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Antiviral Medications for Pregnant Women for Pandemic and Seasonal Influenza:

An Economic Computer Model

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Abstract

OBJECTIVE—To estimate the economic value of administering antiviral medications to pregnant women who have come in contact with an infectious individual with influenza.

METHODS—A computer-simulation model was developed to predict the potential economic effect of antiviral use for postexposure prophylaxis among pregnant women in both seasonal influenza and pandemic influenza scenarios. The model allowed us to examine the effects of varying influenza exposure risk, antiviral efficacy, antiviral cost, and the probability of different influenza outcomes such as hospitalization, preterm delivery, and mortality.

RESULTS—For a variety of pandemic influenza scenarios (attack rate 20% or more, probability of preterm birth for women with influenza 12% or more, mortality for a preterm neonate 2% or more, and probability of influenza-attributable hospitalization 4.8% or more), the postexposure prophylactic use of antiviral medications was strongly cost-effective, with incremental cost-effectiveness ratio values below \$50,000 per quality-adjusted life-year. Antiviral prophylaxis became an economically dominant strategy (that is, less costly and more effective) when the influenza attack rate is 20% or more and preterm birth rate is 36% or more, and when attack rate is 30% or more and preterm birth rate is 24% or more. Antiviral prophylaxis was not cost-effective under seasonal influenza conditions.

CONCLUSION—These findings support the use of antiviral medications for postexposure prophylaxis among pregnant women in a pandemic influenza scenario but not in a seasonal influenza setting.

Pregnant women are at an increased risk for poor outcomes from both seasonal influenza and more novel influenza pandemic strains, such as H1N1.¹ Past reports have suggested that pregnant women experience increased morbidity and rates of hospitalization during influenza season.^{2,3} Historical records of the 1918, 1957, and 1968 influenza pandemics also document markedly higher morbidity and mortality among both pregnant women and neonates.^{4–7} Consistent with historical data, emerging data from the current 2009 H1N1 influenza pandemic also strongly suggest that pregnant women are experiencing

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disproportionately high morbidity and mortality attributable to this novel strain.⁸ Pregnant women who experience severe influenza infections (eg, influenza pneumonia) seem to have increased rates of preterm birth, which, in turn, increases the risk for poor neonate outcomes.^{1,4,7,9} Together, these factors support the high prioritization that the Centers for Disease Control and Prevention (CDC) has given to protecting pregnant women against influenza.

Antiviral medications, including M2 inhibitors (adamantanes) such as amantadine and rimantadine and neuraminidase inhibitors such as oseltamivir and zanamivir, may be useful postexposure prophylaxes for preventing influenza in pregnant women who have come into contact with an infectious individual. Although vaccination may offer some protection against seasonal influenza, this protection is far from perfect, and vaccines for more novel influenza strains may not be available during the early phases of a pandemic outbreak. Moreover, despite recommendations from the Advisory Committee on Immunization Practices and the American College of Obstetrics and Gynecology, a majority of pregnant women either do not receive or refuse the seasonal influenza vaccine.¹⁰⁻¹² Concerns about vaccine safety may further reduce pregnant women's acceptance of an H1N1 influenza vaccine. These barriers to vaccination underscore the potential importance of antiviral medications for use during seasonal and pandemic influenza scenarios and have prompted the CDC to recommend use of antiviral medications in pregnant women for both postexposure prophylaxis and treatment.

We developed a computer simulation model to predict the potential economic effect of using antiviral medications as postexposure prophylaxes for pregnant women in both seasonal influenza and pandemic influenza scenarios. The model allowed us to examine the effects of varying influenza exposure risk, antiviral medication efficacy, antiviral medication cost, and the probability of different influenza outcomes, such as hospitalization, premature birth, and maternal mortality.

MATERIALS AND METHODS

This study was found to be exempt by the University of Pittsburgh Institutional Review Board. Using TreeAge Pro 2009 (TreeAge Software, Williamstown, MA), we constructed decision analytic computer simulation models, with probabilistic sensitivity analyses. The model (Fig. 1) represented the decision of whether to administer antiviral medication to a pregnant woman who may have been exposed to influenza through a close or household contact. The model allowed us to examine the effects of varying influenza exposure risk, antiviral efficacy, antiviral cost, and the probability of different influenza outcomes, such as hospitalization, preterm delivery, and mortality. The time frame for each simulation was the duration of a woman's pregnancy. Simulation runs were conducted from both societal and third-party payer perspectives. The primary difference between the two perspectives was the cost of having a preterm infant. From the third-party payer perspective, this cost totaled \$33,200 and included all costs for increased medical services. The societal perspective added the cost of early intervention services and special education services (associated primarily with cerebral palsy, mental retardation, vision impairment, and hearing loss—all of which are more common among premature infants) and the accompanying lost household and labor market productivity to bring the total up to \$51,600 per preterm infant. These numbers came from an Institute of Medicine report on preterm birth.¹³

A patient's risk of contracting influenza depended on whether she received neuraminidase inhibitors (eg, oseltamivir phosphate), the antiviral efficacy, and her individual risk of exposure. Those receiving antiviral medications had a probability of experiencing adverse effects, such as nausea, which necessitated the use over-the-counter medications. Consistent

with values from the literature, influenza persisted for 7 days (range 3–10 days).^{11,14–17} Of the patients who developed influenza, a percentage required hospitalization. Those who did not require hospitalization either self-treated with over-the-counter medications or visited an outpatient medical clinic. A subset of hospitalized patients did not survive. Hospitalized patients in their third trimester had a risk of premature labor and delivery (above the background risk of 12%), which could result in negative fetal and neonatal outcomes.

The incremental cost-effectiveness ratio is the added cost of an intervention (compared with no intervention) divided by the added favorable effects of the intervention (compared with no intervention). The following equation calculates the incremental cost-effectiveness ratio (ICER) of administering compared with not administering antiviral medications:

$$\text{ICER} = \left(\text{Cost}_{\text{Antiviral Prophylaxis}} - \text{Cost}_{\text{No Antiviral Prophylaxis}} \right) / \left(\text{Effectiveness}_{\text{Antiviral Prophylaxis}} - \text{Effectiveness}_{\text{No Antiviral Prophylaxis}} \right).$$

While some debate exists over the exact threshold below which ICER values indicate cost-effectiveness, \$50,000/quality-adjusted life-year (QALY) is a commonly used cutpoint. Incremental cost-effectiveness ratios \$50,000/QALY or less are considered relatively cost-effective, and values of \$20,000/QALY or less provide strong economic support for adoption of an intervention.¹⁸ When postexposure antiviral prophylaxis is both more effective and less costly than no use of antivirals, suggesting clear benefit, antiviral prophylaxis is considered the economically dominant strategy. Incremental cost-effectiveness ratios \$100,000/QALY or more suggest poor economic evidence for adoption of postexposure antiviral prophylaxis.¹⁹ When antiviral use is less effective and more costly than no antiviral use, postexposure antiviral prophylaxis is a dominated strategy and the practice is discouraged from an economic standpoint.

Table 1 lists the cost and probability inputs for our model and the corresponding distributions and data sources. Each medication's average wholesale price along with its dosing schedule determined its cost.²⁰ The National Inpatient Survey from the Healthcare Utilization Project provided the costs of hospitalization.²¹ Previously published economic decision models used the cost of death in a hospital. A CDC study generated the cost of a birth defect.²² Costs assumed gamma distributions, except for the costs of over-the-counter influenza medications and treatment of antiviral medication adverse effects, which assumed triangular distributions, and the cost of death and preterm birth, which took uniform distributions. Economic models frequently use the gamma distribution to model continuous variables that are always positive and have skewed distributions.^{23,24} Health care costs often have these characteristics, with the majority of costs centered around the lower end of the distribution and a long tail to the right representing a small percentage of much greater costs. Using a triangular distribution is appropriate when a parameter's distribution is asymmetric and only the lower limit, mode, and upper limit are known. Such a distribution is shaped like a triangle with the lower limit at the far left of the base, the upper limit at the far right, and the mode at the point of the triangle with height equal to 2 divided by the width of the base. All probabilities assumed triangular distributions, except for the probabilities of antiviral medication adverse effects, hospitalization, maternal death, and preterm birth, which took on uniform distributions. Where possible, data inputs came from published meta-analyses. All costs were in 2009 U.S. dollars. A 3% discount rate converted all costs from other years into 2009 dollars. Sensitivity analyses examined the effects of changing the discount rate from 0% to 5% and discounting and not discounting QALYs.

The model measured effectiveness in QALYs. Pregnant women who did not experience medication adverse effects or influenza accrued 0.92 QALYs.¹³ Uncomplicated influenza caused a reduction of QALYs to 0.65 (range 0.49–0.81) through the duration of illness.

Hospitalization from influenza resulted in a QALY decrement to 0.50 (range 0.38–0.63) during hospitalization. Antiviral medication adverse effects caused a 0.05 QALY decrement. A normal birth contributed QALYs based on the infant's life expectancy. Medication adverse effects, influenza, and hospitalization each caused different decrements in QALYs.^{25,34} The expected loss of QALYs from death of the pregnant woman and the infant came from the life expectancy (in QALYs) of the pregnant woman and infant, respectively. Life expectancy estimates came from the Human Mortality Database.³⁵

The base case pandemic scenario assumed a 100% risk of exposure to influenza, a 20% influenza attack rate, and the standard cost and efficacy (for healthy adults) of oseltamivir. It also assumed a risk of hospitalization 4.21 times, a preterm labor risk equal to, and mortality equal to that of seasonal influenza. By contrast, the seasonal influenza base case assumed a lower attack rate (a triangular distribution with most likely value 0.125; lower limit 0.05; upper limit 0.20).³⁶

Sensitivity analyses determined the effects of varying different parameter values individually throughout the ranges listed in Table 1. Multidimensional sensitivity analyses were performed on selected parameters. In particular, we examined the effects of varying the risk of exposure (25% to 100%), influenza attack rate (5% to 30%) type of antiviral medication, antiviral medication efficacy in preventing influenza infection (25% to 75%), antiviral medication cost, the probability of premature delivery, the probability of hospitalization from influenza (one, two, three, and four times that of seasonal influenza), and mortality from influenza (one, two, three, and four times that of seasonal influenza) to represent both seasonal and pandemic influenza scenarios. Additional sets of sensitivity analyses varied the risk of birth defects from antiviral use and the discount rate. In addition, probabilistic (Monte Carlo) sensitivity analyses examined the effects of varying all parameters through their entire ranges.

RESULTS

Each pandemic simulation run sent 1,000 hypothetical pregnant women (initially healthy and of median age 27.1 year and gestational age drawn from a distribution between 1 and 40 weeks) through the model 1,000 times (ie, 1,000,000 total trial outcomes). Based on a set of probability rolls, each of the 1,000 women had a set of characteristics (eg, woman number one would have a gestational age of 40 weeks based on a computer dice roll) that helped govern her path through the model. Every time a given woman would travel through the model, she would accrue costs and QALYs. Because these costs and QALY values are drawn from probability distributions, each time the same woman would travel through the model she could accrue different costs and QALYs. Each woman then would go through the model 1,000 times (eg, woman number one would proceed through the model 1,000 times, then woman number two would proceed through the model 1,000 times, etc.).

Administration of antiviral medication was strongly cost-effective for a wide variety of possible H1N1 pandemic influenza scenarios. For a variety of pandemic influenza scenarios (attack rate 20% or more, probability of preterm birth for women with influenza 12% or more, mortality for a preterm neonate 2% or more, and probability of influenza-attributable hospitalization 4.8% or more), the postexposure prophylactic use of antiviral medications had incremental cost-effectiveness ratio values below \$50,000 per quality adjusted life-year. The median ICER for the base case scenario was \$4534.96 from the third-party perspective. Table 2 shows how the ICER values varied by the influenza attack rate, probability of preterm birth, and probability of preterm mortality that is attributable to influenza from the third-party payer perspective. The ICER for antiviral medication use was consistently lower from the societal perspective than from the third-party payer perspective. When the

influenza attack rate reached 30%, the ICER antiviral medication use was well under \$1000 per QALY for all of the scenarios for both the third party and societal perspectives. Antiviral prophylaxis became the economically dominant option (ie, less costly and more effective) for both the third party and societal perspectives when the influenza attack rate was 20% or more and the preterm birth rate 36% or more (three times the background risk), or when the attack rate was 30% or more and preterm birth rate was 24% or more (twice the background risk). Table 3 shows the influenza outcomes averted by antiviral medications per 1,000 patients treated in the baseline pandemic scenarios. For an attack rate of 30%, 0.378 and 0.369 of the simulations did not result in antiviral prophylaxis being cost-effective at willingness-to-pay thresholds of \$25,000 and \$50,000, respectively. For an attack rate of 20%, 0.474 and 0.460 of the simulations did not result in antiviral prophylaxis being cost-effective at willingness-to-pay thresholds of \$25,000 and \$50,000, respectively.

Figure 2 demonstrates how the ICER of administering antiviral medications rapidly decreases as the influenza-attributable preterm birth rate increases. In fact, antiviral medication use becomes economically dominant when the influenza-attributable preterm birth rate reaches 36%. These findings emphasize the importance of considering how influenza may affect preterm birth rates when planning for and making decisions during an influenza pandemic.

These results did not change substantially when ranging maternal age from 20 years to 40 years. For example, whether maternal age was set to 20 years, antiviral use was cost-effective when the attack rate ranged from 20% (ICER=\$165.04/QALY) to 30% (ICER=\$147.23/QALY) at $P<.05$. When maternal age was set to 40 years, antiviral use still was cost-effective when the attack rate varied from 20% (ICER=\$471.56/QALY) to 30% (ICER=\$190.52/QALY) at $P<.05$. Results were also very robust to changes in discount rates from 0% to 5% and discounting and not discounting QALYs. The same cost-effective and economic dominance thresholds held through all changes in discounting.

Conversely, attack rate and gestational age significantly affected the economic value of antiviral use. When the attack rate fell below 15%, antiviral use was no longer cost-effective and, in fact, dominated (ie, avoiding antiviral use saved costs and was more effective). When gestational age was less than 20 weeks, not using antiviral medications dominated antiviral use, even when influenza attack rates were as high as 30%. When gestational age was greater than 20 weeks, antiviral use was economically dominant in all explored scenarios in which the attack rate 20% or more. Thus, much of the economic value of antiviral medications is contingent on their ability to prevent influenza-induced preterm births. When only maternal QALYs were considered in the pandemic base case scenario, not using antiviral medications dominated antiviral use.

Sensitivity analyses delineated the threshold at which antiviral resistance would make antiviral medication use no longer cost-effective. When antiviral medication efficacy dropped to 50%, its use remained cost-effective for preterm mortality 0.02 or more, probability of preterm birth 0.12 or more, and attack rate 20% or more. When efficacy dropped even further to 30%, antiviral use was cost-effective for preterm mortality 0.02 or more, probability of preterm birth 0.24 or more, and attack rate 20% or more. Antiviral use became dominated when efficacy fell to 25% (as long as preterm mortality was 0.08 or more, probability of preterm birth was 0.36 or more, and attack rate was 30% or more). These results suggest that antiviral medications are no longer cost-effective when antiviral resistance causes efficacy to move below 30%.

Varying the risk of birth defects attributable to antiviral use during pregnancy delineated the risk threshold at which antiviral medications were no longer cost-effective in our baseline

pandemic scenarios. When the attack rate was 20%, a 0.1% risk of birth defects yielded an ICER of \$32,685/QALY. Increasing the risk to 0.2% boosted the ICER to \$39,340. The ICER crossed \$50,000/QALY to \$96,876/QALY when the risk increased to 0.3%. At a higher attack rate of 30%, the ICER of antiviral medication use was \$7,641/QALY at a birth defect rate of 0.1%, \$32,224/QALY at a rate of 0.5%, \$43,860 at a rate of 0.7%, and \$54,949/QALY at 0.9%.

Each seasonal influenza simulation run sent 1,000 simulated pregnant women through the model 1,000 times (1,000,000 total trials). For the baseline scenario, as well as many others, administering antiviral medications was definitively not cost-effective. Antiviral administration was dominated in all simulated scenarios (antiviral efficacy from 25–100%, probability of influenza exposure from 25–100%, influenza attack rate 50–100%, probability of maternal mortality from seasonal influenza mortality to four times seasonal influenza mortality, and probability of hospitalization with seasonal influenza and four times this hospitalization rate) by opting not to use antiviral medications. For seasonal influenza, 0.118 and 0.140 of the simulations resulted in antiviral prophylaxis being cost-effective at willingness-to-pay thresholds of \$25,000 and \$50,000, respectively.

DISCUSSION

These study results suggest that postexposure prophylactic use of antiviral medications during pregnancy is a cost-effective (and in many circumstances economically dominant) intervention during a pandemic influenza scenario assuming that the risk of birth defects is negligible. The value of antiviral medications lies not only in their ability to prevent maternal hospitalization and mortality, but also mitigating the risk of preterm birth associated with severe influenza infection during pregnancy. These findings were robust under a variety of pandemic scenarios, offering strong support for the CDC recommendations regardless of the exact characteristics (eg, reproductive rate or virulence) of the predominant H1N1 influenza strain circulating this coming autumn and winter. These results were consistent from both societal and third-party payer perspectives, which suggests that insurers should consider covering the use of antiviral medications for postexposure prophylaxis during pandemic situations, because prevention of influenza and its complications outweighs the cost of antiviral medications. Although no human studies to date have demonstrated a link between antiviral medications and fetal anomalies, the relative dearth of human studies may have to temper any definitive statements about antiviral safety. Our analyses found that antiviral use was no longer a cost-effective strategy when the risk of birth defects attributable to maternal antiviral use exceeded 0.3% given an attack rate of 20%, or when the risk of birth defects was greater than 0.9% given a higher attack rate of 30%.

In our model, the probability of preterm birth had a substantial effect on the cost-effectiveness of postexposure antiviral prophylaxis. Based on prior studies, the model assumed that seasonal influenza would not cause a substantial number of pulmonary complications and increase the risk of preterm birth. However, data from previous influenza pandemics (as well as data on pneumonia in pregnancy in general) have suggested that pregnant women suffering from pneumonia may have at least a twofold to fourfold increased likelihood of delivering preterm.^{2-5,32} Although it is too early to determine if such increased rates will be seen during the current H1N1 influenza pandemic, concerns have prompted the CDC to initiate surveillance for pregnant women infected with the virus.³⁷

Recommendations for prophylactic treatment of pregnant women against 2009 H1N1 pandemic influenza include use of either oseltamivir or zanamivir in standard doses.³⁸ Currently, the large majority of isolates recovered remain susceptible to these two

neuraminidase inhibitor medications. However, changes to the circulating virus could alter susceptibility to either or both, prompting recommendations for use of one or both of the older adamantane medications (amantadine and rimantadine). The CDC recommends that treatment of pregnant women with influenza-like illness begin as soon as possible. Initiation of treatment should not await influenza testing or test results. Treatment and chemoprophylaxis regimens recommended for pregnant women are the same as those recommended for other adults. Pregnancy is not a contraindication to either oseltamivir or zanamivir. Given that zanamivir is an inhaled antiviral prophylactic and may provide reduced systemic effect, oseltamivir should be the treatment of choice and administered within 48 hours of infection for maximal effect.

Our study also suggests that routine use of prophylactic antiviral medications for the prevention of seasonal influenza in the pregnant population is not cost-effective. For otherwise healthy pregnant women (assuming seasonal attack rates and virulence), antiviral prophylaxes may not offer enough protective efficacy to justify their relatively high costs. Not administering antiviral medications dominated administering antiviral medications in most seasonal influenza scenarios. More women experienced adverse effects, such as nausea, than benefitted from avoiding influenza in these simulations. These findings support current practice in that antiviral medications targeting seasonal influenza are rarely used during pregnancy for postexposure prophylaxis. This highlights the importance of influenza vaccination for pregnant women. Vaccination not only is much less costly but also more effectively protects a pregnant woman for a much greater duration of time. Our study suggests that antiviral medications are by no means a substitute for vaccines against seasonal influenza and that providers should emphasize to pregnant patients the importance of immunization.

Before this investigation, few researchers have examined the cost-effectiveness of antiviral medications for prophylaxis against influenza in pregnant women. Systematic reviews of prior economic studies on antiviral postexposure prophylaxis yielded studies of healthy adults, institutionalized and noninstitutionalized elderly, and children, but little information specific to the population of pregnant women.³⁹⁻⁴⁵ These reviews found a wide range of ICERs of antiviral prophylaxis, from \$5,000 to well over \$200,000 per QALY.⁴⁶⁻⁴⁹ An additional nuance is that most of the past economic evaluations were for countries outside the United States, predominantly the United Kingdom.

Economic modeling can help guide decision making with regard to whether antiviral medications should be used for postexposure prophylaxis in pregnant women. The choice of whether to employ an intervention is often a balance between cost and clinical effects. Third-party payers can factor in economic values when determining whether to provide insurance coverage for antiviral medications, and if so, to what extent. Manufacturers can use economic information to guide development and pricing of antiviral medications. Economic value can guide antiviral production and storage, as well as prescription practices. Economic concerns may be particularly paramount during an influenza epidemic or pandemic when antiviral availability may be limited, forcing policy makers and clinicians to prioritize who should receive antiviral medications.

Economic evaluations of influenza disease interventions should critically evaluate the subpopulation of pregnant women and its relevant characteristics rather than assume that findings in a larger population will generalize to this unique subset. An intervention shown to be cost-effective in other populations may not be cost-effective in the pregnant population and vice versa. Pregnancy affects a woman's immune status by producing a relative immune-compromised state that seems to peak in the latter parts of gestation, placing pregnant women and their fetuses at increased risk for untoward outcomes from a variety of

bacterial, viral, and parasitic pathogens. Safety data specific to maternity is limited, but no studies have suggested that pregnant women or their fetuses are at significantly increased risk for major adverse outcomes from antiviral medications.⁵⁰

Economic evaluations for various subpopulations, such as pregnant women, are especially important when there is limited availability of antiviral medication, and rationing may become necessary. In this type of situation, policy makers and clinicians will have to prioritize administration of antiviral medications, and assessment of cost-effectiveness information such as that generated by our model provides valuable insight to the decision-making process. Antiviral medication shortages are highly probable during an influenza pandemic; additionally, governmental, organizational, and personal stockpiling of antiviral medications can further limit resources. These findings support the prioritization of antiviral use among pregnant women from an economic standpoint.

Every computer model is a simplification of real life. No model can fully represent every single event and outcome that may ensue from influenza and antiviral medication use. Our model did not fully represent the pregnant population's heterogeneity and accompanying comorbidities. Comorbidities may increase a person's risk of influenza and influenza-related complications and corresponding resource consumption (eg, intubation and mechanical ventilation). Resource use and probabilities of hospitalization and death may vary by demographic characteristics such as race, ethnicity, and socioeconomic status. Moreover, our model may underestimate the value of antiviral medications by not including the potential effects of antiviral medications on transmission, because antiviral medications may decrease influenza virus shedding and therefore the infectiousness of the pregnant woman.

These results strongly support administering antiviral medications to pregnant women for postexposure prophylaxis in pandemic influenza scenarios. This strategy is highly cost-effective (and, in many cases, economically dominant) for a wide range of pandemic circumstances. Our study does not support the routine use of antiviral medications to prevent seasonal influenza among pregnant women, because the cost outweighs their potential value in preventing disease. Understanding the economic effect of antiviral medications in pregnant women may be useful for clinical, production, distribution, and prioritization decisions.

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Fig. 1.
General model structure.
Lee. Pandemic and Seasonal Influenza Medications. Obstet Gynecol 2009.

Fig. 2.

Incremental cost-effectiveness ratio of antiviral prophylaxis against influenza for pregnant women at different preterm birth and mortality rates.

Lee. Pandemic and Seasonal Influenza Medications. *Obstet Gynecol* 2009.

Table 1
Data Inputs for Model Variables

Description (Units)	Mean	Standard Deviation or Range*	Source (Reference)
Costs (\$U.S.)			
Antiviral medications			
Oseltamivir	99.32	±21.99	20
Zanamivir	62.20	±3.26	20
Amantadine	19.58	±4.64	20
Rimantadine	44.30	±13.48	20
Clinical outcomes			
Over-the-counter medications	15.61	11.70–19.51	20
Hospitalization	3,526.00	±302.10	21
Death in hospital	5,000.00	-	26
Antiviral adverse effects	0.76	0.68–3.82	20
Preterm birth (3rd party payer perspective)	37,366.89	-	27
Preterm birth (societal perspective)	58,076.25	-	27
Birth defect	244,000.00	-	22
Probabilities			
Clinical outcomes			
Antiviral medications adverse effects	0.05	-	25
Influenza	0.125	0.050–0.200	28, 29
Given influenza (base case)			
Hospitalization	0.048	-	8, 21
Maternal death	0.0105	-	28, 30–32
Preterm birth	0.12	-	33
Preterm mortality	0.02	0.0088–0.151	11
Efficacy			
Oseltamivir	0.61	0.08–0.85	28, 30–32
Zanamivir	0.62	0.07–0.85	28, 30–32
Amantadine	0.61	0.35–0.76	28, 30–32
Rimantadine	0.72	0.00–0.92	28, 30–32

* Depending on the type of distribution.

Table 2
Incremental Cost-effectiveness Ratio and 95% Confidence Interval in U.S. Dollars per
Quality-Adjusted Life-Year for Different Pandemic and Seasonal Influenza Scenarios
From the Third-Party Payer Perspective

Probability of Preterm Mortality	Probability of Preterm Birth			
	Base Case: 0.12	2×Base Case: 0.24	3×Base Case: 0.36	4×Base Case: 0.48
Influenza attack rate 10%				
0.02	Antiviral medication use dominated by no antiviral medication use			
Base case: 0.02 (0.0088–0.151)*				
0.04	Antiviral medication use dominated by no antiviral medication use			
0.08	Antiviral medication use dominated by no antiviral medication use			
Influenza attack rate 20%				
0.02	5206.61 (–27571.50 to 46630.05)	654.61 (–53205.80 to 33162.8)	Antiviral medication use dominant (over no antiviral use)	
Base case: 0.02 (0.0088–0.151)*	4534.96 (–31552.40 to 42530.57)	321.17 (–46388.60 to 35200.04)	Antiviral medication use dominant (over no antiviral use)	
0.04	3796.84 (–27651.10 to 44624.73)	689.82 (–46872.40 to 39088.83)	Antiviral medication use dominant (over no antiviral use)	
0.08	3494.15 (–34499.30 to 42084.25)	388.85 (–31933.40 to 28295.94)	Antiviral medication use dominant (over no antiviral use)	
Influenza attack rate 30%				
0.02	161.51 (–46221.40 to 28374.04)	Antiviral medication use dominant (over no antiviral use)		
Base case: 0.02 (0.0088–0.151)*	276.35 (–24695.30 to 27440.22)	Antiviral medication use dominant (over no antiviral use)		
0.04	142.46 (–37128.70 to 26608.83)	Antiviral medication use dominant (over no antiviral use)		
0.08	132.32 (–20474.30 to 25598.20)	Antiviral medication use dominant (over no antiviral use)		

Data in parentheses are 95% confidence intervals.

* Range.

Table 3
Influenza Outcomes Prevented per 1,000 Pregnant Patients Treated With Antiviral Medications for Baseline Pandemic Scenario*

Outcome Prevented	10% Attack Rate			20% Attack Rate			30% Attack Rate		
	Mean	95% Range	Mean	95% Range	Mean	95% Range	Mean	95% Range	Mean
Maternal influenza cases	69	20 128	110	46 167	163	72 246			
Maternal deaths	0	0 1	1	0 5	2	0 6			
Hospitalizations	0	0 2	5	0 13	8	0 18			
Neonatal deaths	0	0 0	0	0 1	0	0 1			
Preterm births	0	0 1	1	0 4	1	0 4			

* Risk of hospitalization 4.21 times, a preterm labor risk equal to and a mortality equal to that of seasonal influenza.