EFFECT OF *INFLUENZA* VACCINATION ON OUTCOME OF HOSPITALIZED ADULTS: CASE CONTROL STUDY

by

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ABSTRACT

Background: *Influenza* is a respiratory illness caused by three different viruses: type A, B, or C. *Influenza* has a large impact on morbidity and mortality globally with an estimated attack rate at 5-10% in adults and 20-30% in children. The *Influenza* vaccine is the most effective way to prevent *Influenza*. The purpose of this epidemiologic study is to determine the efficacy of the *Influenza* vaccines administered between 2013 and 2015, and to address public misconceptions concerning the safety of the vaccine.

Methods: This case control study of adult patients took place at University of Pittsburgh Medical Center Mercy Hospital. The study included 306 adult patients with respiratory illnesses who were admitted to the hospital during 2013-2015 *Influenza* seasons. Of these admitted patients, 206 tested positive for *Influenza* while the other 100 patients tested negative and therefore served as case controls. Data on each patient were collected via medical records, which included vaccination status, demographics such as gender, and outcomes such as length of stay. The data were statistically analyzed using SAS v 9.3 software.

Results: Among *Influenza* positive cases during the 2013-2014 *Influenza* season, 34.4% were vaccinated and 55.6% were between the ages 51 and 79. Among *Influenza* positive cases during the 2014-2015 season, 64.6% were vaccinated and 57% were between the ages 51 and 79. Among *Influenza* negative cases during both *Influenza* seasons, 66.7% were vaccinated and

56.3% were between the ages 51 and 79. Importantly, as a general finding, those patients who received *Influenza* vaccination prior to admission were significantly less likely to have *Influenza* ($p = 0.0132$). Patients who were vaccinated prior to admission were statistically significantly older ($p = 0.0001$) and had higher comorbidity scores ($p = 0.0001$).

Conclusions: *Influenza* vaccination significantly reduces the rate of *Influenza* positivity among inpatients. Patients who are older and have higher comorbidity scores are more likely to be vaccinated. The *Influenza* vaccine is significant to public health because it is cost effective and reduces hospitalizations and mortality due to *Influenza*. This information can be used to educate patients and health care workers about the *Influenza* vaccine and its benefits.

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PREFACE

I would like to thank my thesis director, Dr. Mohamed Yassin from University of Pittsburgh's Medical Center (UPMC) Mercy, Department of Infection Control, for allowing and trusting me to work on this project and for all of his guidance and support throughout this entire process.

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1.0 INTRODUCTION

1.1 GLOBAL IMPACT OF *INFLUENZA*

Influenza has a large impact on morbidity and mortality globally with an estimated attack rate at 5-10% in adults and 20-30% in children, resulting in about three to five million cases of severe illness, and about 250,000 to 500,000 deaths[19]. Therefore, it is essential to better understand and investigate the effects of *Influenza* on global public health in order to decrease these rates.

1.2 *INFLUENZA* EPIDEMIOLOGY

In order to effectively prevent individuals from getting *Influenza*, understanding what the causative infective agent is and how it causes illness is essential. *Influenza* is a respiratory illness that is caused by three different viruses, type A, B, or C, with type A being the most severe and type C being the least severe[29]. Type A *Influenza* can be separated into subtypes based on the surface glycoproteins, hemagglutinin (HA) and neuraminidase (NA), located on the *Influenza* virus[29]. *Influenza* is very pathogenic and difficult to control due to the fact that there are 18 HA subtypes and 11 NA subtypes, which can be combined in numerous combinations to create a large number of possible *Influenza* strains[29].

The *Influenza* virus is spread through infected air droplets when people cough or sneeze and another person inhales the droplets[15]. Once the virus is in an individual's respiratory system, it will begin to infect cells. Hemagglutinin on the virus recognizes and binds sialic acids on carbohydrate side chains of cell-surface glycoproteins and glycolipids, allowing the virus to then fuse with the host cell and replicate. Once replication is finished, neuraminidase removes sialic acid from the infected cell surface so that the newly made viruses can be released and infect more cells[14].

The incubation period for *Influenza* is about two days[19]. Once an individual is infected they may experience the following symptoms: high fever, cough, headache, muscle and joint pain, severe malaise, sore throat and runny nose. These symptoms usually last a week in most people but the virus can cause severe illness or even death in people who are at high risk. Those in the high risk category includes children younger than two years, adults aged 65 or older, pregnant women, those who are immune-compromised and anyone with medical conditions such as chronic heart, lung, kidney, liver or blood disease[19]. An example of a severe illness that these groups may experience is bacterial pneumonia that could lead to death or other complications if not treated properly[12].

As previously mentioned, *Influenza* can be spread through infected air droplets. Another mode of transmission is through direct contact. For example, if a person's hand is contaminated, touching surfaces that other people come in contact with can facilitate the spread[15]. This is why it is so important for people to wash their hands immediately after covering their mouths when coughing and sneezing. Rates of *Influenza* transmission can be decreased if the population practices these simple methods.

1.3 PREVENTION

The most effective way to prevent *Influenza* and therefore epidemics is by vaccination. *Influenza* vaccinations have been used for more than 60 years and are recommended for anyone six months and older[21]. Vaccination can provide protection in healthy individuals but may be less effective in the elderly[19]. However, the vaccine can still help reduce the severity of the illness and mortality risk in the elderly[19]. High-risk individuals are especially encouraged to get vaccinated to help prevent illness or complications from the illness. Unfortunately, the level of effectiveness of the annual vaccine is not extremely consistent, and greatly depends on how well the vaccine matches the antigenic make-up of the circulating viruses at that given time[19]. This is because *Influenza* viruses are continuously changing and highly susceptible to antigenic drift[21]. Therefore, the World Health Organization (WHO) updates its vaccine composition recommendation biannually to target the three (trivalent) most important virus types that are in circulation, which usually includes two subtypes of *Influenza* A viruses and one B virus[19]. Most recently a quadrivalent vaccine composed of two subtypes of *Influenza* A viruses and two B viruses has been recommended because it is expected to increase protection against *Influenza*[19]. While there has been some public resistance towards the vaccine, the following data highlights the steady increase in vaccinations over the past three years in the United States:

- 134.5 million doses in 2013-2014 (by 2/28/14)
- 147.8 million doses in 2014-2015 by (2/6/15)
- 145.6 million doses in 2015-2016 by (1/15/16)

Manufacturers have projected they will provide between 171 and 179 million doses of vaccine by the end of the 2015-2016 season[27].

1.4 BENEFITS OF VACCINATION

There are many benefits of the *Influenza* vaccine. It not only can provide protection to the vaccine recipient, but it can help protect people around them who may be more vulnerable to *Influenza*. This concept is known as 'herd immunity'. The vaccine can also reduce the number of hospitalizations due to *Influenza*. For example, during both the 2010-2012 *Influenza* seasons the vaccine was associated with a 74% reduction in children's risk of *Influenza*-related pediatric intensive care unit admission and as well as a 71% reduction in *Influenza*-related hospitalizations in adults of all ages during the 2011-2012 *Influenza* season[21]. Moreover, studies have shown that the vaccine is also effective for protecting women who are pregnant, as well as their babies for up to six months after they are born[21]. A study showed that the *Influenza* vaccine given to pregnant women was 92% effective in preventing their babies from being hospitalized[5].

1.5 VACCINE EFFECTIVENESS

As mentioned earlier, the vaccine's effectiveness relies on which *Influenza* viruses are circulating at the time. The predominating, circulating virus during the 2013-2014 *Influenza* season was *Influenza* A 2009 H1N1, which was included in the vaccine for that year[16]. Because of this, the vaccine effectiveness was 61% for all age groups[1]. The predominating, circulating virus during the 2014-2015 *Influenza* season was *Influenza* A H3N2, which was different from the *Influenza* A H3N2 component of the vaccine. This caused the vaccine effectiveness to only be 23%, which caused more hospitalizations and deaths compared to the previous *Influenza* season[17]. The 2013-2014 *Influenza* season had 9,586 hospitalizations and 96 laboratory-

confirmed, *Influenza*-associated pediatric deaths[16]. In comparison, the 2014-2015 *Influenza* season had 17,911 hospitalizations and 141 laboratory-confirmed, *Influenza*-associated pediatric deaths[17]. These data highlight the importance of an effective match between the *Influenza* vaccine and the circulating viruses of a given season.

Despite the fact that the viral component of the Influenza vaccine was not a strong match to the circulating viruses during the 2014-2015 *Influenza* season, the vaccine still proved beneficial. There were an estimated 1.9 million *Influenza*-associated illnesses prevented, 966,000 *Influenza*-associated medical visits prevented, and 67,000 *Influenza* hospitalizations prevented[10]. The vaccine still provided protection against vaccine-like *Influenza* A (H3N2) viruses that had not significantly changed due to antigenic drift and against *Influenza* B viruses that predominated late in the season[17]. The more people vaccinated will generally decrease the number of hospitalizations and deaths due to *Influenza.* A modeling study conducted for the 2013-2014 *Influenza* season concluded that if the vaccination rates were improved from 40% to 70%, another 5.9 million *Influenza* illnesses, 2.3 million medically attended illnesses, and 42,000 *Influenza* hospitalizations could have been prevented[24].

1.6 SURVEILLANCE

The Department of Health in Pennsylvania has an *Influenza* surveillance system that keeps a record of the number of reported cases of *Influenza* that occur each week[25]. The system is used more often and looked more closely at during the fall and winter seasons. The official *Influenza* surveillance period begins in October and ends in May of the following year. Reported cases are only those that have had a positive laboratory test for *Influenza*, which is done by a

rapid test, direct fluorescent antibody assay (DFA), polymerase chain reaction (PCR), or culture. A large number of *Influenza* cases go unreported because many individuals do not go to the doctor and/or do not get tested. It is estimated that between 5 to 20% of Pennsylvanians contract *Influenza* on any given year and the number of deaths due to *Influenza*-related complications range between120 to 2,000 annually[25]. From October 3rd, 2015 to March 12th, 2016 there were 10,965 cases of *Influenza*, 8,676 of which were caused by *Influenza* A viruses, 2,178 by *Influenza* B viruses, and 111 by unknown viruses[25].

1.7 LOCAL *INFLUENZA* DATA

It is also important to review *Influenza* on a local level. Allegheny Health Department reported that as of March 12, 2016 there have been 739 cumulative cases, 65 cumulative hospitalizations, and three deaths. These numbers are substantially lower than the previous *Influenza* season, which recorded 4,917 cumulative cases, 732 cumulative hospitalizations, and 23 cumulative deaths[3]. The 739 cumulative cases for this current *Influenza* season can be broken down into 646 cases being caused by *Influenza* A viruses and 93 being caused by *Influenza* B viruses[25]. While the complete data set from this *Influenza* season is not yet complete, the current trend suggests a promising improvement over the previous season.

1.8 RESPIRATORY VIRAL PANEL TEST

As mentioned before, reported cases are only those that have had a positive laboratory test for *Influenza*. One of those tests, the direct fluorescent-antibody assay (DFA), offers a rapid turnaround time for results but is labor-intensive and subjective, and also requires trained technologists and specific monoclonal antibodies. Because of these limitations, a multiplex PCR assay has been developed, called the respiratory virus panel (RVP) test. This can detect several different viruses, including conventional respiratory viruses, common cold viruses, and newly emerging respiratory viruses[22]. The assay works in multiple steps beginning with a multiplex PCR using 14 primer pairs, followed by a multiplex target-specific primer extension (TSPE) using 21 primer pairs, to detect and identify 20 different virus types and subtypes in a single test. This test only requires 5 hours and when contamination precautions are taken, there is a low risk for false positives[22]. In one study, researchers concluded that the test was more sensitive than the standard DFA method and could additionally detect other respiratory virus infections that would otherwise go undetected by methods commonly used[11]. This test could also be a very important tool to use for global surveillance of emerging or reemerging respiratory viruses, such as SARS or the avian *Influenza* virus H5N1[22].

1.9 TREATMENT OPTIONS

Even though the *Influenza* vaccine is the best way to prevent a person from getting *Influenza*, in the event of sickness the best treatment option currently available is use of antiviral prescription drugs. The CDC recommends taking these drugs within the first 48 hours of

infection[31]. These drugs work by binding to the neuraminidase protein on the virus and not allowing it to replicate. Three commonly used FDA approved *Influenza* antiviral drugs include Tamiflu® (generic name oseltamivir), Relenza® (generic name zanamivir), and Rapivab® (generic name peramivir)[31]. These drugs can decrease symptoms and length of illness by one to two days. Importantly, they can also prevent serious *Influenza* complications, which is an essential benefit for high-risk patients. Considering the fact that these antiviral drugs can decrease *Influenza* symptoms, they can have a positive financial impact by limiting *Influenza* associated hospitalization visits and stays.

One major problem with antiviral drugs is antiviral resistance, where the virus can selectively mutate to become resistant to their effects[31]. While the three antiviral drugs listed above are still effective at targeting current circulating *Influenza* viruses the two other antiviral drugs, amantadine and rimantadine, are not used in the United States anymore because of the development of *Influenza* resistance[31]. Because of this fact, the CDC constantly monitors circulating *Influenza* viruses for evidence of antiviral resistance through a variety of laboratory testing methods[31].

1.10 HEALTH CARE INFECTION PREVENTION EFFORTS

Environments where people live in close contact with one another, such as nursing homes or college dorms can contribute to the spread of the *Influenza* virus and therefore put residents at a higher risk of infection. According to the Centers for Medicare & Medicaid Services (CMS), there have been 7,300 *Influenza* deaths in nursing homes annually along with $173 million in inpatient Medicare spending[8]. Today, most nursing home residents receive the *Influenza* vaccine.

However, the vaccine is known to be less effective for elderly and immune-compromised individuals. After observing case reports of outbreaks of *Influenza* in certain nursing homes, it was strongly suggested that health care workers were transmitting the virus to the residents[7]. For these reasons, it is extremely important for health care workers in nursing homes to get vaccinated. One study estimated the vaccination rates in nursing home employees to range from 33% to 61%[28]. In another study that surveyed 37 nursing homes in Florida, Georgia and Wisconsin, the vaccination rates were 36.4%, 58.5%, and 73.4% respectively[8]. Researchers attributed these rates to the employee's beliefs such as the effectiveness of the vaccine. They reported that vaccination rates increased 12 percentage points when employees believed that the vaccine does not cause *Influenza*[8].

Considering the impact that vaccinated employees have on their nursing home residents, it is strongly suggested that employee vaccinations for *Influenza* become mandatory. According to the CDC the vaccination coverage rate for health care workers was 64.3% during the 2014-2015 *Influenza* season and 62.9% during the 2013-2014 *Influenza* season[20]. These rates were measured during the early months of the seasons and *Influenza* vaccination rates increased by 9-12 percentage points by the end of each *Influenza* season. While these coverage rates are impressive, if *Influenza* vaccine was required by all health care workers, the coverage rates would likely be even higher. The American Academy of Pediatrics reported that during the 2013-2014 *Influenza* season, 36% of all health care workers, and 58% of hospital workers were subjected to a mandatory *Influenza* vaccination requirement[18]. They also reported that 500 health care facilities nationally have required their health care workers receive an *Influenza* vaccine. Seattle's Virginia Mason Medical Center mandated *Influenza* vaccinations for all their employees in 2005[18]. Employees who were exempt from the vaccine requirement due to medical

or religious reasons were required to wear a mask at work during the entire *Influenza* season. The medical center reported 97.6% coverage in the first year. This coverage rate was compared to vaccination rates during previous years that were between 29.5% to 54%. This is a great example of how effective a mandatory *Influenza* vaccine policy works to control the disease.

Locally, University of Pittsburgh Medical Center (UPMC) has implemented a universal *Influenza* immunization policy for every staff member working in a clinical location. This policy was put in place in September at the beginning of the 2015-2016 *Influenza* season[30]. Employees who elected not to receive the vaccine were required to complete an education program on the benefits of the vaccine and acknowledge that they understood the risks for themselves and others. After this policy was issued, more than 80 percent of the UPMC staff was vaccinated. This was a greater than ten percent increase compared to previous *Influenza* seasons[30]. UPMC offered hundreds of free vaccination clinics at many different locations, which greatly contributed to their success in increasing staff immunization[30].

1.11 OBJECTIVE

The importance of the *Influenza* vaccine is well recognized, still many people are hesitant to get vaccinated and not aware of the benefits. Because of this, the objective of this study was to evaluate the effectiveness of the *Influenza* vaccine through analysis of patients admitted to the hospital with respiratory illness. The effect was measured by comparing symptomatic patients who tested positive for *Influenza* to those who tested negative.

2.0 METHODS

2.1 STUDY DESIGN

This was a case-control study of adult patients at University of Pittsburgh Medical Center Mercy and was approved as a Quality Improvement project by UPMC Health System. The cases included patients who were admitted to the hospital and had a positive respiratory viral panel result during both the 2013-2014 and the 2014-2015 *Influenza* seasons. Controls included patients who were admitted to the hospital and had a negative respiratory viral panel result, within the same time frame. We define the *Influenza* season as running from the beginning of November to the end of April. This time frame was chosen after determining the range of months that recorded the highest number of *Influenza* cases by studying data from previous *Influenza* seasons.

Considering the study's objective was to evaluate the effectiveness of the *Influenza* vaccine on hospitalized patients, we looked for any demographic and outcome variables that could have any influence on the patient getting their vaccine. Some variables included were age, race, mortality, and vaccination status. These variables were investigated by collecting data on each patient and interpreting the results after the data was statistically analyzed.

2.2 DATA COLLECTION

Data on each patient was obtained via medical records from multiple UPMC databases including Cerner (the primary software for patient data), TheraDoc (infection control for all RVP data) and McKesson (medical imaging database). Demographic data including age, gender, and comorbidities were collected for each patient. Comorbidities were scaled using the Charlson Comorbidity Index, which classifies comorbid conditions by predicting mortality[26]. Patients from older age groups, and those with severe clinical conditions, such as a malignant tumor and leukemia, registered a higher comorbidity index number, whereas younger patients and those with slightly less severe clinical conditions, such as peptic ulcers or mild diabetes, generally had a lower comorbidity index number (the Charlson Comorbidity index can be found in Appendix B). Outcomes including length of stay (LOS), length of intensive care unit (ICU) stays, ventilator use, readmission, and mortality were also collected for each patient. Readmission was determined to either be 1-30 days, 60-90 days or more. Mortality was determined to be either *Influenza* related or non-*Influenza* related. Data on patient vaccination status were also collected, which was found in the medical review in the Cerner database. An example of a spreadsheet with all variables can be found in appendix A.

2.3 DATA ANALYSIS

Once the data was collected and organized into three different Excel spreadsheets, two for cases and one for controls, they were statistically analyzed using the SAS v 9.3 statistical analysis software. For each demographic and outcome variable, a two by two contingency table

of independent and dependent variables was constructed. Fisher's Exact test was performed for every table to observe the statistical significance between variables. This test was also used because of the small sample sizes. Because some data variables were categorical, they were not normally distributed, so consequently a nonparametric measurement was needed for some of the variables. In this instance a Kruskal-Wallis test was performed to observe if variables in the contingency tables were significantly different. Lastly, a box and whisker plot of Wilcoxon scores were used to display the comparative results.

3.0 RESULTS

A total of 306 patients were included in this study. Out of those 306 patients, 206 represented the cases and 100 represented the controls. *Influenza* vaccination status was not known for 30 patients and these were therefore excluded from the study, leaving a total of 276 patients to be analyzed.

Among *Influenza* positive cases during the 2013-2014 season, demographic data were as follows: 34.4% were vaccinated, 65.6% were not, 55.5% were female, 44.4% were male, 60% were Caucasian, 32.2% were African-American, 41.1% were between the ages of 20 and 50, 55.6% were between the ages of 51 and 79, and 3.3% were 80 or older. The outcome variables for these patients were as follows: an average of 5.4 days for LOS, 23.2% stayed in the ICU, 5.6% required a vent, 60% were readmitted, and 8% died. Among *Influenza* positive cases during the 2014-2015 season, demographic data was as follows: 64.6% were vaccinated, 35.4% were not, 64.6% were females, 35% were males, 78% were Caucasian, 22.3% were African-American, 10.1% were between the ages of 20 and 50, 57% were between the ages 51 and 79, and 33% were 80 and up. The outcome variables for these patients were as follows: an average of 5.5 days for LOS, 25.3% stayed in the ICU, 2% required a vent, 43% were readmitted, and 14% died. Among *Influenza* negative cases (controls) during the two *Influenza* seasons, demographic data was as follows: 66.7% were vaccinated, 33.3% were not, 51.7% were female, 48.3% were male, 71.3% were Caucasian, 28.8% were African-American, 28.7% were between

the ages 20 and 50, 56.3% were between the ages 51 and 79, and 14.9% were 80 and older. The outcome variables for these patients were as follows: an average of 7.7 days for LOS, 46% stayed in the ICU, 8.2% required a vent, 69% were readmitted, and 32% died. Table 1 lists all the results in detail.

Table 1. Demographic data broken down by variable and *Influenza* season

Variable* N=276	***Influenza* Positive (13-14) N=90**	***Influenza* Positive (14-15) N=99**	***Influenza* Negative (13-15) N=87**
Vaccination: Yes	31 (34.4%)	64 (64.6%)	58 (66.7%)
Vaccination: No	59 (65.6%)	35 (35.4%)	29 (33.3%)
Age (mean & Std Dev)	53 ± 16	70 ± 18	61 ± 18
Gender	50 (55.5%) Females 40 (44.4%) Males	64 (64.6%) Females 35 (35%) Males	45 (51.7%) Females 42 (48.3%) Males
Race	54 (60%) Caucasian 29 (32.2%) African-American	73 (78%) Caucasian 21 (22.3%) African-American	57 (71.3%) Caucasian 23 (28.8%) African-American
LOS (mean & Std Dev)	5.4 ± 8.4	5.5 ± 5.4	7.7 ± 6.1
ICU	Yes: 23 (23.2%) No: 67 (74.4%)	Yes: 25 (25.3%) No: 74 (74.7%)	Yes: 40 (46%) No: 47 (54%)
Vent Required	Yes: 5 (5.6%) No: 85 (94.4%)	Yes: 2 (2%) No: 97 (98%)	Yes: 7 (8.2%) No: 78 (91.8%)
Readmission	No: 36 (40%) 1-30 Days: 35 (39%) 31-60 Days: 13 (14.4%) 61-90 Days: 6 (7%)	No: 56 (57%) 1-30 Days: 31 (31.3%) 31-60 Days: 8 (8%) 61-90 Days: 4 (4%)	No: 27 (31%) 1-30 Days: 52 (60%) 31-60 Days: 8 (9.2%) 61-90 Days: 0 (0%)
Deceased	No: 83 (92%) Yes: 7 (8%)	No: 85 (86%) Yes: 14 (14%)	No: 59 (68%) Yes: 28 (32%)

*Patients who were determined Unknown for their *Influenza* vaccination prior to admission were excluded from the data.

Univariate and multivariate regression analysis was performed to evaluate the presence of any particular significant risk factors. A p-value less than 0.05 is considered significant. Patients who were vaccinated prior to admission had statistically significantly higher comorbidity scores compared to patients who were not vaccinated before being admitted to the hospital ($p = 0.0001$). Table 2 shows the percentages of patients who had a high Charlson score separated by their vaccination status and that there was a higher percentage of patients who were vaccinated and had a high Charlson index number. Figure 1 displays the distribution of Wilcoxon scores to show that patients who were vaccinated prior to admission and who had a high Charlson score had a higher rank compared to patients who did not get vaccinated and who had a low Charlson score.

Table 2. Prior Vaccination by High Charlson Score

Prior Vaccination	**High Charlson (Charlson > =5)**		
Frequency **Row Percent** **Column Percent**	**No**	**Yes**	**Total**
No	95 77.24% 56.98%	28 22.76% 25.69%	123 44.57%
Yes	72 47.06% 43.11%	81 52.94% 74.31%	153 55.43%
Total	167 60.51%	109 39.49%	276 100%

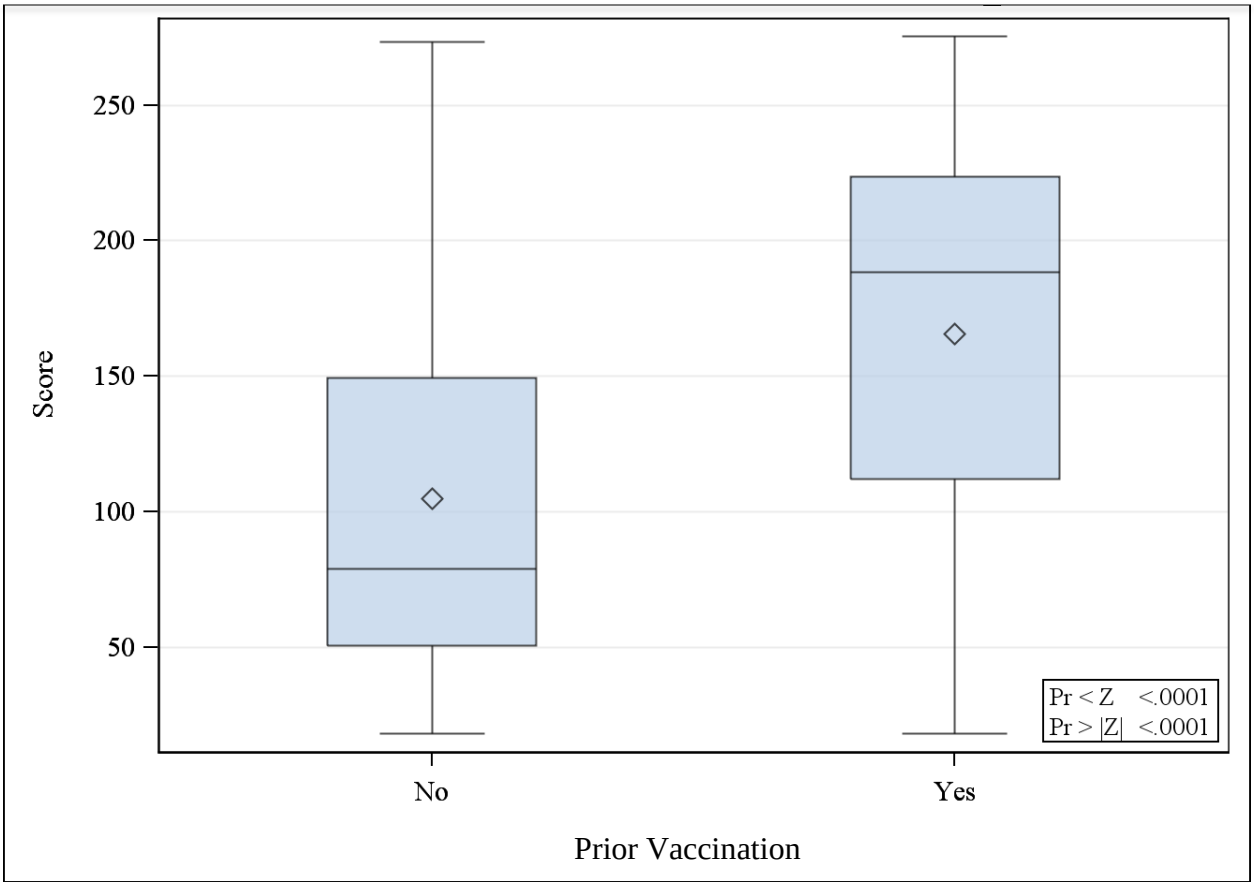

Figure 1. Wilxocon Scores for Charlson Comorbidity Index.

Patients with higher comorbidity index numbers are more likely to receive the *Influenza* vaccine

Patients who were vaccinated prior to admission were statistically significantly older in age ($p = 0.0001$). Figure 2 shows that the distribution of Wilcoxon Scores are uneven so the Kruskal-Wallis test was used to confirm that older patients were more likely to be vaccinated prior to admission ($p = 0.0001$).

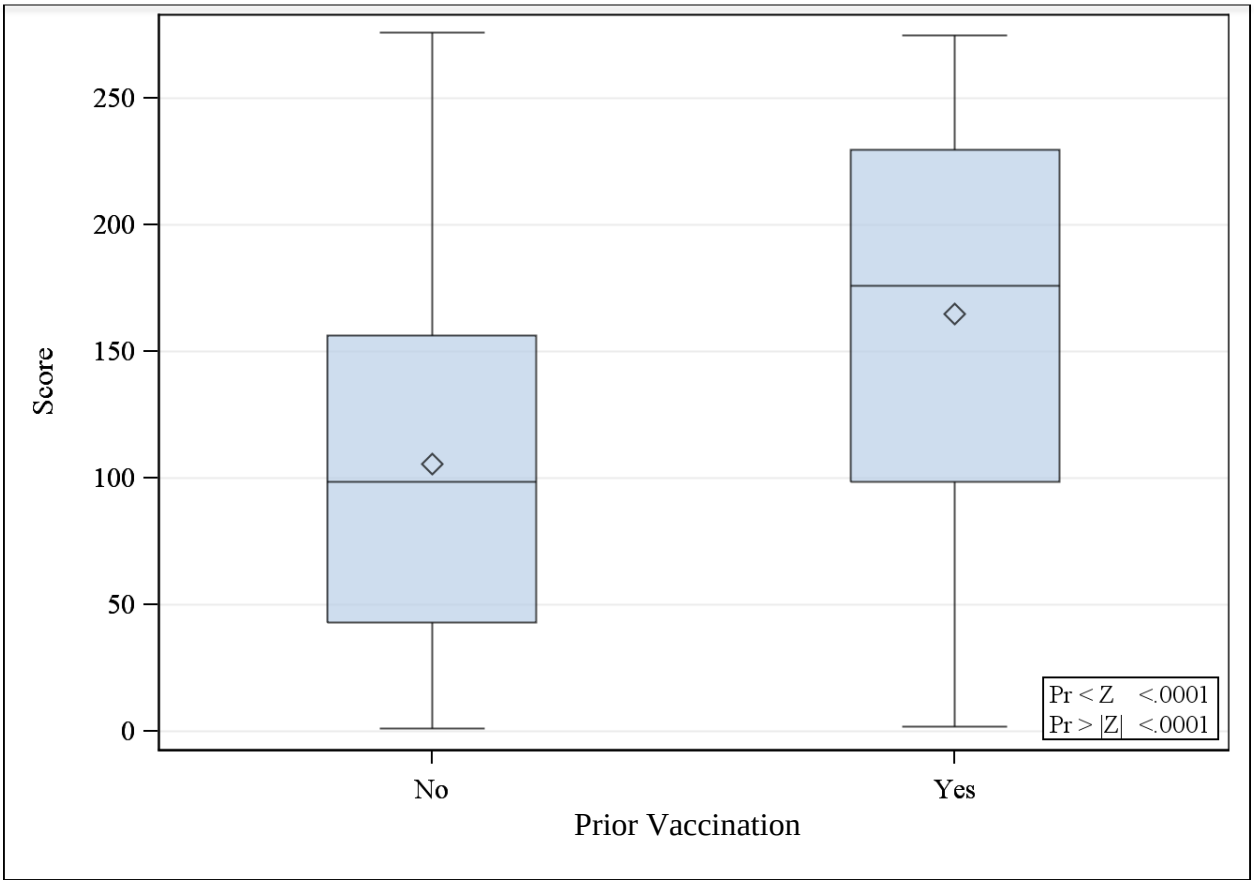

Figure 2. Wilcoxon Scores for Patient ages.

Older patients are more likely to receive the *Influenza* vaccine

After performing Fisher's exact tests using data from the contingency tables, there was no statistically significant difference between genders but racial minorities had lower rates of vaccination ($p = 0.0025$). Table 3 shows percentages of prior vaccination between racial groups and that African-Americans had lower percentages of vaccinations compared to Caucasians. Patients who received *Influenza* vaccination prior to admission were significantly less likely to have *Influenza* ($p = 0.0132$). Table 4 shows the number of patients who were positive or negative for *Influenza* and whether or not they were vaccinated prior to admission. There was no statistically significant difference between patients who stayed in the ICU, required a vent, were

readmitted on different days, or their mortality. The contingency tables for these variables can be found in Appendix B.

Table 3. Percentage of patients who were vaccinated prior to admission separated by race

	Race	
Prior Vaccination	**Caucasian**	**African-American**
No N=115	68 (59%)	47 (41%)
Yes N=142	112 (79%)	30 (21%)

Table 4. Prior vaccination separated by negative and positive cases of *Influenza*

Prior Vaccination	**Case (Positive *Influenza* test)**		
Frequency **Row Percent** **Column Percent**	**No**	**Yes**	**Total**
No	29 23.58% 33.33%	94 76.42% 49.74%	123 44.57%
Yes	58 37.91% 66.67%	95 62.09% 50.26%	153 55.43%
Total	87 31.52%	189 68.48%	276 100%

4.0 DISCUSSION

The most important observed result was *Influenza* vaccination reduced the rate of *Influenza* positivity among patients. There were a larger proportion of patients who were vaccinated prior to admission, who didn't get *Influenza*. In a very similar study, also completed at UPMC, the data analyzed demonstrated that the *Influenza* vaccine was an effective intervention that decreased the likelihood of ICU admission in patients hospitalized for *Influenza* with an odds ratio of 0.15[6]. In yet another similar study, researchers were able to conclude that hospital admissions caused by *Influenza*, pneumonia, bronchitis and emphysema were reduced by 63% due to the *Influenza* vaccine[4]. These three studies, including the present one, indicate how critical it is for people to get their *Influenza* vaccines in order to reduce the risk of illness and other *Influenza*-related complications that could lead to the patient being admitted to the hospital.

During the 2013-2014 *Influenza* season, the median age of patients who were vaccinated for *Influenza* was 53 while during the 2014-2015 *Influenza* season, the median age of patients who were vaccinated was 70. This difference could be because older patients with medical complications are encouraged to get the *Influenza* vaccine more so by their physician because of their increased risk of morbidity if they get *Influenza*[32]. In both seasons there were a higher percentage of females than males that were vaccinated, and a higher percentage of Caucasians vaccinated compared to African-Americans. Overall, there were no significant differences in

outcomes related to LOS, patients staying in the ICU, and patients requiring a ventilator between the two seasons. Readmission percentages were slightly higher in the 2013-2014 *Influenza* season while death percentages were slightly higher in the 2014-2015 *Influenza* season. Increased readmission during the 2013-2014 *Influenza* season could have been the result of lower vaccination rates (34.4% compared to 64.6%) and the observed increase in deaths during the 2014-2015 *Influenza* season was most likely due to the vaccine ineffective coverage (only 23%)[17] of the circulating viral strains.

Patients with a higher comorbidity index, individuals with more than one dangerous health condition, were more likely to be vaccinated. Older patients were also more likely to be vaccinated compared to younger patients. The CDC posted a report that showed similar results in other major cities during the 2014-2015 *Influenza* season. Chicago, New York City, and Philadelphia all had an increase in individuals aged 65 and older who received their *Influenza* vaccine with percentages at 62.1%, 58.2%, and 59.2%, respectively[2]. A lower percentage of racial minorities who were vaccinated prior to admission were observed. One study conducted an online survey that sampled participants from minority racial backgrounds as well as individuals living under the poverty level, to assess their reasons for not getting the *Influenza* vaccine during the 2009-2010 season[13]. In that study, African-Americans were the most likely racial group to have stated that they did not receive the vaccine because it was unavailable to them[13]. They were also the least likely racial group to think the vaccine was safe[13]. These results could reflect why there were a lower percentage of African-American individuals who received their *Influenza* vaccine prior to admission in our study.

4.1 LIMITATIONS

This study had several limitations including being a retrospective study, the small number of patients, the limited number of years included and being a single center study. Another limitation of this type of study is the potential for inaccurate reporting or documentation of prior vaccination by the patient, physician, and/or computer system. The patient being surveyed may not be able to accurately recall related details such as the date when they received their *Influenza* vaccine, or they may falsify information intentionally or unintentionally for whatever reason. Physicians might enter the information wrongly into the computer system or there may be a computer malfunction. This could lead to some errors in the data or skewed results. However, this study has many strengths, including the clearly defined cohorts of *Influenza* positive vs. *Influenza* negative control of patients being admitted to the hospital and undergoing respiratory viral panel testing after presenting with a respiratory illness. Moreover, this study addressed questions regarding both health care utilization as well as individual patient outcomes.

4.2 PUBLIC HEALTH SIGNIFICANCE

The diagnosis and treatment of *Influenza* can be a long and financially burdening experience for most patients. The most precise diagnosis (the RVP test) involves laboratory work and takes time to process. The treatment can vary depending on whether the patient was sick solely with *Influenza* or with a further *Influenza*-associated illness like pneumonia. If the patient had an *Influenza*-associated illness then they might need to be admitted to the ICU and need a vent, which could be costly and life threatening. Anti-viral drugs that are issued to patients can

be costly and have bad side effects. *Influenza* can also be a financial burden on an individual when they have to stay home from work. These factors can largely affect families with low socioeconomic status. For these reasons, it is important to have patients vaccinated against *Influenza*.

According to a study that measured the disease burden and costs of *Influenza* in 2003, the annual direct medical costs were approximately $10.4 billion, with a projected *Influenza* associated lost of earnings to be estimated at $16.3 billion annually, and a total economic impact annually of $87.1 billion[23]. While part of the costs are due to hospitalizations, the majority is due to a loss in productivity resulting from missed workdays and loss of lives[23]. Importantly, the *Influenza* vaccine can have a positive financial impact on a society considering that the vaccine prevented approximately 6.6 million *Influenza*-associated illnesses during the 2012-2013 season and 1.9 million during the 2014-2015 season, while preventing 79,000 hospitalizations and 67,000 hospitalizations in those seasons respectively[9].

4.3 FUTURE DIRECTION

The purpose of this study was to observe the effect of the *Influenza* vaccination on patients admitted to the hospital. Additional activities can be done to better understand the results of this study. An important direction would be to determine the reason behind the poor rates of *Influenza* vaccinations associated with racial minorities. Such a study could lead to a targeted increase the percentage racial minorities being vaccinated. Studies such as the one presented here could also be expanded to more locations in the Pittsburgh area to increase the sample size and to observe the effects of the *Influenza* vaccine on more than one hospital.

5.0 CONCLUSION

Influenza vaccination reduced the rate of *Influenza* positivity among inpatients during the 2013-2015 *Influenza* seasons. Patients who were older in age and/or with a higher comorbidity index were more likely to have been vaccinated prior to being admitted. There was no difference between genders, but racial minorities had a lower rate of vaccination. This information can be used to not only motivate and educate patients about the *Influenza* vaccine and its benefits but health care workers at UPMC Mercy as well.

APPENDIX A: TABLES AND FIGURES

LOS	ICU Care	ICU LOS	Vent Required	Days on Vent	Discharge Date (related)	Deceased Related Admission	Deceased	Death Date	Death related to Flu	Readmission	Readmission related to Flu	Flu Shot Prior to Admit	Month of Flu Shot	Flu Shot Given during Admit	Charlson CI
4.8 Days	No		No		12/18/2014	No	No		No	No		Unknown		No	0
18.9 Days	Yes	1 day	No		1/2/2015	No	No		No	61-90 days	No	No		No	6
2.7 Days	No		No		12/16/2014	No	No		No	No		Yes	October		6
1.6 Days	No		No		12/18/2014	No	No		No	No		No		No	7
4.8 Days	No		No		12/21/2014	No	No		No	No		No		No	6
3.9 Days	No		No		12/21/2014	No	No		No	No		No		No	3
6 Days	Yes	2 days	No		12/23/2014	No	No		No	No		Yes	October		3
5.4 Days	Yes	1 day	No		12/22/2014	No	No		No	No		No		No	3
2 Days	No		No		12/19/2014	No	No		No	1-30 days	No	No		Yes	2
4.9 Days	No		No		12/23/2014	No	No		No	31-60 days	No	No		No	6
6.1 Days	Yes	1 day	No		12/24/2014	No	No		No	1-30 days	No	Yes	September		8

Figure 3. An example of an excel spreadsheet that was used to collect data on patients

Table 5. Contingency table of prior vaccination by sex

Prior Vaccination	Sex		
Frequency Row Percent Column Percent	Female	Male	Total
No	71 57.72% 44.65%	52 42.28% 44.44%	123 44.57%
Yes	88 57.52% 55.35%	65 42.48% 55.56%	153 55.43%
Total	159 57.61%	117 42.39%	276 100%

Table 6. Contingency table of prior vaccination by ICU care

Prior Vaccination	ICU Care		
Frequency Row Percent Column Percent	No	Yes	Total
No	90 73.17% 47.87%	33 26.83% 37.50%	123 44.57%
Yes	98 64.05% 52.13%	55 35.95% 62.50%	153 55.43%
Total	188 68.12%	88 31.88%	276 100%

Table 7. Contingency table of prior vaccination by vent required

Prior Vaccination	Vent Required		
Frequency Row Percent Column Percent	No	Yes	Total
No	117 96.69% 45.00%	4 3.31% 28.57%	121 44.16%
Yes	143 93.46% 55.00%	10 6.54% 71.43%	153 55.84%
Total	260 94.89%	14 5.11%	274 100%

Table 8. Contingency table of prior vaccination by *Influenza* death

Prior Vaccination	*Influenza* Death		
Frequency Row Percent Column Percent	No	Yes	Total
No	117 98.32% 46.99%	2 1.68% 22.22%	119 46.12%
Yes	132 94.96% 53.01%	7 5.04% 77.78%	139 53.88%
Total	249 96.51%	9 3.49%	276 100%

Table 9. Contingency table of prior vaccination by readmission

Prior Vaccination	Readmission				
Frequency **Row Percent** **Column Percent**	**1-30 Days**	**31-60 Days**	**61-90 Days**	**No**	**Total**
No	50 40.65% 42.37%	12 9.76% 41.38%	6 4.88% 60.00%	55 44.72% 46.22%	123 44.57%
Yes	68 44.44% 57.63%	17 11.11% 58.62%	4 2.61% 40.00%	64 41.83% 53.78%	153 55.43%
Total	118 42.75%	29 10.51%	10 3.62%	119 43.12%	276 100%

APPENDIX B: COMORBIDITY INDEX TABLE

Table 10. Comorbidity Index Table

Weight	Clinical Conditions
1	Myocardial Infarct Congestive Cardiac insufficiency Peripheral vascular disease Dementia Cerebrovascular disease Chronic pulmonary disease Connective tissue disease Slight diabetes, without complications Peptic ulcers Chronic liver diseases or cirrhosis
2	Hemiplegia Moderate or severe kidney disease Diabetes with complications Tumors Leukemia Lymphoma
3	Moderate or severe liver disease
6	Malignant tumor, metastasis AIDS
Age Group	**Points**
<40	0
41-50	1
51-60	2
61-70	3
71-80	4
>80	5

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