

Replication of Effects of the angiotensin-receptor blocker telmisartan on cardiovascular events in high-risk patients intolerant to angiotensin-converting enzyme inhibitors: a randomised controlled trial (ONTARGET trial)

July 13, 2020

## 1. RCT Details

This section provides a high-level overview of the RCT that the described real-world evidence study is trying to replicate as closely as possible given the remaining limitations inherent in the healthcare databases.

### 1.1 Title

**Effects of the angiotensin-receptor blocker telmisartan on cardiovascular events in high-risk patients intolerant to angiotensin-converting enzyme inhibitors: a randomised controlled trial ([ONTARGET](#) trial)**

### 1.2 Intended aim(s)

The primary objectives of the study were to determine the effectiveness of 80 mg of telmisartan daily, as compared with 10 mg of ramipril daily. If noninferiority was demonstrated, we would test the superiority of telmisartan over ramipril.

### 1.3 Primary endpoint for replication and RCT finding

Death from cardiovascular causes, myocardial infarction, stroke, or hospitalization for heart failure.

### 1.4 Required power for primary endpoint and noninferiority margin (if applicable)

The original planned sample size of 7800 patients who were followed for a mean of 4.5 years provided a power of 93% for the superiority hypothesis, if the hazard ratio was 0.87. For noninferiority, the expected power was 89%, for a hazard ratio of 1.00. The non-inferiority margin was 1.13.

### 1.5 Primary trial estimate targeted for replication

HR = 1.01 (95% CI 0.94–1.09) comparing telmisartan to ramipril (Yusuf et al., 2008, NEJM)

## 2. Person responsible for implementation of replication in Aetion

Ajinkya Pawar, Ph.D. implemented the study design in the Aetion Evidence Platform. S/he is not responsible for the validity of the design and analytic choices. All implementation steps are recorded and the implementation history is archived in the platform.

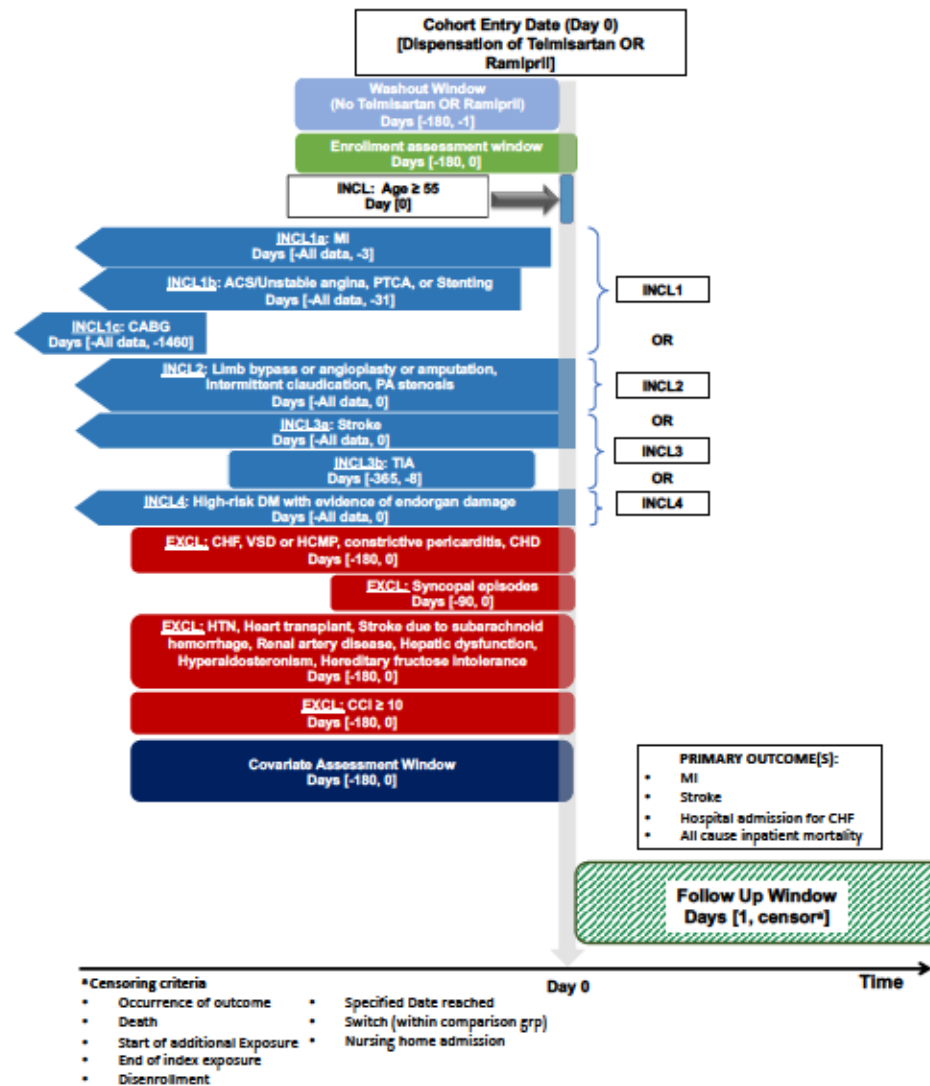
## 3. Data Source(s)

United/Optum, MarketScan

#### 4. Study Design Diagram

The study design diagram visualizes key aspects of the longitudinal study design for expedited review.

##### Design Diagram – ONTARGET TRIAL REPLICATION



## 5. Cohort Identification

### 5.1 Cohort Summary

This study will involve a new user, parallel group, cohort study design comparing telmisartan to ramipril. The patients will be required to have continuous enrollment during baseline period of 180 days before initiation of telmisartan or the comparator drug (cohort entry date). Follow-up for the outcome, begins the day after drug initiation. Patients are also required to have no prior ACE or ARB use during the 3 months before the cohort entry date, but they are allowed to take other antihypertensive medications during the study, as in the trial.

### 5.2 Important steps for cohort formation

#### 5.2.1 Eligible cohort entry dates

Market availability of telmisartan in the U.S. started on November 10, 1998, however, the Marketscan and Optum data are available at BWH only from Jan 1, 2003 and Jan 1, 2004, respectively.

- For Marketscan: Jul 1, 2003 -Dec 2018 (end of data availability).
- For Optum: Jan 1, 2004- Dec 2019 (end of data availability).

#### 5.2.2 Specify inclusion/exclusion criteria for cohort entry and define the index date

Inclusion and exclusion criteria were adapted from the trial as closely as possible. Definitions for all inclusion/exclusion are provided in **Appendix A** and are summarized in the flowcharts below.

### 5.3 Flowchart of the study cohort assembly

	Optum		Truven	
	Remaining Patients		Less Excluded Patients	Remaining Patients
Less Excluded Patients				
All patients		75,894,642		200,203,908
Did not meet cohort entry criteria	-75,250,227	644,415	-198,892,008	1,311,900
Excluded due to insufficient enrollment	-74,705	569,710	-167,142	1,144,758
Excluded due to prior use of referent	-295257	274,453	-639288	505,470

Excluded due to prior use of exposure	-155,795	118,658	-264,031	241,439
Excluded because patient qualified in >1 exposure category	-17	118,641	-25	241,414
Excluded based on Age	0	118,641	0	241,414
Excluded based on Gender	-14	118,627	0	241,414
Excluded based on Inclusion Age >= 55	-29,428	89,199	-59,190	182,224
Excluded based on All inclusion criteria (Coronary artery disease/Peripheral artery disease/Cerebrovascular disease) EXCEPT Age >=55	-28349	60,850	-51572	130,652
Excluded based on Exclusion 2a- Heart failure (CHF) (inpatient/ER)	-2,267	58,583	-4,218	126,434
Excluded based on Exclusion 2b- Hemodynamically significant primary valvular or outflow tract obstruction	-950	57,633	-736	125,698
Excluded based on Exclusion 2c- Constrictive pericarditis	-1	57,632	-3	125,695
Excluded based on Exclusion 2d- Complex congenital heart disease	-246	57,386	-382	125,313
Excluded based on Exclusion 2e- Syncopal episodes of unknown etiology <3 months before informed consent	-471	56,915	-1,178	124,135
Excluded based on Exclusion 2g- Uncontrolled hypertension on treatment (eg, BP >160/100 mm Hg)	-697	56,218	-1080	123,055
Excluded based on Exclusion 2f- Heart transplant recipient	-2	56,216	-2	123,053
Excluded based on Exclusion 2g- Stroke due to subarachnoid hemorrhage	-40	56,176	-85	122,968
Excluded based on Exclusion 3a- Significant renal artery disease	-160	56,016	-224	122,744
Excluded based on Exclusion 3b- Hepatic dysfunction	-297	55,719	-614	122,130
Excluded based on Exclusion 3d- Primary hyperaldosteronism	-1	55,718	-1	122,129
Excluded based on Exclusion 3e- Hereditary fructose intolerance	0	55,718	0	122,129
Excluded based on Exclusion 3f- Other major noncardiac illness expected to reduce life expectancy or interfere with study participation- CCI (180 days)	-222	55,496	-123	122,006
Excluded based on ACE or ARB (prior 3 months)	-5,543	49,953	-7,266	114,740
Final cohort		49,953		114,740

## 6. Variables

### 6.1 Exposure-related variables:

Study drug:

The study exposure of interest is initiation of telmisartan. Initiation will be defined by no use of telmisartan or a comparator in the prior 6 months before treatment initiation (washout period).

Comparator agents-

- Initiators of telmisartan will be compared to initiators of-
  - Ramipril (**primary**)

6.2 Preliminary Covariates:

- Age
- Sex
- Combined Comorbidity Index (CCI), measured over the baseline covariate assessment period, defined as 180 days prior to and including index date

Covariates listed above represent only a small subset of covariates that will ultimately be controlled for in the design and analysis. We use the covariates above only for initial feasibility analyses to judge whether there is likely to be sufficient overlap between treatment groups to proceed with the study. Remaining covariates are defined only after the study has passed the initial feasibility analysis and the initial power assessment and are listed in Table 1 (**Appendix B**). These covariates are based on those used by Patorno et al. (2019).

6.3 Outcome variables and study follow-up:

6.3.1 Outcome variables

Effectiveness outcome of interest (definitions provided in **Appendix A**):

- **Primary outcome:** Composite endpoint including death from cardiovascular causes, myocardial infarction, stroke, and hospitalization for heart failure
- Secondary outcomes: Individual components:
  - Heart failure requiring hospitalization
  - Hospital admission for MI (for purposes of this individual component, fatal MI is included)

- Hospital admission for stroke (for purposes of this individual component, fatal stroke is included)
- All-cause inpatient mortality/CV mortality:
  - Information on CV mortality through data linkage with the National Death Index (NDI) will only be available for CMS.
  - All-cause inpatient mortality identified using discharge status codes will be used as a proxy for “CV mortality” in commercial databases

### 6.3.2 Study follow-up

Both as-treated (AT) and intention-to-treat (ITT) analyses will be conducted with treatment defined as the index drug on day of cohort entry. Because adherence in the real world databases is expected to be much worse than in the trial, the AT analysis is the **primary** analysis, as it targets the relative hazard of outcomes on treatment.

For the AT analyses, the follow-up will start the day after initiation of telmisartan and comparator and will continue until the earliest date of the following events:

- The first occurrence of the outcome of interest, unless otherwise specified for selected outcomes,
- The date of end of continuous registration in the database,
- End of the study period,
- Measured death event occurs,
- Nursing home admission
  - Nursing home admissions are considered a censoring event because the data sources utilized typically provide little to no data on a patient, particularly on drug utilization, after admission. We will utilize this as an exclusion reason for cohorts for the same reason.
- The date of drug discontinuation, defined as the date of the last continuous treatment episode of the index drug (telmisartan and comparator) plus a defined grace period (i.e., 30 days after the end of the last prescription's days' supply in main analyses).
- The date of switching from an exposure to a comparator and vice versa, defined as a prescription fill from the other treatment group.

For the intention-to-treat (ITT) analyses, the censoring based on the switching and treatment discontinuation will be replaced with a maximum allowed follow-up time of 365 days.

## 7. Initial Feasibility Analysis

### Action report name:

Optum- <https://bwh-dope.aetion.com/projects/details/774/results/55701/result/0>

MarketScan- <https://bwh-dope.aetion.com/projects/details/775/results/55702/result/0>

Date conducted: 06/27/2020

Complete Aetion feasibility analysis using age, sex, and CCI as the only covariates and the primary endpoint (Section 6.3.1) as the outcome. No measures of association will be computed nor will incidence rates stratified by treatment group.

- Complete study flowchart from Section 5.3
- Report patient characteristics by treatment group
- Report summary parameters of study population
- Report median follow-up time by treatment group
- Report reasons for censoring in the overall study population

## 8. Initial Power Assessment

### Action report name:

Optum- <https://bwh-dope.aetion.com/#/projects/details/774/results/31496/result/1>

MarketScan- <https://bwh-dope.aetion.com/#/projects/details/775/results/31494/result/1>

Date conducted: 02/11/2019

In order to complete the initial power analysis, the dummy outcome of a 90-day gap in database enrollment will be used. This outcome is used to ensure that no information on the comparative risks of the outcomes of interest are available at this stage. Complete a 1:1 PS-matched comparative analysis using this outcome. PS should include only 3 covariates: age, sex, and combined comorbidity index. Power calculations are based on the formulas from Chow et al. (2008).

- Stop analyses until feasibility and power are reviewed by primary investigators and FDA. Reviewers evaluate the results of the

analyses described above in Sections 7 and 8, including numbers of patients, patient characteristics, follow-up time, and reasons for censoring by treatment group, as well as overall rates of outcomes and study power. These parameters are re-evaluated and reported in the subsequent sections, after incorporating feedback and refining the protocol.

Reviewed by PI:	Jessica Franklin	Date reviewed:	7/16/19
Reviewed by FDA:	Ken Quinto	Date reviewed:	7/30/19
Reasons for stopping analysis (if required):			

## 9. Balance Assessment after PS matching

### **Action report name:**

Optum- <https://bwh-dope.aetion.com/projects/details/774/results/55703/result/0>

MarketScan- <https://bwh-dope.aetion.com/projects/details/775/results/55704/result/0>

**Date conducted:** 06/27/2020

After review of initial feasibility and power analyses, complete creation of the remaining covariates (see Table 1 below for list of covariates). Again, using the dummy outcome of a 90-day gap in database enrollment, complete a 1:1 PS-matched analysis. The PS should include the complete list of covariates (excluding laboratory values, which are missing in some patients).

- Provide plot of PS distributions stratified by treatment group.

Note- Please refer to **Appendix B**.

- Report covariate balance after matching.

Note- For Table 1, please refer to **Appendix B**.

- Report reasons for censoring by treatment group.

	Overall	Referent	Exposure
Dummy Outcome	0 (0.00%)	0 (0.00%)	0 (0.00%)
Death	343 (0.54%)	211 (0.66%)	132 (0.41%)
Start of an additional exposure	189 (0.30%)	95 (0.30%)	94 (0.29%)
End of index exposure	47,275 (74.16%)	22,786 (71.49%)	24,489 (76.84%)
Specified date reached	3,666 (5.75%)	1,949 (6.12%)	1,717 (5.39%)
End of patient enrollment	10,559 (16.56%)	5,864 (18.40%)	4,695 (14.73%)
Nursing home + Pharmacy disenrollment	1,712 (2.69%)	967 (3.03%)	745 (2.34%)

- Report follow-up time by treatment group.

Median Follow-Up Time (Days) [IQR]		
Patient Group	Optum	Marketscan
Overall Patient Population	118 [58-299]	151 [94-365]
Referent	144 [79-342]	177 [99-403]
Exposure	118 [58-260]	128 [91-319]

- Report overall risk of the primary outcome.

	Optum	Marketscan	Pooled
Risk per 1,000 patients (Composite endpoint including death from cardiovascular causes, myocardial infarction, stroke, and hospitalization for heart failure)	52.3	55.2	54.3

## 10. Final Power Assessment

### Date conducted:

- Re-calculate power in the appropriate excel table, using the revised number of matched patients from the PS-match in Section 9. All other parameters in the table should be the same as in Section 8. If the study is to be implemented in more than one database, copy and paste excel sheet to report power for each database separately and for the pooled analysis that uses data from all databases together. Power calculations are based on the formulas from Chow et al. (2008).

#### ▪ Pooled

Superiority Analysis		Non-inferiority Analysis	
Number of patients matched		Number of patients matched	
Reference	31,872	Reference	31,872
Exposed	31,872	Exposed	31,872
Risk per 1,000 patients	54.3	Risk per 1,000 patients	54.30
Desired HR from RCT	0.87	Assumed HR from RCT	1
Alpha (2-sided)	0.05	Alpha (2-sided)	0.05
		Non-inferiority margin	1.13
Number of events expected	3461.2992	Number of events expected	3461.2992
Power	0.983685756	Power	0.949000546

#### ▪ Optum

Superiority Analysis		Non-inferiority Analysis	
Number of patients matched		Number of patients matched	
Reference	10,798	Reference	10,798
Exposed	10,798	Exposed	10,798
Risk per 1,000 patients	52.3	Risk per 1,000 patients	52.3
Desired HR from RCT	0.87	Assumed HR from RCT	1
Alpha (2-sided)	0.05	Alpha (2-sided)	0.05
		Non-inferiority margin	1.13
Number of events expected	1129.4708	Number of events expected	1129.4708
Power	0.648098168	Power	0.537348783

▪ MarketScan

Superiority Analysis		Non-inferiority Analysis	
Number of patients matched		Number of patients matched	
Reference	21,074	Reference	21,074
Exposed	21,074	Exposed	21,074
Risk per 1,000 patients	55.2	Risk per 1,000 patients	55.2
Desired HR from RCT	0.87	Assumed HR from RCT	1
Alpha (2-sided)	0.05	Alpha (2-sided)	0.05
		Non-inferiority margin	1.13
Number of events expected	2326.5696	Number of events expected	2326.5696
Power	0.919041969	Power	0.838323471

- Stop analyses until balance and final power assessment are reviewed by primary investigators, FDA, and assigned members of advisory board. Reviewers evaluate the results of the analyses described above in Sections 9 and 10, including numbers of patients, balance in patient characteristics, follow-up time, and reasons for censoring by treatment group, as well as overall rates of outcomes and study power.

Reviewed by PI:	Jessica Franklin	Date reviewed:	7/6/20
Reviewed by FDA:	Ken Quinto	Date reviewed:	4/5/20
Reasons for stopping analysis (if required):			

## 11. Study Confidence and Concerns

Deadline for voting on study confidence and listing concerns:

Date votes and concerns are summarized:

- If final feasibility and power analyses are reviewed and approved, proceed to the remaining protocol steps.
- All study team and advisory board members that review this protocol should at this stage provide their level of confidence for the success of the RWD study in the [Google Form](#). This form also provides space for reviewers to list any concerns that they feel may contribute to a failure to replicate the findings of the RCT, including differences in study populations, poor measurement of study variables, or residual confounding. All responses will be kept confidential and individual-level results will only be shared with the individual respondent.
- After the deadline for voting has passed, provide the distribution of responses and summarize all concerns here.

## 12. Register study protocol on clinicalTrials.gov

Date conducted:

- Register the study on [clinicalTrials.gov](#) and upload this document.

## 13. Comparative Analyses

Action report name:

Date conducted:

13.1 For **primary analysis**:

- In the PS-matched cohort of telmisartan and ramipril from Section 9, calculate the HR for each outcome for telmisartan versus referent patients using a Cox proportional hazards model.

13.2 For sensitivity analyses:

**14. Requested Results**

14.1 Table 1: Baseline characteristics before and after adjustment

Variable	Before adjustment			After adjustment		
	Referent	Exposure	Std. diff.	Referent	Exposure	Std. diff.
Number of patients			-			-
Age categories						
...						

14.2 Table 2: Follow-up time

Patient Group	Median Follow-Up Time (Days) [IQR]
Overall Patient Population	
Referent	
Exposure	

14.3 Table 3: Censoring events

	Overall	Referent	Exposure
Outcome			
Death			
Start of an additional exposure			
End of index exposure			
Specified date reached			
End of patient data			
End of patient enrollment			
...			

#### 14.4 Table 4: Results from primary analyses;

Analysis	No. exposed events	No. referent events	Exposed rate	Referent rate	HR (95% CI)
Crude					
Analysis 1					
Analysis 2					
...					

HR, Hazard Ratio; CI, Confidence Interval.

#### 14.5 Table 5: Results from secondary analyses;

### 15. References

Chow S, Shao J, Wang H. 2008. *Sample Size Calculations in Clinical Research*. 2nd Ed. Chapman & Hall/CRC Biostatistics Series. **page 177**

Patorno E, Pawar A, Franklin JM, et al. Empagliflozin and the Risk of Heart Failure Hospitalization in Routine Clinical Care: A First Analysis from the Empagliflozin Comparative Effectiveness and Safety (EMPRISE) Study. *Circulation*. 2019; in press.  
<https://www.ahajournals.org/doi/pdf/10.1161/CIRCULATIONAHA.118.039177>

# Appendix A

#	ONTARGET trial definitions	Implementation in routine care	References/Rationale	Color coding
	Trial details- 3- Failed S- No NI margin specified - 3 weeks run in		Please see the following Google Drive for further details or any missing information: <a href="https://drive.google.com/open?id=1W0dL8wvnyV1taFtL-TcU-3Cmb02-gV">https://drive.google.com/open?id=1W0dL8wvnyV1taFtL-TcU-3Cmb02-gV</a>	Criteria
	EXPOSURE vs. COMPARISON		ICD-10 codes are not listed in this document because of excel cell size limitations and excessive number of ICD-10 codes. Full ICD-10 code lists will be available in the above Google Drive Folder (link above). ICD-9 to ICD-10 code conversions were completed using a SAS macro that implements forward/ backward mapping based on the CMS ICD-9 to ICD-10 mapping: <a href="https://www.cms.gov/data/d3/icd-10-cm-and-icd-9-cm-crosswalk-general-equivalence-mapping.html">https://www.cms.gov/data/d3/icd-10-cm-and-icd-9-cm-crosswalk-general-equivalence-mapping.html</a>	Adequate mapping in claims
	ONTARGET: Aimed to determine if the combination of ARB (telmisartan) and the ACE (ramipril) is more effective than ramipril alone, and if telmisartan is at least as effective as ramipril	Telmisartan vs Ramipril (Exclude patients who received any ACE-i or ARB in prior)		Intermediate mapping in claims
	PRIMARY OUTCOME			Poor mapping or cannot be measured in claims
	Death from cardiovascular causes, myocardial infarction, stroke, or hospitalization for heart failure.	Measured 1 day after drug initiation in diagnosis position specified below and inpatient care setting: <u>Composite inpatient mortality (MI/Stroke/CHF -</u> <u>Hospital admission for CHF (inpatient only, any position) ICD-9 diagnosis: 428.x, 398.91, 402.01, 402.11, 402.91, 404.01, 404.11, 404.91, 404.03, 404.13, 404.93</u> <u>MI (inpatient only, any position) ICD-9 diagnosis: 410.x excluding 410.x2</u> <u>Stroke (inpatient only, primary position only) ICD-9 diagnosis: 430.xx, 431.xx, 433.x1, 434.xx (excluding 434.x0), 436.x</u> <u>Mortality- See Mortality Sheet.</u>	For MI: → PPV 94% in Medicare claims data (Kyota Y, Schneeweiss S, Glynn RJ, Cennamo CC, Avorn J, Solomon DH. Accuracy of Medicare claims-based diagnosis of acute myocardial infarction: estimating positive predictive value on the basis of review of hospital records. American heart journal 2004;148:99-104.) → PPV 88.4% in commercially-insured population (Wehl PM, Rodgers K, Schneeweiss S, et al. Validation of claims-based diagnostic and procedure codes for cardiovascular and gastrointestinal serious adverse events in a commercially-insured population. Pharmacoepidemiology and Drug Safety 2010;19:596-603.) For stroke: PPV of 85% or higher for ischemic stroke PPV ranging from 80% to 96% for hemorrhagic stroke → (Andrade SE, Harrold LR, Tjia J, et al. A systematic review of validated methods for identifying cerebrovascular accident or transient ischemic attack using administrative data. Pharmacoepidemiology and Drug Safety 2012;21 Suppl 1:100-28.) → (Trinchese DL, Longstreth WT, Jr. Validating administrative data in stroke research. Stroke; a journal of cerebral circulation 2002;33:2465-70.) → (Roumie CL, Mitchell E, Gideon PS, Varro-Lorenzo C, Castellanos J, Griffin MR. Validation of ICD-9 codes with a high positive predictive value for incident strokes resulting in hospitalization using Medicaid health data. Pharmacoepidemiology and drug safety 2008;17:20-6.)	Can't be measured in claims but not important for the analysis
	INCLUSION CRITERIA			
	Individuals 55 years of age with 1 of the following:	Age ≥55 years at drug initiation		
1	Coronary artery disease			
1a	Previous myocardial infarction (>2 days post uncomplicated MI)	Measured from the start of all available data to 2 days prior to drug initiation in any diagnosis position and the inpatient or outpatient care setting <u>Acute MI</u> ICD-9 diagnosis: 410.xx <u>Old MI</u> ICD-9 diagnosis: 412.xx	Paterno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliiflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 <a href="http://dx.doi.org/10.1136/bmj.k119">http://dx.doi.org/10.1136/bmj.k119</a>  Paterno, Elisabetta et al. "Empagliflozin and the Risk of Heart Failure Hospitalization in Routine Clinical Care: A First Analysis from the Empagliflozin Comparative Effectiveness and Safety (EMPREST) Study." Circulation. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177	
1b	Stable angina or unstable angina >30 days before informed consent and with documented evidence of multivessel coronary artery disease	Measured from the start of all available data to 30 days prior to drug initiation in any diagnosis position and the inpatient or outpatient care setting <u>ACU/Unstable angina</u> ICD-9 diagnosis: 411.xx <u>Stable angina</u> ICD-9 diagnosis: 413.xx	Paterno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliiflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 <a href="http://dx.doi.org/10.1136/bmj.k119">http://dx.doi.org/10.1136/bmj.k119</a>  Paterno, Elisabetta et al. "Empagliflozin and the Risk of Heart Failure Hospitalization in Routine Clinical Care: A First Analysis from the Empagliflozin Comparative Effectiveness and Safety (EMPREST) Study." Circulation. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177	

# Appendix A

1c	Multi-vessel PTCA >30 days before informed consent	Measured from the start of all available data to 30 days prior to drug initiation in any procedure position and the care setting indicated below: <u>PTCA</u> [Inpatient only] CPT-4: 92973, 92982, 92984, 92995, 92996, 92920 – 92921, 92924 – 92925, 92937, 92938, 92941, 92943, 92944 [Inpatient or outpatient] ICD-9 procedure: 00.66, 36.01, 36.02, 36.03, 36.05, 36.09 <u>Stenting</u> [Inpatient only] CPT-4: 92980, 92981, 92928 – 92929, 92933 – 92934 [Inpatient or outpatient] ICD-9 procedure: 36.06, 36.07 <u>Transmyocardial revascularization</u> [Inpatient only] CPT-4: 33140, 33141 [Inpatient or outpatient] ICD-9 procedure: 36.31-36.34	Paterno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliiflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 <a href="http://dx.doi.org/10.1136/bmj.k119">http://dx.doi.org/10.1136/bmj.k119</a>  Paterno, Elisabetta et al. "Empagliflozin and the Risk of Heart Failure Hospitalization in Routine Clinical Care: A First Analysis from the Empagliflozin Comparative Effectiveness and Safety (EMPRESE) Study." Circulation. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177
1d	Multi-vessel CABG surgery >4 years before informed consent, or with recurrent angina following surgery	Measured from the start of all available data to 1460 days (4 years) prior to drug initiation in any procedure position and the inpatient care setting <u>CABG</u> CPT-4: 33510 – 33536, 33545, 33572. ICD-9 procedure: 36.1x, 36.2x	Paterno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliiflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 <a href="http://dx.doi.org/10.1136/bmj.k119">http://dx.doi.org/10.1136/bmj.k119</a>  Paterno, Elisabetta et al. "Empagliflozin and the Risk of Heart Failure Hospitalization in Routine Clinical Care: A First Analysis from the Empagliflozin Comparative Effectiveness and Safety (EMPRESE) Study." Circulation. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177
2	Peripheral artery disease		
2a	Previous limb bypass surgery or Previous limb bypass surgery or angioplasty	Measured from the start of all available data prior to and including day of drug initiation in any procedure position and the inpatient or outpatient care setting <u>Previous limb bypass surgery/Previous limb bypass surgery or angioplasty</u> CPT-4: 35556, 35566, 35570, 35571, 35583-35587, 35623, 35656, 35666, 35671 <u>Lower-extremity endarterectomy, stenting, angioplasty, or atherectomy</u> ICD-9 procedure: 38.18, 38.19 [Outpatient only] CPT-4: 35454, 35456, 35458, 35470, 35473, 35474, 35482, 35483, 35485, 35492, 35493, 35495, 37207, 37208, 37220-37235 <u>Lower-extremity bypass</u> ICD-9 procedure: 39.25, 39.29 [Outpatient only] CPT-4: 35351, 35355, 35361, 35363, 35371, 35372, 35321, 35333, 35341, 35346, 35348, 35349, 35351, 35356, 35358, 35363, 35365, 35366, 35371, 35621, 35623, 35641, 35646, 35647, 35651, 35654, 35656, 35661, 35663, 35666, 35671, 35570, 35582, 35583, 35585, 35587, 35637, 35638, 35681, 35682, 35683 <u>Other peripheral vascular surgery</u> ICD-9 procedure: 38.08, 38.09, 38.38, 38.39, 38.46, 38.49, 39.5x, 39.9x [Outpatient only] CPT-4: 35256, 35286, 35381, 35679	
2b	Previous limb or foot amputation	Measured from the start of all available data prior to and including day of drug initiation in any diagnosis/procedure position and the inpatient or outpatient care setting <u>Lower extremity amputation</u> ICD-9 diagnosis: V49.7x [excluding V49.76, V49.77] ICD-9 procedure: 84.10-84.18 CPT: 27590, 27591, 27592, 27680, 27681, 27682, 27684, 27686, 27688, 27689, 28800, 28805, 28810, 28820, 28825	Paterno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliiflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 <a href="http://dx.doi.org/10.1136/bmj.k119">http://dx.doi.org/10.1136/bmj.k119</a>  Paterno, Elisabetta et al. "Empagliflozin and the Risk of Heart Failure Hospitalization in Routine Clinical Care: A First Analysis from the Empagliflozin Comparative Effectiveness and Safety (EMPRESE) Study." Circulation. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177
2c	Intermittent claudication, with ankle/arm BP ratio <0.80 on at least 1 side	Measured from the start of all available data prior to and including day of drug initiation in any diagnosis position and the inpatient or outpatient care setting <u>Atherosclerosis of native arteries of the extremities with intermittent claudication</u> ICD-9 diagnosis: 440.31	
2d	Significant peripheral artery stenosis (>50%) documented by angiography or non-invasive testing	Measured from the start of all available data prior to and including day of drug initiation as at least two claims on separate days in any diagnosis/procedure position and the inpatient or outpatient care setting (unless otherwise specified): <u>Peripheral vascular disease</u> ICD-9 diagnosis: 440.20 – 440.24, 440.29 – 440.32, 440.3, 440.4, 443.9	Paterno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliiflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 <a href="http://dx.doi.org/10.1136/bmj.k119">http://dx.doi.org/10.1136/bmj.k119</a>  Paterno, Elisabetta et al. "Empagliflozin and the Risk of Heart Failure Hospitalization in Routine Clinical Care: A First Analysis from the Empagliflozin Comparative Effectiveness and Safety (EMPRESE) Study." Circulation. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177
3	Cerebrovascular disease		

# Appendix A

3a	Previous stroke	Measured from the start of all available data prior to and including day of drug initiation in any diagnosis position and the inpatient or outpatient care setting <u>Stroke</u> ICD-9 diagnosis: 430.xx, 431.xx, 433.x1, 434.xx (excluding 434.x0), 436.x	Paterno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliiflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 <a href="http://dx.doi.org/10.1136/bmj.k119">http://dx.doi.org/10.1136/bmj.k119</a>  Paterno, Elisabetta et al. "Empagliflozin and the Risk of Heart Failure Hospitalization in Routine Clinical Care: A First Analysis from the Empagliflozin Comparative Effectiveness and Safety (EMPEROR) Study." Circulation. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177
3b	Transient ischemic attacks >7 days and <1 year before informed consent	Measured 365 days prior to drug initiation to 7 days prior to drug initiation in any diagnosis position and the inpatient or outpatient care setting <u>TIA</u> ICD-9 diagnosis: 435.xx	
4	Diabetes mellitus		
3c	Diabetes mellitus/High-risk diabetics with evidence of endorgan damage	Measured at the start of all available data prior to and including day of drug initiation in any diagnosis position and the inpatient or outpatient care setting <u>Diabetic retinopathy</u> ICD-9 diagnosis: 362.0x <u>Diabetes with other ophthalmic manifestations</u> ICD-9 diagnosis: 250.5x (without mention of 362.01-362.07), 366.A1, 369.A4 <u>Diabetic nephropathy</u> ICD-9 diagnosis: 250.Ax, 583.81 <u>Diabetic neuropathy</u> ICD-9 diagnosis: 250.6x, 357.2x, 337.1 <u>Diabetic foot</u> ICD-9 diagnosis: 707.1x	Paterno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliiflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 <a href="http://dx.doi.org/10.1136/bmj.k119">http://dx.doi.org/10.1136/bmj.k119</a>  Paterno, Elisabetta et al. "Empagliflozin and the Risk of Heart Failure Hospitalization in Routine Clinical Care: A First Analysis from the Empagliflozin Comparative Effectiveness and Safety (EMPEROR) Study." Circulation. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177
Exclusion criteria			
1	Medication use		
1a	Inability to discontinue ACE inhibitors or ARB	N/A	
1b	Known hypersensitivity or intolerance to ACE inhibitors or ARB (patient intolerant of ACE inhibitor can be enrolled in TRANSCEND)	N/A	
2	Cardiovascular disease (ICD)		
2a	Symptomatic congestive heart failure	Measured 180 days prior to and including day of drug initiation in any diagnosis position and the inpatient/emergency room care setting: <u>Heart failure diagnosis requiring hospitalization</u> ICD-9 diagnosis: 428.x, 398.91, 402.01, 402.11, 402.91, 404.01, 404.11, 404.91, 404.03, 404.13, 404.93 ICD-10 diagnosis: I09.81, I11.0, I13.0, I13.2, I50.1, I50.20, I50.21, I50.22, I50.23, I50.31, I50.32, I50.33, I50.40, I50.41, I50.42, I50.43, I50.9	Paterno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliiflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 <a href="http://dx.doi.org/10.1136/bmj.k119">http://dx.doi.org/10.1136/bmj.k119</a>  Paterno, Elisabetta et al. "Empagliflozin and the Risk of Heart Failure Hospitalization in Routine Clinical Care: A First Analysis from the Empagliflozin Comparative Effectiveness and Safety (EMPEROR) Study." Circulation. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177
2b	Hemodynamically significant primary valvular or outflow tract obstruction	Measured 180 days prior to and including day of drug initiation in any diagnosis position and the inpatient or outpatient care setting <u>Ventricular septal defect</u> ICD-9 diagnosis: 745.4x <u>Hypertrophic Cardiomyopathy</u> ICD-9 diagnosis: 425.1x <u>Significant valvular heart disease</u> ICD-9 diagnosis: 394.x, 395.x, 396.x, 397.x, 398.9x, V42.2, V43.3 ICD-9 procedure: 35.1x, 35.2x CPT-4: 33660-33665, 33400-33403, 33405, 33420-33430, 33460, 33463-33468, 33475, 33496, 02577, 02587, 02597, 02627	
2c	Constrictive pericarditis	Measured 180 days prior to and including day of drug initiation in any diagnosis position and the inpatient or outpatient care setting <u>Constrictive pericarditis</u> ICD-9 diagnosis: 423.2	
2d	Complex congenital heart disease	Measured 180 days prior to and including day of drug initiation in any diagnosis position and the inpatient or outpatient care setting <u>Complex congenital heart disease</u> ICD-9 diagnosis: 416.0, 745, 745.0, 745.1, 745.10, 745.11, 745.12, 745.19, 745.2, 745.3, 745.4, 745.5, 745.6, 745.60, 745.61, 745.69, 745.7, 745.8, 745.9, 746, 746.00, 746.01, 746.02, 746.09, 746.1, 746.2, 746.3, 746.5, 746.6, 746.7, 746.8, 746.81, 746.82, 746.83, 746.84, 746.85, 746.86, 746.87, 746.88, 746.89, 747, 747.0, 747.1, 747.10, 747.11, 747.2, 747.20, 747.21, 747.22, 747.29, 747.3, 747.31, 747.32, 747.39, 747.4, 747.40, 747.41, 747.42, 747.49, 747.53	

# Appendix A

2e	Syncopal episodes of unknown etiology <3 months before informed consent	Measured 90 days prior to and including day of drug initiation in any diagnosis position and the inpatient or outpatient care setting <u>Syncope and collapse</u> ICD-9 diagnostic: 780.2	
2f	Planned cardiac surgery or PTCA <3 months of informed consent	N/A	
2g	Uncontrolled hypertension on treatment (eg, BP >160/100 mm Hg)	Measured 180 days prior to and including day of drug initiation in any diagnosis position and the inpatient or outpatient care setting <u>Malignant hypertension</u> ICD-9 diagnostic: 401.0, 402.0, 402.00, 402.01, 403.0, 403.00, 403.01, 404.0, 404.00, 404.01, 404.02, 404.03, 405.0, 405.01, 405.09	
2f	Heart transplant recipient	Measured 180 days prior to and including day of drug initiation in any diagnosis/procedure position and the inpatient or outpatient care setting <u>Heart transplantation</u> ICD-9 diagnostic: V42.1 ICD-9 procedure: 37.51	
2g	Stroke due to subarachnoid hemorrhage	Measured 180 days prior to and including day of drug initiation in any diagnosis position and the inpatient or outpatient care setting <u>Subarachnoid hemorrhage (SAH)</u> ICD-9 diagnostic: 430.xx	
3	Other conditions		
3a	Significant renal artery disease	Measured 180 days prior to and including day of drug initiation in any diagnosis position and the inpatient or outpatient care setting <u>Renovascular hypertension</u> ICD-9 diagnostic: 405.01, 405.11, 405.91, 440.1	
3b	Hepatic dysfunction	Measured 180 days prior to and including day of drug initiation in any diagnosis position and the inpatient or outpatient care setting <u>Hepatitis</u> ICD-9 diagnostic: 070.0, 070.1, 070.20, 070.21, 070.30, 070.31, 070.41, 070.51 <u>Chronic liver disease and cirrhosis</u> ICD-9 diagnostic: 571.x, 572.x, 573.x	
3c	Uncorrected volume or sodium depletion	N/A	
3d	Primary hyperaldosteronism	Measured 180 days prior to and including day of drug initiation in any diagnosis position and the inpatient or outpatient care setting <u>Hyperaldosteronism</u> ICD-9 diagnostic: 255.10	
3e	Hereditary fructose intolerance	Measured 180 days prior to and including day of drug initiation in any diagnosis position and the inpatient or outpatient care setting <u>Hereditary Fructose Intolerance</u> ICD-9 diagnostic: 271.2	
3f	Other major noncardiac illness expected to reduce life expectancy or interfere with study participation	Measured 180 days prior to and including day of drug initiation- CCL ≥ 10	Gagne, Josh J et. al. "A combined comorbidity score predicted mortality in elderly patients better than existing scores." <i>J Clin Epidemiol.</i> 2011 Jul;64(7):749-59. doi: 10.1016/j.jclinepi.2010.10.004.  Sun, Jenny W et. al. "Validation of the Combined Comorbidity Index of Charlson and Elixhauser to Predict 30-Day Mortality Across ICD-9 and ICD-10." <i>Med Care.</i> 2018 Sep;56(9):e12. doi: 10.1097/MLR.0000000000000954.
3g	Simultaneously taking another experimental drug	N/A	
3h	Significant disability precluding regular follow-up visits	N/A	
3i	Unable or unwilling to provide written informed consent	N/A	
4	Additional Exclusions		
	N/A	ACE or ARB dispensing in the prior 3 months	

## Appendix A

<b><u>Trial ID</u></b>	Neg4
<b><u>Trial Name (with web links)</u></b>	<a href="#">ONTARGET</a>
<b><u>Trial Name (with pdf links)</u></b>	<a href="#">ONTARGET</a>
<b><u>NCT</u></b>	<a href="#">NCT00153101</a>
<b><u>Trial category</u></b>	Negative trial
<b><u>Therapeutic Area</u></b>	Cardiology/Vascular Diseases
<b><u>Study batch</u></b>	Antihypertensives (ARBs+aliskiren)
<b><u>RCT Category</u></b>	3- Failed S- No NI margin specified
<b><u>Brand Name</u></b>	Micardis
<b><u>Generic Name</u></b>	telmisartan + ramipril
<b><u>Sponsor</u></b>	Boehringer Ingelheim
<b><u>Year</u></b>	2008
<b><u>Measurable endpoint</u></b>	Primary composite Endpoint of Cardiovascular Death, Non-fatal Myocardial Infarction, Non-fatal Stroke and Hospitalization for Congestive Heart Failure
<b><u>Exposure</u></b>	Telmisartan
<b><u>Comparator</u></b>	Ramipril
<b><u>Population</u></b>	Patients aged 55 years or older with established atherosclerotic vascular disease or with diabetes with end-organ damage
<b><u>Trial finding</u></b>	HR = 1.01 (95% CI 0.94–1.09)
<b><u>Notes</u></b>	
<b><u>No. of Patients</u></b>	31546
<b><u>Non-inferiority margin</u></b>	Not provided
<b><u>Assay Sens. Outcome</u></b>	Angioedema
<b><u>Assay Sens. Endpoint (from trial)</u></b>	Angioedema
<b><u>Finding for potential Assay Sens. Outcome from trial-</u></b>	HR, 0.40; P = .01
<b><u>Power</u></b>	
<b><u>Blinding</u></b>	Double-blinded
<b><u>Statistical Method</u></b>	Non-inferiority margin was 1.13

# Appendix A

## Mortality- Dependent on data source.

1. All-cause mortality / inpatient mortality  
Identified using the vital status file-

Medicare  
Identified using the discharge status codes-

Optum-

- 20 = EXPIRED
- 21 = EXPIRED TO BE DEFINED AT STATE LEVEL
- 22 = EXPIRED TO BE DEFINED AT STATE LEVEL
- 23 = EXPIRED TO BE DEFINED AT STATE LEVEL
- 24 = EXPIRED TO BE DEFINED AT STATE LEVEL
- 25 = EXPIRED TO BE DEFINED AT STATE LEVEL
- 26 = EXPIRED TO BE DEFINED AT STATE LEVEL
- 27 = EXPIRED TO BE DEFINED AT STATE LEVEL
- 28 = EXPIRED TO BE DEFINED AT STATE LEVEL
- 29 = EXPIRED TO BE DEFINED AT STATE LEVEL
- 40 = EXPIRED AT HOME (HOSPICE)
- 41 = EXPIRED IN A MEDICAL FACILITY (HOSPICE)
- 42 = EXPIRED - PLACE UNKNOWN (HOSPICE)

Truven-

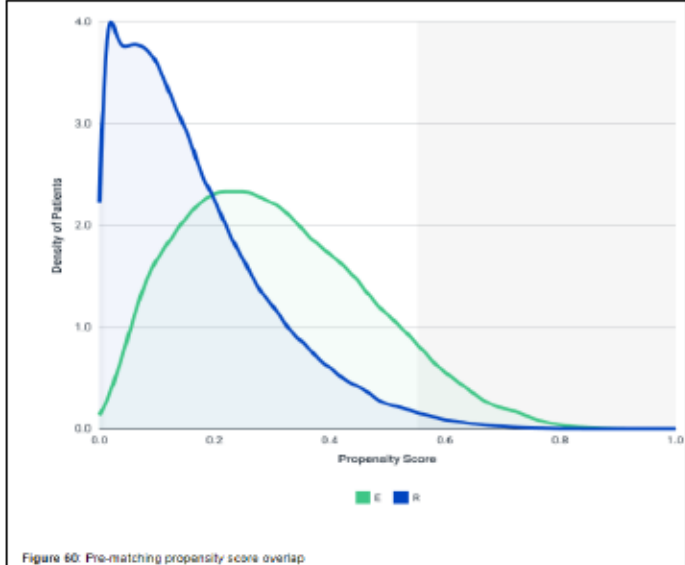
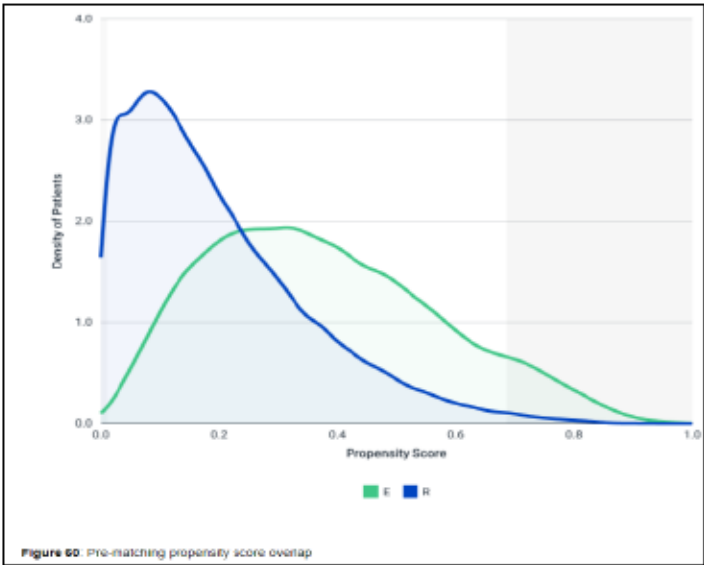
- 20 - Died
- 22 - Died
- 23 - Died
- 24 - Died
- 25 - Died
- 26 - Died
- 27 - Died
- 28 - Died
- 29 - Died
- 40 - Other died status or Expired at home (Hospice claims only) (depends on year)
- 41 - Other died status or Expired in medical facility (Hospice claims only) (depends on year)
- 42 - Other died status or Expired - place unknown (Hospice claims only) (depends on year)
- 21 - Died or Disch./Transf. to court/law enforcement (depends on year)

Appendix B

Optum

MarketScan

BEFORE PS MATCHING



The c-statistics for the propensity score model, pre-matching was 0.772. The post-matching c-statistic was 0.632.

The c-statistics for the propensity score model, pre-matching was 0.762. The post-matching c-statistic was 0.523.

AFTER PS MATCHING

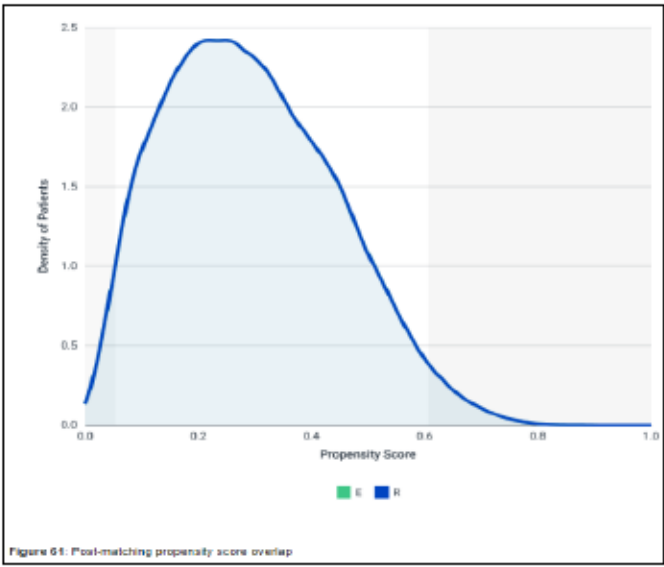
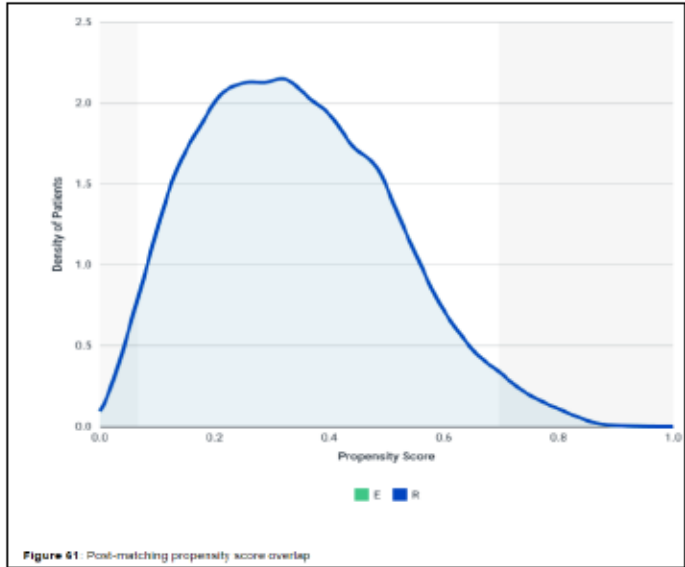


Table 1: Telmisartan vs Ramipril

Variable	Unmatched								
	Optum			Truven			POOLED		
	Ramipril (Any dose)	Telmisartan (Any dose)	St. Diff.	Ramipril (Any dose)	Telmisartan (Any dose)	St. Diff.	Ramipril (Any dose)	Telmisartan (Any dose)	St. Diff.
Number of patients	37,963	11,955		92,821	21,871		130,784	33,826	
Age									
...mean (sd)	68.65 (9.21)	69.57 (9.24)	-0.10	68.25 (9.67)	68.60 (9.78)	-0.04	68.37 (9.54)	68.94 (9.59)	-0.06
...median [IQR]	68.00 [61.00, 75.00]	69.00 [62.00, 76.00]	-0.11	66.00 [60.00, 76.00]	67.00 [60.00, 76.00]	-0.10	66.58 [9.54]	67.71 [9.59]	-0.12
Age categories									
...18 - 54; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	0,000 (0.0%)	0,000 (0.0%)	#DIV/0!
...55 - 64; n (%)	14,313 (37.7%)	3,963 (33.1%)	0.10	42,090 (45.3%)	9,615 (44.0%)	0.03	56,403 (43.1%)	13,578 (40.1%)	0.06
...65 - 74; n (%)	13,132 (34.6%)	4,251 (35.6%)	-0.02	24,764 (26.7%)	5,807 (26.6%)	0.00	37,896 (29.0%)	10,058 (29.7%)	-0.02
...≥ 75; n (%)	10,518 (27.7%)	3,741 (31.3%)	-0.08	25,967 (28.0%)	6,449 (29.5%)	-0.03	36,485 (27.9%)	10,190 (30.1%)	-0.05
Gender									
...Males; n (%)	23,547 (62.0%)	5,225 (43.7%)	0.37	57,804 (62.3%)	9,926 (45.4%)	0.34	81,351 (62.2%)	15,151 (44.8%)	0.35
...Females; n (%)	14,416 (38.0%)	6,730 (56.3%)	-0.37	35,017 (37.7%)	11,945 (54.6%)	-0.34	49,433 (37.8%)	18,675 (55.2%)	-0.35
Region									
...Northeast; n (%)	6,036 (15.9%)	1,167 (9.8%)	0.18	20,614 (22.2%)	3,034 (13.9%)	0.22	26,650 (20.4%)	4,201 (12.4%)	0.22
...South; n (%)	20,157 (53.1%)	7,419 (62.1%)	-0.18	25,327 (27.3%)	5,130 (23.5%)	0.09	45,484 (34.8%)	12,549 (37.1%)	-0.05
...Midwest; n (%)	5,635 (14.8%)	1,385 (11.6%)	0.09	36,314 (39.1%)	10,403 (47.6%)	-0.17	41,949 (32.1%)	11,788 (34.8%)	-0.06
...West; n (%)	6,135 (16.2%)	1,984 (16.6%)	-0.01	9,966 (10.7%)	3,170 (14.5%)	-0.11	16,101 (12.3%)	5,154 (15.2%)	-0.08
...Unknown+missing; n (%)	N/A	N/A	#VALUE!	600 (0.6%)	134 (0.6%)	0.00	600 (0.5%)	134 (0.4%)	0.01
CV Covariates									
Ischemic heart disease; n (%)	19,508 (51.4%)	3,708 (31.0%)	0.42	45,103 (48.6%)	6,024 (27.5%)	0.45	64,611 (49.4%)	9,732 (28.8%)	0.43
Acute MI; n (%)	4,164 (11.0%)	217 (1.8%)	0.38	10,774 (11.6%)	344 (1.6%)	0.41	14938 (11.4%)	561 (1.7%)	0.40
ACS/unstable angina; n (%)	3,085 (8.1%)	327 (2.7%)	0.24	7,863 (8.5%)	666 (3.0%)	0.24	10948 (8.4%)	993 (2.9%)	0.24
Old MI; n (%)	3,612 (9.5%)	516 (4.3%)	0.21	3,971 (4.3%)	354 (1.6%)	0.16	7583 (5.8%)	870 (2.6%)	0.16
Stable angina; n (%)	3,884 (10.2%)	824 (6.9%)	0.12	7,781 (8.4%)	1,206 (5.5%)	0.11	11,665 (8.9%)	2,030 (6.0%)	0.11
Coronary atherosclerosis and other forms of chronic ischemic heart disease; n (%)	18,048 (47.5%)	3,234 (27.1%)	0.43	40,383 (43.5%)	5,175 (23.7%)	0.43	58,431 (44.7%)	8,409 (24.9%)	0.42
Other atherosclerosis with ICD10 ; n (%)	1,228 (3.2%)	218 (1.8%)	0.09	2,275 (2.5%)	358 (1.6%)	0.06	3503 (2.7%)	576 (1.7%)	0.07
Previous cardiac procedure (CABG or PTCA or Stent) ; n (%)	3,749 (9.9%)	141 (1.2%)	0.39	8,424 (9.1%)	293 (1.3%)	0.36	12173 (9.3%)	434 (1.3%)	0.36
History of CABG or PTCA; n (%)	5,500 (14.5%)	791 (6.6%)	0.26	5,538 (6.0%)	526 (2.4%)	0.18	11,038 (8.4%)	1,317 (3.9%)	0.19
Any stroke; n (%)	6,534 (17.2%)	1,771 (14.8%)	0.07	15,361 (16.5%)	3,048 (13.9%)	0.07	21,895 (16.7%)	4,819 (14.2%)	0.07
Ischemic stroke (w and w/o mention of cerebral infarction); n (%)	6,483 (17.1%)	1,758 (14.7%)	0.07	15,281 (16.5%)	3,024 (13.8%)	0.08	21,764 (16.6%)	4,782 (14.1%)	0.07
Hemorrhagic stroke; n (%)	155 (0.4%)	39 (0.3%)	0.02	302 (0.3%)	60 (0.3%)	0.00	457 (0.3%)	99 (0.3%)	0.00
TIA; n (%)	1,799 (4.7%)	502 (4.2%)	0.02	4,340 (4.7%)	854 (3.9%)	0.04	6139 (4.7%)	1356 (4.0%)	0.03
Other cerebrovascular disease; n (%)	1,361 (3.6%)	366 (3.1%)	0.03	2,392 (2.6%)	467 (2.1%)	0.03	3753 (2.9%)	833 (2.5%)	0.02
Late effects of cerebrovascular disease; n (%)	1,141 (3.0%)	280 (2.3%)	0.04	1,693 (1.8%)	296 (1.4%)	0.03	2834 (2.2%)	576 (1.7%)	0.04
Cerebrovascular procedure; n (%)	183 (0.5%)	36 (0.3%)	0.03	460 (0.5%)	87 (0.4%)	0.01	643 (0.5%)	123 (0.4%)	0.01
Heart failure (CHF); n (%)	4,149 (10.9%)	901 (7.5%)	0.12	6,644 (7.2%)	1,019 (4.7%)	0.11	10,793 (8.3%)	1,920 (5.7%)	0.10
Peripheral Vascular Disease (PVD) or PVD Surgery ; n (%)	4,262 (11.2%)	1,255 (10.5%)	0.02	7,315 (7.9%)	1,563 (7.1%)	0.03	11,577 (8.9%)	2,818 (8.3%)	0.02
Atrial fibrillation; n (%)	3,981 (10.5%)	938 (7.8%)	0.09	8,576 (9.2%)	1,430 (6.5%)	0.10	12,557 (9.6%)	2,368 (7.0%)	0.09
Other cardiac dysrhythmia; n (%)	5,611 (14.8%)	1,339 (11.2%)	0.11	10,682 (11.5%)	1,720 (7.9%)	0.12	16,293 (12.5%)	3,059 (9.0%)	0.11

Table 1: Telmisartan vs Ramipril

Cardiac conduction disorders; n (%)	1,740 (4.6%)	360 (3.0%)	0.08	2,943 (3.2%)	394 (1.8%)	0.09	4683 (3.6%)	754 (2.2%)	0.08
Other CVD; n (%)	7,644 (20.1%)	1,732 (14.5%)	0.15	16,519 (17.8%)	2,560 (11.7%)	0.17	24,163 (18.5%)	4,292 (12.7%)	0.16
<b>Diabetes-related complications</b>									
Diabetic retinopathy; n (%)	2,266 (6.0%)	735 (6.1%)	0.00	3,866 (4.2%)	835 (3.8%)	0.02	6,132 (4.7%)	1,570 (4.6%)	0.00
Diabetes with other ophthalmic manifestations; n (%)	128 (0.3%)	60 (0.5%)	-0.03	2,595 (2.8%)	586 (2.7%)	0.01	2,723 (2.1%)	0,646 (1.9%)	0.01
Retinal detachment, vitreous hemorrhage, vitrectomy; n (%)	214 (0.6%)	63 (0.5%)	0.01	344 (0.4%)	79 (0.4%)	0.00	558 (0.4%)	142 (0.4%)	0.00
Retinal laser coagulation therapy; n (%)	309 (0.8%)	93 (0.8%)	0.00	832 (0.9%)	178 (0.8%)	0.01	1141 (0.9%)	271 (0.8%)	0.01
Occurrence of Diabetic Neuropathy ; n (%)	4,676 (12.3%)	1,528 (12.8%)	-0.02	6,411 (6.9%)	1,417 (6.5%)	0.02	11,087 (8.5%)	2,945 (8.7%)	-0.01
Occurrence of diabetic nephropathy with ICD10 ; n (%)	2,627 (6.9%)	1,065 (8.9%)	-0.07	2,726 (2.9%)	745 (3.4%)	-0.03	5,353 (4.1%)	1,810 (5.4%)	-0.06
Hypoglycemia; n (%)	760 (2.0%)	159 (1.3%)	0.05	1,607 (1.7%)	309 (1.4%)	0.02	2,367 (1.8%)	0,468 (1.4%)	0.03
Hyperglycemia; n (%)	1,254 (3.3%)	430 (3.6%)	-0.02	1,298 (1.4%)	312 (1.4%)	0.00	2,552 (2.0%)	0,742 (2.2%)	-0.01
Disorders of fluid electrolyte and acid-base balance; n (%)	2,764 (7.3%)	873 (7.3%)	0.00	4,269 (4.6%)	866 (4.0%)	0.03	7,033 (5.4%)	1,739 (5.1%)	0.01
Diabetic ketoacidosis; n (%)	152 (0.4%)	22 (0.2%)	0.04	269 (0.3%)	27 (0.1%)	0.04	421 (0.3%)	49 (0.1%)	0.04
Hyperosmolar hyperglycemic nonketotic syndrome (HONK); n (%)	107 (0.3%)	25 (0.2%)	0.02	145 (0.2%)	25 (0.1%)	0.03	252 (0.2%)	50 (0.1%)	0.03
Diabetes with peripheral circulatory disorders with ICD-10 ; n (%)	1,596 (4.2%)	482 (4.0%)	0.01	2,032 (2.2%)	364 (1.7%)	0.04	3,628 (2.8%)	0,846 (2.5%)	0.02
Diabetic Foot; n (%)	1,161 (3.1%)	319 (2.7%)	0.02	2,589 (2.8%)	586 (2.7%)	0.01	3750 (2.9%)	905 (2.7%)	0.01
Gangrene; n (%)	121 (0.3%)	22 (0.2%)	0.02	243 (0.3%)	24 (0.1%)	0.04	364 (0.3%)	46 (0.1%)	0.04
Lower extremity amputation; n (%)	239 (0.6%)	66 (0.6%)	0.00	350 (0.4%)	45 (0.2%)	0.04	589 (0.5%)	111 (0.3%)	0.03
Osteomyelitis; n (%)	307 (0.8%)	62 (0.5%)	0.04	612 (0.7%)	91 (0.4%)	0.04	919 (0.7%)	153 (0.5%)	0.03
Skin infections; n (%)	2,117 (5.6%)	635 (5.3%)	0.01	5,025 (5.4%)	1,101 (5.0%)	0.02	7,142 (5.5%)	1,736 (5.1%)	0.02
Erectile dysfunction; n (%)	1,035 (2.7%)	317 (2.7%)	0.00	1,359 (1.5%)	275 (1.3%)	0.02	2,394 (1.8%)	0,592 (1.8%)	0.00
Diabetes with unspecified complication; n (%)	969 (2.6%)	316 (2.6%)	0.00	1,763 (1.9%)	342 (1.6%)	0.02	2,732 (2.1%)	0,658 (1.9%)	0.01
Diabetes mellitus without mention of complications; n (%)	16,496 (43.5%)	5,002 (41.8%)	0.03	34,936 (37.6%)	7,565 (34.6%)	0.06	51,432 (39.3%)	12,567 (37.2%)	0.04
Hypertension: 1 inpatient or 2 outpatient claims within 365 days; n (%)	27,935 (73.6%)	10,512 (87.9%)	-0.37	48,516 (52.3%)	15,315 (70.0%)	-0.37	76,451 (58.5%)	25,827 (76.4%)	-0.39
Hyperlipidemia ; n (%)	25,720 (67.8%)	7,595 (63.5%)	0.09	37,915 (40.8%)	8,384 (38.3%)	0.05	63,635 (48.7%)	15,979 (47.2%)	0.03
Edema; n (%)	2,181 (5.7%)	1,016 (8.5%)	-0.11	3,441 (3.7%)	1,012 (4.6%)	-0.05	5,622 (4.3%)	2,028 (6.0%)	-0.08
Renal Dysfunction (non-diabetic) ; n (%)	5,308 (14.0%)	2,309 (19.3%)	-0.14	7,474 (8.1%)	2,213 (10.1%)	-0.07	12,782 (9.8%)	4,522 (13.4%)	-0.11
Occurrence of acute renal disease ; n (%)	862 (2.3%)	295 (2.5%)	-0.01	1,360 (1.5%)	303 (1.4%)	0.01	2222 (1.7%)	598 (1.8%)	-0.01
Occurrence of chronic renal insufficiency; n (%)	3,832 (10.1%)	1,818 (15.2%)	-0.15	4,683 (5.0%)	1,543 (7.1%)	-0.09	8,515 (6.5%)	3,361 (9.9%)	-0.12
Chronic kidney disease ; n (%)	3,530 (9.3%)	1,739 (14.5%)	-0.16	4,116 (4.4%)	1,430 (6.5%)	-0.09	7,646 (5.8%)	3,169 (9.4%)	-0.14
CKD Stage 3-4; n (%)	2,087 (5.5%)	1,181 (9.9%)	-0.17	2,245 (2.4%)	893 (4.1%)	-0.10	4,332 (3.3%)	2,074 (6.1%)	-0.13
Occurrence of hypertensive nephropathy; n (%)	1,681 (4.4%)	912 (7.6%)	-0.14	1,616 (1.7%)	592 (2.7%)	-0.07	3297 (2.5%)	1504 (4.4%)	-0.10
Occurrence of miscellaneous renal insufficiency ; n (%)	1,850 (4.9%)	712 (6.0%)	-0.05	3,018 (3.3%)	754 (3.4%)	-0.01	4,868 (3.7%)	1,466 (4.3%)	-0.03
Glaucoma or cataracts ; n (%)	6,825 (18.0%)	2,530 (21.2%)	-0.08	14,801 (15.9%)	3,941 (18.0%)	-0.06	21,626 (16.5%)	6,471 (19.1%)	-0.07
Cellulitis or abscess of toe; n (%)	460 (1.2%)	136 (1.1%)	0.01	792 (0.9%)	145 (0.7%)	0.02	1252 (1.0%)	281 (0.8%)	0.02
Foot ulcer; n (%)	1,180 (3.1%)	329 (2.8%)	0.02	2,675 (2.9%)	597 (2.7%)	0.01	3855 (2.9%)	926 (2.7%)	0.01

Table 1: Telmisartan vs Ramipril

Bladder stones; n (%)	58 (0.2%)	16 (0.1%)	0.03	121 (0.1%)	22 (0.1%)	0.00	179 (0.1%)	38 (0.1%)	0.00
Kidney stones; n (%)	728 (1.9%)	250 (2.1%)	-0.01	1,685 (1.8%)	358 (1.6%)	0.02	2,413 (1.8%)	0,608 (1.8%)	0.00
Urinary tract infections (UTIs); n (%)	3,325 (8.8%)	1,215 (10.2%)	-0.05	5,653 (6.1%)	1,384 (6.3%)	-0.01	8,978 (6.9%)	2,599 (7.7%)	-0.03
Dipstick urinalysis; n (%)	12,280 (32.3%)	4,415 (36.9%)	-0.10	21,781 (23.5%)	5,317 (24.3%)	-0.02	34,061 (26.0%)	9,732 (28.8%)	-0.06
Non-dipstick urinalysis; n (%)	7,839 (20.6%)	2,658 (22.2%)	-0.04	11,042 (11.9%)	2,434 (11.1%)	0.03	18,881 (14.4%)	5,092 (15.1%)	-0.02
Urine function test; n (%)	1,152 (3.0%)	335 (2.8%)	0.01	3,048 (3.3%)	705 (3.2%)	0.01	4,200 (3.2%)	1,040 (3.1%)	0.01
Cytology; n (%)	572 (1.5%)	146 (1.2%)	0.03	1,723 (1.9%)	321 (1.5%)	0.03	2295 (1.8%)	467 (1.4%)	0.03
Cystos; n (%)	773 (2.0%)	231 (1.9%)	0.01	2,146 (2.3%)	442 (2.0%)	0.02	2919 (2.2%)	673 (2.0%)	0.01
<b>Other Covariates</b>									
Liver disease; n (%)	633 (1.7%)	298 (2.5%)	-0.06	776 (0.8%)	162 (0.7%)	0.01	1,409 (1.1%)	0,460 (1.4%)	-0.03
Osteoarthritis; n (%)	5,538 (14.6%)	2,189 (18.3%)	-0.10	10,078 (10.9%)	2,895 (13.2%)	-0.07	15,616 (11.9%)	5,084 (15.0%)	-0.09
Other arthritis, arthropathies and musculoskeletal pain; n (%)	13,165 (34.7%)	4,673 (39.1%)	-0.09	27,287 (29.4%)	7,113 (32.5%)	-0.07	40,452 (30.9%)	11,786 (34.8%)	-0.08
Dorsopathies; n (%)	7,713 (20.3%)	2,886 (24.1%)	-0.09	15,687 (16.9%)	4,425 (20.2%)	-0.08	23,400 (17.9%)	7,311 (21.6%)	-0.09
Fractures; n (%)	1,320 (3.5%)	426 (3.6%)	-0.01	3,257 (3.5%)	735 (3.4%)	0.01	4,577 (3.5%)	1,161 (3.4%)	0.01
Falls; n (%)	1,059 (2.8%)	386 (3.2%)	-0.02	567 (0.6%)	136 (0.6%)	0.00	1626 (1.2%)	522 (1.5%)	-0.03
Osteoporosis; n (%)	2,577 (6.8%)	1,053 (8.8%)	-0.07	5,906 (6.4%)	1,733 (7.9%)	-0.06	8,483 (6.5%)	2,786 (8.2%)	-0.07
Hyperthyroidism; n (%)	264 (0.7%)	103 (0.9%)	-0.02	373 (0.4%)	103 (0.5%)	-0.01	637 (0.5%)	206 (0.6%)	-0.01
Hypothyroidism ; n (%)	5,075 (13.4%)	1,932 (16.2%)	-0.08	6,835 (7.4%)	1,915 (8.8%)	-0.05	11,910 (9.1%)	3,847 (11.4%)	-0.08
Other disorders of thyroid gland ; n (%)	1,131 (3.0%)	520 (4.3%)	-0.07	2,105 (2.3%)	640 (2.9%)	-0.04	3,236 (2.5%)	1,160 (3.4%)	-0.05
Depression; n (%)	2,849 (7.5%)	890 (7.4%)	0.00	4,424 (4.8%)	1,054 (4.8%)	0.00	7,273 (5.6%)	1,944 (5.7%)	0.00
Anxiety; n (%)	2,267 (6.0%)	896 (7.5%)	-0.06	2,793 (3.0%)	703 (3.2%)	-0.01	5,060 (3.9%)	1,599 (4.7%)	-0.04
Sleep Disorder; n (%)	2,613 (6.9%)	902 (7.5%)	-0.02	5,740 (6.2%)	1,789 (8.2%)	-0.08	8,353 (6.4%)	2,691 (8.0%)	-0.06
Dementia; n (%)	1,718 (4.5%)	466 (3.9%)	0.03	3,033 (3.3%)	548 (2.5%)	0.05	4751 (3.6%)	1014 (3.0%)	0.03
Delirium; n (%)	579 (1.5%)	134 (1.1%)	0.04	1,192 (1.3%)	168 (0.8%)	0.05	1771 (1.4%)	302 (0.9%)	0.05
Psychosis; n (%)	472 (1.2%)	95 (0.8%)	0.04	853 (0.9%)	124 (0.6%)	0.03	1325 (1.0%)	219 (0.6%)	0.04
Obesity; n (%)	3,470 (9.1%)	1,501 (12.6%)	-0.11	3,759 (4.0%)	1,033 (4.7%)	-0.03	7,229 (5.5%)	2,534 (7.5%)	-0.08
Overweight; n (%)	1,069 (2.8%)	505 (4.2%)	-0.08	606 (0.7%)	173 (0.8%)	-0.01	1,675 (1.3%)	0,678 (2.0%)	-0.05
Smoking; n (%)	4,937 (13.0%)	1,069 (8.9%)	0.13	4,821 (5.2%)	661 (3.0%)	0.11	9,758 (7.5%)	1,730 (5.1%)	0.10
Alcohol abuse or dependence; n (%)	427 (1.1%)	73 (0.6%)	0.05	524 (0.6%)	80 (0.4%)	0.03	951 (0.7%)	153 (0.5%)	0.03
Drug abuse or dependence; n (%)	361 (1.0%)	142 (1.2%)	-0.02	340 (0.4%)	75 (0.3%)	0.02	701 (0.5%)	217 (0.6%)	-0.01
COPD; n (%)	4,437 (11.7%)	1,308 (10.9%)	0.03	8,552 (9.2%)	1,752 (8.0%)	0.04	12,989 (9.9%)	3,060 (9.0%)	0.03
Asthma; n (%)	1,741 (4.6%)	784 (6.6%)	-0.09	3,318 (3.6%)	1,135 (5.2%)	-0.08	5,059 (3.9%)	1,919 (5.7%)	-0.08
Obstructive sleep apnea; n (%)	1,805 (4.8%)	895 (7.5%)	-0.11	3,711 (4.0%)	1,272 (5.8%)	-0.08	5,516 (4.2%)	2,167 (6.4%)	-0.10
Pneumonia; n (%)	1,189 (3.1%)	296 (2.5%)	0.04	3,095 (3.3%)	497 (2.3%)	0.06	4,284 (3.3%)	0,793 (2.3%)	0.06
Imaging; n (%)	166 (0.4%)	24 (0.2%)	0.04	14,801 (15.9%)	17 (0.1%)	0.61	291 (0.2%)	41 (0.1%)	0.03
<b>Other Medications</b>									
Use of ACE inhibitors; n (%)	37,963 (100.0%)	303 (2.5%)	8.83	92,821 (100.0%)	508 (2.3%)	9.22	130,784 (100.0%)	0,811 (2.4%)	9.02
Use of ARBs; n (%)	325 (0.9%)	11,955 (100.0%)	-14.84	833 (0.9%)	21,871 (100.0%)	-14.84	1,158 (0.9%)	33,826 (100.0%)	-14.84
Use of Loop Diuretics - ; n (%)	5,252 (13.8%)	1,577 (13.2%)	0.02	14,397 (15.5%)	3,030 (13.9%)	0.05	19,649 (15.0%)	4,607 (13.6%)	0.04
Use of other diuretics - ; n (%)	1,157 (3.0%)	294 (2.5%)	0.03	2,865 (3.1%)	556 (2.5%)	0.04	4,022 (3.1%)	0,850 (2.5%)	0.04
Use of nitrates - ; n (%)	5,526 (14.6%)	846 (7.1%)	0.24	16,635 (17.9%)	1,960 (9.0%)	0.26	22,161 (16.9%)	2,806 (8.3%)	0.26
Use of other hypertension drugs; n (%)	1,939 (5.1%)	1,098 (9.2%)	-0.16	4,883 (5.3%)	1,796 (8.2%)	-0.12	6,822 (5.2%)	2,894 (8.6%)	-0.13
Use of digoxin - ; n (%)	1,234 (3.3%)	208 (1.7%)	0.10	4,285 (4.6%)	574 (2.6%)	0.11	5519 (4.2%)	782 (2.3%)	0.11
Use of Anti-arrhythmics; n (%)	1,082 (2.9%)	242 (2.0%)	0.06	3,365 (3.6%)	490 (2.2%)	0.08	4447 (3.4%)	732 (2.2%)	0.07
Use of COPD/asthma meds - ; n (%)	4,953 (13.0%)	1,961 (16.4%)	-0.10	14,331 (15.4%)	3,907 (17.9%)	-0.07	19,284 (14.7%)	5,868 (17.3%)	-0.07
Use of statins; n (%)	24,481 (64.5%)	6,411 (53.6%)	0.22	61,328 (66.1%)	11,663 (53.3%)	0.26	85,809 (65.6%)	18,074 (53.4%)	0.25
Use of other lipid-lowering drugs; n (%)	4,845 (12.8%)	1,293 (10.8%)	0.06	14,291 (15.4%)	2,905 (13.3%)	0.06	19,136 (14.6%)	4,198 (12.4%)	0.06

Table 1: Telmisartan vs Ramipril

Use of oral anticoagulants (Dabigatran, Rivaroxaban, Apixaban, Warfarin); n (%)	3,071 (8.1%)	750 (6.3%)	0.07	8,984 (9.7%)	1,533 (7.0%)	0.10	12,055 (9.2%)	2,283 (6.7%)	0.09
Use of heparin and other low-molecular weight heparins; n (%)	251 (0.7%)	60 (0.5%)	0.03	45 (0.0%)	4 (0.0%)	#DIV/0!	296 (0.2%)	64 (0.2%)	0.00
Use of NSAIDs; n (%)	4,320 (11.4%)	1,727 (14.4%)	-0.09	10,853 (11.7%)	3,115 (14.2%)	-0.07	15,173 (11.6%)	4,842 (14.3%)	-0.08
Use of oral corticosteroids; n (%)	5,292 (13.9%)	2,068 (17.3%)	-0.09	14,014 (15.1%)	3,758 (17.2%)	-0.06	19,306 (14.8%)	5,826 (17.2%)	-0.07
Use of bisphosphonate (); n (%)	1,419 (3.7%)	570 (4.8%)	-0.05	4,290 (4.6%)	1,266 (5.8%)	-0.05	5709 (4.4%)	1836 (5.4%)	-0.05
Use of opioids; n (%)	9,421 (24.8%)	3,054 (25.5%)	-0.02	24,882 (26.8%)	6,229 (28.5%)	-0.04	34,303 (26.2%)	9,283 (27.4%)	-0.03
Use of antidepressants; n (%)	7,526 (19.8%)	2,613 (21.9%)	-0.05	19,409 (20.9%)	4,795 (21.9%)	-0.02	26,935 (20.6%)	7,408 (21.9%)	-0.03
Use of antipsychotics; n (%)	699 (1.8%)	186 (1.6%)	0.02	1,810 (1.9%)	386 (1.8%)	0.01	2,509 (1.9%)	0,572 (1.7%)	0.02
Use of anticonvulsants; n (%)	4,282 (11.3%)	1,487 (12.4%)	-0.03	9,523 (10.3%)	2,404 (11.0%)	-0.02	13,805 (10.6%)	3,891 (11.5%)	-0.03
Use of lithium; n (%)	74 (0.2%)	9 (0.1%)	0.03	159 (0.2%)	30 (0.1%)	0.03	233 (0.2%)	39 (0.1%)	0.03
Use of Benzos; n (%)	3,780 (10.0%)	1,435 (12.0%)	-0.06	12,311 (13.3%)	3,365 (15.4%)	-0.06	16,091 (12.3%)	4,800 (14.2%)	-0.06
Use of anxiolytics/hypnotics; n (%)	2,506 (6.6%)	858 (7.2%)	-0.02	7,377 (7.9%)	2,006 (9.2%)	-0.05	9,883 (7.6%)	2,864 (8.5%)	-0.03
Use of dementia meds; n (%)	1,026 (2.7%)	322 (2.7%)	0.00	2,537 (2.7%)	592 (2.7%)	0.00	3563 (2.7%)	914 (2.7%)	0.00
Use of antiparkinsonian meds; n (%)	769 (2.0%)	254 (2.1%)	-0.01	2,048 (2.2%)	575 (2.6%)	-0.03	2,817 (2.2%)	0,829 (2.5%)	-0.02
Entresto (sacubitril/valsartan); n (%)	22 (0.1%)	3 (0.0%)	0.04	17 (0.0%)	1 (0.0%)	#DIV/0!	39 (0.0%)	4 (0.0%)	#DIV/0!
Labs							0	0	
Lab values- HbA1c (%); n (%)	6,272 (16.5%)	2,302 (19.3%)	-0.07	1,279 (1.4%)	286 (1.3%)	0.01	7,551 (5.8%)	2,588 (7.7%)	-0.08
Lab values- HbA1c (%) (within 3 months); n (%)	4,439 (11.7%)	1,572 (13.1%)	-0.04	917 (1.0%)	198 (0.9%)	0.01	5,356 (4.1%)	1,770 (5.2%)	-0.05
Lab values- HbA1c (%) (within 6 months); n (%)	6,272 (16.5%)	2,302 (19.3%)	-0.07	1,279 (1.4%)	286 (1.3%)	0.01	7,551 (5.8%)	2,588 (7.7%)	-0.08
Lab values- BNP; n (%)	242 (0.6%)	82 (0.7%)	-0.01	30 (0.0%)	6 (0.0%)	#DIV/0!	272 (0.2%)	88 (0.3%)	-0.02
Lab values- BNP (within 3 months); n (%)	173 (0.5%)	55 (0.5%)	0.00	21 (0.0%)	3 (0.0%)	#DIV/0!	194 (0.1%)	58 (0.2%)	-0.03
Lab values- BNP (within 6 months); n (%)	242 (0.6%)	82 (0.7%)	-0.01	30 (0.0%)	6 (0.0%)	#DIV/0!	272 (0.2%)	88 (0.3%)	-0.02
Lab values- BUN (mg/dl); n (%)	9,218 (24.3%)	3,511 (29.4%)	-0.12	1,435 (1.5%)	341 (1.6%)	-0.01	10,653 (8.1%)	3,852 (11.4%)	-0.11
Lab values- BUN (mg/dl) (within 3 months); n (%)	6,592 (17.4%)	2,507 (21.0%)	-0.09	1,028 (1.1%)	238 (1.1%)	0.00	7,620 (5.8%)	2,745 (8.1%)	-0.09
Lab values- BUN (mg/dl) (within 6 months); n (%)	9,218 (24.3%)	3,511 (29.4%)	-0.12	1,435 (1.5%)	341 (1.6%)	-0.01	10,653 (8.1%)	3,852 (11.4%)	-0.11
Lab values- Creatinine (mg/dl); n (%)	9,536 (25.1%)	3,630 (30.4%)	-0.12	1,550 (1.7%)	372 (1.7%)	0.00	11,086 (8.5%)	4,002 (11.8%)	-0.11
Lab values- Creatinine (mg/dl) (within 3 months); n (%)	6,818 (18.0%)	2,584 (21.6%)	-0.09	1,127 (1.2%)	260 (1.2%)	0.00	7,945 (6.1%)	2,844 (8.4%)	-0.09
Lab values- Creatinine (mg/dl) (within 6 months); n (%)	9,536 (25.1%)	3,630 (30.4%)	-0.12	1,550 (1.7%)	372 (1.7%)	0.00	11,086 (8.5%)	4,002 (11.8%)	-0.11
Lab values- HDL level (mg/dl); n (%)	7,182 (18.9%)	2,656 (22.2%)	-0.08	1,289 (1.4%)	290 (1.3%)	0.01	8,471 (6.5%)	2,946 (8.7%)	-0.08
Lab values- HDL level (mg/dl) (within 3 months); n (%)	4,912 (12.9%)	1,760 (14.7%)	-0.05	893 (1.0%)	184 (0.8%)	0.02	5,805 (4.4%)	1,944 (5.7%)	-0.06
Lab values- HDL level (mg/dl) (within 6 months); n (%)	7,182 (18.9%)	2,656 (22.2%)	-0.08	1,289 (1.4%)	290 (1.3%)	0.01	8,471 (6.5%)	2,946 (8.7%)	-0.08
Lab values- LDL level (mg/dl); n (%)	8,000 (21.1%)	2,859 (23.9%)	-0.07	1,313 (1.4%)	299 (1.4%)	0.00	9,313 (7.1%)	3,158 (9.3%)	-0.08
Lab values- LDL level (mg/dl) (within 3 months); n (%)	5,499 (14.5%)	1,895 (15.9%)	-0.04	910 (1.0%)	190 (0.9%)	0.01	6,409 (4.9%)	2,085 (6.2%)	-0.06
Lab values- LDL level (mg/dl) (within 6 months); n (%)	8,000 (21.1%)	2,859 (23.9%)	-0.07	1,313 (1.4%)	299 (1.4%)	0.00	9,313 (7.1%)	3,158 (9.3%)	-0.08
Lab values- NT-proBNP; n (%)	38 (0.1%)	22 (0.2%)	-0.03	3 (0.0%)	0 (0.0%)	#DIV/0!	41 (0.0%)	22 (0.1%)	-0.04
Lab values- NT-proBNP (within 3 months); n (%)	24 (0.1%)	12 (0.1%)	0.00	3 (0.0%)	0 (0.0%)	#DIV/0!	27 (0.0%)	12 (0.0%)	#DIV/0!

Table 1: Telmisartan vs Ramipril

Lab values- NT-proBNP (within 6 months); n (%)	38 (0.1%)	22 (0.2%)	-0.03	3 (0.0%)	0 (0.0%)	#DIV/0!	41 (0.0%)	22 (0.1%)	-0.04
Lab values- Total cholesterol (mg/dl); n (%)	8,031 (21.2%)	2,864 (24.0%)	-0.07	1,323 (1.4%)	299 (1.4%)	0.00	9,354 (7.2%)	3,163 (9.4%)	-0.08
Lab values- Total cholesterol (mg/dl) (within 3 months); n (%)	5,524 (14.6%)	1,899 (15.9%)	-0.04	919 (1.0%)	188 (0.9%)	0.01	6,443 (4.9%)	2,087 (6.2%)	-0.06
Lab values- Total cholesterol (mg/dl) (within 6 months); n (%)	8,031 (21.2%)	2,864 (24.0%)	-0.07	1,323 (1.4%)	299 (1.4%)	0.00	9,354 (7.2%)	3,163 (9.4%)	-0.08
Lab values- Triglyceride level (mg/dl); n (%)	7,813 (20.6%)	2,828 (23.7%)	-0.07	1,314 (1.4%)	293 (1.3%)	0.01	9,127 (7.0%)	3,121 (9.2%)	-0.08
Lab values- Triglyceride level (mg/dl) (within 3 months); n (%)	5,376 (14.2%)	1,878 (15.7%)	-0.04	912 (1.0%)	186 (0.9%)	0.01	6,288 (4.8%)	2,064 (6.1%)	-0.06
Lab values- Triglyceride level (mg/dl) (within 6 months); n (%)	7,813 (20.6%)	2,828 (23.7%)	-0.07	1,314 (1.4%)	293 (1.3%)	0.01	9,127 (7.0%)	3,121 (9.2%)	-0.08
Lab result number- HbA1c (%) mean (only 2 to 20 included)	5,992	2,235		1,237	276		0	0	
...mean (sd)	7.19 (1.66)	6.93 (1.58)	0.16	7.59 (1.79)	7.24 (1.63)	0.20	7.47 (1.75)	7.13 (1.61)	0.20
...median [IQR]	6.70 [6.00, 7.85]	6.50 [5.90, 7.55]	0.12	7.10 [6.30, 8.30]	6.75 [6.10, 8.00]	0.20	6.98 (1.75)	6.66 (1.61)	0.19
...Missing; n (%)	31,971 (84.2%)	9,720 (81.3%)	0.08	91,584 (98.7%)	21,595 (98.7%)	0.00	123,555 (94.5%)	31,315 (92.6%)	0.08
Lab result number- BNP mean	242	82		30	6		0	0	
...mean (sd)	231.84 (419.63)	184.35 (414.42)	0.11	8,444.38 (45,622.79)	40.33 (28.20)	0.26	6060.51 (38435.82)	91.23 (247.41)	0.22
...median [IQR]	105.35 [39.08, 225.15]	69.65 [30.48, 152.00]	0.09	74.10 [23.00, 177.00]	42.00 [18.00, 66.00]	0.00	83.17 (38435.82)	51.77 (247.41)	0.00
...Missing; n (%)	37,721 (99.4%)	11,873 (99.3%)	0.01	92,791 (100.0%)	21,865 (100.0%)	#DIV/0!	130,512 (99.8%)	33,738 (99.7%)	0.02
Lab result number- BUN (mg/dl) mean	9,218	3,511		1,435	341		0	0	
...mean (sd)	-18.62 (3,471.95)	-503.49 (19,685.58)	0.03	1,284.61 (16,530.91)	634.14 (8,037.23)	0.05	906.32 (14051.61)	232.07 (13368.79)	0.05
...median [IQR]	17.00 [13.00, 21.00]	17.00 [13.50, 22.00]	0.00	16.67 [13.00, 21.00]	16.50 [14.00, 21.62]	0.00	16.77 (14051.61)	16.68 (13368.79)	0.00
...Missing; n (%)	28,745 (75.7%)	8,444 (70.6%)	0.12	91,386 (98.5%)	21,530 (98.4%)	0.01	120,131 (91.9%)	29,974 (88.6%)	0.11
Lab result number- Creatinine (mg/dl) mean (only 0.1 to 15 included)	8,971	3,488		1,514	364		0	0	
...mean (sd)	1.04 (0.43)	1.08 (0.55)	-0.08	1.00 (0.39)	1.04 (0.46)	-0.09	1.01 (0.40)	1.05 (0.49)	-0.09
...median [IQR]	0.97 [0.82, 1.16]	0.97 [0.80, 1.20]	0.00	0.94 [0.79, 1.10]	0.94 [0.78, 1.15]	0.00	0.95 (0.40)	0.95 (0.49)	0.00
...Missing; n (%)	28,992 (76.4%)	8,467 (70.8%)	0.13	91,307 (98.4%)	21,507 (98.3%)	0.01	120,299 (92.0%)	29,974 (88.6%)	0.12
Lab result number- HDL level (mg/dl) mean (only <=5000 included)	7,182	2,656		1,283	289		0	0	
...mean (sd)	47.33 (17.84)	50.53 (17.48)	-0.18	46.98 (15.84)	48.11 (17.13)	-0.07	47.08 (16.45)	48.97 (17.25)	-0.11
...median [IQR]	46.00 [38.00, 57.00]	49.00 [40.00, 59.62]	-0.17	45.00 [37.50, 54.67]	46.00 [37.00, 57.00]	-0.06	45.29 (16.45)	47.06 (17.25)	-0.11
...Missing; n (%)	30,781 (81.1%)	9,299 (77.8%)	0.08	91,538 (98.6%)	21,582 (98.7%)	-0.01	122,319 (93.5%)	30,881 (91.3%)	0.08
Lab result number- LDL level (mg/dl) mean (only <=5000 included)	7,845	2,824		1,270	293		0	0	
...mean (sd)	-3,429.61 (57,169.13)	-1,780.42 (40,246.04)	-0.03	90.45 (42.42)	94.53 (47.17)	-0.09	-931.33 (30800.83)	-568.13 (23925.88)	-0.01
...median [IQR]	85.00 [61.50, 112.00]	90.00 [67.00, 116.00]	0.00	88.00 [65.00, 113.00]	89.00 [65.00, 121.00]	-0.02	87.13 (30800.83)	89.35 (23925.88)	0.00
...Missing; n (%)	30,118 (79.3%)	9,131 (76.4%)	0.07	91,551 (98.6%)	21,578 (98.7%)	-0.01	121,669 (93.0%)	30,709 (90.8%)	0.08

# Table 1: Telmisartan vs Ramipril

Lab result number- Total cholesterol (mg/dl) mean (only <=5000 included)	8,026	2,862		1,317	297		0	0	
...mean (sd)	163.98 (62.21)	170.82 (54.20)	-0.12	172.04 (54.21)	182.87 (58.76)	-0.19	169.70 (56.65)	178.61 (57.19)	-0.16
...median [IQR]	165.00 [137.00, 198.00]	171.00 [143.38, 201.00]	-0.10	168.00 [141.17, 199.75]	177.75 [151.00, 206.25]	-0.17	167.13 (56.65)	175.36 (57.19)	-0.14
...Missing; n (%)	29,937 (78.9%)	9,093 (76.1%)	0.07	91,504 (98.6%)	21,574 (98.6%)	0.00	121,441 (92.9%)	30,667 (90.7%)	0.08
Lab result number- Triglyceride level (mg/dl) mean (only <=5000 included)	7,812	2,828		1,308	292		0	0	
...mean (sd)	145.34 (119.44)	141.55 (95.58)	0.04	162.46 (135.71)	192.41 (285.64)	-0.13	157.49 (131.20)	174.43 (236.61)	-0.09
...median [IQR]	122.00 [84.00, 177.00]	121.00 [87.00, 172.00]	0.01	136.00 [92.00, 190.50]	145.00 [102.00, 211.75]	-0.04	131.94 (131.20)	136.52 (236.61)	-0.02
...Missing; n (%)	30,151 (79.4%)	9,127 (76.3%)	0.07	91,513 (98.6%)	21,579 (98.7%)	-0.01	121,664 (93.0%)	30,706 (90.8%)	0.08
Lab result number- Hemoglobin mean (only >0 included)	6,569	2,671		990	254		0	0	
...mean (sd)	-1,026.52 (29,854.92)	13.30 (1.68)	-0.05	11,174.87 (318,011.67)	1,071.92 (11,916.90)	0.04	7633.14 (268392.99)	697.78 (9582.42)	0.04
...median [IQR]	13.80 [12.70, 14.90]	13.30 [12.20, 14.40]	0.00	13.90 [12.70, 14.90]	13.40 [12.30, 14.22]	0.00	13.87 (268392.99)	13.36 (9582.42)	0.00
...Missing; n (%)	31,394 (82.7%)	9,284 (77.7%)	0.13	91,831 (98.9%)	21,617 (98.8%)	0.01	123,225 (94.2%)	30,901 (91.4%)	0.11
Lab result number- Serum sodium mean (only >90 and <190 included)	8,774	3,449		1,297	309		0	0	
...mean (sd)	140.07 (2.63)	140.28 (2.88)	-0.08	139.68 (2.44)	139.60 (2.37)	0.03	139.79 (2.50)	139.84 (2.56)	-0.02
...median [IQR]	140.00 [139.00, 142.00]	140.50 [139.00, 142.00]	-0.18	140.00 [138.00, 141.00]	140.00 [138.00, 141.00]	0.00	140.00 (2.50)	140.18 (2.56)	-0.07
...Missing; n (%)	29,189 (76.9%)	8,506 (71.2%)	0.13	91,524 (98.6%)	21,562 (98.6%)	0.00	120,713 (92.3%)	30,068 (88.9%)	0.12
Lab result number- Albumin mean (only >0 and <=10 included)	8,299	3,240		1,218	293		0	0	
...mean (sd)	4.22 (0.34)	4.21 (0.35)	0.03	4.18 (0.66)	4.12 (0.69)	0.09	4.19 (0.59)	4.15 (0.59)	0.07
...median [IQR]	4.20 [4.00, 4.40]	4.20 [4.00, 4.40]	0.00	4.25 [4.06, 4.50]	4.20 [4.00, 4.40]	0.07	4.24 (0.59)	4.20 (0.59)	0.07
...Missing; n (%)	29,664 (78.1%)	8,715 (72.9%)	0.12	91,603 (98.7%)	21,578 (98.7%)	0.00	121,267 (92.7%)	30,293 (89.6%)	0.11
Lab result number- Glucose (fasting or random) mean (only 10-1000 included)	8,610	3,424		1,294	309		0	0	
...mean (sd)	128.64 (56.57)	121.53 (51.47)	0.13	143.08 (62.07)	137.82 (59.51)	0.09	138.89 (60.53)	132.06 (56.80)	0.12
...median [IQR]	109.00 [94.00, 143.00]	105.00 [92.54, 133.00]	0.07	125.00 [102.00, 164.25]	120.00 [100.00, 157.50]	0.08	120.36 (60.53)	114.70 (56.80)	0.10
...Missing; n (%)	29,353 (77.3%)	8,531 (71.4%)	0.14	91,527 (98.6%)	21,562 (98.6%)	0.00	120,880 (92.4%)	30,093 (89.0%)	0.12
Lab result number- Potassium mean (only 1-7 included)	8,888	3,490		1,383	334		0	0	
...mean (sd)	4.44 (0.42)	4.39 (0.44)	0.12	4.41 (0.41)	4.33 (0.43)	0.19	4.42 (0.41)	4.35 (0.43)	0.17
...median [IQR]	4.40 [4.20, 4.70]	4.40 [4.10, 4.70]	0.00	4.40 [4.18, 4.70]	4.30 [4.10, 4.60]	0.24	4.40 (0.41)	4.34 (0.43)	0.14
...Missing; n (%)	29,075 (76.6%)	8,465 (70.8%)	0.13	91,438 (98.5%)	21,537 (98.5%)	0.00	120,513 (92.1%)	30,002 (88.7%)	0.12
Comorbidity Scores									
CCI (180 days)- ICD9 and ICD10									
...mean (sd)	2.43 (1.94)	2.49 (1.89)	-0.03	1.71 (1.64)	1.71 (1.52)	0.00	1.92 (1.73)	1.99 (1.66)	-0.04
...median [IQR]	2.00 [1.00, 3.00]	2.00 [1.00, 3.00]	0.00	1.00 [1.00, 2.00]	1.00 [1.00, 2.00]	0.00	1.29 (1.73)	1.35 (1.66)	-0.04
Frailty Score (mean): Empirical Version 365 days,									
...mean (sd)	0.18 (0.06)	0.17 (0.06)	0.17	0.16 (0.05)	0.16 (0.05)	0.00	0.17 (0.05)	0.16 (0.05)	0.20
...median [IQR]	0.16 [0.14, 0.20]	0.16 [0.14, 0.20]	0.00	0.15 [0.13, 0.18]	0.15 [0.13, 0.18]	0.00	0.15 (0.05)	0.15 (0.05)	0.00

Table 1: Telmisartan vs Ramipril

<b>Healthcare Utilization</b>									
Any hospitalization; n (%)	8,075 (21.3%)	1,130 (9.5%)	0.33	24,371 (26.3%)	2,561 (11.7%)	0.38	32,446 (24.8%)	3,691 (10.9%)	0.37
Any hospitalization during prior 31-180 days; n (%)	3,508 (9.2%)	900 (7.5%)	0.06	11,208 (12.1%)	1,988 (9.1%)	0.10	14,716 (11.3%)	2,888 (8.5%)	0.09
Endocrinologist Visit; n (%)	3,025 (8.0%)	835 (7.0%)	0.04	6,470 (7.0%)	1,263 (5.8%)	0.05	9,495 (7.3%)	2,098 (6.2%)	0.04
Endocrinologist Visit (30 days prior); n (%)	1,441 (3.8%)	300 (2.5%)	0.07	3,063 (3.3%)	475 (2.2%)	0.07	4,504 (3.4%)	0,775 (2.3%)	0.07
Endocrinologist Visit (31 to 180 days prior); n (%)	2,445 (6.4%)	722 (6.0%)	0.02	5,250 (5.7%)	1,105 (5.1%)	0.03	7,695 (5.9%)	1,827 (5.4%)	0.02
Internal medicine/family medicine visits; n (%)	28,199 (74.3%)	9,198 (76.9%)	-0.06	68,739 (74.1%)	17,095 (78.2%)	-0.10	96,938 (74.1%)	26,293 (77.7%)	-0.08
Internal medicine/family medicine visits (30 days prior); n (%)	18,818 (49.6%)	5,859 (49.0%)	0.01	43,764 (47.1%)	10,543 (48.2%)	-0.02	62,582 (47.9%)	16,402 (48.5%)	-0.01
Internal medicine/family medicine visits (31 to 180 days prior); n (%)	23,757 (62.6%)	8,113 (67.9%)	-0.11	59,359 (63.9%)	15,346 (70.2%)	-0.13	83,116 (63.6%)	23,459 (69.4%)	-0.12
Cardiologist visit; n (%)	19,758 (52.0%)	4,641 (38.8%)	0.27	38,839 (41.8%)	7,118 (32.5%)	0.19	58,597 (44.8%)	11,759 (34.8%)	0.21
Number of Cardiologist visits (30 days prior); n (%)	12,595 (33.2%)	1,986 (16.6%)	0.39	23,165 (25.0%)	3,090 (14.1%)	0.28	35,760 (27.3%)	5,076 (15.0%)	0.30
Number of Cardiologist visits (31 to 180 days prior); n (%)	12,948 (34.1%)	3,810 (31.9%)	0.05	27,848 (30.0%)	5,830 (26.7%)	0.07	40,796 (31.2%)	9,640 (28.5%)	0.06
Electrocardiogram ; n (%)	18,432 (48.6%)	4,720 (39.5%)	0.18	44,610 (48.1%)	8,382 (38.3%)	0.20	63,042 (48.2%)	13,102 (38.7%)	0.19
Use of glucose test strips; n (%)	983 (2.6%)	304 (2.5%)	0.01	1,782 (1.9%)	359 (1.6%)	0.02	2,765 (2.1%)	0,663 (2.0%)	0.01
Dialysis; n (%)	97 (0.3%)	38 (0.3%)	0.00	270 (0.3%)	46 (0.2%)	0.02	367 (0.3%)	84 (0.2%)	0.02
number of different/distinct medication prescriptions									
...mean (sd)	8.27 (4.55)	8.49 (4.96)	-0.05	8.96 (4.84)	8.80 (5.02)	0.03	8.76 (4.76)	8.69 (5.00)	0.01
...median [IQR]	7.00 [5.00, 11.00]	8.00 [5.00, 11.00]	-0.21	8.00 [5.00, 12.00]	8.00 [5.00, 11.00]	0.00	7.71 (4.76)	8.00 (5.00)	-0.06
Number of Hospitalizations									
...mean (sd)	0.25 (0.54)	0.11 (0.38)	0.30	0.30 (0.55)	0.13 (0.39)	0.36	0.29 (0.55)	0.12 (0.39)	0.36
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 1.00]	0.00 [0.00, 0.00]	0.00	0.00 (0.55)	0.00 (0.39)	0.00
Number of hospital days									
...mean (sd)	1.43 (4.41)	0.63 (3.03)	0.21	1.68 (4.87)	0.69 (3.02)	0.24	1.61 (4.74)	0.67 (3.02)	0.24
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 2.00]	0.00 [0.00, 0.00]	0.00	0.00 (4.74)	0.00 (3.02)	0.00
Number of Emergency Department (ED) visits									
...mean (sd)	0.49 (1.17)	0.45 (1.17)	0.03	0.38 (2.09)	0.12 (0.99)	0.16	0.41 (1.87)	0.24 (1.06)	0.11
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 (1.87)	0.00 (1.06)	0.00
Number of Office visits									
...mean (sd)	4.96 (4.38)	5.57 (4.52)	-0.14	5.13 (4.53)	5.68 (4.71)	-0.12	5.08 (4.49)	5.64 (4.64)	-0.12
...median [IQR]	4.00 [2.00, 7.00]	5.00 [2.00, 8.00]	-0.22	4.00 [2.00, 7.00]	5.00 [2.00, 8.00]	-0.22	4.00 (4.49)	5.00 (4.64)	-0.22
Number of Endocrinologist visits									
...mean (sd)	0.40 (2.14)	0.33 (1.90)	0.03	0.35 (2.02)	0.27 (1.73)	0.04	0.39 (1.81)	0.33 (1.56)	0.04
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 (1.81)	0.00 (1.56)	0.00
Number of internal medicine/family medicine visits									
...mean (sd)	7.74 (13.04)	8.18 (12.63)	-0.03	6.03 (10.20)	6.47 (9.97)	-0.04	6.53 (11.10)	7.07 (10.98)	-0.05
...median [IQR]	4.00 [0.00, 9.00]	4.00 [1.00, 10.00]	0.00	3.00 [0.00, 8.00]	4.00 [1.00, 8.00]	-0.10	3.29 (11.10)	4.00 (10.98)	-0.06
Number of Cardiologist visits									
...mean (sd)	4.20 (7.38)	2.14 (4.66)	0.33	2.55 (5.30)	1.74 (4.19)	0.17	3.03 (5.98)	1.88 (4.36)	0.22

Table 1: Telmisartan vs Ramipril

...median [IQR]	1.00 [0.00, 6.00]	0.00 [0.00, 2.00]	0.16	0.00 [0.00, 3.00]	0.00 [0.00, 2.00]	0.00	0.29 (5.98)	0.00 (4.36)	0.06
Number electrocardiograms received									
...mean (sd)	1.24 (2.26)	0.79 (1.46)	0.24	0.93 (1.50)	0.66 (1.17)	0.20	1.02 (1.75)	0.71 (1.28)	0.20
...median [IQR]	0.00 [0.00, 2.00]	0.00 [0.00, 1.00]	0.00	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00	0.00 (1.75)	0.00 (1.28)	0.00
Number of HbA1c tests ordered									
...mean (sd)	0.59 (0.86)	0.63 (0.85)	-0.05	0.33 (0.69)	0.31 (0.66)	0.03	0.41 (0.74)	0.42 (0.73)	-0.01
...median [IQR]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 (0.74)	0.00 (0.73)	0.00
Number of glucose tests ordered									
...mean (sd)	0.32 (2.23)	0.30 (1.23)	0.01	0.19 (1.31)	0.18 (0.73)	0.01	0.23 (1.63)	0.22 (0.94)	0.01
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 (1.63)	0.00 (0.94)	0.00
Number of lipid tests ordered									
...mean (sd)	0.83 (1.02)	0.82 (0.96)	0.01	0.49 (0.98)	0.46 (0.91)	0.03	0.59 (0.99)	0.59 (0.93)	0.00
...median [IQR]	1.00 [0.00, 1.00]	1.00 [0.00, 1.00]	0.00	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00	0.29 (0.99)	0.35 (0.93)	-0.06
Number of creatinine tests ordered									
...mean (sd)	0.07 (0.41)	0.08 (0.45)	-0.02	0.05 (0.32)	0.06 (0.34)	-0.03	0.06 (0.35)	0.07 (0.38)	-0.03
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 (0.35)	0.00 (0.38)	0.00
Number of BUN tests ordered									
...mean (sd)	0.05 (0.41)	0.06 (0.51)	-0.02	0.04 (0.32)	0.04 (0.36)	0.00	0.04 (0.35)	0.05 (0.42)	-0.03
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 (0.35)	0.00 (0.42)	0.00
Number of tests for microalbuminuria									
...mean (sd)	0.37 (0.91)	0.40 (0.94)	-0.03	0.19 (0.64)	0.17 (0.61)	0.03	0.24 (0.73)	0.25 (0.74)	-0.01
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 (0.73)	0.00 (0.74)	0.00
Total N distinct ICD9/ICD10 diagnoses at the 3rd digit level									
...mean (sd)	4.10 (6.83)	5.20 (7.87)	-0.15	1.74 (4.15)	1.33 (3.39)	0.11	2.43 (5.08)	2.70 (5.41)	-0.05
...median [IQR]	0.00 [0.00, 6.00]	2.00 [0.00, 8.00]	-0.27	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00	0.00 (5.08)	0.71 (5.41)	-0.14
For PS									
Hemorrhagic stroke+Other cerebrovascular disease+Cerebrovascular procedure (for PS); n (%)	1,573 (4.1%)	420 (3.5%)	0.03	2,937 (3.2%)	576 (2.6%)	0.04	4,510 (3.4%)	996 (2.9%)	0.03
Occurrence of creatinine tests ordered (for PS); n (%)	2,017 (5.3%)	671 (5.6%)	-0.01	3,713 (4.0%)	866 (4.0%)	0.00	5,730 (4.4%)	1,537 (4.5%)	0.00
Occurrence of BUN tests ordered (for PS); n (%)	1,339 (3.5%)	433 (3.6%)	-0.01	2,756 (3.0%)	607 (2.8%)	0.01	4,095 (3.1%)	1,040 (3.1%)	0.00
Occurrence of chronic renal insufficiency w/o CKD (for PS); n (%)	1,645 (4.3%)	672 (5.6%)	-0.06	1,963 (2.1%)	584 (2.7%)	-0.04	3,608 (2.8%)	1,256 (3.7%)	-0.05
Chronic kidney disease Stage 1-2 (for PS); n (%)	779 (2.1%)	344 (2.9%)	-0.05	669 (0.7%)	241 (1.1%)	-0.04	1,448 (1.1%)	585 (1.7%)	-0.05
Chronic kidney disease Stage 3-6 (for PS); n (%)	2,242 (5.9%)	1,272 (10.6%)	-0.17	2,667 (2.9%)	1,012 (4.6%)	-0.09	4,909 (3.8%)	2,284 (6.8%)	-0.13
Bladder stones+Kidney stones (for PS); n (%)	758 (2.0%)	257 (2.1%)	-0.01	1,741 (1.9%)	369 (1.7%)	0.02	2,499 (1.9%)	0,626 (1.9%)	0.00
Diabetes with peripheral circulatory disorders+Gangrene+Osteomyelitis(for PS) with ICD10 ; n (%)	1,851 (4.9%)	532 (4.5%)	0.02	2,580 (2.8%)	460 (2.1%)	0.05	4,431 (3.4%)	0,992 (2.9%)	0.03
Alcohol abuse or dependence+Drug abuse or dependence (for PS); n (%)	750 (2.0%)	210 (1.8%)	0.01	820 (0.9%)	149 (0.7%)	0.02	1,570 (1.2%)	359 (1.1%)	0.01

Table 1: Telmisartan vs Ramipril

Diabetes with other ophthalmic manifestations+Retinal detachment, vitreous hemorrhage, vitrectomy+Retinal laser coagulation therapy (for PS); n (%)	584 (1.5%)	197 (1.6%)	-0.01	3,380 (3.6%)	755 (3.5%)	0.01	3,964 (3.0%)	0,952 (2.8%)	0.01
Other atherosclerosis+Cardiac conduction disorders+Other CVD (for PS) ; n (%)	9,446 (24.9%)	2,138 (17.9%)	0.17	19,987 (21.5%)	3,130 (14.3%)	0.19	29,433 (22.5%)	5,268 (15.6%)	0.18
Previous cardiac procedure (CABG or PTCA or Stent) + History of CABG or PTCA (for PS) ; n (%)	7,667 (20.2%)	847 (7.1%)	0.39	11,938 (12.9%)	721 (3.3%)	0.36	19,605 (15.0%)	1,568 (4.6%)	0.36
Hyperthyroidism + Hypothyroidism + Other disorders of thyroid gland (for PS); n (%)	5,896 (15.5%)	2,314 (19.4%)	-0.10	8,543 (9.2%)	2,435 (11.1%)	-0.06	14,439 (11.0%)	4,749 (14.0%)	-0.09
Delirium + Psychosis (for PS); n (%)	945 (2.5%)	209 (1.7%)	0.06	1,834 (2.0%)	273 (1.2%)	0.06	2779 (2.1%)	482 (1.4%)	0.05
Any use of Meglitinides (for PS); n (%)	315 (0.8%)	72 (0.6%)	0.02	1,137 (1.2%)	239 (1.1%)	0.01	1452 (1.1%)	311 (0.9%)	0.02
Any use of AGIs (for PS); n (%)	64 (0.2%)	17 (0.1%)	0.03	216 (0.2%)	41 (0.2%)	0.00	29,433 (22.5%)	5,268 (15.6%)	0.18
CKD stage 3-6 + dialysis (for PS); n (%)	2,258 (5.9%)	1,280 (10.7%)	-0.17	2,756 (3.0%)	1,015 (4.6%)	-0.08	5,014 (3.8%)	2,295 (6.8%)	-0.13
Use of thiazide; n (%)	3,399 (9.0%)	1,398 (11.7%)	-0.09	8,655 (9.3%)	2,289 (10.5%)	-0.04	69,385 (53.1%)	13,491 (39.9%)	0.27
Use of beta blockers; n (%)	19,309 (50.9%)	4,780 (40.0%)	0.22	50,076 (53.9%)	8,711 (39.8%)	0.29	25,567 (19.5%)	10,073 (29.8%)	-0.24
Use of calcium channel blockers; n (%)	7,144 (18.8%)	3,694 (30.9%)	-0.28	18,423 (19.8%)	6,379 (29.2%)	-0.22	43,200 (33.0%)	10,354 (30.6%)	0.05
All antidiabetic medications except Insulin; n (%)	12,807 (33.7%)	3,883 (32.5%)	0.03	30,393 (32.7%)	6,471 (29.6%)	0.07	12,054 (9.2%)	3,687 (10.9%)	-0.06
DM Medications - Insulin ; n (%)	4,891 (12.9%)	1,386 (11.6%)	0.04	11,894 (12.8%)	2,323 (10.6%)	0.07	16,785 (12.8%)	3,709 (11.0%)	0.06
Use of Low Intensity Statins; n (%)	11,986 (31.6%)	3,096 (25.9%)	0.13	31,153 (33.6%)	5,929 (27.1%)	0.14	43,139 (33.0%)	9,025 (26.7%)	0.14
Use of High Intensity Statins; n (%)	12,278 (32.3%)	3,103 (26.0%)	0.14	28,435 (30.6%)	4,919 (22.5%)	0.18	40,713 (31.1%)	8,022 (23.7%)	0.17
Malignant hypertension; n (%)	1,131 (3.0%)	320 (2.7%)	0.02	28,309 (30.5%)	8,199 (37.5%)	-0.15	29,440 (22.5%)	8,519 (25.2%)	-0.06
Cardiovascular stress test; n (%)	110 (0.3%)	38 (0.3%)	0.00	292 (0.3%)	80 (0.4%)	-0.02	0,402 (0.3%)	118 (0.3%)	0.00
Echocardiogram; n (%)	9,024 (23.8%)	1,883 (15.8%)	0.20	26,426 (28.5%)	3,831 (17.5%)	0.26	35,450 (27.1%)	5,714 (16.9%)	0.25
Number of BNP tests									
...mean (sd)	0.06 (0.32)	0.06 (0.29)	0.00	0.03 (0.22)	0.02 (0.20)	0.05	0.04 (0.25)	0.03 (0.24)	0.04
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 (0.25)	0.00 (0.24)	0.00
Number of Cardiac biomarkers tests (troponin, CK-MBs, Myoglobin, CPK)									
...mean (sd)	0.42 (1.56)	0.29 (1.07)	0.10	0.23 (1.03)	0.17 (0.93)	0.06	0.29 (1.21)	0.21 (0.98)	0.07
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 (1.21)	0.00 (0.98)	0.00
Number of Ambulatory Blood pressure monitoring tests									
...mean (sd)	0.00 (0.06)	0.00 (0.06)	0.00	0.00 (0.06)	0.00 (0.07)	0.00	0.00 (0.06)	0.00 (0.07)	0.00
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 (0.06)	0.00 (0.07)	0.00
N of days on antihypertensive medications during baseline									
...mean (sd)	75.24 (73.17)	86.41 (73.17)	-0.15	86.01 (74.38)	90.27 (72.25)	-0.06	82.88 (74.03)	88.91 (72.58)	-0.08
...median [IQR]	58.00 [1.00, 159.00]	83.00 [1.00, 167.00]	-0.34	82.00 [1.00, 168.00]	87.00 [1.00, 169.00]	-0.07	75.03 (74.03)	85.59 (72.58)	-0.14
N of days in database anytime prior									
...mean (sd)	1,454.93 (1,091.34)	1,700.65 (1,241.25)	-0.21	1,460.72 (1,093.13)	1,710.55 (1,132.92)	-0.22	1459.04 (1092.61)	1707.05 (1172.35)	-0.22
...median [IQR]	1,164.00 [623.00, 1,976.00]	1,383.00 [753.00, 2,317.00]	-0.19	1,140.00 [622.00, 2,024.00]	1,484.00 [789.00, 2,428.00]	-0.31	1146.97 (1092.61)	1448.30 (1172.35)	-0.27

Table 1: Telmisartan vs Ramipril

Mean Copay for per prescription cost (charges in U.S. \$) (180-1 day prior)									
...mean (sd)	32.53 (40.29)	30.00 (37.37)	0.07	23.24 (25.91)	23.56 (26.11)	-0.01	25.94 (30.78)	25.84 (30.57)	0.00
...median [IQR]	23.33 [10.13, 40.52]	21.04 [8.60, 37.65]	0.06	17.35 [6.24, 32.14]	17.74 [6.69, 32.48]	-0.01	19.09 (30.78)	18.91 (30.57)	0.01
...Missing; n (%)	3,106 (8.2%)	738 (6.2%)	0.08	5,692 (6.1%)	1,063 (4.9%)	0.05	8,798 (6.7%)	1801 (5.3%)	0.06
Colonos; n (%)	1,792 (4.7%)	563 (4.7%)	0.00	5,008 (5.4%)	1,161 (5.3%)	0.00	6,800 (5.2%)	1724 (5.1%)	0.00
Fecal occult blood (FOB) test; n (%)	1,914 (5.0%)	611 (5.1%)	0.00	3,485 (3.8%)	800 (3.7%)	0.01	5,399 (4.1%)	1411 (4.2%)	-0.01
Flu vaccine; n (%)	5,787 (15.2%)	1,904 (15.9%)	-0.02	8,869 (9.6%)	2,177 (10.0%)	-0.01	14,656 (11.2%)	4081 (12.1%)	-0.03
Mammogram; n (%)	2,932 (7.7%)	1,576 (13.2%)	-0.18	6,866 (7.4%)	2,526 (11.5%)	-0.14	9,798 (7.5%)	4102 (12.1%)	-0.16
Pap smear; n (%)	1,133 (3.0%)	519 (4.3%)	-0.07	2,971 (3.2%)	1,074 (4.9%)	-0.09	4,104 (3.1%)	1593 (4.7%)	-0.08
Pneumonia vaccine; n (%)	3,129 (8.2%)	1,237 (10.3%)	-0.07	3,097 (3.3%)	695 (3.2%)	0.01	6,226 (4.8%)	1932 (5.7%)	-0.04
PSA test or Prostate exam for DRE; n (%)	6,733 (17.7%)	1,741 (14.6%)	0.08	10,296 (11.1%)	1,977 (9.0%)	0.07	17,029 (13.0%)	3718 (11.0%)	0.06
Bone mineral density; n (%)	1,041 (2.7%)	547 (4.6%)	-0.10	1,784 (1.9%)	684 (3.1%)	-0.08	2,825 (2.2%)	1231 (3.6%)	-0.08
Use of Sympathomimetic agents; n (%)	472 (1.2%)	150 (1.3%)	-0.01	1,832 (2.0%)	444 (2.0%)	0.00	2,304 (1.8%)	594 (1.8%)	0.00
Use of CNS stimulants; n (%)	164 (0.4%)	77 (0.6%)	-0.03	596 (0.6%)	188 (0.9%)	-0.03	0,760 (0.6%)	265 (0.8%)	-0.02
Use of estrogens, progestins, androgens; n (%)	1,423 (3.7%)	612 (5.1%)	-0.07	4,658 (5.0%)	1,612 (7.4%)	-0.10	6,081 (4.6%)	2224 (6.6%)	-0.09
Use of Angiogenesis inhibitors; n (%)	15 (0.0%)	5 (0.0%)	#DIV/0!	60 (0.1%)	12 (0.1%)	0.00	0,075 (0.1%)	17 (0.1%)	0.00
Use of Oral Immunosuppressants; n (%)	70 (0.2%)	25 (0.2%)	0.00	215 (0.2%)	56 (0.3%)	-0.02	0,285 (0.2%)	81 (0.2%)	0.00
Cardiomegaly, LVH, and other cardiopathy due to hypertension; n (%)	4,467 (11.8%)	1,343 (11.2%)	0.02	7,841 (8.4%)	1,788 (8.2%)	0.01	12,308 (9.4%)	3131 (9.3%)	0.00
Ultrasound; n (%)	7,429 (19.6%)	2,288 (19.1%)	0.01	21,445 (23.1%)	4,601 (21.0%)	0.05	28,874 (22.1%)	6889 (20.4%)	0.04
Symptomatic hypotension; n (%)	1,117 (2.9%)	209 (1.7%)	0.08	1,677 (1.8%)	248 (1.1%)	0.06	2,794 (2.1%)	457 (1.4%)	0.05
Syncopal episodes; n (%)	678 (1.8%)	270 (2.3%)	-0.04	1,252 (1.3%)	330 (1.5%)	-0.02	1,930 (1.5%)	600 (1.8%)	-0.02
N of Generic name drugs only									
...mean (sd)	9.94 (11.91)	11.40 (12.37)	-0.12	8.09 (8.46)	8.54 (8.60)	-0.05	8.63 (9.59)	9.55 (10.09)	-0.09
...median [IQR]	6.00 [2.00, 14.00]	8.00 [3.00, 16.00]	-0.16	6.00 [2.00, 11.00]	6.00 [2.00, 12.00]	0.00	6.00 (9.59)	6.71 (10.09)	-0.07
N of Brand name drugs only									
...mean (sd)	4.71 (6.39)	4.59 (6.18)	0.02	5.95 (6.84)	5.70 (6.42)	0.04	5.59 (6.71)	5.31 (6.34)	0.04
...median [IQR]	2.00 [0.00, 7.00]	2.00 [0.00, 6.00]	0.00	4.00 [1.00, 8.00]	4.00 [1.00, 8.00]	0.00	3.42 (6.71)	3.29 (6.34)	0.02
Number of distinct antihypertensive generic medications (180-1 days before index)									
...mean (sd)	0.96 (1.12)	1.13 (1.24)	-0.14	1.05 (1.17)	1.11 (1.22)	-0.05	1.02 (1.16)	1.12 (1.23)	-0.08
...median [IQR]	1.00 [0.00, 2.00]	1.00 [0.00, 2.00]	0.00	1.00 [0.00, 2.00]	1.00 [0.00, 2.00]	0.00	1.00 (1.16)	1.00 (1.23)	0.00
Number of distinct antihypertensive generic medications on CED									
...mean (sd)	1.41 (0.72)	1.25 (0.60)	0.24	1.44 (0.75)	1.26 (0.59)	0.27	1.43 (0.74)	1.26 (0.59)	0.25
...median [IQR]	1.00 [1.00, 2.00]	1.00 [1.00, 1.00]	0.00	1.00 [1.00, 2.00]	1.00 [1.00, 1.00]	0.00	1.00 (0.74)	1.00 (0.59)	0.00
Hypertensive retinopathy; n (%)	271 (0.7%)	122 (1.0%)	-0.03	405 (0.4%)	118 (0.5%)	-0.01	0,676 (0.5%)	240 (0.7%)	-0.03
Commercial vs Medicare Advantage-Business Type Code - CORRECT ONE - TRUVEN									
...Commercial; n (%)	18,308 (48.2%)	5,129 (42.9%)	0.11	51,603 (55.6%)	12,453 (56.9%)	-0.03	69,911 (53.5%)	17582 (52.0%)	0.00
...Medicare Advantage; n (%)	19,655 (51.8%)	6,826 (57.1%)	-0.11	41,218 (44.4%)	9,418 (43.1%)	0.03	60,873 (46.5%)	16244 (48.0%)	0.00
Commercial vs Medicare Advantage-Business Type Code									
...COM = COMMERCIAL; n (%)	18,308 (48.2%)	5,129 (42.9%)	0.11	-	-	#VALUE!	18,308 (48.2%)	5,129 (42.9%)	0.11

Table 1: Telmisartan vs Ramipril

...MCR = MEDICARE; n (%)	19,655 (51.8%)	6,826 (57.1%)	-0.11	-	-	#VALUE!	19,655 (51.8%)	6,826 (57.1%)	-0.11
...MCD = MEDICAID; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	-	-	#VALUE!	0 (0.0%)	0 (0.0%)	#DIV/0!
...NONE = NO BUSINESS LINE CODE (added in 2015); n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	-	-	#VALUE!	0 (0.0%)	0 (0.0%)	#DIV/0!
...UNK = UNKNOWN (added in 2015); n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	-	-	#VALUE!	0 (0.0%)	0 (0.0%)	#DIV/0!
Commercial vs Medicare Advantage- Data Type									
...1 - Fee For Service; n (%)	-	-	#VALUE!	36,614 (39.4%)	8,586 (39.3%)	0.00	36,614 (39.4%)	8,586 (39.3%)	0.00
...2 - Encounter; n (%)	-	-	#VALUE!	4,604 (5.0%)	832 (3.8%)	0.06	4,604 (5.0%)	832 (3.8%)	0.06
...3 - Medicare; n (%)	-	-	#VALUE!	47,043 (50.7%)	11,770 (53.8%)	-0.06	47,043 (50.7%)	11,770 (53.8%)	-0.06
...4 - Medicare Encounter; n (%)	-	-	#VALUE!	4,560 (4.9%)	683 (3.1%)	0.09	4,560 (4.9%)	683 (3.1%)	0.09
Metropolitan Statistical Area - Urban (any MSA) vs Rural (non-MSA)									
...Urban; n (%)	-	-	#VALUE!	64,126 (69.1%)	16,537 (75.6%)	-0.15	64,126 (69.1%)	16,537 (75.6%)	-0.15
...Rural; n (%)	-	-	#VALUE!	844 (0.9%)	203 (0.9%)	0.00	844 (0.9%)	203 (0.9%)	0.00
...Unknown/Missing; n (%)	-	-	#VALUE!	27,851 (30.0%)	5,131 (23.5%)	0.15	27,851 (30.0%)	5,131 (23.5%)	0.15

Table 1: Telmisartan vs Ramipril

PS-matched									
Variable	Optum			Truven			POOLED		
	Ramipril (Any dose)	Telmisartan (Any dose)	St. Diff.	Ramipril (Any dose)	Telmisartan (Any dose)	St. Diff.	Ramipril (Any dose)	Telmisartan (Any dose)	St. Diff.
Number of patients	10,798	10,798		21,074	21,074		31,872	31,872	
Age									
...mean (sd)	69.53 (9.48)	69.41 (9.22)	0.01	68.68 (9.90)	68.55 (9.76)	0.01	68.97 (9.76)	68.84 (9.58)	0.01
...median [IQR]	69.00 [62.00, 76.00]	69.00 [62.00, 76.00]	0.00	67.00 [60.00, 76.00]	67.00 [60.00, 76.00]	0.00	67.68 (9.76)	67.68 (9.58)	0.00
Age categories									
...18 - 54; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	0,000 (0.0%)	0,000 (0.0%)	#DIV/0!
...55 - 64; n (%)	3,668 (34.0%)	3,655 (33.8%)	0.00	9,212 (43.7%)	9,304 (44.1%)	-0.01	12,880 (40.4%)	12,959 (40.7%)	-0.01
...65 - 74; n (%)	3,738 (34.6%)	3,815 (35.3%)	-0.01	5,632 (26.7%)	5,604 (26.6%)	0.00	9,370 (29.4%)	9,419 (29.6%)	0.00
...≥ 75; n (%)	3,392 (31.4%)	3,328 (30.8%)	0.01	6,230 (29.6%)	6,166 (29.3%)	0.01	9,622 (30.2%)	9,494 (29.8%)	0.01
Gender									
...Males; n (%)	4,912 (45.5%)	4,984 (46.2%)	-0.01	9,692 (46.0%)	9,823 (46.6%)	-0.01	14,604 (45.8%)	14,807 (46.5%)	-0.01
...Females; n (%)	5,886 (54.5%)	5,814 (53.8%)	0.01	11,382 (54.0%)	11,251 (53.4%)	0.01	17,268 (54.2%)	17,065 (53.5%)	0.01
Region									
...Northeast; n (%)	1,185 (11.0%)	1,125 (10.4%)	0.02	2,950 (14.0%)	3,023 (14.3%)	-0.01	4,135 (13.0%)	4,148 (13.0%)	0.00
...South; n (%)	6,441 (59.6%)	6,556 (60.7%)	-0.02	5,131 (24.3%)	5,035 (23.9%)	0.01	11,572 (36.3%)	11,591 (36.4%)	0.00
...Midwest; n (%)	1,350 (12.5%)	1,308 (12.1%)	0.01	9,833 (46.7%)	9,916 (47.1%)	-0.01	11,183 (35.1%)	11,224 (35.2%)	0.00
...West; n (%)	1,822 (16.9%)	1,809 (16.8%)	0.00	3,021 (14.3%)	2,968 (14.1%)	0.01	4,843 (15.2%)	4,777 (15.0%)	0.01
...Unknown+missing; n (%)	N/A	N/A	#VALUE!	139 (0.7%)	132 (0.6%)	0.01	139 (0.4%)	132 (0.4%)	0.00
CV Covariates									
Ischemic heart disease; n (%)	3,469 (32.1%)	3,519 (32.6%)	-0.01	5,902 (28.0%)	5,947 (28.2%)	0.00	9,371 (29.4%)	9,466 (29.7%)	-0.01
Acute MI; n (%)	190 (1.8%)	209 (1.9%)	-0.01	340 (1.6%)	344 (1.6%)	0.00	530 (1.7%)	553 (1.7%)	0.00
ACS/unstable angina; n (%)	282 (2.6%)	314 (2.9%)	-0.02	627 (3.0%)	655 (3.1%)	-0.01	909 (2.9%)	969 (3.0%)	-0.01
Old MI; n (%)	494 (4.6%)	504 (4.7%)	0.00	349 (1.7%)	354 (1.7%)	0.00	843 (2.6%)	858 (2.7%)	-0.01
Stable angina; n (%)	721 (6.7%)	768 (7.1%)	-0.02	1,166 (5.5%)	1,174 (5.6%)	0.00	1,887 (5.9%)	1,942 (6.1%)	-0.01
Coronary atherosclerosis and other forms of chronic ischemic heart disease; n (%)	3,081 (28.5%)	3,093 (28.6%)	0.00	5,064 (24.0%)	5,133 (24.4%)	-0.01	8,145 (25.6%)	8,226 (25.8%)	0.00
Other atherosclerosis with ICD10 ; n (%)	231 (2.1%)	208 (1.9%)	0.01	336 (1.6%)	354 (1.7%)	-0.01	567 (1.8%)	562 (1.8%)	0.00
Previous cardiac procedure (CABG or PTCA or Stent) ; n (%)	161 (1.5%)	141 (1.3%)	0.02	329 (1.6%)	293 (1.4%)	0.02	490 (1.5%)	434 (1.4%)	0.01
History of CABG or PTCA; n (%)	756 (7.0%)	771 (7.1%)	0.00	479 (2.3%)	525 (2.5%)	-0.01	1,235 (3.9%)	1,296 (4.1%)	-0.01
Any stroke; n (%)	1,668 (15.4%)	1,634 (15.1%)	0.01	3,038 (14.4%)	2,955 (14.0%)	0.01	4,706 (14.8%)	4,589 (14.4%)	0.01
Ischemic stroke (w and w/o mention of cerebral infarction); n (%)	1,649 (15.3%)	1,622 (15.0%)	0.01	3,018 (14.3%)	2,932 (13.9%)	0.01	4,667 (14.6%)	4,554 (14.3%)	0.01
Hemorrhagic stroke; n (%)	43 (0.4%)	37 (0.3%)	0.02	66 (0.3%)	58 (0.3%)	0.00	109 (0.3%)	95 (0.3%)	0.00
TIA; n (%)	464 (4.3%)	475 (4.4%)	0.00	847 (4.0%)	833 (4.0%)	0.00	1311 (4.1%)	1308 (4.1%)	0.00
Other cerebrovascular disease; n (%)	365 (3.4%)	338 (3.1%)	0.02	508 (2.4%)	456 (2.2%)	0.01	873 (2.7%)	794 (2.5%)	0.01
Late effects of cerebrovascular disease; n (%)	285 (2.6%)	263 (2.4%)	0.01	296 (1.4%)	293 (1.4%)	0.00	581 (1.8%)	556 (1.7%)	0.01
Cerebrovascular procedure; n (%)	40 (0.4%)	35 (0.3%)	0.02	71 (0.3%)	86 (0.4%)	-0.02	111 (0.3%)	121 (0.4%)	-0.02
Heart failure (CHF); n (%)	857 (7.9%)	830 (7.7%)	0.01	1,058 (5.0%)	1,005 (4.8%)	0.01	1,915 (6.0%)	1,835 (5.8%)	0.01
Peripheral Vascular Disease (PVD) or PVD Surgery ; n (%)	1,149 (10.6%)	1,123 (10.4%)	0.01	1,564 (7.4%)	1,518 (7.2%)	0.01	2,713 (8.5%)	2,641 (8.3%)	0.01
Atrial fibrillation; n (%)	871 (8.1%)	864 (8.0%)	0.00	1,409 (6.7%)	1,390 (6.6%)	0.00	2,280 (7.2%)	2,254 (7.1%)	0.00
Other cardiac dysrhythmia; n (%)	1,232 (11.4%)	1,199 (11.1%)	0.01	1,617 (7.7%)	1,665 (7.9%)	-0.01	2,849 (8.9%)	2,864 (9.0%)	0.00

**Table 1: Telmisartan vs Ramipril**

Cardiac conduction disorders; n (%)	307 (2.8%)	322 (3.0%)	-0.01	399 (1.9%)	386 (1.8%)	0.01	706 (2.2%)	708 (2.2%)	0.00
Other CVD; n (%)	1,543 (14.3%)	1,568 (14.5%)	-0.01	2,604 (12.4%)	2,508 (11.9%)	0.02	4,147 (13.0%)	4,076 (12.8%)	0.01
<b>Diabetes-related complications</b>									
Diabetic retinopathy; n (%)	675 (6.3%)	673 (6.2%)	0.00	791 (3.8%)	819 (3.9%)	-0.01	1,466 (4.6%)	1,492 (4.7%)	0.00
Diabetes with other ophthalmic manifestations; n (%)	45 (0.4%)	51 (0.5%)	-0.01	603 (2.9%)	578 (2.7%)	0.01	0,648 (2.0%)	0,629 (2.0%)	0.00
Retinal detachment, vitreous hemorrhage, vitrectomy; n (%)	69 (0.6%)	56 (0.5%)	0.01	74 (0.4%)	79 (0.4%)	0.00	143 (0.4%)	135 (0.4%)	0.00
Retinal laser coagulation therapy; n (%)	79 (0.7%)	87 (0.8%)	-0.01	176 (0.8%)	176 (0.8%)	0.00	255 (0.8%)	263 (0.8%)	0.00
Occurrence of Diabetic Neuropathy ; n (%)	1,350 (12.5%)	1,373 (12.7%)	-0.01	1,384 (6.6%)	1,389 (6.6%)	0.00	2,734 (8.6%)	2,762 (8.7%)	0.00
Occurrence of diabetic nephropathy with ICD10 ; n (%)	945 (8.8%)	926 (8.6%)	0.01	682 (3.2%)	717 (3.4%)	-0.01	1,627 (5.1%)	1,643 (5.2%)	0.00
Hypoglycemia; n (%)	169 (1.6%)	154 (1.4%)	0.02	331 (1.6%)	305 (1.4%)	0.02	0,500 (1.6%)	0,459 (1.4%)	0.02
Hyperglycemia; n (%)	363 (3.4%)	377 (3.5%)	-0.01	290 (1.4%)	297 (1.4%)	0.00	0,653 (2.0%)	0,674 (2.1%)	-0.01
Disorders of fluid electrolyte and acid-base balance; n (%)	746 (6.9%)	737 (6.8%)	0.00	846 (4.0%)	831 (3.9%)	0.01	1,592 (5.0%)	1,568 (4.9%)	0.00
Diabetic ketoacidosis; n (%)	29 (0.3%)	21 (0.2%)	0.02	34 (0.2%)	27 (0.1%)	0.03	63 (0.2%)	48 (0.2%)	0.00
Hyperosmolar hyperglycemic nonketotic syndrome (HONK); n (%)	25 (0.2%)	23 (0.2%)	0.00	27 (0.1%)	23 (0.1%)	0.00	52 (0.2%)	46 (0.1%)	0.03
Diabetes with peripheral circulatory disorders with ICD-10 ; n (%)	428 (4.0%)	434 (4.0%)	0.00	354 (1.7%)	358 (1.7%)	0.00	0,782 (2.5%)	0,792 (2.5%)	0.00
Diabetic Foot; n (%)	323 (3.0%)	301 (2.8%)	0.01	577 (2.7%)	566 (2.7%)	0.00	900 (2.8%)	867 (2.7%)	0.01
Gangrene; n (%)	24 (0.2%)	22 (0.2%)	0.00	23 (0.1%)	24 (0.1%)	0.00	47 (0.1%)	46 (0.1%)	0.00
Lower extremity amputation; n (%)	65 (0.6%)	61 (0.6%)	0.00	48 (0.2%)	44 (0.2%)	0.00	113 (0.4%)	105 (0.3%)	0.02
Osteomyelitis; n (%)	76 (0.7%)	61 (0.6%)	0.01	104 (0.5%)	85 (0.4%)	0.01	180 (0.6%)	146 (0.5%)	0.01
Skin infections; n (%)	622 (5.8%)	581 (5.4%)	0.02	1,087 (5.2%)	1,066 (5.1%)	0.00	1,709 (5.4%)	1,647 (5.2%)	0.01
Erectile dysfunction; n (%)	279 (2.6%)	290 (2.7%)	-0.01	243 (1.2%)	271 (1.3%)	-0.01	0,522 (1.6%)	0,561 (1.8%)	-0.02
Diabetes with unspecified complication; n (%)	291 (2.7%)	286 (2.6%)	0.01	351 (1.7%)	339 (1.6%)	0.01	0,642 (2.0%)	0,625 (2.0%)	0.00
Diabetes mellitus without mention of complications; n (%)	4,622 (42.8%)	4,599 (42.6%)	0.00	7,440 (35.3%)	7,412 (35.2%)	0.00	12,062 (37.8%)	12,011 (37.7%)	0.00
Hypertension: 1 inpatient or 2 outpatient claims within 365 days; n (%)	9,425 (87.3%)	9,377 (86.8%)	0.01	14,509 (68.8%)	14,543 (69.0%)	0.00	23,934 (75.1%)	23,920 (75.1%)	0.00
Hyperlipidemia ; n (%)	6,924 (64.1%)	6,904 (63.9%)	0.00	8,046 (38.2%)	8,175 (38.8%)	-0.01	14,970 (47.0%)	15,079 (47.3%)	-0.01
Edema; n (%)	829 (7.7%)	826 (7.6%)	0.00	968 (4.6%)	944 (4.5%)	0.00	1,797 (5.6%)	1,770 (5.6%)	0.00
Renal Dysfunction (non-diabetic) ; n (%)	1,958 (18.1%)	1,937 (17.9%)	0.01	2,085 (9.9%)	2,082 (9.9%)	0.00	4,043 (12.7%)	4,019 (12.6%)	0.00
Occurrence of acute renal disease ; n (%)	250 (2.3%)	243 (2.3%)	0.00	280 (1.3%)	281 (1.3%)	0.00	530 (1.7%)	524 (1.6%)	0.01
Occurrence of chronic renal insufficiency; n (%)	1,567 (14.5%)	1,508 (14.0%)	0.01	1,458 (6.9%)	1,446 (6.9%)	0.00	3,025 (9.5%)	2,954 (9.3%)	0.01
Chronic kidney disease ; n (%)	1,480 (13.7%)	1,433 (13.3%)	0.01	1,339 (6.4%)	1,336 (6.3%)	0.00	2,819 (8.8%)	2,769 (8.7%)	0.00
CKD Stage 3-4; n (%)	989 (9.2%)	933 (8.6%)	0.02	789 (3.7%)	830 (3.9%)	-0.01	1,778 (5.6%)	1,763 (5.5%)	0.00
Occurrence of hypertensive nephropathy; n (%)	722 (6.7%)	730 (6.8%)	0.00	572 (2.7%)	539 (2.6%)	0.01	1294 (4.1%)	1269 (4.0%)	0.01
Occurrence of miscellaneous renal insufficiency ; n (%)	604 (5.6%)	603 (5.6%)	0.00	728 (3.5%)	718 (3.4%)	0.01	1,332 (4.2%)	1,321 (4.1%)	0.01
Glaucoma or cataracts ; n (%)	2,158 (20.0%)	2,251 (20.8%)	-0.02	3,746 (17.8%)	3,780 (17.9%)	0.00	5,904 (18.5%)	6,031 (18.9%)	-0.01
Cellulitis or abscess of toe; n (%)	143 (1.3%)	120 (1.1%)	0.02	155 (0.7%)	143 (0.7%)	0.00	298 (0.9%)	263 (0.8%)	0.01
Foot ulcer; n (%)	328 (3.0%)	311 (2.9%)	0.01	591 (2.8%)	576 (2.7%)	0.01	919 (2.9%)	887 (2.8%)	0.01

Table 1: Telmisartan vs Ramipril

Bladder stones; n (%)	20 (0.2%)	12 (0.1%)	0.03	29 (0.1%)	21 (0.1%)	0.00	49 (0.2%)	33 (0.1%)	0.03
Kidney stones; n (%)	225 (2.1%)	219 (2.0%)	0.01	335 (1.6%)	349 (1.7%)	-0.01	0,560 (1.8%)	0,568 (1.8%)	0.00
Urinary tract infections (UTIs); n (%)	1,097 (10.2%)	1,071 (9.9%)	0.01	1,349 (6.4%)	1,322 (6.3%)	0.00	2,446 (7.7%)	2,393 (7.5%)	0.01
Dipstick urinalysis; n (%)	3,856 (35.7%)	3,902 (36.1%)	-0.01	5,162 (24.5%)	5,125 (24.3%)	0.00	9,018 (28.3%)	9,027 (28.3%)	0.00
Non-dipstick urinalysis; n (%)	2,413 (22.3%)	2,359 (21.8%)	0.01	2,434 (11.5%)	2,386 (11.3%)	0.01	4,847 (15.2%)	4,745 (14.9%)	0.01
Urine function test; n (%)	344 (3.2%)	298 (2.8%)	0.02	617 (2.9%)	688 (3.3%)	-0.02	0,961 (3.0%)	0,986 (3.1%)	-0.01
Cytology; n (%)	163 (1.5%)	128 (1.2%)	0.03	357 (1.7%)	308 (1.5%)	0.02	520 (1.6%)	436 (1.4%)	0.02
Cystos; n (%)	226 (2.1%)	204 (1.9%)	0.01	471 (2.2%)	428 (2.0%)	0.01	697 (2.2%)	632 (2.0%)	0.01
<b>Other Covariates</b>									
Liver disease; n (%)	230 (2.1%)	249 (2.3%)	-0.01	150 (0.7%)	160 (0.8%)	-0.01	0,380 (1.2%)	0,409 (1.3%)	-0.01
Osteoarthritis; n (%)	1,871 (17.3%)	1,879 (17.4%)	0.00	2,725 (12.9%)	2,734 (13.0%)	0.00	4,596 (14.4%)	4,613 (14.5%)	0.00
Other arthritis, arthropathies and musculoskeletal pain; n (%)	4,118 (38.1%)	4,111 (38.1%)	0.00	6,818 (32.4%)	6,762 (32.1%)	0.01	10,936 (34.3%)	10,873 (34.1%)	0.00
Dorsopathies; n (%)	2,521 (23.3%)	2,520 (23.3%)	0.00	4,212 (20.0%)	4,191 (19.9%)	0.00	6,733 (21.1%)	6,711 (21.1%)	0.00
Fractures; n (%)	386 (3.6%)	394 (3.6%)	0.00	718 (3.4%)	703 (3.3%)	0.01	1,104 (3.5%)	1,097 (3.4%)	0.01
Falls; n (%)	325 (3.0%)	328 (3.0%)	0.00	126 (0.6%)	133 (0.6%)	0.00	451 (1.4%)	461 (1.4%)	0.00
Osteoporosis; n (%)	935 (8.7%)	937 (8.7%)	0.00	1,657 (7.9%)	1,641 (7.8%)	0.00	2,592 (8.1%)	2,578 (8.1%)	0.00
Hyperthyroidism; n (%)	88 (0.8%)	93 (0.9%)	-0.01	96 (0.5%)	96 (0.5%)	0.00	184 (0.6%)	189 (0.6%)	0.00
Hypothyroidism ; n (%)	1,759 (16.3%)	1,686 (15.6%)	0.02	1,896 (9.0%)	1,814 (8.6%)	0.01	3,655 (11.5%)	3,500 (11.0%)	0.02
Other disorders of thyroid gland ; n (%)	396 (3.7%)	460 (4.3%)	-0.03	554 (2.6%)	606 (2.9%)	-0.02	0,950 (3.0%)	1,066 (3.3%)	-0.02
Depression; n (%)	835 (7.7%)	813 (7.5%)	0.01	1,017 (4.8%)	1,012 (4.8%)	0.00	1,852 (5.8%)	1,825 (5.7%)	0.00
Anxiety; n (%)	747 (6.9%)	774 (7.2%)	-0.01	664 (3.2%)	674 (3.2%)	0.00	1,411 (4.4%)	1,448 (4.5%)	0.00
Sleep Disorder; n (%)	825 (7.6%)	818 (7.6%)	0.00	1,721 (8.2%)	1,678 (8.0%)	0.01	2,546 (8.0%)	2,496 (7.8%)	0.01
Dementia; n (%)	440 (4.1%)	435 (4.0%)	0.01	558 (2.6%)	535 (2.5%)	0.01	998 (3.1%)	970 (3.0%)	0.01
Delirium; n (%)	130 (1.2%)	118 (1.1%)	0.01	156 (0.7%)	162 (0.8%)	-0.01	286 (0.9%)	280 (0.9%)	0.00
Psychosis; n (%)	94 (0.9%)	89 (0.8%)	0.01	116 (0.6%)	121 (0.6%)	0.00	210 (0.7%)	210 (0.7%)	0.00
Obesity; n (%)	1,239 (11.5%)	1,229 (11.4%)	0.00	948 (4.5%)	978 (4.6%)	0.00	2,187 (6.9%)	2,207 (6.9%)	0.00
Overweight; n (%)	405 (3.8%)	401 (3.7%)	0.01	175 (0.8%)	160 (0.8%)	0.00	0,580 (1.8%)	0,561 (1.8%)	0.00
Smoking; n (%)	928 (8.6%)	974 (9.0%)	-0.01	660 (3.1%)	655 (3.1%)	0.00	1,588 (5.0%)	1,629 (5.1%)	0.00
Alcohol abuse or dependence; n (%)	78 (0.7%)	67 (0.6%)	0.01	71 (0.3%)	79 (0.4%)	-0.02	149 (0.5%)	146 (0.5%)	0.00
Drug abuse or dependence; n (%)	113 (1.0%)	118 (1.1%)	-0.01	78 (0.4%)	73 (0.3%)	0.02	191 (0.6%)	191 (0.6%)	0.00
COPD; n (%)	1,134 (10.5%)	1,166 (10.8%)	-0.01	1,702 (8.1%)	1,683 (8.0%)	0.00	2,836 (8.9%)	2,849 (8.9%)	0.00
Asthma; n (%)	622 (5.8%)	628 (5.8%)	0.00	1,026 (4.9%)	1,026 (4.9%)	0.00	1,648 (5.2%)	1,654 (5.2%)	0.00
Obstructive sleep apnea; n (%)	731 (6.8%)	720 (6.7%)	0.00	1,187 (5.6%)	1,193 (5.7%)	0.00	1,918 (6.0%)	1,913 (6.0%)	0.00
Pneumonia; n (%)	277 (2.6%)	269 (2.5%)	0.01	465 (2.2%)	479 (2.3%)	-0.01	0,742 (2.3%)	0,748 (2.3%)	0.00
Imaging; n (%)	18 (0.2%)	24 (0.2%)	0.00	11 (0.1%)	17 (0.1%)	0.00	29 (0.1%)	41 (0.1%)	0.00
<b>Other Medications</b>									
Use of ACE inhibitors; n (%)	10,798 (100.0%)	268 (2.5%)	8.83	21,074 (100.0%)	471 (2.2%)	9.43	31,872 (100.0%)	0,739 (2.3%)	9.22
Use of ARBs; n (%)	132 (1.2%)	10,798 (100.0%)	-12.83	268 (1.3%)	21,074 (100.0%)	-12.32	0,400 (1.3%)	31,872 (100.0%)	-12.32
Use of Loop Diuretics - ; n (%)	1,441 (13.3%)	1,399 (13.0%)	0.01	2,988 (14.2%)	2,905 (13.8%)	0.01	4,429 (13.9%)	4,304 (13.5%)	0.01
Use of other diuretics - ; n (%)	246 (2.3%)	249 (2.3%)	0.00	544 (2.6%)	525 (2.5%)	0.01	0,790 (2.5%)	0,774 (2.4%)	0.01
Use of nitrates; n (%)	790 (7.3%)	805 (7.5%)	-0.01	1,974 (9.4%)	1,929 (9.2%)	0.01	2,764 (8.7%)	2,734 (8.6%)	0.00
Use of other hypertension drugs; n (%)	854 (7.9%)	872 (8.1%)	-0.01	1,577 (7.5%)	1,602 (7.6%)	0.00	2,431 (7.6%)	2,474 (7.8%)	-0.01
Use of digoxin - ; n (%)	185 (1.7%)	200 (1.9%)	-0.02	591 (2.8%)	563 (2.7%)	0.01	776 (2.4%)	763 (2.4%)	0.00
Use of Anti-arrhythmics; n (%)	213 (2.0%)	218 (2.0%)	0.00	489 (2.3%)	476 (2.3%)	0.00	702 (2.2%)	694 (2.2%)	0.00
Use of COPD/asthma meds - ; n (%)	1,650 (15.3%)	1,668 (15.4%)	0.00	3,684 (17.5%)	3,673 (17.4%)	0.00	5,334 (16.7%)	5,341 (16.8%)	0.00
Use of statins; n (%)	5,936 (55.0%)	5,891 (54.6%)	0.01	11,370 (54.0%)	11,431 (54.2%)	0.00	17,306 (54.3%)	17,322 (54.3%)	0.00
Use of other lipid-lowering drugs; n (%)	1,241 (11.5%)	1,192 (11.0%)	0.02	2,807 (13.3%)	2,838 (13.5%)	-0.01	4,048 (12.7%)	4,030 (12.6%)	0.00

Table 1: Telmisartan vs Ramipril

Use of oral anticoagulants (Dabigatran, Rivaroxaban, Apixaban, Warfarin); n (%)	699 (6.5%)	702 (6.5%)	0.00	1,505 (7.1%)	1,492 (7.1%)	0.00	2,204 (6.9%)	2,194 (6.9%)	0.00
Use of heparin and other low-molecular weight heparins; n (%)	51 (0.5%)	56 (0.5%)	0.00	14 (0.1%)	4 (0.0%)	0.04	65 (0.2%)	60 (0.2%)	0.00
Use of NSAIDs; n (%)	1,536 (14.2%)	1,493 (13.8%)	0.01	2,962 (14.1%)	2,956 (14.0%)	0.00	4,498 (14.1%)	4,449 (14.0%)	0.00
Use of oral corticosteroids; n (%)	1,734 (16.1%)	1,771 (16.4%)	-0.01	3,556 (16.9%)	3,564 (16.9%)	0.00	5,290 (16.6%)	5,335 (16.7%)	0.00
Use of bisphosphonate (); n (%)	527 (4.9%)	517 (4.8%)	0.00	1,204 (5.7%)	1,200 (5.7%)	0.00	1731 (5.4%)	1717 (5.4%)	0.00
Use of opioids; n (%)	2,755 (25.5%)	2,771 (25.7%)	0.00	5,922 (28.1%)	5,931 (28.1%)	0.00	8,677 (27.2%)	8,702 (27.3%)	0.00
Use of antidepressants; n (%)	2,370 (21.9%)	2,331 (21.6%)	0.01	4,632 (22.0%)	4,623 (21.9%)	0.00	7,002 (22.0%)	6,954 (21.8%)	0.00
Use of antipsychotics; n (%)	190 (1.8%)	171 (1.6%)	0.02	386 (1.8%)	370 (1.8%)	0.00	0,576 (1.8%)	0,541 (1.7%)	0.01
Use of anticonvulsants; n (%)	1,307 (12.1%)	1,295 (12.0%)	0.00	2,347 (11.1%)	2,324 (11.0%)	0.00	3,654 (11.5%)	3,619 (11.4%)	0.00
Use of lithium; n (%)	15 (0.1%)	9 (0.1%)	0.00	35 (0.2%)	30 (0.1%)	0.03	50 (0.2%)	39 (0.1%)	0.03
Use of Benzos; n (%)	1,248 (11.6%)	1,225 (11.3%)	0.01	3,252 (15.4%)	3,189 (15.1%)	0.01	4,500 (14.1%)	4,414 (13.8%)	0.01
Use of anxiolytics/hypnotics; n (%)	766 (7.1%)	751 (7.0%)	0.00	1,917 (9.1%)	1,897 (9.0%)	0.00	2,683 (8.4%)	2,648 (8.3%)	0.00
Use of dementia meds; n (%)	294 (2.7%)	286 (2.6%)	0.01	588 (2.8%)	576 (2.7%)	0.01	882 (2.8%)	862 (2.7%)	0.01
Use of antiparkinsonian meds; n (%)	235 (2.2%)	228 (2.1%)	0.01	519 (2.5%)	551 (2.6%)	-0.01	0,754 (2.4%)	0,779 (2.4%)	0.00
Entresto (sacubitril/valsartan); n (%)	4 (0.0%)	3 (0.0%)	#DIV/0!	2 (0.0%)	1 (0.0%)	#DIV/0!	6 (0.0%)	4 (0.0%)	#DIV/0!
<b>Labs</b>									
Lab values- HbA1c (%); n (%)	2,027 (18.8%)	2,001 (18.5%)	0.01	303 (1.4%)	280 (1.3%)	0.01	2,330 (7.3%)	2,281 (7.2%)	0.00
Lab values- HbA1c (%) (within 3 months); n (%)	1,421 (13.2%)	1,374 (12.7%)	0.01	204 (1.0%)	194 (0.9%)	0.01	1,625 (5.1%)	1,568 (4.9%)	0.01
Lab values- HbA1c (%) (within 6 months); n (%)	2,027 (18.8%)	2,001 (18.5%)	0.01	303 (1.4%)	280 (1.3%)	0.01	2,330 (7.3%)	2,281 (7.2%)	0.00
Lab values- BNP; n (%)	72 (0.7%)	71 (0.7%)	0.00	8 (0.0%)	6 (0.0%)	#DIV/0!	80 (0.3%)	77 (0.2%)	0.02
Lab values- BNP (within 3 months); n (%)	49 (0.5%)	47 (0.4%)	0.01	5 (0.0%)	3 (0.0%)	#DIV/0!	54 (0.2%)	50 (0.2%)	0.00
Lab values- BNP (within 6 months); n (%)	72 (0.7%)	71 (0.7%)	0.00	8 (0.0%)	6 (0.0%)	#DIV/0!	80 (0.3%)	77 (0.2%)	0.02
Lab values- BUN (mg/dl); n (%)	2,965 (27.5%)	3,034 (28.1%)	-0.01	349 (1.7%)	335 (1.6%)	0.01	3,314 (10.4%)	3,369 (10.6%)	-0.01
Lab values- BUN (mg/dl) (within 3 months); n (%)	2,060 (19.1%)	2,165 (20.1%)	-0.03	240 (1.1%)	234 (1.1%)	0.00	2,300 (7.2%)	2,399 (7.5%)	-0.01
Lab values- BUN (mg/dl) (within 6 months); n (%)	2,965 (27.5%)	3,034 (28.1%)	-0.01	349 (1.7%)	335 (1.6%)	0.01	3,314 (10.4%)	3,369 (10.6%)	-0.01
Lab values- Creatinine (mg/dl); n (%)	3,074 (28.5%)	3,133 (29.0%)	-0.01	377 (1.8%)	366 (1.7%)	0.01	3,451 (10.8%)	3,499 (11.0%)	-0.01
Lab values- Creatinine (mg/dl) (within 3 months); n (%)	2,137 (19.8%)	2,224 (20.6%)	-0.02	263 (1.2%)	256 (1.2%)	0.00	2,400 (7.5%)	2,480 (7.8%)	-0.01
Lab values- Creatinine (mg/dl) (within 6 months); n (%)	3,074 (28.5%)	3,133 (29.0%)	-0.01	377 (1.8%)	366 (1.7%)	0.01	3,451 (10.8%)	3,499 (11.0%)	-0.01
Lab values- HDL level (mg/dl); n (%)	2,339 (21.7%)	2,294 (21.2%)	0.01	308 (1.5%)	284 (1.3%)	0.02	2,647 (8.3%)	2,578 (8.1%)	0.01
Lab values- HDL level (mg/dl) (within 3 months); n (%)	1,559 (14.4%)	1,529 (14.2%)	0.01	202 (1.0%)	181 (0.9%)	0.01	1,761 (5.5%)	1,710 (5.4%)	0.00
Lab values- HDL level (mg/dl) (within 6 months); n (%)	2,339 (21.7%)	2,294 (21.2%)	0.01	308 (1.5%)	284 (1.3%)	0.02	2,647 (8.3%)	2,578 (8.1%)	0.01
Lab values- LDL level (mg/dl); n (%)	2,527 (23.4%)	2,492 (23.1%)	0.01	312 (1.5%)	293 (1.4%)	0.01	2,839 (8.9%)	2,785 (8.7%)	0.01
Lab values- LDL level (mg/dl) (within 3 months); n (%)	1,695 (15.7%)	1,662 (15.4%)	0.01	203 (1.0%)	187 (0.9%)	0.01	1,898 (6.0%)	1,849 (5.8%)	0.01
Lab values- LDL level (mg/dl) (within 6 months); n (%)	2,527 (23.4%)	2,492 (23.1%)	0.01	312 (1.5%)	293 (1.4%)	0.01	2,839 (8.9%)	2,785 (8.7%)	0.01
Lab values- NT-proBNP; n (%)	13 (0.1%)	17 (0.2%)	-0.03	0 (0.0%)	0 (0.0%)	#DIV/0!	13 (0.0%)	17 (0.1%)	-0.04
Lab values- NT-proBNP (within 3 months); n (%)	9 (0.1%)	8 (0.1%)	0.00	0 (0.0%)	0 (0.0%)	#DIV/0!	9 (0.0%)	8 (0.0%)	#DIV/0!

# Table 1: Telmisartan vs Ramipril

Lab values- NT-proBNP (within 6 months); n (%)	13 (0.1%)	17 (0.2%)	-0.03	0 (0.0%)	0 (0.0%)	#DIV/0!	13 (0.0%)	17 (0.1%)	-0.04
Lab values- Total cholesterol (mg/dl); n (%)	2,519 (23.3%)	2,497 (23.1%)	0.00	314 (1.5%)	293 (1.4%)	0.01	2,833 (8.9%)	2,790 (8.8%)	0.00
Lab values- Total cholesterol (mg/dl) (within 3 months); n (%)	1,690 (15.7%)	1,665 (15.4%)	0.01	207 (1.0%)	185 (0.9%)	0.01	1,897 (6.0%)	1,850 (5.8%)	0.01
Lab values- Total cholesterol (mg/dl) (within 6 months); n (%)	2,519 (23.3%)	2,497 (23.1%)	0.00	314 (1.5%)	293 (1.4%)	0.01	2,833 (8.9%)	2,790 (8.8%)	0.00
Lab values- Triglyceride level (mg/dl); n (%)	2,479 (23.0%)	2,463 (22.8%)	0.00	314 (1.5%)	287 (1.4%)	0.01	2,793 (8.8%)	2,750 (8.6%)	0.01
Lab values- Triglyceride level (mg/dl) (within 3 months); n (%)	1,659 (15.4%)	1,644 (15.2%)	0.01	206 (1.0%)	183 (0.9%)	0.01	1,865 (5.9%)	1,827 (5.7%)	0.01
Lab values- Triglyceride level (mg/dl) (within 6 months); n (%)	2,479 (23.0%)	2,463 (22.8%)	0.00	314 (1.5%)	287 (1.4%)	0.01	2,793 (8.8%)	2,750 (8.6%)	0.01
Lab result number- HbA1c (%) mean (only 2 to 20 included)	1,968	1,935		296	270		0	0	
...mean (sd)	7.11 (1.65)	6.98 (1.59)	0.08	7.50 (1.79)	7.24 (1.62)	0.15	7.37 (1.74)	7.15 (1.61)	0.13
...median [IQR]	6.62 [6.00, 7.70]	6.50 [5.90, 7.60]	0.07	7.10 [6.30, 8.10]	6.75 [6.10, 8.00]	0.21	6.94 (1.74)	6.67 (1.61)	0.16
...Missing; n (%)	8,830 (81.8%)	8,863 (82.1%)	-0.01	20,778 (98.6%)	20,804 (98.7%)	-0.01	29,608 (92.9%)	29,667 (93.1%)	-0.01
Lab result number- BNP mean	72	71		8	6		0	0	
...mean (sd)	192.43 (286.24)	181.05 (419.77)	0.03	55.18 (41.00)	40.33 (28.20)	0.42	101.68 (169.91)	88.00 (245.40)	0.06
...median [IQR]	98.05 [27.50, 201.60]	69.40 [29.50, 152.00]	0.08	57.95 [20.50, 80.30]	42.00 [18.00, 66.00]	0.45	71.54 (169.91)	51.28 (245.40)	0.10
...Missing; n (%)	10,726 (99.3%)	10,727 (99.3%)	0.00	21,066 (100.0%)	21,068 (100.0%)	#DIV/0!	31,792 (99.7%)	31,795 (99.8%)	-0.02
Lab result number- BUN (mg/dl) mean	2,965	3,034		349	335		0	0	
...mean (sd)	17.98 (8.45)	-585.70 (21,175.88)	0.04	360.96 (6,422.54)	645.23 (8,108.67)	-0.04	244.76 (5222.51)	228.20 (13978.25)	0.00
...median [IQR]	17.00 [13.33, 21.00]	17.00 [13.33, 22.00]	0.00	16.00 [13.00, 21.00]	16.50 [14.00, 21.75]	0.00	16.34 (5222.51)	16.67 (13978.25)	0.00
...Missing; n (%)	7,833 (72.5%)	7,764 (71.9%)	0.01	20,725 (98.3%)	20,739 (98.4%)	-0.01	28,558 (89.6%)	28,503 (89.4%)	0.01
Lab result number- Creatinine (mg/dl) mean (only 0.1 to 15 included)	2,957	3,004		371	358		3,328	3,362	
...mean (sd)	1.04 (0.53)	1.08 (0.55)	-0.07	0.96 (0.36)	1.04 (0.46)	-0.19	0.99 (0.43)	1.05 (0.49)	-0.13
...median [IQR]	0.94 [0.80, 1.15]	0.97 [0.80, 1.19]	-0.06	0.90 [0.74, 1.07]	0.95 [0.78, 1.16]	-0.12	0.91 (0.43)	0.96 (0.49)	-0.11
...Missing; n (%)	7,841 (72.6%)	7,794 (72.2%)	0.01	20,703 (98.2%)	20,716 (98.3%)	-0.01	28,544 (89.6%)	28,510 (89.5%)	0.00
Lab result number- HDL level (mg/dl) mean (only <=5000 included)	2,339	2,294		307	283		2,646	2,577	
...mean (sd)	50.19 (17.83)	50.14 (17.34)	0.00	49.24 (16.21)	48.06 (17.06)	0.07	49.56 (16.78)	48.76 (17.16)	0.05
...median [IQR]	49.00 [40.00, 60.00]	49.00 [40.00, 59.00]	0.00	49.00 [39.50, 57.00]	46.00 [37.00, 57.00]	0.18	49.00 (16.78)	47.02 (17.16)	0.12
...Missing; n (%)	8,459 (78.3%)	8,504 (78.8%)	-0.01	20,767 (98.5%)	20,791 (98.7%)	-0.02	29,226 (91.7%)	29,295 (91.9%)	-0.01
Lab result number- LDL level (mg/dl) mean (only <=5000 included)	2,481	2,458		303	288		2,784	2,746	
...mean (sd)	-2,429.55 (47,296.88)	-2,059.43 (43,132.62)	-0.01	97.05 (47.66)	93.76 (46.96)	0.07	-758.94 (27529.19)	-635.72 (25105.38)	0.00
...median [IQR]	87.50 [65.00, 113.00]	89.00 [67.00, 115.00]	0.00	92.00 [69.00, 122.00]	89.00 [65.00, 119.75]	0.06	90.48 (27529.19)	89.00 (25105.38)	0.00
...Missing; n (%)	8,317 (77.0%)	8,340 (77.2%)	0.00	20,771 (98.6%)	20,786 (98.6%)	0.00	29,088 (91.3%)	29,126 (91.4%)	0.00

Table 1: Telmisartan vs Ramipril

Lab result number- Total cholesterol (mg/dl) mean (only <=5000 included)	2,518	2,495		313	291		2,831	2,786	
...mean (sd)	169.81 (55.72)	170.21 (54.89)	-0.01	179.74 (59.11)	181.98 (58.55)	-0.04	176.38 (57.98)	177.99 (57.34)	-0.03
...median [IQR]	169.00 [142.00, 201.00]	171.00 [143.00, 200.50]	-0.04	174.00 [146.00, 210.00]	177.00 [151.00, 205.00]	-0.05	172.31 (57.98)	174.97 (57.34)	-0.05
...Missing; n (%)	8,280 (76.7%)	8,303 (76.9%)	0.00	20,761 (98.5%)	20,783 (98.6%)	-0.01	29,041 (91.1%)	29,086 (91.3%)	-0.01
Lab result number- Triglyceride level (mg/dl) mean (only <=5000 included)	2,479	2,463		313	286		2,792	2,749	
...mean (sd)	143.65 (99.39)	142.29 (96.50)	0.01	157.67 (107.86)	191.88 (288.25)	-0.16	152.92 (105.07)	175.08 (241.03)	-0.12
...median [IQR]	122.00 [86.50, 174.00]	121.50 [87.00, 174.00]	0.01	133.00 [89.00, 197.00]	144.50 [102.00, 210.25]	-0.05	129.27 (105.07)	136.71 (241.03)	-0.04
...Missing; n (%)	8,319 (77.0%)	8,335 (77.2%)	0.00	20,761 (98.5%)	20,788 (98.6%)	-0.01	29,080 (91.2%)	29,123 (91.4%)	-0.01
Lab result number- Hemoglobin mean (only >0 included)	2,149	2,271		238	248		2,387	2,519	
...mean (sd)	13.51 (1.64)	13.38 (1.69)	0.08	698.10 (10,564.86)	1,097.55 (12,059.62)	-0.04	466.17 (8590.85)	730.24 (9806.31)	-0.03
...median [IQR]	13.60 [12.50, 14.60]	13.40 [12.30, 14.50]	0.12	13.40 [12.34, 14.52]	13.40 [12.30, 14.30]	0.00	13.47 (8590.85)	13.40 (9806.31)	0.00
...Missing; n (%)	8,649 (80.1%)	8,527 (79.0%)	0.03	20,836 (98.9%)	20,826 (98.8%)	0.01	29,485 (92.5%)	29,353 (92.1%)	0.02
Lab result number- Serum sodium mean (only >90 and <190 included)	2,899	2,971		310	303		3,209	3,274	
...mean (sd)	140.25 (2.70)	140.22 (2.86)	0.01	139.96 (2.35)	139.62 (2.36)	0.14	140.06 (2.47)	139.82 (2.54)	0.10
...median [IQR]	140.20 [139.00, 142.00]	140.50 [139.00, 142.00]	-0.11	140.00 [139.00, 141.50]	140.00 [138.00, 141.00]	0.00	140.07 (2.47)	140.17 (2.54)	-0.04
...Missing; n (%)	7,899 (73.2%)	7,827 (72.5%)	0.02	20,764 (98.5%)	20,771 (98.6%)	-0.01	28,663 (89.9%)	28,598 (89.7%)	0.01
Lab result number- Albumin mean (only >0 and <=10 included)	2,731	2,785		293	288		3,024	3,073	
...mean (sd)	4.22 (0.34)	4.21 (0.34)	0.03	4.16 (0.62)	4.12 (0.70)	0.06	4.18 (0.54)	4.15 (0.60)	0.05
...median [IQR]	4.25 [4.00, 4.40]	4.20 [4.00, 4.40]	0.15	4.20 [4.00, 4.40]	4.20 [4.00, 4.40]	0.00	4.22 (0.54)	4.20 (0.60)	0.04
...Missing; n (%)	8,067 (74.7%)	8,013 (74.2%)	0.01	20,781 (98.6%)	20,786 (98.6%)	0.00	28,848 (90.5%)	28,799 (90.4%)	0.00
Lab result number- Glucose (fasting or random) mean (only 10-1000 included)	2,878	2,947		303	302		3,181	3,249	
...mean (sd)	126.20 (54.75)	122.77 (52.41)	0.06	140.15 (65.72)	138.06 (59.88)	0.03	135.42 (62.22)	132.88 (57.46)	0.04
...median [IQR]	107.00 [93.00, 139.50]	106.00 [93.00, 134.00]	0.02	121.00 [100.00, 157.00]	120.00 [100.00, 157.25]	0.02	116.26 (62.22)	115.26 (57.46)	0.02
...Missing; n (%)	7,920 (73.3%)	7,851 (72.7%)	0.01	20,771 (98.6%)	20,772 (98.6%)	0.00	28,691 (90.0%)	28,623 (89.8%)	0.01
Lab result number- Potassium mean (only 1-7 included)	2,941	3,005		333	328		3,274	3,333	
...mean (sd)	4.43 (0.43)	4.39 (0.44)	0.09	4.35 (0.41)	4.33 (0.43)	0.05	4.38 (0.42)	4.35 (0.43)	0.07
...median [IQR]	4.40 [4.15, 4.70]	4.40 [4.10, 4.70]	0.00	4.35 [4.10, 4.60]	4.30 [4.10, 4.60]	0.12	4.37 (0.42)	4.33 (0.43)	0.09
...Missing; n (%)	7,857 (72.8%)	7,793 (72.2%)	0.01	20,741 (98.4%)	20,746 (98.4%)	0.00	28,598 (89.7%)	28,539 (89.5%)	0.01
Comorbidity Scores									
CCI (180 days)- ICD9 and ICD10									
...mean (sd)	2.46 (1.91)	2.44 (1.87)	0.01	1.71 (1.57)	1.70 (1.52)	0.01	1.96 (1.69)	1.95 (1.65)	0.01
...median [IQR]	2.00 [1.00, 3.00]	2.00 [1.00, 3.00]	0.00	1.00 [1.00, 2.00]	1.00 [1.00, 2.00]	0.00	1.34 (1.69)	1.34 (1.65)	0.00
Frailty Score (mean): Empirical Version 365 days,									
...mean (sd)	0.17 (0.06)	0.17 (0.06)	0.00	0.16 (0.05)	0.16 (0.05)	0.00	0.16 (0.05)	0.16 (0.05)	0.00
...median [IQR]	0.16 [0.14, 0.20]	0.16 [0.14, 0.20]	0.00	0.15 [0.13, 0.18]	0.15 [0.13, 0.18]	0.00	0.15 (0.05)	0.15 (0.05)	0.00

Table 1: Telmisartan vs Ramipril

<b>Healthcare Utilization</b>									
Any hospitalization; n (%)	1,039 (9.6%)	1,047 (9.7%)	0.00	2,526 (12.0%)	2,508 (11.9%)	0.00	3,565 (11.2%)	3,555 (11.2%)	0.00
Any hospitalization during prior 31-180 days; n (%)	796 (7.4%)	817 (7.6%)	-0.01	1,965 (9.3%)	1,935 (9.2%)	0.00	2,761 (8.7%)	2,752 (8.6%)	0.00
Endocrinologist Visit; n (%)	775 (7.2%)	760 (7.0%)	0.01	1,210 (5.7%)	1,226 (5.8%)	0.00	1,985 (6.2%)	1,986 (6.2%)	0.00
Endocrinologist Visit (30 days prior); n (%)	285 (2.6%)	279 (2.6%)	0.00	462 (2.2%)	468 (2.2%)	0.00	0,747 (2.3%)	0,747 (2.3%)	0.00
Endocrinologist Visit (31 to 180 days prior); n (%)	668 (6.2%)	659 (6.1%)	0.00	1,050 (5.0%)	1,072 (5.1%)	0.00	1,718 (5.4%)	1,731 (5.4%)	0.00
Internal medicine/family medicine visits; n (%)	8,235 (76.3%)	8,214 (76.1%)	0.00	16,197 (76.9%)	16,428 (78.0%)	-0.03	24,432 (76.7%)	24,642 (77.3%)	-0.01
Internal medicine/family medicine visits (30 days prior) ; n (%)	5,405 (50.1%)	5,194 (48.1%)	0.04	10,493 (49.8%)	10,094 (47.9%)	0.04	15,898 (49.9%)	15,288 (48.0%)	0.04
Internal medicine/family medicine visits (31 to 180 days prior) ; n (%)	7,225 (66.9%)	7,227 (66.9%)	0.00	14,210 (67.4%)	14,711 (69.8%)	-0.05	21,435 (67.3%)	21,938 (68.8%)	-0.03
Cardiologist visit; n (%)	4,248 (39.3%)	4,215 (39.0%)	0.01	6,932 (32.9%)	6,906 (32.8%)	0.00	11,180 (35.1%)	11,121 (34.9%)	0.00
Number of Cardiologist visits (30 days prior); n (%)	1,865 (17.3%)	1,875 (17.4%)	0.00	3,056 (14.5%)	3,045 (14.4%)	0.00	4,921 (15.4%)	4,920 (15.4%)	0.00
Number of Cardiologist visits (31 to 180 days prior); n (%)	3,390 (31.4%)	3,420 (31.7%)	-0.01	5,653 (26.8%)	5,635 (26.7%)	0.00	9,043 (28.4%)	9,055 (28.4%)	0.00
Electrocardiogram ; n (%)	4,169 (38.6%)	4,291 (39.7%)	-0.02	8,178 (38.8%)	8,113 (38.5%)	0.01	12,347 (38.7%)	12,404 (38.9%)	0.00
Use of glucose test strips; n (%)	296 (2.7%)	275 (2.5%)	0.01	336 (1.6%)	353 (1.7%)	-0.01	0,632 (2.0%)	0,628 (2.0%)	0.00
Dialysis; n (%)	35 (0.3%)	33 (0.3%)	0.00	64 (0.3%)	43 (0.2%)	0.02	99 (0.3%)	76 (0.2%)	0.02
number of different/distinct medication prescriptions									
...mean (sd)	8.42 (4.74)	8.35 (4.89)	0.01	8.79 (5.01)	8.75 (4.98)	0.01	8.66 (4.92)	8.61 (4.95)	0.01
...median [IQR]	8.00 [5.00, 11.00]	8.00 [5.00, 11.00]	0.00	8.00 [5.00, 11.00]	8.00 [5.00, 11.00]	0.00	8.00 (4.92)	8.00 (4.95)	0.00
Number of Hospitalizations									
...mean (sd)	0.11 (0.37)	0.12 (0.39)	-0.03	0.13 (0.39)	0.13 (0.39)	0.00	0.12 (0.38)	0.13 (0.39)	-0.03
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 (0.38)	0.00 (0.39)	0.00
Number of hospital days									
...mean (sd)	0.61 (2.77)	0.64 (3.07)	-0.01	0.72 (2.86)	0.70 (3.05)	0.01	0.68 (2.83)	0.68 (3.06)	0.00
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 (2.83)	0.00 (3.06)	0.00
Number of Emergency Department (ED) visits									
...mean (sd)	0.43 (1.17)	0.45 (1.15)	-0.02	0.12 (0.90)	0.12 (1.01)	0.00	0.23 (1.00)	0.23 (1.06)	0.00
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 (1.00)	0.00 (1.06)	0.00
Number of Office visits									
...mean (sd)	5.51 (4.70)	5.46 (4.45)	0.01	5.62 (4.90)	5.60 (4.62)	0.00	5.58 (4.83)	5.55 (4.56)	0.01
...median [IQR]	4.00 [2.00, 7.00]	4.00 [2.00, 7.00]	0.00	4.00 [2.00, 8.00]	5.00 [2.00, 8.00]	-0.21	4.00 (4.83)	4.66 (4.56)	-0.14
Number of Endocrinologist visits									
...mean (sd)	0.33 (1.76)	0.34 (1.95)	-0.01	0.27 (1.70)	0.27 (1.74)	0.00	0.32 (1.54)	0.33 (1.57)	-0.01
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 (1.54)	0.00 (1.57)	0.00
Number of internal medicine/family medicine visits									
...mean (sd)	7.93 (12.42)	8.01 (12.57)	-0.01	6.43 (10.52)	6.42 (9.97)	0.00	6.94 (11.20)	6.96 (10.92)	0.00
...median [IQR]	4.00 [1.00, 10.00]	4.00 [1.00, 10.00]	0.00	3.00 [1.00, 8.00]	4.00 [1.00, 8.00]	-0.10	3.34 (11.20)	4.00 (10.92)	-0.06
Number of Cardiologist visits									
...mean (sd)	2.26 (5.11)	2.19 (4.76)	0.01	1.74 (4.37)	1.77 (4.23)	-0.01	1.92 (4.63)	1.91 (4.42)	0.00

Table 1: Telmisartan vs Ramipril

...median [IQR]	0.00 [0.00, 2.00]	0.00 [0.00, 2.00]	0.00	0.00 [0.00, 2.00]	0.00 [0.00, 2.00]	0.00	0.00 (4.63)	0.00 (4.42)	0.00
Number electrocardiograms received									
...mean (sd)	0.77 (1.52)	0.79 (1.47)	-0.01	0.67 (1.21)	0.67 (1.18)	0.00	0.70 (1.32)	0.71 (1.29)	-0.01
...median [IQR]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00	0.00 (1.32)	0.00 (1.29)	0.00
Number of HbA1c tests ordered									
...mean (sd)	0.62 (0.87)	0.62 (0.85)	0.00	0.33 (0.67)	0.32 (0.67)	0.01	0.43 (0.74)	0.42 (0.74)	0.01
...median [IQR]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 (0.74)	0.00 (0.74)	0.00
Number of glucose tests ordered									
...mean (sd)	0.32 (1.98)	0.30 (1.24)	0.01	0.19 (2.25)	0.18 (0.74)	0.01	0.23 (2.16)	0.22 (0.94)	0.01
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 (2.16)	0.00 (0.94)	0.00
Number of lipid tests ordered									
...mean (sd)	0.81 (0.97)	0.82 (0.96)	-0.01	0.47 (0.99)	0.47 (0.92)	0.00	0.59 (0.98)	0.59 (0.93)	0.00
...median [IQR]	1.00 [0.00, 1.00]	1.00 [0.00, 1.00]	0.00	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00	0.34 (0.98)	0.34 (0.93)	0.00
Number of creatinine tests ordered									
...mean (sd)	0.08 (0.46)	0.08 (0.44)	0.00	0.06 (0.35)	0.06 (0.34)	0.00	0.07 (0.39)	0.07 (0.38)	0.00
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 (0.39)	0.00 (0.38)	0.00
Number of BUN tests ordered									
...mean (sd)	0.06 (0.53)	0.06 (0.49)	0.00	0.04 (0.36)	0.04 (0.36)	0.00	0.05 (0.43)	0.05 (0.41)	0.00
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 (0.43)	0.00 (0.41)	0.00
Number of tests for microalbuminuria									
...mean (sd)	0.39 (0.92)	0.39 (0.93)	0.00	0.17 (0.61)	0.18 (0.62)	-0.02	0.24 (0.73)	0.25 (0.74)	-0.01
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 (0.73)	0.00 (0.74)	0.00
Total N distinct ICD9/ICD10 diagnoses at the 3rd digit level									
...mean (sd)	4.68 (7.40)	4.67 (7.41)	0.00	1.33 (3.41)	1.34 (3.40)	0.00	2.46 (5.12)	2.47 (5.12)	0.00
...median [IQR]	1.00 [0.00, 7.00]	1.00 [0.00, 7.00]	0.00	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00	0.34 (5.12)	0.34 (5.12)	0.00
For PS									
Hemorrhagic stroke+Other cerebrovascular disease+Cerebrovascular procedure (for PS); n (%)	415 (3.8%)	390 (3.6%)	0.01	600 (2.8%)	563 (2.7%)	0.01	1015 (3.2%)	953 (3.0%)	0.01
Occurrence of creatinine tests ordered (for PS); n (%)	608 (5.6%)	592 (5.5%)	0.00	874 (4.1%)	832 (3.9%)	0.01	1,482 (4.6%)	1,424 (4.5%)	0.00
Occurrence of BUN tests ordered (for PS); n (%)	391 (3.6%)	382 (3.5%)	0.01	613 (2.9%)	590 (2.8%)	0.01	1,004 (3.2%)	972 (3.0%)	0.01
Occurrence of chronic renal insufficiency w/o CKD (for PS); n (%)	620 (5.7%)	575 (5.3%)	0.02	555 (2.6%)	547 (2.6%)	0.00	1,175 (3.7%)	1,122 (3.5%)	0.01
Chronic kidney disease Stage 1-2 (for PS); n (%)	294 (2.7%)	293 (2.7%)	0.00	233 (1.1%)	225 (1.1%)	0.00	527 (1.7%)	518 (1.6%)	0.01
Chronic kidney disease Stage 3-6 (for PS); n (%)	1,058 (9.8%)	1,009 (9.3%)	0.02	945 (4.5%)	939 (4.5%)	0.00	2,003 (6.3%)	1,948 (6.1%)	0.01
Bladder stones+Kidney stones (for PS); n (%)	236 (2.2%)	226 (2.1%)	0.01	353 (1.7%)	360 (1.7%)	0.00	0,589 (1.8%)	0,586 (1.8%)	0.00
Diabetes with peripheral circulatory disorders+Gangrene+Osteomyelitis(for PS) with ICD10 ; n (%)	485 (4.5%)	484 (4.5%)	0.00	450 (2.1%)	448 (2.1%)	0.00	0,935 (2.9%)	0,932 (2.9%)	0.00
Alcohol abuse or dependence+Drug abuse or dependence (for PS); n (%)	184 (1.7%)	181 (1.7%)	0.00	147 (0.7%)	146 (0.7%)	0.00	331 (1.0%)	327 (1.0%)	0.00

Table 1: Telmisartan vs Ramipril

Diabetes with other ophthalmic manifestations+Retinal detachment, vitreous hemorrhage, vitrectomy+Retinal laser coagulation therapy (for PS); n (%)	171 (1.6%)	178 (1.6%)	0.00	777 (3.7%)	745 (3.5%)	0.01	0,948 (3.0%)	0,923 (2.9%)	0.01
Other atherosclerosis+Cardiac conduction disorders+Other CVD (for PS) ; n (%)	1,890 (17.5%)	1,940 (18.0%)	-0.01	3,122 (14.8%)	3,069 (14.6%)	0.01	5,012 (15.7%)	5,009 (15.7%)	0.00
Previous cardiac procedure (CABG or PTCA or Stent) + History of CABG or PTCA (for PS) ; n (%)	819 (7.6%)	827 (7.7%)	0.00	696 (3.3%)	720 (3.4%)	-0.01	1,515 (4.8%)	1,547 (4.9%)	0.00
Hyperthyroidism + Hypothyroidism + Other disorders of thyroid gland (for PS); n (%)	2,036 (18.9%)	2,026 (18.8%)	0.00	2,345 (11.1%)	2,302 (10.9%)	0.01	4,381 (13.7%)	4,328 (13.6%)	0.00
Delirium + Psychosis (for PS); n (%)	205 (1.9%)	188 (1.7%)	0.02	246 (1.2%)	264 (1.3%)	-0.01	451 (1.4%)	452 (1.4%)	0.00
Any use of Meglitinides (for PS); n (%)	69 (0.6%)	70 (0.6%)	0.00	229 (1.1%)	236 (1.1%)	0.00	298 (0.9%)	306 (1.0%)	-0.01
Any use of AGIs (for PS); n (%)	13 (0.1%)	14 (0.1%)	0.00	3,122 (14.8%)	3,069 (14.6%)	0.01	5,012 (15.7%)	5,009 (15.7%)	0.00
CKD stage 3-6 + dialysis (for PS); n (%)	1,062 (9.8%)	1,017 (9.4%)	0.01	966 (4.6%)	942 (4.5%)	0.00	2,028 (6.4%)	1,959 (6.1%)	0.01
Use of thiazide; n (%)	1,217 (11.3%)	1,206 (11.2%)	0.00	2,245 (10.7%)	2,192 (10.4%)	0.01	12,766 (40.1%)	12,770 (40.1%)	0.00
Use of beta blockers; n (%)	4,323 (40.0%)	4,313 (39.9%)	0.00	8,443 (40.1%)	8,457 (40.1%)	0.00	9,032 (28.3%)	8,944 (28.1%)	0.00
Use of calcium channel blockers; n (%)	3,057 (28.3%)	3,052 (28.3%)	0.00	5,975 (28.4%)	5,892 (28.0%)	0.01	9,980 (31.3%)	9,933 (31.2%)	0.00
All antidiabetic medications except Insulin; n (%)	3,614 (33.5%)	3,591 (33.3%)	0.00	6,366 (30.2%)	6,342 (30.1%)	0.00	3,462 (10.9%)	3,398 (10.7%)	0.01
DM Medications - Insulin ; n (%)	1,311 (12.1%)	1,288 (11.9%)	0.01	2,346 (11.1%)	2,279 (10.8%)	0.01	3,657 (11.5%)	3,567 (11.2%)	0.01
Use of Low Intensity Statins; n (%)	2,886 (26.7%)	2,867 (26.6%)	0.00	5,753 (27.3%)	5,812 (27.6%)	-0.01	8639 (27.1%)	8,679 (27.2%)	0.00
Use of High Intensity Statins; n (%)	2,896 (26.8%)	2,809 (26.0%)	0.02	4,972 (23.6%)	4,837 (23.0%)	0.01	7868 (24.7%)	7,646 (24.0%)	0.02
Malignant hypertension; n (%)	314 (2.9%)	304 (2.8%)	0.01	7,681 (36.4%)	7,737 (36.7%)	-0.01	7995 (25.1%)	8,041 (25.2%)	0.00
Cardiovascular stress test; n (%)	34 (0.3%)	34 (0.3%)	0.00	79 (0.4%)	75 (0.4%)	0.00	0,113 (0.4%)	109 (0.3%)	0.02
Echocardiogram; n (%)	1,689 (15.6%)	1,723 (16.0%)	-0.01	3,801 (18.0%)	3,752 (17.8%)	0.01	5,490 (17.2%)	5475 (17.2%)	0.00
Number of BNP tests									
...mean (sd)	0.05 (0.29)	0.05 (0.29)	0.00	0.03 (0.20)	0.03 (0.20)	0.00	0.04 (0.23)	0.04 (0.23)	0.00
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 (0.23)	0.00 (0.23)	0.00
Number of Cardiac biomarkers tests (troponin, CK-MBs, Myoglobin, CPK)									
...mean (sd)	0.28 (1.16)	0.29 (1.07)	-0.01	0.18 (0.89)	0.17 (0.94)	0.01	0.21 (0.99)	0.21 (0.99)	0.00
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 (0.99)	0.00 (0.99)	0.00
Number of Ambulatory Blood pressure monitoring tests									
...mean (sd)	0.00 (0.05)	0.00 (0.06)	0.00	0.00 (0.09)	0.00 (0.07)	0.00	0.00 (0.08)	0.00 (0.07)	0.00
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 (0.08)	0.00 (0.07)	0.00
N of days on antihypertensive medications during baseline									
...mean (sd)	84.64 (73.97)	83.37 (72.98)	0.02	90.02 (73.50)	89.44 (72.27)	0.01	88.20 (73.66)	87.38 (72.51)	0.01
...median [IQR]	81.00 [1.00, 167.00]	78.00 [1.00, 165.00]	0.04	89.00 [1.00, 170.00]	86.00 [1.00, 168.00]	0.04	86.29 (73.66)	83.29 (72.51)	0.04
N of days in database anytime prior									
...mean (sd)	1,658.62 (1,202.43)	1,646.78 (1,190.83)	0.01	1,693.01 (1,137.33)	1,698.81 (1,133.02)	-0.01	1681.36 (1159.79)	1681.18 (1152.93)	0.00
...median [IQR]	1,366.00 [726.00, 2,255.00]	1,353.50 [731.00, 2,246.00]	0.01	1,441.00 [781.00, 2,363.25]	1,464.00 [780.00, 2,408.00]	-0.02	1415.59 (1159.79)	1426.56 (1152.93)	-0.01

Table 1: Telmisartan vs Ramipril

Mean Copay for per prescription cost (charges in U.S. \$) (180-1 day prior)									
...mean (sd)	30.82 (38.30)	30.67 (37.74)	0.00	23.28 (26.42)	23.56 (26.22)	-0.01	25.83 (30.96)	25.97 (30.61)	0.00
...median [IQR]	21.88 [9.56, 38.75]	21.54 [9.00, 38.59]	0.01	17.14 [6.66, 31.86]	17.67 [6.64, 32.50]	-0.02	18.75 (30.96)	18.98 (30.61)	-0.01
...Missing; n (%)	692 (6.4%)	702 (6.5%)	0.00	1,075 (5.1%)	1,043 (4.9%)	0.01	1,767 (5.5%)	1745 (5.5%)	0.00
Colonos; n (%)	529 (4.9%)	511 (4.7%)	0.01	1,182 (5.6%)	1,124 (5.3%)	0.01	1,711 (5.4%)	1635 (5.1%)	0.01
Fecal occult blood (FOB) test; n (%)	560 (5.2%)	559 (5.2%)	0.00	773 (3.7%)	775 (3.7%)	0.00	1,333 (4.2%)	1334 (4.2%)	0.00
Flu vaccine; n (%)	1,686 (15.6%)	1,725 (16.0%)	-0.01	2,082 (9.9%)	2,106 (10.0%)	0.00	3,768 (11.8%)	3831 (12.0%)	-0.01
Mammogram; n (%)	1,305 (12.1%)	1,335 (12.4%)	-0.01	2,335 (11.1%)	2,365 (11.2%)	0.00	3,640 (11.4%)	3700 (11.6%)	-0.01
Pap smear; n (%)	465 (4.3%)	464 (4.3%)	0.00	1,011 (4.8%)	1,005 (4.8%)	0.00	1,476 (4.6%)	1469 (4.6%)	0.00
Pneumonia vaccine; n (%)	1,049 (9.7%)	1,038 (9.6%)	0.00	673 (3.2%)	683 (3.2%)	0.00	1,722 (5.4%)	1721 (5.4%)	0.00
PSA test or Prostate exam for DRE; n (%)	1,615 (15.0%)	1,643 (15.2%)	-0.01	1,947 (9.2%)	1,950 (9.3%)	0.00	3,562 (11.2%)	3593 (11.3%)	0.00
Bone mineral density; n (%)	459 (4.3%)	464 (4.3%)	0.00	627 (3.0%)	648 (3.1%)	-0.01	1,086 (3.4%)	1112 (3.5%)	-0.01
Use of Sympathomimetic agents; n (%)	137 (1.3%)	138 (1.3%)	0.00	399 (1.9%)	427 (2.0%)	-0.01	0,536 (1.7%)	565 (1.8%)	-0.01
Use of CNS stimulants; n (%)	73 (0.7%)	66 (0.6%)	0.01	163 (0.8%)	170 (0.8%)	0.00	0,236 (0.7%)	236 (0.7%)	0.00
Use of estrogens, progestins, androgens; n (%)	567 (5.3%)	532 (4.9%)	0.02	1,428 (6.8%)	1,495 (7.1%)	-0.01	1,995 (6.3%)	2027 (6.4%)	0.00
Use of Angiogenesis inhibitors; n (%)	6 (0.1%)	5 (0.0%)	0.04	14 (0.1%)	12 (0.1%)	0.00	0,020 (0.1%)	17 (0.1%)	0.00
Use of Oral Immunosuppressants; n (%)	35 (0.3%)	18 (0.2%)	0.02	70 (0.3%)	54 (0.3%)	0.00	0,105 (0.3%)	72 (0.2%)	0.02
Cardiomegaly, LVH, and other cardiopathy due to hypertension; n (%)	1,211 (11.2%)	1,184 (11.0%)	0.01	1,704 (8.1%)	1,699 (8.1%)	0.00	2,915 (9.1%)	2883 (9.0%)	0.00
Ultrasound; n (%)	1,986 (18.4%)	2,015 (18.7%)	-0.01	4,463 (21.2%)	4,409 (20.9%)	0.01	6,449 (20.2%)	6424 (20.2%)	0.00
Symptomatic hypotension; n (%)	178 (1.6%)	187 (1.7%)	-0.01	265 (1.3%)	238 (1.1%)	0.02	0,443 (1.4%)	425 (1.3%)	0.01
Syncopal episodes; n (%)	234 (2.2%)	231 (2.1%)	0.01	321 (1.5%)	315 (1.5%)	0.00	0,555 (1.7%)	546 (1.7%)	0.00
N of Generic name drugs only									
...mean (sd)	11.16 (12.36)	11.01 (12.23)	0.01	8.52 (8.59)	8.48 (8.55)	0.00	9.41 (10.03)	9.34 (9.95)	0.01
...median [IQR]	8.00 [3.00, 15.00]	7.00 [3.00, 15.00]	0.08	6.00 [2.00, 12.00]	6.00 [2.00, 12.00]	0.00	6.68 (10.03)	6.34 (9.95)	0.03
N of Brand name drugs only									
...mean (sd)	4.71 (6.40)	4.64 (6.19)	0.01	5.72 (6.82)	5.67 (6.39)	0.01	5.38 (6.68)	5.32 (6.32)	0.01
...median [IQR]	2.00 [0.00, 7.00]	2.00 [0.00, 6.00]	0.00	4.00 [1.00, 8.00]	4.00 [1.00, 8.00]	0.00	3.32 (6.68)	3.32 (6.32)	0.00
Number of distinct antihypertensive generic medications (180-1 days before index)									
...mean (sd)	1.07 (1.21)	1.07 (1.20)	0.00	1.09 (1.21)	1.08 (1.20)	0.01	1.08 (1.21)	1.08 (1.20)	0.00
...median [IQR]	1.00 [0.00, 2.00]	1.00 [0.00, 2.00]	0.00	1.00 [0.00, 2.00]	1.00 [0.00, 2.00]	0.00	1.00 (1.21)	1.00 (1.20)	0.00
Number of distinct antihypertensive generic medications on CED									
...mean (sd)	1.26 (0.57)	1.26 (0.61)	0.00	1.26 (0.58)	1.26 (0.60)	0.00	1.26 (0.58)	1.26 (0.60)	0.00
...median [IQR]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	0.00	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	0.00	1.00 (0.58)	1.00 (0.60)	0.00
Hypertensive retinopathy; n (%)	95 (0.9%)	104 (1.0%)	-0.01	119 (0.6%)	117 (0.6%)	0.00	0	0	#VALUE!
Commercial vs Medicare Advantage-Business Type Code - CORRECT ONE - TRUVEN									
...Commercial; n (%)	4,759 (44.1%)	4,766 (44.1%)	0.00	12,068 (57.3%)	11,960 (56.8%)	0.01	16,827 (52.8%)	16726 (52.5%)	0.01
...Medicare Advantage; n (%)	6,039 (55.9%)	6,032 (55.9%)	0.00	9,006 (42.7%)	9,114 (43.2%)	-0.01	15,045 (47.2%)	15146 (47.5%)	-0.01
Commercial vs Medicare Advantage-Business Type Code									
...COM = COMMERCIAL; n (%)	4,759 (44.1%)	4,766 (44.1%)	0.00	-	-	#VALUE!	4,759 (44.1%)	4,766 (44.1%)	0.00

**Table 1: Telmisartan vs Ramipril**

...MCR = MEDICARE; n (%)	6,039 (55.9%)	6,032 (55.9%)	0.00	-	-	#VALUE!	6,039 (55.9%)	6,032 (55.9%)	0.00
...MCD = MEDICAID; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	-	-	#VALUE!	0 (0.0%)	0 (0.0%)	#DIV/0!
...NONE = NO BUSINESS LINE CODE (added in 2015); n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	-	-	#VALUE!	0 (0.0%)	0 (0.0%)	#DIV/0!
...UNK = UNKNOWN (added in 2015); n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	-	-	#VALUE!	0 (0.0%)	0 (0.0%)	#DIV/0!
Commercial vs Medicare Advantage- Data Type	-	-	#VALUE!	0	0	#VALUE!	0	0	#VALUE!
...1 - Fee For Service; n (%)	-	-	#VALUE!	8,196 (38.9%)	8,292 (39.3%)	-0.01	8,196 (38.9%)	8,292 (39.3%)	-0.01
...2 - Encounter; n (%)	-	-	#VALUE!	810 (3.8%)	822 (3.9%)	-0.01	810 (3.8%)	822 (3.9%)	-0.01
...3 - Medicare; n (%)	-	-	#VALUE!	11,407 (54.1%)	11,287 (53.6%)	0.01	11,407 (54.1%)	11,287 (53.6%)	0.01
...4 - Medicare Encounter; n (%)	-	-	#VALUE!	661 (3.1%)	673 (3.2%)	-0.01	661 (3.1%)	673 (3.2%)	-0.01
Metropolitan Statistical Area - Urban (any MSA) vs Rural (non-MSA)									
...Urban; n (%)	-	-	#VALUE!	15,898 (75.4%)	15,898 (75.4%)	0.00	15,898 (75.4%)	15,898 (75.4%)	0.00
...Rural; n (%)	-	-	#VALUE!	220 (1.0%)	199 (0.9%)	0.01	220 (1.0%)	199 (0.9%)	0.01
...Unknown/Missing; n (%)	-	-	#VALUE!	4,956 (23.5%)	4,977 (23.6%)	0.00	4,956 (23.5%)	4,977 (23.6%)	0.00