

Outcomes of Antiviral Treatment for Influenza in Type 2 Diabetes

Benjamin D. Lewing, PhD; Christopher Wallick, PharmD; Tu My To, PhD; Henry Masters III, MD; Parul Dayal, PhD; Stephan W. Korom, MD; and Selina Tam, PharmD

Type 2 diabetes (T2D) is a chronic metabolic disease characterized by increased blood glucose levels arising from inadequate insulin secretion and impaired response to insulin. The prevalence of T2D in the United States is estimated at more than 30 million (~10.5% of the population), and an additional 88 million adults in the United States (34.5%) have prediabetes.¹ Influenza is a contagious viral infection of the respiratory tract that can lead to complications resulting in hospitalization or death. Since 2010, influenza has resulted in up to 45 million illnesses, 810,000 hospitalizations, and 61,000 deaths annually.² Although infection with an influenza virus typically causes a self-limited illness, the consequences of influenza are more serious in individuals with T2D. Approximately 30% of adults recently reported to be hospitalized for influenza have diabetes.³ Influenza infection can act as a trigger for acute complications in patients with cardiovascular or cerebrovascular disease⁴⁻⁶ and enhance the already-increased risk of heart attack and stroke in patients with diabetes.⁷ Glucose metabolism may also be dysregulated, resulting in poor glucose control that can lead to metabolic complications such as diabetic ketoacidosis.^{8,9} In turn, diabetes increases the severity of influenza infection, and patients with diabetes have worse outcomes after influenza infection than patients without diabetes, including higher rates of hospitalization, intensive care unit admission, and death.^{10,11} Many patients with diabetes also have comorbidities, such as obesity, that can influence the severity of the infection.¹²⁻¹⁴

Vaccination remains the principal strategy to control influenza and its complications in patients with chronic conditions.^{3,15} Patients with T2D derive substantial benefits from seasonal vaccination, but coverage rates remain suboptimal.^{16,17} To provide a second line of defense after vaccination by shortening the duration of illness and reducing the risk of complications, guidelines recommend early treatment (within 48 hours of symptom onset) with antivirals, particularly among high-risk patients such as those with diabetes.^{18,19} Currently recommended antivirals include the neuraminidase inhibitors oseltamivir (Tamiflu), zanamivir (Relenza), and peramivir (Rapivab) and the cap-dependent endonuclease inhibitor baloxavir marboxil

ABSTRACT

OBJECTIVES: To evaluate the long-term effects of antiviral treatment on influenza-related health care resource utilization (HCRU) and costs in patients with type 2 diabetes (T2D) and a diagnosis of influenza.

STUDY DESIGN: Retrospective cohort study.

METHODS: Claims data from the IBM MarketScan Commercial Claims Database were used to identify patients with T2D and a diagnosis of influenza between October 1, 2016, and April 30, 2017. Patients who received antiviral treatment within 2 days of influenza diagnosis were identified and propensity score-matched 1:1 with a comparator cohort of untreated patients. HCRU (number of outpatient visits, emergency department visits, hospitalizations, and duration of hospitalization) and costs were assessed over 1 full year and over each quarter after influenza diagnosis.

RESULTS: Treated and untreated matched cohorts consisted of 2459 patients each. In the treated cohort vs the untreated cohort, emergency department visits were reduced 24.6% over 1 year after influenza diagnosis (mean [SD], 0.94 [1.76] vs 1.24 [2.47] visits; $P < .0001$) and were also reduced significantly during each quarter; the duration of hospitalization decreased 35.6% in the treated cohort vs the untreated cohort over 1 full year (mean [SD], 0.71 [3.36] vs 1.11 [5.60] days; $P < .0023$). Mean (SD) total health care costs were 17.68% lower in the treated cohort (\$20,212 [\$58,627]) than in the untreated cohort (\$24,552 [\$71,830]) over a whole year following the index influenza visit ($P = .0203$).

CONCLUSIONS: Antiviral treatment in patients with T2D and influenza was associated with significantly lower HCRU and costs over at least 1 year after infection.

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TAKEAWAY POINTS

- We used insurance claims data to evaluate the long-term effects of antiviral treatment on health care resource utilization and costs in patients with type 2 diabetes and a diagnosis of influenza.
- ▶ After adjusting for differences between treated and untreated groups in baseline clinical and demographic characteristics, antiviral treatment was associated with a reduced number of emergency department visits, shorter duration of hospitalization, and lower total health care costs both over a full year and in each quarter.
- ▶ Prompt antiviral treatment may reduce influenza-related health care resource utilization and costs in patients with type 2 diabetes.

METHODS

Data Source

Data for this study were extracted from the IBM MarketScan Commercial Claims Database. These data included health insurance claims across the continuum of care (eg, inpatient, outpatient, outpatient pharmacy, carve-out behavioral health care) and enrollment data from large employers and health plans across the United States that provide private health care coverage for more than 203 million employees, their spouses, and

dependents.³¹ The study used deidentified data and was exempt from institutional review board review. The research was compliant with the Health Insurance Portability and Accountability Act.

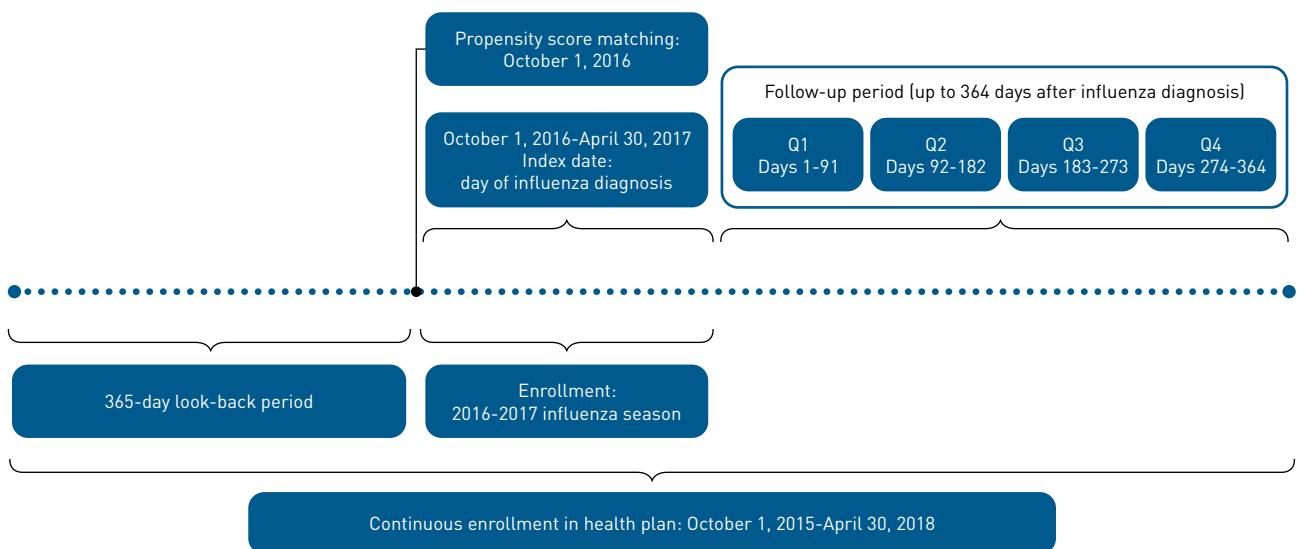
Study Design

This was a retrospective cohort study (Figure 1). Patients 18 years and older with T2D were identified using *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)* codes and *International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM)* codes. A previously validated algorithm was used to define patients with a diagnosis of T2D as those with at least 2 outpatient claims that included a diagnosis of T2D within 2 years or 1 inpatient claim with a diagnosis of T2D, together with at least 1 prescribed antihyperglycemic drug during the look-back period (October 1, 2015–October 1, 2016).³² Patients with a diagnosis of type 1 diabetes (defined as those with 3 outpatient or 2 inpatient claims) were excluded.

(Xofluza).¹⁸ In the general population, early treatment with antivirals has been shown to reduce the severity and duration of illness, as well as influenza-related complications and hospitalization.²⁰⁻²² In patients with preexisting cardiovascular disease, antiviral agents may protect against recurrent cardiac events.²³ However, rates of antiviral prescribing are low both in the general population²⁴⁻²⁶ and among high-risk patients with respiratory illness.^{27,28}

We recently showed that influenza infection has a significant long-term impact on morbidity in patients with T2D, including worsening of diabetes.²⁹ However, scant data are available on antiviral treatment in patients with diabetes,³⁰ and there is an unmet need to quantify the long-term treatment effect of antivirals in patients with T2D. In this study, we used real-world US claims data from the 2016–2017 influenza season to investigate the long-term effect of antiviral treatment on influenza-related health care resource utilization (HCRU) and costs in patients with T2D over a 1-year period following infection.

FIGURE 1. Study Design



Q, quarter.

The study enrolled patients with T2D who received a diagnosis of influenza between October 1, 2016, and April 30, 2017. Patients were included if they had a claim associated with a diagnosis suggesting influenza (*ICD-9-CM* codes 487.xx or 488.xx; *ICD-10-CM* codes J09.xx, J10.xx, or J11.xx). Patients with an inpatient diagnosis of influenza were excluded because less than 3% of the study population received this diagnosis in an inpatient setting; additionally, patients with an inpatient influenza diagnosis are not comparable with those with a diagnosis outside an inpatient setting. Patients also needed to be continuously enrolled in their health plan from October 1, 2015, through April 30, 2018. The study included a look-back period (October 1, 2015–October 1, 2016). The index date was the date of first influenza diagnosis between October 1, 2016, and April 30, 2017. The follow-up period was the 364 days following the index date.

The treated cohort consisted of patients who had a claim for an antiviral agent (oseltamivir, zanamivir, rimantadine, or peramivir) within 2 days of the index date. Treated patients were propensity score–matched 1:1 with untreated control patients using caliper matching (caliper equal to 0.2 of the SD of the logit of the propensity score). Patients were matched on October 1, 2016, with a 1-year look-back period to create the propensity scores. The propensity score model used several covariates that predicted treatment with antivirals. These included age; sex; region; health plan type; receipt of influenza vaccine; conditions considered to increase risk of severe influenza complications (neurologic disorders, blood disorders, liver disease, pulmonary disorders, heart disease, kidney disease, and obesity)³³; Diabetes Complications Severity Index (DCSI), a 14-level metric validated for use in claims analyses to quantify the severity of diabetes complications (cardiovascular, cerebrovascular, or metabolic complications; retinopathy; nephropathy; neuropathy; and peripheral vascular disease) and updated using *ICD-10-CM* codes^{34,35}; diabetes drug classification (a proxy for the severity of diabetes based on the American Diabetes Association diabetes pharmacologic step therapy guidelines³⁶ as described in earlier work²⁹); all-cause hospitalization in the preceding 12 months; and an emergency department (ED) visit in the preceding 12 months. A comorbidity index was not used because of overlap with the DCSI and the number of conditions considered to increase risk of severe influenza complications.

Outcomes

Outcomes were assessed for the full year and for each of the 4 quarters (each 91 days) following the diagnosis of influenza. Metrics included mean number of outpatient visits, ED visits, and hospitalizations; mean duration of hospitalization; and total medical costs (defined as total costs of all outpatient, inpatient, and ED visit claims, adjusted to 2018 US\$).

Statistical Analysis

Following propensity score matching, the cohort balance was compared using the standardized difference, with a standardized

difference of less than 0.10 considered to indicate negligible correlation.³⁷ To assess differences between the 2 cohorts, prematch and postmatch variables were compared using the *t* test for continuous variables and the χ^2 test for categorical variables.

Outcomes for each time period (quarters 1–4 [Q1–Q4] and the full year) were compared between treated and matched untreated cohorts using the *t* test. Analyses were conducted with SAS version 9.4 (SAS Institute Inc), with statistical significance set at 0.05.

RESULTS

Study Population

Of 7776 patients with T2D who received a diagnosis of influenza in the 2016–2017 influenza season, 5115 patients were treated with an antiviral agent and 2463 were untreated; 198 patients whose influenza was diagnosed in the inpatient setting were excluded (**eAppendix Figure** [available at ajmc.com]). Following propensity score matching, treated and untreated cohorts of 2459 patients each were identified. Other than 1 patient who received zanamivir and 1 patient who received rimantadine, all patients in the treated cohort had received oseltamivir.

Several characteristics differed between the cohorts before propensity score matching, including the number of high-risk conditions for severe influenza complications, DCSI score, sex, age group, receipt of influenza vaccine, and ED visit in preceding 12 months (**Table 1**). Following propensity score matching, the cohorts were well balanced, and the standardized difference did not exceed the threshold of 0.1 for any characteristic (**Table 2**). The mean age of patients was 52 years (with more than two-thirds of patients in the group aged 50–64 years), with a mean of 1.5 high-risk conditions and a mean DCSI score of 2.3. Most patients (61%) were taking insulin or an antihyperglycemic drug other than or in addition to metformin. Less than one-third of patients had received the influenza vaccine. Approximately 8% had been hospitalized in the preceding year, and approximately 27% had visited the ED in the preceding year.

HCRU

Antiviral treatment was associated with a significant reduction in the mean number of ED visits over 1 year following influenza infection (mean [SD], 0.94 [1.76] vs 1.24 [2.47]; $P < .0001$), resulting in a reduction in ED visits of approximately 25% compared with the untreated cohort (**Table 3** and **Figure 2**). A significant reduction in ED visits was also observed during each quarter and ranged from 29.2% in Q1 to 21.3% in Q4. No significant differences were observed between treated and untreated cohorts in the number of outpatient visits over the full year or during each quarter, with the exception of Q3, in which treated patients experienced a significantly higher number of visits.

For all time periods examined, the number of hospitalizations among the treated cohort was lower compared with the untreated cohort; however, the differences were not significant. The duration

CLINICAL

TABLE 1. Prematch Baseline Demographic and Clinical Characteristics of Untreated and Treated Patients With Type 2 Diabetes and Influenza During the 2016-2017 Influenza Season

Characteristic	Untreated (n = 2463)	Treated (n = 5115)	P ^a	Standardized difference ^b
Age in years, mean (SD)	51.86 (8.25)	52.12 (7.88)	.2936	0.0212
Number of conditions considered to increase risk of severe influenza complications, mean (SD)	1.53 (1.32)	1.42 (1.24)	.0006	0.1021
DCSI, mean (SD)	2.29 (2.27)	2.17 (2.14)	.0206	0.0729
Sex, n (%)			.0027	0.0630
Male	1062 (43.1%)	2393 (46.8%)		
Female	1401 (56.9%)	2722 (53.2%)		
Age group, n (%)			.9896	0.0016
18-49 years	811 (32.9%)	1685 (32.9%)		
50-64 years	1652 (67.1%)	3430 (67.1%)		
Region, n (%)			< .0001	0.2372
South	336 (13.6%)	494 (9.7%)		
North Central	366 (14.9%)	572 (11.2%)		
Northeast	1534 (62.3%)	3746 (73.2%)		
West	214 (8.7%)	295 (5.8%)		
Unknown	13 (0.5%)	8 (0.2%)		
Health plan type, n (%)			.3270	0.0374
PPO	570 (23.1%)	1106 (21.5%)		
HMO	254 (10.3%)	541 (10.6%)		
Other/unknown	1639 (66.5%)	3468 (67.8%)		
Received influenza vaccine, n (%)			.0003	0.0880
No reported influenza vaccine	1748 (71.0%)	3418 (66.8%)		
Yes	715 (29.0%)	1697 (33.2%)		
Drug category, n (%)			.5994	0.0468
Metformin only	960 (39.0%)	1979 (38.7%)		
Other antihyperglycemic drugs	913 (37.0%)	1952 (38.2%)		
Insulin	590 (24.0%)	1184 (23.1%)		
Prior-year hospitalization, n (%)			.9464	0.0402
No	2271 (92.2%)	4714 (92.2%)		
Yes	192 (7.8%)	401 (7.8%)		
Prior-year ED visit, n (%)			.0002	0.1030
No	1769 (71.8%)	3879 (75.8%)		
Yes	694 (28.2%)	1236 (24.2%)		

DCSI, Diabetes Complications Severity Score; ED, emergency department; HMO, health maintenance organization; PPO, preferred provider organization.

^aP value was calculated using the *t* test for continuous variables and the χ^2 test for categorical variables.

^bA threshold of 0.1 was used to indicate significant differences in the mean value of the characteristic between groups.

of hospitalization, however, was significantly reduced in the treated cohort compared with the untreated cohort over the full year (mean [SD], 0.71 [3.36] days vs 1.11 [5.60] days; $P < .0023$) and in Q1 (mean [SD], 0.29 [1.75] vs 0.48 [3.27] days; $P = .0075$), representing a reduction in hospitalization days of 35.6% and 40.5%, respectively (Table 3 and Figure 2). Hospitalization duration was also lower in the treated cohort during Q2, Q3, and Q4, but the difference was not significant.

year after the index influenza episode.

To ensure the comparability of the 2 cohorts in this study, patients were propensity score–matched for variables that could influence outcomes. We used both the DCSI, a metric that encompasses a variety of diabetic complications, and diabetes drug classification to control for the severity of diabetes. Additionally, to ensure that baseline morbidity was comparable between the groups, we matched

Health Care Costs

Mean (SD) total health care costs were significantly lower in the treated cohort (\$20,212 [\$58,627]) than in the untreated cohort (\$24,552 [\$71,830]) over a whole year following the index influenza visit ($P = .0203$), representing a cost reduction of 17.7% (Table 3 and Figure 2). A significant reduction in costs of 21.7% was also realized in Q1 (\$5042 [\$19,272] vs \$6443 [\$26,382]; $P = .0335$). Costs in Q2, Q3, and Q4 were also lower in the treated cohort but did not reach statistical significance.

DISCUSSION

Patients with T2D are at increased risk for severe medical outcomes and increased HCRU following influenza compared with the general population.^{38,39} Interventions that can limit the impact of influenza may provide clinical and economic benefits. Although vaccination remains the most effective way to prevent influenza, vaccine effectiveness varies from season to season depending on the match between vaccine components and the dominant circulating strains,⁴⁰ and vaccination rates among high-risk patients remain suboptimal.⁴¹ Antiviral treatment is also recommended for high-risk groups, including individuals with diabetes. The impact of antiviral treatment for influenza on outcomes in patients with T2D, however, remains largely undocumented. In this study we used real-world claims data from the 2016-2017 influenza season to assess short-term and long-term HCRU and costs of antiviral treatment in patients with diabetes. This study showed that patients with diabetes who received an antiviral within 2 days of an influenza diagnosis had significantly fewer ED visits, significantly reduced duration of hospitalization, and significantly lower medical costs compared with untreated patients. Importantly, the beneficial effect of antiviral treatment was long-lasting and was observed not only in the acute postinfluenza period but also over a full

for health conditions associated with a higher risk of severe influenza complications and for hospitalization and ED use in the preceding year.

The results show that both HCRU and costs were lower in the treated cohort than in the untreated cohort over multiple time periods. Importantly, the beneficial impact of antiviral treatment was sustained for a full year. The reduction in number of ED visits during each quarter over a full year ranged from 21.3% to 29.2%. Although the number of hospitalizations was not significantly reduced in the treated cohort, the duration of hospitalization was reduced significantly both in Q1 and over the full ensuing year, with a nonsignificant reduction in duration also observed for Q2, Q3, and Q4. Although the proportion of patients who needed to be hospitalized was not significantly different between the cohorts, the duration of hospitalization—as a surrogate for severity of condition—was shortened significantly in the treated cohort. Costs over a full year were reduced significantly in the treated group compared with the untreated group, with lower costs reported in all quarters for the treated group.

Some notable trends are apparent in the study results. Although reductions in all categories of postinfluenza HCRU were not statistically significant in all quarters, the treated cohort had consistently lower numerical HCRU for each quarter. The exception to this trend was the number of outpatient visits, which increased in the treated cohort by 7.1% and 4.2% in Q3 and Q4, respectively. However, the consistent trend in reduction of HCRU for the treated cohort in each quarter following influenza infection is compelling. Future studies should evaluate whether these results are generalizable to other high-risk patient populations. Also, the current study evaluated outcomes up to 1 year following influenza infection, but based on the results, benefits of antiviral treatment may extend beyond 1 year. The duration of the benefit of antiviral treatment beyond 1 year would therefore also be worth examining. In addition, future investigations could examine differences in the long-term effect of antivirals in the treatment of influenza among a variety of patients with diabetes, such as those who are receiving oral antihyperglycemics vs insulin.

This is the first study to show the long-term benefit of timely antiviral treatment of an acute episode of influenza in patients with T2D. A previous subgroup analysis of a retrospective claims-based

TABLE 2. Postmatch Baseline Demographic and Clinical Characteristics of Untreated and Treated Patients With Type 2 Diabetes and Influenza During the 2016-2017 Influenza Season

Characteristic	Untreated (n = 2459)	Treated (n = 2459)	P ^a	Standardized difference ^b
Age in years, mean (SD)	51.85 (8.26)	52.14 (8.06)	.2153	0.0330
Number of conditions considered to increase risk of severe influenza complications, mean (SD)	1.53 (1.32)	1.53 (1.27)	.9561	0.0016
DCSI, mean (SD)	2.29 (2.27)	2.25 (2.18)	.5859	0.0051
Sex, n (%)			.4901	0.0197
Male	1059 (43.1%)	1083 (44.0%)		
Female	1400 (56.9%)	1376 (56.0%)		
Age group, n (%)			.5631	0.0165
18-49 years	810 (32.9%)	791 (32.2%)		
50-64 years	1649 (67.1%)	1668 (67.8%)		
Region, n (%)			.9687	0.0300
South	336 (13.7%)	326 (13.3%)		
North Central	366 (14.8%)	365 (14.8%)		
Northeast	1534 (62.4%)	1555 (63.2%)		
West	214 (8.7%)	205 (8.3%)		
Unknown	9 (0.4%)	8 (0.3%)		
Health plan type, n (%)			.7393	0.0240
PPO	570 (23.2%)	583 (23.7%)		
HMO	254 (10.3%)	239 (9.7%)		
Other/unknown	1635 (66.5%)	1637 (66.6%)		
Received influenza vaccine, n (%)			1.0000	0.0000
No reported influenza vaccine	1745 (71.0%)	1745 (71.0%)		
Yes	714 (29.0%)	714 (29.0%)		
Drug category, n (%)			.8494	0.0000
Metformin only	958 (38.9%)	966 (39.3%)		
Other antihyperglycemic drugs	912 (37.1%)	921 (37.5%)		
Insulin	589 (24.0%)	572 (23.2%)		
Prior-year hospitalization, n (%)			.5629	0.0076
No	2268 (92.2%)	2257 (91.8%)		
Yes	191 (7.8%)	202 (8.2%)		
Prior-year ED visit, n (%)			.3544	0.0579
No	1768 (71.9%)	1797 (73.1%)		
Yes	691 (28.1%)	662 (26.9%)		

DCSI, Diabetes Complications Severity Index; ED, emergency department; HMO, health maintenance organization; PPO, preferred provider organization.

^aP value was calculated using the t test for continuous variables and χ^2 test for categorical variables.

^bA threshold of 0.1 was used to indicate significant differences in the mean value of the characteristic between groups.

study in patients with diabetes showed a reduction in short-term outcomes (within 14 days of influenza diagnosis) in patients treated with oseltamivir following influenza diagnosis; treated patients had a significant 17% reduction in risk of respiratory illnesses and a 30% reduction in risk of hospitalization for any reason compared with an unmatched group of untreated patients.³⁰ Another study documented a reduction in hospitalization following antiviral treatment of a cohort of patients with high-risk conditions that

TABLE 3. Health Care Resource Utilization and Costs Over 1 Year and in Each Quarter in Untreated and Treated Patients With Type 2 Diabetes and Influenza During the 2016-2017 Influenza Season

Health care resource utilization and costs	Untreated (n = 2459)	Treated (n = 2459)	P
Outpatient visits, n, mean (SD)			
Full year	18.70 (18.07)	19.24 (18.84)	.2995
Q1	5.39 (5.29)	5.37 (5.25)	.9073
Q2	4.41 (5.35)	4.47 (5.46)	.7019
Q3	4.48 (5.39)	4.80 (5.84)	.0472
Q4	4.42 (5.48)	4.62 (5.48)	.232
ED visits, n, mean (SD)			
Full year	1.24 (2.47)	0.94 (1.76)	<.0001
Q1	0.46 (0.98)	0.32 (0.74)	<.0001
Q2	0.27 (0.79)	0.21 (0.60)	.0018
Q3	0.26 (0.75)	0.21 (0.62)	.004
Q4	0.25 (0.83)	0.20 (0.62)	.0093
Hospitalizations, n, mean (SD)			
Full year	0.15 (0.53)	0.13 (0.49)	.1351
Q1	0.04 (0.24)	0.03 (0.20)	.1011
Q2	0.03 (0.20)	0.03 (0.20)	.615
Q3	0.04 (0.26)	0.04 (0.24)	.3007
Q4	0.03 (0.22)	0.03 (0.20)	.7382
Duration of hospitalization, days, mean (SD)			
Full year	1.11 (5.60)	0.71 (3.36)	.0023
Q1	0.48 (3.27)	0.29 (1.75)	.0075
Q2	0.18 (1.70)	0.13 (1.03)	.1485
Q3	0.21 (1.77)	0.16 (1.27)	.2003
Q4	0.23 (2.06)	0.14 (1.40)	.0804
Total costs, US\$, mean (SD)*			
Full year	24,552 (71,830)	20,212 (58,627)	.0203
Q1	6443 (26,382)	5042 (19,272)	.0335
Q2	5612 (21,586)	5284 (30,108)	.6607
Q3	5746 (20,730)	4855 (18,900)	.115
Q4	6750 (41,225)	5032 (20,041)	.0613

ED, emergency department; Q, quarter.

*Total costs include inpatient + outpatient + ED visits in 2018 US\$.

included diabetes.⁴² The long-term impact of influenza in patients with T2D has recently been documented in a claims-based study that showed significantly higher HCRU (outpatient visits, ED visits, and hospitalizations) and medical expenditures for up to at least 1 year after a diagnosis of influenza compared with no influenza diagnosis.²⁹ A diagnosis of influenza was also associated with a higher prevalence of new or worsening diabetic complications, particularly cardiovascular and cerebrovascular complications, over a year of follow-up compared with those without influenza.

Our study shows that timely antiviral treatment of an index influenza episode in patients with diabetes may improve health

care outcomes and reduce costs for a full year after infection and mitigate the long-term deleterious impact of influenza. The data support current recommendations, which advocate antiviral treatment for patients in high-risk groups. However, as shown in this study, a substantial proportion of patients in this high-risk group remained untreated; only two-thirds of patients with T2D who sought care for influenza received an antiviral agent, supporting previous reports of low antiviral prescribing rates, even among high-risk individuals.^{27,28} The low rate of antiviral prescribing coupled with inadequate influenza prophylaxis (more than one-third of US adults with diabetes are estimated to be unvaccinated)^{16,17} is reflective of suboptimal adherence to treatment guidelines following influenza infection and overall poor standard of care in this high-risk group.

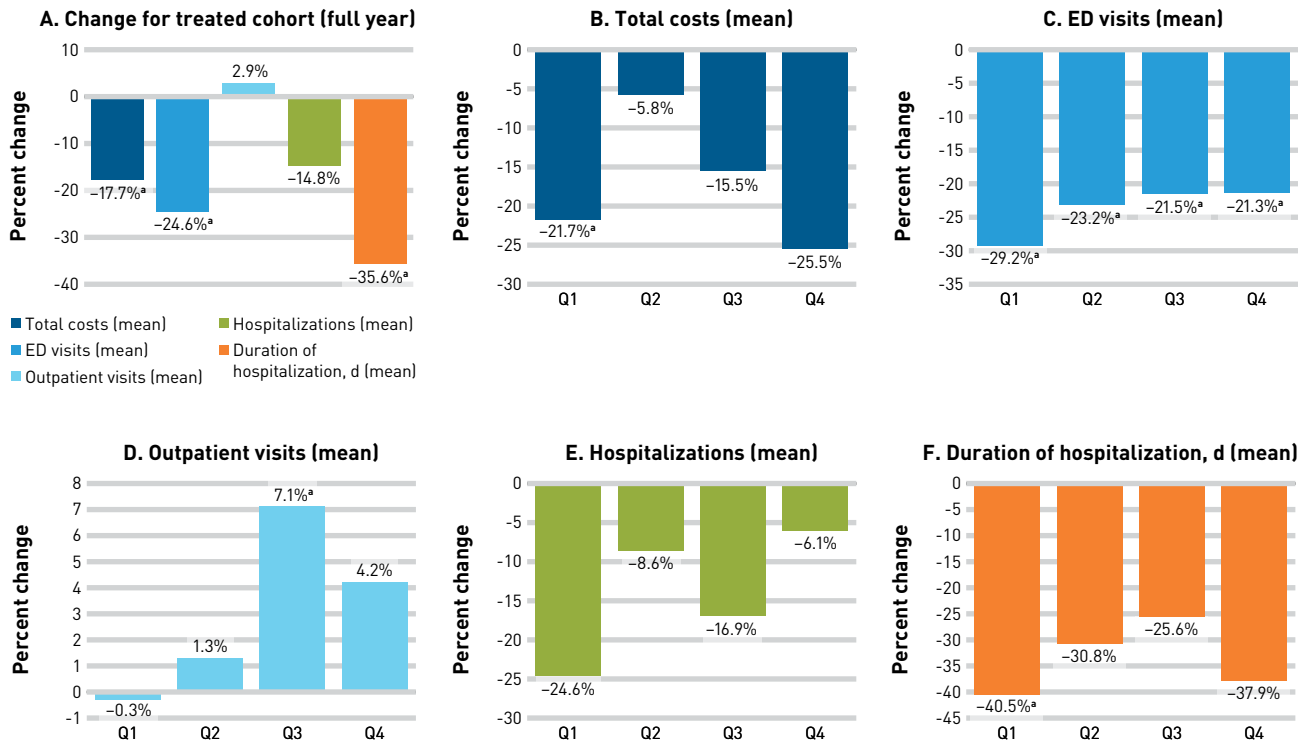
Limitations

This study has a number of limitations. Because this was a claims-based study, the possibility of residual bias exists even though propensity score matching was used to reduce selection bias. The study used data from US commercial insurance plans, and results may not be generalizable to other populations such as the Medicare or Medicaid populations. Patients who received a diagnosis of influenza in the inpatient setting were excluded. Because claims are collected for billing purposes, data may be incomplete or inaccurate and diagnoses may also be miscoded. Documentation of influenza vaccination may be unreliable in claims analysis; however, this covariate was still selected as a variable for the propensity score model because its absence may cause bias. The study design required patients to be continuously enrolled in the health plan, so those who died or who were lost to follow-up were not included, leading to selection bias. Cases of influenza were identified using claims data, and the diagnosis was not verified by medical record review or confirmed with a laboratory diagnosis, resulting in potential inclusion of patients with influenza-like illness in the analysis. If misclassification of influenza was nondifferential between treated and untreated cohorts, there would likely be minimal impact on this study's results, but if misclassification was significantly different between cohorts, results could be biased. Because the index date was the date of first diagnosis of influenza associated with a medical service and not with symptom onset, any delay in seeking care could have resulted in antiviral therapy being initiated after the 48-hour window for optimal drug efficacy and therefore an underestimation of antiviral efficacy. Further, the study evaluated all-cause HCRU, which includes conditions that may not be affected by influenza infection in the past year.

CONCLUSIONS

Claims data for the 2016-2017 influenza season showed that antiviral treatment of patients with T2D and a diagnosis of influenza was associated with reduced HCRU. In particular, the number of ED visits and the duration of hospitalization were significantly lower

FIGURE 2. Percent Change in Outcomes Following Antiviral Treatment in Patients With Type 2 Diabetes and Influenza During the 2016-2017 Influenza Season: (A) Change in All Outcomes Over 1 Year and (B-F) Quarterly Change in Individual Outcomes



D, days; ED, emergency department; Q, quarter.
 *P < .05 for difference between untreated and treated patients.

in treated patients with T2D compared with untreated patients over the full year after the influenza diagnosis and during Q1. Costs in treated patients were significantly lower over the first full year and numerically lower during each quarter. These findings suggest that prompt antiviral treatment of patients with T2D confers immediate and long-term benefits after a diagnosis of influenza. ■

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Author Affiliations: Genentech, Inc (BDL, CW, TMT, HM, PD, ST), South San Francisco, CA; University of Houston (BDL), Houston, TX; Roche (SWK), Basel, Switzerland.

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Address Correspondence to: Benjamin D. Lewing, PhD, University of Houston, 4849 Calhoun, HB2, R4058, Houston, TX 77204-5047. Email: BLewing2@central.uh.edu.

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eAppendix Figure.

