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Differential effects of outpatient use of ACE inhibitors and angiotensin receptor blockers on outcomes of acute respiratory illness during the COVID-19 pandemic: a cohort study

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Title: Differential effects of outpatient use of ACE inhibitors and angiotensin receptor blockers on outcomes of acute respiratory illness during the COVID-19 pandemic: a cohort study

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Competing interests

None.

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ABSTRACT

Objectives: Evaluate the associations between patients taking ACE inhibitors (ACEis) and angiotensin receptor blockers (ARBs) and their clinical outcomes after an acute viral respiratory illness (AVRI) due to COVID-19.

Design: Retrospective cohort.

Setting: The USA; 2017-2018 influenza season, 2018-2019 influenza season, and 2019-2020 influenza/COVID-19 season.

Participants: People with hypertension (HTN) taking an ACEi, ARB or other HTN medications, and experiencing AVRI.

Main outcome measures: Change in hospital admission, intensive care unit (ICU) or coronary care unit (CCU), acute respiratory distress (ARD), ARD syndrome (ARDS), and all-cause mortality, comparing COVID-19 to pre-COVID-19 influenza seasons.

Results: The cohort included 1,059,474 episodes of AVRI (653,797 filled an ACEi or ARB, and 405,677 other HTN medications). 58.6% were women and 72.9% with age ≥ 65. The ACEi/ARB cohort saw a larger increase in risk in the COVID-19 influenza season than the other HTN medication cohort for four out of five outcomes, with an additional 1.5 percentage point (pp) increase in risk of an inpatient stay (95% CI 1.2 to 1.9 pp) and of ICU/CCU use (95% CI 0.3 to 2.7 pp), as well as a 0.7 pp (0.1 to 1.2 pp) additional increase in risk of ARD and 0.9 pp (0.4 to 1.3 pp) additional increase in risk of ARDS. There was no statistically significant difference in the absolute risk of death (-0.2 pp, 95% CI -0.4 to 0.1 pp). However, the relative risk of death in 2019/2020 vs. 2017/2018 for the ACEi/ARB group was larger (1.40 [1.36 to 1.44]) than for the other HTN medication cohort (1.24 [1.21 to 1.28]).

Conclusions: People with AVRI using ACEi/ARBs for hypertension had a greater increase in poor outcomes during the COVID-19 pandemic than those using other medications to treat hypertension. The small absolute magnitude of the differences likely does not support changes in clinical practice.

Keywords: ACE inhibitors, angiotensin receptor blockers, COVID-19, acute viral respiratory illness.

ARTICLE SUMMARY

Strengths and limitations of this study

- It uses an approach of difference-in-differences that mitigates some of the limitations of observational studies.
- The cohort includes a diverse sample of US residents including people with commercial insurance and Medicare Advantage.
- The cohort is not representative of people without insurance or people with Medicaid or other insurance types.
- Given the observational design, it is not possible to make causal claims.

INTRODUCTION

The renin-angiotensin-aldosterone system (RAAS) is a hormone system responsible for several physiologic functions including vascular resistance, electrolyte homeostasis, and fluid balance. Medications such as angiotensin-converting enzyme inhibitors (ACEi) and angiotensin-receptor blockers (ARBs) interrupt different steps in this system and are commonly used in clinical practice for outpatient blood pressure or heart failure management. Early in the coronavirus disease 2019 (COVID-19) pandemic, pre-clinical studies raised concerns about the association between use of ACEi or ARBs and severe illness in hypertensive patients with COVID-19. Angiotensin-converting-enzyme 2 (ACE-2) is the binding site for respiratory viruses including the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and two opposing theories on the potential effects of these medications have been debated: one postulating an increased susceptibility to SARS-CoV-2 through upregulation of ACE-2 receptors, and one postulating a protection against severe disease through suppression of angiotensin II and subsequent prevention of virus-mediated acute lung injury.

Since the hypothesis that the prior use of RAAS inhibitors could be associated with worse clinical outcomes in hypertensive patients diagnosed with COVID-19 was raised, several clinical studies were published.² In the latest update of a living systematic review addressing this question by Mackey and colleagues, the authors reported high confidence based on 78 studies (77 observational studies, 1 randomized controlled trial [RCTs]) in the finding that ACEi/ARB use is not associated with COVID-19 severity.² Another 21 systematic reviews and/or meta-analyses have been consistent with this conclusion as well.³⁻²³ Furthermore, two recently published RCTs do not support the discontinuation of these drugs in hypertensive patients admitted to the hospital with COVID-19.²⁴25

Most existing studies, however, are of relatively small sample size with low methodological quality. In this study, we aimed to evaluate the associations between patients taking ACEis and ARBs and their clinical outcomes after an acute viral respiratory illness (AVRI) due to COVID-19. We assessed severity of illness and mortality in AVRI across cohorts of patients with hypertension (HTN) using ACEis, ARBs, and other HTN medications, and we compared the differential effects of these medications on outcomes of AVRI in the 2017/2018 and 2018/2019 influenza seasons to those in the 2019/2020 influenza/COVID-19 season in the United States.

METHODS

We adhered to the RECORD statement (REporting of studies Conducted using Observational Routinely collected health Data).²⁶

Data source and study setting

We used de-identified administrative claims data from the OptumLabs Data Warehouse (OLDW) to identify episodes of AVRI in people with Medicare Advantage or commercial health insurance in the United States. The OLDW includes medical and pharmacy claims, laboratory results, and enrollment records for commercial and Medicare Advantage enrollees.²⁷ The database contains longitudinal health information on enrollees and patients, representing a diverse mixture of ages, ethnicities, and geographical regions across the United States.

Study design and participants

We created a cohort of patients with one or more episodes of AVRI with an initial date of service (index date) between October 1, 2017, and November 30, 2020. AVRI was defined

using ICD-10 diagnosis codes for viral causes of respiratory illness: bronchitis, pneumonia, influenza, influenza like illness, and lower respiratory infections. (**Supplementary Material S1**). Each episode of AVRI started on the first date on which the patient had a claim with an AVRI diagnosis code and continued until the patient experienced a 30-day span with no AVRI diagnoses.

We required 180 days of continuous insurance enrollment before the index date of the AVRI episode. Insurance claims during this period were used to identify hypertension diagnoses, as well as other comorbidities that could be associated with COVID-19 morbidity and mortality risk or with the choice of medications to treat hypertension, as explained below.

Variables and measurements

Patient age, sex, residence state, and insurance enrollments dates and coverage type (commercial vs. Medicare Advantage) were taken from insurance enrollment data.

Hypertension and comorbidities

Hypertension and most comorbidities were defined based on the Quan enhanced Elixhauser comorbidity ICD-10 codes;²⁸ codes used to define comorbidities not included in the Elixhauser index (coronary artery disease, stroke, deep vein thrombosis, and pulmonary embolism) are available in the **Supplementary Material S1.** Hypertension and diabetes were coded hierarchically such that people with both complicated and uncomplicated disease were coded as complicated. All comorbidities required at least one inpatient or two outpatient diagnoses on different dates of service in the 6 months before the index date. Inpatient and outpatient settings were defined using procedure and revenue codes using code lists developed

for use with Healthcare Effectiveness Data and Information Set (HEDIS) performance measures.²⁹

Hypertension medications

We developed a comprehensive list of hypertension medications (see **Supplementary Material S1**), then identified all National Drug Codes (NDCs) for these medications in a table that is part of the OLDW. We searched for prescription fills in the 90 days before the index date for each episode of AVRI and categorized fill patterns as ACEi or ARB only, ACEi or ARB with other (i.e., not ACEi or ARB) hypertension medications, other hypertension medications only, or no hypertension medications. In primary analyses, ACEi or ARB users with and without other hypertension medications were combined and compared with people using only other hypertension medications; information on people who did not use hypertension medications is provided in summary tables for reference, but they were excluded from the analyses. A small number of people who filled both an ACEi and an ARB were also excluded from the analysis (N=10,933).

Outcomes

We specified 5 outcomes associated with more serious cases of AVRI: death, hospitalization, and, conditional on hospitalization: intensive care unit (ICU) or coronary care unit (CCU) services (revenue codes 0200 to 0219), a diagnosis of acute respiratory distress (ARD) (ICD-10 diagnosis code R06.03), and a diagnosis of acute respiratory distress syndrome (ARDS) (ICD-10 diagnosis code J80).

Data on death in OLDW includes only the month and year of death to maintain deidentification. It is sourced from the Death Master File, claims information, and insurance enrollment information. The mortality outcome in this study assessed whether the person was reported to have died in the same month as the index date or in the following month.

Data analysis

We used a difference-in-differences approach to assess the association between use of ACEis or ARBs and poor outcomes from COVID-19. The comparison group is people with hypertension using hypertension medications other than ACEis or ARBs; the exposure of interest is the COVID-19 pandemic. We compared outcomes of AVRI in the 2017/2018 and 2018/2019 influenza seasons to those in the 2019/2020 influenza/COVID-19 season. The premise is that the design will control for both differences in underlying health between the two medication groups (by comparing each to people taking those same medications in the years before COVID-19) and differences in healthcare service use during COVID-19 that are common to all people with hypertension. The inclusion of two pre-COVID-19 influenza seasons allows for a comparison of differences in outcomes between the medication groups due to changes in overall AVRI illness mix unrelated to COVID-19. Cases, inpatient admission rates, and mortality rates can vary substantially with different influenza strains.³⁰

We used a linear probability approach to model each of the five outcomes, in 3 time periods (2017/2018, 2018/2019, and 2019/2020 seasons) for two patient medication groups (people using ACEis or ARBs vs. those using other HTN medications). Regression models included patient sex, age (categorical), insurance type (Medicare Advantage vs. commercial), Census region of residence, race/ethnicity, and flags for comorbidities described above. Huber-

White standard errors were specified to adjust for repeated observations of some patients across separate episodes of AVRI. The model is specified such that the coefficient on the interaction between the 2019/2020 influenza/COVID-19 season and the ACEi/ARB group provides a statistical test for whether the ACEi/ARB group was differently affected by COVID-19 than the other HTN medication cohort. A coefficient greater than 0 indicates the ACEi/ARB group had a larger absolute increase in risk of the outcome than the other HTN medication cohort.

A linear probability model provides estimates of absolute risk differences rather than relative changes in risk. As a result, the differences are not scaled to the baseline probability of the event: a one percentage point risk difference may have different importance for an event with an incidence of 10% (relative increase 10%) compared to one with an incidence of 1% (relative increase 100%). To ease interpretation of results, we calculated average marginal effects for each flu season over the medication groups (in other words, the adjusted probabilities were calculated keeping the actual medication group rather than changing the medication group of each individual). We calculated ratios of these adjusted probabilities in the 2018/2019 flu season and the 2019/2020/COVID-19 flu season versus the baseline 2017/2018 flu season, along with p-values for the hypothesis test that the ratios were equal to 1 (i.e., the baseline year and the later year had no difference in outcome risk for that medication group). These ratios provide the percentage relative increase in the outcome risk.

Model result interpretation

If the presence of COVID-19 affects the ACEi/ARB group more than the other HTN medication group, we would expect to see a positive and statistically significant coefficient for the interaction term ACEi/ARB by season=2019/2020. We would place more credence in the

COVID-19 season findings if we find that outcomes in the 2018/2019 season did not differ much from those in the 2017/18 season, which would suggest that COVID-19 is fundamentally different from the general year-to-year shifts in flu strain. This would be supported by finding 1) a smaller coefficient for season=2018/2019 than for season=2019/2020, and 2) a smaller coefficient for the interaction term ACEi/ARB by season=2018/2019 than for the interaction term ACEi/ARB by season=2019/2020. Stata/MP version 16.0 was used for all analyses (StataCorp College Station, TX, 2019). The first author (MMJ) conducted all analyses and had access to all study data; all other authors had access to summary data and complete analysis results. No additional data available.

Patient and public involvement

Patients and/or public were not involved in this study.

RESULTS

We identified 1,247,393 episodes of AVRI in the study period among people with hypertension. Of these, 15.1% (187,919) did not fill a hypertension medication in the 90 days before the index date and were excluded from further analysis. Of the remaining 1,059,474, 61.7% (653,797) filled at least one ACEi or ARB, and 38.3% (405,677) filled no ACEi or ARBs (**Table 1**). Most episodes were in female patients (58.6%; n=620,810) and in older patients, with 72.9% of AVRI episodes in people aged 65 and older (n=772,210). The most common comorbidities were chronic pulmonary diseases (35.2%; n=372,735), cardiac arrhythmias (27.2%, n=288,478), coronary artery disease (26.3%; n=279,098), diabetes with complications (25.6%; n=271,700), and congestive heart failure (24.0%; n=254,773).

Compared to AVRI episodes in those using other HTN medications, AVRI episodes in people using ACEi or ARB were more frequently identified in those with Commercial insurance (vs. Medicare Advantage), uncomplicated diabetes, and Hispanic ethnicity, among other patient characteristics (Table 1). AVRI episodes in people using ACEi/ARB were less likely to be associated with the oldest age group and with most comorbidities, including complicated hypertension, congestive heart failure, kidney failure, liver failure, cancer, arrhythmia, coagulopathy, deep vein thrombosis or pulmonary embolism, stroke, and valvular disease, among other patient characteristics compared to AVRI episodes in people using other HTN medications. (Table 1)

<u>Unadjusted outcome rates</u>

Across all study years, 15.8% of AVRI episodes included an inpatient stay (n=167,330), including 14.0% of episodes in ACEi/ARB users (n=91,660) and 18.7% in other HTN medication users (n=75,670; **Table 1**). Episode mortality rates were 5.2% overall (n=55,164), 4.0% for ACEi/ARB users (n=26,411), and 7.1% in other HTN medication users (n=28,753). About half of inpatient stays included ICU or CCU use.

Primary analysis

Table 2 presents key model results and marginal effects and ratios for season and medication cohort effects for all five outcomes. Complete regression results are available in **Supplementary Material S2**. The ACEi/ARB cohort had a somewhat lower risk of three of the five outcomes in the baseline 2017-2018 flu season compared to the other HTN medication cohort, with a 1.9 percentage point (pp) (95% CI -2.2 to -1.6 percentage points) lower risk of an

inpatient stay, a 0.9 pp lower risk of death (95% CI -1.1 to -0.8 pp), and a 0.7 pp (95% CI -1.1 to -0.2 pp) lower risk of an ARD diagnosis conditional on having an inpatient stay. The point estimates for the risk differences of ICU/CCU use or an ARDS diagnosis in an inpatient stay also showed a lower risk for the ACEi/ARB cohort, but this difference was not statistically significant. The COVID-19 flu season was associated with a higher risk of all five outcomes in both the ACEi/ARB and the other HTN medication cohorts. Risk differences ranged from 1.3 pp higher risk of an ARD (95% CI: 0.8 to 1.7 pp) or ARDS (95% CI: 0.9 to 1.6 pp) diagnosis in an inpatient stay to a 3.5 pp (2.6 to 4.4 pp) higher risk of ICU/CCU use in an inpatient stay. (**Table 2**)

The ACEi/ARB cohort saw a larger risk difference than the other HTN medication cohort in four out of the five outcomes, with an additional 1.5 pp increase in risk of an inpatient stay (95% CI 1.2 to 1.9 pp) and of ICU/CCU use in an inpatient stay (95% CI 0.3 to 2.7 pp), as well as a 0.7 pp (0.1 to 1.2 pp) additional increase in risk of ARD and 0.9 pp (0.4 to 1.3 pp) additional increase in risk of ARDS. There was no statistically significant difference in the absolute risk of death (-0.2 pp, 95% CI -0.4 to 0.1 pp) for the ACEi/ARB group beyond that seen by the other medication group. However, the relative increased risk of death in 2019/2020 vs. 2017/2018 for the ACEi/ARB group was larger (1.40 [1.36 to 1.44]) than for the other HTN medication cohort (1.24 [1.21 to 1.28]). In other words, each group experienced roughly the same absolute change in risk (an increase of about 1.6 pp), but the baseline risk of death for the ACEi/ARB group was lower, so the relative increase was greater.

Sensitivity analyses

ACEi/ARB monotherapy

When we separated people using only ACEi/ARB from those using ACEi/ARB plus other HTN medications, results were somewhat different for the two groups. In both the 2018/2019 and 2019/2020 seasons, the monotherapy group had a 3.5 to 4.0 pp higher risk of ICU/CCU use in an inpatient stay than the polytherapy group. (**Supplementary Material S3**)

People with no comorbidities

The primary effect being studied (ACEi/ARB use during COVID-19) was attenuated when the cohort was limited to people who did not have any of the comorbidities we identified (other than hypertension). A large (5.0 pp; 95% CI -0.6 pp to 10.6 pp) increase in the risk of an inpatient stay with ICU/CCU services was not statistically significant because of the small sample size (N=7,696 episodes). (**Supplementary Material S3**)

Strict flu season

Limiting the 2017/18 and 2018/19 cohorts to cases of AVRI occurring in the strict flu season (generally October to May) had minimal effect on the results, which were similar to the primary analysis. (Supplementary Material S3)

DISCUSSION

In this large observational study, we found that hypertensive patients with an AVRI who were taking ACEis or ARBs for management of their HTN had larger risk differences during the COVID-19 period in the outcomes of inpatient stay, inpatient stay with ICU/CCU, inpatient stay with ARD, and inpatient stay with ARDS when compared with people on other antihypertensive

medications. This suggests that people taking ACEi/ARB were more affected by COVID-19 than people taking other HTN medications.

People with AVRI who were using ACEi/ARB had fewer comorbidities compared to people taking other medications to control their blood pressure, which might explain their lower baseline risk of poor outcomes. Prior to the COVID-19 season, among people with hypertension experiencing an episode of AVRI, those who used ACEi/ARB were less likely to have an inpatient stay, less likely to experience ARDS and ARD, and less likely to die compared to people on other antihypertensives at baseline.

During the COVID-19 flu season, all patients (ACEi/ARB and other HTN) had higher risk of all outcomes, compared to prior years. This is consistent with evidence that patients with hypertension experience worse outcomes from COVID-19.³¹⁻³⁵ The ACEi/ARB group had a larger increase in poor outcomes from baseline compared to patients taking other HTN medication, including higher rates of hospitalization, ICU admission, ARD and ARDS. There was no significant difference in the absolute risk of death for those on ACEi/ARB versus other medication group.

While relative changes in poor AVRI outcomes associated with ACEi/ARB use during COVID-19 were moderate to large, the absolute differences were relatively small, ranging from 0.7 to 1.9 percentage points. The effects demonstrated in this study may support the theoretical biological effect of ACEi/ARB in the clinical outcomes of people with COVID-19.

Nevertheless, it is very uncertain whether these effects were mediated through upregulation of ACE-2 receptors and subsequent susceptibility to SARS-CoV-2, as previously proposed.
Moreover, in translating these findings to clinical practice, the small absolute risk differences observed here are unlikely to outweigh the clinical benefits of ACEi/ARB therapy for managing

hypertension and heart failure. Therapy selection for these diseases should follow existing clinical guidelines of nephrology, cardiology, and other societies.

LIMITATIONS

The use of health insurance claims data limits the findings of this study to the populations included in the OptumLabs Data Warehouse; in particular, we do not observe outcomes of people who are uninsured or those who have Medicaid insurance (i.e., people with low incomes and no employer-based insurance). The study only captures people who received health care for AVRI, which may be different in important ways during COVID-19 compared to earlier years; early in the pandemic, many people avoided seeking in-person care, likely to avoid exposure to COVID-19 or to preserve access to care for others.³⁶ However, the difference-in-differences design of the study addresses this problem by comparing changes in outcomes for two similar populations; as long as people with hypertension who used ACEi/ARB and those who used other medications changed their care seeking behavior in similar ways, this effect should be minimized.

CONCLUSIONS

People with acute viral respiratory illnesses using ACEi/ARBs to treat hypertension had a greater increase in poor outcomes during the COVID-19 pandemic than those using other medications to treat hypertension. This may support the existence of the theoretical biological effect of ACEi/ARB in increasing susceptibility to COVID-19. Small absolute differences in risks of hospitalization, ICU use, and diagnosis of ARD or ARDS suggest that this effect likely does not warrant changes in clinical practice.

CONTRIBUTORSHIP STATEMENT

Conceptualization: MMJ, LOJS, FB, VDG, TMD, AHL, NWC. Formal analysis: MMJ. Investigation: MMJ, LOJS, FB, VDG, TMD, AHL, NWC. Methodology: MMJ, LOJS, FB. Project administration: MMJ. Supervision: MMJ, NWC. Validation: MMJ, NWC. Writing-original draft: MMJ. Writing-review and editing: MMJ, LOJS, FB, VSD, TMD, AHL, NWC. Guarantor: MMJ, NWC. All authors provided critical revision and contribution for important intellectual content.

COMPETING INTERESTS

None.

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DATA SHARING STATEMENT

No additional data available.

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LEGENDS

Table 1. Cohort characteristics.

Table 2. Main analysis results from linear probability model; full results in supplementary materials.



Table 1. Cohort characteristics.

	Comparison only (not included sample)	Included Sample			
	No HTN meds	Other HTN meds only	ACEi or ARB	Total included sample	
	N (%)	N (%)	N (%)	N (%)	
Insurance type					
Medicare Advantage	145,045 (77.2%)	348,583 (85.9%)	518,670 (79.3%)	867,253 (81.9%)	
Commercial	42,874 (22.8%)	57,094 (14.1%)	135,127 (20.7%)	192,221 (18.1%)	
Female	99,755 (53.1%)	246,659 (60.8%)	374,151 (57.2%)	620,810 (58.6%)	
Age (categories)					
<35	3,922 (2.1%)	3,354 (0.8%)	4,537 (0.7%)	7,891 (0.7%)	
35-44	8,337 (4.4%)	9,784 (2.4%)	17,780 (2.7%)	27,564 (2.6%)	
45-54	17,704 (9.4%)	24,916 (6.1%)	51,926 (7.9%)	76,842 (7.3%)	
55-64	32,637 (17.4%)	59,872 (14.8%)	115,095 (17.6%)	174,967 (16.5%)	
65-74	54,862 (29.2%)	120,039 (29.6%)	218,160 (33.4%)	338,199 (31.9%)	
75-84	44,330 (23.6%)	115,011 (28.4%)	171,276 (26.2%)	286,287 (27.0%)	
85+	26,127 (13.9%)	72,701 (17.9%)	75,023 (11.5%)	147,724 (13.9%)	
Race/ethnicity					
White	109,223 (58.1%)	238,439 (58.8%)	372,987 (57.0%)	611,426 (57.7%)	
Black	28,990 (15.4%)	70,774 (17.4%)	103,284 (15.8%)	174,058 (16.4%)	
Hispanic	20,302 (10.8%)	36,478 (9.0%)	82,374 (12.6%)	118,852 (11.2%)	
Asian	4,449 (2.4%)	8,003 (2.0%)	15,063 (2.3%)	23,066 (2.2%)	
Unknown/other	24,955 (13.3%)	51,983 (12.8%)	80,089 (12.2%)	132,072 (12.5%)	
Census Division					
New England	7,217 (3.8%)	18,358 (4.5%)	25,557 (3.9%)	43,915 (4.1%)	
Mid Atlantic	18,655 (9.9%)	43,354 (10.7%)	59,385 (9.1%)	102,739 (9.7%)	
South Atlantic	66,206 (35.2%)	154,483 (38.1%)	252,798 (38.7%)	407,281 (38.4%)	
E North Central	24,489 (13.0%)	59,277 (14.6%)	86,110 (13.2%)	145,387 (13.7%)	
E South Central	12,743 (6.8%)	28,786 (7.1%)	47,182 (7.2%)	75,968 (7.2%)	
W North Central	18,292 (9.7%)	28,065 (6.9%)	42,997 (6.6%)	71,062 (6.7%)	
W South Central	25,743 (13.7%)	48,406 (11.9%)	92,517 (14.2%)	140,923 (13.3%)	
Mountain	8,484 (4.5%)	14,224 (3.5%)	27,963 (4.3%)	42,187 (4.0%)	
Pacific	5,902 (3.1%)	10,612 (2.6%)	19,087 (2.9%)	29,699 (2.8%)	
Unknown/Other	188 (0.1%)	112 (0.0%)	201 (0.0%)	313 (<0.1%)	

Hypertension

	Comparison only (not included sample)	Included Sample		
	No HTN meds	Other HTN meds only	ACEi or ARB	Total included sample
	N (%)	N (%)	N (%)	N (%)
No complications	164,325 (87.4%)	334,180 (82.4%)	572,570 (87.6%)	906,750 (85.6%)
With complications	23,594 (12.6%)	71,497 (17.6%)	81,227 (12.4%)	152,724 (14.4%)
Comorbidities				
Diabetes				
No complications	22,002 (11.7%)	42,302 (10.4%)	99,778 (15.3%)	142,080 (13.4%)
With complications	37,742 (20.1%)	99,365 (24.5%)	172,335 (26.4%)	271,700 (25.6%)
Chronic pulmonary disease	66,355 (35.3%)	163,682 (40.3%)	209,053 (32.0%)	372,735 (35.2%)
Coronary artery disease	41,083 (21.9%)	122,633 (30.2%)	156,465 (23.9%)	279,098 (26.3%)
Congestive heart failure	30,910 (16.4%)	123,355 (30.4%)	131,418 (20.1%)	254,773 (24.0%)
Cardia arrhythmia	47,176 (25.1%)	138,713 (34.2%)	149,765 (22.9%)	288,478 (27.2%)
Valvular disease	15,929 (8.5%)	50,011 (12.3%)	55,342 (8.5%)	105,353 (9.9%)
Chronic/acute deep vein thrombosis or pulmonary	6,657 (3.5%)	13,846 (3.4%)	13,883 (2.1%)	27,729 (2.6%)
embolism	24,473 (13.0%)	66,643 (16.4%)	74,909 (11.5%)	141,552 (13.4%)
Peripheral vascular disorders	15,912 (8.5%)	34,297 (8.5%)	39,064 (6.0%)	73,361 (6.9%)
Hemorrhagic or ischemic stroke	10,197 (5.4%)	25,467 (6.3%)	22,109 (3.4%)	47,576 (4.5%)
Coagulopathy	2,928 (1.6%)	6,095 (1.5%)	6,086 (.9%)	12,181 (1.1%)
Lymphoma	6,506 (3.5%)	11,323 (2.8%)	11,808 (1.8%)	23,131 (2.2%)
Metastatic cancer	17,654 (9.4%)	35,097 (8.7%)	42,177 (6.5%)	77,274 (7.3%)
Solid tumor without mets	29,431 (15.7%)	104,877 (25.9%)	107,485 (16.4%)	212,362 (20.0%)
Renal failure	8,676 (4.6%)	19,071 (4.7%)	19,875 (3.0%)	38,946 (3.7%)
Liver failure Rheumatoid arthritis/collagen vascular diseases	8,584 (4.6%)	20,953 (5.2%)	27,768 (4.2%)	48,721 (4.6%)
Obesity	17,709 (9.4%)	44,279 (10.9%)	72,278 (11.1%)	116,557 (11.0%)
Total	187,919 (100.0%)	405,677 (100.0%)	653,797 (100.0%)	1,059,474 (100.0%)
Unadjusted outcome incidence				
Inpatient stay	33,058 (17.6%)	75,670 (18.7%)	91,660 (14.0%)	167,330 (15.8%)
ICU/CCU services during inpatient stay	15,360 (46.5%)	37,894 (50.1%)	45,129 (49.2%)	83,023 (49.6%)
ARDS diagnosis during inpatient stay	1,051 (3.2%)	2,598 (3.4%)	3,403 (3.7%)	6,001 (3.6%)
ARD diagnosis during inpatient stay	1,781 (5.4%)	4,749 (6.3%)	5,388 (5.9%)	10,137 (6.1%)
Died same or following calendar month	12,933 (6.9%)	28,753 (7.1%)	26,411 (4.0%)	55,164 (5.2%)

Table 2. Main analysis results from linear probability model; full results in supplementary materials.

	(1)	(2)	(3)	(4)	(5)
	Inpatient stay	Inpatient stay with ICU/CCU	Inpatient stay with ARD dx	Inpatient stay with ARDS dx	Died same or following month
	Key coefficie	nt estimates (95%	6 confidence inte	rval)	
Season	C	C	C	C	C
2017-2018 flu season	ref.	ref.	ref.	ref.	ref.
2018-2019 flu season	-0.001	0.008	0.013***	-0.007***	0.000
	(-0.004, 0.002)	(-0.002, 0.018)	(0.008, 0.017)	(-0.010,-0.004)	(-0.002,0.002)
2019-2020 flu season	0.018***	0.035***	0.013***	0.013***	0.016***
	(0.015, 0.021)	(0.026, 0.044)	(0.008, 0.017)	(0.009, 0.016)	(0.014, 0.017)
HTN medication group					
Other medications only	ref.	ref.	ref.	ref.	ref.
Other inedications only					
ACEi or ARB	-0.019***	-0.009	-0.007**	-0.003	-0.009***
plus/minus other	(-0.022,-0.016)	(-0.019,0.001)	(-0.011,-0.002)	(-0.007,0.000)	(-0.011,-0.008)
medications	(0.022, 0.010)	(0.01),0.001)	(0.011, 0.002)	(0.007,0.000)	(0.011, 0.000)
Season/medication interactions					
2018-2019 season:	0.004*	0.010	0.004	0.000	0.000
ACEi or ARB	(0.001,0.008)	(-0.004,0.023)	(-0.003,0.010)	(-0.004,0.004)	(-0.002,0.002)
plus/minus other medications	(0.001,0.000)	(0.004,0.023)	(0.003,0.010)	(0.004,0.004)	(0.002,0.002)
2019-2020 season:	0.015***	0.015*	0.007*	0.009***	-0.002
ACEi or ARB plus/minus other medications Note: p value for coefficien	(0.012,0.019)	(0.003,0.027)	(0.001,0.012)	(0.004,0.013)	(-0.004,0.001)

Note: p-value for coefficients is for the null hypothesis that the coefficient = 0; presented in probability units (e.g., coefficient of -0.001 represents -0.1 percentage points)

Marginal effects/predicted probability (95% confidence interval)

Other hypertension medications only					
2017/18	0.179	0.482	0.053	0.030	0.064
	(0.177, 0.181)	(0.474, 0.489)	(0.050, 0.056)	(0.028, 0.033)	(0.062, 0.065)
2018/19	0.178	0.490	0.066	0.023	0.064
	(0.176, 0.180)	(0.483, 0.496)	(0.062, 0.069)	(0.021, 0.025)	(0.063, 0.065)
2019/20	0.196	0.516	0.066	0.043	0.080

	(1)	(2)	(3)	(4)	(5)
	Inpatient stay	Inpatient stay with ICU/CCU	Inpatient stay with ARD dx	Inpatient stay with ARDS dx	Died same or following month
	(0.195, 0.198)	(0.511,0.521)	(0.063, 0.068)	(0.041, 0.045)	(0.078, 0.081)
ACEi or ARB plus/minus other medications					
2017/18	0.125	0.463	0.045	0.029	0.035
2018/19	(0.124,0.127) 0.128	(0.456,0.470) 0.481	0.042,0.048)	(0.027,0.031) 0.021	(0.034,0.035) 0.034
2019/20	(0.127,0.130) 0.158	(0.475,0.487) 0.512	(0.058,0.064) 0.064	(0.020,0.023) 0.050	(0.034,0.035) 0.049
	(0.157, 0.160)	(0.508, 0.517)	(0.062, 0.066)	(0.048, 0.052)	(0.048, 0.049)
	Ratios of ma	rginal effects (95%	% confidence inte	rval)	
Other hypertension		· ·		,	
medications only	(V			
2018/19 season vs. 2017/18	0.994 (0.977,1.011)	1.017 (0.996,1.038)	1.236*** (1.136,1.337)	0.759*** (0.668,0.850)	0.999 (0.969,1.030)
2019/20 season vs.	1.099***	1.072***	1.238***	1.414***	1.244***
2017/18	(1.081, 1.116)	(1.053, 1.092)	(1.147,1.330)	(1.278, 1.550)	(1.210, 1.278)
ACEi or ARB plus/minus other medications					
2018/19 season vs.	1.025**	1.039***	1.360***	0.739***	0.993
2017/18	(1.009, 1.042)	(1.019,1.058)	(1.251,1.469)	(0.656, 0.822)	(0.961,1.025)
2019/20 season vs.	1.264***	1.107***	1.437***	1.731***	1.404***
2017/18	(1.245,1.282)	(1.088,1.126)	(1.332,1.542)	(1.580,1.882)	(1.363,1.444)

Note: p-value for risk ratios is for the null hypothesis that the risk ratio = 1 p<0.05, ** p<0.01, *** p<0.001

ref.: reference category

^{*} p<0.05, ** p<0.01, *** p<0.001

SUPPLEMENTARY MATERIAL S1

SUPPLEMENT T1: Codes used to define AVRI, CAD, stroke, DVT, and PE

Condition	Codes
Acute viral respiratory illness (AVRI)	B9721, B9729, J09*, J10*, J11*, J12*, J16,
	J168, J18, J180, J181, J182, J188, J189, J20,
	J201, J203, J204, J205, J206, J207, J208,
	J209, J22, J40, J440, J470, J8411, J84111,
	U071, U072
Coronary artery disease (CAD)	120*, 121*, 122*, 123*, 124*, 125*
Stroke	I63*, Z8673*, I60*, I61*, I62*
Deep vein thrombosis (DVT) and pulmonary	I8249, I824Y, I824Z, I8251, I8259, I825Y,
embolism (PE)	I825Z, I8262, I8272, I26*, I2782

SUPPLEMENT T2: Hypertension medications

Medication type	Included medications (generic name)
ACEi	captopril, lisinopril, enalapril, benazepril,
	perindopril, quinapril, fosinopril, moexipril,
	ramipril, trandolapril
ARB	losartan, valsartan, irbesartan, candesartan,
	eprosartan, telmisartan, azilsartan, Olmesartan
Other (excluding topical, ophthalmic, and	Bendroflumethiazide, chlorothiazide,
drops preparations)	indapamide, metolazone, bumetanide,
	furosemide, torsemide, ethacrynic, amiloride,
	triamterene, eplerenone, spironolactone,
	aliskiren, diltiazem, verapamil, amlodipine,
	nicardipine, felodipine, nifedipine, torsemide,
	ethacrynic, isradipine, nisoldipine, doxazosin,
	prazosin, terazosin, clonidine, guanfacine,
	methyldopa, reserpine, hydralazine,
	minoxidil, acebutolol, atenolol, betaxolol,
	bisoprolol, carvedilol, labetalol, metoprolol,
	nadolol, nebivolol, penbutolol, pindolol,
	propranolol, timolol

2		(4)	(2)	Primary analysis	(4)	(5)
3		(1) Inpatient stay (95% confidence interval)		(3) Inpatient stay with ARD dx (95% confidence interval)	(4) Inpatient stay with ARDS dx (95% confidence interval)	(5) Died same or following month (95% confidence interval)
5	Flu season / medication type					
	2017-2018 flu season	ref.	ref.	ref.	ref.	ref.
6	2018-2019 flu season	-0.001	0.008	0.013***	-0.007***	0.000
7	2018-2019 Hu Season	(-0.004,0.002)	(-0.002,0.018)	(0.008,0.017)	(-0.010,-0.004)	(-0.002,0.002)
8	2019-2020 flu season	0.018***	0.035***	0.013***	0.013***	0.016***
9		(0.015,0.021)	(0.026,0.044)	(0.008, 0.017)	(0.009,0.016)	(0.014, 0.017)
10	Other medications only	ref.	ref.	ref.	ref.	ref.
11	ACEi or ARB plus/minus other medications	-0.019***	-0.009	-0.007**	-0.003	-0.009***
12	ACEI OF AND plus/Illinus other medications	(-0.022,-0.016)	(-0.019,0.001)	(-0.011,-0.002)	(-0.007,0.000)	(-0.011,-0.008)
13	ACEi or ARB monotherapy	(3325) 3321,	(,,	(0.022)	(,,	(3.322)
14						
	2018-2019 season: ACEi or ARB +- other	0.004*	0.01	0.004	0	0
15	2018-2019 season: ACEi or ARB monotherapy	(0.001,0.008)	(-0.004,0.023)	(-0.003,0.010)	(-0.004,0.004)	(-0.002,0.002)
16	2016-2019 Season. ACEI of AND Infoliationapy					
17	2019-2020 season: ACEi or ARB +/- other	0.015***	0.015*	0.007*	0.009***	-0.002
18		(0.012,0.019)	(0.003,0.027)	(0.001,0.012)	(0.004,0.013)	(-0.004,0.001)
19	2019-2020 season: ACEi or ARB monotherapy					
20	Demographics					
21	Female	-0.016***	-0.023***	0	-0.004***	-0.011***
22		(-0.017,-0.014)	(-0.028,-0.018)	(-0.002,0.003)	(-0.006,-0.002)	(-0.012,-0.010)
23	Age categories					
23 24	<35	-0.006*	-0.029	0.02	-0.01	-0.001
	35-44	(-0.011,-0.000) -0.008***	(-0.078,0.019) -0.028	(-0.006,0.045) 0.006	(-0.028,0.008) -0.004	(-0.003,0.001) 0.001
25	35-44	(-0.012,-0.005)	(-0.056,0.000)	(-0.008,0.019)	(-0.016,0.008)	(-0.000,0.002)
26	45-54	ref.	ref.	ref.	ref.	ref.
27						
28	55-64	0.010***	0.005	0.001	0.001	0.001*
29	65-74	(0.008,0.013) 0.011***	(-0.009,0.020) -0.003	(-0.005,0.008) 0.001	(-0.005,0.007) -0.001	(0.000,0.002) 0.009***
30	03 74	(0.008,0.014)	(-0.017,0.011)	(-0.006,0.008)	(-0.007,0.004)	(0.007,0.010)
31	75-84	0.029***	-0.026***	-0.002	-0.005	0.024***
32		(0.025,0.032)	(-0.041,-0.012)	(-0.009,0.004)	(-0.011,0.001)	(0.023,0.026)
33	85+	0.045***	-0.071***	-0.010**	-0.014***	0.063***
34	Insurance coverage type Medicare Advantage	(0.041,0.048) ref.	(-0.086,-0.056) ref.	(-0.017,-0.003) ref.	(-0.020,-0.008) ref.	(0.061,0.065) ref.
	Wedicare Advantage	TCT.	ici.	ici.	ici.	ici.
35	Commercial	-0.032***	0.01	0.001	0.003	-0.001*
36	Census region	(-0.034,-0.030)	(-0.001,0.020)	(-0.004,0.006)	(-0.002,0.007)	(-0.002,-0.000)
37	Unknown/other	-0.046**	0.194*	-0.011	0.009	-0.023*
38	New England	(-0.075,-0.016) ref.	(0.014,0.373) ref.	(-0.086,0.064) ref.	(-0.068,0.087) ref.	(-0.044,-0.002) ref.
39	New Liigianu	iei.	iei.	iei.	ici.	ici.
40	Mid Atlantic	-0.008***	0.017*	0.021***	0.021***	-0.005**
41		(-0.012,-0.003)	(0.003,0.031)	(0.015,0.028)	(0.016,0.026)	(-0.008,-0.002)
	South Atlantic	-0.001	0.122***	0.016***	0.003	-0.016***
42		(-0.005,0.003)	(0.110,0.134)	(0.011,0.021)	(-0.002,0.007)	(-0.018,-0.013)
43						
44		Fanna annual annual	.l			
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E North Central

E South Central

W North Central

W South Central

Unknown/other

Mountain

Pacific Race/ethnicity

White

Black

Asian

Hispanic

Comorbidities

Diabetes without CC

Uncomp hypertension

Coronary artery disease

Congestive heart failure

Chronic pulmonary diseases

Non-metastatic solid tumor

Peripheral vascular disorders

Cardiac arrhythmias

Comp hypertension

Renal failure

Liver failure

Lymphoma

Metastatic cancer

Diabetes with CC

No diabetes

		Primary analysis		
(1)	(2)	(3)	(4)	(5)
Inpatient stay	Inpatient stay with ICU/CCU	Inpatient stay with ARD dx	Inpatient stay with ARDS dx	Died same or following month
(95% confidence interval)	(95% confidence interval)	(95% confidence interval)	(95% confidence interval)	(95% confidence interval)
0.018***	0.073***	0.003	0	-0.009***
(0.013,0.022)	(0.060,0.086)	(-0.002,0.009)	(-0.004,0.004)	(-0.012,-0.007)
0.011***	0.071***	0.018***	-0.001	-0.009***
(0.007,0.016)	(0.056,0.085)	(0.011,0.024)	(-0.006,0.005)	(-0.011,-0.006)
0.027***	0.093***	0.004	0.006*	-0.007***
(0.022,0.032)	(0.079,0.107)	(-0.002,0.010)	(0.001,0.011)	(-0.010,-0.004)
0.014***	0.111***	0.017***	0.003	-0.011***
(0.010,0.018)	(0.097,0.124)	(0.011,0.023)	(-0.002,0.007)	(-0.014,-0.009)
-0.033***	0.122***	-0.007	0.008*	-0.019***
(-0.037,-0.028) -0.002	(0.103,0.140) 0.170***	(-0.015,0.000)	(0.001,0.016) 0.001	(-0.022,-0.016) -0.016***
(-0.007,0.004)		0.008 (-0.000,0.017)	(-0.006,0.007)	
-0.007***	(0.151,0.189) 0.020***	0.004*	0.009***	(-0.019,-0.013) -0.002**
(-0.010,-0.005)	(0.013,0.028)	(0.001,0.008)	(0.006,0.012)	(-0.003,-0.001)
ref.	ref.	(0.001,0.008) ref.	ref.	ref.
Tel.	iei.	iei.	iei.	iei.
0.011***	-0.010**	0.005**	0.008***	0.004***
(0.009,0.013)	(-0.017,-0.003)	(0.002,0.008)	(0.006,0.011)	(0.002,0.005)
-0.016***	0.086***	0.011***	0.010***	-0.008***
(-0.018,-0.013)	(0.077,0.095)	(0.006,0.015)	(0.007,0.014)	(-0.009,-0.006)
-0.011***	0.020*	0.002	0.007	-0.001
(-0.016,-0.007)	(0.002,0.039)	(-0.007,0.010)	(-0.000,0.014)	(-0.004,0.002)
ref.	ref.	ref.	ref.	ref.
0.011***	0.012**	0.005**	0.004**	0.005***
(0.009,0.013)	(0.004,0.019)	(0.001,0.009)	(0.001,0.007)	(0.004,0.006)
0.029***	0.008**	-0.002	0.002	0.008***
(0.027,0.031)	(0.002,0.014)	(-0.005,0.001)	(-0.000,0.004)	(0.006,0.009)
ref.	ref.	ref.	ref.	ref.
0.023***	-0.012**	-0.003	-0.003*	-0.001
(0.020,0.026)	(-0.012,-0.005)	(-0.006,0.000)	(-0.005,-0.000)	(-0.003,0.001)
0.020,0.026)	0.028***	0.001	-0.002	0.007***
(0.018,0.022)	(0.022,0.033)	(-0.001,0.004)	(-0.004,0.000)	(0.006,0.009)
0.093***	0.077***	0.018***	0.002*	0.036***
(0.090,0.095)	(0.072,0.083)	(0.015,0.020)	(0.000,0.004)	(0.034,0.037)
0.061***	-0.010***	0.015***	-0.007***	-0.002***
(0.059,0.063)	(-0.015,-0.005)	(0.013,0.018)	(-0.009,-0.006)	(-0.003,-0.001)
0.019***	0.012***	-0.001	0.001	0.023***
(0.017,0.022)	(0.005,0.018)	(-0.004,0.003)	(-0.001,0.004)	(0.021,0.025)
0.046***	0.035***	-0.003	0	0.059***
(0.042,0.051)	(0.025,0.045)	(-0.008,0.002)	(-0.004,0.004)	(0.056,0.063)
0.122***	0.01	0.003	-0.010***	0.136***
(0.115,0.130)	(-0.003,0.024)	(-0.004,0.009)	(-0.014,-0.006)	(0.130,0.142)
0.064***	-0.008	-0.001	-0.010***	0.027***
(0.056,0.073)	(-0.025,0.009)	(-0.009,0.007)	(-0.015,-0.004)	(0.021,0.033)
0.036***	0.018***	0	-0.003*	0.028***
(0.033,0.040)	(0.009,0.027)	(-0.004,0.005)	(-0.006,-0.000)	(0.026,0.030)
-0.008***	0.017***	0.004**	0.001	0.018***
(-0.011,-0.006)	(0.010,0.023)	(0.001,0.008)	(-0.001,0.003)	(0.017,0.020)
0.062***	0.062***	0.005***	-0.002*	0.024***

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			Primary analysis		
	(1)	(2)	(3)	(4)	(5)
	Inpatient stay	Inpatient stay with ICU/CCU	Inpatient stay with ARD dx	Inpatient stay with ARDS dx	Died same or following month
	(95% confidence interval)	(95% confidence interval)	(95% confidence interval)	(95% confidence interval)	(95% confidence interval)
	(0.060,0.064)	(0.057,0.067)	(0.002,0.007)	(-0.004,-0.000)	(0.023,0.025)
Rheumatoid arthritis/collagen vascular diseases	0.016***	-0.005	-0.007**	0	0.004***
	(0.013,0.020)	(-0.016,0.005)	(-0.012,-0.002)	(-0.004,0.004)	(0.002,0.006)
Coagulopathy	0.029***	0.032***	-0.004	0.002	0.035***
	(0.024,0.033)	(0.023,0.041)	(-0.008,0.000)	(-0.001,0.005)	(0.032,0.038)
Obesity	-0.002	0.013***	0.004	0.009***	-0.009***
	(-0.005,0.000)	(0.006,0.021)	(-0.000,0.007)	(0.006,0.012)	(-0.010,-0.007)
Chronic/acute deep vein thrombosis or pulmonary embolism	0.061***	0.050***	0.003	0.002	0.030***
	(0.056,0.067)	(0.039,0.061)	(-0.003,0.009)	(-0.003,0.006)	(0.026,0.034)
Hemorrhagic or ischemic stroke	0.016***	0.032***	0.002	-0.004**	0.043***
	(0.013,0.020)	(0.024,0.040)	(-0.001,0.006)	(-0.007,-0.001)	(0.040,0.045)
Valvular disease	-0.009***	0.045***	0.007***	-0.002	0.017***
	(-0.012,-0.006)	(0.038,0.052)	(0.003,0.010)	(-0.004,0.001)	(0.015,0.019)
Constant	0.058***	0.310***	0.020***	0.034***	0.012***
	(0.053,0.063)	(0.291,0.330)	(0.011,0.029)	(0.027,0.041)	(0.009,0.015)
N	1059474	167330	167330	167330	1057707
N_clust	728455	147846	147846	147846	727311
p	<0.001	<0.001	<0.001	<0.001	<0.001
R-squared	0.081	0.037	0.006	0.008	0.076
				0.008	

	Sensitivity analysis: ACEi/ARB monother	ару			
	(6)	(7)	(8)	(9)	(10)
	Inpatient stay	Inpatient stay with ICU/CCU	Inpatient stay with ARD dx	Inpatient stay with ARDS dx	Died same or following month
	(95% confidence interval)	(95% confidence interval)	(95% confidence interval)	(95% confidence interval)	(95% confidence interval)
Flu season / medication type					
2017-2018 flu season	ref.	ref.	ref.	ref.	ref.
2018-2019 flu season	-0.001	0.008	0.013***	-0.007***	0
	(-0.004,0.002)	(-0.002,0.018)	(0.008,0.017)	(-0.010,-0.004)	(-0.002,0.002)
2019-2020 flu season	0.018***	0.035***	0.013***	0.013***	0.016***
	(0.015,0.021)	(0.026,0.044)	(0.008,0.017)	(0.009,0.016)	(0.014,0.017)
Other medications only	ref.	ref.	ref.	ref.	ref.
ACEi or ARB plus/minus other medications	-0.020***	-0.004	-0.007**	-0.002	-0.010***
	(-0.023,-0.017)	(-0.014,0.006)	(-0.011,-0.002)	(-0.006,0.001)	(-0.012,-0.009)
ACEi or ARB monotherapy	-0.016***	-0.039***	-0.007	-0.009**	-0.004***
	(-0.020,-0.012)	(-0.057,-0.020)	(-0.015,0.001)	(-0.015,-0.003)	(-0.006,-0.002)
2018-2019 season: ACEi or ARB +- other	0.004*	0.004	0.004	-0.001	-0.001
	(0.000,0.008)	(-0.009,0.018)	(-0.003,0.010)	(-0.005,0.004)	(-0.003,0.002)
2018-2019 season: ACEi or ARB monotherapy	0.005	0.040**	0.002	0.002	0.001
	(-0.001,0.010)	(0.015,0.065)	(-0.009,0.013)	(-0.006,0.009)	(-0.002,0.004)
2019-2020 season: ACEi or ARB +/- other	0.015***	0.011	0.007*	0.008***	-0.001
	(0.011,0.019)	(-0.001,0.024)	(0.002,0.013)	(0.003,0.013)	(-0.004,0.001)
2019-2020 season: ACEi or ARB monotherapy	0.017***	0.035**	0.004	0.012**	-0.003*
5	(0.012,0.022)	(0.013,0.057)	(-0.006,0.013)	(0.004,0.020)	(-0.006,-0.000)
Demographics	0.045***	0.000444		0.004***	0.044**
Female	-0.016***	-0.023***	0	-0.004***	-0.011***
Annual control	(-0.017,-0.014)	(-0.028,-0.018)	(-0.002,0.003)	(-0.006,-0.002)	(-0.012,-0.010)
Age categories	0.000*	0.000	0.03	0.04	0.004
<35	-0.006*	-0.029	0.02	-0.01	-0.001
35-44	(-0.012,-0.000) -0.008***	(-0.078,0.020) -0.028	(-0.005,0.045) 0.006	(-0.028,0.008) -0.004	(-0.003,0.001) 0.001
55-44	(-0.012,-0.005)	(-0.056,0.000)			
45-54	(-0.012,-0.005) ref.	(-0.056,0.000) ref.	(-0.008,0.019) ref.	(-0.016,0.008) ref.	(-0.001,0.002) ref.
43-34	iei.	iei.	iei.	iei.	iei.
55-64	0.010***	0.005	0.001	0.001	0.001*
33 04	(0.008,0.013)	(-0.009,0.020)	(-0.005,0.008)	(-0.005,0.007)	(0.000,0.002)
65-74	0.011***	-0.003	0.001	-0.001	0.009***
03 / 4	(0.008,0.014)	(-0.017,0.011)	(-0.006,0.008)	(-0.007,0.004)	(0.007,0.010)
75-84	0.029***	-0.026***	-0.002	-0.005	0.024***
,5 0.	(0.026,0.032)	(-0.041,-0.012)	(-0.009,0.004)	(-0.011,0.001)	(0.023,0.026)
85+	0.045***	-0.072***	-0.010**	-0.014***	0.063***
Insurance coverage type	(0.041,0.049)	(-0.087,-0.057)	(-0.017,-0.003)	(-0.020,-0.008)	(0.061,0.065)
Medicare Advantage	ref.	ref.	ref.	ref.	ref.
•					
Commercial	-0.032***	0.01	0.001	0.003	-0.001**
Census region	(-0.035,-0.030)	(-0.001,0.021)	(-0.004,0.006)	(-0.002,0.007)	(-0.002,-0.000)
Unknown/other	-0.045**	0.196*	-0.011	0.009	-0.023*
	(-0.075,-0.016)	(0.016,0.375)	(-0.086,0.064)	(-0.068,0.087)	(-0.044,-0.002)
New England	ref.	ref.	ref.	ref.	ref.
Mid Atlantic	-0.008***	0.017*	0.021***	0.021***	-0.005**
	(-0.012,-0.003)	(0.003,0.031)	(0.015,0.028)	(0.016,0.026)	(-0.008,-0.002)
South Atlantic	-0.001	0.122***	0.016***	0.003	-0.016***
	(-0.005,0.003)	(0.110,0.134)	(0.011,0.021)	(-0.002,0.007)	(-0.018,-0.013)

	(6)	(7)	(8)	(9)	(10)
	Inpatient stay	Inpatient stay with ICU/CCU	Inpatient stay with ARD dx	Inpatient stay with ARDS dx	Died same or following mont
	(95% confidence interval)	(95% confidence interval)	(95% confidence interval)	(95% confidence interval)	(95% confidence interval)
North Central	0.018***	0.073***	0.003	0	-0.009***
	(0.013,0.022)	(0.060,0.086)	(-0.002,0.009)	(-0.004,0.004)	(-0.012,-0.007)
South Central	0.011***	0.070***	0.018***	-0.001	-0.008***
	(0.007,0.016)	(0.056,0.085)	(0.011,0.024)	(-0.006,0.004)	(-0.011,-0.006)
V North Central	0.027***	0.093***	0.004	0.006*	-0.007***
	(0.022,0.032)	(0.079,0.107)	(-0.002,0.010)	(0.001,0.011)	(-0.010,-0.004)
/ South Central	0.014***	0.111***	0.017***	0.003	-0.011***
	(0.010,0.018)	(0.097,0.124)	(0.011,0.023)	(-0.002,0.007)	(-0.014,-0.009)
l ountain	-0.033***	0.122***	-0.007	0.008*	-0.019***
	(-0.037,-0.028)	(0.103,0.141)	(-0.015,0.000)	(0.001,0.016)	(-0.022,-0.016)
acific	-0.002	0.170***	0.008	0.001	-0.016***
ace/ethnicity	(-0.007,0.004)	(0.151,0.189)	(-0.000,0.017)	(-0.006,0.007)	(-0.019,-0.013)
Inknown/other	-0.007***	0.020***	0.004*	0.009***	-0.002**
	(-0.010,-0.005)	(0.013,0.028)	(0.001,0.008)	(0.006, 0.012)	(-0.003,-0.001)
Vhite	ref.	ref.	ref.	ref.	ref.
lack	0.011***	-0.010**	0.005**	0.008***	0.004***
	(0.009,0.013)	(-0.017,-0.003)	(0.002,0.008)	(0.006,0.011)	(0.003,0.005)
lispanic	-0.016***	0.086***	0.011***	0.010***	-0.008***
	(-0.018,-0.013)	(0.077,0.095)	(0.006, 0.015)	(0.007,0.014)	(-0.009,-0.006)
sian	-0.012***	0.020*	0.002	0.007	-0.001
omorbidities	(-0.016,-0.007)	(0.002,0.039)	(-0.007,0.010)	(-0.000,0.014)	(-0.004,0.001)
lo diabetes	ref.	ref.	ref.	ref.	ref.
iabetes without CC	0.011***	0.012**	0.005**	0.004**	0.005***
	(0.009,0.013)	(0.004,0.019)	(0.001,0.009)	(0.001,0.007)	(0.004,0.006)
iabetes with CC	0.029***	0.008**	-0.002	0.002	0.008***
	(0.027,0.031)	(0.002,0.014)	(-0.005,0.001)	(-0.000,0.004)	(0.006,0.009)
Jncomp hypertension	ref.	ref.	ref.	ref.	ref.
Comp hypertension	0.023***	-0.012**	-0.003	-0.003*	-0.001
omp hypertension	(0.020,0.026)	(-0.019,-0.005)	(-0.006,0.000)	(-0.005,-0.000)	(-0.003,0.001)
oronary artery disease	0.020***	0.027***	0.001	-0.002	0.008***
oronary artery disease	(0.018,0.022)	(0.022,0.033)	(-0.001,0.004)	(-0.004,0.000)	(0.006,0.009)
ongestive heart failure	0.016,0.022)	0.022,0.033)	0.017***	0.002	0.036***
ongestive near randic	(0.091,0.096)	(0.071,0.082)	(0.015,0.020)	(-0.000,0.004)	(0.035,0.038)
hronic pulmonary diseases	0.061***	-0.010***	0.015,0.020)	-0.007***	-0.002***
mone pullionary diseases	(0.059,0.063)	(-0.015,-0.005)	(0.013,0.018)	(-0.009,-0.006)	(-0.003,-0.001)
enal failure	0.019***	(-0.015,-0.005) 0.012***	-0.001	0.001	0.023***
charranule	(0.017,0.022)	(0.005,0.018)	(-0.001	(-0.001,0.003)	(0.021,0.025)
iver failure	(0.017,0.022) 0.046***	0.005,0.018)	-0.004,0.003)	(-0.001,0.003) O	(0.021,0.025)
iver ranule			-0.003 (-0.008,0.002)	· ·	
Antastatic cancer	(0.042,0.051) 0.122***	(0.025,0.045) 0.01	0.003	(-0.004,0.004) -0.010***	(0.056,0.063) 0.136***
Metastatic cancer					
	(0.115,0.130)	(-0.003,0.024)	(-0.004,0.009)	(-0.014,-0.006)	(0.130,0.142)
ymphoma	0.064***	-0.008	-0.001	-0.010***	0.027***
	(0.056,0.073)	(-0.025,0.009)	(-0.009,0.007)	(-0.015,-0.004)	(0.021,0.033)
Ion-metastatic solid tumor	0.036***	0.018***	0	-0.003*	0.028***
	(0.033,0.040)	(0.009,0.027)	(-0.004,0.005)	(-0.006,-0.000)	(0.026,0.030)
eripheral vascular disorders	-0.008***	0.017***	0.004**	0.001	0.018***
	(-0.011,-0.006)	(0.010,0.023)	(0.001,0.008)	(-0.001,0.003)	(0.017,0.020)
Cardiac arrhythmias	0.062***	0.062***	0.005***	-0.002*	0.024***

Sei	nsitivity analysis: ACEi/ARB monothera	ару			
	(6)	(7)	(8)	(9)	(10)
	Inpatient stay	Inpatient stay with ICU/CCU	Inpatient stay with ARD dx	Inpatient stay with ARDS dx	Died same or following month
	(95% confidence interval)	(95% confidence interval)	(95% confidence interval)	(95% confidence interval)	(95% confidence interval)
	(0.060,0.064)	(0.057,0.067)	(0.002,0.007)	(-0.004,-0.000)	(0.023,0.026)
Rheumatoid arthritis/collagen vascular diseases	0.016***	-0.005	-0.007**	0	0.004***
	(0.013,0.020)	(-0.016,0.006)	(-0.012,-0.002)	(-0.004,0.004)	(0.002,0.006)
Coagulopathy	0.029***	0.032***	-0.004	0.002	0.035***
	(0.024,0.033)	(0.023, 0.041)	(-0.008,0.000)	(-0.001,0.005)	(0.032,0.038)
Obesity	-0.002	0.013***	0.004	0.009***	-0.008***
	(-0.004,0.000)	(0.006, 0.021)	(-0.000,0.007)	(0.006,0.012)	(-0.010,-0.007)
Chronic/acute deep vein thrombosis or pulmonary embolism	0.061***	0.050***	0.003	0.002	0.030***
	(0.055,0.067)	(0.039,0.061)	(-0.003,0.009)	(-0.002,0.006)	(0.026,0.034)
Hemorrhagic or ischemic stroke	0.016***	0.032***	0.002	-0.004**	0.043***
	(0.013,0.019)	(0.024,0.040)	(-0.001,0.006)	(-0.007,-0.001)	(0.040,0.045)
Valvular disease	-0.009***	0.045***	0.007***	-0.002	0.017***
	(-0.012,-0.006)	(0.038,0.052)	(0.003,0.010)	(-0.004,0.001)	(0.015,0.019)
Constant	0.058***	0.312***	0.020***	0.034***	0.012***
	(0.053,0.063)	(0.292,0.332)	(0.011,0.029)	(0.027,0.042)	(0.009,0.015)
N	1059474	167330	167330	167330	1057707
N_clust	728455	147846	147846	147846	727311
p	<0.001	<0.001	<0.001	<0.001	<0.001
R-squared	0.081	0.037	0.006	0.008	0.076
		0.037			

	Sensitivity analysis: Dropping people with comorbidities (other than hypertension)						
	(11)	(12)	(13)	(14)	(15)		
	Inpatient stay (95% confidence interval)	Inpatient stay with ICU/CCU (95% confidence interval)	Inpatient stay with ARD dx (95% confidence interval)	Inpatient stay with ARDS dx (95% confidence interval)	Died same or following month (95% confidence interval)		
Flu season / medication type							
2017-2018 flu season	ref.	ref.	ref.	ref.	ref.		
2018-2019 flu season	0.002	0.02	0.030**	0.006	0		
2019-2020 flu season	(-0.001,0.006) 0.032***	(-0.032,0.072) 0.068**	(0.009,0.051) 0.029***	(-0.005,0.017) 0.052***	(-0.002,0.002) 0.007***		
	(0.028,0.035)	(0.024,0.111)	(0.014,0.045)	(0.039,0.065)	(0.005,0.009)		
Other medications only	ref.	ref.	ref.	ref.	ref.		
ACEi or ARB plus/minus other medications	-0.006***	-0.001	0.009	0.003	-0.003***		
	(-0.009,-0.003)	(-0.049,0.046)	(-0.008,0.026)	(-0.007,0.013)	(-0.004,-0.001)		
ACEi or ARB monotherapy							
2018-2019 season: ACEi or ARB +- other	-0.003	0.004	-0.013	0.001	0.001		
	(-0.007,0.001)	(-0.062,0.071)	(-0.041,0.014)	(-0.015,0.017)	(-0.001,0.003)		
2018-2019 season: ACEi or ARB monotherapy							
2019-2020 season: ACEi or ARB +/- other	-0.001	0.05	-0.022*	-0.001	-0.001		
	(-0.006,0.003)	(-0.006,0.106)	(-0.043,-0.001)	(-0.019,0.016)	(-0.003,0.001)		
2019-2020 season: ACEi or ARB monotherapy							
Demographics							
Female	-0.010***	-0.025*	-0.01	-0.008	-0.003***		
	(-0.012,-0.008)	(-0.048,-0.003)	(-0.019,0.000)	(-0.018,0.002)	(-0.004,-0.002)		
Age categories <35	-0.013***	-0.125	0.089	-0.017	-0.001**		
35	(-0.017,-0.010)	(-0.286,0.037)	(-0.025,0.202)	(-0.074,0.040)	(-0.002,-0.000)		
5-44	-0.007***	-0.151***	0.014	-0.022	-0.001		
	(-0.009,-0.004)	(-0.229,-0.074)	(-0.026,0.055)	(-0.053,0.009)	(-0.001,0.000)		
15-54	ref.	ref.	ref.	ref.	ref.		
55-64	0.003**	-0.041	-0.004	0.006	0.001***		
	(0.001,0.006)	(-0.091,0.009)	(-0.027,0.018)	(-0.018,0.029)	(0.001,0.002)		
55-74	0.006***	-0.056*	-0.017	0.009	0.001*		
	(0.003,0.009)	(-0.109,-0.003)	(-0.041,0.008)	(-0.015,0.032)	(0.000,0.002)		
75-84	0.028***	-0.077**	-0.011	0.005	0.008***		
DF .	(0.024,0.032) 0.074***	(-0.132,-0.022) -0.139***	(-0.037,0.014) -0.022	(-0.019,0.029) -0.007	(0.007,0.010) 0.036***		
85+	(0.068,0.079)	(-0.196,-0.083)	-0.022 (-0.048,0.004)	-0.007 (-0.032,0.017)	(0.032,0.039)		
nsurance coverage type Medicare Advantage	(0.008,0.079) ref.	ref.	(-0.048,0.004) ref.	(-0.032,0.017) ref.	(0.032,0.039) ref.		
vieuicare Advantage	ici.	ici.	iei.	ici.	iei.		
Commercial	-0.013***	-0.043*	-0.01	0.006	-0.004***		
Census region	(-0.015,-0.010)	(-0.083,-0.002)	(-0.028,0.009)	(-0.011,0.024)	(-0.005,-0.003)		
Jnknown/other	-0.034***	0.755***	-0.025*	-0.062***	0.008		
New England	(-0.053,-0.014) ref.	(0.693,0.816) ref.	(-0.050,-0.000) ref.	(-0.089,-0.035) ref.	(-0.018,0.034) ref.		
1id Atlantic	-0.002	0.065*	0.015	0.025	0.002		
	(-0.007,0.004)	(0.008,0.123)	(-0.008,0.038)	(-0.003,0.053)	(-0.001,0.005)		
South Atlantic	-0.004	0.164***	0.012	-0.009	-0.001		

		Sensitivity and
	(11)	(12)
	Inpatient stay	Inpatient stay with
	(95% confidence interval)	(95% confidence
E North Central	0.007**	0.111***
	(0.002,0.013)	(0.058,0.16
E South Central	0.001	0.116***
	(-0.005,0.007)	(0.055,0.17
W North Central	0.009**	0.124***
	(0.003,0.015)	(0.063,0.18
W South Central	0.001	0.142***
	(-0.004,0.007)	(0.086,0.19
Mountain	-0.005	0.161***
	(-0.011,0.001)	(0.087,0.23
Pacific	0	0.173***
Race/ethnicity	(-0.007,0.006)	(0.093,0.25
Unknown/other	0.001	0.056**
•	(-0.002,0.004)	(0.022,0.08
White	ref.	ref.
······································		
Black	0.008***	0
DIACK	(0.006,0.011)	(-0.031,0.03
Hispania	-0.001	0.092***
Hispanic		
A - t	(-0.004,0.001)	(0.054,0.13
Asian	-0.007**	0.029
Comorbidities	(-0.011,-0.002)	(-0.045,0.10
No diabetes		
Diabetes without CC		
Diabetes with CC		
Uncomp hypertension	ref.	ref.
Comp hypertension	0.014***	-0.009
	(0.007,0.021)	(-0.068,0.05
Coronary artery disease		
Congestive heart failure		
Chronic pulmonary diseases		
Renal failure		
Liver failure		
Metastatic cancer		
Lymphoma		
Non-metastatic solid tumor		
Peripheral vascular disorders		
Cardiac arrhythmias		

	Sensitivity analysis: Dro	pping people with comorbidi	ties (other than hypertension)	
(11)	(12)	(13)	(14)	(15)
Inpatient stay	Inpatient stay with ICU/CCU	Inpatient stay with ARD dx	Inpatient stay with ARDS dx	Died same or following month
(95% confidence interval)	(95% confidence interval)	(95% confidence interval)	(95% confidence interval)	(95% confidence interval)
0.007**	0.111***	0.018	0	0
(0.002,0.013)	(0.058,0.165)	(-0.003,0.039)	(-0.024,0.024)	(-0.003,0.002)
0.001	0.116***	0.01	-0.004	-0.001
(-0.005,0.007)	(0.055,0.176)	(-0.014,0.034)	(-0.030,0.023)	(-0.003,0.002)
0.009**	0.124***	0.021	-0.002	0.002
(0.003,0.015)	(0.063,0.184)	(-0.004,0.046)	(-0.028,0.025)	(-0.001,0.004)
0.001	0.142***	0.025*	0.007	0
(-0.004,0.007)	(0.086,0.199)	(0.002,0.049)	(-0.019,0.034)	(-0.002,0.003)
-0.005	0.161***	-0.005	0.019	-0.002
(-0.011,0.001)	(0.087,0.235)	(-0.031,0.020)	(-0.017,0.055)	(-0.005,0.001)
0	0.173***	-0.004	-0.008	-0.003
(-0.007,0.006)	(0.093,0.253)	(-0.032,0.024)	(-0.041,0.025)	(-0.005,0.000)
0.001	0.056**	0.002	0.009	0
(-0.002,0.004)	(0.022,0.089)	(-0.012,0.016)	(-0.006,0.023)	(-0.001,0.001)
ref.	ref.	ref.	ref.	ref.
0.008***	0	0.003	0.01	0.001
(0.006,0.011)	(-0.031,0.032)	(-0.010,0.016)	(-0.003,0.023)	(-0.000,0.002)
-0.001	0.092***	0.016	0.035***	-0.001*
(-0.004,0.001)	(0.054,0.130)	(-0.001,0.034)	(0.015,0.055)	(-0.003,-0.000)
-0.007**	0.029	-0.018	0.018	-0.002
(-0.011,-0.002)	(-0.045,0.103)	(-0.042,0.007)	(-0.018,0.055)	(-0.004,0.000)
ref.	ref.	ref.	ref.	ref.
0.014***	-0.009	-0.009	-0.017	0.006**
(0.007,0.021)	(-0.068,0.050)	(-0.032,0.013)	(-0.036,0.003)	(0.002,0.010)

1			Sensitivity analysis: Dro	opping people with comorbid	ities (other than hypertension)
2 3 4		(11) Inpatient stay (95% confidence interval)	(12) Inpatient stay with ICU/CCU	(13)	(14) Inpatient stay with ARDS dx	(15) Died same or following month (95% confidence interval)
5	Rheumatoid arthritis/collagen vascular diseases					
6 7	Coagulopathy					
8	Obesity					
9 10	Chronic/acute deep vein thrombosis or pulmonary embolism					
11 12	Hemorrhagic or ischemic stroke					
13	Valvular disease					
14 15	Constant	0.027*** (0.020,0.033)	0.268*** (0.190,0.347)	0.027 (-0.003,0.058)	0.006 (-0.026,0.038)	0.006*** (0.003,0.009)
16	N N_clust	200778	7696	7696	7696	200508
17	р	<0.001	7647	7647	7647	<0.001
18 19	R-squared	0.022	0.033	0.007	0.023	0.015
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		Sensitivity analysis: limiting analysis to strict flu season (dropping summer months)					
2017-2019 flu season		Inpatient stay	Inpatient stay with ICU/CCU	Inpatient stay with ARD dx	Inpatient stay with ARDS dx	Died same or following month	
	**	ref.	ref.	ref.	ref.	ref.	
2019-2020 Season: ACE or ARB montherapy C0.0024** C0.012** C0.0024**	2018-2019 flu season						
Other medications only ref. coops. 0.0007 0.001 0.000 0.000,0001 0.001 0.00 0.000,0001 0.000 0.000,0001 0.000,0000 <td>2019-2020 flu season</td> <td>0.003*</td> <td>0.030***</td> <td>0.017***</td> <td>0.010***</td> <td>0.017***</td>	2019-2020 flu season	0.003*	0.030***	0.017***	0.010***	0.017***	
ACE! or ARB monotherapy 2018- 2019 season: ACE! or ARB + other (0.002, 0.001) (-0.002,0.006) (-0.002,0.006) (-0.002,0.006) (-0.002,0.006) (-0.002,0.006) (-0.002,0.006) (-0.002,0.006) (-0.006,0.008) (-0.005,0.004) (-0.003,0.002) 2019- 2020 season: ACE! or ARB monotherapy 2019- 2020	Other medications only	, , ,					
ACE or ARB monotherapy	ACEi or ARB plus/minus other medications						
	ACEi or ARB monotherapy		, , ,	, ,	, , ,	, , ,	
2019-2020 season: ACEi or ARB +/- other 0.008*** 0.008*** 0.0008*** 0.0008*** 0.0008*** 0.0008*** 0.0008*** 0.0008*** 0.0008*** 0.0008*** 0.0008*** 0.0008*** 0.0008*** 0.0008*** 0.0008*** 0.0008*** 0.0008*** 0.0008*** 0.0009**** 0.0001 0.0001 0.0009*** 0.0009*** 0.0001 0.0001 0.0001 0.0009*** 0.0008*** 0.0001	2018-2019 season: ACEi or ARB +- other						
	2018-2019 season: ACEi or ARB monotherapy						
Demographics Female -0.011*** -0.024*** 0.001 -0.001 -0.001 -0.001 -0.003 -0.001 -0.003 -0.001 -0.003 -0.001 -0.003 -0.001 -0.003 -0.001 -0.003 -0.001 -0.001 -0.001 -0.001 -0.001 -0.001 -0.001 -0.001 -0.001 -0.001 -0.003 -0.001 -0.002 0.001 -0.001 -0.002 0.001 -0.001 -0.002 0.001 -0.002 0.001 -0.002 0.001 -0.002 0.001 -0.002 0.001 -0.002 0.001 -0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.003 -0.002 0.002 0.003 -0.002 0.002 0.003 -0.002 0.003 -0.002 0.002 0.003 -0.002 0.003 -0.003 -0.002 0.002 0.003 -0.003 -0.003 -0.002 0.003 -0.003 -0.003 -0.003 -0.003 -0.003 -0.003 -0.003 -0.003	,						
Pemale							
Age categories (-0.012,-0.009) (-0.030,-0.017) (-0.002,0.004) (-0.003,0.001) (-0.010,-0.008) -35 0 -0.051 0.012 -0.014 -0.001 35-44 -0.005*** -0.027 0.005 -0.008 0.001 45-54 ref. ref. ref. ref. ref. ref. 55-64 0.009*** -0.005 0 -0.002 0 65-74 0.009*** -0.009 -0.002 0 -0.001 0 65-74 0.009*** -0.009 -0.002 -0.003 0.006*** 65-74 0.005** -0.002 -0.003 0.006*** 75-84 0.027*** -0.033*** -0.002 -0.003 0.006*** 10065,0121 (-0.014,0023) (-0.011,007) (-0.010,0004) (0.005,008) 75-84 0.027*** -0.033**** -0.002 -0.003 0.006*** 100405**** -0.028*** -0.001 (-0.011,0007) (-0.010,0004) (0.002,002)		0.011***	0.024***	0.001	0.001	0.000***	
Commercial Com							
35-44		0	-0.051	0.012	-0.014	-0.001	
C-0.009,-0.002		(-0.006,0.006)	(-0.111,0.009)	(-0.020,0.044)	(-0.035,0.006)	(-0.003,0.001)	
45-54 ref. ref. ref. ref. ref. ref. ref. ref.	35-44						
(0.006,0.012) (-0.014,0.023) (-0.009,0.009) (-0.009,0.005) (-0.001,0.001) (-0.001,0.001) (-0.002) (-0.002) (-0.003) (-0.001,0.001) (-0.002,0.002) (-0.003) (-0.002) (-0.003) (-0.002,0.008) (-0.002,0.008) (-0.002,0.008) (-0.005,0.008) (-0.005,0.008) (-0.005,0.008) (-0.005,0.008) (-0.005,0.008) (-0.005,0.008) (-0.005,0.008) (-0.005,0.008) (-0.005,0.008) (-0.005,0.008) (-0.005,0.008) (-0.005,0.008) (-0.005,0.008) (-0.005,0.008) (-0.005,0.008) (-0.013,0.004) (-0.014,0.000) (0.022,0.023) (-0.022,0.008) (-0.002,0.008) (-0.002,0.008) (-0.002,0.008) (-0.002,0.008) (-0.002,0.008) (-0.002,0.008) (-0.002,0.008) (-0.002,0.008) (-0.002,0.008) (-0.002,0.008) (-0.002,0.008) (-0.002,0.008) (-0.002,0.008) (-0.002,0.008) (-0.002,0.008) (-0.002,0.008) (-0.002,0.008) (-0.002,0.008) (-0.003,0.008) (-0.002,0.008) (-0.003,0.00	45-54	• • •	, , ,		, , ,		
65-74	55-64						
10.006,0.012	65.74			, , ,			
75-84 0.027*** -0.033*** -0.005 -0.007 0.022*** 85+ 0.049*** -0.078*** -0.012* -0.015*** 0.062*** Insurance coverage type (0.045,0.053) (-0.097,-0.059) (-0.021,-0.003) (-0.022,-0.008) (0.060,0.065) Medicare Advantage ref. ref. ref. ref. ref. ref. ref. ref. ref. 0.002 0.004 0.001 0.001 0.002 0.004 0.001 0.001 0.002 0.004 0.001 0.002 0.004 0.001 0.002 0.004 0.001 0.002 0.004 0.001 0.002 0.004 0.001 0.002 0.004 0.001 0.002 0.004 0.001 0.002 0.004 0.001 0.002 0.004 0.001 0.002 0.002 0.004 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 <td>65-74</td> <td></td> <td></td> <td></td> <td></td> <td></td>	65-74						
85+ 0.049*** -0.078*** -0.012* -0.015*** 0.062*** Insurance coverage type (0.045,0.053) (-0.097,-0.059) (-0.021,-0.003) (-0.022,-0.008) (0.060,0.065) Medicare Advantage ref. 0.002 0.004 0.001 0.001 0.002 0.004 0.001 0.001 0.002 0.004 0.001 0.001 0.002 0.004 0.001 0.001 0.002 0.004 0.001 0.002 0.001 0.002 0.001 0.001 0.002 0.001 0.001 0.002 0.001 0.001 0.002 0.001 0.001 0.002 0.001 0.001 0.002 0.001 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.001 0.002 0.001 0.002 0.001 0.001 0.001 0.001	75-84		, , ,	, , ,	· • • • • • • • • • • • • • • • • • • •		
Insurance coverage type (0.045,0.053) (-0.097,-0.059) (-0.021,-0.003) (-0.022,-0.008) (0.060,0.065) (-0.022,-0.008) (-0.002,0.008) (-0.002,		(0.023,0.030)	(-0.051,-0.015)	(-0.013,0.004)	(-0.014,0.000)	(0.020,0.023)	
Medicare Advantage ref. 0.002 0.004 0.001 0.001 0.002 0.003,0009 (-0.001,0.009) (-0.000,0.002) 0.0024* 0.0024* 0.004 0.004 0.004 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.003 0.002 0.002 0.002 0.002 0.002 0.003 0.002 0.003 0.002 0.003 0.002 0.003	85+						
Commercial -0.028*** 0.006 0.002 0.004 0.001 Census region (-0.030,-0.025) (-0.007,0.019) (-0.005,0.008) (-0.001,0.009) (-0.000,0.002) Unknown/other -0.035 0.219* -0.003 0.016 -0.024* New England ref. ref. ref. ref. ref. ref. ref. ref. ref. 0.002*** 0.002 0.002*** 0.002 0.002*** 0.002 0.002*** 0.002 0.002*** 0.002*** 0.002 0.001,0.006 0.014*** 0.001,0.006 0.001,0.006 0.014*** 0.004*** 0.004 -0.001,0.006 0.019*** 0.001,0.006 0.014*** 0.004 -0.001,0.006 0.019*** 0.001,0.006	- ··						
Census region (-0.030,-0.025) (-0.007,0.019) (-0.005,0.008) (-0.001,0.009) (-0.000,0.002) Unknown/other -0.035 0.219* -0.003 0.016 -0.024* (-0.071,0.000) (0.012,0.426) (-0.099,0.094) (-0.085,0.117) (-0.048,-0.000) New England ref. ref. ref. ref. ref. ref. ref. ref. 0.022*** 0.002 0.002 0.018* 0.021*** 0.022*** 0.002<	Medicare Advantage	ref.	ref.	ref.	ref.	ref.	
Unknown/other -0.035 0.219* -0.003 0.016 -0.024* (-0.071,0.000) (0.012,0.426) (-0.099,0.094) (-0.085,0.117) (-0.048,-0.000) New England ref. ref. ref. ref. ref. ref. ref. o.022*** 0.002 Mid Atlantic (-0.005,0.005) (0.002,0.035) (0.014,0.029) (0.015,0.028) (-0.001,0.006) South Atlantic -0.012*** 0.121*** 0.014*** -0.004 -0.019***	Commercial	-0.028***	0.006	0.002	0.004	0.001	
New England (-0.071,0.000) (0.012,0.426) (-0.099,0.094) (-0.085,0.117) (-0.048,-0.000) New England ref. ref. ref. ref. ref. ref. ref. 0.002*** 0.002 0.002 0.002*** 0.002 0.002 0.002*** 0.002	Census region	(-0.030,-0.025)	(-0.007,0.019)	(-0.005,0.008)	(-0.001,0.009)	(-0.000,0.002)	
New England ref. 0.002 0.002 ref. 0.014**** <td>Unknown/other</td> <td></td> <td></td> <td></td> <td></td> <td></td>	Unknown/other						
Mid Atlantic 0 0.018* 0.021*** 0.022*** 0.002 (-0.005,0.005) (0.002,0.035) (0.014,0.029) (0.015,0.028) (-0.001,0.006) South Atlantic -0.012*** 0.121*** 0.014*** -0.004 -0.019***	Now England	, , ,	, , ,	, , ,	, , ,	, , ,	
(-0.005,0.005) (0.002,0.035) (0.014,0.029) (0.015,0.028) (-0.001,0.006) South Atlantic -0.012*** 0.121*** 0.014*** -0.004 -0.019***	ivew Eligialiu	rei.	rei.	rei.	rei.	rei.	
South Atlantic -0.012*** 0.121*** 0.014*** -0.004 -0.019***	Mid Atlantic						
		• • • •	, , ,			• • •	
(-0.017,-0.008) (0.107,0.135) (0.007,0.020) (-0.009,0.001) (-0.022,-0.016)	South Atlantic						
		(-0.017,-0.008)	(0.107,0.135)	(0.007,0.020)	(-0.009,0.001)	(-0.022,-0.016)	

	Sensitivity analysis: limiting analysis to strict flu season (dropping summer months) (16) (17) (18) (19) (20)						
	` ,	` '	` '	` '	Died same or following mon		
	Inpatient stay (95% confidence interval)	(95% confidence interval)	(95% confidence interval)	(95% confidence interval)	(95% confidence interval)		
North Control	0.008***	0.073***	0.004	-0.008**	-0.012***		
North Central							
Coult Coulty	(0.003,0.013)	(0.058,0.089)	(-0.003,0.011)	(-0.013,-0.002)	(-0.015,-0.009)		
South Central	-0.006*	0.069***	0.015***	-0.010**	-0.014***		
	(-0.011,-0.001)	(0.051,0.087)	(0.007,0.023)	(-0.016,-0.004)	(-0.017,-0.010)		
V North Central	0.013***	0.091***	0.003	-0.004	-0.012***		
	(0.008,0.018)	(0.074,0.109)	(-0.005,0.011)	(-0.010,0.002)	(-0.015,-0.009)		
V South Central	-0.002	0.100***	0.016***	-0.008**	-0.017***		
	(-0.007,0.002)	(0.083,0.116)	(0.008,0.024)	(-0.014,-0.003)	(-0.020,-0.014)		
Mountain	-0.040***	0.115***	-0.009	-0.006	-0.020***		
	(-0.046,-0.035)	(0.091,0.138)	(-0.019,0.001)	(-0.014,0.002)	(-0.024,-0.017)		
acific	-0.008*	0.180***	0.005	-0.006	-0.017***		
ace/ethnicity	(-0.014,-0.001)	(0.158,0.203)	(-0.006,0.015)	(-0.014,0.002)	(-0.021,-0.013)		
Inknown/other	-0.007***	0.013*	0.003	0.005**	0		
•	(-0.010,-0.005)	(0.003,0.023)	(-0.002,0.009)	(0.001,0.009)	(-0.001,0.002)		
/hite	ref.	ref.	ref.	ref.	ref.		
lack	0.011***	-0.012**	0.005*	0.010***	0.004***		
Idek	(0.009,0.014)	(-0.021,-0.004)	(0.000,0.009)	(0.007,0.014)	(0.002,0.005)		
llanania	-0.015***	0.079***					
lispanic			0.010***	0.007**	-0.008***		
	(-0.018,-0.013)	(0.068,0.090)	(0.004,0.015)	(0.003,0.011)	(-0.010,-0.007)		
sian	-0.011***	0.005	0.002	0.006	-0.002		
omorbidities	(-0.016,-0.005)	(-0.017,0.027)	(-0.009,0.012)	(-0.002,0.015)	(-0.005,0.001)		
Io diabetes	ref.	ref.	ref.	ref.	ref.		
Diabetes without CC	0.006***	0.012*	0.004	0.003	0.004***		
	(0.004,0.009)	(0.003,0.022)	(-0.000,0.009)	(-0.001,0.006)	(0.003,0.005)		
piabetes with CC	0.026***	0.006	-0.003	0	0.007***		
	(0.024,0.028)	(-0.001,0.013)	(-0.006,0.001)	(-0.002,0.003)	(0.006,0.008)		
Incomp hypertension	ref.	ref.	ref.	ref.	ref.		
	0.000***	0.000#		•	2 224		
omp hypertension	0.023***	-0.009*	-0.004	0	-0.001		
	(0.020,0.026)	(-0.018,-0.000)	(-0.008,0.000)	(-0.003,0.003)	(-0.003,0.001)		
oronary artery disease	0.018***	0.031***	0	-0.001	0.006***		
	(0.016,0.020)	(0.025,0.038)	(-0.003,0.004)	(-0.003,0.001)	(0.004,0.007)		
ongestive heart failure	0.101***	0.078***	0.018***	0.004***	0.038***		
	(0.098,0.104)	(0.072,0.085)	(0.015,0.022)	(0.002,0.007)	(0.037,0.040)		
hronic pulmonary diseases	0.074***	-0.010**	0.015***	-0.005***	0		
	(0.072,0.076)	(-0.016,-0.004)	(0.012,0.018)	(-0.007,-0.002)	(-0.001,0.001)		
enal failure	0.019***	0.012**	0	0.001	0.023***		
	(0.016,0.022)	(0.004,0.020)	(-0.004,0.004)	(-0.002,0.004)	(0.021,0.025)		
iver failure	0.041***	0.037***	0.004,0.004)	0.004	0.057***		
iver randie	(0.036,0.047)	(0.024,0.050)	(-0.006,0.007)	(-0.001,0.009)	(0.053,0.062)		
Astrologic	, , ,	, , ,	, , ,				
Metastatic cancer	0.118***	0.007	0.001	-0.008**	0.138***		
	(0.109,0.127)	(-0.010,0.023)	(-0.007,0.010)	(-0.013,-0.003)	(0.131,0.146)		
ymphoma	0.064***	-0.009	-0.001	-0.009**	0.023***		
	(0.054,0.073)	(-0.030,0.012)	(-0.011,0.009)	(-0.015,-0.002)	(0.016,0.029)		
Ion-metastatic solid tumor	0.038***	0.021***	0.002	-0.004*	0.030***		
	(0.034,0.042)	(0.010,0.032)	(-0.003,0.008)	(-0.007,-0.000)	(0.027,0.033)		
eripheral vascular disorders	-0.001	0.016***	0.005*	0.004**	0.023***		
eripheral vascular disorders	, , ,	0.016*** (0.008,0.024)	0.005* (0.001,0.009)	0.004** (0.001,0.007)	0.023*** (0.021,0.025)		

	Sensitivity analysis: limiting analysis to strict flu season (dropping summer months)				
	(16)	(17)	(18)	(19)	(20)
	Inpatient stay	Inpatient stay with ICU/CCU	Inpatient stay with ARD dx	Inpatient stay with ARDS dx	Died same or following month
	(95% confidence interval)	(95% confidence interval)	(95% confidence interval)	(95% confidence interval)	(95% confidence interval)
	(0.061,0.066)	(0.058,0.071)	(0.002,0.008)	(-0.003,0.002)	(0.021,0.025)
Rheumatoid arthritis/collagen vascular diseases	0.015***	-0.013	-0.008*	-0.001	0.002
	(0.010,0.019)	(-0.026,0.001)	(-0.014,-0.002)	(-0.005,0.004)	(-0.000,0.005)
Coagulopathy	0.035***	0.032***	-0.002	0.001	0.039***
	(0.030,0.041)	(0.021,0.043)	(-0.008,0.003)	(-0.004,0.005)	(0.035,0.043)
Obesity	-0.002	0.016***	0.004	0.008***	-0.008***
	(-0.005,0.000)	(0.007,0.026)	(-0.001,0.009)	(0.005,0.012)	(-0.010,-0.006)
Chronic/acute deep vein thrombosis or pulmonary embolism	0.053***	0.052***	0.005	0.002	0.026***
	(0.046,0.061)	(0.038,0.066)	(-0.003,0.012)	(-0.004,0.007)	(0.021,0.031)
Hemorrhagic or ischemic stroke	0.018***	0.030***	0.005	-0.003	0.044***
	(0.014,0.022)	(0.020,0.040)	(-0.000,0.010)	(-0.007,0.000)	(0.041,0.047)
Valvular disease	-0.008***	0.053***	0.008***	-0.001	0.016***
	(-0.012,-0.005)	(0.044,0.061)	(0.003, 0.012)	(-0.004,0.003)	(0.014,0.019)
Constant	0.057***	0.314***	0.022***	0.037***	0.013***
	(0.051,0.063)	(0.290,0.338)	(0.010,0.033)	(0.028,0.046)	(0.010,0.017)
N	738240	106917	106917	106917	737059
N_clust	556579	97383	97383	97383	555729
p	<0.001	<0.001	<0.001	<0.001	<0.001
R-squared	0.094	0.039	0.007	0.008	0.082
				0.008	

	Primary analysis				
_	(1)	(2)	(3)	(4)	(5)
	Inpatient stay	Inpatient stay with ICU/CCU	Inpatient stay with ARD dx	Inpatient stay with ARDS dx	Died same or following month
Key coefficient estimates					
Season 2017-2018 flu season	ref.	ref.	ref.	ref.	ref.
2018-2019 flu season	-0.001	0.008	0.013***	-0.007***	0.000
2019-2020 flu season	(-0.004,0.002) 0.018***	(-0.002,0.018) 0.035***	(0.008,0.017) 0.013***	(-0.010,-0.004) 0.013***	(-0.002,0.002) 0.016***
HTN medication group	(0.015,0.021)	(0.026,0.044)	(0.008,0.017)	(0.009,0.016)	(0.014,0.017)
Other medications only	ref.	ref.	ref.	ref.	ref.
ACEi or ARB plus/minus other medications	-0.019***	-0.009	-0.007**	-0.003	-0.009***
ACEi or ARB monotherapy	(-0.022,-0.016) N/A	(-0.019,0.001) N/A	(-0.011,-0.002) N/A	(-0.007,0.000) N/A	(-0.011,-0.008) N/A
Season/medication interactions					
2018-2019 season: ACEi or ARB +- other	0.004*	0.01	0.004	0	0
2018-2019 season: ACEi or ARB monotherapy	(0.001,0.008) N/A	(-0.004,0.023) N/A	(-0.003,0.010) N/A	(-0.004,0.004) N/A	(-0.002,0.002) N/A
2019-2020 season: ACEi or ARB +/- other	0.015***	0.015*	0.007*	0.009***	-0.002
2019-2020 season: ACEi or ARB monotherapy	(0.012,0.019) N/A	(0.003,0.027) N/A	(0.001,0.012) N/A	(0.004,0.013) N/A	(-0.004,0.001) N/A
Note: p-value for coefficients is for the null hypothe	esis that the coefficient =	U			
Marginal effects/predicted probability Other hypertension medications only					
2017/18	0.179 (0.177,0.181)	0.482 (0.474,0.489)	0.053 (0.050,0.056)	0.030 (0.028,0.033)	0.064 (0.062,0.065)
2018/19	0.178 (0.176,0.180)	0.490 (0.483,0.496)	0.066 (0.062,0.069)	0.023 (0.021,0.025)	0.064 (0.063,0.065)
2019/20	0.196 (0.195,0.198)	0.516 (0.511,0.521)	0.066 (0.063,0.068)	0.043 (0.041,0.045)	0.080 (0.078,0.081)
	(0.133,0.130)	(0.311,0.321)	(0.003,0.003)	(0.041,0.043)	(0.070,0.001)

Primary analysis

	(1)	(2)	(3)	(4)	(5)
		Inpatient stay with	Inpatient stay with ARD	Inpatient stay with ARDS	Died same or following
	Inpatient stay	ICU/CCU	dx	dx	month
ACEi or ARB plus/minus other medications					
2017/18	0.125	0.463	0.045	0.029	0.035
	(0.124,0.127)	(0.456,0.470)	(0.042,0.048)	(0.027,0.031)	(0.034,0.035)
2018/19	0.128	0.481	0.061	0.021	0.034
	(0.127,0.130)	(0.475,0.487)	(0.058,0.064)	(0.020,0.023)	(0.034,0.035)
2019/20	0.158	0.512	0.064	0.050	0.049
	(0.157,0.160)	(0.508,0.517)	(0.062,0.066)	(0.048,0.052)	(0.048,0.049)
ACEi or ARB monotherapy					
2017/18	N/A	N/A	N/A	N/A	N/A
====					
2018/19	N/A	N/A	N/A	N/A	N/A
2019/20	N/A	N/A	N/A	N/A	N/A
Risk ratios of marginal effects					
Other hypertension medications only					
2018/19 season vs. 2017/18	0.994	1.017	1.236***	0.759***	0.999
	(0.977,1.011)	(0.996,1.038)	(1.136,1.337)	(0.668, 0.850)	(0.969,1.030)
2019/20 season vs. 2017/18	1.099***	1.072***	1.238***	1.414***	1.244***
,	(1.081,1.116)	(1.053,1.092)	(1.147,1.330)	(1.278,1.550)	(1.210,1.278)
ACEi or ARB plus/minus other medications					
2018/19 season vs. 2017/18	1.025**	1.039***	1.360***	0.739***	0.993
2020, 20 000000 100 2027, 20	(1.009,1.042)	(1.019,1.058)	(1.251,1.469)	(0.656,0.822)	(0.961,1.025)
2019/20 season vs. 2017/18	1.264***	1.107***	1.437***	1.731***	1.404***
	(1.245,1.282)	(1.088,1.126)	(1.332,1.542)	(1.580,1.882)	(1.363,1.444)
ACEi or ARB monotherapy	(=== := /= := = /	(=:====================================	(=:===,=:=,	(=====)	(======================================
2018/19 season vs. 2017/18	N/A	N/A	N/A	N/A	N/A
2019/20 season vs. 2017/18	N/A	N/A	N/A	N/A	N/A
Number of episodes	1,059,474	167,330	167,330	167,330	1,057,707
Number of people	728,455	147,846	147,846	147,846	727,311
Note: p-value for risk ratios is for the null hypoth	esis that the risk ratio = 1				

N/A: variable not included in model

Sensitivity analysis: ACEi/ARB monotherapy

	(6)	(7)	(8)	(9)	(10)
	Inpatient stay	Inpatient stay with ICU/CCU	Inpatient stay with ARD dx	Inpatient stay with ARDS dx	Died same or following month
Key coefficient estimates					
Season					
2017-2018 flu season	ref.	ref.	ref.	ref.	ref.
2018-2019 flu season	-0.001	0.008	0.013***	-0.007***	0
	(-0.004,0.002)	(-0.002,0.018)	(0.008, 0.017)	(-0.010,-0.004)	(-0.002,0.002)
2019-2020 flu season	0.018***	0.035***	0.013***	0.013***	0.016***
	(0.015,0.021)	(0.026, 0.044)	(0.008, 0.017)	(0.009, 0.016)	(0.014,0.017)
HTN medication group					
Other medications only	ref.	ref.	ref.	ref.	ref.
ACEi or ARB plus/minus other medications	-0.020***	-0.004	-0.007**	-0.002	-0.010***
	(-0.023,-0.017)	(-0.014,0.006)	(-0.011,-0.002)	(-0.006,0.001)	(-0.012,-0.009)
ACEi or ARB monotherapy	-0.016***	-0.039***	-0.007	-0.009**	-0.004***
	(-0.020,-0.012)	(-0.057,-0.020)	(-0.015,0.001)	(-0.015,-0.003)	(-0.006,-0.002)
Season/medication interactions					
2018-2019 season: ACEi or ARB +- other	0.004*	0.004	0.004	-0.001	-0.001
	(0.000,0.008)	(-0.009,0.018)	(-0.003,0.010)	(-0.005,0.004)	(-0.003,0.002)
2018-2019 season: ACEi or ARB monotherapy	0.005	0.040**	0.002	0.002	0.001
	(-0.001,0.010)	(0.015, 0.065)	(-0.009,0.013)	(-0.006,0.009)	(-0.002,0.004)
2019-2020 season: ACEi or ARB +/- other	0.015***	0.011	0.007*	0.008***	-0.001
	(0.011,0.019)	(-0.001,0.024)	(0.002,0.013)	(0.003,0.013)	(-0.004,0.001)
2019-2020 season: ACEi or ARB monotherapy	0.017***	0.035**	0.004	0.012**	-0.003*
Note: p-value for coefficients is for the null hypotl	(0.012,0.022)	(0.013,0.057)	(-0.006,0.013)	(0.004,0.020)	(-0.006,-0.000)
Marginal effects/predicted probability					
Other hypertension medications only					
2017/18	0.179	0.481	0.053	0.030	0.064
	(0.177,0.181)	(0.474,0.489)	(0.050,0.056)	(0.028, 0.033)	(0.062,0.065)
2018/19	0.178	0.490	0.066	0.023	0.064
	(0.176,0.180)	(0.483,0.496)	(0.062,0.069)	(0.021,0.025)	(0.063,0.065)
2019/20	0.196	0.516	0.066	0.043	0.079
	(0.195,0.198)	(0.511,0.521)	(0.063,0.068)	(0.041,0.045)	(0.078,0.081)

(10)

(6)

Sensitivity analysis: ACEi/ARB monotherapy

N/A: variable not included in model

* p<0.05, ** p<0.01, *** p<0.001

	Inpatient stay	Inpatient stay with ICU/CCU	Inpatient stay with ARD dx	Inpatient stay with ARDS dx	Died same or following month
ACEi or ARB plus/minus other medications	inpatient stay	100/000	ux	ux	month
2017/18	0.133	0.473	0.046	0.030	0.037
2017/10	(0.132,0.135)	(0.466,0.480)	(0.043,0.049)	(0.027,0.032)	(0.036,0.038)
2018/19	0.136	0.486	0.062	0.022	0.037
2010/13	(0.135,0.138)	(0.479,0.492)	(0.059,0.065)	(0.020,0.024)	(0.036,0.038)
2019/20	0.166	0.519	0.066	0.050	0.052
2013/20	(0.164,0.167)	(0.514,0.524)	(0.063,0.068)	(0.048,0.052)	(0.051,0.053)
	(6.27.),1.21.7	(0.02.70.02.7)	(4.444)	(5.5.5)5.55=/	(======================================
ACEi or ARB monotherapy					
2017/18	0.093	0.408	0.040	0.024	0.024
	(0.090,0.096)	(0.392,0.425)	(0.033, 0.047)	(0.019,0.029)	(0.022, 0.025)
2018/19	0.096	0.456	0.054	0.018	0.025
	(0.094,0.099)	(0.441,0.472)	(0.047, 0.061)	(0.014,0.022)	(0.023, 0.026)
2019/20	0.127	0.478	0.056	0.048	0.036
	(0.125,0.130)	(0.467, 0.489)	(0.051,0.061)	(0.043,0.053)	(0.034, 0.037)
Risk ratios of marginal effects					
Other hypertension medications only					
2018/19 season vs. 2017/18	0.994	1.017	1.236***	0.759***	0.999
	(0.977,1.011)	(0.996,1.038)	(1.136,1.337)	(0.668, 0.850)	(0.969,1.030)
2019/20 season vs. 2017/18	1.098***	1.072***	1.238***	1.414***	1.243***
	(1.081,1.116)	(1.053,1.092)	(1.147,1.330)	(1.278,1.550)	(1.209,1.278)
ACEi or ARB plus/minus other medications					
2018/19 season vs. 2017/18	1.023*	1.027*	1.360***	0.735***	0.985
	(1.005,1.041)	(1.006, 1.048)	(1.243,1.476)	(0.647,0.824)	(0.950,1.019)
2019/20 season vs. 2017/18	1.244***	1.097***	1.441***	1.690***	1.382***
	(1.225,1.264)	(1.077,1.118)	(1.329,1.554)	(1.532,1.848)	(1.339,1.425)
ACEi or ARB monotherapy					
2018/19 season vs. 2017/18	1.037	1.117***	1.358*	0.766	1.047
	(0.993,1.080)	(1.058,1.177)	(1.055,1.660)	(0.526,1.006)	(0.958,1.136)
2019/20 season vs. 2017/18	1.369***	1.170***	1.412**	2.028***	1.526***
	(1.318,1.420)	(1.115,1.226)	(1.129,1.694)	(1.537,2.519)	(1.412,1.640)
Number of episodes	1,059,474	167,330	167,330	167,330	1,057,70
Number of people	728,455	147,846	147,846	147,846	727,31

Sensitivity analysis: Dropping people with comorbidities (other than hypertension)

_	(1.1)	(12)	(12)	(1.4)	(15)
	(11)	(12)	(13)	(14)	(15)
		Innationt stay with	Innationt stay with ABD	Innationt stay with ADDC	Died same or following
	In mation to story	Inpatient stay with ICU/CCU	Inpatient stay with ARD dx	Inpatient stay with ARDS	
	Inpatient stay	ICU/CCU	ux	dx	month
Key coefficient estimates					
Season					
2017-2018 flu season		af	ef		not.
2017-2018 Hu Season	ref.	ref.	ref.	ref.	ref.
2018-2019 flu season	0.002	0.02	0.030**	0.006	0
2016-2019 IIU SedS0II					
2040 2020 [(-0.001,0.006) 0.032***	(-0.032,0.072) 0.068**	(0.009,0.051) 0.029***	(-0.005,0.017) 0.052***	(-0.002,0.002) 0.007***
2019-2020 flu season				****	
	(0.028,0.035)	(0.024,0.111)	(0.014,0.045)	(0.039,0.065)	(0.005,0.009)
HTN medication group					
			•	•	•
Other medications only	ref.	ref.	ref.	ref.	ref.
ACE: ADD I / : II II II II	0.000***	0.004	0.000	0.000	0.002***
ACEi or ARB plus/minus other medications	-0.006***	-0.001	0.009	0.003	-0.003***
	(-0.009,-0.003)	(-0.049,0.046)	(-0.008,0.026)	(-0.007,0.013)	(-0.004,-0.001)
ACEi or ARB monotherapy	N/A	N/A	N/A	N/A	N/A
Season/medication interactions					
2010 2010					2 224
2018-2019 season: ACEi or ARB +- other	-0.003	0.004	-0.013	0.001	0.001
	(-0.007,0.001)	(-0.062,0.071)	(-0.041,0.014)	(-0.015,0.017)	(-0.001,0.003)
2018-2019 season: ACEi or ARB monotherapy	N/A	N/A	N/A	N/A	N/A
2019-2020 season: ACEi or ARB +/- other	-0.001	0.05	-0.022*	-0.001	-0.001
	(-0.006,0.003)	(-0.006, 0.106)	(-0.043,-0.001)	(-0.019,0.016)	(-0.003,0.001)
2019-2020 season: ACEi or ARB monotherapy	N/A	N/A	N/A	N/A	N/A
Note: p-value for coefficients is for the null hypotl					
Marginal effects/predicted probability					
Other hypertension medications only					
2017/18	0.031	0.312	0.023	0.009	0.007
	(0.029,0.034)	(0.275,0.350)	(0.011,0.035)	(0.002, 0.016)	(0.006,0.009)
2018/19	0.033	0.332	0.053	0.015	0.007
	(0.031,0.036)	(0.296,0.368)	(0.036,0.070)	(0.006, 0.024)	(0.006,0.008)
2019/20	0.063	0.380	0.053	0.061	0.014
	(0.060,0.066)	(0.357,0.403)	(0.042,0.063)	(0.050,0.073)	(0.013, 0.016)

Sensitivity analysis: Dropping people with comorbidities (other than hypertension)

	(11)	(12)	(13)	(14)	(15)
		Inpatient stay with	Inpatient stay with ARD	Inpatient stay with ARDS	Died same or following
	Inpatient stay	ICU/CCU	dx	dx	month
ACEi or ARB plus/minus other medications		2.212		0.046	
2017/18	0.023	0.319	0.033	0.016	0.004
2040/40	(0.022,0.025)	(0.289,0.349)	(0.021,0.044)	(0.008,0.023)	(0.003,0.004)
2018/19	0.022	0.343	0.049	0.023	0.004
2040/20	(0.021,0.024)	(0.313,0.373)	(0.036,0.063)	(0.014,0.032)	(0.004,0.005)
2019/20	0.054 (0.052,0.055)	0.436 (0.418,0.454)	0.040 (0.033,0.048)	0.067 (0.058,0.076)	0.010 (0.009,0.011)
ACEi or ARB monotherapy					
2017/18	N/A	N/A	N/A	N/A	N/A
2018/19	N/A	N/A	N/A	N/A	N/A
2019/20	N/A	N/A	N/A	N/A	N/A
Risk ratios of marginal effects					
Other hypertension medications only					
2018/19 season vs. 2017/18	1.069	1.064	2.291	1.633	0.973
	(0.953,1.186)	(0.893,1.235)	(0.893,3.688)	(0.078,3.189)	(0.744,1.203)
2019/20 season vs. 2017/18	2.008***	1.216**	2.270*	6.718*	1.942***
	(1.823,2.193)	(1.053,1.379)	(1.013,3.526)	(1.473,11.963)	(1.561,2.323)
ACEi or ARB plus/minus other medications					
2018/19 season vs. 2017/18	0.961	1.076	1.510	1.432	1.128
	(0.875,1.047)	(0.939,1.213)	(0.842,2.177)	(0.544,2.320)	(0.879,1.377)
2019/20 season vs. 2017/18	2.291***	1.369***	1.234	4.210**	2.624***
	(2.124,2.458)	(1.228,1.509)	(0.754,1.713)	(2.113,6.308)	(2.142,3.107)
ACEi or ARB monotherapy					
2018/19 season vs. 2017/18	N/A	N/A	N/A	N/A	N/A
2019/20 season vs. 2017/18	N/A	N/A	N/A	N/A	N/A
Number of episodes	200,778	7,696	7,696	7,696	200,508
Number of people	175,494	7,647	7,647	7,647	175,251
Note: p-value for risk ratios is for the null hypothe					
N/A: variable not included in model * p<0.05, ** p<0.01, *** p<0.001					

	(16)	(17)	(18)	(19)	(20)
	Inpatient stay	Inpatient stay with ICU/CCU	Inpatient stay with ARD dx	Inpatient stay with ARDS dx	Died same or following
	,	323, 323			
Key coefficient estimates					
Season 2017-2018 flu season	ref.	ref.	ref.	ref.	ref.
2018-2019 flu season	0	0.009	0.017***	-0.007***	0
	(-0.004,0.003)	(-0.002,0.019)	(0.012,0.022)	(-0.010,-0.003)	(-0.002,0.002)
2019-2020 flu season	0.003*	0.030***	0.017***	0.010***	0.017***
HTN medication group	(0.000,0.007)	(0.020,0.041)	(0.011,0.022)	(0.006,0.014)	(0.015,0.020)
The medication group					
Other medications only	ref.	ref.	ref.	ref.	ref.
ACEi or ARB plus/minus other medications	-0.016***	-0.01	-0.007**	-0.003	-0.009***
Acet of Auto prosymmus other medications	(-0.019,-0.013)	(-0.021,0.000)	(-0.011,-0.002)	(-0.006,0.001)	(-0.010,-0.007)
ACEi or ARB monotherapy	N/A	N/A	N/A	N/A	N/A
Season/medication interactions					
2018-2019 season: ACEi or ARB +- other	0.002	0.01	0.001	0	0
	(-0.002,0.006)	(-0.004,0.025)	(-0.006,0.008)	(-0.005,0.004)	(-0.003,0.002)
2018-2019 season: ACEi or ARB monotherapy	N/A	N/A	N/A	N/A	N/A
2019-2020 season: ACEi or ARB +/- other	0.008***	0.012	0.008*	0.008**	-0.005***
	(0.004,0.012)	(-0.003,0.026)	(0.001,0.014)	(0.002,0.013)	(-0.008,-0.002)
2019-2020 season: ACEi or ARB monotherapy	N/A	N/A	N/A	N/A	N/A
Note: p-value for coefficients is for the null hypotl					
Marginal effects/predicted probability Other hypertension medications only					
2017/18	0.175	0.480	0.053	0.030	0.061
2027,120	(0.173,0.178)	(0.472,0.487)	(0.049,0.056)	(0.028,0.033)	(0.060,0.063)
2018/19	0.175	0.488	0.070	0.024	0.061
,	(0.172,0.177)	(0.480,0.496)	(0.066,0.074)	(0.021,0.026)	(0.060,0.063)
2019/20	0.179	0.510	0.069	0.041	0.079
	(0.176,0.181)	(0.503,0.517)	(0.066, 0.073)	(0.038, 0.044)	(0.077,0.080)

Page 52 of 57

Sensitivity analysis: limiting analysis to strict flu season (dropping summer months)

* p<0.05, ** p<0.01, *** p<0.001

Inpatient stay ICU/CCU		(16)	(17)	(18)	(19)	(20)
ACEI or ARB monotherapy 2017/18 ACEI or ARB monotherapy 2018/19 ACEI or ARB monotherapy 2018/19 ACEI or ARB monotherapy 2017/18 ACEI or ARB monotherapy 2018/19 ACEI or ARB monotherapy 2017/18 ACEI or ARB monotherapy 2018/19 season vs. 2017/18 ACEI or ARB monotherapy 2018/19 season vs. 2017/18 ACEI or ARB monotherapy 2019/20 season vs. 2017/18 ACEI or ARB monotherapy 2019/20 season vs. 2017/18 ACEI or ARB plus/minus other medications 2018/19 season vs. 2017/18 ACEI or ARB plus/minus other medications 2018/19 season vs. 2017/18 ACEI or ARB plus/minus other medications 2018/19 season vs. 2017/18 ACEI or ARB plus/minus other medications 2018/19 season vs. 2017/18 ACEI or ARB plus/minus other medications 2019/20 season vs. 2017/18 ACEI or ARB plus/minus other medications 2019/20 season vs. 2017/18 ACEI or ARB monotherapy 2019/20 season vs. 2017/18		In mation to story	•			Died same or following
2017/18	ACFi or ARR plus/minus other medications	inpatient stay	ico/cco	ux	ux	month
(0.120,0.123)	• •	0.122	0.459	0.044	0.028	0.033
2018/19	, -					
2019/20	2018/19	0.124	0.478	0.063	0.021	
(0.131,0.134) (0.494,0.508) (0.065,0.072) (0.044,0.049) (0.044,0.046) ACE or ARB monotherapy 2017/18 N/A N/A N/A N/A N/A N/A N/A N/		(0.122,0.125)	(0.470,0.485)	(0.059,0.066)	(0.019, 0.023)	(0.032,0.033)
N/A	2019/20	0.133	0.501	0.069	0.046	0.045
2017/18 N/A		(0.131,0.134)	(0.494,0.508)	(0.065,0.072)	(0.044,0.049)	(0.044,0.046)
2017/18 N/A	ACEi or ARR monotherany					
2019/20 N/A	• •	N/A	N/A	N/A	N/A	N/A
Risk ratios of marginal effects Other hypertension medications only 2018/19 season vs. 2017/18 0.998 1.018 1.024**** (0.979,1.017) (0.995,1.041) (1.208,1.440) (0.673,0.879) (0.967,1.036) 2019/20 season vs. 2017/18 1.019 1.064*** 1.313*** 1.343*** 1.282*** (1.000,1.039) (1.041,1.087) (1.201,1.425) (1.190,1.495) (1.190,1.495) (1.241,1.324) ACEI or ARB plus/minus other medications 2018/19 season vs. 2017/18 1.017 1.041*** 1.041*** 1.411*** 0.750*** 0.997 (0.999,1.035) (1.019,1.063) (1.289,1.533) (0.655,0.846) (0.960,1.034) 2019/20 season vs. 2017/18 1.091*** 1.092*** 1.542*** 1.634*** 1.380*** 4.426** 1.380*** 1.380*** 4.426** 4.411*** 0.750*** 0.997 0.9	2018/19	N/A	N/A	N/A	N/A	N/A
Other hypertension medications only 2018/19 season vs. 2017/18 0.998 1.018 1.324*** 0.776*** 1.002 2019/20 season vs. 2017/18 1.019 1.064*** 1.313*** 1.343*** 1.282*** 2019/20 season vs. 2017/18 1.019 1.064*** 1.313*** 1.343*** 1.282*** ACEi or ARB plus/minus other medications 2018/19 season vs. 2017/18 1.017 1.041*** 1.411*** 0.750*** 0.997 2019/20 season vs. 2017/18 1.091*** 1.092*** 1.542*** 1.634*** 1.380*** 4CEi or ARB monotherapy (1.071,1.110) (1.069,1.114) (1.413,1.671) (1.465,1.803) (1.331,1.428) ACEi or ARB monotherapy 2018/19 season vs. 2017/18 N/A	2019/20	N/A	N/A	N/A	N/A	N/A
2018/19 season vs. 2017/18	Risk ratios of marginal effects					
2019/20 season vs. 2017/18	Other hypertension medications only					
2019/20 season vs. 2017/18 1.019 (1.000,1.039) (1.041,1.087) (1.201,1.425) (1.190,1.495) (1.190,1.495) (1.241,1.324) ACEi or ARB plus/minus other medications 2018/19 season vs. 2017/18 1.017 1.041*** 1.411*** 0.750*** 0.997 (0.999,1.035) (1.019,1.063) (1.289,1.533) (0.655,0.846) (0.960,1.034) 2019/20 season vs. 2017/18 1.091*** 1.092*** 1.542*** 1.634*** 1.380*** (1.071,1.110) (1.069,1.114) (1.413,1.671) (1.465,1.803) (1.331,1.428) ACEi or ARB monotherapy 2018/19 season vs. 2017/18 N/A	2018/19 season vs. 2017/18	0.998	1.018	1.324***	0.776***	1.002
(1.000,1.039) (1.041,1.087) (1.201,1.425) (1.190,1.495) (1.241,1.324) ACEi or ARB plus/minus other medications 2018/19 season vs. 2017/18 1.017 1.041*** 1.411*** 0.750*** 0.997 0.999,1.035) (1.019,1.063) (1.289,1.533) (0.655,0.846) (0.960,1.034) 1.091*** 1.092*** 1.542*** 1.634*** 1.380*** ACEi or ARB monotherapy 2018/19 season vs. 2017/18 N/A			• • • • • • • • • • • • • • • • • • • •			
ACEi or ARB plus/minus other medications 2018/19 season vs. 2017/18 1.017 1.041*** 1.411*** 0.750*** 0.997 (0.999,1.035) (1.019,1.063) (1.289,1.533) (0.655,0.846) (0.960,1.034) 1.091*** 1.092*** 1.542*** 1.634*** 1.380*** ACEi or ARB monotherapy 2018/19 season vs. 2017/18 N/A	2019/20 season vs. 2017/18					
2018/19 season vs. 2017/18 1.017 1.041*** 1.411*** 0.750*** 0.997 (0.999,1.035) 1.019,1.063) (1.289,1.533) (0.655,0.846) (0.960,1.034) 2019/20 season vs. 2017/18 1.091*** 1.092*** 1.542*** 1.634*** 1.380*** (1.071,1.110) 1.069,1.114) 1.413,1.671) 1.415,1.803) 1.331,1.428) ACEi or ARB monotherapy 2018/19 season vs. 2017/18 N/A		(1.000,1.039)	(1.041,1.087)	(1.201,1.423)	(1.190,1.493)	(1.241,1.324)
(0.999,1.035) (1.019,1.063) (1.289,1.533) (0.655,0.846) (0.960,1.034) (1.091/20 season vs. 2017/18						
2019/20 season vs. 2017/18 1.091*** 1.092*** 1.542*** 1.634*** 1.634*** 1.380*** (1.071,1.110) (1.069,1.114) (1.413,1.671) (1.465,1.803) (1.331,1.428) ACEi or ARB monotherapy 2018/19 season vs. 2017/18 N/A N/A N/A N/A N/A N/A N/A N/	2018/19 season vs. 2017/18	1.017	1.041***	1.411***		0.997
(1.071,1.110) (1.069,1.114) (1.413,1.671) (1.465,1.803) (1.331,1.428) ACEi or ARB monotherapy 2018/19 season vs. 2017/18 N/A N/A N/A N/A N/A N/A N/A 2019/20 season vs. 2017/18 N/A N/A N/A N/A N/A N/A Number of episodes 738,240 106,917 106,917 106,917 737,05 Number of people 556,579 97,383 97,383 97,383 555,72			, , ,	, , ,		, , ,
ACEi or ARB monotherapy 2018/19 season vs. 2017/18 N/A N/A N/A N/A N/A N/A N/A N/	2019/20 season vs. 2017/18					
2018/19 season vs. 2017/18 N/A <		(1.071,1.110)	(1.069,1.114)	(1.413,1.671)	(1.465,1.803)	(1.331,1.428)
2019/20 season vs. 2017/18 N/A N/A N/A N/A N/A N/A Number of episodes 738,240 106,917 106,917 106,917 737,05 Number of people 556,579 97,383 97,383 97,383 555,72						
Number of episodes 738,240 106,917 106,917 106,917 737,05 Number of people 556,579 97,383 97,383 97,383 555,72	2018/19 season vs. 2017/18	N/A	N/A	N/A	N/A	N/A
Number of people 556,579 97,383 97,383 97,383 555,72	2019/20 season vs. 2017/18	N/A	N/A	N/A	N/A	N/A
	Number of episodes	738,240	106,917	106,917	106,917	737,059
Note: p-value for risk ratios is for the null hypothe	Number of people	556,579	97,383	97,383	97,383	555,729
	Note: p-value for risk ratios is for the null hypothe					
N/A: variable not included in model						

The RECORD statement - checklist of items, extended from the STROBE statement, that should be reported in observational studies using routinely collected health data.

	Item No.	STROBE items	Location in manuscript where items are reported	RECORD items	Location in manuscript where items are reported
Title and abstra	ct				_
	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found		RECORD 1.1: The type of data used should be specified in the title or abstract. When possible, the name of the databases used should be included. RECORD 1.2: If applicable, the geographic region and timeframe within which the study took place should be reported in the title or abstract. RECORD 1.3: If linkage between databases was conducted for the study, this should be clearly stated in the title or abstract.	
Introduction		T 1: 4 :	I	T	T
Background rationale	2	Explain the scientific background and rationale for the investigation being reported			
Objectives	3	State specific objectives, including any prespecified hypotheses			
Methods					
Study Design	4	Present key elements of study design early in the paper			
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection			
Participants	6	(a) Cohort study - Give the	http://bmjopen.bmj.com/si	RECORD 6.1: The methods of study	

BMJ Open	Page 54 of 57
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		eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> - Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> - Give the eligibility criteria, and the sources and methods of selection of participants (b) Cohort study - For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> - For matched studies, give matching criteria and the number of controls per case	population selection (such as codes or algorithms used to identify subjects) should be listed in detail. If this is not possible, an explanation should be provided. RECORD 6.2: Any validation studies of the codes or algorithms used to select the population should be referenced. If validation was conducted for this study and not published elsewhere, detailed methods and results should be provided. RECORD 6.3: If the study involved linkage of databases, consider use of a flow diagram or other graphical display to demonstrate the data linkage process, including the number of individuals with linked data at each stage.
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable.	RECORD 7.1: A complete list of codes and algorithms used to classify exposures, outcomes, confounders, and effect modifiers should be provided. If these cannot be reported, an explanation should be provided.
Data sources/ measurement	8	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	
Bias	9	Describe any efforts to address potential sources of bias	

Study size	10	Explain how the study size was arrived at	
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) Cohort study - If applicable, explain how loss to follow-up was addressed Case-control study - If applicable, explain how matching of cases and controls was addressed Cross-sectional study - If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses	
Data access and cleaning methods			RECORD 12.1: Authors should describe the extent to which the investigators had access to the database population used to create the study population. RECORD 12.2: Authors should provide information on the data
Linkage			cleaning methods used in the study. RECORD 12.3: State whether the

Dozulta				study included person-level, institutional-level, or other data linkage across two or more databases. The methods of linkage and methods of linkage quality evaluation should be provided.	
Results	12	(a) Donor at the consultance of		DECORD 12.1. December in detail the	
Participants	13	(a) Report the numbers of individuals at each stage of the study (<i>e.g.</i> , numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed) (b) Give reasons for non-participation at each stage. (c) Consider use of a flow diagram		RECORD 13.1: Describe in detail the selection of the persons included in the study (<i>i.e.</i> , study population selection) including filtering based on data quality, data availability and linkage. The selection of included persons can be described in the text and/or by means of the study flow diagram.	
Descriptive data	14	(a) Give characteristics of study participants (<i>e.g.</i> , demographic, clinical, social) and information on exposures and potential confounders (b) Indicate the number of participants with missing data for each variable of interest (c) <i>Cohort study</i> - summarise follow-up time (<i>e.g.</i> , average and total amount)			
Outcome data	15	Cohort study - Report numbers of outcome events or summary measures over time Case-control study - Report numbers in each exposure category, or summary measures of exposure Cross-sectional study - Report numbers of outcome events or	tp://bmjopen.bmj.com/si t		

		summary measures		
Main results	16	(a) Give unadjusted estimates		
		and, if applicable, confounder-		
		adjusted estimates and their		
		precision (e.g., 95% confidence		
		interval). Make clear which		
		confounders were adjusted for		
		and why they were included		
		(b) Report category boundaries		
		when continuous variables were		
		categorized		
		(c) If relevant, consider		
		translating estimates of relative		
		risk into absolute risk for a		
		meaningful time period		
Other analyses	17	Report other analyses		
		done—e.g., analyses of		
		subgroups and interactions, and		
		sensitivity analyses		
Discussion				
Key results	18	Summarise key results with		
		reference to study objectives		
Limitations	19	Discuss limitations of the study,	RECORD 19.1: Discuss the	
		taking into account sources of	implications of using data that were not	
		potential bias or imprecision.	created or collected to answer the	
		Discuss both direction and	specific research question(s). Include	
		magnitude of any potential bias	discussion of misclassification bias,	
			unmeasured confounding, missing	
			data, and changing eligibility over	
			time, as they pertain to the study being	
			reported.	
Interpretation	20	Give a cautious overall		
		interpretation of results		
		considering objectives,		
		limitations, multiplicity of		
		analyses, results from similar		
		studies, and other relevant		
		evidence		

Generalisability	21	Discuss the generalisability (external validity) of the study results				
Other Information	Other Information					
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based				
Accessibility of protocol, raw data, and programming code			RECORD 22.1: Authors should provide information on how to access any supplemental information such as the study protocol, raw data, or programming code.			

^{*}Reference: Benchimol EI, Smeeth L, Guttmann A, Harron K, Moher D, Petersen I, Sørensen HT, von Elm E, Langan SM, the RECORD Working Committee. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) Statement. *PLoS Medicine* 2015; in press.

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Association of outpatient use of renin-angiotensinaldosterone system blockers on outcomes of acute respiratory illness during the COVID-19 pandemic: a cohort study

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Title: Association of outpatient use of renin-angiotensin-aldosterone system blockers on outcomes of acute respiratory illness during the COVID-19 pandemic: a cohort study

Authors

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Investigation: MMJ, LOJS, FB, VDG, TMD, AHL, NWC. Methodology: MMJ, LOJS, FB.

Project administration: MMJ. Supervision: MMJ, NWC. Validation: MMJ, NWC. Writing-

original draft: MMJ. Writing-review and editing: MMJ, LOJS, FB, VSD, TMD, AHL, NWC.

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Competing interests

None.

Patient consent for publication

Not applicable / Not required.

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ABSTRACT

Objectives: Evaluate the associations between patients taking ACE inhibitors (ACEis) and angiotensin receptor blockers (ARBs) and their clinical outcomes after an acute viral respiratory illness (AVRI) due to COVID-19.

Design: Retrospective cohort.

Setting: The USA; 2017-2018 influenza season, 2018-2019 influenza season, and 2019-2020 influenza/COVID-19 season.

Participants: People with hypertension (HTN) taking an ACEi, ARB or other HTN medications, and experiencing AVRI.

Main outcome measures: Change in hospital admission, intensive care unit (ICU) or coronary care unit (CCU), acute respiratory distress (ARD), ARD syndrome (ARDS), and all-cause mortality, comparing COVID-19 to pre-COVID-19 influenza seasons.

Results: The cohort included 1,059,474 episodes of AVRI (653,797 filled an ACEi or ARB, and 405,677 other HTN medications). 58.6% were women and 72.9% with age ≥ 65. The ACEi/ARB cohort saw a larger increase in risk in the COVID-19 influenza season than the other HTN medication cohort for four out of five outcomes, with an additional 1.5 percentage point (pp) increase in risk of an inpatient stay (95% CI 1.2 to 1.9 pp) and of ICU/CCU use (95% CI 0.3 to 2.7 pp), as well as a 0.7 pp (0.1 to 1.2 pp) additional increase in risk of ARD and 0.9 pp (0.4 to 1.3 pp) additional increase in risk of ARDS. There was no statistically significant difference in the absolute risk of death (-0.2 pp, 95% CI -0.4 to 0.1 pp). However, the relative risk of death in 2019/2020 vs. 2017/2018 for the ACEi/ARB group was larger (1.40 [1.36 to 1.44]) than for the other HTN medication cohort (1.24 [1.21 to 1.28]).

Conclusions: People with AVRI using ACEi/ARBs for hypertension had a greater increase in poor outcomes during the COVID-19 pandemic than those using other medications to treat hypertension. The small absolute magnitude of the differences likely does not support changes in clinical practice.

Keywords: ACE inhibitors, angiotensin receptor blockers, COVID-19, acute viral respiratory illness.

ARTICLE SUMMARY

Strengths and limitations of this study

- It uses an approach of difference-in-differences that mitigates some of the limitations of observational studies.
- The cohort includes a diverse sample of US residents including people with commercial insurance and Medicare Advantage.
- The cohort is not representative of people without insurance or people with Medicaid or other insurance types.
- Given the observational design, it is not possible to make causal claims.

INTRODUCTION

The renin-angiotensin-aldosterone system (RAAS) is a hormone system responsible for several physiologic functions including vascular resistance, electrolyte homeostasis, and fluid balance. Medications such as angiotensin-converting enzyme inhibitors (ACEi) and angiotensin-receptor blockers (ARBs) interrupt different steps in this system and are commonly used in clinical practice for outpatient blood pressure or heart failure management. Early in the coronavirus disease 2019 (COVID-19) pandemic, pre-clinical studies raised concerns about the association between use of ACEi or ARBs and severe illness in hypertensive patients with COVID-19. Angiotensin-converting-enzyme 2 (ACE-2) is the binding site for respiratory viruses including the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and two opposing theories on the potential effects of these medications have been debated: one postulating an increased susceptibility to SARS-CoV-2 through upregulation of ACE-2 receptors, and one postulating a protection against severe disease through suppression of angiotensin II and subsequent prevention of virus-mediated acute lung injury.

Since the hypothesis that the prior use of RAAS inhibitors could be associated with worse clinical outcomes in hypertensive patients diagnosed with COVID-19 was raised, several clinical studies were published.² In the latest update of a living systematic review addressing this question by Mackey and colleagues, the authors reported high confidence based on 78 studies (77 observational studies, 1 randomized controlled trial [RCTs]) in the finding that ACEi/ARB use is not associated with COVID-19 severity.² Another 21 systematic reviews and/or meta-analyses have been consistent with this conclusion as well.³⁻²³ Furthermore, two recently published RCTs do not support the discontinuation of these drugs in hypertensive patients admitted to the hospital with COVID-19.²⁴.²⁵

Most existing studies, however, are of relatively small sample size with low methodological quality. The RCTs addressing discontinuation of ACEi/ARBs in people hospitalized with COVID-19, while reassuring for clinicians and patients, do not directly address the question of whether the risk of hospitalization may be increased in this population. In this study, we aimed to evaluate the associations between prescription fills for ACEis and ARBs and clinical outcomes with an acute viral respiratory illness (AVRI) due to COVID-19. We use a difference-in-differences approach comparing the COVID-19 period to prior AVRI seasons and comparing users of ACEis or ARBs vs. other HTN medications in order to control for otherwise unobserved differences in underlying health and healthcare seeking behavior between the medication cohorts. We assessed severity of illness and mortality in AVRI across cohorts of patients with hypertension (HTN) using ACEis, ARBs, and other HTN medications, and we compared the differential effects of these medications on outcomes of AVRI in the 2017/2018 and 2018/2019 influenza seasons to those in the 2019/2020 influenza/COVID-19 season in the United States.

METHODS

We adhered to the RECORD statement (REporting of studies Conducted using Observational Routinely collected health Data).²⁶

Data source and study setting

We used de-identified administrative claims data from the OptumLabs® Data Warehouse (OLDW) to identify episodes of AVRI in people with Medicare Advantage or commercial health insurance in the United States. The OLDW includes medical and pharmacy claims, laboratory results, and enrollment records for commercial and Medicare Advantage enrollees.²⁷ The

database contains longitudinal health information on enrollees and patients, representing a diverse mixture of ages, ethnicities, and geographical regions across the United States. This study was deemed exempt by the Institutional Review Board.

Study design and participants

We created a cohort of patients with one or more episodes of AVRI with an initial date of service (index date) between October 1, 2017, and November 30, 2020. AVRI was defined using ICD-10 diagnosis codes for viral causes of respiratory illness: bronchitis, pneumonia, influenza, influenza like illness, and lower respiratory infections. (**Supplementary Material S1**). Each episode of AVRI started on the first date on which the patient had a claim with an AVRI diagnosis code and continued until the patient experienced a 30-day span with no AVRI diagnoses.

We required 180 days of continuous insurance enrollment before the index date of the AVRI episode. Insurance claims during this period were used to identify hypertension diagnoses, as well as other comorbidities that could be associated with COVID-19 morbidity and mortality risk or with the choice of medications to treat hypertension, as explained below.

Variables and measurements

Patient age, sex, residence state, and insurance enrollments dates and coverage type (commercial vs. Medicare Advantage) were taken from insurance enrollment data.

Hypertension and comorbidities

Hypertension and most comorbidities were defined based on the Quan enhanced Elixhauser comorbidity ICD-10 codes;²⁸ codes used to define comorbidities not included in the Elixhauser index (coronary artery disease, stroke, deep vein thrombosis, and pulmonary embolism) are available in the **Supplementary Material S1.** Hypertension and diabetes were coded hierarchically such that people with both complicated and uncomplicated disease were coded as complicated. All comorbidities required at least one inpatient or two outpatient diagnoses on different dates of service in the 6 months before the index date. Inpatient and outpatient settings were defined using procedure and revenue codes using code lists developed for use with Healthcare Effectiveness Data and Information Set (HEDIS) performance measures ²⁹

Hypertension medications

We developed a comprehensive list of hypertension medications (see **Supplementary Material S1**), then identified all National Drug Codes (NDCs) for these medications in a table that is part of the OLDW. We searched for prescription fills in the 90 days before the index date for each episode of AVRI and categorized fill patterns as ACEi or ARB only, ACEi or ARB with other (i.e., not ACEi or ARB) hypertension medications, other hypertension medications only, or no hypertension medications. In primary analyses, ACEi or ARB users with and without other hypertension medications were combined and compared with people using only other hypertension medications; information on people who did not use hypertension medications is provided in summary tables for reference, but they were excluded from the analyses. A small number of people who filled both an ACEi and an ARB were also excluded from the analysis (N=10.933).

Outcomes

We specified 5 outcomes associated with more serious cases of AVRI: death, hospitalization, and, conditional on hospitalization: intensive care unit (ICU) or coronary care unit (CCU) services (revenue codes 0200 to 0219), a diagnosis of acute respiratory distress (ARD) (ICD-10 diagnosis code R06.03), and a diagnosis of acute respiratory distress syndrome (ARDS) (ICD-10 diagnosis code J80).

Data on death in OLDW includes only the month and year of death to maintain deidentification. It is sourced from the Death Master File, claims information, and insurance enrollment information. The mortality outcome in this study assessed whether the person was reported to have died in the same month as the index date or in the following month.

Data analysis

We used a difference-in-differences approach to assess the association between use of ACEis or ARBs and poor outcomes from COVID-19. The comparison group is people with hypertension using hypertension medications other than ACEis or ARBs; the exposure of interest is the COVID-19 pandemic. We compared outcomes of AVRI in the 2017/2018 and 2018/2019 influenza seasons to those in the 2019/2020 influenza/COVID-19 season. The premise is that the design will control for both differences in underlying health between the two medication groups (by comparing each to people taking those same medications in the years before COVID-19) and differences in healthcare service use during COVID-19 that are common to all people with hypertension. The inclusion of two pre-COVID-19 influenza seasons allows for a comparison of differences in outcomes between the medication groups due to changes in overall AVRI illness

mix unrelated to COVID-19. Cases, inpatient admission rates, and mortality rates can vary substantially with different influenza strains.³⁰

We used a linear probability approach to model each of the five outcomes, in 3 time periods (2017/2018, 2018/2019, and 2019/2020 seasons) for two patient medication groups (people using ACEis or ARBs vs. those using other HTN medications). Regression models included patient sex, age (categorical), insurance type (Medicare Advantage vs. commercial), Census region of residence, race/ethnicity, and flags for comorbidities described above. Huber-White standard errors were specified to adjust for repeated observations of some patients across separate episodes of AVRI. The model is specified such that the coefficient on the interaction between the 2019/2020 influenza/COVID-19 season and the ACEi/ARB group provides a statistical test for whether the ACEi/ARB group was differently affected by COVID-19 than the other HTN medication cohort. A coefficient greater than 0 indicates the ACEi/ARB group had a larger absolute increase in risk of the outcome than the other HTN medication cohort.

A linear probability model provides estimates of absolute risk differences rather than relative changes in risk. As a result, the differences are not scaled to the baseline probability of the event: a one percentage point risk difference may have different importance for an event with an incidence of 10% (relative increase 10%) compared to one with an incidence of 1% (relative increase 100%). To ease interpretation of results, we calculated average marginal effects for each flu season over the medication groups (in other words, the adjusted probabilities were calculated keeping the actual medication group rather than changing the medication group of each individual). We calculated ratios of these adjusted probabilities in the 2018/2019 flu season and the 2019/2020/COVID-19 flu season versus the baseline 2017/2018 flu season, along with p-values for the hypothesis test that the ratios were equal to 1 (i.e., the baseline year and the later

year had no difference in outcome risk for that medication group). These ratios provide the percentage relative increase in the outcome risk.

Model result interpretation

If the presence of COVID-19 affects the ACEi/ARB group more than the other HTN medication group, we would expect to see a positive and statistically significant coefficient for the interaction term ACEi/ARB by season=2019/2020. We would place more credence in the COVID-19 season findings if we find that outcomes in the 2018/2019 season did not differ much from those in the 2017/18 season, which would suggest that COVID-19 is fundamentally different from the general year-to-year shifts in flu strain. This would be supported by finding 1) a smaller coefficient for season=2018/2019 than for season=2019/2020, and 2) a smaller coefficient for the interaction term ACEi/ARB by season=2018/2019 than for the interaction term ACEi/ARB by season=2018/2019 than for the interaction term ACEi/ARB by season=2019/2020. Stata/MP version 16.0 was used for all analyses (StataCorp College Station, TX, 2019). The first author (MMJ) conducted all analyses and had access to all study data; all other authors had access to summary data and complete analysis results. No additional data available.

Patient and public involvement

Patients and/or public were not involved in this study.

RESULTS

We identified 1,247,393 episodes of AVRI in the study period among people with hypertension. Of these, 15.1% (187,919) did not fill a hypertension medication in the 90 days

before the index date and were excluded from further analysis. Of the remaining 1,059,474, 61.7% (653,797) filled at least one ACEi or ARB, and 38.3% (405,677) filled no ACEi or ARBs (**Table 1**). Most episodes were in female patients (58.6%; n=620,810) and in older patients, with 72.9% of AVRI episodes in people aged 65 and older (n=772,210). The most common comorbidities were chronic pulmonary diseases (35.2%; n=372,735), cardiac arrhythmias (27.2%, n=288,478), coronary artery disease (26.3%; n=279,098), diabetes with complications (25.6%; n=271,700), and congestive heart failure (24.0%; n=254,773).

Compared to AVRI episodes in those using other HTN medications, AVRI episodes in people using ACEi or ARB were more frequently identified in those with Commercial insurance (vs. Medicare Advantage), uncomplicated diabetes, and Hispanic ethnicity, among other patient characteristics (Table 1). AVRI episodes in people using ACEi/ARB were less likely to be associated with the oldest age group and with most comorbidities, including complicated hypertension, congestive heart failure, kidney failure, liver failure, cancer, arrhythmia, coagulopathy, deep vein thrombosis or pulmonary embolism, stroke, and valvular disease, among other patient characteristics compared to AVRI episodes in people using other HTN medications. (Table 1)

Unadjusted outcome rates

Across all study years, 15.8% of AVRI episodes included an inpatient stay (n=167,330), including 14.0% of episodes in ACEi/ARB users (n=91,660) and 18.7% in other HTN medication users (n=75,670; **Table 1**). Episode mortality rates were 5.2% overall (n=55,164), 4.0% for ACEi/ARB users (n=26,411), and 7.1% in other HTN medication users (n=28,753). About half of inpatient stays included ICU or CCU use.

Primary analysis

Table 2 presents key model results and marginal effects and ratios for season and medication cohort effects for all five outcomes. Complete regression results are available in Supplementary Material S2. The ACEi/ARB cohort had a somewhat lower risk of three of the five outcomes in the baseline 2017-2018 flu season compared to the other HTN medication cohort, with a 1.9 percentage point (pp) (95% CI -2.2 to -1.6 percentage points) lower risk of an inpatient stay, a 0.9 pp lower risk of death (95% CI -1.1 to -0.8 pp), and a 0.7 pp (95% CI -1.1 to -0.2 pp) lower risk of an ARD diagnosis conditional on having an inpatient stay. The point estimates for the risk differences of ICU/CCU use or an ARDS diagnosis in an inpatient stay also showed a lower risk for the ACEi/ARB cohort, but this difference was not statistically significant. The COVID-19 flu season was associated with a higher risk of all five outcomes in both the ACEi/ARB and the other HTN medication cohorts. Risk differences ranged from 1.3 pp higher risk of an ARD (95% CI: 0.8 to 1.7 pp) or ARDS (95% CI: 0.9 to 1.6 pp) diagnosis in an inpatient stay to a 3.5 pp (2.6 to 4.4 pp) higher risk of ICU/CCU use in an inpatient stay. (Table 2)

The ACEi/ARB cohort saw a larger risk difference than the other HTN medication cohort in four out of the five outcomes, with an additional 1.5 pp increase in risk of an inpatient stay (95% CI 1.2 to 1.9 pp) and of ICU/CCU use in an inpatient stay (95% CI 0.3 to 2.7 pp), as well as a 0.7 pp (0.1 to 1.2 pp) additional increase in risk of ARD and 0.9 pp (0.4 to 1.3 pp) additional increase in risk of ARDS. There was no statistically significant difference in the absolute risk of death (-0.2 pp, 95% CI -0.4 to 0.1 pp) for the ACEi/ARB group beyond that seen by the other medication group. However, the relative increased risk of death in 2019/2020 vs. 2017/2018 for

the ACEi/ARB group was larger (1.40 [1.36 to 1.44]) than for the other HTN medication cohort (1.24 [1.21 to 1.28]). In other words, each group experienced roughly the same absolute change in risk (an increase of about 1.6 pp), but the baseline risk of death for the ACEi/ARB group was lower, so the relative increase was greater.

Sensitivity analyses

ACEi/ARB monotherapy

When we separated people using only ACEi/ARB from those using ACEi/ARB plus other HTN medications, results were somewhat different for the two groups. In both the 2018/2019 and 2019/2020 seasons, the monotherapy group had a 3.5 to 4.0 pp higher risk of ICU/CCU use in an inpatient stay than the polytherapy group. (**Supplementary Material S3**)

People with no comorbidities

The primary effect being studied (ACEi/ARB use during COVID-19) was attenuated when the cohort was limited to people who did not have any of the comorbidities we identified (other than hypertension). A large (5.0 pp; 95% CI -0.6 pp to 10.6 pp) increase in the risk of an inpatient stay with ICU/CCU services was not statistically significant because of the small sample size (N=7,696 episodes). (**Supplementary Material S3**)

Strict flu season

Limiting the 2017/18 and 2018/19 cohorts to cases of AVRI occurring in the strict flu season (generally October to May) had minimal effect on the results, which were similar to the primary analysis. (Supplementary Material S3)

DISCUSSION

In this large observational study, we found that hypertensive patients with an AVRI who were taking ACEis or ARBs for management of their HTN had larger risk differences during the COVID-19 period in the outcomes of inpatient stay, inpatient stay with ICU/CCU, inpatient stay with ARD, and inpatient stay with ARDS when compared with people on other antihypertensive medications. This suggests that people taking ACEi/ARB were more affected by COVID-19 than people taking other HTN medications.

People with AVRI who were using ACEi/ARB had fewer comorbidities compared to people taking other medications to control their blood pressure, which might explain their lower baseline risk of poor outcomes. Prior to the COVID-19 season, among people with hypertension experiencing an episode of AVRI, those who used ACEi/ARB were less likely to have an inpatient stay, less likely to experience ARDS and ARD, and less likely to die compared to people on other antihypertensives at baseline.

Recent observational studies assessing association between ACEi/ARB use and COVID-19 outcomes have generally found lower risk of poor outcomes for ACEi/ARB users, 31-35 however, these studies have differed from ours in important ways. Our finding of lower baseline risk of poor outcomes with AVRI in people taking ACEis/ARBs even after extensively controlling for observed differences in health status highlights the importance of using methods that can control for unobserved differences in health status. Our difference-in-differences approach does this by using non-COVID AVRI outcome differences to control for unobserved differences in underlying health and health care seeking behavior.

During the COVID-19 flu season, all patients (ACEi/ARB and other HTN) had higher risk of all outcomes, compared to prior years. This is consistent with evidence that patients with hypertension experience worse outcomes from COVID-19.³⁶⁻⁴⁰ The ACEi/ARB group had a larger increase in poor outcomes from baseline compared to patients taking other HTN medication, including higher rates of hospitalization, ICU admission, ARD and ARDS. There was no significant difference in the absolute risk of death for those on ACEi/ARB versus other medication group.

While relative changes in poor AVRI outcomes associated with ACEi/ARB use during COVID-19 were moderate to large, the absolute differences were relatively small, ranging from 0.7 to 1.9 percentage points. The effects demonstrated in this study may support the theoretical biological effect of ACEi/ARB in the clinical outcomes of people with COVID-19.

Nevertheless, it is very uncertain whether these effects were mediated through upregulation of ACE-2 receptors and subsequent susceptibility to SARS-CoV-2, as previously proposed.¹

Moreover, in translating these findings to clinical practice, the small absolute risk differences observed here are unlikely to outweigh the clinical benefits of ACEi/ARB therapy for managing hypertension and heart failure. Therapy selection for these diseases should follow existing clinical guidelines of nephrology, cardiology, and other societies.

LIMITATIONS

The use of health insurance claims data limits the findings of this study to the populations included in the OptumLabs Data Warehouse; in particular, we do not observe outcomes of people who are uninsured or those who have Medicaid insurance (i.e., people with low incomes and no employer-based insurance). The study only captures people who received health care for

AVRI, which may be different in important ways during COVID-19 compared to earlier years; early in the pandemic, many people avoided seeking in-person care, likely to avoid exposure to COVID-19 or to preserve access to care for others. However, the difference-in-differences design of the study addresses this problem by comparing changes in outcomes for two similar populations; as long as people with hypertension who used ACEi/ARB and those who used other medications changed their care seeking behavior in similar ways, this effect should be minimized. Lastly, although analyses were adjusted for age, sex, race/ethnicity and comorbidities, residual confounding is still a possibility given the observational study design and other potential confounders that were not evaluated such as number of previous respiratory infections, number of previous hospitalization, and duration of treatment with ACEi/ARBs.

CONCLUSIONS

People with acute viral respiratory illnesses using ACEi/ARBs to treat hypertension had a greater increase in poor outcomes during the COVID-19 pandemic than those using other medications to treat hypertension. This may support the existence of the theoretical biological effect of ACEi/ARB in increasing susceptibility to COVID-19. Small absolute differences in risks of hospitalization, ICU use, and diagnosis of ARD or ARDS suggest that this effect likely does not warrant changes in clinical practice.

CONTRIBUTORSHIP STATEMENT

Conceptualization: MMJ, LOJS, FB, VDG, TMD, AHL, NWC. Formal analysis: MMJ. Investigation: MMJ, LOJS, FB, VDG, TMD, AHL, NWC. Methodology: MMJ, LOJS, FB. Project administration: MMJ. Supervision: MMJ, NWC. Validation: MMJ, NWC. Writing-

original draft: MMJ. Writing-review and editing: MMJ, LOJS, FB, VSD, TMD, AHL, NWC. Guarantor: MMJ, NWC. All authors provided critical revision and contribution for important intellectual content.

COMPETING INTERESTS

None.

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DATA SHARING STATEMENT

No additional data available.

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LEGENDS

Table 1. Cohort characteristics.

Table 2. Main analysis results from linear probability model; full results in supplementary materials.



Table 1. Cohort characteristics.

	Comparison only (not included sample)	Included			
	No HTN meds	Other HTN meds	ACEi or ARB	Total included	
	N (%)	only N (%)	N (%)	sample N (%)	
Insurance type					
Medicare Advantage	145,045 (77.2%)	348,583 (85.9%)	518,670 (79.3%)	867,253 (81.9%)	
Commercial	42,874 (22.8%)	57,094 (14.1%)	135,127 (20.7%)	192,221 (18.1%)	
Female	99,755 (53.1%)	246,659 (60.8%)	374,151 (57.2%)	620,810 (58.6%)	
Age (categories)					
<35	3,922 (2.1%)	3,354 (0.8%)	4,537 (0.7%)	7,891 (0.7%)	
35-44	8,337 (4.4%)	9,784 (2.4%)	17,780 (2.7%)	27,564 (2.6%)	
45-54	17,704 (9.4%)	24,916 (6.1%)	51,926 (7.9%)	76,842 (7.3%)	
55-64	32,637 (17.4%)	59,872 (14.8%)	115,095 (17.6%)	174,967 (16.5%)	
65-74	54,862 (29.2%)	120,039 (29.6%)	218,160 (33.4%)	338,199 (31.9%)	
75-84	44,330 (23.6%)	115,011 (28.4%)	171,276 (26.2%)	286,287 (27.0%)	
85+	26,127 (13.9%)	72,701 (17.9%)	75,023 (11.5%)	147,724 (13.9%)	
Race/ethnicity					
White	109,223 (58.1%)	238,439 (58.8%)	372,987 (57.0%)	611,426 (57.7%)	
Black	28,990 (15.4%)	70,774 (17.4%)	103,284 (15.8%)	174,058 (16.4%)	
Hispanic	20,302 (10.8%)	36,478 (9.0%)	82,374 (12.6%)	118,852 (11.2%)	
Asian	4,449 (2.4%)	8,003 (2.0%)	15,063 (2.3%)	23,066 (2.2%)	
Unknown/other	24,955 (13.3%)	51,983 (12.8%)	80,089 (12.2%)	132,072 (12.5%)	
Census Division					
New England	7,217 (3.8%)	18,358 (4.5%)	25,557 (3.9%)	43,915 (4.1%)	
Mid Atlantic	18,655 (9.9%)	43,354 (10.7%)	59,385 (9.1%)	102,739 (9.7%)	
South Atlantic	66,206 (35.2%)	154,483 (38.1%)	252,798 (38.7%)	407,281 (38.4%)	
E North Central	24,489 (13.0%)	59,277 (14.6%)	86,110 (13.2%)	145,387 (13.7%)	
E South Central	12,743 (6.8%)	28,786 (7.1%)	47,182 (7.2%)	75,968 (7.2%)	
W North Central	18,292 (9.7%)	28,065 (6.9%)	42,997 (6.6%)	71,062 (6.7%)	
W South Central	25,743 (13.7%)	48,406 (11.9%)	92,517 (14.2%)	140,923 (13.3%)	
Mountain	8,484 (4.5%)	14,224 (3.5%)	27,963 (4.3%)	42,187 (4.0%)	
Pacific	5,902 (3.1%)	10,612 (2.6%)	19,087 (2.9%)	29,699 (2.8%)	
Unknown/Other	188 (0.1%)	112 (0.0%)	201 (0.0%)	313 (<0.1%)	

Hypertension

	Comparison only (not included sample)	Included Sample		
	No HTN meds	Other HTN meds only	ACEi or ARB	Total included sample
	N (%)	N (%)	N (%)	N (%)
No complications	164,325 (87.4%)	334,180 (82.4%)	572,570 (87.6%)	906,750 (85.6%)
With complications	23,594 (12.6%)	71,497 (17.6%)	81,227 (12.4%)	152,724 (14.4%)
Comorbidities				
Diabetes				
No complications	22,002 (11.7%)	42,302 (10.4%)	99,778 (15.3%)	142,080 (13.4%)
With complications	37,742 (20.1%)	99,365 (24.5%)	172,335 (26.4%)	271,700 (25.6%)
Chronic pulmonary disease	66,355 (35.3%)	163,682 (40.3%)	209,053 (32.0%)	372,735 (35.2%)
Coronary artery disease	41,083 (21.9%)	122,633 (30.2%)	156,465 (23.9%)	279,098 (26.3%)
Congestive heart failure	30,910 (16.4%)	123,355 (30.4%)	131,418 (20.1%)	254,773 (24.0%)
Cardia arrhythmia	47,176 (25.1%)	138,713 (34.2%)	149,765 (22.9%)	288,478 (27.2%)
Valvular disease	15,929 (8.5%)	50,011 (12.3%)	55,342 (8.5%)	105,353 (9.9%)
Chronic/acute deep vein	6,657 (3.5%)	13,846 (3.4%)	13,883 (2.1%)	27,729 (2.6%)
thrombosis or pulmonary embolism				
Peripheral vascular disorders	24,473 (13.0%)	66,643 (16.4%)	74,909 (11.5%)	141,552 (13.4%)
Hemorrhagic or ischemic stroke	15,912 (8.5%)	34,297 (8.5%)	39,064 (6.0%)	73,361 (6.9%)
Coagulopathy	10,197 (5.4%)	25,467 (6.3%)	22,109 (3.4%)	47,576 (4.5%)
Lymphoma	2,928 (1.6%)	6,095 (1.5%)	6,086 (.9%)	12,181 (1.1%)
Metastatic cancer	6,506 (3.5%)	11,323 (2.8%)	11,808 (1.8%)	23,131 (2.2%)
Solid tumor without mets	17,654 (9.4%)	35,097 (8.7%)	42,177 (6.5%)	77,274 (7.3%)
Renal failure	29,431 (15.7%)	104,877 (25.9%)	107,485 (16.4%)	212,362 (20.0%)
Liver failure	8,676 (4.6%)	19,071 (4.7%)	19,875 (3.0%)	38,946 (3.7%)
Rheumatoid arthritis/collagen vascular diseases	8,584 (4.6%)	20,953 (5.2%)	27,768 (4.2%)	48,721 (4.6%)
Obesity	17,709 (9.4%)	44,279 (10.9%)	72,278 (11.1%)	116,557 (11.0%)
Total	187,919 (100.0%)	405,677 (100.0%)	653,797 (100.0%)	1,059,474 (100.0%)
Unadjusted outcome incidence				
Inpatient stay	33,058 (17.6%)	75,670 (18.7%)	91,660 (14.0%)	167,330 (15.8%)
ICU/CCU services during inpatient stay	15,360 (46.5%)	37,894 (50.1%)	45,129 (49.2%)	83,023 (49.6%)
ARDS diagnosis during inpatient stay	1,051 (3.2%)	2,598 (3.4%)	3,403 (3.7%)	6,001 (3.6%)
ARD diagnosis during inpatient stay	1,781 (5.4%)	4,749 (6.3%)	5,388 (5.9%)	10,137 (6.1%)
Died same or following calendar month	12,933 (6.9%)	28,753 (7.1%)	26,411 (4.0%)	55,164 (5.2%)

Table 2. Main analysis results from linear probability model; full results in supplementary materials.

	(1)	(2)	(2) (3)		(5)					
	Inpatient stay	Inpatient stay with ICU/CCU	Inpatient stay with ARD dx	Inpatient stay with ARDS dx	Died same or following month					
	Key coefficie	nt estimates (95%	6 confidence inte	rval)						
Season										
2017-2018 flu season	ref.	ref.	ref.	ref.	ref.					
2018-2019 flu season	-0.001	0.008	0.013***	-0.007***	0.000					
	(-0.004, 0.002)	(-0.002, 0.018)	(0.008, 0.017)	(-0.010,-0.004)	(-0.002, 0.002)					
2019-2020 flu season	0.018***	0.035***	0.013***	0.013***	0.016***					
2017 2020 114 8448011	(0.015, 0.021)	(0.026, 0.044)	(0.008, 0.017)	(0.009, 0.016)	(0.014, 0.017)					
HTN medication group										
Other medications only	ref.	ref.	ref.	ref.	ref.					
Other medications only										
ACEi or ARB	-0.019***	-0.009	-0.007**	-0.003	-0.009***					
plus/minus other	(-0.022,-0.016)	(-0.019,0.001)	(-0.011,-0.002)	(-0.007, 0.000)	(-0.011,-0.008)					
medications	, , ,			, , ,	, , ,					
G / 1										
Season/medication interactions										
2018-2019 season:	0.004*	0.010	0.004	0.000	0.000					
ACEi or ARB	(0.001, 0.008)	(-0.004,0.023)	(-0.003,0.010)	(-0.004,0.004)	(-0.002,0.002)					
plus/minus other	, , ,	, , ,		, , ,	, , ,					
medications										
2019-2020 season:	0.015***	0.015*	0.007*	0.009***	-0.002					
ACEi or ARB	(0.012,0.019)	(0.003,0.027)	(0.001,0.012)	(0.004,0.013)	(-0.004,0.001)					
plus/minus other	(0.012,0.019)	(0.003,0.027)	(0.001,0.012)	(0.004,0.013)	(0.004,0.001)					
medications	ata ia faritha n11 h-		acafficient = 0:	agantad in nucleatil	itita (a. a.					

Note: p-value for coefficients is for the null hypothesis that the coefficient = 0; presented in probability units (e.g., coefficient of -0.001 represents -0.1 percentage points)

Marginal effects/predicted probability (95% confidence interval)

0.179	0.482	0.053	0.030	0.064
(0.177, 0.181)	(0.474, 0.489)	(0.050, 0.056)	(0.028, 0.033)	(0.062, 0.065)
0.178	0.490	0.066	0.023	0.064
(0.176, 0.180)	(0.483, 0.496)	(0.062, 0.069)	(0.021, 0.025)	(0.063, 0.065)
0.196	0.516	0.066	0.043	0.080
	(0.177,0.181) 0.178 (0.176,0.180)	(0.177,0.181) (0.474,0.489) 0.178 0.490 (0.176,0.180) (0.483,0.496)	(0.177,0.181) (0.474,0.489) (0.050,0.056) 0.178 0.490 0.066 (0.176,0.180) (0.483,0.496) (0.062,0.069)	(0.177,0.181) (0.474,0.489) (0.050,0.056) (0.028,0.033) 0.178 0.490 0.066 0.023 (0.176,0.180) (0.483,0.496) (0.062,0.069) (0.021,0.025)

	(1)	(2)	(3)	(4)	(5)
	Inpatient stay (0.195,0.198)	Inpatient stay with ICU/CCU (0.511,0.521)	Inpatient stay with ARD dx (0.063,0.068)	Inpatient stay with ARDS dx (0.041,0.045)	Died same or following month (0.078,0.081)
ACEi or ARB plus/minus other medications					
2017/18	0.125	0.463	0.045	0.029	0.035
	(0.124, 0.127)	(0.456, 0.470)	(0.042, 0.048)	(0.027, 0.031)	(0.034, 0.035)
2018/19	0.128	0.481	0.061	0.021	0.034
	(0.127, 0.130)	(0.475, 0.487)	(0.058, 0.064)	(0.020, 0.023)	(0.034, 0.035)
2019/20	0.158	0.512	0.064	0.050	0.049
	(0.157, 0.160)	(0.508, 0.517)	(0.062, 0.066)	(0.048, 0.052)	(0.048, 0.049)
	Ratios of mai	rginal effects (95%	6 confidence inte	rval)	
Other hypertension medications only 2018/19 season vs.	0.994	1.017	1.236***	0.759***	0.999
2017/18	(0.977,1.011)	(0.996,1.038)	(1.136,1.337)	(0.668, 0.850)	(0.969,1.030)
2019/20 season vs.	1.099***	1.072***	1.238***	1.414***	1.244***
2017/18	(1.081,1.116)	(1.053,1.092)	(1.147,1.330)	(1.278, 1.550)	(1.210,1.278)
ACEi or ARB plus/minus other medications					
2018/19 season vs.	1.025**	1.039***	1.360***	0.739***	0.993
2017/18	(1.009, 1.042)	(1.019, 1.058)	(1.251,1.469)	(0.656, 0.822)	(0.961,1.025)
2019/20 season vs.	1.264***	1.107***	1.437***	1.731***	1.404***
2017/18	(1.245,1.282)	(1.088,1.126)	(1.332,1.542)	(1.580,1.882)	(1.363,1.444)

Note: p-value for risk ratios is for the null hypothesis that the risk ratio = 1 p<0.05, ** p<0.01, *** p<0.001

ref.: reference category

^{*} p<0.05, ** p<0.01, *** p<0.001

SUPPLEMENTARY MATERIAL S1

SUPPLEMENT T1: Codes used to define AVRI, CAD, stroke, DVT, and PE

Condition	Codes
Acute viral respiratory illness (AVRI)	B9721, B9729, J09*, J10*, J11*, J12*, J16,
	J168, J18, J180, J181, J182, J188, J189, J20,
	J201, J203, J204, J205, J206, J207, J208,
	J209, J22, J40, J440, J470, J8411, J84111,
	U071, U072
Coronary artery disease (CAD)	120*, 121*, 122*, 123*, 124*, 125*
Stroke	I63*, Z8673*, I60*, I61*, I62*
Deep vein thrombosis (DVT) and pulmonary	I8249, I824Y, I824Z, I8251, I8259, I825Y,
embolism (PE)	I825Z, I8262, I8272, I26*, I2782

SUPPLEMENT T2: Hypertension medications

Medication type	Included medications (generic name)
ACEi	captopril, lisinopril, enalapril, benazepril,
	perindopril, quinapril, fosinopril, moexipril,
	ramipril, trandolapril
ARB	losartan, valsartan, irbesartan, candesartan,
	eprosartan, telmisartan, azilsartan, Olmesartan
Other (excluding topical, ophthalmic, and	Bendroflumethiazide, chlorothiazide,
drops preparations)	indapamide, metolazone, bumetanide,
	furosemide, torsemide, ethacrynic, amiloride,
	triamterene, eplerenone, spironolactone,
	aliskiren, diltiazem, verapamil, amlodipine,
	nicardipine, felodipine, nifedipine, torsemide,
	ethacrynic, isradipine, nisoldipine, doxazosin,
	prazosin, terazosin, clonidine, guanfacine,
	methyldopa, reserpine, hydralazine,
	minoxidil, acebutolol, atenolol, betaxolol,
	bisoprolol, carvedilol, labetalol, metoprolol,
	nadolol, nebivolol, penbutolol, pindolol,
	propranolol, timolol

	Primary analysis					
	(1) Inpatient stay	(2) Inpatient stay with ICU/CCU	(3)	(4) Inpatient stay with ARDS dx	(5) Died same or following month	
	(95% confidence interval)	(95% confidence interval)	(95% confidence interval)	(95% confidence interval)	(95% confidence interval)	
Flu season / medication type 2017-2018 flu season	ref.	ref.	ref.	ref.	ref.	
2018-2019 flu season	-0.001 (-0.004,0.002)	0.008 (-0.002,0.018)	0.013*** (0.008,0.017)	-0.007*** (-0.010,-0.004)	0.000 (-0.002,0.002)	
2019-2020 flu season	0.018*** (0.015,0.021)	0.035*** (0.026,0.044)	0.013*** (0.008,0.017)	0.013*** (0.009,0.016)	0.016*** (0.014,0.017)	
Other medications only	ref.	ref.	ref.	ref.	ref.	
ACEi or ARB plus/minus other medications	-0.019*** (-0.022,-0.016)	-0.009 (-0.019,0.001)	-0.007** (-0.011,-0.002)	-0.003 (-0.007,0.000)	-0.009*** (-0.011,-0.008)	
ACEi or ARB monotherapy						
2018-2019 season: ACEi or ARB +- other	0.004* (0.001,0.008)	0.01 (-0.004,0.023)	0.004 (-0.003,0.010)	0 (-0.004,0.004)	0 (-0.002,0.002)	
2018-2019 season: ACEi or ARB monotherapy						
2019-2020 season: ACEi or ARB +/- other	0.015*** (0.012,0.019)	0.015* (0.003,0.027)	0.007* (0.001,0.012)	0.009*** (0.004,0.013)	-0.002 (-0.004,0.001)	
2019-2020 season: ACEi or ARB monotherapy						
Demographics	0.045***	0.022***	•	0.004***	0.044***	
Female	-0.016*** (-0.017,-0.014)	-0.023*** (-0.028,-0.018)	0 (-0.002,0.003)	-0.004*** (-0.006,-0.002)	-0.011*** (-0.012,-0.010)	
Age categories	-0.006*	-0.029	0.02	-0.01	-0.001	
<35	(-0.011,-0.000)	(-0.078,0.019)	(-0.006,0.045)	(-0.028,0.008)	(-0.003,0.001)	
35-44	-0.008***	-0.028	0.006	-0.004	0.001	
	(-0.012,-0.005)	(-0.056,0.000)	(-0.008,0.019)	(-0.016,0.008)	(-0.000,0.002)	
45-54	ref.	ref.	ref.	ref.	ref.	
55-64	0.010***	0.005	0.001	0.001	0.001*	
	(0.008,0.013)	(-0.009,0.020)	(-0.005,0.008)	(-0.005,0.007)	(0.000,0.002)	
65-74	0.011***	-0.003	0.001	-0.001	0.009***	
75-84	(0.008,0.014) 0.029***	(-0.017,0.011) -0.026***	(-0.006,0.008) -0.002	(-0.007,0.004) -0.005	(0.007,0.010) 0.024***	
73-84	(0.025,0.032)	(-0.041,-0.012)	(-0.009,0.004)	(-0.011,0.001)	(0.023,0.026)	
85+	0.045***	-0.071***	-0.010**	-0.014***	0.063***	
Insurance coverage type	(0.041,0.048)	(-0.086,-0.056)	(-0.017,-0.003)	(-0.020,-0.008)	(0.061,0.065)	
Medicare Advantage	ref.	ref.	ref.	ref.	ref.	
Commercial	-0.032***	0.01	0.001	0.003	-0.001*	
Census region	(-0.034,-0.030)	(-0.001,0.020)	(-0.004,0.006)	(-0.002,0.007)	(-0.002,-0.000)	
Unknown/other	-0.046**	0.194*	-0.011	0.009	-0.023*	
	(-0.075,-0.016)	(0.014,0.373)	(-0.086,0.064)	(-0.068,0.087)	(-0.044,-0.002)	
New England	ref.	ref.	ref.	ref.	ref.	
Mid Atlantic	-0.008***	0.017*	0.021***	0.021***	-0.005**	
	(-0.012,-0.003)	(0.003,0.031)	(0.015,0.028)	(0.016,0.026)	(-0.008,-0.002)	
South Atlantic	-0.001	0.122***	0.016***	0.003	-0.016***	
	(-0.005,0.003)	(0.110,0.134)	(0.011,0.021)	(-0.002,0.007)	(-0.018,-0.013)	

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1				Drimon, analysis		
2		(1)	(2)	Primary analysis (3)	(4)	(5)
3		Inpatient stay	• •	` '	` '	Died same or following month
4		(95% confidence interval)	(95% confidence interval)	(95% confidence interval)	(95% confidence interval)	(95% confidence interval)
5	E North Central	0.018***	0.073***	0.003	0	-0.009***
		(0.013,0.022)	(0.060,0.086)	(-0.002,0.009)	(-0.004,0.004)	(-0.012,-0.007)
6	E South Central	0.011***	0.071***	0.018***	-0.001	-0.009***
7	W North Central	(0.007,0.016) 0.027***	(0.056,0.085) 0.093***	(0.011,0.024) 0.004	(-0.006,0.005) 0.006*	(-0.011,-0.006) -0.007***
8	w North Central	(0.022,0.032)	(0.079,0.107)	(-0.002,0.010)	(0.001,0.011)	(-0.010,-0.004)
9	W South Central	0.014***	0.111***	0.017***	0.003	-0.011***
10		(0.010,0.018)	(0.097,0.124)	(0.011,0.023)	(-0.002,0.007)	(-0.014,-0.009)
	Mountain	-0.033***	0.122***	-0.007	0.008*	-0.019***
11		(-0.037,-0.028)	(0.103,0.140)	(-0.015,0.000)	(0.001,0.016)	(-0.022,-0.016)
12	Pacific	-0.002	0.170***	0.008	0.001	-0.016***
13	Race/ethnicity	(-0.007,0.004)	(0.151,0.189)	(-0.000,0.017)	(-0.006,0.007)	(-0.019,-0.013)
14	Unknown/other	-0.007***	0.020***	0.004*	0.009***	-0.002**
15	White	(-0.010,-0.005) ref.	(0.013,0.028) ref.	(0.001,0.008) ref.	(0.006,0.012) ref.	(-0.003,-0.001) ref.
16	Wille	iei.	ici.	iei.	ici.	Tel.
	Black	0.011***	-0.010**	0.005**	0.008***	0.004***
17		(0.009,0.013)	(-0.017,-0.003)	(0.002,0.008)	(0.006,0.011)	(0.002,0.005)
18	Hispanic	-0.016***	0.086***	0.011***	0.010***	-0.008***
19		(-0.018,-0.013)	(0.077,0.095)	(0.006,0.015)	(0.007,0.014)	(-0.009,-0.006)
20	Asian	-0.011***	0.020*	0.002	0.007	-0.001
21	Comorbidities	(-0.016,-0.007)	(0.002,0.039)	(-0.007,0.010)	(-0.000,0.014)	(-0.004,0.002)
	No diabetes	ref.	ref.	ref.	ref.	ref.
22	Diabetes without CC	0.011***	0.012**	0.005**	0.004**	0.005***
23	State tes William Ce	(0.009,0.013)	(0.004,0.019)	(0.001,0.009)	(0.001,0.007)	(0.004,0.006)
24	Diabetes with CC	0.029***	0.008**	-0.002	0.002	0.008***
25		(0.027,0.031)	(0.002,0.014)	(-0.005,0.001)	(-0.000,0.004)	(0.006,0.009)
26	Uncomp hypertension	ref.	ref.	ref.	ref.	ref.
27						
	Comp hypertension	0.023***	-0.012**	-0.003	-0.003*	-0.001
28	Coronary artery disease	(0.020,0.026) 0.020***	(-0.018,-0.005) 0.028***	(-0.006,0.000) 0.001	(-0.005,-0.000) -0.002	(-0.003,0.001) 0.007***
29	Coronary artery disease	(0.018,0.022)	(0.022,0.033)	(-0.001,0.004)	(-0.004,0.000)	(0.006,0.009)
30	Congestive heart failure	0.093***	0.077***	0.018***	0.002*	0.036***
31	3	(0.090,0.095)	(0.072,0.083)	(0.015,0.020)	(0.000,0.004)	(0.034,0.037)
32	Chronic pulmonary diseases	0.061***	-0.010***	0.015***	-0.007***	-0.002***
		(0.059,0.063)	(-0.015,-0.005)	(0.013,0.018)	(-0.009,-0.006)	(-0.003,-0.001)
33	Renal failure	0.019***	0.012***	-0.001	0.001	0.023***
34		(0.017,0.022)	(0.005,0.018)	(-0.004,0.003)	(-0.001,0.004)	(0.021,0.025)
35	Liver failure	0.046***	0.035***	-0.003	0	0.059***
36	Metastatic cancer	(0.042,0.051) 0.122***	(0.025,0.045) 0.01	(-0.008,0.002) 0.003	(-0.004,0.004) -0.010***	(0.056,0.063) 0.136***
37	ivietastatic caricer	(0.115,0.130)	(-0.003,0.024)	(-0.004,0.009)	(-0.014,-0.006)	(0.130,0.142)
	Lymphoma	0.064***	-0.008	-0.001	-0.010***	0.027***
38	, ,	(0.056,0.073)	(-0.025,0.009)	(-0.009,0.007)	(-0.015,-0.004)	(0.021,0.033)
39	Non-metastatic solid tumor	0.036***	0.018***	0	-0.003*	0.028***
40		(0.033,0.040)	(0.009,0.027)	(-0.004,0.005)	(-0.006,-0.000)	(0.026,0.030)
41	Peripheral vascular disorders	-0.008***	0.017***	0.004**	0.001	0.018***
	Conflict and thereby	(-0.011,-0.006)	(0.010,0.023)	(0.001,0.008)	(-0.001,0.003)	(0.017,0.020)
42	Cardiac arrhythmias	0.062***	0.062***	0.005***	-0.002*	0.024***
43						
44						

			Primary analysis		
	(1)	(2)	(3)	(4)	(5)
	Inpatient stay	Inpatient stay with ICU/CCU	Inpatient stay with ARD dx	Inpatient stay with ARDS dx	Died same or following month
	(95% confidence interval)	(95% confidence interval)	(95% confidence interval)	(95% confidence interval)	(95% confidence interval)
	(0.060,0.064)	(0.057,0.067)	(0.002,0.007)	(-0.004,-0.000)	(0.023,0.025)
Rheumatoid arthritis/collagen vascular diseases	0.016***	-0.005	-0.007**	0	0.004***
	(0.013,0.020)	(-0.016,0.005)	(-0.012,-0.002)	(-0.004,0.004)	(0.002,0.006)
Coagulopathy	0.029***	0.032***	-0.004	0.002	0.035***
	(0.024,0.033)	(0.023,0.041)	(-0.008,0.000)	(-0.001,0.005)	(0.032,0.038)
Obesity	-0.002	0.013***	0.004	0.009***	-0.009***
	(-0.005,0.000)	(0.006,0.021)	(-0.000,0.007)	(0.006,0.012)	(-0.010,-0.007)
Chronic/acute deep vein thrombosis or pulmonary embolism	0.061***	0.050***	0.003	0.002	0.030***
	(0.056,0.067)	(0.039,0.061)	(-0.003,0.009)	(-0.003,0.006)	(0.026,0.034)
Hemorrhagic or ischemic stroke	0.016***	0.032***	0.002	-0.004**	0.043***
	(0.013,0.020)	(0.024,0.040)	(-0.001,0.006)	(-0.007,-0.001)	(0.040,0.045)
Valvular disease	-0.009***	0.045***	0.007***	-0.002	0.017***
	(-0.012,-0.006)	(0.038,0.052)	(0.003,0.010)	(-0.004,0.001)	(0.015,0.019)
Constant	0.058***	0.310***	0.020***	0.034***	0.012***
	(0.053,0.063)	(0.291,0.330)	(0.011,0.029)	(0.027,0.041)	(0.009,0.015)
N	1059474	167330	167330	167330	1057707
N_clust	728455	147846	147846	147846	727311
p	<0.001	<0.001	<0.001	<0.001	<0.001
R-squared	0.081	0.037	0.006	0.008	0.076
				0.008	

	(6)	(7)	(8)	(9)	(10)
	Inpatient stay (95% confidence interval)	Inpatient stay with ICU/CCU (95% confidence interval)	Inpatient stay with ARD dx (95% confidence interval)	Inpatient stay with ARDS dx (95% confidence interval)	Died same or following mon (95% confidence interval)
lu season / medication type	_	_	_	_	_
2017-2018 flu season	ref.	ref.	ref.	ref.	ref.
018-2019 flu season	-0.001	0.008	0.013***	-0.007***	0
	(-0.004,0.002)	(-0.002,0.018)	(0.008, 0.017)	(-0.010,-0.004)	(-0.002,0.002)
019-2020 flu season	0.018***	0.035***	0.013***	0.013***	0.016***
	(0.015,0.021)	(0.026,0.044)	(0.008,0.017)	(0.009,0.016)	(0.014,0.017)
Other medications only	ref.	ref.	ref.	ref.	ref.
CEi or ARB plus/minus other medications	-0.020***	-0.004	-0.007**	-0.002	-0.010***
	(-0.023,-0.017)	(-0.014,0.006)	(-0.011,-0.002)	(-0.006,0.001)	(-0.012,-0.009)
ACEi or ARB monotherapy	-0.016***	-0.039***	-0.007	-0.009**	-0.004***
	(-0.020,-0.012)	(-0.057,-0.020)	(-0.015,0.001)	(-0.015,-0.003)	(-0.006,-0.002)
018-2019 season: ACEi or ARB +- other	0.004*	0.004	0.004	-0.001	-0.001
	(0.000,0.008)	(-0.009,0.018)	(-0.003,0.010)	(-0.005,0.004)	(-0.003,0.002)
018-2019 season: ACEi or ARB monotherapy	0.005	0.040**	0.002	0.002	0.001
	(-0.001,0.010)	(0.015,0.065)	(-0.009,0.013)	(-0.006,0.009)	(-0.002,0.004)
019-2020 season: ACEi or ARB +/- other	0.015***	0.011	0.007*	0.008***	-0.001
	(0.011,0.019)	(-0.001,0.024)	(0.002,0.013)	(0.003,0.013)	(-0.004,0.001)
1019-2020 season: ACEi or ARB monotherapy	0.017***	0.035**	0.004	0.012**	-0.003*
No	(0.012,0.022)	(0.013,0.057)	(-0.006,0.013)	(0.004,0.020)	(-0.006,-0.000)
Demographics Semale	-0.016***	-0.023***	0	-0.004***	-0.011***
eniale	(-0.017,-0.014)	(-0.028,-0.018)	(-0.002,0.003)	(-0.006,-0.002)	(-0.012,-0.010)
age categories	(0.017, 0.014)	(0.028, 0.018)	(0.002,0.003)	(0.000, 0.002)	(0.012, 0.010)
35	-0.006*	-0.029	0.02	-0.01	-0.001
	(-0.012,-0.000)	(-0.078,0.020)	(-0.005,0.045)	(-0.028,0.008)	(-0.003,0.001)
15-44	-0.008***	-0.028	0.006	-0.004	0.001
	(-0.012,-0.005)	(-0.056,0.000)	(-0.008,0.019)	(-0.016,0.008)	(-0.001,0.002)
5-54	ref.	ref.	ref.	ref.	ref.
5-64	0.010***	0.005	0.001	0.001	0.001*
3-04	(0.008,0.013)	(-0.009,0.020)	(-0.005,0.008)	(-0.005,0.007)	(0.000,0.002)
55-74	0.011***	-0.003	0.001	-0.001	0.009***
3 74	(0.008,0.014)	(-0.017,0.011)	(-0.006,0.008)	(-0.007,0.004)	(0.007,0.010)
75-84	0.029***	-0.026***	-0.002	-0.005	0.024***
	(0.026,0.032)	(-0.041,-0.012)	(-0.009,0.004)	(-0.011,0.001)	(0.023,0.026)
S5+	0.045***	-0.072***	-0.010**	-0.014***	0.063***
nsurance coverage type	(0.041,0.049)	(-0.087,-0.057)	(-0.017,-0.003)	(-0.020,-0.008)	(0.061,0.065)
Medicare Advantage	ref.	ref.	ref.	ref.	ref.
Commercial	-0.032***	0.01	0.001	0.003	-0.001**
Census region	(-0.035,-0.030)	(-0.001,0.021)	(-0.004,0.006)	(-0.002,0.007)	(-0.002,-0.000)
Jnknown/other	-0.045**	0.196*	-0.011	0.009	-0.023*
The state of the s	(-0.075,-0.016)	(0.016,0.375)	(-0.086,0.064)	(-0.068,0.087)	(-0.044,-0.002)
New England	ref.	ref.	ref.	ref.	ref.
Aid Atlantic	-0.008***	0.017*	0.021***	0.021***	-0.005**
outh Atlantic	(-0.012,-0.003)	(0.003,0.031)	(0.015,0.028)	(0.016,0.026)	(-0.008,-0.002)
	-0.001	0.122***	0.016***	0.003	-0.016***

	Sensitivity analysis: ACEi/ARB monother				
	(6)	(7)	(8)	(9)	(10)
	Inpatient stay	Inpatient stay with ICU/CCU	Inpatient stay with ARD dx	Inpatient stay with ARDS dx	Died same or following month
	(95% confidence interval)	(95% confidence interval)	(95% confidence interval)	(95% confidence interval)	(95% confidence interval)
E North Central	0.018***	0.073***	0.003	0	-0.009***
	(0.013,0.022)	(0.060,0.086)	(-0.002,0.009)	(-0.004,0.004)	(-0.012,-0.007)
E South Central	0.011***	0.070***	0.018***	-0.001	-0.008***
	(0.007,0.016)	(0.056,0.085)	(0.011,0.024)	(-0.006,0.004)	(-0.011,-0.006)
W North Central	0.027***	0.093***	0.004	0.006*	-0.007***
	(0.022,0.032)	(0.079,0.107)	(-0.002,0.010)	(0.001,0.011)	(-0.010,-0.004)
W South Central	0.014***	0.111***	0.017***	0.003	-0.011***
	(0.010,0.018)	(0.097,0.124)	(0.011,0.023)	(-0.002,0.007)	(-0.014,-0.009)
Mountain	-0.033***	0.122***	-0.007	0.008*	-0.019***
	(-0.037,-0.028)	(0.103,0.141)	(-0.015,0.000)	(0.001,0.016)	(-0.022,-0.016)
Pacific	-0.002	0.170***	0.008	0.001	-0.016***
Race/ethnicity	(-0.007,0.004)	(0.151,0.189)	(-0.000,0.017)	(-0.006,0.007)	(-0.019,-0.013)
Unknown/other	-0.007***	0.020***	0.004*	0.009***	-0.002**
Officiowity offici	(-0.010,-0.005)	(0.013,0.028)	(0.001,0.008)	(0.006,0.012)	(-0.003,-0.001)
White	(-0.010,-0.003)	(0.013,0.028) ref.	ref.	ref.	ref.
write	iei.	iei.	iei.	iei.	iei.
Black	0.011***	-0.010**	0.005**	0.008***	0.004***
Black	(0.009,0.013)	(-0.017,-0.003)	(0.002,0.008)	(0.006,0.011)	(0.003,0.005)
Hispania	-0.016***	0.086***	0.011***	0.010***	-0.008***
Hispanic					
A. da .	(-0.018,-0.013) -0.012***	(0.077,0.095)	(0.006,0.015)	(0.007,0.014)	(-0.009,-0.006)
Asian		0.020*	0.002	0.007	-0.001
Comorbidities	(-0.016,-0.007)	(0.002,0.039)	(-0.007,0.010)	(-0.000,0.014)	(-0.004,0.001)
No diabetes	ref.	ref.	ref.	ref.	ref.
Diabetes without CC	0.011***	0.012**	0.005**	0.004**	0.005***
Diabetes without ee	(0.009,0.013)	(0.004,0.019)	(0.001,0.009)	(0.001,0.007)	(0.004,0.006)
Diabetes with CC	0.029***	0.008**	-0.002	0.002	0.008***
Diabetes with CC	(0.027,0.031)	(0.002,0.014)	(-0.005,0.001)	(-0.000,0.004)	(0.006,0.009)
Uncomp hypertension	(0.027,0.031) ref.	(0.002,0.014) ref.	ref.	ref.	ref.
Oncomp hypertension	iei.	iei.	iei.	iei.	iei.
Comp hypertension	0.023***	-0.012**	-0.003	-0.003*	-0.001
comp hypertension	(0.020,0.026)	(-0.019,-0.005)	(-0.006,0.000)	(-0.005,-0.000)	(-0.003,0.001)
Coronary artery disease	0.020***	0.027***	0.001	-0.002	0.008***
coronary artery disease	(0.018,0.022)	(0.022,0.033)	(-0.001,0.004)	(-0.004,0.000)	(0.006,0.009)
Congestive heart failure	0.093***	0.077***	0.017***	0.002	0.036***
congestive heart randic	(0.091,0.096)	(0.071,0.082)	(0.015,0.020)	(-0.000,0.004)	(0.035,0.038)
Chronic pulmonary diseases	0.061***	-0.010***	0.015***	-0.007***	-0.002***
chronic parmonary discuses	(0.059,0.063)	(-0.015,-0.005)	(0.013,0.018)	(-0.009,-0.006)	(-0.003,-0.001)
Renal failure	0.019***	0.012***	-0.001	0.001	0.023***
iverial failure	(0.017,0.022)	(0.005,0.018)	(-0.004,0.003)	(-0.001,0.003)	(0.021,0.025)
Liver failure	0.046***	0.035***	-0.003	(-0.001,0.003)	0.059***
Liver randre	(0.042,0.051)		(-0.008,0.002)	(-0.004,0.004)	
Motostatic cancer	0.122***	(0.025,0.045) 0.01	0.003	-0.010***	(0.056,0.063) 0.136***
Metastatic cancer					
London	(0.115,0.130)	(-0.003,0.024)	(-0.004,0.009)	(-0.014,-0.006)	(0.130,0.142)
Lymphoma	0.064***	-0.008	-0.001	-0.010***	0.027***
And the second s	(0.056,0.073)	(-0.025,0.009)	(-0.009,0.007)	(-0.015,-0.004)	(0.021,0.033)
Non-metastatic solid tumor	0.036***	0.018***	0	-0.003*	0.028***
	(0.033,0.040)	(0.009,0.027)	(-0.004,0.005)	(-0.006,-0.000)	(0.026,0.030)
Peripheral vascular disorders	-0.008***	0.017***	0.004**	0.001	0.018***
	(-0.011,-0.006)	(0.010,0.023)	(0.001,0.008)	(-0.001,0.003)	(0.017,0.020)
Cardiac arrhythmias	0.062***	0.062***	0.005***	-0.002*	0.024***

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_	Sensitivity analysis: ACEi/ARB monothe	rapy			
	(6)	(7)	(8)	(9)	(10)
	Inpatient stay				Died same or following month
	(95% confidence interval)	(95% confidence interval)	(95% confidence interval)	(95% confidence interval)	(95% confidence interval)
	(0.060,0.064)	(0.057,0.067)	(0.002,0.007)	(-0.004,-0.000)	(0.023,0.026)
Rheumatoid arthritis/collagen vascular diseases	0.016***	-0.005	-0.007**	0	0.004***
	(0.013,0.020)	(-0.016,0.006)	(-0.012,-0.002)	(-0.004,0.004)	(0.002,0.006)
Coagulopathy	0.029***	0.032***	-0.004	0.002	0.035***
	(0.024,0.033)	(0.023,0.041)	(-0.008,0.000)	(-0.001,0.005)	(0.032,0.038)
Obesity	-0.002	0.013***	0.004	0.009***	-0.008***
	(-0.004,0.000)	(0.006,0.021)	(-0.000,0.007)	(0.006,0.012)	(-0.010,-0.007)
Chronic/acute deep vein thrombosis or pulmonary embolism	0.061***	0.050***	0.003	0.002	0.030***
Harrist Anna Carata Anna Carata Anna Carata	(0.055,0.067)	(0.039,0.061) 0.032***	(-0.003,0.009)	(-0.002,0.006)	(0.026,0.034) 0.043***
Hemorrhagic or ischemic stroke	0.016*** (0.013,0.019)		0.002	-0.004**	***
Valvular disease	-0.009***	(0.024,0.040) 0.045***	(-0.001,0.006) 0.007***	(-0.007,-0.001) -0.002	(0.040,0.045) 0.017***
valvular uisease	(-0.012,-0.006)	(0.038,0.052)	(0.003,0.010)	(-0.004,0.001)	(0.015,0.019)
Constant	0.058***	0.312***	0.020***	0.034***	0.013,0.013)
Constant	(0.053,0.063)	(0.292,0.332)	(0.011,0.029)	(0.027,0.042)	(0.009,0.015)
N	1059474	167330	167330	167330	1057707
N clust	728455	147846	147846	147846	727311
p					<0.001
R-squared	0.081	0.037	0.006	0.008	0.076
		<0.001 0.037			

		Sensitivity analysis: Dro	pping people with comorbidi	ties (other than hypertension)
	(11)	(12)	(13)	(14)	(15)
	Inpatient stay			• •	Died same or following month
	(95% confidence interval)	(95% confidence interval)	(95% confidence interval)	(95% confidence interval)	(95% confidence interval)
Flu season / medication type		_			_
2017-2018 flu season	ref.	ref.	ref.	ref.	ref.
2010 2010 fly	0.002	0.02	0.030**	0.006	0
2018-2019 flu season	(-0.001,0.006)	(-0.032,0.072)	(0.009,0.051)	(-0.005,0.017)	(-0.002,0.002)
2019-2020 flu season	0.032***	0.068**	0.029***	0.052***	0.007***
2013 2020 Hu 3cu30H	(0.028,0.035)	(0.024,0.111)	(0.014,0.045)	(0.039,0.065)	(0.005,0.009)
Other medications only	ref.	ref.	ref.	ref.	ref.
, , , , , , , , , , , , , , , , , , ,					
ACEi or ARB plus/minus other medications	-0.006***	-0.001	0.009	0.003	-0.003***
	(-0.009,-0.003)	(-0.049,0.046)	(-0.008,0.026)	(-0.007,0.013)	(-0.004,-0.001)
ACEi or ARB monotherapy					
2018-2019 season: ACEi or ARB +- other	-0.003	0.004	-0.013	0.001	0.001
	(-0.007,0.001)	(-0.062,0.071)	(-0.041,0.014)	(-0.015,0.017)	(-0.001,0.003)
2018-2019 season: ACEi or ARB monotherapy					
2010 2020 ACE: ARR - / -+h	-0.001	0.05	-0.022*	0.001	0.001
2019-2020 season: ACEi or ARB +/- other	(-0.006,0.003)	0.05 (-0.006,0.106)		-0.001	-0.001 (-0.003,0.001)
2019-2020 season: ACEi or ARB monotherapy	(-0.000,0.003)	(-0.000,0.100)	(-0.043,-0.001)	(-0.019,0.016)	(-0.003,0.001)
2013 2020 3cd3011. ACEI OF ARB Monotherapy					
Demographics					
Female	-0.010***	-0.025*	-0.01	-0.008	-0.003***
	(-0.012,-0.008)	(-0.048,-0.003)	(-0.019,0.000)	(-0.018,0.002)	(-0.004,-0.002)
Age categories					
<35	-0.013***	-0.125	0.089	-0.017	-0.001**
	(-0.017,-0.010)	(-0.286,0.037)	(-0.025,0.202)	(-0.074,0.040)	(-0.002,-0.000)
35-44	-0.007***	-0.151***	0.014	-0.022	-0.001
	(-0.009,-0.004)	(-0.229,-0.074)	(-0.026,0.055)	(-0.053,0.009)	(-0.001,0.000)
45-54	ref.	ref.	ref.	ref.	ref.
55-64	0.003**	-0.041	-0.004	0.006	0.001***
33-04	(0.001,0.006)	(-0.091,0.009)	(-0.027,0.018)	(-0.018,0.029)	(0.001,0.002)
65-74	0.006***	-0.056*	-0.017	0.009	0.001*
	(0.003,0.009)	(-0.109,-0.003)	(-0.041,0.008)	(-0.015,0.032)	(0.000,0.002)
75-84	0.028***	-0.077**	-0.011	0.005	0.008***
	(0.024,0.032)	(-0.132,-0.022)	(-0.037,0.014)	(-0.019,0.029)	(0.007,0.010)
85+	0.074***	-0.139***	-0.022	-0.007	0.036***
Insurance coverage type	(0.068, 0.079)	(-0.196,-0.083)	(-0.048,0.004)	(-0.032,0.017)	(0.032,0.039)
Medicare Advantage	ref.	ref.	ref.	ref.	ref.
Commercial	-0.013***	-0.043*	-0.01	0.006	-0.004***
Census region	(-0.015,-0.010)	(-0.083,-0.002)	(-0.028,0.009)	(-0.011,0.024)	(-0.005,-0.003)
Unknown/other	-0.034*** (-0.053,-0.014)	0.755*** (0.693,0.816)	-0.025* (-0.050,-0.000)	-0.062*** (-0.089,-0.035)	0.008 (-0.018,0.034)
New England	(-0.055,-0.014) ref.	(0.695,0.616) ref.	(-0.050,-0.000) ref.	(-0.069,-0.055) ref.	(-0.018,0.034) ref.
New England	iCi.	ici.	ici.	ici.	161.
Mid Atlantic	-0.002	0.065*	0.015	0.025	0.002
	(-0.007,0.004)	(0.008,0.123)	(-0.008,0.038)	(-0.003,0.053)	(-0.001,0.005)
South Atlantic	-0.004	0.164***	0.012	-0.009	-0.001
	(-0.009,0.001)	(0.113,0.214)	(-0.007,0.032)	(-0.032,0.014)	(-0.004,0.001)

	(11)	(12)	(13)	(14)	(15)
	Inpatient stay	• •	• •	, ,	Died same or following mon
	(95% confidence interval)				
E North Central	0.007**	0.111***	0.018	0	0
	(0.002,0.013)	(0.058,0.165)	(-0.003,0.039)	(-0.024,0.024)	(-0.003,0.002)
E South Central	0.001	0.116***	0.01	-0.004	-0.001
M. North Control	(-0.005,0.007) 0.009**	(0.055,0.176) 0.124***	(-0.014,0.034)	(-0.030,0.023)	(-0.003,0.002)
W North Central	(0.003,0.015)	(0.063,0.184)	0.021 (-0.004,0.046)	-0.002 (-0.028,0.025)	0.002 (-0.001,0.004)
W South Central	0.001	0.142***	0.025*	0.007	0
	(-0.004,0.007)	(0.086,0.199)	(0.002,0.049)	(-0.019,0.034)	(-0.002,0.003)
Mountain	-0.005	0.161***	-0.005	0.019	-0.002
	(-0.011,0.001)	(0.087,0.235)	(-0.031,0.020)	(-0.017,0.055)	(-0.005,0.001)
Pacific	0	0.173***	-0.004	-0.008	-0.003
ace/ethnicity	(-0.007,0.006)	(0.093,0.253)	(-0.032,0.024)	(-0.041,0.025)	(-0.005,0.000)
Jnknown/other	0.001	0.056**	0.002	0.009	0
/hite	(-0.002,0.004) ref.	(0.022,0.089) ref.	(-0.012,0.016) ref.	(-0.006,0.023) ref.	(-0.001,0.001)
Tille	rei.	rei.	rei.	rei.	ref.
lack	0.008***	0	0.003	0.01	0.001
	(0.006,0.011)	(-0.031,0.032)	(-0.010,0.016)	(-0.003,0.023)	(-0.000,0.002)
ispanic	-0.001	0.092***	0.016	0.035***	-0.001*
	(-0.004,0.001)	(0.054,0.130)	(-0.001,0.034)	(0.015,0.055)	(-0.003,-0.000)
sian	-0.007**	0.029	-0.018	0.018	-0.002
omorbidities	(-0.011,-0.002)	(-0.045,0.103)	(-0.042,0.007)	(-0.018,0.055)	(-0.004,0.000)
o diabetes					
abetes without CC					
Diabetes with CC					
Jncomp hypertension	ref.	ref.	ref.	ref.	ref.
comp hypertension	0.014***	-0.009	-0.009	-0.017	0.006**
Coronary artery disease	(0.007,0.021)	(-0.068,0.050)	(-0.032,0.013)	(-0.036,0.003)	(0.002,0.010)
ongestive heart failure					
Chronic pulmonary diseases					
Renal failure					
iver failure					
Metastatic cancer					
ymphoma					
Non-metastatic solid tumor					
Peripheral vascular disorders					
reliplieral vascular disorders					

Sensitivity analysis: Dropping people with comorbidities (other than hypertension)					
(11) Inpatient stay (95% confidence interval)				(15) Died same or following month (95% confidence interval)	
0.027*** (0.020,0.033) 200778 175494 <0.001 0.022	0.268*** (0.190,0.347) 7696 7647 0.033	0.027 (-0.003,0.058) 7696 7647 0.007	0.006 (-0.026,0.038) 7696 7647 0.023	0.006*** (0.003,0.009) 200508 175251 <0.001 0.015	
	0.027*** (0.020,0.033) 200778 175494 <0.001	(11) (12) Inpatient stay Inpatient stay with ICU/CCU (95% confidence interval) (95% confidence interval) 0.027*** 0.268*** (0.020,0.033) (0.190,0.347) 200778 7696 175494 7647 <0.001 0.022 0.033	(11) (12) (13) Inpatient stay Inpatient stay with ICU/CCU Inpatient stay with ARD dx (95% confidence interval) (95% confidence interval) (95% confidence interval) 0.027*** 0.268*** 0.027 (0.020,0.033) (0.190,0.347) (-0.003,0.058) 200778 7696 7696 175494 7647 7647 <0.001 0.022 0.033 0.007	(11) (12) (13) (14) Inpatient stay Inpatient stay with ICU/CCU Inpatient stay with ARD dx (95% confidence interval) 0.027*** 0.268*** 0.027 0.006 (0.020,0.033) (0.190,0.347) (-0.003,0.058) (-0.026,0.038) 200778 7696 7696 7696 7696 175494 7647 7647 7647 7647	

	Sensitivity analysis: limiting analysis to strict flu season (dropping summer months)						
	(16) Inpatient stay (95% confidence interval)	(17) Inpatient stay with ICU/CCU (95% confidence interval)	(18) Inpatient stay with ARD dx (95% confidence interval)	(19) Inpatient stay with ARDS dx (95% confidence interval)	(20) Died same or following month (95% confidence interval)		
Flu season / medication type	(93% confidence interval)	(93% confidence interval)	(93% confidence interval)	(93% confidence interval)	(93% confidence interval)		
2017-2018 flu season	ref.	ref.	ref.	ref.	ref.		
2018-2019 flu season	0 (-0.004,0.003)	0.009 (-0.002,0.019)	0.017*** (0.012,0.022)	-0.007*** (-0.010,-0.003)	0 (-0.002,0.002)		
2019-2020 flu season	0.003* (0.000,0.007)	0.030*** (0.020,0.041)	0.012,0.022) 0.017*** (0.011,0.022)	0.010*** (0.006,0.014)	0.017*** (0.015,0.020)		
Other medications only	ref.	ref.	ref.	ref.	ref.		
ACEi or ARB plus/minus other medications	-0.016*** (-0.019,-0.013)	-0.01 (-0.021,0.000)	-0.007** (-0.011,-0.002)	-0.003 (-0.006,0.001)	-0.009*** (-0.010,-0.007)		
ACEi or ARB monotherapy	(0.013, 0.013)	(0.021,0.000)	(0.011, 0.002)	(0.000,0.001)	(0.010, 0.007)		
2018-2019 season: ACEi or ARB +- other	0.002 (-0.002,0.006)	0.01 (-0.004,0.025)	0.001 (-0.006,0.008)	0 (-0.005,0.004)	0 (-0.003,0.002)		
2018-2019 season: ACEi or ARB monotherapy	(0.002,0.000)	(0.004,0.023)	(0.000,0.000)	(0.003,0.004)	(0.003,0.002)		
2019-2020 season: ACEi or ARB +/- other	0.008*** (0.004,0.012)	0.012 (-0.003,0.026)	0.008* (0.001,0.014)	0.008** (0.002,0.013)	-0.005*** (-0.008,-0.002)		
2019-2020 season: ACEi or ARB monotherapy	(0.004,0.012)	(-0.003,0.020)	(0.001,0.014)	(0.002,0.013)	(-0.008,-0.002)		
Demographics	-0.011***	-0.024***	0.001	0.001	0.000***		
Female	(-0.012,-0.009)	(-0.030,-0.017)	0.001 (-0.002,0.004)	-0.001 (-0.003,0.001)	-0.009*** (-0.010,-0.008)		
Age categories							
<35	0	-0.051	0.012	-0.014	-0.001		
35-44	(-0.006,0.006) -0.005**	(-0.111,0.009) -0.027	(-0.020,0.044) 0.005	(-0.035,0.006) -0.008	(-0.003,0.001) 0.001		
i5-44	(-0.009,-0.002)	(-0.063,0.009)	(-0.013,0.023)	(-0.022,0.006)	(-0.000,0.002)		
15-54	ref.	ref.	ref.	ref.	ref.		
55-64	0.009***	0.005	0	-0.002	0		
CF 74	(0.006,0.012)	(-0.014,0.023)	(-0.009,0.009)	(-0.009,0.005)	(-0.001,0.001)		
5-74	0.009*** (0.006,0.012)	-0.009 (-0.027,0.009)	-0.002 (-0.011,0.007)	-0.003 (-0.010,0.004)	0.006*** (0.005,0.008)		
'5-84	0.027***	-0.033***	-0.005	-0.007	0.022***		
3 04	(0.023,0.030)	(-0.051,-0.015)	(-0.013,0.004)	(-0.014,0.000)	(0.020,0.023)		
85+	0.049***	-0.078***	-0.012*	-0.015***	0.062***		
nsurance coverage type	(0.045,0.053)	(-0.097,-0.059)	(-0.021,-0.003)	(-0.022,-0.008)	(0.060,0.065)		
Medicare Advantage	ref.	ref.	ref.	ref.	ref.		
Commercial	-0.028***	0.006	0.002	0.004	0.001		
Census region	(-0.030,-0.025)	(-0.007,0.019)	(-0.005,0.008)	(-0.001,0.009)	(-0.000,0.002)		
Unknown/other	-0.035	0.219*	-0.003	0.016	-0.024*		
New England	(-0.071,0.000) ref.	(0.012,0.426) ref.	(-0.099,0.094) ref.	(-0.085,0.117) ref.	(-0.048,-0.000) ref.		
Mid Atlantic	0	0.018*	0.021***	0.022***	0.002		
	(-0.005,0.005) -0.012***	(0.002,0.035) 0.121***	(0.014,0.029) 0.014***	(0.015,0.028) -0.004	(-0.001,0.006) -0.019***		
South Atlantic							

		Sensitivity analysis: limiting analysis to strict flu season (dropping summer months)						
		(16)	(17)	(18)	(19)	(20)		
Eventhe 0,008*** 0,073*** 0,0004 0,008*** 0,012****		Inpatient stay	Inpatient stay with ICU/CCU	Inpatient stay with ARD dx	Inpatient stay with ARDS dx	Died same or following month		
Control Cont		(95% confidence interval)	(95% confidence interval)	(95% confidence interval)	(95% confidence interval)	(95% confidence interval)		
South Central 0.005	E North Central	0.008***	0.073***	0.004	-0.008**	-0.012***		
		(0.003,0.013)	(0.058,0.089)	(-0.003,0.011)	(-0.013,-0.002)	(-0.015,-0.009)		
N North Central 0.003*** 0.003 -0.004 -0.012*** W South Central 0.002 0.007*** 0.016*** -0.004** 0.001*** Mountain -0.004*** 0.018*** -0.009** -0.001*** -0.001*** Pacific -0.040*** 0.011**** -0.009 -0.006 -0.021*** Pacific -0.046** 0.019*** -0.009 -0.006 -0.021*** Pacific -0.008** 0.138*** -0.009 -0.006 -0.012*** Race/ethnicty -0.008** 0.138*** -0.006 -0.012*** -0.012** -0.006*** -0.012*** Mine -0.000**** -0.012*** -0.013** -0.001*** -0.012*** -0.012*** -0.001*** -0.012*** -0.012*** -0.012*** -0.012*** -0.012*** -0.012*** -0.012*** -0.012*** -0.012*** -0.012*** -0.012*** -0.002*** -0.002*** -0.002*** -0.002*** -0.002*** -0.002*** -0.002*** -0.002*** -0.002*** -0.002*** <th>E South Central</th> <th>-0.006*</th> <th>0.069***</th> <th>0.015***</th> <th>-0.010**</th> <th>-0.014***</th>	E South Central	-0.006*	0.069***	0.015***	-0.010**	-0.014***		
		(-0.011,-0.001)	(0.051,0.087)	(0.007, 0.023)	(-0.016,-0.004)	(-0.017,-0.010)		
W bott central -0.002 0.001*** 0.016*** -0.008** -0.017** Mountain -0.040*** 0.115*** -0.009 -0.006 -0.020** Pacific -0.046*** 0.115*** -0.009 -0.006 -0.020** Pacific -0.008** 0.188*** -0.005 -0.016 -0.017** Pacific -0.009** 0.188*** -0.005 -0.006 -0.017** Reac/ethnicity (-0.01, 0.001) (-0.01, 0.002) (-0.01, 0.002) (-0.01, 0.002) (-0.01, 0.002) White ref. ref	W North Central	0.013***	0.091***	0.003	-0.004	-0.012***		
		(0.008,0.018)	(0.074,0.109)	(-0.005,0.011)	(-0.010,0.002)	(-0.015,-0.009)		
Nountrin	W South Central	-0.002	0.100***	0.016***	-0.008**	-0.017***		
				(0.008,0.024)	(-0.014,-0.003)			
Pacific 0.008* 0.180** 0.008* 0.008* 0.0017*** 0.0017*** 0.0018** 0.00	Mountain	-0.040***	0.115***	-0.009	-0.006	-0.020***		
Race/Hmicity C.0034, 0.001 C.006, 0.015 C.0014, 0.002 C.0021, 0.013 C.006, 0.005 C.0014, 0.002 C.0015, 0.003 C.0014, 0.002 C.0015, 0.003 C.0014, 0.003		, , ,	, , ,	, , ,	, , ,			
Compone Comp	Pacific	-0.008*	0.180***	0.005	-0.006	-0.017***		
White (-0.01,0.005) (0.003,0.023) (-0.002,0.009) (-0.01,0.009) (-0.01,0.009) Black 0.011*** -0.012** 0.005* 0.010*** 0.004*** Hispanic (-0.015*** 0.010*** 0.000** 0.007*,0.14) (0.002,0.005) Asian (-0.018**,0.013) (0.668,0.090) (0.040,0.015) (0.003,0.011) (-0.101-0.007) Asian (-0.018**,0.013) (0.668,0.090) (0.040,0.015) (0.003,0.011) (-0.007) Asian (-0.016**,0.005) (-0.017,0.027) (-0.009,0.012) (-0.002,0.015) (-0.002,0.007) No diabetes (**e**) ref. r						(-0.021,-0.013)		
White ref. ref. ref. ref. ref. Black 0.011*** -0.012** 0.005** 0.010*** 0.004*** Hispanic 0.015*** 0.079*** 0.010*** 0.007** -0.008*** Asian -0.011*** 0.005 0.002 0.006 -0.002 Comorbidities -0.011*** 0.005 0.002 0.006 -0.002 No diabetes ref. <	Unknown/other							
Black				(-0.002,0.009)	(0.001,0.009)	(-0.001,0.002)		
	White	ref.	ref.	ref.	ref.	ref.		
Hispanic	Black	0.011***	-0.012**	0.005*	0.010***	0.004***		
Control Cont		` ' '		, , ,	, , ,	, , ,		
Asian	Hispanic							
Composition No diabetes (-0.016, -0.005) ref. (-0.017, 0.027) ref. (-0.009, 0.012) ref. (-0.002, 0.015) ref. (-0.002, 0.003) ref. (-0.000, 0.009) ref. (-0.002, 0.003) ref. (-0.003, 0.004) ref. (-0.0					, , ,			
No diabetes ref. 0.003								
Diabetes without CC 0.006*** 0.012* 0.004 0.003 0.004**** Diabetes with CC (0.004,0.009) (0.003,0.002) (-0.000,0.009) (-0.001,0.006) (0.003,0.005) Uncomp hypertension ref.								
Diabetes with CC (0.004,0.009) (0.003,0.022) (-0.000,0.009) (-0.001,0.066) (0.003,0.005) (0.007***) (0.004,0.028) (-0.001,0.013) (-0.006,0.001) (-0.002,0.003) (0.006,0.008) Uncomp hypertension ref. 0.001 0.0061 0.0061 <th< th=""><th>No diabetes</th><th>ref.</th><th>ref.</th><th>ref.</th><th>ref.</th><th>ref.</th></th<>	No diabetes	ref.	ref.	ref.	ref.	ref.		
Diabetes with CC (0.004,0.009) (0.003,0.022) (-0.000,0.009) (-0.001,0.066) (0.003,0.005) (0.007***) (0.004,0.028) (-0.001,0.013) (-0.006,0.001) (-0.002,0.003) (0.006,0.008) Uncomp hypertension ref. 0.001 0.0061 0.0061 <th< th=""><th>Diahetes without CC</th><td>0.006***</td><td>0.012*</td><td>0.004</td><td>0.003</td><td>0.004***</td></th<>	Diahetes without CC	0.006***	0.012*	0.004	0.003	0.004***		
Diabetes with CC	blubetes without ee							
Uncomp hypertension (0.024,0.028) ref. (-0.001,0.013) ref. (-0.006,0.001) ref. (-0.002,0.003) ref. (0.006,0.008) ref. Comp hypertension 0.023**** -0.009* -0.004 0 -0.001 Coronary artery disease 0.018*** 0.031*** 0 -0.001 0.006*** Congestive heart failure 0.101*** 0.078*** 0.018*** 0.004,0007) 0.031*** 0.003,0004 (-0.003,0001) (0.004,0007) Chronic pulmonary diseases 0.074*** 0.078*** 0.015*** -0.005** 0 0 0.033*** 0 0 0.004*** 0.038*** 0 0 0.004*** 0.038*** 0 0 0.004*** 0.038*** 0 0 0.004*** 0.038*** 0 0 0.004*** 0.038*** 0	Diabetes with CC							
Uncomp hypertension ref. 0004*** 0.001 0.001 0.001 0.003,0001) (-0.003,0003) (-0.003,0003) (-0.003,0001) (0.004,0007) 0.003,0004 (-0.003,0001) (0.004,0007) 0.001 0.003,0004 (-0.003,0001) 0.003,0004 0.003,0004 0.004**********************************	State test with de							
Coronary artery disease (0.020,0.026) (-0.018,-0.000) (-0.008,0.000) (-0.003,0.003) (-0.003,0.001) Coronary artery disease (0.016,0.020) (0.025,0.038) (-0.003,0.004) (-0.003,0.001) (0.004,0.007) Congestive heart failure (0.101*** (0.078*** (0.018*** (0.004,0.007) (0.037,0.040) Chronic pulmonary diseases (0.072,0.076) (-0.010** (0.015,0.022) (0.002,0.007) (0.037,0.040) Renal failure (0.072,0.076) (-0.016,0.004) (0.012,0.018) (-0.007,-0.002) (-0.001,0.01) Liver failure (0.016,0.022) (0.004,0.020) (-0.004,0.004) (-0.007,-0.002) (-0.001,0.001) Liver failure (0.016,0.022) (0.004,0.020) (-0.004,0.004) (-0.002,0.004) (0.021,0.025) Liver failure (0.016,0.022) (0.004,0.020) (-0.004,0.004) (-0.002,0.004) (0.021,0.025) Liver failure (0.034,0.022) (0.004,0.004) (-0.001,0.004) (0.001,0.004) (0.021,0.025) Liver failure (0.018,0.002) (0.004,0.004) (-0.001,0.004) (-0.00	Uncomp hypertension	, , ,						
Coronary artery disease (0.020,0.026) (-0.018,-0.000) (-0.008,0.000) (-0.003,0.003) (-0.003,0.001) Coronary artery disease (0.016,0.020) (0.025,0.038) (-0.003,0.004) (-0.003,0.001) (0.004,0.007) Congestive heart failure (0.101*** (0.078*** (0.018*** (0.004,0.007) (0.037,0.040) Chronic pulmonary diseases (0.072,0.076) (-0.010** (0.015,0.022) (0.002,0.007) (0.037,0.040) Renal failure (0.072,0.076) (-0.016,0.004) (0.012,0.018) (-0.007,-0.002) (-0.001,0.01) Liver failure (0.016,0.022) (0.004,0.020) (-0.004,0.004) (-0.007,-0.002) (-0.001,0.001) Liver failure (0.016,0.022) (0.004,0.020) (-0.004,0.004) (-0.002,0.004) (0.021,0.025) Liver failure (0.016,0.022) (0.004,0.020) (-0.004,0.004) (-0.002,0.004) (0.021,0.025) Liver failure (0.034,0.022) (0.004,0.004) (-0.001,0.004) (0.001,0.004) (0.021,0.025) Liver failure (0.018,0.002) (0.004,0.004) (-0.001,0.004) (-0.00								
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· (-0.004,0.002) (0.008,0.024) (0.001,0.009) (0.001,0.007) (0.021,0.025)	Desireheard conserving dispudent							
	Peripheral vascular disorders							
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	Carulac arrnythmias	0.063***	0.065***	0.005**	-0.001	0.023***		

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	Sensitivity analysis: limiting analysis to strict flu season (dropping summer months)				
	(16)	(17)	(18)	(19)	(20)
	Inpatient stay	Inpatient stay with ICU/CCU	Inpatient stay with ARD dx	Inpatient stay with ARDS dx	Died same or following month
	(95% confidence interval)	(95% confidence interval)	(95% confidence interval)	(95% confidence interval)	(95% confidence interval)
	(0.061,0.066)	(0.058,0.071)	(0.002,0.008)	(-0.003,0.002)	(0.021,0.025)
Rheumatoid arthritis/collagen vascular diseases	0.015***	-0.013	-0.008*	-0.001	0.002
	(0.010,0.019)	(-0.026,0.001)	(-0.014,-0.002)	(-0.005,0.004)	(-0.000,0.005)
Coagulopathy	0.035***	0.032***	-0.002	0.001	0.039***
	(0.030,0.041)	(0.021,0.043)	(-0.008,0.003)	(-0.004,0.005)	(0.035,0.043)
Obesity	-0.002	0.016***	0.004	0.008***	-0.008***
	(-0.005,0.000)	(0.007,0.026)	(-0.001,0.009)	(0.005,0.012)	(-0.010,-0.006)
Chronic/acute deep vein thrombosis or pulmonary embolism	0.053***	0.052***	0.005	0.002	0.026***
	(0.046,0.061)	(0.038,0.066)	(-0.003,0.012)	(-0.004,0.007)	(0.021,0.031)
Hemorrhagic or ischemic stroke	0.018***	0.030***	0.005	-0.003	0.044***
	(0.014,0.022)	(0.020,0.040)	(-0.000,0.010)	(-0.007,0.000)	(0.041,0.047)
Valvular disease	-0.008***	0.053***	0.008***	-0.001	0.016***
	(-0.012,-0.005)	(0.044,0.061)	(0.003,0.012)	(-0.004,0.003)	(0.014,0.019)
Constant	0.057***	0.314***	0.022***	0.037***	0.013***
	(0.051,0.063)	(0.290,0.338)	(0.010,0.033)	(0.028,0.046)	(0.010,0.017)
N	738240	106917	106917	106917	737059
N_clust	556579	97383	97383	97383	555729
p	<0.001	<0.001	<0.001	<0.001	<0.001
R-squared	0.094	0.039	0.007	0.008	0.082
				0.008	

	Primary analysis						
_	(1)	(2)	(3)	(4)	(5)		
	Inpatient stay	Inpatient stay with ICU/CCU	Inpatient stay with ARD dx	Inpatient stay with ARDS dx	Died same or following month		
Key coefficient estimates Season							
2017-2018 flu season	ref.	ref.	ref.	ref.	ref.		
2018-2019 flu season	-0.001	0.008	0.013***	-0.007***	0.000		
2019-2020 flu season	(-0.004,0.002) 0.018***	(-0.002,0.018) 0.035***	(0.008,0.017) 0.013***	(-0.010,-0.004) 0.013***	(-0.002,0.002) 0.016***		
HTN medication group	(0.015,0.021)	(0.026,0.044)	(0.008,0.017)	(0.009,0.016)	(0.014,0.017)		
Other medications only	ref.	ref.	ref.	ref.	ref.		
ACEi or ARB plus/minus other medications	-0.019***	-0.009	-0.007**	-0.003	-0.009***		
ACEi or ARB monotherapy	(-0.022,-0.016) N/A	(-0.019,0.001) N/A	(-0.011,-0.002) N/A	(-0.007,0.000) N/A	(-0.011,-0.008) N/A		
Season/medication interactions							
2018-2019 season: ACEi or ARB +- other	0.004* (0.001,0.008)	0.01 (-0.004,0.023)	0.004 (-0.003,0.010)	0 (-0.004,0.004)	0 (-0.002,0.002)		
2018-2019 season: ACEi or ARB monotherapy	N/A	N/A	N/A	N/A	N/A		
2019-2020 season: ACEi or ARB +/- other	0.015*** (0.012,0.019)	0.015* (0.003,0.027)	0.007* (0.001,0.012)	0.009*** (0.004,0.013)	-0.002 (-0.004,0.001)		
2019-2020 season: ACEi or ARB monotherapy Note: p-value for coefficients is for the null hypothe	N/A	N/A	N/A	N/A	N/A		
Marginal effects/predicted probability							
Other hypertension medications only							
2017/18	0.179	0.482	0.053	0.030	0.064		
2012/12	(0.177,0.181)	(0.474,0.489)	(0.050,0.056)	(0.028,0.033)	(0.062,0.065)		
2018/19	0.178	0.490	0.066	0.023	0.064		
2010/20	(0.176,0.180) 0.196	(0.483,0.496)	(0.062,0.069) 0.066	(0.021,0.025) 0.043	(0.063,0.065) 0.080		
2019/20	(0.195,0.198)	0.516 (0.511,0.521)	(0.063,0.068)	(0.041,0.045)	(0.078,0.081)		
	(0.133,0.130)	(0.311,0.321)	(0.003,0.000)	(0.041,0.043)	(0.070,0.001)		

Primary analysis

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	(1)	(2)	(3)	(4)	(5)
		Inpatient stay with	Inpatient stay with ARD	Inpatient stay with ARDS	Died same or following
	Inpatient stay	ICU/CCU	dx	dx	month
ACEi or ARB plus/minus other medications					
2017/18	0.125	0.463	0.045	0.029	0.035
	(0.124,0.127)	(0.456,0.470)	(0.042,0.048)	(0.027, 0.031)	(0.034,0.035)
2018/19	0.128	0.481	0.061	0.021	0.034
	(0.127,0.130)	(0.475,0.487)	(0.058,0.064)	(0.020,0.023)	(0.034,0.035)
2019/20	0.158	0.512	0.064	0.050	0.049
	(0.157,0.160)	(0.508, 0.517)	(0.062,0.066)	(0.048,0.052)	(0.048,0.049)
ACEi or ARB monotherapy					
2017/18	N/A	N/A	N/A	N/A	N/A
2018/19	N/A	N/A	N/A	N/A	N/A
2019/20	N/A	N/A	N/A	N/A	N/A
Risk ratios of marginal effects					
Other hypertension medications only					
2018/19 season vs. 2017/18	0.994	1.017	1.236***	0.759***	0.999
	(0.977,1.011)	(0.996, 1.038)	(1.136,1.337)	(0.668,0.850)	(0.969,1.030)
2019/20 season vs. 2017/18	1.099***	1.072***	1.238***	1.414***	1.244***
	(1.081,1.116)	(1.053,1.092)	(1.147,1.330)	(1.278,1.550)	(1.210,1.278)
ACEi or ARB plus/minus other medications					
2018/19 season vs. 2017/18	1.025**	1.039***	1.360***	0.739***	0.993
	(1.009, 1.042)	(1.019,1.058)	(1.251,1.469)	(0.656, 0.822)	(0.961,1.025)
2019/20 season vs. 2017/18	1.264***	1.107***	1.437***	1.731***	1.404***
	(1.245,1.282)	(1.088,1.126)	(1.332,1.542)	(1.580, 1.882)	(1.363,1.444)
ACEi or ARB monotherapy					
2018/19 season vs. 2017/18	N/A	N/A	N/A	N/A	N/A
2019/20 season vs. 2017/18	N/A	N/A	N/A	N/A	N/A
Number of episodes	1,059,474	167,330	167,330	167,330	1,057,707
Number of people	728,455	147,846	147,846	147,846	727,311
Note: p-value for risk ratios is for the null hypoth	esis that the risk ratio = 1				

N/A: variable not included in model

^{*} p<0.05, ** p<0.01, *** p<0.001

	Sensitivity analysis: ACEi/ARB monotherapy					
	(6)	(7)	(8)	(9)	(10)	
	Inpatient stay	Inpatient stay with ICU/CCU	Inpatient stay with ARD dx	Inpatient stay with ARDS dx	Died same or following month	
Key coefficient estimates						
Season						
2017-2018 flu season	ref.	ref.	ref.	ref.	ref.	
2018-2019 flu season	-0.001	0.008	0.013***	-0.007***	0	
	(-0.004,0.002)	(-0.002,0.018)	(0.008, 0.017)	(-0.010,-0.004)	(-0.002,0.002)	
2019-2020 flu season	0.018***	0.035***	0.013***	0.013***	0.016***	
	(0.015, 0.021)	(0.026, 0.044)	(0.008, 0.017)	(0.009, 0.016)	(0.014, 0.017)	
HTN medication group		, , ,	, , ,	, , ,	, , ,	
Other medications only	ref.	ref.	ref.	ref.	ref.	
ACEi or ARB plus/minus other medications	-0.020***	-0.004	-0.007**	-0.002	-0.010***	
Action And prosymmos other medications	(-0.023,-0.017)	(-0.014,0.006)	(-0.011,-0.002)	(-0.006,0.001)	(-0.012,-0.009)	
ACEi or ARB monotherapy	-0.016***	-0.039***	-0.007	-0.009**	-0.004***	
ACLI OF AND MONOTHERAPY	(-0.020,-0.012)	(-0.057,-0.020)	(-0.015,0.001)	(-0.015,-0.003)	(-0.006,-0.002)	
Season/medication interactions	(0.020) 0.022)	(0.007) 0.020)	(0.015)0.001)	(0.025) 0.005)	(0.000) 0.002)	
2018-2019 season: ACEi or ARB + other	0.004*	0.004	0.004	-0.001	-0.001	
2020 2023 30000	(0.000,0.008)	(-0.009,0.018)	(-0.003,0.010)	(-0.005,0.004)	(-0.003,0.002)	
2018-2019 season: ACEi or ARB monotherapy	0.005	0.040**	0.002	0.002	0.001	
2020 2023 30000 m / O21 01 / m 2 m o m o m o m o p y	(-0.001,0.010)	(0.015,0.065)	(-0.009,0.013)	(-0.006,0.009)	(-0.002,0.004)	
2019-2020 season: ACEi or ARB +/- other	0.015***	0.011	0.007*	0.008***	-0.001	
2020 2020 30000	(0.011,0.019)	(-0.001,0.024)	(0.002,0.013)	(0.003,0.013)	(-0.004,0.001)	
2019-2020 season: ACEi or ARB monotherapy	0.017***	0.035**	0.004	0.012**	-0.003*	
Note: p-value for coefficients is for the null hypotl	(0.012,0.022)	(0.013,0.057)	(-0.006,0.013)	(0.004,0.020)	(-0.006,-0.000)	
Marginal effects/predicted probability						
Other hypertension medications only						
2017/18	0.179	0.481	0.053	0.030	0.064	
	(0.177,0.181)	(0.474,0.489)	(0.050,0.056)	(0.028,0.033)	(0.062,0.065)	
2018/19	0.178	0.490	0.066	0.023	0.064	
,	(0.176,0.180)	(0.483,0.496)	(0.062,0.069)	(0.021,0.025)	(0.063,0.065)	
2019/20	0.196	0.516	0.066	0.043	0.079	
, -	(0.195,0.198)	(0.511,0.521)	(0.063,0.068)	(0.041,0.045)	(0.078,0.081)	

(6)

Sensitivity analysis: ACEi/ARB monotherapy

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N/A: variable not included in model * p<0.05, ** p<0.01, *** p<0.001

					, ,
		Inpatient stay with	Inpatient stay with ARD	Inpatient stay with ARDS	Died same or following
	Inpatient stay	ICU/CCU	dx	dx	month
ACEi or ARB plus/minus other medications	inputient stay	100/000	un.	ux	month
2017/18	0.133	0.473	0.046	0.030	0.037
2017/10	(0.132,0.135)	(0.466,0.480)	(0.043,0.049)	(0.027,0.032)	(0.036,0.038)
2018/19	0.136	0.486	0.062	0.022	0.037
2010/13	(0.135,0.138)	(0.479,0.492)	(0.059,0.065)	(0.020,0.024)	(0.036,0.038)
2019/20	0.166	0.519	0.066	0.050	0.052
2013/20	(0.164,0.167)	(0.514,0.524)	(0.063,0.068)	(0.048,0.052)	(0.051,0.053)
	(0.104,0.107)	(0.314,0.324)	(0.003,0.008)	(0.048,0.032)	(0.031,0.033)
ACEi or ARB monotherapy					
2017/18	0.093	0.408	0.040	0.024	0.024
	(0.090,0.096)	(0.392,0.425)	(0.033,0.047)	(0.019,0.029)	(0.022,0.025)
2018/19	0.096	0.456	0.054	0.018	0.025
2020,25	(0.094,0.099)	(0.441,0.472)	(0.047,0.061)	(0.014,0.022)	(0.023,0.026)
2019/20	0.127	0.478	0.056	0.048	0.036
2023,20	(0.125,0.130)	(0.467,0.489)	(0.051,0.061)	(0.043,0.053)	(0.034,0.037)
isk ratios of marginal effects	(0.123,0.130)	(0.107,0.103)	(0.031,0.001)	(0.013,0.033)	(0.031,0.037)
ther hypertension medications only					
2018/19 season vs. 2017/18	0.994	1.017	1.236***	0.759***	0.999
2010,10 0000011 10. 2017,10	(0.977,1.011)	(0.996,1.038)	(1.136,1.337)	(0.668,0.850)	(0.969,1.030)
2019/20 season vs. 2017/18	1.098***	1.072***	1.238***	1.414***	1.243***
2013/20 3003011 V3. 2017/10	(1.081,1.116)	(1.053,1.092)	(1.147,1.330)	(1.278,1.550)	(1.209,1.278)
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CEi or ARB plus/minus other medications					
2018/19 season vs. 2017/18	1.023*	1.027*	1.360***	0.735***	0.985
	(1.005,1.041)	(1.006, 1.048)	(1.243,1.476)	(0.647,0.824)	(0.950,1.019)
2019/20 season vs. 2017/18	1.244***	1.097***	1.441***	1.690***	1.382***
	(1.225,1.264)	(1.077,1.118)	(1.329,1.554)	(1.532,1.848)	(1.339,1.425)
CEi or ARB monotherapy					
2018/19 season vs. 2017/18	1.037	1.117***	1.358*	0.766	1.047
·	(0.993,1.080)	(1.058,1.177)	(1.055, 1.660)	(0.526,1.006)	(0.958,1.136)
2019/20 season vs. 2017/18	1.369***	1.170***	1.412**	2.028***	1.526***
•	(1.318,1.420)	(1.115,1.226)	(1.129,1.694)	(1.537,2.519)	(1.412,1.640)
lumber of episodes	1,059,474	167,330	167,330	167,330	1,057,707
lumber of people	728,455	147,846	147,846	147,846	727,311
lote: p-value for risk ratios is for the null hypothe	, 20, 155	11,040	117,040	117,540	, _,,511

	Sensitivity analysis: Dropping people with comorbidities (other than hypertension)					
_	(11)	(12)	(13)	(14)	(15)	
	Inpatient stay	Inpatient stay with ICU/CCU	Inpatient stay with ARD dx	Inpatient stay with ARDS dx	Died same or following month	
Key coefficient estimates						
Season 2017-2018 flu season	ref.	ref.	ref.	ref.	ref.	
2018-2019 flu season	0.002 (-0.001,0.006)	0.02 (-0.032,0.072)	0.030** (0.009,0.051)	0.006 (-0.005,0.017)	0 (-0.002,0.002)	
2019-2020 flu season	0.032*** (0.028,0.035)	0.068**	0.029***	0.052***	0.007***	
HTN medication group	(0.028,0.033)	(0.024,0.111)	(0.014,0.045)	(0.039,0.065)	(0.005,0.009)	
Other medications only	ref.	ref.	ref.	ref.	ref.	
ACEi or ARB plus/minus other medications	-0.006*** (-0.009,-0.003)	-0.001 (-0.049,0.046)	0.009 (-0.008,0.026)	0.003 (-0.007,0.013)	-0.003*** (-0.004,-0.001)	
ACEi or ARB monotherapy	(-0.009,-0.003) N/A	(-0.049,0.046) N/A	(-0.008,0.028) N/A	(-0.007,0.013) N/A	(-0.004,-0.001) N/A	
Season/medication interactions						
2018-2019 season: ACEi or ARB +- other	-0.003 (-0.007,0.001)	0.004 (-0.062,0.071)	-0.013 (-0.041,0.014)	0.001 (-0.015,0.017)	0.001 (-0.001,0.003)	
2018-2019 season: ACEi or ARB monotherapy	N/A	N/A	N/A	N/A	N/A	
2019-2020 season: ACEi or ARB +/- other	-0.001 (-0.006,0.003)	0.05 (-0.006,0.106)	-0.022* (-0.043,-0.001)	-0.001 (-0.019,0.016)	-0.001 (-0.003,0.001)	
2019-2020 season: ACEi or ARB monotherapy Note: p-value for coefficients is for the null hypotl	N/A	N/A	N/A	N/A	N/A	
Marginal effects/predicted probability						
Other hypertension medications only						
2017/18	0.031	0.312	0.023	0.009	0.007	
2018/19	(0.029,0.034) 0.033	(0.275,0.350) 0.332	(0.011,0.035) 0.053	(0.002,0.016) 0.015	(0.006,0.009) 0.007	
2010/13	(0.031,0.036)	(0.296,0.368)	(0.036,0.070)	(0.006,0.024)	(0.006,0.008)	
2019/20	0.063	0.380	0.053	0.061	0.014	
2013/20	0.005	0.500	0.055	0.001	0.014	

Sensitivity analysis: Dropping people with comorbidities (other than hypertension)

	(11)	(12)	(13)	(14)	(15)
		Inpatient stay with	Inpatient stay with ARD	Inpatient stay with ARDS	Died same or following
	Inpatient stay	ICU/CCU	dx	dx	month
ACEi or ARB plus/minus other medications					
2017/18	0.023	0.319	0.033	0.016	0.004
	(0.022,0.025)	(0.289,0.349)	(0.021,0.044)	(0.008, 0.023)	(0.003,0.004)
2018/19	0.022	0.343	0.049	0.023	0.004
	(0.021,0.024)	(0.313,0.373)	(0.036,0.063)	(0.014,0.032)	(0.004,0.005)
2019/20	0.054	0.436	0.040	0.067	0.010
	(0.052,0.055)	(0.418,0.454)	(0.033,0.048)	(0.058,0.076)	(0.009,0.011)
ACEi or ARB monotherapy					
2017/18	N/A	N/A	N/A	N/A	N/A
2018/19	N/A	N/A	N/A	N/A	N/A
2019/20	N/A	N/A	N/A	N/A	N/A
Risk ratios of marginal effects					
Other hypertension medications only					
2018/19 season vs. 2017/18	1.069	1.064	2.291	1.633	0.973
•	(0.953,1.186)	(0.893,1.235)	(0.893,3.688)	(0.078,3.189)	(0.744,1.203)
2019/20 season vs. 2017/18	2.008***	1.216**	2.270*	6.718*	1.942***
	(1.823,2.193)	(1.053,1.379)	(1.013,3.526)	(1.473,11.963)	(1.561,2.323)
ACEi or ARB plus/minus other medications					
2018/19 season vs. 2017/18	0.961	1.076	1.510	1.432	1.128
·	(0.875,1.047)	(0.939,1.213)	(0.842,2.177)	(0.544,2.320)	(0.879,1.377)
2019/20 season vs. 2017/18	2.291***	1.369***	1.234	4.210**	2.624***
•	(2.124,2.458)	(1.228,1.509)	(0.754,1.713)	(2.113,6.308)	(2.142,3.107)
ACEi or ARB monotherapy	(, ==-,	(-,,	(/		(, /
2018/19 season vs. 2017/18	N/A	N/A	N/A	N/A	N/A
2019/20 season vs. 2017/18	N/A	N/A	N/A	N/A	N/A
Number of episodes	200,778	7,696	7,696	7,696	200,508
Number of people	175,494	7,647	7,647	7,647	175,251
Note: p-value for risk ratios is for the null hypothe	, -	,-	,-	,-	-, -
N/A: variable not included in model					
* p<0.05, ** p<0.01, *** p<0.001					

	Sensitivity	y analysis: limiting an	alysis to strict flu seas	son (dropping summe	r months)
	(16)	(17)	(18)	(19)	(20)
	Inpatient stay	Inpatient stay with ICU/CCU	Inpatient stay with ARD dx	Inpatient stay with ARDS dx	Died same or following month
Key coefficient estimates Season					
2017-2018 flu season	ref.	ref.	ref.	ref.	ref.
2018-2019 flu season	0 (-0.004,0.003)	0.009 (-0.002,0.019)	0.017*** (0.012,0.022)	-0.007*** (-0.010,-0.003)	0 (-0.002,0.002)
2019-2020 flu season	0.003*	0.030***	0.017***	0.010***	0.017***
HTN medication group	(0.000,0.007)	(0.020,0.041)	(0.011,0.022)	(0.006,0.014)	(0.015,0.020)
Other medications only	ref.	ref.	ref.	ref.	ref.
ACEi or ARB plus/minus other medications	-0.016***	-0.01	-0.007**	-0.003	-0.009***
ACEi or ARB monotherapy	(-0.019,-0.013) N/A	(-0.021,0.000) N/A	(-0.011,-0.002) N/A	(-0.006,0.001) N/A	(-0.010,-0.007) N/A
Season/medication interactions					
2018-2019 season: ACEi or ARB +- other	0.002 (-0.002,0.006)	0.01 (-0.004,0.025)	0.001 (-0.006,0.008)	0 (-0.005,0.004)	0 (-0.003,0.002)
2018-2019 season: ACEi or ARB monotherapy	N/A	N/A	N/A	N/A	N/A
2019-2020 season: ACEi or ARB +/- other	0.008*** (0.004,0.012)	0.012 (-0.003,0.026)	0.008*	0.008** (0.002,0.013)	-0.005*** (-0.008,-0.002)
2019-2020 season: ACEi or ARB monotherapy Note: p-value for coefficients is for the null hypotl	N/A	N/A	N/A	N/A	N/A
Marginal effects/predicted probability Other hypertension medications only					
2017/18	0.175	0.480	0.053	0.030	0.061
	(0.173,0.178)	(0.472,0.487)	(0.049,0.056)	(0.028, 0.033)	(0.060,0.063)
2018/19	0.175	0.488	0.070	0.024	0.061
	(0.172,0.177)	(0.480,0.496)	(0.066,0.074)	(0.021,0.026)	(0.060,0.063)
2019/20	0.179	0.510	0.069	0.041	0.079
	(0.176,0.181)	(0.503,0.517)	(0.066,0.073)	(0.038,0.044)	(0.077,0.080)

Sensitivity analysis: limiting analysis to strict flu season (dropping summer months)

Inpatient stay with ARD Inpatient stay with art Inpatient stay with ARD Inpatient stay with art Inpatient stay w	month 0.033 (0.032,0.033) 0.032 (0.032,0.033)
ACEI or ARB plus/minus other medications 2017/18	0.033 (0.032,0.033) 0.032 (0.032,0.033)
2017/18 0.122 0.459 0.044 0.028 2018/19 0.124 0.452,0.466) (0.041,0.047) (0.026,0.031) 2018/19 0.124 0.478 0.063 0.021 2019/20 0.133 0.501 0.069 0.046 2019/20 0.133 0.501 0.069 0.046 2017/18 N/A N/A N/A N/A N/A 2018/19 N/A N/A N/A N/A N/A N/A 2019/20 N/A N/A N/A N/A N/A N/A N/A 2018/19 N/A N/A N/A N/A N/A N/A N/A Risk ratios of marginal effects Other hypertension medications only 1.018 1.324**** 0.776**** 2018/19 season vs. 2017/18 0.998 1.018 1.324**** 0.776**** 2019/20 season vs. 2017/18 1.019 1.064**** 1.313*** 1.343**** 2018/19 season vs. 2017/18 1.017	(0.032,0.033) 0.032 (0.032,0.033)
10.120, 0.123	(0.032,0.033) 0.032 (0.032,0.033)
2018/19	0.032 (0.032,0.033)
2019/20	(0.032,0.033)
2019/20	
ACEi or ARB monotherapy 2017/18 N/A N/A N/A N/A N/A N/A N/A N/	
2017/18 N/A N/A N/A N/A N/A N/A 2018/19 N/A N/A N/A N/A N/A N/A 2019/20 N/A N/A N/A N/A N/A N/A Risk ratios of marginal effects Other hypertension medications only 2018/19 season vs. 2017/18 0.998 1.018 1.324*** 0.776*** (0.979,1.017) (0.995,1.041) (1.208,1.440) (0.673,0.879) 2019/20 season vs. 2017/18 1.019 1.064*** 1.313*** 1.343*** (1.000,1.039) (1.041,1.087) (1.201,1.425) (1.190,1.495) ACEi or ARB plus/minus other medications 2018/19 season vs. 2017/18 1.017 1.041*** 1.411*** 0.750*** 2019/20 season vs. 2017/18 1.091*** 1.092*** 1.542*** 1.634*** (0.999,1.035) (1.019,1.063) (1.289,1.533) (0.655,0.846) 2019/20 season vs. 2017/18 1.091*** 1.092*** 1.542*** 1.634*** (1.071,1.110) (1.069,1.114) (1.413,1.671) (1.465,1.803)	0.045 (0.044,0.046)
2017/18 N/A N/A N/A N/A N/A N/A 2018/19 N/A N/A N/A N/A N/A N/A 2019/20 N/A N/A N/A N/A N/A N/A Risk ratios of marginal effects Other hypertension medications only 2018/19 season vs. 2017/18 0.998 1.018 1.324*** 0.776*** (0.979,1.017) (0.995,1.041) (1.208,1.440) (0.673,0.879) 2019/20 season vs. 2017/18 1.019 1.064*** 1.313*** 1.343*** (1.000,1.039) (1.041,1.087) (1.201,1.425) (1.190,1.495) ACEi or ARB plus/minus other medications 2018/19 season vs. 2017/18 1.017 1.041*** 1.411*** 0.750*** 2019/20 season vs. 2017/18 1.091*** 1.092*** 1.542*** 1.634*** (0.999,1.035) (1.019,1.063) (1.289,1.533) (0.655,0.846) 2019/20 season vs. 2017/18 1.091*** 1.092*** 1.542*** 1.634*** (1.071,1.110) (1.069,1.114) (1.413,1.671) (1.465,1.803)	
2019/20 N/A N/A N/A N/A N/A N/A Risk ratios of marginal effects Other hypertension medications only 2018/19 season vs. 2017/18 0.998 1.018 1.324*** 0.776*** (0.979,1.017) (0.995,1.041) (1.208,1.440) (0.673,0.879) 2019/20 season vs. 2017/18 1.019 1.064*** 1.313*** 1.343*** (1.000,1.039) (1.041,1.087) (1.201,1.425) (1.190,1.495) ACEi or ARB plus/minus other medications 2018/19 season vs. 2017/18 1.017 1.041*** 1.411*** 0.750*** (0.999,1.035) (1.019,1.063) (1.289,1.533) (0.655,0.846) 2019/20 season vs. 2017/18 1.091*** 1.092*** 1.542*** 1.634*** (1.071,1.110) (1.069,1.114) (1.413,1.671) (1.465,1.803) ACEi or ARB monotherapy	N/A
Risk ratios of marginal effects Other hypertension medications only 2018/19 season vs. 2017/18 0.998 1.018 1.324*** 0.776*** (0.979,1.017) (0.995,1.041) (1.208,1.440) (0.673,0.879) 2019/20 season vs. 2017/18 1.019 1.064*** 1.313*** 1.343*** 1.343*** (1.000,1.039) ACEi or ARB plus/minus other medications 2018/19 season vs. 2017/18 1.017 1.041*** 1.041*** 1.411*** 0.750*** (0.999,1.035) (1.019,1.063) (1.289,1.533) (0.655,0.846) 2019/20 season vs. 2017/18 1.091*** 1.092*** 1.542*** 1.634*** (1.071,1.110) ACEi or ARB monotherapy	N/A
Other hypertension medications only 2018/19 season vs. 2017/18 0.998 1.018 1.324*** 0.776*** 2019/20 season vs. 2017/18 1.019 1.064*** 1.313*** 1.343*** 2019/20 season vs. 2017/18 1.019 1.041*** 1.201,1.425) (1.190,1.495) ACEi or ARB plus/minus other medications 2018/19 season vs. 2017/18 1.017 1.041*** 1.411*** 0.750*** 2019/20 season vs. 2017/18 1.091*** 1.092*** 1.542*** 1.634*** 4CEi or ARB monotherapy 1.071,1.110) (1.069,1.114) (1.413,1.671) (1.465,1.803)	N/A
2018/19 season vs. 2017/18	
2019/20 season vs. 2017/18 (0.979,1.017) (0.995,1.041) (1.208,1.440) (0.673,0.879) 1.019 (1.000,1.039) (1.041,1.087) (1.201,1.425) (1.313*** 1.343*** (1.000,1.039) ACEi or ARB plus/minus other medications 2018/19 season vs. 2017/18 1.017 1.041*** 1.411*** 0.750*** (0.999,1.035) (1.019,1.063) (1.289,1.533) (0.655,0.846) 2019/20 season vs. 2017/18 1.091*** 1.092*** 1.542*** 1.634*** (1.071,1.110) (1.069,1.114) (1.413,1.671) (1.465,1.803)	
2019/20 season vs. 2017/18 1.019 1.064*** 1.313*** 1.343*** (1.000,1.039) ACEi or ARB plus/minus other medications 2018/19 season vs. 2017/18 1.017 1.041*** 1.411*** 0.750*** (0.999,1.035) 1.091*** 1.092*** 1.542*** 1.634*** (1.071,1.110) 1.069,1.114) 1.1413,1.671) 1.465,1.803) ACEi or ARB monotherapy	1.002
ACEi or ARB plus/minus other medications 2018/19 season vs. 2017/18 1.017 1.041*** 1.411*** 0.750*** (0.999,1.035) (1.019,1.063) 1.092*** 1.542*** 1.634*** (1.071,1.110) 1.069,1.114) 1.413,1.671) 1.465,1.803) ACEi or ARB monotherapy	(0.967,1.036)
ACEi or ARB plus/minus other medications 2018/19 season vs. 2017/18 1.017 1.041*** (0.999,1.035) 2019/20 season vs. 2017/18 1.091*** 1.092*** 1.542*** 1.634*** (1.071,1.110) (1.069,1.114) (1.413,1.671) (1.465,1.803)	1.282***
2018/19 season vs. 2017/18	(1.241,1.324)
(0.999,1.035) (1.019,1.063) (1.289,1.533) (0.655,0.846) 2019/20 season vs. 2017/18 1.091*** 1.092*** 1.542*** 1.634*** (1.071,1.110) (1.069,1.114) (1.413,1.671) (1.465,1.803) ACEi or ARB monotherapy	
2019/20 season vs. 2017/18 1.091*** 1.092*** 1.542*** 1.634*** (1.071,1.110) (1.069,1.114) (1.413,1.671) (1.465,1.803) ACEi or ARB monotherapy	0.997
(1.071,1.110) (1.069,1.114) (1.413,1.671) (1.465,1.803) ACEi or ARB monotherapy	(0.960,1.034)
ACEi or ARB monotherapy	1.380***
• •	(1.331,1.428)
2018/19 season vs. 2017/18 N/A N/A N/A N/A N/A	N/A
2019/20 season vs. 2017/18 N/A N/A N/A N/A N/A	N/A
Number of episodes 738,240 106,917 106,917 106,9	17 737,059
Number of people 556,579 97,383 97,383 97,383	83 555,729
Note: p-value for risk ratios is for the null hypothe	
N/A: variable not included in model * p<0.05, ** p<0.01, *** p<0.001	

The RECORD statement – checklist of items, extended from the STROBE statement, that should be reported in observational studies using routinely collected health data.

	Item No.	STROBE items	Location in manuscript where items are reported	RECORD items	Location in manuscript where items are reported
Title and abstra	ict				
	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found		RECORD 1.1: The type of data used should be specified in the title or abstract. When possible, the name of the databases used should be included. RECORD 1.2: If applicable, the geographic region and timeframe within which the study took place should be reported in the title or abstract. RECORD 1.3: If linkage between databases was conducted for the study, this should be clearly stated in the title or abstract.	
Introduction					
Background rationale	2	Explain the scientific background and rationale for the investigation being reported			
Objectives	3	State specific objectives, including any prespecified hypotheses			
Methods	,				
Study Design	4	Present key elements of study design early in the paper			
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection			
Participants	6	(a) Cohort study - Give the		RECORD 6.1: The methods of study	

	eligibility criteria, and the	population selection (such as codes or
	sources and methods of selection	algorithms used to identify subjects)
	of participants. Describe	should be listed in detail. If this is not
		possible, an explanation should be
		provided.
		RECORD 6.2: Any validation studies
	ascertainment and control	of the codes or algorithms used to
	selection. Give the rationale for	select the population should be
	the choice of cases and controls	referenced. If validation was conducted
	<i>Cross-sectional study</i> - Give the	for this study and not published
		elsewhere, detailed methods and
		results should be provided.
		RECORD 6.3: If the study involved
	(b) Cohort study - For matched	linkage of databases, consider use of a
		flow diagram or other graphical
		display to demonstrate the data linkage
		process, including the number of
		individuals with linked data at each
		stage.
	criteria and the number of	
	controls per case	
7		RECORD 7.1: A complete list of codes
	exposures, predictors, potential	and algorithms used to classify
	1 1 1 1	exposures, outcomes, confounders, and
		effect modifiers should be provided. If
	_	these cannot be reported, an
	, 11	explanation should be provided.
8	For each variable of interest,	•
	of methods of assessment	
	(measurement).	
	assessment methods if there is	
	more than one group	
9	Describe any efforts to address	
		of participants. Describe methods of follow-up Case-control study - Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls Cross-sectional study - Give the eligibility criteria, and the sources and methods of selection of participants (b) Cohort study - For matched studies, give matching criteria and number of exposed and unexposed Case-control study - For matched studies, give matching criteria and the number of controls per case Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable. For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group

Page 54 of 56

Study size	10	Explain how the study size was arrived at	
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) Cohort study - If applicable, explain how loss to follow-up was addressed Case-control study - If applicable, explain how matching of cases and controls was addressed Cross-sectional study - If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses	
Data access and cleaning methods			RECORD 12.1: Authors should describe the extent to which the investigators had access to the database population used to create the study population. RECORD 12.2: Authors should provide information on the data cleaning methods used in the study.
Linkage			RECORD 12.3: State whether the

Results				study included person-level, institutional-level, or other data linkage across two or more databases. The methods of linkage and methods of linkage quality evaluation should be provided.	
Participants	13	(a) Report the numbers of		RECORD 13.1: Describe in detail the	
	13	individuals at each stage of the study (<i>e.g.</i> , numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed) (b) Give reasons for non-participation at each stage. (c) Consider use of a flow diagram		selection of the persons included in the study (<i>i.e.</i> , study population selection) including filtering based on data quality, data availability and linkage. The selection of included persons can be described in the text and/or by means of the study flow diagram.	
Descriptive data	14	(a) Give characteristics of study participants (<i>e.g.</i> , demographic, clinical, social) and information on exposures and potential confounders (b) Indicate the number of participants with missing data for each variable of interest (c) <i>Cohort study</i> - summarise follow-up time (<i>e.g.</i> , average and total amount)			
Outcome data	15	Cohort study - Report numbers of outcome events or summary measures over time Case-control study - Report numbers in each exposure category, or summary measures of exposure Cross-sectional study - Report numbers of outcome events or	ttp://bmjopen.bmj.com/sit		

		summary measures		
Main results	16	(a) Give unadjusted estimates and, if applicable, confounderadjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period		
Other analyses	17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses		
Discussion				
Key results	18	Summarise key results with reference to study objectives		
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	RECORD 19.1: Discuss the implications of using data that were not created or collected to answer the specific research question(s). Include discussion of misclassification bias, unmeasured confounding, missing data, and changing eligibility over time, as they pertain to the study being reported.	
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence		

Generalisability	21	Discuss the generalisability (external validity) of the study results	
Other Information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	
Accessibility of protocol, raw data, and programming code			RECORD 22.1: Authors should provide information on how to access any supplemental information such as the study protocol, raw data, or programming code.

^{*}Reference: Benchimol EI, Smeeth L, Guttmann A, Harron K, Moher D, Petersen I, Sørensen HT, von Elm E, Langan SM, the RECORD Working Committee. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) Statement. *PLoS Medicine* 2015; in press.

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