect knowledge and thought processes at the time of questionnaire administration rather than those that occurred at the time the oseltamivir prescription was obtained. The high proportion of patients who responded "don't know" to certain questions may have limited our ability to detect differences between case patients and control subjects for those questions, but nonetheless highlights similar uncertainty in both groups. Our study also may have been underpowered to detect modest differences between case patients and control subjects for some survey questions. The assessment of indications for oseltamivir was limited by our use of a retrospective record review. Finally, we could not determine that all prescriptions for which the indications were not clearly elucidated were definitely intended for personal stockpiling. In particular, 4 individuals classified as probable stockpilers responded that they were not at all worried about avian influenza and that avian influenza would never come to the United States. Analyses were performed that excluded

these individuals, and the results were not substantially different. However, with respect to other case patients, the widespread reports of stockpiling around the country, the lack of a documented appropriate indication, and the absence of similar prescriptions during the prior influenza season for all persons in this group suggest that stockpiling is likely to have occurred.

Future outbreaks of emerging infectious diseases and the possibility of bioterrorism are, at the present time, unavoidable. By evaluating the receipt of oseltamivir prescriptions prior to the onset of influenza season and during a period of heightened media coverage of avian influenza, our study is the first we know of that closely examines, on a patient-specific level, the attitudes associated with personal stockpiling. Although personal stockpiling was common, subsequent consumption of oseltamivir for inappropriate reasons was not. In a comparison of case patients and control subjects with respect to their knowledge, beliefs, concerns, and expectations regarding avian influenza, we found very few differences between persons who stockpiled oseltamivir and those who did not. Although our findings may not apply to all stockpiling scenarios, they suggest that there may be few patient-specific modifiable factors associated with stockpiling of antimicrobials and that self-medication with stockpiled drugs need not be a major concern in all circumstances. Strategies aimed at limiting prescribing by healthcare providers may be a more effective approach for minimizing personal stockpiling in instances where resources are scarce. The results of this study provide information that may be useful in formulating a public health response to other emerging infectious diseases and/or bioterrorism scenarios that prompt a high demand for antimicrobials.

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**TABLE 1**  
 Responses to Questions Assessing Knowledge and Understanding of the Transmission of Avian Influenza

Question, response group	Response				
	People never catch bird flu from birds	It is not easy, but it can happen	It is somewhat easy	It is extremely easy	Don't know
Is it easy for people to catch bird flu from birds?					
Case patients (n = 44)	1 (2.3)	26 (59.1)	6 (13.6)	1 (2.3)	10 (22.7)
Control subjects (n = 426)	8 (1.9)	235 (55.2)	39 (9.2)	7 (1.6)	137 (32.2)
Is it easy for people to catch bird flu from other people?					
Case patients (n = 44)	3 (6.8)	14 (31.8)	7 (15.9)	4 (9.1)	16 (36.4)
Control subjects (n = 425)	43 (10.1)	96 (22.6)	59 (13.9)	44 (10.4)	183(43.1)

NOTE. Data are no. (%) of respondents who selected each response.

**TABLE 2**  
Responses to the Question Assessing Knowledge and Understanding of the Severity of Avian Influenza

Question, response group	Response					
	Less than a quarter	Between a quarter and half	About half	Between half and three-quarters	More than three-quarters	Don't know
Of all the people who have had bird flu, how many have died?						
Case patients (n = 44)	18 (40.9)	6 (13.6)	6 (13.6)	5 (11.4)	2 (4.6)	7 (15.9)
Control subjects (n = 429)	188 (43.8)	68 (15.8)	60 (14.0)	43 (10.05)	27 (6.3)	43 (10.0)

NOTE. Data are no. (%) of respondents who selected each response.

**TABLE 3**

Responses to the Question Assessing Knowledge and Understanding of Influenza Vaccination

Question, response group	Response		
	Yes	No	Don't know
Does the current vaccine for the flu also protect you from bird flu?			
Case patients ( <i>n</i> = 44)	2 (4.6)	24 (54.6)	18 (40.9)
Control subjects ( <i>n</i> = 421)	2 (0.5)	284 (67.5)	135 (32.1)

NOTE. Data are no. (%) of respondents who selected each response.

Responses to Questions Assessing Concerns and Expectations Regarding an Avian Influenza Outbreak

TABLE 4

Question, response group	Response				
	No, definitely not	No, probably not	Yes, probably	Yes, definitely	Don't know
Do you think bird flu will spread to people in the United States?					
Case patients (n = 44)	0 (0.0)	3 (6.8)	18 (40.9)	2 (4.6)	21 (47.7)
Control subjects (n = 428)	11 (2.6)	82 (19.2)	135 (31.5)	16 (3.7)	184 (43.0)
If bird flu comes to the United States, do you think you, or someone you care about will catch it?					
Case patients (n = 44)	1 (2.3)	8 (18.2)	6 (13.6)	0 (0.0)	29 (65.9)
Control subjects (n = 424)	23 (5.4)	145 (34.2)	47 (11.1)	0 (0.0)	209 (49.3)
If bird flu comes to the United States, do you think you, or someone you care about will die from it?					
Case patients (n = 44)	2 (4.6)	15 (34.1)	5 (11.4)	0 (0.0)	22 (50.0)
Control subjects (n = 424)	42 (9.9)	150 (35.4)	29 (6.8)	1 (0.2)	202 (47.6)
Do you think the United States is prepared to deal with bird flu in an outbreak right now?					
Case patients (n = 44)	19 (43.2)	20 (45.5)	3 (6.8)	0 (0.0)	2 (4.5)
Control subjects (n = 425)	112 (26.4)	198 (46.6)	48 (11.3)	3 (0.7)	64 (15.1)
If an outbreak occurred, do you think most people could get medicine to treat it if needed?					
Case patients (n = 44)	7 (15.9)	23 (52.3)	7 (15.9)	0 (0.0)	7 (15.9)
Control subjects (n = 425)	66 (15.5)	161 (37.9)	107 (25.2)	5 (1.2)	86 (20.2)

NOTE. Data are no. (%) of respondents who selected each response.

**TABLE 5**  
**Responses to Question Assessing Concerns and Expectations Regarding the Timing of an Avian Influenza Outbreak**

Question, response group	Response					Don't know
	Within 1 year	Within 2 to 3 years	Within 4 to 5 years	More than 5 years from now	Never, it won't spread to people in the United States	
If bird flu were to spread to people in the United States, when would this occur?						
Case patients (n = 44)	6 (13.6)	18 (40.9)	6 (13.6)	5 (11.4)	4 (9.1)	5 (11.4)
Control subjects (n = 429)	63 (14.7)	179 (41.7)	73 (17.0)	49 (11.4)	48 (11.2)	17 (4.0)

NOTE. Data are no. (%) of respondents who selected each response.