

ABSTRACT

- Influenza causes substantial morbidity in people with Diabetes; annual vaccination is recommended. We conducted a retrospective study of influenza-related outcomes (IRO) among fully insured Type 2 diabetics from a large US payer over a 1 year period covering the 2016-17 influenza season. We used bivariate analysis (54,656 diabetics, mean age 54.8 yr, s.d. = 10.2) to compare IRO's inferred from claims data against IRO's for 113,016 age and gender matched non-diabetics
- Diabetics had more influenza events (per ICD-9 and ICD-10 codes¹, 1.96% vs 1.37%, p<0.001), and were prescribed more influenza antivirals (27.1 vs 22 per 100 people, p<0.001). Within 2-weeks before and 4-weeks after a medical claim for influenza, diabetics with influenza had more observed hyperglycemic² events than in a comparable non-influenza period in the same year (3.81% vs 2.18%, p<0.001), with substantial increases in pneumonia, sepsis and coronary disease (5.5% vs 0.7%, 5.5% vs 3.5%, 1.6% vs 0.3%, p<0.001), and more outpatient antibiotic use per 100 people (54.5 vs 16.9, p<0.001)
- 8.2% of Type 2 Diabetics (vs. 9.1% controls, p<0.001) used commercially available activity and sleep trackers, sharing data through an insurer provided wellness platform. Activity trackers showed that diabetics slept fewer hours compared to controls (6.48 vs 6.69 hrs, p<0.001), and had statistically significant changes in sleep and walking habits in the days around an influenza event as compared to baseline (about 2% more of the night spent restless and 10k fewer steps)
- This is the first population scale study to use medical claims linked with activity tracking data to quantify the behavioral and clinical effects of influenza in Type 2 Diabetes. These data highlight the impact of influenza on glycemic control and the daily lives of the Diabetic population, and reinforce the need for annual influenza vaccine, as recommended by the WHO and other global public health bodies



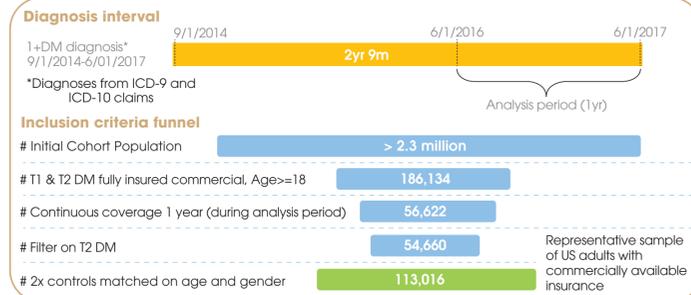
BACKGROUND

- Influenza is a major public health and medical concern. Particularly among persons with Type 2 Diabetes it imposes a high burden of morbidity, mortality and economic costs
- Surveillance of influenza offers valuable information for understanding the burden of influenza in a given population and also to evaluate the impact of vaccination
- Conventional surveillance methods rely on data derived from patient interactions with the health care system - i.e. clinics, pharmacies or hospitals. Recent efforts to use novel digital markers have shown promise as a surveillance method in the general population. For example, the use of Google searches, Twitter feeds, or over-the-counter pharmacy sales may offer earlier detection of outbreaks as well as insights on the symptoms from text analysis of the searches or feeds
- The advent of mobile health technologies (mHealth) such as exercise trackers, digital scales or app-enabled smartphones can potentially add more individualized insights by providing person-level data at granularities up to minute level for a number of behavioral types such as walking, exercise, sleeping and diet
- In this study, we explore the first effort integrating conventional medical claims with mHealth data to characterize influenza and its impact on persons with Type 2 Diabetes Mellitus

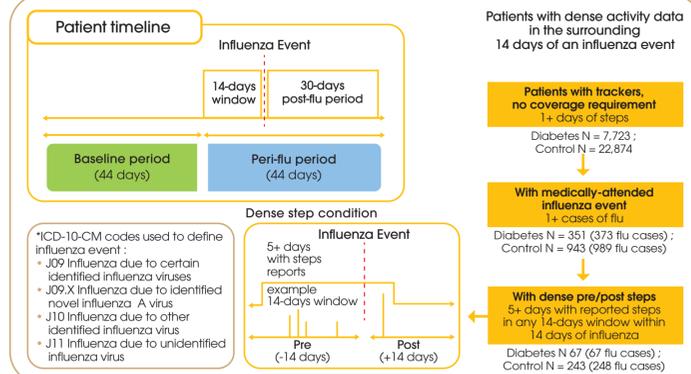
¹ICD 9 codes 487, 488, ICD 10 codes J09, J10, J11 / ²ICD 9 790.2 and ICD 10 code r73

METHODS

- Study design is a retrospective population based cohort of persons with Type 2 Diabetes compared to age and gender matched non-diabetic controls and a self controlled study centered around incident influenza diagnosis among persons with Type 2 Diabetes
- Study setting is a large national insurance payer in the United States. Potential participant data is drawn from a nearly three year period during which participants were enrolled in the insurance plan
- The analysis covers a one year period from June 1, 2016 to June 1, 2017, thereby focusing on incident outcomes during the 2016-2017 influenza season in the US
- Eligible participants were adults over the age of 18, with evidence of commercial coverage during the analysis period
- Participants included in the retrospective cohort and case-control pre-post analysis were required to have at least one year of continuous commercial coverage that included the 2016-2017 analysis period



- The insurance payer provides a digital wellness app that connects a variety of consumer wearable fitness devices
- The wellness app works on mobile phones using the Apple iOS or the Google Android operating system
- The wearable fitness devices provide passively collected behavioral activity data in the form of steps taken and sleep, as well as heart rate data
- Bivariate analysis compared influenza related medical outcomes among persons with Type 2 Diabetes to age and gender matched non-diabetic controls
- P values were computed with Student's t-test, chi-square or Mann-Whitney U tests where appropriate. False discovery rate threshold of 10% used to select significant p values



- Activity behaviors and medical outcomes were examined with a pre-post study design comparing the peri-influenza period (the 2 weeks before and 4 weeks after an incident influenza diagnosis) to the 6 week period preceding the peri-influenza period (baseline) at the individual level. We also looked at a sub-cohort of patients with dense data in the 14 days surrounding an influenza event

RESULTS

Demographics and Influenza Outcomes Full Cohort		
	T2DM	Controls
Number	54,656	113,016
Percent male	53.7%	53.7%
Mean Age (s.d.)	54.8 (10.2)	54.8 (10.2)
Lipid disorder*	67.1%	27.3%
Hypertension*	69.3%	28.1%
Respiratory illness*	41.5%	32.2%
Activity Trackers*	8.2%	9.1%
Influenza Event (medically-attended)*	1.96%	1.37%
Influenza vaccination*	34.3%	24.3%

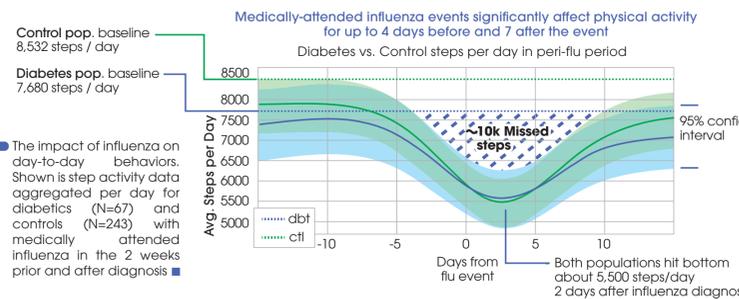
*p < 0.001

Demographics, Influenza Outcomes and Behaviors-Trackers Only		
	T2DM	Controls
Number of trackers	4,459	10,321
% Days with tracked steps	78.7%**	80.7%
Charlson Comorbidity index (CCI)	2.28**	0.37
Influenza Vaccination	46.9%**	38.8%
Mean nightly sleep duration (hours)	6.48**	6.69
Sleep Regularity Index (SRI)*	0.72**	0.77
Resting heart rate (bpm)	71.2**	66.0
Mean Daily Stepcount	6,256**	7,374
Average daily cardio exercise sessions	0.20**	0.41

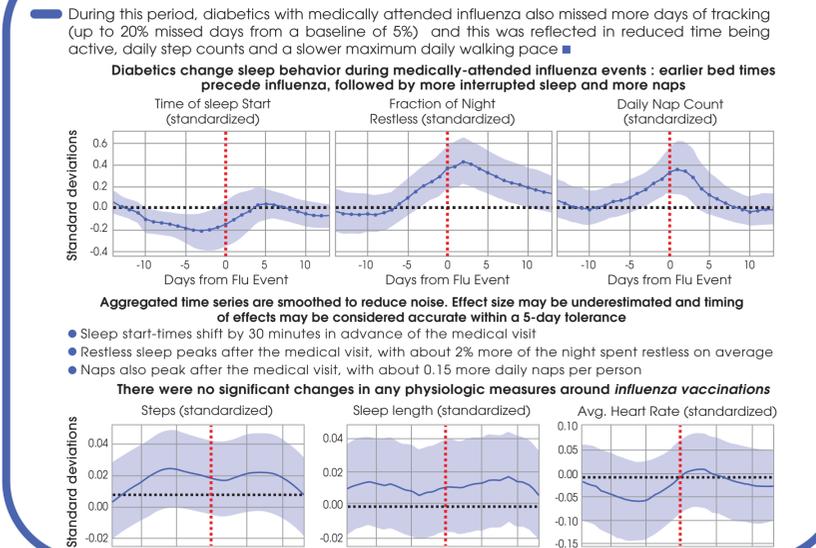
*p < 0.05, **p < 0.001

	Diabetics (N = 1,100)			Control (N = 1,567)			
	Baseline	Peri-Flu	Increase (n-fold)	Baseline	Peri-Flu	Increase (n-fold)	N-fold ²
Abnormal Glucose Events*	2.18%	3.81%	1.63% (1.75)	---	---	---	---
Pneumonia*	0.70%	5.50%	4.8% (7.8)	0.25%	3.3%	3.05% (13.2)	1.57
Ischemic heart disease*	3.45%	5.54%	2.09% (1.6)	1.47%	1.72%	0.25% (1.2)	8.36
Sepsis*	0.30%	1.60%	2.09% (1.6)	0%	0%	0%	NA
Antibiotic Rx (per 100 people)*	16.9	54.5	37.6 (3.2)	15.8	44.1	28.4 (2.8)	1.32
INFLUENZA antiviral Rx (per 100 people)	0.4	67.7	67.3 (169.3)	0.3	69.7	69.4 (232.3)	0.97
ER visits (per 100 people)*	5.9	21.3	15.4 (3.6)	2.2	14.4	12.2 (6.5)	1.26
Hospital visits (per 100 people)**	1.4	6.9	5.5 (4.9)	0.9	3.0	2.1 (3.3)	2.62

*p < 0.05, **p < 0.001. Significance is in a pre/post case/control framework. It indicates that the diabetic peri-influenza change is significantly larger than that for the matched control group
¹n-fold compares the increase from baseline to peri-flu period in each group
²N-fold compares the increase from baseline to peri-flu period among diabetics to the increase among controls



RESULTS



DISCUSSION

- Influenza occurs more frequently among persons with Type 2 Diabetes Mellitus compared with controls. This suggests that diabetes increases the risk of influenza infection, and highlights the importance of vaccination in this population
- No adverse effects of influenza vaccination on activity behaviors or physiologic signals were observed, confirming the lack of evidence for a common misperception that vaccination can lead to flu effects
- Among mHealth users, persons with Type 2 Diabetes differ from non-diabetic trackers in a number of behaviors related to sleep, walking and exercise. Diabetics with influenza also saw more acute events in the peri-influenza period compared to baseline, such as a 75% increase in abnormal glucose events. Among persons with Type 2 Diabetes, mHealth devices detected substantial changes in walking, exercise and sleep in the immediate period before and after an influenza episode. These changes likely lead to further adverse effects on daily living and activities both in work and in personal life. Taken together, these results are the first describing the immediate effects of influenza on the daily life of people with diabetes at a population level
- These findings confirm the potential of mHealth for quantifying the impact of influenza on diabetics. As mHealth devices become more ubiquitous, their applications for individual and population surveillance and for prevention and management of acute and chronic disease will show greater value. This needs to be assessed with further prospective studies

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