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Pandemic 2009 Influenza A(H1N1) Virus Illness Among Pregnant Women in the United States

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Abstract

Context—Early data on pandemic 2009 influenza A(H1N1) suggest pregnant women are at increased risk of hospitalization and death.

Objective—To describe the severity of 2009 influenza A(H1N1) illness and the association with early antiviral treatment among pregnant women in the United States.

Design, Setting, and Patients—Surveillance of 2009 influenza A(H1N1) in pregnant women reported to the Centers for Disease Control and Prevention (CDC) with symptom onset from April through December 2009.

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Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the CDC.

Online-Only Material: eTable is available at http://www.jama.com.

Main Outcome Measures—Severity of illness (hospitalizations, intensive care unit [ICU] admissions, and deaths) due to 2009 influenza A(H1N1) among pregnant women, stratified by timing of antiviral treatment and pregnancy trimester at symptom onset.

Results—We received reports on 788 pregnant women in the United States with 2009 influenza A(H1N1) with symptom onset from April through August 2009. Among those, 30 died (5% of all reported 2009 influenza A[H1N1] influenza deaths in this period). Among 509 hospitalized women, 115 (22.6%) were admitted to an ICU. Pregnant women with treatment more than 4 days after symptom onset were more likely to be admitted to an ICU (56.9% vs 9.4%; relative risk [RR], 6.0; 95% confidence interval [CI], 3.5-10.6) than those treated within 2 days after symptom onset. Only 1 death occurred in a patient who received treatment within 2 days of symptom onset. Updating these data with the CDC's continued surveillance of ICU admissions and deaths among pregnant women with symptom onset through December 31, 2009, identified an additional 165 women for a total of 280 women who were admitted to ICUs, 56 of whom died. Among the deaths, 4 occurred in the first trimester (7.1%), 15 in the second (26.8%), and 36 in the third (64.3%);

Conclusions—Pregnant women had a disproportionately high risk of mortality due to 2009 influenza A(H1N1). Among pregnant women with 2009 influenza A(H1N1) influenza reported to the CDC, early antiviral treatment appeared to be associated with fewer admissions to an ICU and fewer deaths.

On April 21, 2009, THE Centers for Disease Control and Prevention (CDC) reported that 2 children from southern California were identified with a novel influenza A virus infection.[1] Since that time, the 2009 influenza A(H1N1) has rapidly spread worldwide, and on June 11, 2009, the World Health Organization raised the pandemic alert level to the highest level of 6.2 Although 2009 influenza A(H1N1) has generally been characterized as a self-limited uncomplicated infection, severe illnesses and deaths have been reported among some patients.[3–5] Recent studies have shown that health conditions typically associated with risk for seasonal influenza complications were also found among individuals with 2009 influenza A(H1N1) admitted to an intensive care unit (ICU), including chronic lung disease, neurological disorders, diabetes, and pregnancy.[4–6]

Changes in the immune, cardiac, and respiratory systems are likely reasons that pregnant women are at increased risk for severe illness with influenza.[7,8] During previous pandemics, mortality rates among pregnant women appeared elevated,[9–12] and data from seasonal influenza demonstrate that pregnant women are at higher risk for hospitalization than women a year before pregnancy[13] or 6 months after delivery.[14] A study of pregnant US women with confirmed or probable 2009 influenza A(H1N1) during the first month of the outbreak as reported to the CDC showed that 11 of the 34 cases (32.4%) were hospitalized and that hospital admission rates for pregnant women were 4 times higher than those for the general population.[15]

The objective of this project was to further describe the effects of 2009 influenza A(H1N1) on pregnant women. We present data on all influenza cases of pregnant women reported to the CDC with symptom onset from April through August 21, 2009, including data on maternal characteristics, underlying illness, severity of illness, and maternal outcomes

related to timing of antiviral treatment. In addition, we provide an update of all pregnant women with influenza who were admitted to an intensive care unit (ICU) or who died, with symptom onset from August 21 through December 31, 2009, who were reported to the CDC Pregnancy Flu Line by January 31, 2010.

METHODS

On August 24 and 26, 2009, the CDC requested that all state health departments and the local health departments for Chicago, New York City, and the District of Columbia (N=53) provide additional information on all pregnant women reported with confirmed or probable 2009 influenza A(H1N1) from the beginning of the outbreak in April 2009 through August 21, 2009, using a standardized case report form. A confirmed case was defined as an individual reported with acute respiratory illness and laboratory-confirmed 2009 influenza A(H1N1) by real-time reverse-transcriptase polymerase chain reaction (rRT-PCR) or viral culture. A probable case was defined as an individual with an acute febrile respiratory illness, a positive test for influenza, and a negative influenza rRT-PCR test result for H1 and H3.[16] The case report form included data elements to assess demographics, gestational age, underlying conditions, treatment, illness onset, and severity including hospitalization and maternal and infant outcomes. Gestational weeks at illness on set were computed as 40 weeks− (estimated delivery date−illness onset date)/7. Some jurisdictions chose to provide gestational age as either month of pregnancy or gestational weeks. For those women who delivered, gestational age at delivery was computed as 40 weeks−(estimated delivery date −actual delivery date)/7. Delivery at gestational age less than 37 completed weeks was categorized as a preterm delivery. Underlying conditions were entered as open text and were classified into the following categories: asthma, chronic lung disease, pregestational and gestational diabetes, obesity, thyroid disease, immune suppression, autoimmune disease, neurological disease, cardiovascular disease, hypertension, anemia, and other. Hospitalization was defined as admission and discharge dates occurring 1 or more days apart; patients with admission and discharge dates occurring on the same day were included in the analyses but were designated as not being hospitalized. Hospital length of stay was computed as (discharge date)−(admission date). Several health departments chose to provide hospital length of stay directly. Among hospitalized women, a yes, no, or unknown response was requested for ICU admission and mechanical ventilation. Hospitalized patients who were reported to have mechanical ventilation were classified as having received ICU care, even if ICU status was not provided on the report form. Maternal outcome was recorded by reporting jurisdictions as survived, died, or unknown. Delivery method included precoded responses: spontaneous vaginal delivery, vacuum-assisted vaginal delivery, forceps-assisted vaginal delivery, cesarean delivery, spontaneous abortion, or therapeutic abortion; and the following imputed responses: delivered—type unknown or estimated delivery date occurring on or before November 6, 2009, and not yet delivered or estimated delivery date occurring after November 6, 2009. Race/ethnicity was recorded based on abstraction of medical records by state and local health departments.

Demographic and clinical characteristics of women with severe outcomes (hospitalization, ICU admission, and maternal deaths) were assessed. However, because these groups are not mutually exclusive and therefore not independent (maternal deaths are a subset of ICU

admission, and ICU admission is a subset of all hospitalizations), statistical tests comparing these groups were not performed.

Relative risks (RRs) and 95% confidence intervals (CIs) were calculated for severe outcomes (hospital and ICU admission, mechanical ventilation, and maternal death) by timing of antiviral treatment: none; late, more than 4 days after symptom onset; intermediate, 3 to 4 days after symptom onset; and early, within 2 days of symptom onset. Stratified analysis for ICU admission or death among hospitalized patients was used to compare intermediate and late treatment with early treatment by pregnancy trimester at illness symptom onset. We decided a priori to use the early-treatment group as the referent instead of the no-treatment group because the latter includes pregnant women who might have had mild illness and recovered without treatment.

A significant amount of data on some variables was missing. Among the 465 women hospitalized with known ICU status, 153 (32.9%) did not have information on antiviral treatment or timing of treatment. Pregnancy trimester at illness onset was missing for 100 women, 73 (15.7%) of whom had intermediate or late treatment, resulting in their exclusion from the analysis of treatment timing by trimester.

States and municipalities provided de-identified information to the CDC electronically. Data were imported, merged, and analyzed using Microsoft Office Access version 2003 (Microsoft Corp, Redmond, Washington) and SAS version 9.2 (SAS Institute Inc, Cary, North Carolina). The Mantel-Haenszel^2 test, and for small sample size comparisons, the Fisher exact test were used to test for statistical significance.

In mid-October 2009, the CDC Pregnancy Flu Line was launched, which requested reports from all state and metropolitan health department so fall severely ill pregnant women (ICU admissions and deaths) with confirmed influenza diagnosed by (1) a positive rapid test result, (2) rRT-PCR positive result for influenza, (3) direct or indirect fluorescent antibody assay, or (4) viral culture. Reports were requested for all cases with symptom onset after August 21, 2009. Case reports included maternal and infant diagnostic, treatment, and outcome data. Health departments sent reports via secure email, fax, or telephone. This includes all CDC Pregnancy Flu Line reports with symptom onset on or before December 31, 2009, and reported to the CDC by January 31, 2010. These cases were all assumed to be 2009 influenza A(H1N1) influenza, based on US virological surveillance suggesting that nearly all influenza activity during this time was 2009 H1N1.[17]

Data collection was conducted as part of public health response and was deemed exempt from review by an institutional review board.

RESULTS

During our initial period of data collection (April-August 2009), we received responses from 50 of the 53 state and local health departments contacted, which reported a total 788 cases. The number of total cases reported per health department ranged from 1 from 11 states to 135 from a single state. Two states reported no cases. The 48 health departments that reported at least 1 case covered service areas representing approximately 97% of all US

births.[18] Among the health departments reporting on pregnant women with 2009 influenza A(H1N1), 5 reported only on hospitalized pregnant women. The 3 health departments that reported the most cases—representing 37% of the total cases—reported that 92% of pregnant women with influenza in their jurisdictions had been hospitalized.

The most commonly reported racial-ethnic groups among 788 reported cases were Hispanic (32.8%), non-Hispanic white (22.7%), non-Hispanic black (19.1%), and Asian/Pacific Islander (5.7%; TABLE 1). Among the 30 deaths, 44.8% were non-Hispanic white, 27.6% were Hispanic, and 13.8% were Asian/Pacific Islander, and 6.9% were non-Hispanic black. Maternal median age was 25 (range, 14-43) years and was similar among patients who died (Table 1). Eleven states accounted for 76% of the pregnant women reported to the CDC, and 37% of the pregnant women with 2009 influenza A(H1N1) influenza reported from these states were of Hispanic ethnicity, the same proportion as observed among live births from these states.[18]

The earliest date of influenza illness onset was April 14, 2009, and the latest was August 21, 2009, the last day of the requested data collection. Of the 592 women with available information on trimester, 11.3% were in their first, 42.2% were in their second, and 46.5% were in their third trimester of pregnancy. Among the 30 women who died, 3 (10.0%) were in their first, 9 (30.0%) were in their second, and 18 (60.0%) were in their third trimester.

Health departments provided information on the presence or absence of underlying conditions for 432 pregnant women (54.8%), of whom 213 had 1 or more underlying condition (49.3%). The most frequently reported conditions were asthma (22.9%), obesity (13.0%), pregestational or gestational diabetes (6.7%), anemia (3.5%), and hypertension (3.0%; Table 1). Underlying conditions were more common among hospitalized women (55.3%), women admitted to the ICU (62.8%), and deaths (78.3%). Among pregnant women who died, asthma was the most common underlying condition reported in 10 (43.5%).

Among the 588 women for whom treatment information was provided, 509 (86.6%) received antiviral treatment; 492 (83.6%) of women received oseltamivir alone or in combinations with zanamivir, amantadine, or rimantadine. Thirteen women received zanamivir alone. The treatment among women admitted to the hospital or the ICU or who had died was distributed similarly. Information about the timing of treatment initiation was available for 384 patients (65.3%). Two hundred nineteen women (43.0%) received treatment early, including 2 women who received prophylaxis 1 and 2 days before illness onset; 84 (16.5%) received intermediate treatment; and 81 (15.9%) received late treatment (Table 1). Only 13 women (15.9%) in the ICU received treatment within 2 days and only 15 (18.3%) in 3 to 4 days. Among the women who died, only 1 received treatment within 2 days and 4 received treatment in 3 to 4 days. The median time to treatment initiation increased from 2 days among hospitalized patients to 5 days among patients in the ICU and to 6 days among patients who died.

Illness severity indicators included hospitalization, ICU admission, mechanical ventilation, and death (TABLE 2). Among those hospitalized, 115 (24.7%) were admitted to an ICU, and

77 (18.8%) received mechanical ventilation. Among 169 live-birth deliveries for which gestational age was known, 51 (30.2%) were preterm.

Sixty-eight percent of women receiving antiviral treatment early vs 79% of women receiving intermediate treatment were hospitalized (RR, 1.2; 95% CI, 1.0-1.3); 9% of hospitalized women receiving early antiviral treatment vs 23% receiving intermediate treatment were admitted to the ICU (RR, 2.4; 95% CI, 1.2-4.8); and 5% of hospitalized women receiving antiviral treatment early vs 17% of women receiving intermediate treatment required mechanical ventilation (RR, 3.8; 95% CI, 1.4-9.9; TABLE 3). Compared with 9% of hospitalized women receiving early treatment, 57% of hospitalized women receiving late treatment were admitted to the ICU, a 6-fold increased risk (RR, 6.0; 95% CI, 3.5-10.6), and they experienced 12-fold increased risk of mechanical ventilation (5% early vs 56% late treatment; RR, 12.3; 95% CI, 5.4-27.7). Compared with women receiving early treatment, those who received no treatment had no increased risk of being hospitalized (68% early vs 58% no treatment; RR, 0.8; 95% CI, 0.7-1.0), but they had an increased risk of ICU admission (9% early vs 35% no treatment; RR, 3.7; 95% CI, 1.9-7.2) and had an increased risk of mechanical ventilation (5% early vs 21% no treatment; RR, 4.7; 95% CI, 1.8-12.4), Women who received intermediate treatment were more likely to die than those who received early treatment (0.5% early vs 5.0% intermediate treatment; RR, 9.9; 95% CI, 1.1-87.2), whereas those who received late treatment were 54 times more likely to die than those who received early treatment (27% late vs 0.5% early; RR, 53.5; 95% CI, 7.3-391.7).

To further examine the association between antiviral treatment with illness severity and any interaction with pregnancy trimester, we stratified analyses for ICU admission among hospitalized women by trimester (TABLE 4). We combined all trimesters for an early-treatment group and used this as the referent. Women in the first and second trimester receiving intermediate treatment did not differ statistically from women who received early treatment; however, women in their third trimester who received intermediate treatment were 3.5 times more likely to be admitted to the ICU (95% CI, 1.7-7.4) than those treated early. Compared with women in any trimester treated early, women in the first trimester receiving late treatment had an increased risk of ICU admission in all 3 trimesters (RR, 8.0; 95% CI, 3.7-17.1) and those in the second and third trimester had a 6-fold increased risk of an ICU admission.

Among pregnant women with symptom onset from April 14 to August 21, 2009, 30 women died. During this same period, 593 deaths associated with 2009 influenza A(H1N1) were reported to the CDC (M. Jhung, MD, medical epidemiologist, Influenza Division, CDC, oral communication, February 25, 2010); thus, pregnant women represented 5% of these deaths.

Based on reports to the CDC Pregnancy Flu line (pregnant women with confirmed influenza with symptom onset after August 21 and on or before December 31, 2009), an additional 165 women were admitted to an ICU (including 26 deaths). Thus, in total from April through December 2009, 280 pregnant women (including 56 deaths) were admitted to the ICU due to 2009 influenza A(H1N1) reported to the CDC (eTable, available at http://www.jama.com). Women with symptom onset in the third trimester accounted for a higher proportion of severe illness (49% of ICU admissions and 64% of deaths), but severe illness

occurred in all 3 trimesters and 7% of deaths had symptom onset in the first trimester. In the first 4 months of the pandemic, 77 women admitted to the ICU (67%) received mechanical ventilation compared with 91 in the latter 4 months of the pandemic (55%; *P*=.09).

COMMENT

This report, which summarizes data on 788 pregnant women with confirmed or probable 2009 influenza A(H1N1) illness reported to the CDC from 50 of 53 state and local health departments, represents the most complete national description of the experience of pregnant women in the United States during the H1N1 pandemic, from April to August 2009. In addition, this report includes the first data to become available from the CDC Pregnancy Flu Line, showing a total of 280 ICU admissions and 56 deaths among pregnant women in the first 8 months of the pandemic. Although several series of pregnant women with 2009 influenza A(H1N1) have been reported,[15,19–23] including a large case series from California[21] and 1 from New York City[24] included herein, a nationwide summary of infected pregnant women has not been published since early in the pandemic when a series of 34 infected pregnant women in the first month of the outbreak was reported.[15]

Pregnant women represent approximately 1% of the US population,[15] yet they accounted for 5% of US deaths from 2009 influenza A(H1N1) reported to the CDC. The data reported herein are consistent with previous studies[15,21 5,6,25] that demonstrate that pregnant women with influenza are at increased risk of serious illness and death. In addition, delayed treatment of antiviral therapy was associated with more severe illness and death as previously shown for both seasonal influenza and 2009 influenza A(H1N1), whereas early treatment initiation has been associated with reduced illness duration, symptom severity, mortality, and incidence of secondary complications, hospitalizations, and need for antibiotics.[21,26–31] Our analysis supports current public health recommendations for pregnant women that include vaccination with 2009 influenza A(H1N1) monovalent vaccine[32] and early treatment of women who present with possible 2009 influenza A(H1N1) with antiviral medications.[33]

Data from previous pandemics and seasonal influenza suggest that risk of influenza complications might be higher in the second and third trimester of pregnancy than in the first trimester.[10,11,13,14] Consistent with this, we observed a higher proportion of ICU admissions and deaths occurring in the second and especially third trimester; however, pregnant women in all 3 trimesters were at increased risk of influenza-associated complications, especially when early antiviral treatment was not instituted.

Among hospitalized women, treatment administered within 2 days and from 3 to 4 days was associated with less severe disease. These data suggest that some benefit might be achieved even if treatment is delayed as many as 4 days after symptom onset,[33] similar to data on hospitalized patients with seasonal influenza in which benefit is observed when treatment is initiated more than 48 hours after symptom onset.[30] The reasons for delayed treatment are unknown but could indicate reluctance of pregnant women or clinicians to use antiviral medication because of concern for risk to the fetus, despite available evidence suggesting that treatment benefit likely outweighs the potential risk.[34,35] In addition, although we did

not collect information on date of presentation to medical care, some women may have delayed seeking medical care. Other reasons for delayed treatment could include inappropriate reliance on influenza diagnostic testing, such as rapid influenza diagnostic tests that have been shown to have low sensitivity (10%-70%) for the 2009 influenza A(H1N1) influenza virus.[36–41] During the current outbreak, pregnant women with suspected influenza should be given empirical treatment as early as possible. Decisions regarding treatment should not be based on diagnostic testing, given issues with performance and timeliness of currently available tests.[42]

The proportion of women reported to have a condition (in addition to pregnancy) that would place them at higher risk for influenza-associated complications[43] increased from 55.3% among hospitalized patients to 78.3% among those who died. The most common underlying condition was asthma, seen in 23.0% of hospitalized patients, 25.6% of ICU admissions, and 43.5% of deaths. The prevalence of obesity in our cases was slightly higher than that reported among women of childbearing age.[44] Although limited information on obesity was obtained from health department reports, documentation of prepregnancy body mass index was unavailable, so the definitions of obesity during pregnancy are nonstandardized. Other studies have also suggested a higher than expected prevalence of obesity among hospitalized and severely ill patients with 2009 influenza A(H1N1),[5,6,45] although many obese patients had other underlying conditions that placed them at higher risk.

Among women in our series for whom data on pregnancy outcomes were available, the rate of preterm birth (30.2%) was higher than the rate of preterm births (13%) reported nationally for the year 2007,[46] consistent with data suggesting a high rate of preterm delivery during previous pandemics.[11,12,47] However, it should be noted that complete follow-up on all pregnancy outcomes, which would be needed to produce an unbiased estimate of preterm births, was not available. In addition, pregnant women in our series had a higher rate of underlying conditions, which may have predisposed them to preterm delivery.

These data support recommendations of the Advisory Committee on Immunization Practices, identifying pregnant women as 1 of 5 initial target groups for the 2009 influenza A(H1N1) monovalent vaccine.[32] Despite recommendations from the Advisory Committee on Immunization Practices and the American College of Obstetricians and Gynecologists[43,48] and from studies that show no evidence of increased maternal or fetal risk from immunization,[49] pregnant women appear to be reluctant to receive[50] and clinicians appear to be reluctant to offer[51] seasonal influenza vaccination. Preliminary data from a time of limited vaccine availability, based on a survey of only 150 women, suggest that the uptake of 2009 influenza A(H1N1) vaccine among pregnant women (38%; 95% CI, 24%-52%) may be higher than that observed in previous years for seasonal influenza vaccine.[52] To increase uptake further, pregnant women and their clinicians should be educated about the risks associated with influenza during pregnancy and made aware of the recommendations that vaccine can prevent illness from both seasonal influenza and 2009 influenza A(H1N1). Other strategies that might increase vaccination include instituting standing orders and reminder systems, and designating certain health care workers as vaccine champions.[53,54]

This study includes data on the largest number of pregnant women with 2009 influenza A(H1N1) influenza reported thus far; however, several limitations need to be considered. Our findings likely represent an underestimate of the total number of pregnant women with 2009 influenza A(H1N1) during this time period and an overestimate of the proportion of pregnant women with severe illness. It is likely that some reported cases of illness may not include relevant pregnancy status information, particularly among women in the first trimester who may be unaware of their pregnancy. Later in the study time period, confirmatory testing for 2009 influenza A(H1N1) influenza was limited to individuals with severe disease, and case-based reporting was limited to severe or hospitalized cases as the outbreak progressed and resources became limited. Therefore, the cases presented herein are likely an overrepresentation of severe cases. In addition, given that data were collected by public health authorities in the midst of a national public health emergency, the data requested were limited to an abbreviated data-collection instrument; thus, not all information of interest (eg, details of medical care provided, preexisting conditions, insurance coverage, socioeconomic status) was available for review. Although information on race and ethnicity was abstracted, it was not formally analyzed because we believe its distribution was reflective of the population of reporting states rather than a meaningful risk factor.

Another limitation is that data were often not available for all variables, especially for those not hospitalized; we noted that the level of missing data decreased as severity of illness increased. Missing information was highest for presence or absence of high-risk conditions and lowest for maternal age and hospital admission status. Missing data were also an issue for pregnancy outcomes, either because delivery had not yet occurred or because this information had not been reported to the health department. Finally, the numbers of cases available for some analyses, especially those related to treatment timing by trimester, were small and have sometimes resulted in unstable estimates.

In conclusion, based on data from the first 4 months of the H1N1 pandemic and corroborated by data through December of 2009, pregnant women are disproportionately represented among deaths due to 2009 H1N1. Among pregnant women with 2009 influenza A(H1N1) influenza reported to the CDC, early antiviral treatment appears to be associated with fewer admissions to an ICU and fewer deaths.

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Dr Siston had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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Table 1

Characteristics of Pregnant Women With 2009 Influenza A(H1N1) Illness Through August 21, 2009, United States[a]

Characteristics	No. (%) of Pregnant Women			
	Total (n = 788)	Hospitalized (n = 509)[b]	Intensive Care Unit Admission (n = 115)[c]	Maternal Deaths (n = 30)
Race/ethnicity				
White, non-Hispanic	167 (22.7)	89 (18.2)	31 (29.0)	13 (44.8)
Black, non-Hispanic	141 (19.1)	103 (21.0)	15 (14.0)	2 (6.9)
Hispanic	242 (32.8)	175 (35.7)	39 (36.4)	8 (27.6)
Asian/Pacific Islander	42 (5.7)	28 (5.7)	9 (8.4)	4 (13.8)
Alaskan Native/American Indian	9 (1.2)	7 (1.4)	0	0
Multiracial	4 (0.5)	2 (0.4)	0	0
Other/unknown	132 (17.9)	86 (17.6)	13 (12.1)	2 (6.9)
Missing	51	19	8	1
Maternal age, y				
<20	124 (16.0)	80 (15.9)	12 (10.4)	2 (6.7)
20-24	249 (32.2)	164 (32.5)	36 (31.3)	10 (33.3)
25-29	195 (25.2)	133 (26.4)	31 (27.0)	8 (26.7)
30-34	122 (15.8)	73 (14.5)	22 (19.1)	6 (20.0)
35-39	69 (8.9)	42 (8.3)	12 (10.4)	3 (10.0)
≥40	15 (1.9)	12 (2.4)	2 (1.7)	1 (3.3)
Unknown/missing	14	5	0	0
Age, median (range)	25 (14-43)	25 (15-43)	26 (17-43)	25 (18-43)
Trimester of pregnancy at symptom onset (wk)				
First trimester (0-13)	67 (11.3)	30 (7.6)	8 (8.2)	3 (10.0)
Second trimester (14-28)	250 (42.2)	151 (38.3)	38 (39.2)	9 (30.0)
Third trimester (≥29)	275 (46.5)	213 (54.1)	51 (52.6)	18 (60.0)
Unknown/missing	196	115	18	0
Month of symptom onset				
April (14 to 30 only)	28 (3.9)	10 (2.2)	2 (1.8)	1 (3.3)
May	182 (25.6)	103 (22.2)	22 (20.0)	9 (30.0)
June	296 (41.6)	182 (39.1)	39 (35.5)	9 (30.0)
July	149 (20.9)	126 (27.1)	35 (31.8)	8 (26.7)
August (1 to 21 only)	57 (8.0)	44 (9.5)	12 (10.9)	3 (10.0)
Unknown/missing	76	44	5	0
Underlying illness/condition				
Asthma	99 (22.9)	73 (23.0)	22 (25.6)	10 (43.5)
Obesity[d]	56 (13.0)	53 (16.7)	19 (22.1)	9 (39.1)

Characteristics	No. (%) of Pregnant Women			
	Total (n = 788)	Hospitalized (n = 509)[b]	Intensive Care Unit Admission (n = 115)[c]	Maternal Deaths (n = 30)
Pregestational diabetes	17 (3.9)	14 (4.4)	3 (3.5)	1 (4.3)
Anemia	15 (3.5)	15 (4.7)	4 (4.7)	0
Hypertension	13 (3.0)	9 (2.8)	3 (3.5)	1 (4.3)
Gestational diabetes	12 (2.8)	10 (3.1)	1 (1.2)	1 (4.3)
Cardiovascular disease (excluding hypertension)	10 (2.3)	10 (3.1)	6 (7.0)	3 (13.0)
Thyroid disease	8 (1.9)	5 (1.6)	2 (2.3)	2 (8.7)
Immune suppression (due to underlying disease or meds)	8 (1.9)	8 (2.5)	5 (5.8)	2 (8.7)
Neurological disease	7 (1.6)	7 (2.2)	4 (4.7)	2 (8.7)
Chronic lung disease (excluding asthma)	7 (1.6)	7 (2.2)	4 (4.7)	1 (4.3)
Autoimmune disease	3 (0.7)	3 (0.9)	3 (3.5)	2 (8.7)
Other	33 (7.6)	30 (9.4)	10 (11.6)	4 (17.4)
Any of the above underlying conditions	213 (49.3)	176 (55.3)	54 (62.8)	18 (78.3)
No underlying conditions	219 (50.7)	142 (44.7)	32 (37.2)	5 (21.7)
Unknown/missing	356	191	29	7
Antiviral medication prescribed				
Oseltamivir only	476 (81.0)	329 (82.5)	71 (73.2)	21 (70.0)
Zanamivir only	13 (2.2)	8 (2.0)	3 (3.1)	0
Oseltamivir and zanamivir	12 (2.0)	11 (2.8)	4 (4.1)	1 (3.3)
Oseltamivir and adamantine	4 (0.7)	3 (0.8)	2 (2.1)	1 (3.3)
Antiviral prescribed, but not specified	4 (0.7)	3 (0.8)	2 (2.1)	2 (6.7)
Refused treatment	5 (0.9)	0	0	0
No treatment	74 (12.6)	45 (11.3)	15 (15.5)	5 (16.7)
Unknown/missing	200	110	18	0
Antiviral treatment timing from symptom onset, d[e]				
≤2	219 (43.0)	148 (41.8)	13 (15.9)	1 (4.0)
3-4	84 (16.5)	66 (18.6)	15 (18.3)	4 (16.0)
>4	81 (15.9)	67 (18.9)	37 (45.1)	20 (80.0)
Antiviral treatment, but timing not known	125 (24.6)	73 (20.6)	17 (20.7)	0
Median (range)[f]	2 (−2 to 21)	2 (−2 to 21)	5 (−1 to 21)	6 (2 to 21)
Unknown/missing	200	110	18	0

[a] Percentages are based on women with complete information in the respective categories.

[b] Includes intensive care unit admission and maternal deaths.

[c] Includes maternal deaths.

[d] Data are based on reports to Centers for Disease Control and Prevention from state and local health departments; prepregnancy body mass index was not available.

[e] Does not include “no treatment.”

[f] Negative numbers represent prophylaxis administered before symptom onset.

Table 2

Clinical Outcomes Among Pregnant Women With Pandemic 2009 Influenza A(H1N1) Illness Through August 21, 2009, United States[a]

Outcome	No. (%) of Pregnant Women
All Pregnant Women (n = 788)	
Hospital admission	
Yes	509 (65.9)
No	263 (34.1)
Unknown/missing	16
Maternal death	
Yes	30 (4.3)
No	662 (95.7)
Unknown/missing	96
Preterm delivery[b]	
Yes (<37 wk gestation)	51 (30.2)
No (≥37 wk gestation)	118 (69.8)
Delivery type	
Spontaneous abortion	8 (1.4)
Therapeutic abortion	4 (0.7)
Vaginal delivery	79 (13.5)
Cesarean delivery	109 (18.6)
Delivered, type unknown or estimated delivery date on or before November 6, 2009	263 (45.0)
Not yet delivered or estimated delivery date after November 6, 2009	122 (20.9)
Unknown/missing	203
Among Hospitalized Pregnant Women (n = 509)	
Hospital length of stay, d	
Median (range)	3 (1–73)
Unknown/missing	122
Admission to intensive care unit	
Yes	115 (24.7)
No	350 (75.3)
Unknown/missing	44
Mechanical ventilation	
Yes	77 (18.8)
No	332 (81.2)
Unknown/missing	100

[a] Percentages are based on women with complete information in the respective categories.

[b] Among live births with known gestational age at delivery (n=169).

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Table 3

Comparison of Maternal Outcomes by Timing of Antiviral (Oseltamivir or Zanamivir) Treatment[a]

	No. (%) of Women							
	Hospital Admission[b]		ICU Admission Among Hospitalized Patients[c]		Mechanical Ventilation Among Hospitalized Patients[c]		Maternal Death[b]	
Treatment	**Yes (n = 509)**	**No (n = 263)**	**Yes (n = 115)**	**No (n = 350)**	**Yes (n = 77)**	**No (n = 332)**	**Yes (n = 30)**	**No (n = 662)**
Timing after symptom onset, d								
≤2	148 (67.6)	71 (32.4)	13 (9.4)	125 (90.6)	6 (4.6)	125 (95.4)	1 (0.5)	197 (99.5)
3-4	66 (78.6)	18 (21.4)	15 (22.7)	51 (77.3)	10 (17.2)	48 (82.8)	4 (5.0)	76 (95.0)
>4	67 (82.7)	14 (17.3)	37 (56.9)	28 (43.1)	32 (56.1)	25 (43.9)	20 (27.0)	54 (73.0)
No treatment	45 (57.7)	33 (42.3)	15 (34.9)	28 (65.1)	9 (21.4)	33 (78.6)	5 (6.9)	67 (93.1)
Treated, timing unknown[d]	73	52	17	47	10	41	0	115
Unknown treatment status[d]	110	75	18	71	10	60	0	153
Treatment Timing Comparisons								
3-4 vs ≤2 d								
Relative risk (95% CI)	1.2 (1.0-1.3)		2.4 (1.2-4.8)		3.8 (1.4-9.9)		9.9 (1.1-87.2)	
P Value	.06		.01		.008[e]		.03[e]	
>4 vs ≤2 d								
Relative risk (95% CI)	1.2 (1.1-1.4)		6.0 (3.5-10.6)		12.3 (5.4-27.7)		53.5 (7.3-391.7)	
P Value	.01		.001		.001		.001	
None vs ≤2 d								
Relative risk (95% CI)	0.8 (0.7-1.0)		3.7 (1.9-7.2)		4.7 (1.8-12.4)		13.8 (1.6-115.7)	
P Value	.12		.001		.002[e]		.006[e]	

Abbreviation: CI, confidence interval.

[a]The referent is early treatment within 2 days of symptom onset. Percentages are based on women with complete information in the respective categories.

[b] Among 788 cases, 16 had missing or unknown data for hospital admission status and 96 had missing or unknown data for maternal death.

[c] Among 509 hospitalized cases, 44 had missing or unknown data for ICU admission status and 100 had missing or unknown data for ventilator use.

[d] Pregnant women who were treated, but timing was unknown and those with unknown treatment status were excluded from relative risk computations.

[e] Fisher exact test.

Table 4

Impact of Trimester and Timing of Antiviral Treatment on Admission to an Intensive Care Unit Among Hospitalized Patients

Trimester and Treatment Timing[a]	No. (%) of Women		Relative Risk (95% CI)	*P* Value
	Intensive Care Admission (n = 61)	No Intensive Care Admission (n = 192)		
Any trimester ≤2 d after symptom onset	13 (9.4)	125 (90.6)	1.0 [Referent]	
3-4 d after symptom onset, trimester				
First	1 (16.7)	5 (83.3)	1.8 (0.3-11.4)	.47[b]
Second	3 (14.3)	18 (85.7)	1.5 (0.5-4.9)	.45[b]
Third	9 (33.3)	18 (66.7)	3.5 (1.7-7.4)	.003[b]
>4 d after symptom onset, trimester				
First	3 (75.0)	1 (25.0)	8.0 (3.7-17.1)	.004[b]
Second	14 (58.3)	10 (41.7)	6.2 (3.3-11.5)	<.001[b]
Third	18 (54.5)	15 (45.5)	5.8 (3.2-10.6)	<.001

Abbreviation: CI, confidence interval.

[a] Sixty-four pregnant women who were treated, but timing was unknown, and 89 with unknown treatment status were excluded from relative risk computations. Pregnant women receiving intermediate or late treatment with unknown pregnancy trimester (n=73) were also excluded.

[b] Fisher exact test.