Influenza hospitalizations in New York State 2007-2013: impact of vaccine and antiviral treatment effectiveness in reducing severity of illness

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Influenza Hospitalizations in New York State 2007-2013: Impact of vaccine and antiviral treatment effectiveness in reducing severity of illness

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Abstract

Background: Underlying medical conditions are known risk factors for increased severity of infectious diseases, including influenza. Although most studies on disease severity, underlying medical conditions, and prevention/treatment effectiveness occurred during the pandemic 2009-2010 season, data is also available for seasons when influenza virus B and influenza virus A subtypes pH1N1, seasonal H1N1, and H3N2 were circulating.

Methods: Population-based, laboratory-confirmed influenza hospitalization surveillance data from the 2007-2008 season to the 2012-2013 season were used to examine the association between underlying medical conditions and severe influenza outcomes. Multivariable analysis explored virus type/subtype, prompt antiviral treatment, medical conditions, and age as predictors for severity (hospital stay of five or more days, intensive care unit admission, and death).

Results: Immunosuppressive conditions (OR: 2.64, 95% CI: 1.24, 5.61) were significantly associated with death and antiviral treatment received within two days of admission (OR: 0.3, 95% CI: 0.13, 0.69) was inversely associated with death. Cardiovascular disease (OR: 1.7, 95% CI: 1.22, 2.37), chronic lung disease (OR: 1.74, 95% CI: 1.25, 2.42), neuromuscular abnormalities (OR: 2.19, 95% CI: 1.52, 3.14) were significant risk factors for intensive care unit admission, while antiviral treatment within two days of admission was a significant protective factor (OR: 0.53, 95% CI: 0.32, 0.89) for intensive care unit admission. Similarly, cardiovascular disease (OR: 1.31, 95% CI: 1.01, 1.71), chronic metabolic disease (OR: 1.29, 95% CI: 1.00, 1.67), neuromuscular abnormality (OR: 1.7, 95% CI: 1.23, 2.33), immunosuppressive conditions (OR: 1.5, 95% CI: 1.04, 21.7) were significant risk factors for a hospital stay of five or more days, and antiviral treatment within two days of admission (OR: 0.11, 95% CI: 0.06, 0.22) was a significant protective factor for the same condition.

Conclusion: Underlying medical conditions associated with an increased risk in influenza severity include immunosuppressive conditions, cardiovascular disease, neuromuscular abnormalities, chronic lung disease, and chronic metabolic disease. Antiviral treatment within two days of arrival was a protective factor against longer hospital stay, intensive care, and death.
1: Background

1.1 Historical context

Influenza epidemics and pandemics have been affecting humans throughout history (Beveridge, 1991). According to the World Health Organization (WHO), influenza infections occur across the globe every year, seasonally and sporadically. It has been estimated that seasonal influenza affects a range of 5%-20% of the United States’ population, 25-50 million cases per season (Fiore, 2010). The WHO estimates that worldwide there are one billion infections, 3-5 million cases of severe disease, and 300,000-500,000 deaths annually (WHO, 2009).

Over the past three centuries there have been at least ten influenza pandemics (Beveridge, 1991). The most notable was the 1918 pandemic, also known as the Spanish flu, which is estimated to have resulted in the deaths of 20 to 50 million people worldwide with a case fatality rate of 2% (Johnson, 2002; Taubenberger, 2006). The pandemic in 1957, known as the Asian flu, resulted in the deaths of 1 to 1.5 million people, and another pandemic in 1968, known as the Hong Kong flu, resulted in the deaths of 0.75 to 1 million people (WHO, 2012). Most recently, the 2009 influenza pandemic, also known as the swine flu, disproportionately affected young adults (aged <65), and resulted in 105,700 to 395,600 deaths worldwide (Dawood, 2012).

1.2 Influenza viruses and antigenic change

Influenza has been described as "an invariable disease caused by a variable virus" (Potter, 2001). Although millions of people are affected by influenza every season, the virus goes through rapid mutations which prevent immunity in following seasons as the
circulating virus changes (Oxford, 1979). According to the Centers for Disease Control and Prevention (CDC), there are two influenza virus types, A and B, which infect humans. Influenza A viruses are classified into subtypes based on the hemagglutinin (H) and neuraminidase (N) proteins found on the surface of the virus. Influenza A subtypes most commonly associated with human illness are H1N1, H1N2, H2N2, and H3N2 (McHardy, 2009; Morens, 2009). The influenza B viruses are not classified by strains and are thought to cause less severe infections than A viruses, although they have also been shown to result in significant hospitalizations and severe infection (CDC, 2011; Paul Glezen, 2013).

According to a virology study by Stray et al, circulating influenza B virus and influenza A virus subtypes change over time due to antigenic drift and antigenic shift. Antigenic drift occurs as the virus goes through small mutations over time, sometimes to the antibody binding site on the virus, making it unrecognizable to the immune system each year (Stray, 2012). This phenomenon is the reason it is recommended by the CDC and WHO that individuals are vaccinated annually as the immune system does not recognize the new virus. Antigenic shift is a major change in the influenza A virus type which results in a new hemagglutinin and/or neuraminidase protein, creating a new subtype (Shindo, 2012). Typically, antigenic shift is caused by the combination of two influenza strains to make a new subtype which could have the potential to infect humans. Since the new subtype is substantially different from previous circulating subtypes, most people will not have immunity to it, typically resulting in an epidemic or pandemic (Potter, 2001). The 2009 pandemic was caused by an H1N1 virus that is believed to be a reassortment of the human H1N1 virus when it was combined with a Eurasian pig
influenza virus (Trifanov, 2009). During the 2009 pandemic, adults over the age of 64 were not as affected as they would be in typical seasons, instead, over 80% of the mortality resulting from pH1N1 occurred in those under 65 (Dawood, 2012). As a result of the disproportionate effect on young and middle aged adults, surveillance and testing was increased during this season and it has been the focus of many recent studies. There have also been other cases of influenza transmission across species due to antigenic shift. Avian influenza, an H5N1 strain, has been circulating in Asia since 2003 and reached Europe, the Middle East, and Africa a few years later (Nguyen-Van-Tam, 2006).

1.3 Influenza transmission

A typical case of influenza human-to-human transmission usually occurs by direct contact with an infected individual, contact with fomites, or inhalation of virus-laden aerosols (Tellier, 2006). Virus is often contained in cough or sneeze droplets of an infected person. Droplets are propelled during coughing or sneezing from three to six feet and, depending on the size, can drop to the ground within a few meters or remain suspended for an extended period of time (Tellier, 2006). Although this is the main source of transmission in humans, direct contact with an infected individual can spread infection if the infected individual has recently touched their nose or conjunctiva (Lowen, 2009; Brankston, 2007). Less typically, transmission through contact with fomites can also occur when an infected individual has touched their nose or conjunctiva and then touched an object which could be touched by another person (Brankston, 2007). A study in 2009 by Lowen et al, showed that this form of transmission is variable, dependent on environmental characteristics such as temperature and humidity (Lowen, 2009).
The incubation period for influenza is two days with a range of one to four days post-exposure (Kuiken, 2008). Peak viral shedding usually occurs from one day prior to symptom onset to three days following onset of symptoms in adults and may be longer in children (Lau, 2010). As maximum virus shedding may occur prior to peak of symptoms, precautionary measures are very important in reducing transmission of influenza. Transmission can be reduced by an infected individual covering their nose and mouth when coughing or sneezing and by washing hands often with soap and water or alcohol based hand cleaners (CDC, 2011).

1.4 Influenza symptoms and complications

Common symptoms of influenza include fever, cough, sore throat, runny or stuffy nose, aches, and fatigue in adults but some children may also experience nausea, vomiting, and diarrhea (Nicholson, 1992). Infants present with similar symptoms to adults and children but may also appear with suspected sepsis (Rojo, 2006). A hallmark of influenza infection is a sudden onset of symptoms. Severity of influenza infection can range from asymptomatic or mildly symptomatic to having secondary infections, exacerbation of underlying medical conditions, and death (CDC, 2011).

According to the CDC, infection with influenza is usually self-limiting and most of those affected will recover from symptoms within two weeks while others may develop a more severe infection and require hospitalization with complications, such as pneumonia, myocarditis, and encephalitis, which could be life threatening.
1.5 Influenza-associated hospitalizations

In the United States, there is in excess of 200,000 hospitalizations and between 3,000 and 49,000 deaths each year attributed to influenza (CDC, 2012). Results from one study using data from the 2003-2004 influenza season, estimated that the annual influenza season results in approximately 600,000 years of life lost, 3 million hospitalized days, and 30 million outpatient visits, with a total cost of $10 billion a year in the United States (Molinari, 2007). When including lost earnings, the total economic burden of an annual influenza epidemic is estimated to cost $87.1 billion (Molinari, 2007).

Incidence rates of influenza in the population fluctuate considerably by season, which in turn, impacts the rates of hospitalization. Circulating subtype strains, virulence factors, populations at risk for certain strains, climate, how well the vaccine matches the circulating strains, vaccination rates, and other factors all impact the seasonal rates of infection (Tscherne, 2011; Kostova, 2013; van Noort, 2012). For example, during the 2009-2010 season when the pH1N1 subtype was circulating, those aged less than 65 were disproportionately affected by influenza, causing higher hospitalization rates among these ages (CDC, 2009). This has been shown to be caused by increased vulnerability in younger people to this virus strain (CDC, 2012).

In a study on laboratory confirmed hospitalizations during the 2009 pandemic, hospitalization rates by age were compared to previous seasons when different influenza strains were circulating. During the pandemic, rates of hospitalization due to laboratory-confirmed influenza per 100,000 among those aged 5–17 years and 18–49 years increased five times (6 to 31) and six times (4 to 27) respectively, while the incidence rates for
those age 75 and older decreased compared with incidence rates from previous influenza seasons (Cox, 2012). Although the ages affected during the 2009 pandemic influenza season was not characteristic of a typical season, it did share many of the same risk factors.

1.6 Risk factors for severe illness

Despite the highest rates of infection occurring in school-aged children, the highest rates of influenza hospitalizations occur among those over the age of 64, among infants and children under the age of five, and among people of any age with underlying medical conditions (Dawood, 2011; Dao, 2010). Underlying medical conditions have been shown to put people at higher risk of severe infection for most infectious diseases, influenza included (Dhainaut, 2005). Asthma, chronic lung disease, chronic cardiovascular disease, chronic metabolic disease, renal disease, neuromuscular disorders, immunosuppressive conditions, pregnancy, and obesity are all medical conditions which are considered risk factors for severe illness with an influenza infection (Chong, 2013; Mertz, 2013). Rates of hospitalizations are higher among those with underlying medical conditions than those who are otherwise healthy among people in the same age category (Mertz, 2013). In one meta-analysis, it was found that for having any medical condition the estimated odds ratio of death was 2.77 with a 95% confidence interval of 1.94 to 4.05 with the pandemic 2009 H1N1 influenza and 2.04 with a confidence interval of 1.74 to 2.39 for seasonal influenza (Mertz, 2013).

Asthma is a chronic lung disease that affects more than 25 million people in the United States (CDC, 2012) and is the most reported underlying medical condition among
children hospitalized with an influenza infection (Neuzil, 2000). Although having asthma has not been associated with increasing an individual’s risk of contracting influenza, it has been shown to increase the risk of severe illness and death (O’Riordan, 2010).

Results are equivocal on whether or not it increases hospitalization rates (O’Riordan, 2010; Neuzil, 2000). In a study comparing hospitalizations due to influenza from 2003-2008 with the 2009 pandemic season, it was demonstrated that children with asthma were at a high risk for complications and death (Dawood, 2011). Study results showed that 16% of the children with asthma hospitalized with an influenza infection from 2003-2009 required intensive care and 22% of those during the 2009-2010 season required intensive care (Dawood, 2011). In another study of influenza-hospitalized patients, specifically among children under the age of 18, patients with asthma had significantly higher odds of death than patients without asthma (Chong, 201). It has also been demonstrated that children with asthma are at a higher risk of an occurrence of an asthma attack while infected with influenza compared to those without an influenza infection. It has been estimated that 24% to 85% of all asthma attacks in children are associated with viral respiratory tract infections, such as influenza (Rothbath, 1995; Johnston; 1996).

Cardiovascular disease is the most reported underlying medical condition among adults hospitalized with an influenza infection (Mertz, 2013); 37% of influenza-hospitalized adults reported having cardiovascular disease in the 2010-2011 season (Chaves, 2013). Cardiovascular disease includes a range of conditions including coronary artery disease, heart failure, hypertensive heart disease, pulmonary heart disease, heart valve disorders, arrhythmias, and congenital heart defects (CDC, 2011). Those with cardiovascular disease are at a higher risk of hospitalization, pneumonia infection, and
death when infected with influenza compared to those without cardiovascular disease (Warren-Gash, 2009; Mertz, 2013). Those with cardiovascular disease had 2.92 (95% CI 1.76-1.86) times higher odds of death than those without disease when infected with pandemic 2009 H1N1 influenza and 1.97 (95% CI 1.06-3.67) times increased odds of death when infected with seasonal influenza (Mertz, 2013). Patients with cardiovascular diseases are also more likely to have a cardiac event while hospitalized with influenza and die as a result (Warren-Gash, 2009).

Chronic metabolic disorders are any conditions that interfere with normal metabolism, the chemical processes of breaking down or synthesizing substances that are necessary for life or to yield energy. This definition includes diabetes, mitochondrial disorders and thyroid dysfunction. It has been demonstrated that people with diabetes are three times more likely to die as a result of an influenza infection (Mertz, 2013). In a study of influenza-hospitalized patients during the 2009-2010, having a chronic metabolic disease increased the odds of severe infection, defined as either intensive care unit (ICU) admission or death, by 5.23 times in children (Chaves, 2013).

Chronic lung diseases, other than asthma, include emphysema, chronic obstructive pulmonary disease (COPD), cystic fibrosis, and restrictive lung diseases. Chronic lung disease symptoms have been shown to worsen in people with an influenza infection (Rothbath, 1995; Johnston; 1996; Mertz, 2013). Among those infected with influenza, people with chronic lung disease have been shown to be more likely to develop a severe respiratory illness, be admitted to intensive care, and placed on mechanical ventilation than those without a chronic lung condition (Rothbath, 1995; Johnston; 1996).
Among those hospitalized with influenza, patients having any chronic lung disease had 1.71 (95% CI 1.17-2.51) times higher odds of death than those hospitalized with influenza without any lung disease (Mertz, 2013). When ICU admission and death were looked at as a composite outcome for disease severity, patients with chronic lung disease still had significantly higher odds for severe illness (OR 1.46 (95% CI 1.12-1.89)) than patients without chronic lung disease (Chaves, 2013).

Immunosuppressive conditions are disorders which inhibit the immune system from functioning properly, which could occur in those who have received a solid organ transplant, those infected with human immunodeficiency virus (HIV), or those who take medications which decrease immune system efficacy (CDC, 2011). An immunosuppressive condition is an independent risk factor for death in patients hospitalized with an influenza infection (Li, 2009). In a study among hospitalized immunocompromised patients with an influenza infection, more than 50% developed pneumonia (Schnell, 2010) and among pediatric organ transplant recipients, infection with influenza has been a significant cause of death (Apalsh, 1995). Among influenza patients with an HIV infection, as with most other infections, the severity of disease and duration of symptoms is increased compared to influenza patients without HIV (Klein, 2007).

Neurological disorders are disorders that affect the nervous system, and include multiple sclerosis, myasthenia gravis, cerebral palsy, dementia, and developmental delays among many others. Those with a neuromuscular disorder had more than 2.5 times higher odds of death with the pH1N1 influenza and 3.21 times higher odds of death with
the seasonal influenza (Mertz, 2013). In a study of children hospitalized with influenza, those with a neurological disorder had significantly higher odds of being admitted to an ICU (Bagdure, 2010). Another study of both children and adults hospitalized with influenza showed a 4.84 (95% CI: 2.02–11.58) times higher odds among children and 1.68 (95% CI: 1.11–2.52) times higher odds among adults for severe outcomes in those with neuromuscular disorders (Chaves, 2013).

Pregnancy is considered an underlying medical condition for influenza-associated hospitalizations. Pregnancy increases the risk for influenza-related severe illness (Rasmussen, 2012; Jamieson, 2009). Data from the pandemic in 2009 indicated that pregnant women were four times more likely to be hospitalized (Jamieson, 2009). There is evidence to suggest that women are at a greater risk of influenza complications and death within the four weeks following delivery (Ailes, 2013). Infants delivered while mothers were ill with influenza were at an increased risk of severe outcomes including low birth weight and preterm birth (Rasmussen, 2012).

Obesity is defined as having a body mass index (BMI) of 30 or above for adults or being above the 95th BMI percentile in children 2-19 years of age. Obesity has been associated with many comorbidities including coronary heart disease, type 2 diabetes, certain cancers, hypertension, dyslipidemia, a stroke, liver and gallbladder disease, respiratory problems, osteoarthritis, and gynecological problems. However, even those obese without any other conditions are at a higher risk of morbidity or mortality (Ward, 2011). Early in the 2009 pandemic, a hospital study found approximately 90% of patients requiring intensive care with pH1N1, were obese (CDC, 2009). In adults, obesity was
independently associated with an increased risk of requiring mechanical ventilation (Ward, 2011) Those identified as obese were almost two times as likely to have lower pulmonary disease manifestations than those who were not obese, almost three times as likely to be admitted to a hospital, and were more than three times as likely to require a hospital stay of five or more days with an influenza infection (Morgan, 2010). Among children hospitalized with laboratory confirmed influenza, obesity was shown to significantly increase the odds of complications including secondary infections, ICU admission, requiring mechanical ventilation, and death (Chen, 2012; Ren, 2013).

1.7 Influenza detection

In the past, infections were identified based solely on symptomology and epidemics were identified by an increase in hospitalizations of patients with bronchopneumonia or Staphylococcus aureus infections as well as an increase of deaths in the elderly and those with chronic disease (Potter, 2001). When the influenza virus was first isolated in humans by Patrick Laidlaw in 1932 (Smith, 1933), infections could be confirmed with a laboratory diagnosis. Many physicians still rely on patients’ symptoms to diagnose and treat influenza, especially when the virus is known to be circulating (Call, 2005). However, this method is not as effective at discerning an influenza infection outside of peak periods. It also leaves a gap in data which could be used to estimate prevalence of infection as well as information on circulating virus strains. Laboratory testing is becoming more commonplace in recent years (Call, 2005). The number and reliability of available influenza diagnostic tests has increased greatly and during the
2009 influenza pandemic, the WHO recommended laboratory testing for all influenza-like-illnesses (WHO, 2009) leading to an increase in laboratory testing and confirmation.

There are currently several different types of laboratory tests for the influenza virus available and the market is ever expanding. Each of these tests has their own merits and limitations (Mehlmann, 2007) and can be used for different purposes depending on the need. For the most accurate results, the Infectious Disease Society of America (IDSA) recommends the following test methods from high to low in order of accuracy: reverse-transcriptase polymer chain reaction (RT-PCR), immunofluorescence, or commercial rapid influenza testing (Harper, 2009).

The viral culture is considered the “gold standard” for influenza detection (Uyeki, 2003), with the highest sensitivity and specificity of all influenza diagnostics widely available (Ginocchio, 2009; Mehlmann, 2007). It can detect influenza virus types A and B as well as differentiate between the influenza A virus subtypes. Unfortunately, the results from a viral culture can take from three to ten days to be obtained, too long a period to make it useful from a clinical management perspective.

A recent study has shown RT-PCR to be more sensitive and specific than viral culture (de Vries, 2012) and test results only take between one to six hours, making it more practical. However, it is still not widely available, although there is an increase in the number of laboratories using RT-PCR to diagnose influenza.

Rapid influenza diagnostic tests (RIDTs), or rapid cell cultures, for influenza diagnostic testing is the most commonly used diagnostic testing method mainly because it
is widely available, easy to use, can be used at point-of-care, and results are received in 10-30 minutes. The rapid tests, however, have low sensitivities (50%-70%) and high specificities (90%-95%). The positive predictive value is dependent on prevalence of influenza, resulting in more false positives using RIDTs when prevalence of influenza is low (Grijalva, 2007).

Immunofluorescence direct (DFA) or indirect (IFA) antibody staining can also be used to detect influenza infections, although they have slightly lower sensitivities and specificities than viral culture (Harper, 2009). Test results can be returned in one to four hours, faster than a viral culture and more widely available than RT-PCR (Harper, 2009).

1.8 Influenza treatment

While influenza detection is important for surveillance and research purposes, it is not a requirement for prescribing treatment. It is currently recommended by CDC to prescribe antiviral treatment as soon as possible (within 2 days of symptom onset) for patients with confirmed or suspected influenza who have severe, complicated, or progressive illness or who require hospitalization. It is also recommended as soon as possible for outpatients with confirmed or suspected influenza that are at a higher risk for influenza complications on the basis of age or underlying medical conditions. It may be considered on the basis of clinical judgment for outpatients with confirmed or suspected influenza who do not have any known risk factors for severe illness as well (CDC, 2011).

Although there are four licensed influenza antiviral agents, oseltamivir and zanamivir are currently the only recommended treatments. Due to high levels of antiviral
resistance to circulating influenza virus type A strains (pH1N1 and H3N2), the two other antiviral drugs (amantadine and rimantadine) are not currently recommended. This could change in the future, if the strains evolve and are no longer resistant to these antiviral treatments. There have also been sporadic occurrences of antiviral resistance to oseltamivir with limited public health impact (CDC, 2011). For infants less than one year of age, only oseltamivir is recommended for treatment or chemoprophylaxis (CDC, 2011).

Antiviral medications work to stop or slow down replication of the virus within the body. It has been demonstrated in randomized, controlled trials among those with mild illness, that zanamivir or oseltamivir treatment within two days of symptom onset reduced the duration of illness by one day when compared to placebo treatment (Hayden, 1999; Hedrick, 2000; Lalezari, 2001). Children who received antiviral therapy within 24 hours of symptom onset had a decrease of duration of illness by three days (Lalezari, 2001). An observational study of hospitalized children and adults showed a reduction in severe clinical outcomes, including pneumonia and death, when treated with oseltamivir versus a placebo (McGeer, 2007). Another study of influenza-hospitalized adults showed that antiviral treatment within two days significantly reduced the odds of either being admitted to an ICU or death (OR 0.47 (95% CI 0.33-0.68)) (Chaves, 2013).

Antiviral treatments are also recommended for both post- and pre-exposure prophylaxis purposes and have been shown to prevent influenza infection in 72%-82% of exposures to the virus with zanamivir and 68%-89% of exposures to the virus with oseltamivir (Hayden, 1999, 2000; Monto, 1999).
1.9 Influenza vaccination

While chemoprophylaxis with influenza antiviral agents appears to be an effective method of preventing illness, the most effective method to prevent influenza infection and influenza-related complications is still vaccination (CDC, 2011). In the 2009-2010 season, the CDC expanded its recommendation for annual vaccination to all individuals aged six months or older, regardless of health status or underlying medical conditions (CDC, 2009, 2011). Before the 2009-2010 season, the CDC recommended only persons aged over 50 years, children aged 6 months–17 years, pregnant women, health-care personnel (HCP), and those 18–49 years with underlying medical conditions for annual vaccination (CDC, 2009).

There are many options for influenza vaccines on the market, some targeting particular populations. Although some contraindications against use of certain vaccines in specific populations (i.e. those with egg allergies, history of reaction to vaccine), there is a vaccine available for virtually all people six months of age and older. These include the standard dose trivalent vaccine, standard dose trivalent vaccine containing virus grown in cell culture, egg free standard dose trivalent vaccine, high dose trivalent vaccine, intradermal trivalent vaccine, quadrivalent vaccine, and quadrivalent influenza vaccine given as a nasal spray. High dose immunizations are recommended for older adults ≥65 because they have been shown in clinical trials to mount a stronger immune response than when given the standard dose vaccine.

The trivalent vaccines include three strains of influenza, one influenza B and two influenza A virus strains. The quadrivalent vaccines contain two B and two A virus
strains. The strains used in the vaccines are chosen during the WHO Vaccine Composition Meeting based on what is circulating around the world. The decision is made in February of the year prior to the season they will be used in so that there will be enough time for manufacturers to prepare vaccine.

Vaccine production can take six to nine months. Standard influenza vaccines are made using the recommended virus strains injected into chicken eggs to grow before being harvested for vaccines (CDC, 2012). Vaccines grown in cell culture are produced much faster. The first step is cell propagation of the Madin-Darby Canine Kidney (MDCK) cell line, then virus propagation after the virus strains are introduced to the cells. The virus is then removed from the cells using a centrifuge, inactivated, and antigens from each virus strain are combined (Novartis, 2012). To produce egg-free vaccines, only the hemagglutinin protein of the influenza virus is used, copied in cells and packaged into the vaccine (CDC, 2012).

Vaccination rates vary by population and year, often due to perceived threat of influenza infection. For example, during the 2011-2012 season those aged six months to 17 years had a 56.7% vaccination rate according to the National Health Information Survey (NHIS) (Lu, 2013). That same year adults aged 18 years and older had a vaccination rate of 38.3% (Lu, 2013). Children aged 6 months to 23 months had a 44.3% vaccination rate (CDC, 2013). These rates are well below the Healthy People 2020 Goal of 70% for children and adults 6 months and older. The goal for healthcare workers is a 90% vaccination rate but it was only 62.4% in the 2011-2012 season according to NHIS (Lu, 2013).
Efficacy for influenza vaccines vary by year due to difference in circulating strains from the strains used in the vaccine for that season. Influenza illnesses averted by vaccination ranged from a low of approximately 1.1 million (95% CI 0.6–1.7 million) during the 2006–2007 season to a high of 5 million (CI 2.9–8.6 million) during the 2010–2011 season (Kostova, 2013).

The influenza vaccine has been shown to not only reduce incidence of infection with influenza but also reduce the incidence of influenza-associated hospitalizations and decrease disease severity in most populations. A study of the 2011–2012 season showed that the vaccine effectiveness in preventing influenza associated hospitalizations was 71.4% (95% CI 17.1%-94.9%) for all adults and 76.8% (95% CI 24.0%-97.9%) for adults aged 50 and older (Kostova, 2013). Vaccinating is also associated with fewer days of illness among all age groups (Kostova, 2013). In a study of healthy adults 18–49 years old, vaccinated recipients had 26% fewer febrile upper-respiratory illness episodes, 27% fewer lost days of work, 18-37% fewer days of health care provider visits, and a reduction of 40-45% of days of antibiotic use compared to non-vaccinated individuals. One study estimated that influenza hospitalizations averted by vaccination ranged from a low of 7,700 (CI 3,700 to 14,100) in 2009–2010 to a high of 40,400 (CI 20,800 to 73,000) in 2010–2011 (Kostova, 2013).

1.10 Surveillance

During influenza season, the CDC monitors influenza and influenza-like-illness across the United States. Data from this surveillance is used to determine prevalence of
infection and assess the possibility of an epidemic. This data is released in weekly reports throughout the season.

Systems that collect information on influenza in the United States include the Influenza Like Illness Network (ILINET), Hospital Acquired Reporting (HAI), World Health Organization (WHO) and National Respiratory & Enteric Virus Surveillance System (NREVSS), and the Influenza Hospitalization Surveillance Network (FluSurv-NET) which is run by the Emerging Infections Program (EIP).

2: Specific Aims

Data on the impact of underlying medical conditions, antiviral treatment within two days of hospital admission, and seasonal vaccination on death, ICU admission, and a hospital stay of five or more days separately was limited, as found in the literature review. Studies differed on the definition of a severe illness. Two studies defined severe illness as a composite outcome of death and ICU admission (Chaves, 2013; Chong, 2013), two studies defined severe illness as death (Vivek, 2011; Chen, 2012), one study defined severe illness as a composite of fever lasting over three days, elevated cardiac enzymes, altered mental status, and aggravation of any other medical conditions (Ren, 2013), and another study defined severe illness as ICU admission (Bagdure, 2010).

Studies also differed on the underlying medical conditions assessed, adjustment for early antiviral treatment, and availability of varying influenza types and subtypes included. Two of the studies looked only at children under the age of 18 (Chong, 2013;
Bagdure, 2010), two combined factors of disease severity (Chaves, 2013; Ren, 2013), and two did not separate out underlying medical conditions to evaluate the effects individually (Ren, 2010; Chen, 2012).

The purpose of this study will be to assess each underlying medical condition individually for each of the three outcomes indicating severe infection (death, ICU admission, and a hospital stay of five or more days) as well as look at the general population from which the hospitalized patients came.

The specific aims of this study are to:

1. Describe the pattern of influenza hospitalizations in New York State.

2. Evaluate whether associations exist between severe influenza infection and underlying medical conditions after adjusting for vaccination and prompt antiviral treatment.

3. Evaluate whether associations exist between vaccine and early antiviral treatment effectiveness adjusting for the presence of underlying medical conditions.
3: Study Background & Methods

3.1 Study Background

The Emerging Infections Program (EIP) was established by the CDC in 1994 and the grant funds ten state health departments, (California, Colorado, Connecticut, Georgia, Maryland, Minnesota, New Mexico, New York, Oregon, and Tennessee) and their academic partners. The entire catchment area includes over 44 million people and is considered representative of the United States based on demographic characteristics.

Core activities conducted by the EIP include several active enhanced population-based surveillance systems for certain reportable diseases and conditions. Three core areas for population-based surveillance are:

1. Active Bacterial Core surveillance (ABCs), which is an active enhanced population based laboratory surveillance for 5 invasive bacterial disease;

2. Foodborne Diseases Active Surveillance Network (FoodNet), which is an active population based surveillance designed to monitor trends for specific foodborne disease incidence and;

3. Influenza Surveillance Network (FluSurv-NET), an enhanced population-based surveillance for laboratory confirmed influenza-associated hospitalizations.

FluSurv-NET involves collaborations between the CDC, state health departments, and universities. This network has been conducting population-based active surveillance for the influenza-associated hospitalizations in the ten EIP states beginning in the 2003-
2004 season in children under the age of 18. The EIP starting collecting information on adult hospitalizations in the 2005-2006 season. In the 2009-2010 season, the network was expanded to include five additional states.

Today this network conducts surveillance in 81 selected counties in California, Colorado, Connecticut, Georgia, Idaho, Maryland, Michigan, Minnesota, New Mexico, New York, Oklahoma, Ohio, Oregon, Rhode Island, Tennessee, and Utah.

FluSurv-NET in New York State covers counties in two areas of the state, the western region, which includes seven counties in the Rochester area, and the Capital District, which includes eight counties around Albany. Residents within this catchment area who are hospitalized with a laboratory confirmed influenza infection are identified by surveillance officers through routine department of health using the Electronic Clinical Laboratory Reporting System (ECLRS) and constant communication with the hospitals’ Infection Preventionists (IPs). Hospitals can send samples to be tested to Wadsworth Center, the NYS laboratory, which have been instrumental in testing and subtyping as part of this surveillance activity. It is recommended that hospitals with suspected cases of influenza in patients who tested negative with a rapid influenza test to send the sample to Wadsworth for a more specific test.

Information on demographic characteristics, medical history, influenza vaccination status, clinical course during hospitalization, and treatment with antiviral medications are then collected through review of medical charts using a standardized case report form. Vaccination status, if not included in the hospital chart, is obtained from the New York State Immunization Information System (NYSIIS) for children, by calling the
patient's primary medical care provider, or by directly contacting the patient. The standard case report form is shown in Appendix 1.

3.2 Case Definition

A case was defined as any resident of a NYS catchment county who was hospitalized with laboratory confirmed influenza from October 1st to April 30th during the 2007-2008, 2008-2009, 2010-2011, 2011-2012, and 2012-2013 seasons. During 2009-2010 season, the season was extended from April 15 2009 to April 30\textsuperscript{th} 2010. The case must have tested positive for influenza \(\leq 14\) days before or \(\leq 3\) days after hospital admission. Individuals who tested positive for influenza \(>3\) days post-hospitalization were not included as they were considered hospital acquired infections. For this analysis, pregnant women were also excluded because their health outcomes are generally different from individuals with other underlying medical conditions. Obesity was defined as a body mass index \(\geq 30\) kg/m\(^2\) for adults and as a body mass index \(\geq 95\text{th percentile}\) for children aged 2 years and older.

Descriptive analyses were used to summarize patients’ demographic and clinical characteristics, such as age, gender, underlying chronic medical conditions, influenza virus type and subtype, prompt antiviral treatment (received within two days of admission), death, a hospital stay of five or more days, and intensive care unit admission. Indexes of disease severity include death, ICU admission, and a hospital stay of 5 or more days.
Influenza-associated hospitalization incidence rates were calculated using the National Center for Health Statistics’ vintage 2010 bridged-race postcensal population estimates for the counties included in the NYS surveillance catchment area.

For analyses on severe illness, cases were defined as those who were hospitalized with laboratory confirmed influenza that either died during hospitalization, were admitted to an intensive care unit, or were hospitalized for five or more days, depending on the analysis. Controls for the patients that died were those influenza-hospitalized with patients that did not die, controls for the patients that required intensive care were influenza-hospitalized patients that did not require intensive care, and controls for patients that were hospitalized for five or more days were influenza-hospitalized patients that were in the hospital for four or fewer days.

Covariates for the analyses included race, sex, age, influenza type and subtype, vaccination status, and prompt antiviral use, which is defined as treatment within two days of hospital admission. Age was categorized as follows: 0-1, 2-4, 5-17, 18-49, 50-64, 65-79, and 80+. Influenza types include type B and influenza A subtypes pH1N1, seasonal H1N1, and H3N2. Prompt antiviral use is categorized by antivirals administered within two days of hospital admission and antivirals administered three or more days from admission.

3.3 Statistical Analysis

Unconditional logistic regression modeling was used to estimate odds ratios for an outcome of death, ICU admission, and length of stay of five or more days by
underlying medical condition categories, vaccination status, and antiviral use within two days for all covariates. Crude and adjusted models were evaluated, with models adjusted for some or all the covariates described above. A p < 0.05 was considered statistically significant. This analysis was conducted using SAS 9.3.

4: Results

Demographic & Clinical Characteristics of Hospitalized Influenza Patients in NYS FluSurv-Net Counties

Table 1 shows demographic characteristics among those hospitalized with laboratory confirmed influenza within the NYS FluSurv-NET catchment area from the 2007-2008 season through to the 2012-2013 season. The number of hospitalized cases ranged from a low of 93 in the 2011-2012 season to a high of 1559 in the 2012-2013 season. The season with the second most hospitalized patients was the pandemic 2009-2010 season. This pandemic season had the highest percentages of children aged 5-17 and adults aged 18-49 with 16.2% and 39.3% respectively, which was expected because those were the ages disproportionately affected by the pH1N1 virus. Seasons 2010-2011 and 2012-2013 had the highest percentages of hospitalized patients aged 64-79 and 80+ with 18.2% and 25%, respectively and 24.1% and 32.7%, respectively, in the two seasons. The elderly were shown to be more susceptible to A (H3N2) strain circulating those years.
The prevalence of underlying medical conditions ranged from 72.8% in the 2008-2009 season to 88.7% in the 2012-2013 season, as shown in Table 2. The percentage of patients hospitalized with asthma in the 2009-2010 season was the highest, which was expected as the highest percent of children were also hospitalized during this season and asthma is more commonly found in children.

Overall vaccination rates among those 6 months of age and older, shown in Table 3, ranged from 33.8% in the 2009-2010 season to 55.4% in the 2007-2008 season. The 2007-2008 season aside, vaccination rates among those hospitalized with influenza increase through the seasons. Use of antiviral treatment varied through the seasons with the lowest treatment percent in the 2008-2009 season at 26.5% to the highest in the 2012-2013 season at 79.4%.

Morbidity did not vary greatly across the seasons, staying between 2.7% in the 2012-2013 season and 4.0% in the 2010-2011 season. The slightly higher percent in the 2010-2011 season is not unexpected as there was a higher percent of older adults (≥65) hospitalized that season. ICU admission exhibits a wider range, starting in the 2007-2008 season at 40.1% then decreasing to an average of 15% in the following seasons. However, during the 2007-2008 season, there were 371 missing values for ICU admission, which could be responsible for artificially inflating that percent. A low of 23.5% of hospitalized influenza patients had a length of stay of 5 or more days in 2008-2009 compared to 42.4% of patients in the 2010-2011 season.
Risk of Severe Influenza Infection by Underlying Medical Condition

Adjusted models indicated significant associations between some underlying medical conditions and the severe outcomes of interest. Table 4 shows odds ratios and 95% confidence intervals adjusted for age, influenza virus type and subtype, and the use of antiviral treatment within two days of hospital admission for each of the underlying medical conditions. For an outcome of death, the only statistically significant odds ratio among the underlying medical conditions was immunosuppressive condition with an odds ratio of 2.64 (95% CI: 1.24, 5.61). For admission to an intensive care unit, the medical conditions having statistically significant higher odds were cardiovascular disease, chronic lung disease, and a neuromuscular abnormality with odds ratios of 1.70 (95% CI: 1.22, 2.37), 1.74 (95% CI: 1.25, 2.42), and 2.19 (95% CI: 1.52, 3.14), respectively. For a length of stay in the hospital of 5 or more days, the medical conditions with statistically significant adjusted odds ratios were cardiovascular disease, chronic metabolic disease, neuromuscular abnormality, and an immunosuppressive condition with odds ratios of 1.31 (95% CI: 1.01, 1.71), 1.29 (95% CI: 1.00, 1.67), 1.7 (95% CI: 1.23, 2.33), and 1.5 (95% CI: 1.04, 21.7), respectively.

Association Between Severe Influenza Infection and Prompt Antiviral Treatment

Table 4 shows adjusted odds ratios for early antiviral treatment with age, influenza virus type and subtype, and underlying medical conditions included in the model. For the outcome of death, admission to an intensive care unit, and a hospital stay of five or more days, all odds ratios were statistically significant showing a protective effect of antiviral treatment, if started within two days of hospital admission. The odds of
death were 0.3 (0.13, 0.69) in those who received antiviral treatment within two days of hospital admission compared to those who received treatment after two days. The odds of intensive care unit admission were 0.53 (0.32, 0.89) in those who received antiviral treatment within two days of hospital admission compared to those who received treatment after two days. The odds of having a hospital stay of five or more days were 0.11 (0.06, 0.22) in those who received antiviral treatment within two days of hospital admission compared to those who received treatment after two days.

**Comparison of Vaccination Rates Between Those Hospitalized with Laboratory Confirmed Influenza Infection and Un-hospitalized Populations.**

Although, vaccination status was not statistically significant in decreasing disease severity among those hospitalized in this study, vaccination may reduce the likelihood of being hospitalized. Table 5 shows the percent of vaccinated individuals in the NYS FluSurv-NET counties that were hospitalized with laboratory confirmed influenza. Also included, is the estimate of the percent of vaccinated adults in the United States according to the Behavioral Risk Factor Surveillance System (BRFSS) data for the 2007-2008 and 2008-2009 seasons. The estimated percent of those under the age of 18 vaccinated in the 2009-2010 season was determined for all ages between 6 months and 18 years of age as a whole in New York State according to data collected by BRFSS. Estimates for adults aged 18 and older in the 2009-2010 season and all age categories in the 2010-2011, 2011-2012, and 2012-2013 seasons are for all of New York State. Chi-squared tests or Fisher exact tests, if there were few observations, were conducted in order to determine if there was a difference in the incidence of vaccinations among those hospitalized compared to
the general populations of either New York State or of the United States. During the 2012-2013 season, the vaccinated percentages in all age categories were lower for those who were hospitalized and the 0-4, 5-12, and 65+ age categories were statistically significant with p-values of <0.001, 0.001, and 0.005, respectively. During the 2011-2012 season, vaccination percentages for all age categories, except for 13-17, were lower in those who were hospitalized. During the 2010-2011 season, vaccination percentages were also lower for those hospitalized in all age categories and those 0-4, 18-49, 50-64, and 65+ were statistically significant with p-values of 0.001, 0.004, 0.001, and 0.001, respectively. During the 2009-2010 season, the vaccination percentages were lower among those hospitalized. Age categories 5-12, 13-17, 50-64, and 65+ had significantly lower vaccination incidences with p-values of 0.004, 0.002, 0.002, and 0.0003, respectively. During the 2007-2008 and 2008-2009 seasons, the vaccination percentages vary between being higher or lower among those hospitalized compared to the general population estimates.

**Relative Risks of Influenza Hospitalization**

In Table 6, the relative risks of hospitalization by gender and age are presented. Denominators were obtained from CDC Wonder bridged-race population data stratified for gender and age category for residents of NYS FluSurv-NET counties during 2007-2012. Relative risks and 95% confidence intervals were calculated for males versus females. Results indicate that 5-17 year old males had a 1.44 (1.12, 1.83) times greater risk for influenza-hospitalization than 5-17 year old females. Males aged 80 and over were also at significant increased risk of hospitalization with 1.41 (1.23, 1.60) times
greater risk than females of the same age. However, males aged 18-49 and 50-64, had a lower risk of hospitalization. 18-49 year old males had 0.69 (0.60, 0.80) times lower risk for influenza- hospitalization than women of the same age and males aged 50-64 had 0.49 (0.42, 0.58) times lower risk of influenza- hospitalization than women of the same age. When age categories were collapsed, women appeared to have a higher risk with men having 0.76 times lower risk of flu hospitalization. Table 7 shows relative risk of hospitalization with laboratory confirmed influenza within the NYS FluSurv-NET catchment area between the age categories 0-17, 18-64, and 65 and older. The results showed that children under 18 years of age were 1.21 times more likely to be hospitalized with influenza than adults aged 18-64 and 0.23 times less likely than adults aged 65 and older. Adults aged 18-64 were 0.19 times less likely than adults aged 65 and older to be hospitalized with influenza.

5: Discussion

The results of the unconditional logistic regression analyses are consistent with some of the previous studies on the risk of severe illness. The significantly higher odds of intensive care unit admission among those with chronic lung disease and neuromuscular disorders are consistent with the findings from the study on influenza-hospitalizations from the 2010-2011 season (Chaves, 2013). Antiviral treatment within two days of hospital admission also significantly lowered the odds for severe illness. However, patients with chronic metabolic disease did not have significantly higher odds for either death or ICU admission in these analyses while they did have significantly higher odds in
the Chaves study (2013). This study defined severe illness as a composite of ICU admission and death, and looked at FluSurv-NET data for all US catchment areas during one season (2010-2011), which could have contributed to the differing results.

A study of those hospitalized during the 2009 pandemic, also defining severe illness as a composite of ICU admission and death, found asthma and obesity to be significant comorbidities (Chong, 2013). Another study by Ren et al of influenza-hospitalized patients during the 2009 pandemic with confirmed pH1N1 infection also showed being overweight or obese to be significantly associated with severe illness, which was defined as a composite of a fever lasting more than three days, elevated cardiac enzymes, altered mental status, and aggravation of medical conditions (Ren, 2010). Neither asthma nor obesity was found to be a significantly associated with death or ICU admission in the analyses for this paper. Asthma and obesity were both very prevalent among those hospitalized with influenza during the 2009 pandemic season, the season their analyses are based on. Since the analyses completed for this paper included data from six seasons, with several influenza types and subtypes, the difference in results is not unexpected.

In a study of influenza-hospitalized patients admitted to the ICU during the pandemic 2009 season, prompt antiviral treatment (received within 48 hours from hospital admission) was significantly associated with death (Chen, 2012). Although the population for this study is not limited to those admitted to an ICU or the pandemic 2009 season, those who received prompt antiviral treatment also had a lower odds of death. Treatment with antiviral medication within two days of hospital admission had consistent
results lowering the odds of severe illness among the studies reviewed and the analyses for this paper.

Influenza vaccine is currently recommended for everyone over the age of six months. Populations recommended for vaccination by the CDC increased over the period assessed in this study to include everyone aged six months and over so the general increase in vaccination rates is expected. However, the percent of influenza-hospitalized patients vaccinated do not match the vaccination rates for the NYS population. In some age categories, the vaccination rates of those hospitalized were almost half that of the general population. This is especially concerning, considering the high percent of those hospitalized with underlying medical conditions and the emphasis on vaccination for these individuals (CDC, 2012). However, when comparing the vaccination rates among those captured in the NYS FluSurv-NET and the general population estimates for NYS, overall, vaccination status appears to be protective against becoming hospitalized with influenza, in agreement with previous studies (Kostova, 2013).

Limitations

This study had several limitation including potential selection bias and information bias. Only laboratory confirmed positive influenza infections were used in this study. Patients hospitalized with an influenza infection that were not tested or had a false negative test result would not have been included. Depending on prevalence of infection, the RIDTs are more likely to give false negative results. However, it is recommended that hospitals send suspected influenza cases that have come back negative using an RIDT to Wadsworth for confirmation using Polymerase Chain Reaction (PCR).
Testing is at the discretion of doctor or hospital and patients may be treated with influenza like illness without testing.

Physicians may be more likely to be prescribe antiviral treatment to patients that appear to have more severe illness upon admission, although it is recommended for anyone hospitalized with suspected influenza. This could bias the results for antiviral use. However, this study attempted to control for this potential bias by only assessing those patients who were prescribed antivirals and categorizing them by time to antiviral treatment.

Missing values for variables could have also led to some bias in these study results. There were 371 missing values for ICU admission in the 2007-2008 season and 422 values missing for obesity in the 2009-2010 season. The missing ICU admission reports may be more likely to be among patients who were not admitted to an ICU which may bias the data. Since values for obesity were collected starting later in the season and because this data would be collected prior to a severe outcome, it is unlikely that it would have biased the results.

Data collected in the earlier seasons of the NYS FluSurv-NET surveillance had more missing values for vaccination, which could have biased the incidence rates if more of the missing values were unvaccinated. Data on influenza vaccinations for those under 18 was not collected for the general population prior to 2009 because that was the first year that it was recommended for children by ACIP and the CDC.
**Strengths**

Since FluSurv-NET is a population-based surveillance, this study was able to compare characteristics of hospitalized patients with the population from which they came. This was helpful in comparing vaccination rates among those hospitalized to the general population as well as to show relative risks for hospitalization by age groups and gender.

This study also accounts for the different influenza virus types and subtypes across six seasons, which could make it more generalizable for future seasons.

**Further Study**

A potential future study would be to replicate this study including data from all of the FluSurv-NET catchment sites, which would increase the generalizability of the results. Also, evaluate the reasons that those hospitalized with underlying medical conditions have such a low incidence of being vaccinated despite the recommendation for those at high risk (Lu, 2012). Another potential area for further research would be to look at antiviral use at any time among those who experienced a severe outcome.

**Public Health Significance & Recommendations**

The results of this study show the benefit of prompt antiviral treatment in those hospitalized with influenza. Currently, the CDC recommend that anyone hospitalized with confirmed or suspected influenza receive antiviral treatment within two days of symptom onset (CDC, 2012). The percent of those treated with antiviral medications
ranged from 26.5% in the 2008-2009 season to 79.4% in the 2012-2013 season, showing an increase in the use of antiviral treatment throughout the seasons studied, however, there was a decrease in treatment during the 2010-2011 season which was consistent with results from a study of all FluSurv-NET hospitalized patients for that season (Garg, 2014). The antiviral treatments are also recommended for those considered to be at a high risk for influenza complications prior to hospitalization. Increasing antiviral treatment among these populations, while still in the community, could lower hospitalization rates and reduce the incidences of severe infection as they could potentially be receiving the treatment earlier than if they waited until hospitalization.

The results should also be used to attempt to increase vaccination rates overall to prevent or reduce influenza-hospitalizations, particularly among those who fall under high-risk categories. Even though almost 80% of those hospitalized with influenza had at least one underlying medical condition that put them into the high-risk category, vaccination rates among those hospitalized were significantly lower than the general NYS population.

Patients with underlying medical conditions made up 72%-90% of those hospitalized with an influenza infection. Many of these hospitalizations may have been mitigated if underlying medical conditions had been treated prior to influenza infection. Although data on asthma severity and control measures were not available for this study, it is known that asthma symptoms can be exacerbated to the point of an asthma attack when infected with influenza (Rothbath, 1995; Johnston; 1996). The use of medications to control asthma symptoms may help to lower the incidence of influenza-hospitalization
as well as severe outcomes among those with asthma. Cardiovascular diseases can also be exacerbated with an influenza infection. Among those with cardiovascular disease, the risk of having a cardiac event is increased while hospitalized with influenza (Warren-Gash, 2009). Treatment for cardiovascular disease should also be utilized, especially during the influenza season, in order to reduce the risk of a cardiac event.

6: Conclusion

Those with certain underlying medical conditions, including cardiovascular disease, chronic lung disease, chronic metabolic disease, neuromuscular abnormality, and immunosuppressive condition, are at a higher risk of death, intensive care unit admission, or a hospital stay of five or more days. Use of antiviral treatment within two days of hospital admission was significantly associated with lower odds of death, ICU admission, and a hospital stay of five or more days. Those hospitalized with influenza have a lower overall incidence of being vaccinated against influenza for the current season than the general population showing the protective effect of the vaccine against hospitalization. Adults over the age of 65 are at the highest relative risks of hospitalization due to laboratory confirmed influenza, followed by children under 18, and then adults aged 18 to 64 years.
Table 1. Demographic characteristics of influenza-hospitalized cases: New York State (NYS) FluSurv-NET catchment, 2007-2013

<table>
<thead>
<tr>
<th></th>
<th>2007-2008 (n=518)</th>
<th>2008-2009 (n=103)</th>
<th>2009-2010 (n=749)</th>
<th>2010-2011 (n=549)</th>
<th>2011-2012 (n=93)</th>
<th>2012-2013 (n=1559)</th>
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<tbody>
<tr>
<td><strong>Age</strong></td>
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<td>0-1</td>
<td>24 (4.6)</td>
<td>9 (8.7)</td>
<td>45 (6.0)</td>
<td>31 (5.7)</td>
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<td>2-4</td>
<td>7 (1.4)</td>
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<td>5-17</td>
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<td>12 (11.7)</td>
<td>121 (16.2)</td>
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<td>275 (50.1)</td>
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<td>A</td>
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<td>66 (65.4)</td>
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<td>439 (86.3)</td>
<td>69 (79.3)</td>
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<td>B</td>
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<td>A(pH1N1)</td>
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<td>-</td>
<td>504 (100.0)</td>
<td>72 (17.8)</td>
<td>24 (40.7)</td>
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<td>A(H3N2)</td>
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<td>-</td>
<td>0.0</td>
<td>333 (82.2)</td>
<td>35 (59.3)</td>
<td>643 (99.4)</td>
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Table 2. Underlying medical conditions among influenza-hospitalized cases: NYS FluSurv-NET catchment, 2007-2013

<table>
<thead>
<tr>
<th>Underlying Medical Condition*</th>
<th>2007-2008 (n=518)</th>
<th>2008-2009 (n=103)</th>
<th>2009-2010 (n=749)</th>
<th>2010-2011 (n=549)</th>
<th>2011-2012 (n=93)</th>
<th>2012-2013 (n=1559)</th>
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<td>Asthma</td>
<td>80 (15.4)</td>
<td>29 (28.2)</td>
<td>275 (36.7)</td>
<td>105 (19.1)</td>
<td>20 (21.5)</td>
<td>325 (20.8)</td>
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<td>Cardiovascular Disease</td>
<td>201 (38.8)</td>
<td>19 (18.5)</td>
<td>155 (20.7)</td>
<td>215 (39.2)</td>
<td>35 (37.6)</td>
<td>714 (45.7)</td>
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<td>Chronic Lung Disease</td>
<td>140 (27.0)</td>
<td>14 (13.6)</td>
<td>85 (11.4)</td>
<td>131 (23.9)</td>
<td>40 (43.0)</td>
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<td>Chronic Metabolic Disease</td>
<td>197 (38.0)</td>
<td>18 (17.5)</td>
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<td>577 (37.0)</td>
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<td>5 (4.9)</td>
<td>28 (3.7)</td>
<td>68 (12.4)</td>
<td>24 (25.8)</td>
<td>422 (27.0)</td>
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<td>Immunosuppressive Condition</td>
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<td>5 (4.9)</td>
<td>61 (8.1)</td>
<td>44 (8.0)</td>
<td>10 (10.8)</td>
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<td>99 (19.1)</td>
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<td>86 (15.7)</td>
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<td>264 (16.9)</td>
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<td>Obese</td>
<td>-</td>
<td>-</td>
<td>151 (46.2)</td>
<td>143 (41.8)</td>
<td>30 (32.3)</td>
<td>483 (30.9)</td>
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<td>More than one underlying condition</td>
<td>250 (48.3)</td>
<td>26 (25.2)</td>
<td>228 (30.4)</td>
<td>235 (42.8)</td>
<td>62 (66.7)</td>
<td>1047 (67.0)</td>
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*Underlying medical conditions include asthma, chronic lung disease, chronic cardiovascular disease, renal disease, neuromuscular disorder, immunosuppressive condition, and obesity.
Table 3. Clinical Characteristics of influenza-hospitalized cases: NYS FluSurv-NET catchment, 2007-2012

<table>
<thead>
<tr>
<th></th>
<th>2007-2008 (n=518)</th>
<th>2008-2009 (n=103)</th>
<th>2009-2010 (n=749)</th>
<th>2010-2011 (n=549)</th>
<th>2011-2012 (n=93)</th>
<th>2012-2013 (n=1559)</th>
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<tbody>
<tr>
<td>Vaccinated*</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>279 (55.4)</td>
<td>38 (38.4)</td>
<td>246 (33.8)</td>
<td>225 (42.1)</td>
<td>38 (42.2)</td>
<td>816 (49.7)</td>
</tr>
<tr>
<td>No</td>
<td>225 (44.6)</td>
<td>61 (61.6)</td>
<td>482 (66.2)</td>
<td>309 (57.9)</td>
<td>52 (57.8)</td>
<td>601 (42.4)</td>
</tr>
<tr>
<td>Antiviral treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>214 (41.3)</td>
<td>27 (26.5)</td>
<td>570 (76.5)</td>
<td>385 (73.6)</td>
<td>53 (57.6)</td>
<td>1227 (79.4)</td>
</tr>
<tr>
<td>No</td>
<td>304 (58.7)</td>
<td>75 (75.5)</td>
<td>175 (23.5)</td>
<td>138 (26.4)</td>
<td>39 (42.4)</td>
<td>318 (20.6)</td>
</tr>
<tr>
<td>Antiviral therapy in &lt; 3 days**</td>
<td>191 (89.3)</td>
<td>25 (92.6)</td>
<td>537 (94.2)</td>
<td>349 (90.7)</td>
<td>50 (94.3)</td>
<td>1149 (93.6)</td>
</tr>
<tr>
<td>Severe hospitalization</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>17 (3.3)</td>
<td>3 (2.9)</td>
<td>22 (2.9)</td>
<td>21 (4.0)</td>
<td>3 (3.3)</td>
<td>42 (2.7)</td>
</tr>
<tr>
<td>ICU admission***</td>
<td>59 (40.1)</td>
<td>12 (11.8)</td>
<td>146 (19.7)</td>
<td>83 (15.9)</td>
<td>20 (21.7)</td>
<td>210 (13.7)</td>
</tr>
<tr>
<td>Hospital stay of 5+ days</td>
<td>201 (39.0)</td>
<td>24 (23.5)</td>
<td>253 (33.8)</td>
<td>228 (42.4)</td>
<td>32 (34.8)</td>
<td>624 (40.1)</td>
</tr>
</tbody>
</table>

* Does not include infants < 6 months of age.
** Among those treated with influenza antiviral medication.
*** Intensive care unit admission
Table 4: Unconditional regression of factors associated with severe outcomes adjusted by age, and influenza virus type and subtype: NYS FluSURV-NET catchment 2007-2013

<table>
<thead>
<tr>
<th></th>
<th>Death (n=2176)</th>
<th>Intensive Care Unit Admission (n=1984)</th>
<th>Hospital Stay of 5+ Days (n=2176)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>aOR 95% CI</td>
<td>aOR 95% CI</td>
<td>aOR 95% CI</td>
</tr>
<tr>
<td>Underlying Medical Condition</td>
<td>1.40 (0.41, 4.75)</td>
<td>2.26 (1.36, 3.78)</td>
<td>2.14 (1.42, 3.22)</td>
</tr>
<tr>
<td>Asthma</td>
<td>0.90 (0.43, 1.90)</td>
<td>1.00 (0.73, 1.38)</td>
<td>1.12 (0.85, 1.47)</td>
</tr>
<tr>
<td>Cardiovascular Disease</td>
<td>1.47 (0.75, 2.89)</td>
<td>1.70 (1.22, 2.37)</td>
<td>1.31 (1.01, 1.71)</td>
</tr>
<tr>
<td>Chronic Lung Disease</td>
<td>0.79 (0.37, 1.66)</td>
<td>1.74 (1.25, 2.42)</td>
<td>1.24 (0.94, 1.64)</td>
</tr>
<tr>
<td>Chronic Metabolic Disease</td>
<td>1.76 (0.93, 3.33)</td>
<td>1.35 (0.99, 1.83)</td>
<td>1.29 (1.0, 1.67)</td>
</tr>
<tr>
<td>Neuromuscular Abnormality</td>
<td>1.83 (0.86, 3.92)</td>
<td>2.19 (1.52, 3.14)</td>
<td>1.70 (1.23, 2.33)</td>
</tr>
<tr>
<td>Immunosuppressive Condition</td>
<td>2.64 (1.24, 5.61)</td>
<td>1.08 (0.7, 1.67)</td>
<td>1.50 (1.04, 2.17)</td>
</tr>
<tr>
<td>Renal Disease</td>
<td>1.13 (0.50, 2.55)</td>
<td>0.95 (0.63, 1.42)</td>
<td>1.26 (0.92, 1.74)</td>
</tr>
<tr>
<td>Obese</td>
<td>2.04 (0.99, 4.15)</td>
<td>1.08 (0.77, 1.52)</td>
<td>1.19 (0.9, 1.57)</td>
</tr>
<tr>
<td>More than one underlying condition</td>
<td>1.41 (0.72, 2.74)</td>
<td>1.70 (1.25, 2.32)</td>
<td>1.44 (1.12, 1.84)</td>
</tr>
<tr>
<td>Antiviral Treatment within &lt;3 Days</td>
<td>0.30 (0.13, 0.69)</td>
<td>0.53 (0.32, 0.89)</td>
<td>0.11 (0.06, 0.22)</td>
</tr>
</tbody>
</table>

Adjusted for age category (0-1, 2-4, 5-17, 18-49, 50-64, 65-79, 80+), influenza virus type and subtype (B, pH1N1, and H3N2), early use of influenza antiviral medication (received within 2 days of admission, received 3 or more days from admission), and all variables shown in table.

Vaccine was included in the model but did not affect odds ratio so it was excluded for a better model fit.
Table 5: Comparison of vaccination incidences among those hospitalized with laboratory confirmed influenza in NYS FluSurv-NET counties and either NYS or United States estimates.

<table>
<thead>
<tr>
<th>Influenza Season</th>
<th>Age Category</th>
<th>0-4</th>
<th>5-12</th>
<th>13-17</th>
<th>18-49</th>
<th>50-64</th>
<th>65+</th>
</tr>
</thead>
<tbody>
<tr>
<td>2007-2008*</td>
<td>FluSurv-NET</td>
<td>41.2</td>
<td>14.3</td>
<td>33.3</td>
<td>30.3</td>
<td>50.5</td>
<td>70.0</td>
</tr>
<tr>
<td></td>
<td>USA</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>17.7</td>
<td>36.2</td>
</tr>
<tr>
<td></td>
<td>p-value</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0.999</td>
<td>0.998</td>
</tr>
<tr>
<td>2008-2009*</td>
<td>FluSurv-NET</td>
<td>36.4</td>
<td>20.0</td>
<td>42.9</td>
<td>13.9</td>
<td>57.9</td>
<td>66.7</td>
</tr>
<tr>
<td></td>
<td>USA</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>20.0</td>
<td>39.5</td>
</tr>
<tr>
<td></td>
<td>p-value</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0.247</td>
<td>0.968</td>
</tr>
<tr>
<td>2009-2010**</td>
<td>FluSurv-NET</td>
<td>29.2</td>
<td>29.6</td>
<td>33.7</td>
<td>13.9</td>
<td>57.9</td>
<td>66.7</td>
</tr>
<tr>
<td></td>
<td>NYS</td>
<td>47.8</td>
<td></td>
<td>31.4</td>
<td>45.3</td>
<td>71.9</td>
<td></td>
</tr>
<tr>
<td></td>
<td>p-value</td>
<td>&lt;0.001</td>
<td>0.291</td>
<td>0.002</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2010-2011</td>
<td>FluSurv-NET</td>
<td>35.3</td>
<td>48.1</td>
<td>25.0</td>
<td>18.6</td>
<td>29.6</td>
<td>57.1</td>
</tr>
<tr>
<td></td>
<td>NYS</td>
<td>62.7</td>
<td>62.3</td>
<td>37.2</td>
<td>31.2</td>
<td>45.0</td>
<td>67.6</td>
</tr>
<tr>
<td></td>
<td>p-value</td>
<td>0.001</td>
<td>0.098</td>
<td>0.525</td>
<td>0.004</td>
<td>0.001</td>
<td>0.001</td>
</tr>
<tr>
<td>2011-2012</td>
<td>FluSurv-NET</td>
<td>33.3</td>
<td>42.9</td>
<td>50.0</td>
<td>17.6</td>
<td>36.8</td>
<td>55.0</td>
</tr>
<tr>
<td></td>
<td>NYS</td>
<td>72.3</td>
<td>57.3</td>
<td>36.8</td>
<td>25.8</td>
<td>43.7</td>
<td>62.5</td>
</tr>
<tr>
<td></td>
<td>p-value</td>
<td>0.055</td>
<td>0.346</td>
<td>0.865</td>
<td>0.326</td>
<td>0.361</td>
<td>0.211</td>
</tr>
<tr>
<td>2012-2013</td>
<td>FluSurv-NET</td>
<td>41.7</td>
<td>43.9</td>
<td>42.9</td>
<td>31.1</td>
<td>44.5</td>
<td>63.2</td>
</tr>
<tr>
<td></td>
<td>NYS</td>
<td>70.2</td>
<td>64.7</td>
<td>48.0</td>
<td>31.6</td>
<td>46.8</td>
<td>68.3</td>
</tr>
<tr>
<td></td>
<td>p-value</td>
<td>&lt;0.001</td>
<td>0.001</td>
<td>0.368</td>
<td>0.463</td>
<td>0.258</td>
<td>0.005</td>
</tr>
</tbody>
</table>

*Data on estimated influenza vaccination incidences from 2007-2008 and 2008-2009 seasons were only available for adults in the United States.
**Data on estimated influenza vaccination incidences during the 2009-2010 season were collected for age categories: 6 months-17 years, 18-49 years, 50-64 years, 65+ years.
Table 6: Relative risk of hospitalization with laboratory confirmed influenza by sex and age in NYS FluSurv-NET catchment area 2007-2013

<table>
<thead>
<tr>
<th>Age</th>
<th>Male Hospitalized/Total</th>
<th>Female Hospitalized/Total</th>
<th>Relative Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-1</td>
<td>86/144879</td>
<td>73/138697</td>
<td>1.13 (0.83, 1.54)</td>
</tr>
<tr>
<td>2-4</td>
<td>50/221811</td>
<td>44/212030</td>
<td>1.09 (0.72, 1.63)</td>
</tr>
<tr>
<td>5-17</td>
<td>169/1101331</td>
<td>112/1051676</td>
<td><strong>1.44 (1.13, 1.83)</strong></td>
</tr>
<tr>
<td>18-49</td>
<td>319/2786191</td>
<td>464/2812159</td>
<td><strong>0.69 (0.60, 0.80)</strong></td>
</tr>
<tr>
<td>50-64</td>
<td>346/2672022</td>
<td>356/1367320</td>
<td><strong>0.49 (0.42, 0.58)</strong></td>
</tr>
<tr>
<td>65-79</td>
<td>305/593813</td>
<td>349/704075</td>
<td>1.03 (0.89, 1.21)</td>
</tr>
<tr>
<td>80+</td>
<td>393/206566</td>
<td>507/374658</td>
<td><strong>1.41 (1.23, 1.60)</strong></td>
</tr>
<tr>
<td>Total</td>
<td>1668/7726613</td>
<td>1905/6660615</td>
<td><strong>0.76 (0.71, 0.81)</strong></td>
</tr>
</tbody>
</table>

Data for denominators came from CDC Wonder bridged-race population data stratified for age and gender within the 15 NYS FluSurv-NET catchment counties.

Table 7: Relative risk of hospitalization with laboratory confirmed influenza by age in NYS FluSurv-NET catchment area 2007-2013

<table>
<thead>
<tr>
<th>Age</th>
<th>0-17</th>
<th>18-64</th>
<th>65+</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-17</td>
<td>-</td>
<td><strong>1.21 (1.09, 1.33)</strong></td>
<td>0.23 (0.20, 0.25)</td>
</tr>
<tr>
<td>18-64</td>
<td>-</td>
<td>-</td>
<td><strong>0.19 (0.17, 0.20)</strong></td>
</tr>
<tr>
<td>65+</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Data for denominator came from CDC Wonder bridged-race population data stratified for age within the 15 NYS FluSurv-NET catchment counties.
References:


*Recommendations and reports/Centers for Disease Control, 57*(RR-7), 1-60.


Appendix 1: FluSurv-NET Case Report Form

### 2012-13 FluSurv-NET Influenza Hospitalization Surveillance Project Case Report Form

#### A. Patient Data – THIS INFORMATION IS NOT SENT TO CDC

<table>
<thead>
<tr>
<th>Field</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Last Name</td>
<td></td>
</tr>
<tr>
<td>First Name</td>
<td></td>
</tr>
<tr>
<td>Phone Number 1</td>
<td></td>
</tr>
<tr>
<td>Phone Number 2</td>
<td></td>
</tr>
<tr>
<td>Street Address</td>
<td></td>
</tr>
<tr>
<td>City</td>
<td></td>
</tr>
<tr>
<td>Zip</td>
<td></td>
</tr>
<tr>
<td>Chart Number</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Emergency Contact 1</td>
<td></td>
</tr>
<tr>
<td>Emergency Contact Phone</td>
<td></td>
</tr>
<tr>
<td>Primary Provider Name</td>
<td></td>
</tr>
<tr>
<td>Provider Phone Number</td>
<td></td>
</tr>
<tr>
<td>Provider Fax Number</td>
<td></td>
</tr>
<tr>
<td>Date Used 1</td>
<td></td>
</tr>
<tr>
<td>Date Used 2</td>
<td></td>
</tr>
</tbody>
</table>

#### B. Reporter Information – THIS INFORMATION IS NOT SENT TO CDC

<table>
<thead>
<tr>
<th>Field</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reporter Name</td>
<td></td>
</tr>
<tr>
<td>Date Reported</td>
<td></td>
</tr>
</tbody>
</table>

#### C. Enrollment Information

<table>
<thead>
<tr>
<th>Field</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case Classification</td>
<td></td>
</tr>
<tr>
<td>State</td>
<td></td>
</tr>
<tr>
<td>County</td>
<td></td>
</tr>
<tr>
<td>Case Type</td>
<td></td>
</tr>
<tr>
<td>Date of Birth</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>Male/Female</td>
</tr>
<tr>
<td>Race</td>
<td>White/Black/Asian/Pacific/Other/American/Non-Hispanic/Mult/Not Specified</td>
</tr>
<tr>
<td>Hospital ID Where Patient Treated</td>
<td></td>
</tr>
<tr>
<td>Admission Date</td>
<td></td>
</tr>
<tr>
<td>Discharge Date</td>
<td></td>
</tr>
<tr>
<td>Was patient transferred from another hospital?</td>
<td>Yes/No/Unknown</td>
</tr>
<tr>
<td>Transfer Hospital ID</td>
<td></td>
</tr>
<tr>
<td>Transfer Hospital Admission Date</td>
<td></td>
</tr>
<tr>
<td>Transfer Date</td>
<td></td>
</tr>
<tr>
<td>If yes, indicate Type of facility:</td>
<td>Nursing home/Rehabilitation Facility/Group home/Assisted living/Homeless Shelter/Unknown/Other, specify</td>
</tr>
<tr>
<td>Indicate NAME of facility</td>
<td></td>
</tr>
</tbody>
</table>

#### D. Influenza Testing Results

<table>
<thead>
<tr>
<th>Test Subject</th>
<th>Method</th>
<th>Result</th>
<th>Other Specimen Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>First</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Second</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Third</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fourth</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

---

V14 1
### E. Admission and Patient History

1. Was patient discharged from any hospital within one week prior to the current admission date?  
   - Yes  
   - No  
   - Unknown

2. Reason for current admission (Check all that apply):  
   - Acute respiratory illness  
   - Asthma and/or COPD exacerbation  
   - Fever/febrile  
   - Pneumonia  
   - Other respiratory or cardiac conditions  
   - Other, neither respiratory nor cardiac conditions  
   - Unknown

3. Date of onset of acute illness resulting in hospitalization:  
   - / /  
   - Unknown

4. Date of onset of respiratory symptoms:  
   - / /  
   - Unknown

5. Body Mass Index  
   -  
   - Unknown

6. Height:  
   -  
   - Unknown

7. Weight:  
   -  
   - Unknown

8. Sex:  
   - Male  
   - Female  
   - Unknown

9. Alcohol abuse:  
   - Yes  
   - No  
   - Unknown

10. Did patient have any of the following pre-existing medical conditions? (Check all that apply)  
    - Yes  
    - No  
    - Unknown

   a. Asthma/Reactive Airway Disease  
   - Yes  
   - No/Unknown

   b. Chronic Lung Disease  
   - Yes  
   - No/Unknown

   c. Chronic Metabolic Disease  
   - Yes  
   - No/Unknown

   d. Blood disorders/Hematopoiesis  
   - Yes  
   - No/Unknown

   e. Cardiovascular Disease  
   - Yes  
   - No/Unknown

   f. Neurovascular disorder  
   - Yes  
   - No/Unknown

   g. Neurologic disorder  
   - Yes  
   - No/Unknown

   h. History of Guillain-Barre Syndrome  
   - Yes  
   - No/Unknown

   i. Immunosuppressed Condition  
   - Yes  
   - No/Unknown

   j. Salivary gland cancer (e.g., nasopharyngeal carcinoma)  
   - Yes  
   - No/Unknown

   k. History of head and neck cancer  
   - Yes  
   - No/Unknown

   l. History of breast cancer  
   - Yes  
   - No/Unknown

   m. History of ovarian cancer  
   - Yes  
   - No/Unknown

   n. History of melanoma  
   - Yes  
   - No/Unknown

   o. History of multiple myeloma  
   - Yes  
   - No/Unknown

   p. History of lymphoma  
   - Yes  
   - No/Unknown

   q. History of hematologic malignancy  
   - Yes  
   - No/Unknown

11. Other:  
   - Yes  
   - No/Unknown

12. Pediatric cases only:  
   - Yes  
   - No/Unknown

   a. Anomalies of upper airway  
   - Yes  
   - No/Unknown

   b. History of febrile seizures  
   - Yes  
   - No/Unknown

   c. Long-term aspirin therapy  
   - Yes  
   - No/Unknown

   d. Prematurity  
   - Yes  
   - No/Unknown

   e. Gestational age in weeks:  
   -  

   f. If yes, specify gestational age at birth in weeks:  
   -  

   g. Unknown gestational age at birth  
   - Yes  
   - No/Unknown
## F. Intensive Care Unit and Interventions

1. Was the patient admitted to an intensive care unit (ICU)?
   - Yes
   - No
   - Unknown

2. Date of ICU Admission:
   - Month/Day/Year

3. Date of ICU Discharge:
   - Month/Day/Year

4. Did patient receive mechanical ventilation?
   - Yes
   - No
   - Unknown

5. Did patient receive extracorporeal membrane oxygenation (ECMO or "on bypass")?
   - Yes
   - No
   - Unknown

## G. Bacterial Pathogens – Sterile or respiratory site only

1. Were any bacterial culture tests performed with a collection date within three days of admission?
   - Yes
   - No
   - Unknown

2. If yes, was there culture confirmation of a bacterial infection?
   - Yes
   - No
   - Unknown

3. If yes, specify pathogen:
   --Staphylococcus aureus:
     - Meticillin-resistant (MRSA)
     - Meticillin-sensitive (MSSA)
     - Sensitivity unknown

4. If Haemophilus influenzae, specify if type B:
   - Yes
   - No
   - Unknown

5. If Nontypeable Haemophilus influenzae, specify serogroup:
   - B
   - C
   - Y
   - Other
   - Specify:

6. Site where pathogen identified:
   - Blood
   - Cerebrospinal fluid (CSF)
   - Bronchoalveolar lavage (BAL)
   - Urine
   - Pleural fluid
   - Endotracheal aspirate
   - Other:

## H. Viral Pathogens

1. Was patient tested for any of the following viral pathogens within 5 days of admission?
   - Yes
   - No
   - Unknown

2. Respiratory syncytial virus (RSV):
   - Yes, positive
   - Yes, negative
   - Not tested/Unknown
   - Date:

3. Adenovirus:
   - Yes, positive
   - Yes, negative
   - Not tested/Unknown
   - Date:

4. Parainfluenza 1:
   - Yes, positive
   - Yes, negative
   - Not tested/Unknown
   - Date:

5. Parainfluenza 2:
   - Yes, positive
   - Yes, negative
   - Not tested/Unknown
   - Date:

6. Parainfluenza 3:
   - Yes, positive
   - Yes, negative
   - Not tested/Unknown
   - Date:

7. Influenza A (H1N1) (human seasonal):
   - Yes, positive
   - Yes, negative
   - Not tested/Unknown
   - Date:

8. Other:
   - Yes, positive
   - Yes, negative
   - Not tested/Unknown
   - Date:

## I. Influenza Treatment

1. Did patient receive antiviral medication treatment for influenza during the course of this illness?
   - Yes
   - No
   - Unknown

2. Treatment 1:
   - Oseltamivir (Tamiflu)
   - Zanamivir (Relenza)
   - Other:

3. Method of Administration:
   - Oral
   - Intravenous (IV)
   - Inhaled

4. Start Date:
   - Month/Day/Year
   - End Date:
   - Month/Day/Year
   - Dose:
   - Frequency:

5. Treatment 2:
   - Oseltamivir (Tamiflu)
   - Zanamivir (Relenza)
   - Other:

6. Method of Administration:
   - Oral
   - Intravenous (IV)
   - Inhaled

7. Start Date:
   - Month/Day/Year
   - End Date:
   - Month/Day/Year
   - Dose:
   - Frequency:

8. Treatment 3:
   - Oseltamivir (Tamiflu)
   - Zanamivir (Relenza)
   - Other:

9. Method of Administration:
   - Oral
   - Intravenous (IV)
   - Inhaled

10. Start Date:
    - Month/Day/Year
    - End Date:
    - Month/Day/Year
    - Dose:
    - Frequency:

11. Treatment 4:
    - Oseltamivir (Tamiflu)
    - Zanamivir (Relenza)
    - Other:

12. Method of Administration:
    - Oral
    - Intravenous (IV)
    - Inhaled

13. Start Date:
    - Month/Day/Year
    - End Date:
    - Month/Day/Year
    - Dose:
    - Frequency:

14. Additional Treatment Comment:

### J. Chest Radiograph – Based on radiology report only

1. Was a chest x-ray taken within 3 days of admission?  
   - Yes ☐  
   - No ☐  
   - Unknown ☐  

2. Were any of these chest x-rays abnormal?  
   - Yes ☐  
   - No ☐  
   - Unknown ☐  

2a. Date of first abnormal chest x-ray: __/__/____

2b. For first abnormal chest x-ray, please check all that apply:
   - Report not available ☐  
   - Bronchopneumonia/pneumonia ☐  
   - Cardiomegaly ☐  
   - Air space opacity or opacity ☐  
   - Consolidation/consolidation ☐  
   - Interstitial infiltrate ☐  
   - Pleural effusion ☐  
   - Single lobe infiltrate ☐  
   - Multiple lobe infiltrate (unilateral or bilateral) ☐  
   - Other: specify: ____________________________

### X. Discharge Summary

1. Did the patient have any of the following diagnoses at discharge (check all that apply)?
   - Pneumonia ☐  
   - Pneumonia: Yes ☐ No ☐ Unknown ☐
   - Cellulitis-Buried syndrome: Yes ☐ No ☐ Unknown ☐
   - Enteritis: Yes ☐ No ☐ Unknown ☐
   - Pneumonia: Yes ☐ No ☐ Unknown ☐
   - Acute respiratory distress syndrome (ARDS): Yes ☐ No ☐ Unknown ☐
   - Seizures: Yes ☐ No ☐ Unknown ☐
   - Bronchitis: Yes ☐ No ☐ Unknown ☐
   - Thyroiditis: Yes ☐ No ☐ Unknown ☐
   - Hemophagocytic syndrome: Yes ☐ No ☐ Unknown ☐

2. What was the outcome of the patient?  
   - Alive ☐  
   - Dead ☐  
   - Unknown ☐

2a. If discharged alive, please indicate to where:  
   - Home ☐  
   - Other hospital ☐  
   - Hospice ☐  
   - Rehabilitation Facility ☐  
   - Other long-term care facility ☐  
   - Other: specify: ____________________________

3. If patient was pregnant on admission, indicate pregnancy status at discharge  
   - Still pregnant ☐  
   - No longer pregnant ☐

3a. If patient was pregnant on admission but no longer pregnant at discharge, indicate pregnancy outcome at discharge:  
   - Miscarriage ☐  
   - Stillborn ☐  
   - Healthy newborn ☐  
   - Stillborn died ☐  
   - Unknown ☐

4. Additional notes regarding discharge:

### L. ICD-9 Discharge Diagnoses – To be recorded in order of appearance

1. ____________________________  
2. ____________________________  
3. ____________________________  
4. ____________________________

### M. Vaccination History

**For mothers of patient < 6 months:**

1. Did patient’s mother receive the influenza vaccine during fall or winter of the current influenza season?  
   - Yes ☐  
   - No ☐  
   - Unknown ☐  

1a. If yes, specify mother’s vaccine type:  
   - Inactivated Vaccine – Trivalent inactivated influenza vaccine (TIV) ☐  
   - Nasal Spray-Live attenuated influenza vaccine (LAIV) ☐  
   - Vaccine type unknown ☐

2. Did patient receive the influenza vaccine during fall or winter of the current influenza season?  
   - Yes ☐  
   - No ☐  
   - Unknown ☐  

2a. If yes, specify patient’s vaccine type:  
   - Inactivated Vaccine – Trivalent inactivated influenza vaccine (TIV) ☐  
   - Nasal Spray-Live attenuated influenza vaccine (LAIV) ☐  
   - Vaccine type unknown ☐

2b. If patient ≥ 18 years and received injected vaccine (TIV), please specify type:  
   - Regular IM ☐  
   - High dose IM ☐  
   - Intradermal ☐  
   - TIV type unknown ☐

3. If patient < 18 years, did patient receive any seasonal influenza vaccine in previous season?  
   - Yes ☐  
   - No ☐  
   - Unknown ☐

3a. Specify dose date:  
   - 1/__/____ Date Unknown ☐  
   - 2/__/____ Date Unknown ☐  
   - 3/__/____ Date Unknown ☐  
   - 4/__/____ Date Unknown ☐

5. What is the source of vaccination history (check all that apply)?  
   - Medical Chart ☐  
   - Vaccine Registry ☐  
   - Primary Care Provider ☐  
   - Interview ☐  
   - Patient refused ☐

5a. If vaccination history obtained by phone interview, please specify source of interview:  
   - Patient ☐  
   - Proxy ☐  
   - Other, specify: ____________________________

### V. Miscellaneous

1. Case Finding ☐  
   - Hospital Log ☐  
   - Laboratory List ☐  
   - Discharge Database ☐  
   - Reportable Disease ☐  
   - Other, specify: ____________________________

2. Additional Comments:
Appendix 2: Research Ethics

This study was exempt from NYS Department of Health and University at Albany Institutional Review Board (IRB) approval for human research protections. The data collected through FluSurv-NET was determined by the IRB to be for routine public health surveillance. Data was de-identified prior to this study being done.
Appendix 3: IRB Exemption Approval

UNIVERSITY AT ALBANY
State University of New York

IRB 0000568
FWA 0001970
Notice of Approval
IRB Protocol Number: 14-X-086-01

Approval Date: April 11, 2014
Expiration Date: April 10, 2015

Title: Influenza Hospitalizations in New York State Emerging Infections Program Counties from the 2007-2008 Season to the 2012-2013 Season. Is there a difference in Prevention/Treatment effectiveness among different Age Categories and Medical Conditions

Principal Investigator: Mary Dundas

Review Type: Exempt #4

☑ New ☐ Modification

Approved under Exempt Category:

☐ 1 – Research conducted in established/commonly accepted educational settings involving normal educational practices.

☐ 2 – Research involving the use of educational tests, survey procedures, interview procedures or observation of public behavior.

☐ 3 – Research involving the use of educational tests, interview procedures not exempt under Category 2 if subjects are appointed public officials or research conducted under federal statute requiring confidentiality be maintained throughout the research and thereafter.

☐ 4 – Research involving collection or study of existing data, documents, records, pathological specimens or diagnostic specimens.

☐ 5 – Research and demonstration projects conducted by or subject to approval of federal Department or Agency heads and designed to study, evaluate, examine public benefit or service programs.

☐ 6 – Taste and food quality and evaluation/consumer acceptance studies.

1. Provisions of Approval: The determination is valid until the expiration date above. If your research is expected to continue beyond the expiration date, you must submit a new protocol. You are required to maintain IRB approval for as long as the study remains active.

2. All recruitment materials and methods must be approved by the IRB (as part of the determination of exempt from IRB review) prior to being used.

3. Informed Consent: An adequate standard of informed consent has been met when required.

4. Principal Investigator Responsibilities: It is the responsibility of the PI to ensure that all investigators and staff associated with this study meet the training requirements for conducting research involving human subjects, promptly report any changes in research activity to ORRC, keep appropriate research records, and comply with all University at Albany Policies, federal, state and local laws, Declaration of Helsinki and the Belmont Report.

5. Research Records: Accurate and detailed research records must be maintained. All research records (including all IRB correspondence) must be kept for a minimum of 3 years after the completion of the research. This research is subject to an audit under the terms of the IRB’s Quality Improvement Program.

6. Modifications: All protocol modifications must be IRB approved prior to implementation. Modifications include (but are not limited to) study personnel, research instruments, protocol procedures, and/or addition of funding source.

7. Funded Research: If your research is funded or otherwise sponsored research, you must submit any changes to the grant to ORRC with the human subjects section(s) highlighted. This is true whether the source of funding is internal or external.

8. Study Closure: A study is considered to be open and active until the protocol has reached its Expiration Date or the investigator has submitted a Closure Form (available at www.albany.edu/research/compliance/Forms.htm). Until a Closure Form is received, IRB oversight of the research will remain active. A closure notice/reminder will be sent to you, but it is your responsibility to ensure that you submit an updated protocol and receive an approval in a timely manner.

9. Unanticipated or adverse events: All unanticipated or adverse events must be reported to the IRB within 5 days.

10. Other:

cc: Shelley Zansky

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