

# Antiviral Use Is Associated with a Decrease in the Rate of Influenza-Related Complications and Healthcare Resource Utilization

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## INTRODUCTION

- The 2017-18 influenza season in the United States was considered highly severe due to increased rates of outpatient and emergency department (ED) visits and hospitalizations<sup>1</sup>
- Cumulative hospitalizations among younger age groups (50-65 years) were among the highest recorded (113.6 per 100,000 people compared with 62.6, 45.2, and 53.4 in the preceding 3 seasons)<sup>2</sup>
- Pneumonia and influenza-associated mortality rates exceeded 10.0% over 4 consecutive weeks during the 2017-18 season
- Among adults hospitalized for influenza >90% have an underlying medical condition that increases the risk for complications<sup>1</sup>
- The Centers for Disease Control and Prevention (CDC) recommends antiviral treatment with neuraminidase inhibitors within 48 hours of illness onset for individuals at higher risk for influenza complications<sup>3</sup>
- Evidence suggests that early antiviral treatment can shorten the duration of illness and reduce complications<sup>4-6</sup>
- However, the effectiveness of early antiviral treatment in reducing complications and improving health outcomes remains somewhat controversial<sup>7</sup>
- Although symptom relief has been seen as the most common measure of flu treatment efficacy, it may be of value to understand the importance of using antivirals and seeing their effects on rates and severity of flu complications
- The following study uses real-world US claims data from 3 influenza seasons (2014, 2015, 2016) to understand the frequency of influenza complications and to understand how intervention with antivirals may affect their occurrence

## METHODS

### Data source

- Data were extracted from the MarketScan Commercial Claims and Encounters Database and the MarketScan Medicare Supplemental and Coordination of Benefits Database (IBM Watson Health, Cambridge, MA).
- The databases include employees, dependents, and retirees insured by employer-sponsored commercial and Medicare insurance
- The claims files capture inpatient and outpatient care, use of facilities and services, prescription fills, and payment information

### Study cohorts

- The index date was defined as the first influenza event in the season. Patients had to be continuously enrolled from 1 year preceding to 91 days after the index date.
- The study sample included patients with a billed diagnosis of influenza during 3 influenza seasons:
  - 2014: 05/01/2014-04/30/2015
  - 2015: 05/01/2015-04/30/2016
  - 2016: 05/01/2016-04/30/2017
- The treated cohort had to have received any of the following influenza treatments within 48 hours of the index date as identified via appropriate NDC and HCPCS codes: oseltamivir phosphate, oral; zanamivir, inhalation powder; rimantadine hydrochloride; or peramivir injection
- Untreated patients were propensity score matched to treated patients, and had exact match on age categories, gender, region, CCI categories, and months of index events.

### Outcomes

- Outcomes were assessed at days 30 and 90 after the index date

### Complications

- Any newly diagnosed respiratory-related complications occurring during the 2 follow-up windows were identified using relevant ICD-9 and ICD-10 codes. These were categorized as:
  - All respiratory-related complications
  - Selected respiratory conditions: influenza, asthma, chronic obstructive pulmonary disease (COPD), or infection

### Healthcare resource utilization (HRU)

- Healthcare resource utilization included: outpatient visits, hospitalizations, ED visits, intensive care/critical care unit (ICU/CCU) stay, prescriptions filled, and mechanical ventilator use

### Costs

- Costs were calculated as medical (hospitalization, ED, and outpatient), prescription (outpatient pharmacy services), and total costs (medical + prescription)
- Costs were adjusted to 2017 dollars using the Medical Component of Consumer Price Index (CPI)

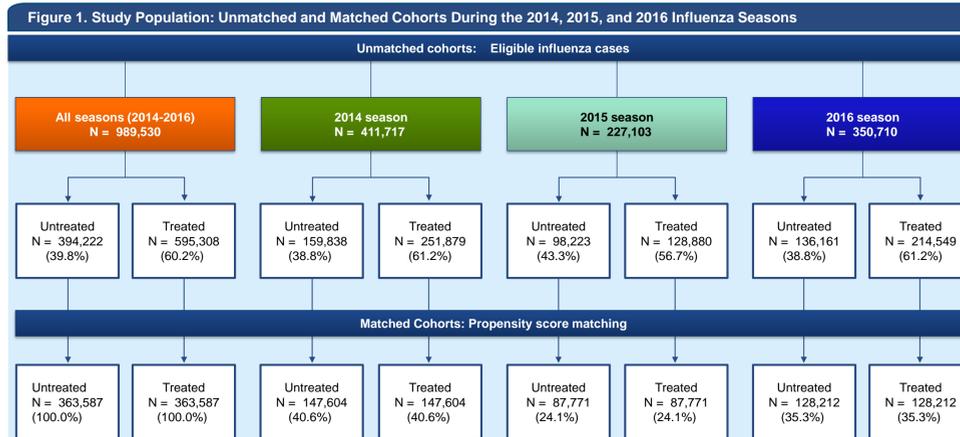
### Statistical analyses

- Complications and HRU in the 30 and 90 days post diagnosis were compared between patients who received antiviral treatment and those who did not
- Patients who received an antiviral within 48 hours of the first influenza-related encounter were identified and propensity score-matched to a comparative cohort without antiviral use but with comparable baseline characteristics; main covariates are listed in Table 1
- Cohorts were compared with chi-squared test for categorical measures, Wilcoxon signed-rank test for counts and costs, and Student's t test for age

## RESULTS

### Study population

- Overall, 989,530 cases of influenza were identified over 3 influenza seasons, with 60.2% of patients receiving antiviral treatment (Figure 1)
- The percentage of patients receiving antiviral treatment in each flu season ranged between 56.7% and 61.2%
- Patients with any flu diagnosis/visit comprised 2.4%, 1.2%, and 2.3% of all commercially insured patients for the 2014, 2015, and 2016 influenza seasons, respectively
- Using propensity score matching, a treated and an untreated cohort with 363,587 patients each was identified (Figure 1)



### Baseline characteristics

- Treated and untreated groups were well matched overall and by season for the listed variables (Table 1)
- In the study population overall:
  - The mean age was ~29 years, 10.1% were younger than 5 years and 4.7% were older than 65 years
  - ~25% of patients overall had been hospitalized or visited the ED in the preceding year;
  - 83% had no baseline comorbidities; the most common comorbidities were chronic pulmonary disease (~12%), asthma (8.4%), diabetes with or without complications (7.2%), and obesity (5.8%)

Table 1. Baseline Demographic and Clinical Characteristics of Matched Cohorts During the 2014, 2015, and 2016 Influenza Seasons

	Untreated N=363,587	Treated N=363,587	Untreated N=363,587	Treated N=363,587
<b>Index setting</b>			CCI, mean (SD)	0.28 (0.82)
Inpatient	38,341 (10.5%)	27,206 (7.5%)	CCI=0	300,709 (82.7%)
ED	7,748 (2.1%)	1,313 (0.4%)	CCI=1	43,120 (11.9%)
Outpatient	317,498 (87.3%)	335,068 (92.2%)	CCI=2	43,015 (11.8%)
<b>Index age, mean (SD)</b>	28.91 (21.7)	28.98 (21.4)	CCI=3+	8,044 (2.2%)
0-4 y	36,919 (10.2%)	36,919 (10.2%)	<b>Month of index event</b>	
5-17 y	117,477 (32.3%)	117,477 (32.3%)	May-September	22,089 (6.1%)
18-49 y	130,721 (36.0%)	130,721 (36.0%)	October-November	20,464 (5.6%)
50-64 y	61,560 (16.9%)	61,560 (16.9%)	December	55,782 (15.3%)
65+ y	16,910 (4.7%)	16,910 (4.7%)	January	71,282 (19.6%)
<b>Sex</b>			February	89,566 (24.6%)
Male	166,790 (45.9%)	166,790 (45.9%)	March-April	104,404 (28.7%)
Female	196,797 (54.1%)	196,797 (54.1%)	<b>HRU in previous 12 months</b>	
<b>Region</b>			Any inpatient	15,734 (4.3%)
Northeast	55,778 (15.3%)	55,778 (15.3%)	Any ED	75,885 (20.9%)
Northcentral	59,919 (16.5%)	59,919 (16.5%)	<b>Special conditions</b>	
South	208,585 (57.4%)	208,585 (57.4%)	Asthma	30,648 (8.4%)
West	37,785 (10.4%)	37,785 (10.4%)	COPD	11,598 (3.2%)
Unknown	1,520 (0.4%)	1,520 (0.4%)	Cystic fibrosis	2,342 (0.6%)
<b>Health plan type</b>			Overweight/obesity	20,956 (5.8%)
HMO	31,722 (8.7%)	31,094 (8.6%)	Pregnancy	5,122 (1.4%)
PPO	211,093 (58.1%)	212,056 (58.3%)	Diabetes (with or without complications)	26,196 (7.2%)
POS	24,421 (6.7%)	24,277 (6.7%)		
Other	96,351 (26.5%)	96,160 (26.4%)		

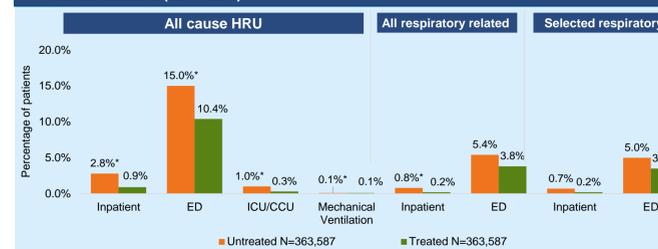
CCI, Charlson comorbidity index; COPD, chronic obstructive pulmonary disease; ED, emergency department; HMO, health maintenance organization; HRU, healthcare resource utilization; POS, point of service; PPO, preferred provider organization; SD, standard deviation.

### Healthcare Resource Utilization

#### Incidence of hospital resource use

- Healthcare resource utilization over the first 30 days in individual and all 3 seasons combined (Figure 2) showed that there were significantly fewer patients in the treated cohort that utilized inpatient, ICU/CCU, or ED services or mechanical ventilation for any cause in comparison to the untreated cohort (P < 0.0001 for all comparisons)
- A similar trend was identified when 90-day HRU was examined, with significantly lower HRU in the treated vs the untreated cohort (for all seasons combined: hospitalization, 1.6% vs 3.5%; ED visits 13.5% vs 18.2%; ICU/CCU admission, 0.5% vs 1.2%; and mechanical ventilator use, 0% vs 0.1%) (P < 0.0001 for all comparisons)
- Healthcare resource utilization for all respiratory conditions and for selected respiratory conditions was lower among treated patients than among untreated patients during the first 30 days post diagnosis (Figure 2 and Table 2)
- Healthcare resource utilization over 90 days was also lower for all respiratory-related conditions (hospitalization, 0.3% vs 0.9%; ED visits, 4.3% vs 6.0%) and the selected respiratory conditions (hospitalization, 0.2% vs 0.7%; ED visits, 3.7% vs 5.2%)

Figure 2. Healthcare Resource Utilization Over the First 30 Days in Matched Cohorts for All Influenza Seasons (2014-2016)



ED, emergency department; CCU, critical care unit; ICU, intensive care unit.

\*P < 0.0001 for untreated vs treated cohort

- In the first 30 days, the mean number of hospitalizations and ED visits for any cause was lower in the treated cohort than in the untreated cohort, but the number of prescriptions filled was higher in the treated group (Table 2)
- This trend was also observed for individual seasons and was similar over the 90-day post-diagnosis period

Table 2. Mean Number of Visits/Stays/Refills Over the First 30 Days in Matched Cohorts for All Influenza Seasons

	Untreated N=363,587	Treated N=363,587
<b>All cause, mean (SD)</b>		
Inpatient stays	0.03 (0.18)*	0.01 (0.10)
ED visits	0.19 (0.50)*	0.13 (0.41)
Outpatient visits	1.92 (1.85)*	1.84 (1.58)
Prescription fills	1.19 (1.42)*	1.83 (1.27)
<b>All respiratory-related, mean (SD)</b>		
Inpatient stays	0.01 (0.09)*	0.00 (0.05)
ED visits	0.06 (0.29)*	0.04 (0.23)
Outpatient	0.56 (0.98)*	0.54 (0.83)
<b>Selected respiratory-related, mean (SD)</b>		
Inpatient stays	0.01 (0.08)*	0.00 (0.40)
ED visits	0.06 (0.26)*	0.04 (0.22)
Outpatient visits	0.47 (0.77)*	0.47 (0.64)

ED, emergency department; SD, standard deviation.

\*P < 0.0001, \*\*P < 0.05, for untreated vs treated cohort.

### Costs

- Influenza treatment resulted in significantly lower mean all-cause total costs and medical costs (inpatient, ED, and outpatient) over the first 30 days in the combined treated cohort compared with the untreated cohort (\$1125 vs \$1637), despite higher prescription costs (\$305 vs \$140) (Table 3)

- Mean 90-day all-cause total and medical costs were also lower in the treated group in each season and all 3 seasons combined (Total costs: \$2282 vs \$3001; medical: \$1705 vs \$2621; prescription: \$578 vs \$380)
- Mean medical costs for all respiratory-related complications were significantly lower in the treated group both at day 30 (Table 3) and at day 90
- Mean medical costs for selected respiratory-related complications did not differ between treated and untreated cohorts

Table 3. Mean (SE) Costs Over the First 30 Days in Treated and Untreated Cohorts for All Influenza Seasons

	Untreated N=363,587	Treated N=363,587
<b>All cause costs</b>		
Total (include prescriptions)	1637 (16)*	1125 (9)
Medical (exclude prescriptions)	1498 (16)*	820 (9)
Inpatient	717 (14)*	212 (8)
ED	267 (2)*	187 (2)
Outpatient	514 (4)**	421 (3)
Prescriptions	140 (2)*	305 (2)
<b>All respiratory-related costs</b>		
Medical (exclude prescriptions)	349 (6)**	183 (3)
Inpatient	156 (5)*	33 (2)
ED	78 (1)*	58 (1)
Outpatient	115 (2)*	92 (1)
<b>Selected respiratory-related costs</b>		
Medical (exclude prescriptions)	264 (5)	140 (2)
Inpatient	119 (4)*	23 (2)
ED	64 (1)*	50 (1)
Outpatient	81 (1)*	66 (0)

ED, emergency department.

\*P < 0.0001, \*\*P < 0.05, for untreated vs treated cohort.

## CONCLUSIONS

- Data for the last 3 available influenza seasons (2014, 2015, 2016) showed that anti-influenza treatment significantly reduced HRU in the treated cohort in comparison to the untreated cohort over 30-day and 90-day periods post diagnosis for the following:
  - Hospitalizations, ED use, ICU/CCU admission, and ventilator use
- Healthcare resource utilization was also reduced in treated patients for all respiratory complications and for selected respiratory conditions, including influenza, asthma, COPD, and infections
- Overall costs and medical costs were reduced significantly with antiviral treatment, despite higher prescription costs
- These findings suggest that treatment for influenza may improve outcomes and lower costs

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