Mortality and Economic Burden of Seasonal Influenza Among Elderly Medicare Beneficiaries With and Without Antiviral Treatment

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BACKGROUND & OBJECTIVE

- Older adults are at high risk of influenza infection and complications leading to high healthcare resource utilization (HCRU) and death[1,2]
- Antiviral medications (antivirals) that improve clinical outcomes and reduce mortality are available;[3] however, more than half of the elderly and other persons at high risk do not receive antiviral therapy[1]
- The literature lacks a recent, real-world comparison of clinical and economic burden between antiviral treated and untreated Medicare beneficiaries diagnosed with influenza[4]
- Objective: To examine acute complications, HCRU and costs, and mortality associated with seasonal influenza in elderly Medicare beneficiaries who are treated vs. untreated with antivirals

[1] Nichol KL, et al. *N Engl J Med*. 1994;331(12):778-84. [2] Putri WCWS, et al. *Vaccine*. 2018;36(27):3960-6. [3] Nichol KL, et al. *Clin Infect Dis*. 2009;48(3):292-8. [4] Gilman BH, et al. *Am J Prev Med*. 2007;32(2):107-15.

METHODS

Study design

- Retrospective analysis using 2015-2019 claims data from the 100% Medicare Research Identifiable Files

Patient population

- Medicare beneficiaries ≥66 years old who received an influenza diagnosis in the outpatient setting (≥1 outpatient medical claim with ICD-10-CM influenza diagnosis code: J09.xx, J10.xx, J11.xx) during the identification period of October-March each year between 2016 and 2019 (i.e., 3 full flu seasons)
- Index date: date of first claim with influenza diagnosis within each flu season
  - For patients with flu in multiple seasons, one season was randomly picked
- Of the above, 2 cohorts were created: 1) Treated patients who received an approved antiviral for influenza (claims with a drug code for zanamivir, oseltamivir, peramivir, or baloxavir) ≤2 days after index date; 2) untreated patients who did not receive treatment within 6 months post-index
- Untreated patients were matched 1:1 to treated patients using propensity score matching (greedy nearest neighbor with caliper width of 0.1 of the standard deviation of the logit of the propensity score)
  - The propensity for initiating antiviral was estimated using logistic regression with independent variables of flu season year, age, sex, geographic region, race, flu vaccine status, usual physician specialty, Charlson Comorbidity Index, number of chronic conditions, dual-eligible status, and each individual high-risk condition
  - Patients were also matched exactly on the flu season year and flu vaccine status
- Continuous enrollment in Medicare FFS Parts A/B and Part D during the 1-year period prior to the index date (baseline) and during the 6 months after index (follow-up), or until death, whichever occurred first, was required
- Exclusion criteria:
  - Antiviral for influenza ≤2 months prior to the index date
  - For treated patients: antiviral medication used for prophylaxis as indicated by a total days' supply of antiviral of ≥10 days within 10 days of the first antiviral claim

METHODS (cont'd)

Measures

- Baseline measures included demographics and comorbidities
- Outcome variables, measured during the follow-up period, included:
  - Acute complications during an inpatient hospitalization
  - HCRU: inpatient hospitalization, emergency department (ED) visits, outpatient visits (excluding ED visits), other (skilled nursing facility [SNF], home health agency [HHA], hospice, received durable medical equipment [DME]), pharmacy
  - Costs (all-cause and respiratory-related [defined as a claim with a primary diagnosis of respiratory disease: ICD-10-CM: J00.xx-J99.xx])
  - Mortality

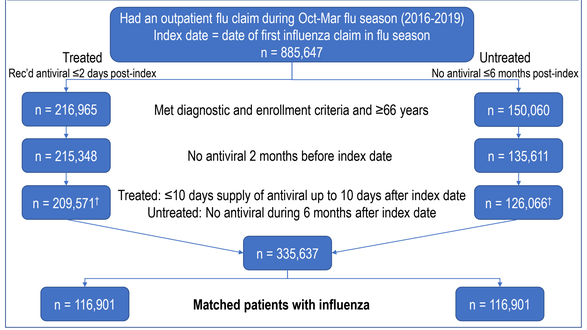
Statistical analysis

- Balance diagnostics after matching were assessed using standardized mean difference
- Descriptive statistics for all baseline and outcome measures were reported by treatment status
- All outcome measures between matched treated and untreated patients with influenza were compared using t-test or Chi-square test for continuous and categorical variables, respectively

RESULTS

- The final matched cohort consisted of 116,901 matched pairs (**Figure 1**)
- Demographics and clinical characteristics are presented in **Table 1**
- During follow-up, 8.3% of treated patients experienced an acute complication vs.15.7% of untreated patients **(Figure 2)**

Figure 1. Patient attrition



† 18,155 (8.7%) treated and 29,411 (23.3%) untreated patients had an inpatient or outpatient hospital claim within 2 days since the index date.

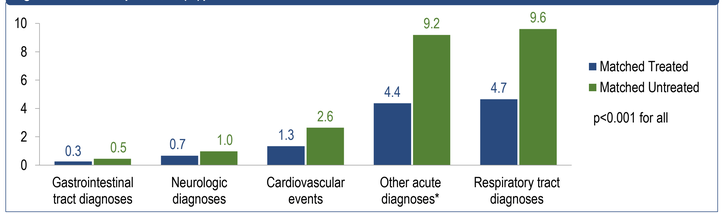
RESULTS (cont'd)

Table 1. Baseline characteristics and measures

	Matched Treated N = 116,901 (50.0%)	Matched Untreated N = 116,901 (50.0%)	Standardized Mean Difference[a]
Age, year, mean (SD)	75.6 (7.0)	75.6 (7.3)	-0.001
Age group			0.046
66-74, n (%)	61,206 (52.4)	62,325 (53.3)	
75-84, n (%)	40,715 (34.8)	38,448 (32.9)	
85+, n (%)	14,980 (12.8)	16,128 (13.8)	
Female, n (%)	71,427 (61.1)	71,904 (61.5)	-0.008
Race, n (%)			0.001
White	106,716 (91.3)	106,594 (91.2)	
Black	4,875 (4.2)	4,914 (4.2)	
Other/Unknown	5,310 (4.5)	5,393 (4.6)	
Year of flu season,[b] n (%)			n/a[c]
2016	28,976 (24.8)	28,976 (24.8)	
2017	57,028 (48.8)	57,028 (48.8)	
2018	30,897 (26.4)	30,897 (26.4)	
Charlson Comorbidity Index, mean (SD)	2.4 (2.6)	2.4 (2.6)	0.014
Number of chronic conditions, mean (SD)	5.8 (2.4)	5.8 (2.5)	0.003
Received flu vaccine for the current season prior to the index date, n (%)	71,730 (61.4)	71,730 (61.4)	n/a[c]
CDC-defined high-risk conditions, n (%)	107,564 (92.0)	107,090 (91.6)	0.015
Asthma	13,948 (11.9)	13,793 (11.8)	0.004
Chronic lung disease	35,212 (30.1)	34,663 (29.7)	0.010
Heart disease	47,970 (41.0)	47,913 (41.0)	0.001
Blood disorders	37,510 (32.1)	37,388 (32.0)	0.002
Endocrine disorders	63,060 (53.9)	63,288 (54.1)	-0.004
Kidney disorders	19,796 (16.9)	19,309 (16.5)	0.011
Liver disorders	7,287 (6.2)	7,250 (6.2)	0.001
Metabolic disorders	92,370 (79.0)	92,207 (78.9)	0.003
Extreme obesity	3,507 (3.0)	3,508 (3.0)	-0.000
COPD	19,674 (16.8)	19,135 (16.4)	0.012
Immunosuppressive conditions (MS, HIV, RA)	5,033 (4.3)	5,092 (4.4)	-0.002

[a] The absolute value of standardized mean difference <0.2 is considered small effect size; therefore, an indicator of good match. [b] Flu season defined as October-March of each year (2016-2019). [c] Matched exactly.

Figure 2. Acute complications (%)†



† Percentages <0.50 not shown (treated vs. untreated): endocrine diagnoses (0.06% vs. 0.11%), influenza with other manifestations (0.07% vs. 0.18%), hematologic diagnoses (0.07% vs. 0.11%). * Includes acute kidney failure (3.2% vs. 6.3%), sepsis (2.1% vs. 4.9%), bacteremia (0.14% vs. 0.34%), rhabdomyolysis (0.09% vs. 0.29%), complications of transplanted organ (0.04% vs. 0.10%), and anaphylaxis (not reported per CMS cell suppression policy).

Healthcare utilization and costs (Table 2)

- Rates of all-cause hospitalizations for treated vs. untreated were 13.9% vs. 22.7% (p<0.001); rates of respiratory-related hospitalizations for treated vs. untreated were 4.2% vs. 9.0% (p<0.001)
- Mean (SD) total all-cause and respiratory-related costs for treated vs. untreated were $9,830 ($18,616.0) and $900 ($4,016.4) vs. $13,207 ($24,405.1) and $2,024 ($7,623.7), respectively (p<0.001 for all)

Mortality

- All-cause mortality ≤6 months from index was 1.6% vs. 4.3% among treated vs. untreated (p<0.001) (results not shown)

Table 2. Healthcare utilization and costs[a]

	N = 116,901 (50.0%)	N = 116,901 (50.0%)
ALL-CAUSE		
Any inpatient hospitalizations, n (%)	16,293 (13.9)	26,501 (22.7)
Hospital stay days among utilizers, mean (SD)	6.2 (8.4)	8.5 (11.2)
Any ICU, n (%)	4,971 (4.3)	9,206 (7.9)
Any inpatient hospitalizations with ventilator use, n (%)	1,042 (0.9)	2,508 (2.1)
Any ED visits, n (%)	22,066 (18.9)	25,125 (21.5)
No. of office visits, mean (SD)	9.8 (8.1)	9.3 (8.1)
Any outpatient hospitalizations (excluding ED visits), n (%)	74,510 (63.7)	72,676 (62.2)
SNF care, n (%)	2,890 (2.5)	8,519 (7.3)
Hospice care, n (%)	1,372 (1.2)	3,410 (2.9)
HHA visit, n (%)	7,695 (6.6)	14,408 (12.3)
DME claim, n (%)	32,944 (28.2)	33,750 (28.9)
Total healthcare costs ($), mean (SD)	9,830 (18,616.0)	13,207 (24,405.1)
RESPIRATORY-RELATED[b]		
Any respiratory inpatient hospitalizations, n (%)	4,899 (4.2)	10,534 (9.0)
Respiratory hospital stay days among utilizers, mean (SD)	4.1 (4.9)	6.1 (7.4)
Any respiratory ED visits, n (%)	3,813 (3.3)	4,699 (4.0)
No. of respiratory office visits, mean (SD)	1.4 (2.1)	1.2 (2.0)
Any respiratory outpatient hospitalizations (excluding ED visits), n (%)	8,469 (7.2)	9,421 (8.1)
Respiratory SNF care, n (%)	662 (0.6)	3,193 (2.7)
Respiratory hospice care, n (%)	199 (0.2)	645 (0.6)
Respiratory HHA visit, n (%)	1,615 (1.4)	3,696 (3.2)
Respiratory DME claim, mean (SD)	6,599 (5.6)	8,216 (7.0)
Respiratory costs ($), mean (SD)	900 (4,016.4)	2,024 (7,623.7)

ED: emergency department visits; DME: durable medical equipment; HHA: home health agency; SD: standard deviation; SNF: skilled nursing facility. [a] P<0.001 for all outcomes. [b] Respiratory-related defined as a claim with a primary diagnosis of respiratory disease: ICD-10-CM: J00.xx-J99.xx.

CONCLUSION

- Our study shows that lack of antiviral treatment is associated with increased mortality, healthcare resource utilization, and economic burden in elderly Medicare beneficiaries with seasonal influenza, a population already at risk for increased resource use and associated costs compared to their counterparts without influenza
- Future study should assess whether choice of influenza antivirals affect real-world clinical and economic outcomes in older adults and other high-risk patients

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