Replication of the SAVOR-TIMI Diabetes Trial in Healthcare Claims
NCT03936023

December 27, 2019

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

Saxagliptin and Cardiovascular Outcomes in Patients with Type 2 Diabetes Mellitus (SAVOR- TIMI 53 trial)

1.2 Intended aim(s)

The cardiovascular safety and efficacy of many current antihyperglycemic agents, including saxagliptin, a dipeptidyl peptidase 4 (DPP-4) inhibitor, are unclear. This trial was designed to evaluate the safety and efficacy of saxagliptin with respect to cardiovascular outcomes in patients with diabetes mellitus who are at risk for cardiovascular events.

1.3 Primary endpoint for replication and RCT finding

Composite of CV death, nonfatal myocardial infarction, or nonfatal ischemic stroke

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

85% power to identify a 17% relative reduction of the primary end point with saxagliptin versus placebo and 98% power to test for noninferiority of saxagliptin versus placebo (reject the upper limit of 95% CI for an HR 1.3 at a 1-sided α of .025)

1.5 Primary trial estimate targeted for replication

HR = 1.00 (95% CI 0.89-1.12) comparing saxagliptin to placebo (Scirica et al., 2013)

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.

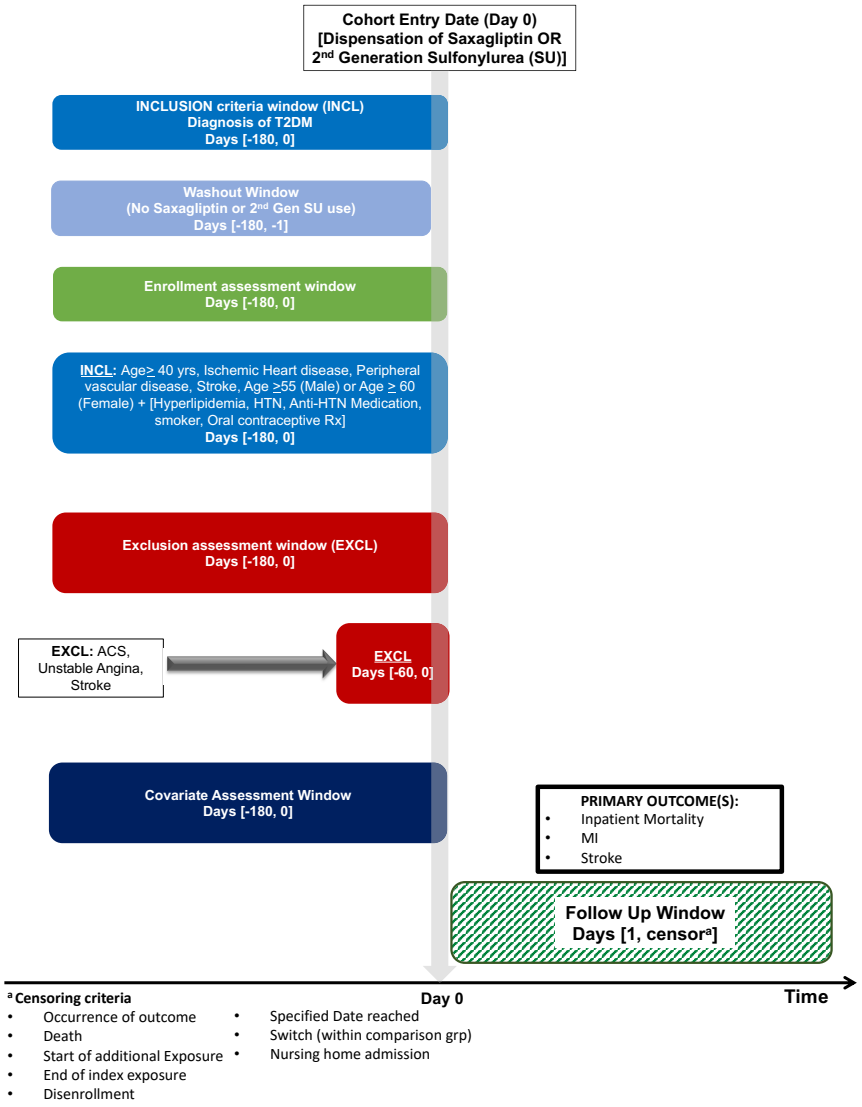
3. Data Source(s)

United/Optum, MarketScan, Medicare

4. Study Design Diagram

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

Design Diagram – SAVOR-TIMI 53 TRIAL REPLICATION



5. Cohort Identification

5.1 Cohort Summary

This study will involve a new user, parallel group, cohort study design comparing saxagliptin to the 2nd generation sulfonylurea (SU) antidiabetic class as a proxy for placebo. 2nd generation SUs are not known to have an impact on the outcome of interest. In addition, SUs were the most frequent background treatment in SAVOR-TIMI53 (after metformin), and DPP4i and SUs are preferentially prescribed to similarly older patients in real world (Patorno et al., 2019). The patients will be required to have continuous enrollment during the baseline period of 180 days before initiation of saxagliptin or a comparator drug (cohort entry date). Follow-up for the outcome (3P-MACE), begins the day after drug initiation. As in the trial, patients are allowed to take other antidiabetic medications during the study

5.2 Important steps for cohort formation

5.2.1 Eligible cohort entry dates

Market availability of saxagliptin in the U.S. started on July 31, 2009

- For Marketscan: July 31, 2009-Dec 31, 2017 (end of data availability).
- For Medicare: Jan 1, 2012-Dec 31, 2017 (start- end of data availability).
- For Optum: July 31, 2009-March 31, 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**	**Medicare**

	Less Excluded Patients	Remaining Patients	Less Excluded Patients	Remaining Patients	Less Excluded Patients	Remaining Patients
All patients in the database		74,864,884		191,990,035		23,466,175
Patients who used exposure or a reference between 20 January 2010 to Dec 2017 (for Marketscan)/March 2019 (for Optum) and 01 January 2012-December 2017 for Medicare	-73,333,681	1,531,203	-189,850,391	2,139,644	-20,002,243	3,463,932
Patients who have continuous 6 months registration in the database	-198,718	1,332,485	-233,411	1,906,233	-926,605	2,537,327
Patients without prior use of reference	-837,680	494,805	-1,282,498	623,735	-1,516,234	1,021,093
Patients without prior use of exposure	-58,834	435,971	-71,555	552,180	-57,547	963,546
Excluded because patient qualified in >1 exposure category	-193	435,778	-301	551,879	-111	963,435
Patients who did not have missing age information	-13	435,765	0	551,879	0	963,435
Patients who did not have missing gender information	-26	435,739	0	551,879	0	963,435
Excluded based on Inclusion 1- DM Type 2	-20,512	415,227	-49,327	502,552	-8,942	954,493
Excluded based on Inclusion 2- Age >=40	-8,101	407,126	-17,260	485,292	0	954,493
Excluded based on Inclusion 4- High risk for a CV event defined as having either established CV disease and/or multiple risk factors	-34,138	372,988	-73,801	411,491	-3,577	950,916
Excluded based on Exclusion1- CCI >=10	-3,466	369,522	-1,659	409,832	-17,277	933,639
Excluded based on Exclusion 2- treatment with an incretin-based therapy such as DPP-4 inhibitors and/or GLP-1 mimetics	-13,198	356,324	-18,748	391,084	-33,418	900,221
Excluded based on Exclusion 3- Acute vascular (cardiac or stroke) event <2 months [i.e. ACS/unstable angina OR Any stroke (inpatient, any)]	-766	355,558	-1,546	389,538	-1,979	898,242
Excluded based on Exclusion 4- chronic dialysis or renal transplant	-592	354,966	-434	389,104	-2,718	895,524
Excluded based on Exclusion 5- Pregnancy	-7	354,959	-11	389,093	-9	895,515
Excluded based on Exclusion 6- HIV/AIDS (dx and meds) with ICD10 CODES	-129	354,830	-104	388,989	-206	895,309
Excluded based on Exclusion 7- Lupus	-174	354,656	-122	388,867	-517	894,792
Excluded based on Exclusion 8- long-term (>30 consecutive days) oral corticosteroids use	-2,286	352,370	-2,495	386,372	-7,501	887,291
Excluded based on Exclusion 9- Morbid Obesity	-3,600	348,770	-2,126	384,246	-6,087	881,204
Excluded based on Exclusion 13- Non-compliance	-1408	347,362	-447	383,799	-2,954	878,250

Final cohort		347,362		383,799		878,250

* Medicare database includes only patients with at least one diagnosis for diabetes, heart failure, or cerebrovascular disease.

6. Variables

6.1 Exposure-related variables:

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

Comparator agents:

- Initiators of saxagliptin will be compared to initiators of-
    - 2nd generation sulfonylureas

Because saxagliptin and comparators are frequently used as second or third line treatments of T2DM, we expect it to be unlikely that saxagliptin and comparators are initiated in patients with substantially different baseline risk for proposed outcomes.

6.2 Preliminary covariates:

- Age
- Sex
- Combined Comorbidity Index (CCI), measured over the default 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 outcomes of interest (definitions provided in **Appendix A**):

- **Primary outcome**: 3-point major adverse cardiovascular events (MACE), i.e., non-fatal myocardial infarction, non-fatal stroke, or CV mortality
- Secondary outcomes: Individual MACE components:
  - 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 mortality/CV mortality:
    - All-cause inpatient mortality identified using discharge status codes will be used as a proxy for "CV mortality" in commercial databases
    - Information on CV mortality through data linkage with the National Death Index (NDI) will only become available at a later date for Medicare and will be used in secondary analyses.

Control outcomes of interest (control outcomes only serve to assess aspects of study validity but are not further interpreted):

1. Severe hypoglycemia (we expect to see protective effect; American Diabetes Association, 2018)

Control outcome definitions

Outcome	Hospital Discharge Code(s)	Comments
Severe hypoglycemia	**Severe hypoglycemia** Any-position ED or primary inpatient ICD-9 diagnosis: 251.0, 251.1x, 251.2x, or 250.8x. Outcomes identified by 250.8x are not included if they co-occur with one of the following diagnoses: 259.8, 272.7, 681.xx, 682.xx, 686.9, 707.1x, 707.2x, 707.8, 707.9, 709.3, 730.0x, 730.1x, 730.2x, 731.8	Note- The corresponding ICD-10 codes will be used also

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 the 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 liraglutide 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 (saxagliptin 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 augmentation or switching from an exposure to a comparator or any other agent in the comparator class and vice versa (e.g. switching from glimepiride to glipizide would be a censoring event);
    - A dosage change on the index treatment does not fulfill this criterion
    - An added treatment that is not part of the exposure or comparator group does not fulfill this criterion (e.g. if a saxagliptin user adds insulin, he or she does not get censored at the time of insulin augmentation)

For the ITT analyses, the censoring based on the augmentation/switching and treatment discontinuation will be replaced with a maximum allowed follow-up time of 365 days.

7. Initial Feasibility Analysis

Aetion report links:
Optum- https://bwh-dope.aetion.com/#/projects/details/641/results/29994/result/0
Marketscan- https://bwh-dope.aetion.com/#/projects/details/642/results/29995/result/0
Medicare- https://bwh-dope.aetion.com/#/projects/details/643/results/29996/result/0

Date conducted: rerun on 01/07/2019

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.

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

8. Initial Power Assessment

Aetion report links:
Optum- https://bwh-dope.aetion.com/#/projects/details/641/results/29997/result/1
Marketscan- https://bwh-dope.aetion.com/#/projects/details/642/results/29998/result/1
Medicare- https://bwh-dope.aetion.com/#/projects/details/643/results/29999/result/1

Date conducted: rerun on 01/07/2019

- 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 M. Franklin	Date reviewed:	10/26/18
Reviewed by FDA:	Ken Quinto	Date reviewed:	12/19/18
Reasons for stopping analysis (if required):			

9. Balance Assessment after PS matching

Aetion report name:
Optum- https://bwh-dope.aetion.com/projects/details/641/results/44771/result/0
Marketscan- https://bwh-dope.aetion.com/projects/details/642/results/44772/result/0
Medicare- https://bwh-dope.aetion.com/projects/details/643/results/45431/result/0

Date conducted: 11/18/2019 (Medicare 11/30/2019)

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	1,783 (0.98%)	1,051 (1.15%)	732 (0.80%)
Start of an additional exposure	10,211 (5.61%)	976 (1.07%)	9,235 (10.14%)
End of index exposure	122,449 (67.23%)	61,560 (67.60%)	60,889 (66.86%)
Specified date reached	11,855 (6.51%)	7,184 (7.89%)	4,671 (5.13%)
End of patient enrollment	25,411 (13.95%)	13,085 (14.37%)	12,326 (13.54%)

Switch to other SUs (for censoring) + nursing home admission	10,419 (5.72%)	7,208 (7.92%)	3,211 (3.53%)

- Report follow-up time by treatment group.

	Median Follow-Up Time (Days) [IQR]		
Patient Group	**Optum**	**Marketscan**	**Medicare**
Overall Patient Population	139 [58-344]	153 [82-367]	155 [85-373]
Referent	144 [78-354]	180 [102-432]	180 [102-432]
Exposure	132 [58-331]	140 [58-323]	140 [58-323]

- Report overall risk of the primary outcome.

	Optum	**Marketscan**	**Medicare**
Risk per 1,000 patients	13.68	16.21	38.38

10. Final Power Assessment

Date conducted: 2/1/2019

- 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

Non-inferiority Analysis	
Number of patients matched	
Reference	91,063
Exposed	91,063
Risk per 1,000 patients	22.76
Assumed HR from RCT	1
Alpha (2-sided)	0.05
Non-inferiority margin	1.3
Number of events expected	4145.18776
Power	1

Superiority Analysis	
Number of patients matched	
Reference	91,063
Exposed	91,063
Risk per 1,000 patients	22.76
Desired HR from RCT	0.83
Alpha (2-sided)	0.05
Number of events expected	4145.18776
Power	0.999973077

- Optum

Non-inferiority Analysis	
Number of patients matched	
Reference	20,772
Exposed	20,772
Risk per 1,000 patients	13.68
Assumed HR from RCT	1
Alpha (2-sided)	0.05
Non-inferiority margin	1.3
Number of events expected	568.32192
Power	0.878466057

Superiority Analysis	
Number of patients matched	
Reference	20,772
Exposed	20,772
Risk per 1,000 patients	13.68
Desired HR from RCT	0.83
Alpha (2-sided)	0.05
Number of events expected	568.32192
Power	0.602983034

- Marketscan

Non-inferiority Analysis	
Number of patients matched	
Reference	29,150
Exposed	29,150
Risk per 1,000 patients	16.21
Assumed HR from RCT	1
Alpha (2-sided)	0.05
Non-inferiority margin	1.3
Number of events expected	945.043
Power	0.980903542

Superiority Analysis	
Number of patients matched	
Reference	29,150
Exposed	29,150
Risk per 1,000 patients	16.21
Desired HR from RCT	0.83
Alpha (2-sided)	0.05
Number of events expected	945.043
Power	0.817020552

- Medicare

Non-inferiority Analysis	
Number of patients matched	
Reference	41,141
Exposed	41,141
Risk per 1,000 patients	38.38
Assumed HR from RCT	1
Alpha (2-sided)	0.05
Non-inferiority margin	1.3
Number of events expected	3157.98316
Power	0.999999969

Superiority Analysis	
Number of patients matched	
Reference	41,141
Exposed	41,141
Risk per 1,000 patients	38.38
Desired HR from RCT	0.83
Alpha (2-sided)	0.05
Number of events expected	3157.98316
Power	0.999472659

- 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:	12/9/19
Reviewed by FDA:	Ken Quinto	Date reviewed:	12/20/19
Reasons for stopping analysis (if required):			

11. Study Confidence and Concerns

Deadline for voting on study confidence and listing concerns: 12/20/19

- 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.

12. Register study protocol on clinicalTrials.gov

Date conducted:

- Register the study on clinicalTrials.gov and upload this document.

13. Comparative Analyses

Aetion report name:
Date conducted:

13.1 For **primary analysis:**

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

13.2 For secondary analyses:

- In the pre-matched cohort, perform asymmetrical trimming to remove patients with PS values below the 2.5th percentile of treated patients and above the 97.5th percentile of untreated patients. In the trimmed cohort, calculate the HR for Saxagliptin versus referent patients using a Cox proportional hazards model, adjusting for deciles of the PS.

14. Requested Results

14.1 Results from primary and secondary analyses:

Separately for each endpoint:

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

HR, Hazard Ratio; CI, Confidence Interval.

15. References

American Diabetes Association. 8. Pharmacologic Approaches to Glycemic Treatment: Standards of Medical Care in Diabetes-2018. Diabetes Care. 2018;41(Suppl 1):S73-S85. doi:10.2337/dc18-S008.

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)

Scirica BM, Bhatt DL, Braunwald E, Steg PG, Davidson J, Hirshberg B, Ohman P, Frederich R, Wiviott SD, Hoffman EB, Cavender MA. Saxagliptin and cardiovascular outcomes in patients with type 2 diabetes mellitus. New England Journal of Medicine. 2013; 369(14):1317-26.

Appendix A

#	SAVOR-TIMI 53 trial definitions	Implementation in routine care	References/Rationale	Color coding
	Trial details- Negative trial		**Please see the following Google Drive for further details or any missing information:** https://drive.google.com/open?id=1WD618wrywYjEaXzfLTcuK-VCcnb6b-gV	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:** https://www.nber.org/data/icd9-icd-10-cm-and-pcs-crosswalk-general-equivalence-mapping.html	Adequate mapping in claims
	Saxagliptin 5 mg QD (2.5 mg in subjects with moderate/severe renal impairment) vs placebo	Saxagliptin vs. 2nd generation sulfonylurea		Intermediate mapping in claims
				Poor mapping or cannot be measured in claims
	PRIMARY OUTCOME			
	Composite of cardiovascular death, nonfatal myocardial infarction, or nonfatal ischemic stroke **HR = 1.00 (95% CI 0.89-1.12)**	**Measured 1 days after drug initiation in diagnosis position specified below and inpatient care setting:** **Inpatient mortality/MI/Stroke --** **For MI** Any diagnosis position in inpatient care setting ICD-9 Dx 410.X (acute myocardial infarction) excluding 410.x2 (subsequent episode of care), as the principal (primary) or the next (secondary) diagnosis **For stroke** Primary diagnosis position in inpatient care setting ICD-9 discharge diagnosis: 430.xx Subarachnoid hemorrhage (SAH) 431.xx Intracerebral hemorrhage (ICH) 433.x1 Occlusion and stenosis of precerebral arteries with cerebral infarction 434.xx (excluding 434.x0) Occlusion and stenosis of cerebral arteries with cerebral infarction 436.x Acute, but ill-defined cerebrovascular events **Mortality- See Mortality Sheet.**	**For MI:** ➔PPV 94% in Medicare claims data [Kiyota Y, Schneeweiss S, Glynn RJ, Cannuscio 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 [Wahl 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 98% 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.] ➔[Tirschwell DL, Longstreth WT, Jr. Validating administrative data in stroke research. Stroke; a journal of cerebral circulation 2002;33:2465-70.] ➔[Roumie CL, Mitchel E, Gideon PS, Varas-Lorenzo C, Castellsague 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			
1	Diagnosed with T2DM based on the current American Diabetes Association guidelines	Patients with a diagnosis of **T2DM** (ICD-9 Dx code of 250.x0 or 250.x2) in the **180 days prior to drug initiation in any diagnosis position and inpatient or outpatient care setting.**	Patorno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 http://dx.doi.org/10.1136/bmj.k119 Patorno, 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 (EMPRISE) Study." Circulation. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177	
2	Age ≥40 years	Age ≥40 years **at drug initiation**		
3	Glycated hemoglobin level of ≥6.5% (based on the last measured and documented laboratory measurement in the previous 6 months)	N/A		
4	High risk for a CV event defined as having either established CV disease and/or	-		
	• History of established cardiovascular disease	-		
	–Ischemic heart disease, and/or	**Measured 180 days prior to drug initiation in any diagnosis position and inpatient or outpatient care setting - Ischemic heart disease** 410.xx-414.xx	Patorno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 http://dx.doi.org/10.1136/bmj.k119 Patorno, 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 (EMPRISE) Study." Circulation. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177	

Appendix A

4a	– Peripheral vascular disease (eg, intermittent claudication), and/or	**Measured 180 days prior to drug initiation in any diagnosis position and inpatient or outpatient care setting- Peripheral vascular disease** ICD9 diagnosis: 440.20 – 440.24, 440.29 – 440.32, 440.3, 440.4, 443.9	Patorno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 http://dx.doi.org/10.1136/bmj.k119 Patorno, 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 (EMPRISE) Study." Circulation. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177
	– Ischemic stroke	**Measured 180 days prior to drug initiation in any diagnosis position and inpatient or outpatient care setting - Any stroke:** ICD-9 Dx: 433.xx, 434.xx, 436.xx	
4b	• Multiple risk factors for vascular disease	-	
	– At least 55 years of age (men) or 60 years of age (women), AND at least one of the following additional risk factors	At least 55 years of age (men) or 60 years of age (women) **at drug initiation**, AND	
	* Dyslipidemia (based on the last measured and documented laboratory measurement in the previous 6 months and defined as at least 1 of the following):	**Measured 180 days prior to drug initiation in any diagnosis position and inpatient or outpatient care setting - Hyperlipidemia** 272.0x-272.4x	Patorno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 http://dx.doi.org/10.1136/bmj.k119 Patorno, 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 (EMPRISE) Study." Circulation. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177
	◦ High level of low-density lipoprotein cholesterol (LDL-C), defined as N130 mg/dL (N 3.36 mmol/L) regardless of lipid-lowering therapy	N/A/Use the labs whenever possible	Patorno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 http://dx.doi.org/10.1136/bmj.k119 Patorno, 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 (EMPRISE) Study." Circulation. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177
	◦ Low level of high-density lipoprotein cholesterol (HDL-C), defined as b40 mg/dL (b1.04 mmol/L) for men or b50 mg/dL (b1.30 mmol/L) for women	N/A/Use the labs whenever possible	Patorno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 http://dx.doi.org/10.1136/bmj.k119 Patorno, 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 (EMPRISE) Study." Circulation. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177
	* Hypertension, as confirmed at the enrolment visit	**Measured 180 days prior to drug initiation in any diagnosis position and inpatient or outpatient care setting - Hypertension** ICD-9 codes 401.x – 405.x	Patorno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 http://dx.doi.org/10.1136/bmj.k119 Patorno, 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 (EMPRISE) Study." Circulation. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177
	◦ BP N140/N90 mm Hg, or		
	◦ BP N130/N80 mm Hg on BP-lowering agent	**Measured as a dispensing for one of the following180 days prior to drug initiation** - Diuretics/ACE/ARB/Calcium channel blockers/Beta blockers	
	* Currently smoking, as confirmed at the enrolment visit	**Measured 180 days prior to drug initiation in any diagnosis position and inpatient or outpatient care setting - Smoking** ICD codes V15.82 305.1x 984.84 CPT codes 99406, 99407, G0436, G0437, G9016 S9453 S4995 G9276, G9458 1034F 4004F, 4001F OR dispensing of at least one nicotine or varenicline prescription	Patorno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 http://dx.doi.org/10.1136/bmj.k119 Patorno, 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 (EMPRISE) Study." Circulation. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177 Desai, Rishi J et al. "Identification of smoking using Medicare data--a validation study of claims-based algorithms." Pharmacoepidemiology and drug safety vol. 25,4 (2016): 472-5. doi:10.1002/pds.3953

Appendix A

5	Women of childbearing potential must take precautions to avoid pregnancy throughout the study and for 4 weeks after intake of the last dose. Men participating in the study should also take precautions not to father a child while participating in the study and for 4 weeks after intake of the last dose.	Since this is an inclusion criteria, it's difficult to implement the contraceptive use requirement here, but we have pregnancy as an exclusion criteria later, so this requirement is implemented then.	
6	Provision of informed consent before any study specific procedures	N/A	
	EXCLUSION CRITERIA		
1	Any conditions that, in the opinion of the investigator, may render the patient unable to complete the study including non-CV disease (eg, active malignancy, cardiomyopathy, cirrhosis, or chronic lung disease) with a likely fatal outcome within 5 years	**Measured 180 days prior to drug initiation** - CCI >= 95 percentile	Gagne, Josh J et. al. "A combined comorbidity score predicted mortality in elderly patients better than existing scores." J Clin Epidemiol. 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." Med Care. 2018 Sep;56(9):812. doi: 10.1097/MLR.0000000000000954.
2	Current or previous (within 6 months) treatment with an incretin-based therapy such as DPP-4 inhibitors and/or GLP-1 mimetics	**Measured 180 days prior to drug initiation** - Current or previous (prior 6 months) occurrence of incretin-based mimetics. Drugs in the incretin mimetic class include exenatide, liraglutide, sitagliptin, saxagliptin, alogliptin, and linagliptin	Source- https://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm343516.htm
3	Acute vascular (cardiac or stroke) event <2 months before randomization	**Measured 60 days prior to drug initiation in any diagnosis/procedure position and inpatient care setting -** **ACS/unstable angina** 411.xx **Any stroke** ICD-9 Dx: 430.xx, 431.xx, 433.xx, 434.xx, 436.xx	Patorno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 http://dx.doi.org/10.1136/bmj.k119 Patorno, 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 (EMPRISE) Study." Circulation. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177
4	Initiation of chronic dialysis and/or renal transplant and/or a serum creatinine >6.0 mg/dL	**Measured 180 days prior to drug initiation in any diagnosis position and inpatient or outpatient care setting -** **Kidney transplant** Codes include: -ICD9 dx codes: o V42.0x, Kidney transplant status o 996.81 Complications of transplanted kidney -ICD9 prox codes: o 55.6x, Transplant of kidney (Exclude 55.61) - CPT4 codes: o 50360, Renal allotransplantation, implantation, graft, w/o donor & recipient nephrectomy o 50365, Renal allotransplantation, implantation, graft, w/ donor & recipient nephrectomy **Dialysis (Please see Dialysis sheet)**	Patorno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 http://dx.doi.org/10.1136/bmj.k119 Patorno, 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 (EMPRISE) Study." Circulation. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177
5	Pregnant or breastfeeding	**Measured 180 days prior to drug initiation in any diagnosis position and inpatient or outpatient care setting-** **Pregnancy : Please see Pregnancy sheet.**	
6	History of human immunodeficiency virus	**Measured 180 days prior to drug initiation in any diagnosis/procedure position and inpatient care setting or a dispensing of one of the following drugs -** **HIV** 042 Human immunodeficiency virus [HIV] disease 079.53 Human immunodeficiency virus, type 2 [HIV-2] V08 Asymptomatic human immunodeficiency virus [HIV] infection status OR filled prescription for HIV treatment: Please see **HIV Treatment sheet.**	Patorno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 http://dx.doi.org/10.1136/bmj.k119 Patorno, 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 (EMPRISE) Study." Circulation. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177

Appendix A

7	Patients being treated for severe autoimmune diseases such as lupus	**Measured 180 days prior to drug initiation in any diagnosis/procedure position and inpatient care setting** **Lupus** 373.34 - (ICD9) DISCOID LUPUS ERYTHEMATOSUS OF EYELID 710.0 - (ICD9) SYSTEMIC LUPUS ERYTHEMATOSUS	
8	Any patient currently receiving long-term (>30 consecutive days) treatment with an oral steroid	**Measured 180 days prior to drug initiation as a dispensing of one of the following drugs -** **Oral corticosteroids**:- Cortisone, hydrocortisone, prednisone, prednisolone, methylprednisolone, triamcinolone, dexamethasone, betamethasone.	Patorno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 http://dx.doi.org/10.1136/bmj.k119 Patorno, 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 (EMPRISE) Study." Circulation. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177
9	Patients with		
9a	• Body mass index >50 kg/m2	**Measured 180 days prior to drug initiation in any diagnosis/procedure position and inpatient care setting-** **Morbid Obesity** 278.01 - (ICD9) MORBID OBESITY	
9b	• Last measured HbA1c ≥12%	N/A	
9c	• Sustained BP >180/100 mm Hg	N/A	
9d	• LDL-C >250 mg/dL (>6.48 mmol/L) (based on the last measured and documented laboratory measurement in the previous 6 months) regardless of lipid-lowering therapy	N/A	
9e	• Triglycerides >1,000 mg/dL (N11.3 mmol/L) (based on the last measured and documented laboratory measurement in the previous 6months)	N/A	
9f	• HDL-C b25 mg/dL (<0.64 mmol/L) (based on the last measured and documented laboratory measurement in the previous 6 months)	N/A	
9g	• Known liver function tests >3 times upper limit of normal (ULN) (based on the last measured and documented laboratory measurement in the previous 6 months)	N/A	
10	Involvement in the planning and/or conduct of the study (applies to both AstraZeneca and Bristol– Myers Squibb or representative staff and/or staff at the study site)	N/A	
11	Previous randomization in the present study	N/A	
12	Participation in another clinical study with an investigational product and/or intervention within 30 days before visit 1	N/A	
13	Individuals at risk for poor protocol or medication compliance	**Measured 180 days prior to drug initiation in any diagnosis/procedure position and inpatient care setting-** **Non-compliance** V15.81 - (ICD9) PERSONAL HISTORY OF NONCOMPLIANCE WITH MEDICAL TREATMENT PRESENTING HAZARDS TO HEALTH V45.12 - (ICD9) NONCOMPLIANCE WITH RENAL DIALYSIS	

Appendix A

Trial ID	Neg5
Trial Name (with web links)	SAVOR- TIMI 53
Trial Name (with pdf links)	SAVOR- TIMI 53
NCT	NCT01107886
Trial category	Negative trial
Therapeutic Area	Endocrinology
RCT Category	2b- Failed S with NI- No label change
Brand Name	Onglyza
Generic Name	saxagliptin
Sponsor	AstraZeneca|Bristol-Myers Squibb
Year	2013
Measurable endpoint	Primary composite endpoint of Cardiovascular Death (CV Death), Non-fatal Myocardial Infarction (MI), or Non-fatal Ischaemic Stroke
Exposure	Saxagliptin
Comparator	Placebo
Population	patients with type 2 diabetes who had a history of, or were at risk for, cardiovascular events. The concomitant Anti-hyperglycemic and Cardiovascular Medications- 75% aspirin, 78% statins, 53% ACE, 61% beta-blockers
Trial finding	HR = 1.00 (95% CI 0.89-1.12)
Notes	
No. of Patients	18,206
Non-inferiority margin	HR = 1.3
Assay Sens. Endpoint	From trial- Hospitalization for heart failure. Alternative suggestion- all-cause mortality/MACE/hypoglycemia
Assay Sens. Finding	3.5% vs. 2.8%; hazard ratio, 1.27; 95% CI, 1.07 to 1.51; P=0.007
Comments/Notes	It is hard to replicate, so alternative option would be to replicate "all-cause mortality"/ MACE/hypoglycemia as shown in this Taiwan study comparing DPP4i to sulfonylureas - http://annals.org/aim/article-abstract/2456123/effects-clinical-outcomes-adding-dipeptidyl-peptidase-4-inhibitors-versus-sulfonylureas
Power	0.85 power to identify a 17% relative reduction of the primary end point with saxagliptin versus placebo and 98% power to test for noninferiority of saxagliptin versus placebo (reject the upper limit of 95% CI for a hazard ratio <1.3 at a 1-sided α of .025)
Blinding	Double-blinded
Statistical Method	Superiority and non-inferiority
Approval indication	

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)

2. CV mortality

Information on CV mortality through data linkage with the National Death Index (NDI) will be available for Medicare and Optum Clinformatics at a later date. We will conduct secondary analyses using CV mortality at that time.

Appendix A

ESRD, defined as 2 codes (either inpatient or outpatient), separated by at least 30 days
ESRD, defined as 2 codes (either inpatient or outpatient), separated by at least 30 days Codes include: - ICD9 prox codes: 39.95, Hemodialysis 54.98, Peritoneal dialysis - ICD9 dx codes: 585.5x, Chronic kidney disease, Stage V (for ESRD with no mention of dialysis) 585.6x, End stage renal disease (for ESRD with dialysis) V56.0x, encounter for dialysis NOS V56.8x, encounter for peritoneal dialysis V45.1x, renal dialysis status - CPT4 codes: 90957, 90960, ESRD related services monthly, for patients 12-19 and 20 years of age and older; with 4 or more face-to-face physician visits per month 90958, 90961, ESRD related services monthly, for patients 12-19 and 20 years of age and older; with 2-3 face-to-face physician visits per month 90959, 90962, ESRD related services monthly, for patients 12-19 and 20 years of age and older; with 1 face-to-face physician visit per month 90920, 90921, ESRD related services per full month; for patients 12-19 and twenty years of age and over 90924, 90925, ESRD related services (less than full month), per day; for patients 12-19 and twenty years of age and over 90935, Hemodialysis procedure with single physician evaluation 90937, Hemodialysis procedure requiring repeated evaluation(s) with or without substantial revision of dialysis prescription 90945, Dialysis procedure other than hemodialysis (eg, peritoneal dialysis, hemofiltration, or other continuous renal replacement therapies), with single physician evaluation 90947, Dialysis procedure other than hemodialysis (eg, peritoneal dialysis, hemofiltration, or other continuous renal replacement therapies) requiring repeated physician evaluations, with or without substantial revision of dialysis prescription 90965, 90966, ESRD related services for home dialysis per full month, for patients 12-19 and 20 years of age and older 90969, 90970, ESRD related services for dialysis less than a full month of service, per day; for patients 12-19 and

Appendix A

90969, 90970, ESRD related services for dialysis less than a full month of service, per day, for patients 12-19 and 20 years of age and older
90989, Dialysis training, patient, including helper where applicable, any mode, completed course
90993, Dialysis training, patient, including helper where applicable, any mode, course not completed, per training session
90999, Unlisted dialysis procedure, inpatient or outpatient
99512, Home visit for hemodialysis
- HCPCS codes:
G0257, Unscheduled or emergency dialysis treatment for ESRD patient in a hospital outpatient dept. that is not certified as an ESRD facility
G0314, G0317, ESRD related services during the course of treatment, for patients 12-19 and 20 yrs of age an over to include monitoring for the adequacy of nutrition, etc. w/4 or more physician visit per month
G0315, G0318, ESRD related services during the course of treatment, for patients 12-19 and 20yrs of age and over to include monitoring for the adequacy of nutrition, etc. w/2 or 3 physician visit per month
G0316, G0319, ESRD related services during the course of treatment, for patients 12-19 and 20 yrs of age and

G0316, G0319, ESRD related services during the course of treatment, for patients 12-19 and 20 yrs of age and over to include monitoring for the adequacy of nutrition, etc. w/1 physician visit per month
G0322, G0323, ESRD related services for home dialysis patients per full month: for patients 12-19 and 20 yrs of age and over to include monitoring for adequacy of nutrition and etc.
G0326, G0327, ESRD related services for home dialysis (less than full month), per day; for patients 12-19 and 20 yrs of age and over
S9335, Home therapy, hemodialysis; administrative services, professional pharmacy services, care coordination, and all necessary supplies and equipment (drugs and nursing services coded separately), per diem
S9339, Home therapy, peritoneal dialysis, administrative services, care coordination and all necessary supplies and equipment, per diem

OR

Kidney transplant, defined as either 1 inpatient or 1 outpatient code
Codes include:
-ICD9 dx codes:
V42.0x, Kidney transplant status
996.81 Complications of transplanted kidney
-ICD9 prox codes:
55.6x, Transplant of kidney (Exclude 55.61)
- CPT4 codes:
50360, Renal allotransplantation, implantation, graft, w/o donor & recipient nephrectomy
50365, Renal allotransplantation, implantation, graft, w/ donor & recipient nephrectomy

Appendix A

HIV Treatment
Abacavir
Amprenavir
Atazanavir
Darunavir
Delavirdine
Didanosine
Efavirenz
Emtricitabine
Enfuvirtide
Etravirine
Fosamprenavir
Indinavir
Lamivudine-Zidovudine
Maraviroc
Nelfinavir
Nevirapine
Raltegravir
Rilpivirine
Ritonavir
Ritonavir-Lopinavir
Saquinavir
Stavudine
Tipranavir
Zalcitabine
Zidovudine

Appendix A

Pregnancy
Dx codes
650 NORMAL DELIVERY
660 OBSTRUCTED LABOR
661 ABNORMALITY OF FORCES OF LABOR
662 LONG LABOR
663 UMBILICAL CORD COMPLICATIONS DURING LABOR AND DELIVERY
664 TRAUMA TO PERINEUM AND VULVA DURING DELIVERY
665 OTHER OBSTETRICAL TRAUMA
667 RETAINED PLACENTA OR MEMBRANES WITHOUT HEMORRHAGE
668 COMPLICATIONS OF THE ADMINISTRATION OF ANESTHETIC OR OTHER SEDATION IN LABOR AND DELIVERY
669.94 UNSPECIFIED COMPLICATION OF LABOR AND DELIVERY POSTPARTUM CONDITION OR COMPLICATION
V24 POSTPARTUM CARE AND EXAMINATION
V24.0 POSTPARTUM CARE AND EXAMINATION IMMEDIATELY AFTER DELIVERY
V24.1 POSTPARTUM CARE AND EXAMINATION OF LACTATING MOTHER
V24.2 ROUTINE POSTPARTUM FOLLOW
V27 OUTCOME OF DELIVERY
V27.0 MOTHER WITH SINGLE LIVEBORN
V27.1 MOTHER WITH SINGLE STILLBORN
V27.2 MOTHER WITH TWINS BOTH LIVEBORN
V27.3 MOTHER WITH TWINS ONE LIVEBORN AND ONE STILLBORN
V27.4 MOTHER WITH TWINS BOTH STILLBORN
V27.5 MOTHER WITH OTHER MULTIPLE BIRTH ALL LIVEBORN
V27.6 MOTHER WITH OTHER MULTIPLE BIRTH SOME LIVEBORN
V27.7 MOTHER WITH OTHER MULTIPLE BIRTH ALL STILLBORN
V27.9 MOTHER WITH UNSPECIFIED OUTCOME OF DELIVERY
Procedure codes
72.0 LOW FORCEPS OPERATION
72.1 LOW FORCEPS OPERATION WITH EPISIOTOMY
72.2 MID FORCEPS OPERATION
72.21 MID FORCEPS OPERATION WITH EPISIOTOMY
72.29 OTHER MID FORCEPS OPERATION
72.3 HIGH FORCEPS OPERATION
72.31 HIGH FORCEPS OPERATION WITH EPISIOTOMY
72.39 OTHER HIGH FORCEPS OPERATION

72.4 FORCEPS ROTATION OF FETAL HEAD
72.5 BREECH EXTRACTION
72.51 PARTIAL BREECH EXTRACTION WITH FORCEPS TO AFTERCOMING HEAD
72.52 OTHER PARTIAL BREECH EXTRACTION
72.53 TOTAL BREECH EXTRACTION WITH FORCEPS TO AFTERCOMING HEAD
72.54 OTHER TOTAL BREECH EXTRACTION
72.6 FORCEPS APPLICATION TO AFTERCOMING HEAD
72.7 VACUUM EXTRACTION
72.71 VACUUM EXTRACTION WITH EPISIOTOMY
72.79 OTHER VACUUM EXTRACTION
72.8 OTHER SPECIFIED INSTRUMENTAL DELIVERY
72.9 UNSPECIFIED INSTRUMENTAL DELIVERY
73.0 ARTIFICIAL RUPTURE OF MEMBRANES
73.01 INDUCTION OF LABOR BY ARTIFICIAL RUPTURE OF MEMBRANES
73.09 OTHER ARTIFICIAL RUPTURE OF MEMBRANES
73.1 OTHER SURGICAL INDUCTION OF LABOR
73.2 INTERNAL AND COMBINED VERSION AND EXTRACTION
73.21 INTERNAL AND COMBINED VERSION WITHOUT EXTRACTION
73.22 INTERNAL AND COMBINED VERSION WITH EXTRACTION
73.3 FAILED FORCEPS
73.4 MEDICAL INDUCTION OF LABOR
73.5 MANUALLY ASSISTED DELIVERY
73.51 MANUAL ROTATION OF FETAL HEAD
73.59 OTHER MANUALLY ASSISTED DELIVERY
73.6 EPISIOTOMY
73.8 OPERATIONS ON FETUS TO FACILITATE DELIVERY
73.9 OTHER OPERATIONS ASSISTING DELIVERY
73.91 EXTERNAL VERSION ASSISTING DELIVERY
73.92 REPLACEMENT OF PROLAPSED UMBILICAL CORD
73.93 INCISION OF CERVIX TO ASSIST DELIVERY
73.94 PUBIOTOMY TO ASSIST DELIVERY
73.99 OTHER OPERATIONS ASSISTING DELIVERY
74.0 CLASSICAL CESAREAN SECTION
74.1 LOW CERVICAL CESAREAN SECTION
74.2 EXTRAPERITONEAL CESAREAN SECTION

74.3 REMOVAL OF EXTRATUBAL ECTOPIC PREGNANCY
74.4 CESAREAN SECTION OF OTHER SPECIFIED TYPE
74.9 CESAREAN SECTION OF UNSPECIFIED TYPE
74.91 HYSTEROTOMY TO TERMINATE PREGNANCY
74.99 OTHER CESAREAN SECTION OF UNSPECIFIED TYPE
75.4 MANUAL REMOVAL OF RETAINED PLACENTA
75.5 REPAIR OF CURRENT OBSTETRIC LACERATION OF UTERUS
75.6 REPAIR OF OTHER CURRENT OBSTETRIC LACERATION
75.7 MANUAL EXPLORATION OF UTERINE CAVITY, POSTPARTUM
75.9 OTHER OBSTETRIC OPERATIONS

Appendix B

Optum	MarketScan	Medicare

BEFORE PS MATCHING

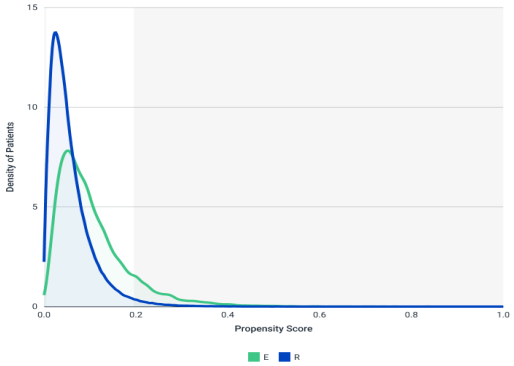


Figure 49: Pre-matching propensity score overlap

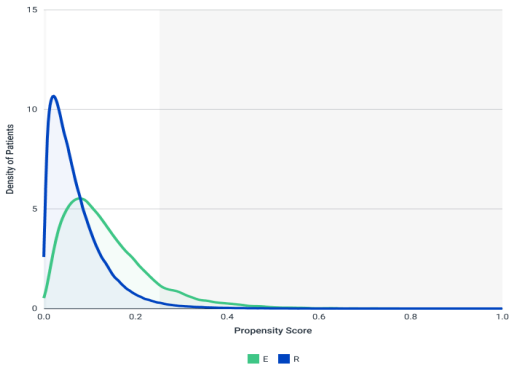


Figure 49: Pre-matching propensity score overlap

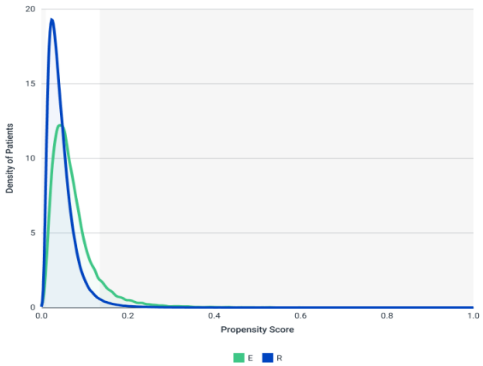


Figure 24: Pre-matching propensity score overlap

The c-statistics for the propensity score model, pre-matching was 0.724. The post-matching c-statistic was 0.524.	The c-statistics for the propensity score model, pre-matching was 0.742. The post-matching c-statistic was 0.521.	The c-statistics for the propensity score model, pre-matching was 0.69. The post-matching c-statistic was 0.519.

AFTER PS MATCHING

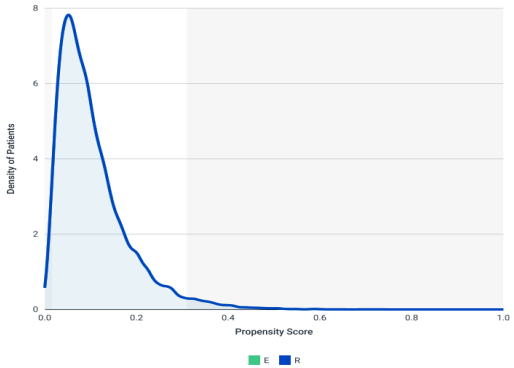


Figure 50: Post-matching propensity score overlap

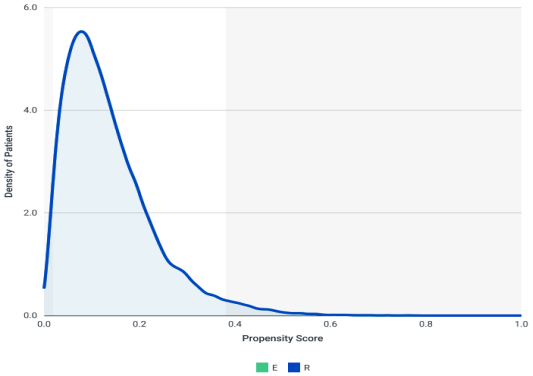
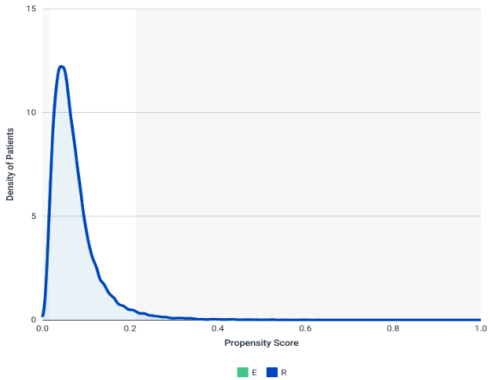


Figure 50: Post-matching propensity score overlap



igure 25: Post-matching propensity score overlap

Table 1: Saxagliptin vs 2nd Generation Sulfonylureas

	Unmatched								
	Optum		MarketScan		Medicare		POOLED		
Variable	Reference- 2nd Generation SUs	Exposure- Saxagliptin	Reference- 2nd Generation SUs	Exposure- Saxagliptin	Reference- 2nd Generation SUs	Exposure- Saxagliptin	Reference- 2nd Generation SUs	Exposure- Saxagliptin	St. Diff.
Number of patients	**326,256**	**20,779**	**354,219**	**29,159**	**833,830**	**41,144**	**1,514,305**	**91,082**	
Age									
...mean (sd)	69.39 (8.53)	66.00 (8.42)	66.17 (9.47)	64.01 (8.25)	74.47 (7.32)	73.88 (6.93)	71.43 (8.13)	68.92 (7.72)	0.32
...median [IQR]	69.00 [64.00, 75.00]	65.00 [60.00, 71.00]	64.00 [60.00, 72.00]	62.00 [59.00, 68.00]	73.00 [68.00, 79.00]	3.00 [68.00, 78.00]	70.03 (8.13)	67.65 (7.72)	0.30
Age categories									
...18 - 54; n (%)	8,369 (2.6%)	923 (4.4%)	14,650 (4.1%)	1,527 (5.2%)	0 (0.0%)	0 (0.0%)	23,019 (1.5%)	2,450 (2.7%)	-0.08
...55 - 64; n (%)	81,938 (25.1%)	8,844 (42.6%)	180,842 (51.1%)	17,427 (59.8%)	14,366 (1.7%)	758 (1.8%)	277,146 (18.3%)	27,029 (29.7%)	-0.27
...65 - 74; n (%)	144,642 (44.3%)	7,473 (36.0%)	86,662 (24.5%)	6,582 (22.6%)	457,643 (54.9%)	23,716 (57.6%)	688,947 (45.5%)	37,771 (41.5%)	0.08
...>= 75; n (%)	91,307 (28.0%)	3,539 (17.0%)	72,065 (20.3%)	3,623 (12.4%)	361,821 (43.4%)	16,670 (40.5%)	525,193 (34.7%)	23,832 (26.2%)	0.19
Gender									
...Males; n (%)	182,712 (56.0%)	12,150 (58.5%)	220,912 (62.4%)	18,053 (61.9%)	392,996 (47.1%)	18,280 (44.4%)	796,620 (52.6%)	48,483 (53.2%)	-0.01
...Females; n (%)	143,544 (44.0%)	8,629 (41.5%)	133,307 (37.6%)	11,106 (38.1%)	440,834 (52.9%)	22,864 (55.6%)	717,685 (47.4%)	42,599 (46.8%)	0.01
Race									
...White; n (%)	N/A	N/A	N/A	N/A	646,820 (77.6%)	30,782 (74.8%)	646,820 (77.6%)	30,782 (74.8%)	0.07
...Black; n (%)	N/A	N/A	N/A	N/A	96,934 (11.6%)	4,514 (11.0%)	96,934 (11.6%)	4,514 (11.0%)	0.02
...Asian; n (%)	N/A	N/A	N/A	N/A	27,110 (3.3%)	1,951 (4.7%)	27,110 (3.3%)	1,951 (4.7%)	-0.07
...Hispanic; n (%)	N/A	N/A	N/A	N/A	32,513 (3.9%)	1,896 (4.6%)	32,513 (3.9%)	1,896 (4.6%)	-0.03
...North American Native; n (%)	N/A	N/A	N/A	N/A	5,488 (0.7%)	541 (1.3%)	5,488 (0.7%)	541 (1.3%)	-0.06
...Other/Unknown; n (%)	N/A	N/A	N/A	N/A	24,965 (3.0%)	1,460 (3.5%)	24,965 (3.0%)	1,460 (3.5%)	-0.03
Region (lumping missing&other category with West)									
...Northeast; n (%)	33,392 (10.2%)	2,359 (11.4%)	57,349 (16.2%)	5,959 (20.4%)	140,063 (16.8%)	8,083 (19.6%)	230,804 (15.2%)	16,401 (18.0%)	-0.08
...South; n (%)	150,301 (46.1%)	11,451 (55.1%)	102,784 (29.0%)	6,008 (20.6%)	354,867 (42.6%)	18,938 (46.0%)	607,952 (40.1%)	36,397 (40.0%)	0.00
...Midwest; n (%)	66,450 (20.4%)	3,702 (17.8%)	136,078 (38.4%)	14,097 (48.3%)	201,736 (24.2%)	7,132 (17.3%)	404,264 (26.7%)	24,931 (27.4%)	-0.02
...West; n (%)	76,113 (23.3%)	3,267 (15.7%)	54,627 (15.4%)	2,738 (9.4%)	137,164 (16.4%)	6,991 (17.0%)	267,904 (17.7%)	12,996 (14.3%)	0.09
...Unknown+missing; n (%)	N/A	N/A	3,381 (1.0%)	357 (1.2%)	N/A	N/A	3,381 (1.0%)	357 (1.2%)	-0.02
CV Covariates									
Ischemic heart disease; n (%)	77,524 (23.8%)	4,616 (22.2%)	77,899 (22.0%)	6,045 (20.7%)	244,727 (29.3%)	11,984 (29.1%)	400,150 (26.4%)	22,645 (24.9%)	0.03
Acute MI; n (%)	5,645 (1.7%)	244 (1.2%)	5,977 (1.7%)	300 (1.0%)	13,796 (1.7%)	471 (1.1%)	25,418 (1.7%)	1,015 (1.1%)	0.05
ACS/unstable angina; n (%)	5,370 (1.6%)	311 (1.5%)	5,093 (1.4%)	374 (1.3%)	12,672 (1.5%)	589 (1.4%)	23,135 (1.5%)	1,274 (1.4%)	0.01
Old MI; n (%)	11,253 (3.4%)	524 (2.5%)	6,653 (1.9%)	415 (1.4%)	32,969 (4.0%)	1,318 (3.2%)	50,875 (3.4%)	2,257 (2.5%)	0.05
Stable angina; n (%)	11,196 (3.4%)	662 (3.2%)	9,411 (2.7%)	729 (2.5%)	28,061 (3.4%)	1,494 (3.6%)	48,668 (3.2%)	2,885 (3.2%)	0.00
Coronary atherosclerosis and other forms of chronic ischer	71,276 (21.8%)	4,252 (20.5%)	71,475 (20.2%)	5,543 (19.0%)	232,887 (27.9%)	11,360 (27.6%)	375,638 (24.8%)	21,155 (23.2%)	0.04
Other atherosclerosis with ICD10 ; n (%)	3,928 (1.2%)	253 (1.2%)	3,704 (1.0%)	366 (1.3%)	15,620 (1.9%)	937 (2.3%)	23,252 (1.5%)	1,556 (1.7%)	-0.02
Previous cardiac procedure (CABG or PTCA or Stent) ; n (%)	3,263 (1.0%)	166 (0.8%)	4,032 (1.1%)	199 (0.7%)	6,282 (0.8%)	233 (0.6%)	13,577 (0.9%)	598 (0.7%)	0.02
History of CABG or PTCA; n (%)	18,034 (5.5%)	932 (4.5%)	9,694 (2.7%)	693 (2.4%)	68,080 (8.2%)	2,852 (6.9%)	95,808 (6.3%)	4,477 (4.9%)	0.06
Any stroke; n (%)	21,878 (6.7%)	1,285 (6.2%)	20,004 (5.6%)	1,583 (5.4%)	77,966 (9.4%)	3,882 (9.4%)	119,848 (7.9%)	6,750 (7.4%)	0.02
Ischemic stroke (w and w/o mention of cerebral infarction)	21,575 (6.6%)	1,270 (6.1%)	19,796 (5.6%)	1,569 (5.4%)	76,960 (9.2%)	3,839 (9.3%)	118,331 (7.8%)	6,678 (7.3%)	0.02
Hemorrhagic stroke; n (%)	640 (0.2%)	30 (0.1%)	511 (0.1%)	33 (0.1%)	2,152 (0.3%)	90 (0.2%)	3,303 (0.2%)	153 (0.2%)	0.00
TIA; n (%)	4,889 (1.5%)	289 (1.4%)	4,657 (1.3%)	335 (1.1%)	17,677 (2.1%)	873 (2.1%)	27,223 (1.8%)	1,497 (1.6%)	0.02
Other cerebrovascular disease; n (%)	6,171 (1.9%)	298 (1.4%)	4,655 (1.3%)	289 (1.0%)	23,758 (2.8%)	984 (2.4%)	34,584 (2.3%)	1,571 (1.7%)	0.04
Late effects of cerebrovascular disease; n (%)	6,142 (1.9%)	291 (1.4%)	3,963 (1.1%)	220 (0.8%)	22,614 (2.7%)	826 (2.0%)	32,719 (2.2%)	1,337 (1.5%)	0.05
Cerebrovascular procedure; n (%)	295 (0.1%)	15 (0.1%)	335 (0.1%)	29 (0.1%)	801 (0.1%)	26 (0.1%)	1,431 (0.1%)	70 (0.1%)	0.00
Heart failure (CHF); n (%)	29,195 (8.9%)	1,231 (5.9%)	23,300 (6.6%)	1,274 (4.4%)	99,329 (11.9%)	4,239 (10.3%)	151,824 (10.0%)	6,744 (7.4%)	0.09
Peripheral Vascular Disease (PVD) or PVD Surgery ; n (%)	25,929 (7.9%)	1,480 (7.1%)	20,526 (5.8%)	1,704 (5.8%)	94,220 (11.3%)	4,860 (11.8%)	140,675 (9.3%)	8,044 (8.8%)	0.02
Atrial fibrillation; n (%)	26,603 (8.2%)	1,219 (5.9%)	23,512 (6.6%)	1,393 (4.8%)	104,219 (12.5%)	4,452 (10.8%)	154,334 (10.2%)	7,064 (7.8%)	0.08
Other cardiac dysrhythmia; n (%)	29,510 (9.0%)	1,327 (6.4%)	23,209 (6.6%)	1,413 (4.8%)	105,401 (12.6%)	4,442 (10.8%)	158,120 (10.4%)	7,182 (7.9%)	0.09
Cardiac conduction disorders; n (%)	9,152 (2.8%)	406 (2.0%)	7,170 (2.0%)	396 (1.4%)	35,402 (4.2%)	1,404 (3.4%)	51,724 (3.4%)	2,206 (2.4%)	0.06
Other CVD; n (%)	37,124 (11.4%)	1,993 (9.6%)	32,930 (9.3%)	2,357 (8.1%)	126,705 (15.2%)	6,323 (15.4%)	196,759 (13.0%)	10,673 (11.7%)	0.04
Diabetes-related complications									
Diabetic retinopathy; n (%)	18,310 (5.6%)	1,007 (4.8%)	13,846 (3.9%)	1,018 (3.5%)	51,299 (6.2%)	2,806 (6.8%)	83,455 (5.5%)	4,831 (5.3%)	0.01
Diabetes with other ophthalmic manifestations; n (%)	1,878 (0.6%)	75 (0.4%)	10,886 (3.1%)	927 (3.2%)	21,591 (2.6%)	1,320 (3.2%)	34,355 (2.3%)	2,322 (2.5%)	-0.01
Retinal detachment, vitreous hemorrhage, vitrectomy; n (%	1,193 (0.4%)	81 (0.4%)	1,053 (0.3%)	86 (0.3%)	3,016 (0.4%)	146 (0.4%)	5,262 (0.3%)	313 (0.3%)	0.00
Retinal laser coagulation therapy; n (%)	1,780 (0.5%)	105 (0.5%)	2,021 (0.6%)	164 (0.6%)	4,269 (0.5%)	275 (0.7%)	8,070 (0.5%)	544 (0.6%)	-0.01
Occurrence of Diabetic Neuropathy ; n (%)	53,488 (16.4%)	2,860 (13.8%)	34,395 (9.7%)	2,354 (8.1%)	141,342 (17.0%)	7,059 (17.2%)	229,225 (15.1%)	12,273 (13.5%)	0.05
Occurrence of diabetic nephropathy with ICD10; n (%)	42,970 (13.2%)	1,931 (9.3%)	18,676 (5.3%)	1,038 (3.6%)	70,413 (8.4%)	3,133 (7.6%)	132,059 (8.7%)	6,102 (6.7%)	0.08

Table 1: Saxagliptin vs 2nd Generation Sulfonylureas

Hypoglycemia ; n (%)	8,609 (2.6%)	520 (2.5%)	11,572 (3.3%)	710 (2.4%)	24,098 (2.9%)	1,309 (3.2%)	44,279 (2.9%)	2,539 (2.8%)	0.01
Hyperglycemia; n (%)	14,232 (4.4%)	915 (4.4%)	10,618 (3.0%)	934 (3.2%)	40,740 (4.9%)	1,907 (4.6%)	65,590 (4.3%)	3,756 (4.1%)	0.01
Disorders of fluid electrolyte and acid-base balance; n (%)	27,078 (8.3%)	1,202 (5.8%)	20,401 (5.8%)	1,090 (3.7%)	87,411 (10.5%)	3,443 (8.4%)	134,890 (8.9%)	5,735 (6.3%)	0.10
Diabetic ketoacidosis; n (%)	1,479 (0.5%)	80 (0.4%)	1,620 (0.5%)	97 (0.3%)	3,796 (0.5%)	185 (0.4%)	6,895 (0.5%)	362 (0.4%)	0.01
Hyperosmolar hyperglycemic nonketotic syndrome (HONK	1,713 (0.5%)	98 (0.5%)	1,402 (0.4%)	88 (0.3%)	4,210 (0.5%)	190 (0.5%)	7,325 (0.5%)	376 (0.4%)	0.01
Diabetes with peripheral circulatory disorders with ICD-10	22,010 (6.7%)	1,121 (5.4%)	12,150 (3.4%)	836 (2.9%)	61,626 (7.4%)	2,985 (7.3%)	95,786 (6.3%)	4,942 (5.4%)	0.04
Diabetic Foot; n (%)	7,372 (2.3%)	325 (1.6%)	7,747 (2.2%)	424 (1.5%)	24,279 (2.9%)	1,019 (2.5%)	39,398 (2.6%)	1,768 (1.9%)	0.05
Gangrene ; n (%)	948 (0.3%)	38 (0.2%)	1,009 (0.3%)	41 (0.1%)	2,368 (0.3%)	65 (0.2%)	4,325 (0.3%)	144 (0.2%)	0.02
Lower extremity amputation; n (%)	2,039 (0.6%)	72 (0.3%)	1,321 (0.4%)	53 (0.2%)	5,746 (0.7%)	177 (0.4%)	9,106 (0.6%)	302 (0.3%)	0.04
Osteomyelitis; n (%)	2,044 (0.6%)	90 (0.4%)	2,207 (0.6%)	123 (0.4%)	5,461 (0.7%)	192 (0.5%)	9,712 (0.6%)	405 (0.4%)	0.03
Skin infections ; n (%)	18,023 (5.5%)	972 (4.7%)	19,814 (5.6%)	1,383 (4.7%)	58,702 (7.0%)	2,771 (6.7%)	96,539 (6.4%)	5,126 (5.6%)	0.03
Erectile dysfunction; n (%)	9,449 (2.9%)	765 (3.7%)	8,064 (2.3%)	706 (2.4%)	18,682 (2.2%)	1,044 (2.5%)	36,195 (2.4%)	2,515 (2.8%)	-0.03
Diabetes with unspecified complication; n (%)	14,017 (4.3%)	812 (3.9%)	10,738 (3.0%)	799 (2.7%)	35,652 (4.3%)	1,619 (3.9%)	60,407 (4.0%)	3,230 (3.5%)	0.03
Diabetes mellitus without mention of complications; n (%)	292,730 (89.7%)	19,178 (92.3%)	332,349 (93.8%)	28,174 (96.6%)	787,651 (94.5%)	39,585 (96.2%)	1,412,730 (93.3%)	86,937 (95.4%)	-0.09
Hypertension: 1 inpatient or 2 outpatient claims within 36	265,847 (81.5%)	16,982 (81.7%)	231,281 (65.3%)	19,548 (67.0%)	738,732 (88.6%)	36,794 (89.4%)	1,235,860 (81.6%)	73,324 (80.5%)	0.03
Hyperlipidemia ; n (%)	232,236 (71.2%)	16,351 (78.7%)	197,940 (55.9%)	18,164 (62.3%)	622,378 (74.6%)	33,571 (81.6%)	1,052,554 (69.5%)	68,086 (74.8%)	-0.12
Edema; n (%)	21,485 (6.6%)	1,155 (5.6%)	15,660 (4.4%)	1,142 (3.9%)	79,196 (9.5%)	3,623 (8.8%)	116,341 (7.7%)	5,920 (6.5%)	0.05
Renal Dysfunction (non-diabetic) ; n (%)	70,481 (21.6%)	3,338 (16.1%)	43,795 (12.4%)	2,667 (9.1%)	188,756 (22.6%)	8,462 (20.6%)	303,032 (20.0%)	14,467 (15.9%)	0.11
Occurrence of acute renal disease ; n (%)	12,784 (3.9%)	473 (2.3%)	10,177 (2.9%)	435 (1.5%)	39,490 (4.7%)	1,234 (3.0%)	62,451 (4.1%)	2,142 (2.4%)	0.10
Occurrence of chronic renal insufficiency; n (%)	56,143 (17.2%)	2,604 (12.5%)	29,119 (8.2%)	1,715 (5.9%)	147,896 (17.7%)	6,643 (16.1%)	233,158 (15.4%)	10,962 (12.0%)	0.10
Chronic kidney disease ; n (%)	53,648 (16.4%)	2,483 (11.9%)	27,764 (7.8%)	1,645 (5.6%)	139,695 (16.8%)	6,214 (15.1%)	221,107 (14.6%)	10,342 (11.4%)	0.10
CKD Stage 3-4; n (%)	35,821 (11.0%)	1,590 (7.7%)	17,504 (4.9%)	994 (3.4%)	94,805 (11.4%)	4,042 (9.8%)	148,130 (9.8%)	6,626 (7.3%)	0.09
Occurrence of hypertensive nephropathy; n (%)	24,104 (7.4%)	1,008 (4.9%)	11,427 (3.2%)	636 (2.2%)	66,301 (8.0%)	2,658 (6.5%)	101,832 (6.7%)	4,302 (4.7%)	0.09
Occurrence of miscellaneous renal insufficiency ; n (%)	19,938 (6.1%)	1,040 (5.0%)	14,640 (4.1%)	974 (3.3%)	65,967 (7.9%)	3,095 (7.5%)	100,545 (6.6%)	5,109 (5.6%)	0.04
Glaucoma or cataracts ; n (%)	65,950 (20.2%)	3,870 (18.6%)	55,781 (15.7%)	4,474 (15.3%)	215,464 (25.8%)	11,810 (28.7%)	337,195 (22.3%)	20,154 (22.1%)	0.00
Cellulitis or abscess of toe; n (%)	3,999 (1.2%)	184 (0.9%)	3,342 (0.9%)	184 (0.6%)	10,892 (1.3%)	352 (0.9%)	18,233 (1.2%)	720 (0.8%)	0.04
Foot ulcer; n (%)	7,328 (2.2%)	320 (1.5%)	7,845 (2.2%)	438 (1.5%)	24,448 (2.9%)	1,031 (2.5%)	39,621 (2.6%)	1,789 (2.0%)	0.04
Bladder stones; n (%)	514 (0.2%)	33 (0.2%)	456 (0.1%)	33 (0.1%)	1,745 (0.2%)	75 (0.2%)	2,715 (0.2%)	141 (0.2%)	0.00
Kidney stones; n (%)	7,301 (2.2%)	502 (2.4%)	7,485 (2.1%)	627 (2.2%)	22,828 (2.7%)	1,199 (2.9%)	37,614 (2.5%)	2,328 (2.6%)	-0.01
Urinary tract infections (UTIs); n (%)	31,174 (9.6%)	1,703 (8.2%)	22,900 (6.5%)	1,726 (5.9%)	121,013 (14.5%)	6,278 (15.3%)	175,087 (11.6%)	9,707 (10.7%)	0.03
Dipstick urinalysis; n (%)	112,162 (34.4%)	7,907 (38.1%)	100,855 (28.5%)	9,925 (34.0%)	333,745 (40.0%)	18,914 (46.0%)	546,762 (36.1%)	36,746 (40.3%)	-0.09
Non-dipstick urinalysis; n (%)	122,036 (37.4%)	8,383 (40.3%)	95,471 (27.0%)	9,302 (31.9%)	302,108 (36.2%)	16,602 (40.4%)	519,615 (34.3%)	34,287 (37.6%)	-0.07
Urine function test; n (%)	8,516 (2.6%)	522 (2.5%)	9,123 (2.6%)	798 (2.7%)	30,598 (3.7%)	1,710 (4.2%)	48,237 (3.2%)	3,030 (3.3%)	-0.01
Cytology; n (%)	3,963 (1.2%)	221 (1.1%)	5,092 (1.4%)	393 (1.3%)	13,903 (1.7%)	757 (1.8%)	22,958 (1.5%)	1,371 (1.5%)	0.00
Cystos; n (%)	5,503 (1.7%)	351 (1.7%)	6,722 (1.9%)	535 (1.8%)	19,356 (2.3%)	979 (2.4%)	31,581 (2.1%)	1,865 (2.0%)	0.01
Other Covariates									
Liver disease; n (%)	15,381 (4.7%)	1,008 (4.9%)	13,265 (3.7%)	952 (3.3%)	40,486 (4.9%)	2,120 (5.2%)	69,132 (4.6%)	4,080 (4.5%)	0.00
Osteoarthritis; n (%)	49,801 (15.3%)	2,939 (14.1%)	39,609 (11.2%)	3,067 (10.5%)	183,282 (22.0%)	9,595 (23.3%)	272,692 (18.0%)	15,601 (17.1%)	0.02
Other arthritis, arthropathies and musculoskeletal pain; n	109,875 (33.7%)	6,759 (32.5%)	103,014 (29.1%)	8,257 (28.3%)	361,926 (43.4%)	18,292 (44.5%)	574,815 (38.0%)	33,308 (36.6%)	0.03
Dorsopathies; n (%)	66,258 (20.3%)	4,112 (19.8%)	59,248 (16.7%)	4,994 (17.1%)	213,504 (25.6%)	11,236 (27.3%)	339,010 (22.4%)	20,342 (22.3%)	0.00
Fractures; n (%)	10,142 (3.1%)	464 (2.2%)	9,882 (2.8%)	624 (2.1%)	35,412 (4.2%)	1,478 (3.6%)	55,436 (3.7%)	2,566 (2.8%)	0.05
Falls ; n (%)	11,108 (3.4%)	421 (2.0%)	3,800 (1.1%)	172 (0.6%)	39,560 (4.7%)	1,361 (3.3%)	54,468 (3.6%)	1,954 (2.1%)	0.09
Osteoporosis; n (%)	16,292 (5.0%)	1,166 (5.6%)	11,172 (3.2%)	1,105 (3.8%)	61,430 (7.4%)	4,453 (10.8%)	88,894 (5.9%)	6,724 (7.4%)	-0.06
Hyperthyroidism; n (%)	1,991 (0.6%)	142 (0.7%)	1,498 (0.4%)	145 (0.5%)	7,561 (0.9%)	456 (1.1%)	11,050 (0.7%)	743 (0.8%)	-0.01
Hypothyroidism ; n (%)	46,694 (14.3%)	3,122 (15.0%)	31,244 (8.8%)	2,932 (10.1%)	125,308 (15.0%)	8,092 (19.7%)	203,246 (13.4%)	14,146 (15.5%)	-0.06
Other disorders of thyroid gland ; n (%)	9,131 (2.8%)	731 (3.5%)	7,621 (2.2%)	889 (3.0%)	30,404 (3.6%)	2,249 (5.5%)	47,156 (3.1%)	3,869 (4.2%)	-0.06
Depression; n (%)	25,425 (7.8%)	1,395 (6.7%)	20,171 (5.7%)	1,455 (5.0%)	90,154 (10.8%)	4,150 (10.1%)	135,750 (9.0%)	7,000 (7.7%)	0.05
Anxiety; n (%)	20,439 (6.3%)	1,110 (5.3%)	13,227 (3.7%)	976 (3.3%)	69,211 (8.3%)	3,190 (7.8%)	102,877 (6.8%)	5,276 (5.8%)	0.04
Sleep_Disorder; n (%)	22,256 (6.8%)	1,819 (8.8%)	29,227 (8.3%)	2,945 (10.1%)	65,850 (7.9%)	3,795 (9.2%)	117,333 (7.7%)	8,559 (9.4%)	-0.06
Dementia; n (%)	14,761 (4.5%)	513 (2.5%)	9,793 (2.8%)	417 (1.4%)	70,951 (8.5%)	2,659 (6.5%)	95,505 (6.3%)	3,589 (3.9%)	0.11
Delirium; n (%)	4,546 (1.4%)	127 (0.6%)	3,729 (1.1%)	136 (0.5%)	19,145 (2.3%)	577 (1.4%)	27,420 (1.8%)	840 (0.9%)	0.08
Psychosis; n (%)	3,765 (1.2%)	125 (0.6%)	2,978 (0.8%)	139 (0.5%)	19,739 (2.4%)	696 (1.7%)	26,482 (1.7%)	960 (1.1%)	0.05
Obesity; n (%)	40,498 (12.4%)	2,590 (12.5%)	25,265 (7.1%)	1,801 (6.2%)	85,113 (10.2%)	4,257 (10.3%)	150,876 (10.0%)	8,648 (9.5%)	0.02
Overweight; n (%)	13,422 (4.1%)	748 (3.6%)	4,458 (1.3%)	279 (1.0%)	24,959 (3.0%)	1,164 (2.8%)	42,839 (2.8%)	2,191 (2.4%)	0.03
Smoking; n (%)	33,167 (10.2%)	1,667 (8.0%)	17,912 (5.1%)	1,207 (4.1%)	107,772 (12.9%)	4,199 (10.2%)	158,851 (10.5%)	7,073 (7.8%)	0.09
Alcohol abuse or dependence; n (%)	3,462 (1.1%)	152 (0.7%)	2,699 (0.8%)	134 (0.5%)	7,115 (0.9%)	249 (0.6%)	13,276 (0.9%)	535 (0.6%)	0.03
Drug abuse or dependence; n (%)	3,665 (1.1%)	169 (0.8%)	1,731 (0.5%)	101 (0.3%)	7,330 (0.9%)	281 (0.7%)	12,726 (0.8%)	551 (0.6%)	0.02
COPD; n (%)	31,399 (9.6%)	1,481 (7.1%)	23,290 (6.6%)	1,501 (5.1%)	100,010 (12.0%)	4,618 (11.2%)	154,699 (10.2%)	7,600 (8.3%)	0.07
Asthma; n (%)	15,300 (4.7%)	1,013 (4.9%)	13,235 (3.7%)	1,110 (3.8%)	47,155 (5.7%)	2,619 (6.4%)	75,690 (5.0%)	4,742 (5.2%)	-0.01
Obstructive sleep apnea; n (%)	22,004 (6.7%)	1,612 (7.8%)	25,186 (7.1%)	2,287 (7.8%)	46,520 (5.6%)	2,191 (5.3%)	93,710 (6.2%)	6,090 (6.7%)	-0.02

Table 1: Saxagliptin vs 2nd Generation Sulfonylureas

Pneumonia; n (%)	10,170 (3.1%)	378 (1.8%)	10,127 (2.9%)	466 (1.6%)	34,226 (4.1%)	1,258 (3.1%)	54,523 (3.6%)	2,102 (2.3%)	0.08
Imaging; n (%)	538 (0.2%)	19 (0.1%)	348 (0.1%)	17 (0.1%)	1,552 (0.2%)	51 (0.1%)	2,438 (0.2%)	87 (0.1%)	0.03
Diabetes Medications									
DM Medications - AGIs; n (%)	985 (0.3%)	65 (0.3%)	1,078 (0.3%)	80 (0.3%)	2,837 (0.3%)	193 (0.5%)	4,900 (0.3%)	338 (0.4%)	-0.02
DM Medications - Glitazones; n (%)	27,778 (8.5%)	2,623 (12.6%)	41,989 (11.9%)	5,550 (19.0%)	52,109 (6.2%)	4,431 (10.8%)	121,876 (8.0%)	12,604 (13.8%)	-0.19
DM Medications - GLP-1 RA; n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	#VALUE!	#VALUE!	#VALUE!
DM Medications - Insulin; n (%)	41,105 (12.6%)	3,173 (15.3%)	44,462 (12.6%)	3,879 (13.3%)	128,124 (15.4%)	7,653 (18.6%)	213,691 (14.1%)	14,705 (16.1%)	-0.06
DM Medications - Meglitinides; n (%)	2,106 (0.6%)	338 (1.6%)	3,358 (0.9%)	778 (2.7%)	8,523 (1.0%)	1,131 (2.7%)	13,987 (0.9%)	2,247 (2.5%)	-0.12
DM Medications - Metformin; n (%)	207,824 (63.7%)	14,677 (70.6%)	226,946 (64.1%)	21,126 (72.5%)	513,950 (61.6%)	27,402 (66.6%)	948,720 (62.7%)	63,205 (69.4%)	-0.14
Concomitant initiation or current use of SGLT2i; n (%)	3,977 (1.2%)	540 (2.6%)	3,386 (1.0%)	349 (1.2%)	6,088 (0.7%)	516 (1.3%)	13,451 (0.9%)	1,405 (1.5%)	-0.06
Concomitant initiation or current use of AGIs; n (%)	723 (0.2%)	45 (0.2%)	806 (0.2%)	49 (0.2%)	2,021 (0.2%)	125 (0.3%)	3,550 (0.2%)	219 (0.2%)	0.00
Concomitant initiation or current use of Glitazones; n (%)	20,847 (6.4%)	1,496 (7.2%)	32,237 (9.1%)	3,195 (11.0%)	39,728 (4.8%)	2,670 (6.5%)	92,812 (6.1%)	7,361 (8.1%)	-0.08
Concomitant initiation or current use of GLP-1 RA; n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	#VALUE!	#VALUE!	#VALUE!
Concomitant initiation or current use of Insulin; n (%)	28,494 (8.7%)	2,341 (11.3%)	32,172 (9.1%)	2,912 (10.0%)	90,757 (10.9%)	5,821 (14.1%)	151,423 (10.0%)	11,074 (12.2%)	-0.07
Concomitant initiation or current use of Meglitinides; n (%	1,207 (0.4%)	240 (1.2%)	2,091 (0.6%)	562 (1.9%)	5,382 (0.6%)	801 (1.9%)	8,680 (0.6%)	1,603 (1.8%)	-0.11
Concomitant initiation or current use of Metformin; n (%)	176,567 (54.1%)	12,740 (61.3%)	193,813 (54.7%)	18,432 (63.2%)	434,419 (52.1%)	23,283 (56.6%)	804,799 (53.1%)	54,455 (59.8%)	-0.14
Past use of SGLT2i; n (%)	1,845 (0.6%)	234 (1.1%)	1,223 (0.3%)	119 (0.4%)	3,419 (0.4%)	197 (0.5%)	6,487 (0.4%)	550 (0.6%)	-0.03
Past use of AGIs; n (%)	262 (0.1%)	20 (0.1%)	272 (0.1%)	31 (0.1%)	816 (0.1%)	68 (0.2%)	1,350 (0.1%)	119 (0.1%)	0.00
Past use of Glitazones; n (%)	6,931 (2.1%)	1,127 (5.4%)	9,754 (2.8%)	2,355 (8.1%)	12,381 (1.5%)	1,761 (4.3%)	29,066 (1.9%)	5,243 (5.8%)	-0.20
Past use of GLP-1 RA; n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	#VALUE!	000 (0.0%)	#VALUE!
Past use of Insulin; n (%)	12,612 (3.9%)	832 (4.0%)	12,290 (3.5%)	967 (3.3%)	37,375 (4.5%)	1,832 (4.5%)	62,277 (4.1%)	3,631 (4.0%)	0.01
Past use of Meglitinides; n (%)	899 (0.3%)	98 (0.5%)	1,267 (0.4%)	216 (0.7%)	3,141 (0.4%)	330 (0.8%)	5,307 (0.4%)	644 (0.7%)	-0.04
Past use of metformin (final); n (%)	31,257 (9.6%)	1,937 (9.3%)	33,134 (9.4%)	2,694 (9.2%)	79,531 (9.5%)	4,119 (10.0%)	143,922 (9.5%)	8,750 (9.6%)	0.00
Other Medications									
Use of ACE inhibitors; n (%)	155,292 (47.6%)	8,589 (41.3%)	168,841 (47.7%)	12,185 (41.8%)	380,058 (45.6%)	16,298 (39.6%)	704,191 (46.5%)	37,072 (40.7%)	0.12
Use of ARBs; n (%)	74,753 (22.9%)	6,018 (29.0%)	85,503 (24.1%)	9,060 (31.1%)	213,647 (25.6%)	13,949 (33.9%)	373,903 (24.7%)	29,027 (31.9%)	-0.16
Use of Loop Diuretics ; n (%)	45,732 (14.0%)	2,095 (10.1%)	47,287 (13.3%)	2,970 (10.2%)	163,097 (19.6%)	7,190 (17.5%)	256,116 (16.9%)	12,255 (13.5%)	0.09
Use of other diuretics; n (%)	9,584 (2.9%)	491 (2.4%)	10,328 (2.9%)	707 (2.4%)	30,836 (3.7%)	1,357 (3.3%)	50,748 (3.4%)	2,555 (2.8%)	0.03
Use of nitrates-United; n (%)	19,150 (5.9%)	970 (4.7%)	22,344 (6.3%)	1,429 (4.9%)	67,077 (8.0%)	3,287 (8.0%)	108,571 (7.2%)	5,686 (6.2%)	0.04
Use of other hypertension drugs; n (%)	25,970 (8.0%)	1,250 (6.0%)	26,097 (7.4%)	1,535 (5.3%)	75,683 (9.1%)	3,334 (8.1%)	127,750 (8.4%)	6,119 (6.7%)	0.06
Use of digoxin; n (%)	7,924 (2.4%)	368 (1.8%)	9,532 (2.7%)	605 (2.1%)	30,623 (3.7%)	1,512 (3.7%)	48,079 (3.2%)	2,485 (2.7%)	0.03
Use of Anti-arrhythmics; n (%)	5,069 (1.6%)	211 (1.0%)	6,091 (1.7%)	348 (1.2%)	19,073 (2.3%)	819 (2.0%)	30,233 (2.0%)	1,378 (1.5%)	0.04
Use of COPD/asthma meds; n (%)	40,979 (12.6%)	2,796 (13.5%)	46,482 (13.1%)	4,170 (14.3%)	129,633 (15.5%)	7,675 (18.7%)	217,094 (14.3%)	14,641 (16.1%)	-0.05
Use of statins; n (%)	206,872 (63.4%)	13,609 (65.5%)	220,717 (62.3%)	18,979 (65.1%)	541,625 (65.0%)	28,292 (68.8%)	969,214 (64.0%)	60,880 (66.8%)	-0.06
Use of other lipid-lowering drugs; n (%)	34,054 (10.4%)	2,947 (14.2%)	47,664 (13.5%)	4,901 (16.8%)	90,399 (10.8%)	5,974 (14.5%)	172,117 (11.4%)	13,822 (15.2%)	-0.11
Use of antiplatelet agents; n (%)	39,164 (12.0%)	2,606 (12.5%)	49,626 (14.0%)	4,089 (14.0%)	120,312 (14.4%)	6,953 (16.9%)	209,102 (13.8%)	13,648 (15.0%)	-0.03
Use of oral anticoagulants (Dabigatran, Rivaroxaban, Apixa	22,175 (6.8%)	1,078 (5.2%)	23,822 (6.7%)	1,445 (5.0%)	84,094 (10.1%)	3,537 (8.6%)	130,091 (8.6%)	6,060 (6.7%)	0.07
Use of heparin and other low-molecular weight heparins; n	1,612 (0.5%)	90 (0.4%)	105 (0.0%)	1 (0.0%)	4,807 (0.6%)	169 (0.4%)	6,524 (0.4%)	260 (0.3%)	0.02
Use of NSAIDs; n (%)	45,323 (13.9%)	3,100 (14.9%)	48,638 (13.7%)	4,344 (14.9%)	125,605 (15.1%)	7,302 (17.7%)	219,566 (14.5%)	14,746 (16.2%)	-0.05
Use of oral corticosteroids; n (%)	43,644 (13.4%)	2,665 (12.8%)	46,469 (13.1%)	3,678 (12.6%)	134,781 (16.2%)	6,572 (16.0%)	224,894 (14.9%)	12,915 (14.2%)	0.02
Use of bisphosphonate (United); n (%)	8,508 (2.6%)	603 (2.9%)	7,182 (2.0%)	637 (2.2%)	25,961 (3.1%)	1,971 (4.8%)	41,651 (2.8%)	3,211 (3.5%)	-0.04
Use of opioids; n (%)	78,095 (23.9%)	4,736 (22.8%)	88,854 (25.1%)	6,978 (23.9%)	219,576 (26.3%)	10,565 (25.7%)	386,525 (25.5%)	22,279 (24.5%)	0.02
Use of antidepressants; n (%)	67,097 (20.6%)	4,035 (19.4%)	69,354 (19.6%)	5,621 (19.3%)	205,107 (24.6%)	10,384 (25.2%)	341,558 (22.6%)	20,040 (22.0%)	0.01
Use of antipsychotics; n (%)	7,040 (2.2%)	369 (1.8%)	6,306 (1.8%)	432 (1.5%)	29,618 (3.6%)	1,457 (3.5%)	42,964 (2.8%)	2,258 (2.5%)	0.02
Use of anticonvulsants; n (%)	44,305 (13.6%)	2,376 (11.4%)	37,580 (10.6%)	2,730 (9.4%)	135,780 (16.3%)	6,460 (15.7%)	217,665 (14.4%)	11,566 (12.7%)	0.05
Use of lithium; n (%)	406 (0.1%)	23 (0.1%)	511 (0.1%)	26 (0.1%)	1,154 (0.1%)	44 (0.1%)	2,071 (0.1%)	093 (0.1%)	0.00
Use of Benzos; n (%)	25,438 (7.8%)	1,649 (7.9%)	36,367 (10.3%)	2,964 (10.2%)	81,585 (9.8%)	3,787 (9.2%)	143,390 (9.5%)	8,400 (9.2%)	0.01
Use of anxiolytics/hypnotics; n (%)	17,416 (5.3%)	1,301 (6.3%)	21,131 (6.0%)	1,988 (6.8%)	51,549 (6.2%)	3,336 (8.1%)	90,096 (5.9%)	6,625 (7.3%)	-0.06
Use of dementia meds; n (%)	8,507 (2.6%)	361 (1.7%)	7,359 (2.1%)	365 (1.3%)	42,615 (5.1%)	2,350 (5.7%)	58,481 (3.9%)	3,076 (3.4%)	0.03
Use of antiparkinsonian meds; n (%)	7,238 (2.2%)	410 (2.0%)	7,186 (2.0%)	556 (1.9%)	27,741 (3.3%)	1,332 (3.2%)	42,165 (2.8%)	2,298 (2.5%)	0.02
Any use of pramlintide; n (%)	32 (0.0%)	11 (0.1%)	139 (0.0%)	38 (0.1%)	64 (0.0%)	12 (0.0%)	235 (0.0%)	061 (0.1%)	-0.04
Any use of 1st generation sulfonylureas; n (%)	133 (0.0%)	5 (0.0%)	465 (0.1%)	8 (0.0%)	538 (0.1%)	19 (0.0%)	1,136 (0.1%)	032 (0.0%)	0.00
Entresto (sacubitril/valsartan); n (%)	250 (0.1%)	16 (0.1%)	58 (0.0%)	1 (0.0%)	320 (0.0%)	11 (0.0%)	628 (0.0%)	028 (0.0%)	0.00
Initiation as monotherapy ; n (%)	58,625 (18.0%)	4,352 (20.9%)	57,540 (16.2%)	5,432 (18.6%)	121,960 (14.6%)	6,427 (15.6%)	238,125 (15.7%)	16,211 (17.8%)	-0.06
Labs							680,475	49,938	
Lab values- HbA1c (%) ; n (%)	100,016 (30.7%)	7,392 (35.6%)	21,446 (6.1%)	1,595 (5.5%)	N/A	N/A	121,462 (17.8%)	8,987 (18.0%)	-0.01
Lab values- HbA1c (%) (within 3 months) ; n (%)	77,689 (23.8%)	5,930 (28.5%)	16,948 (4.8%)	1,266 (4.3%)	N/A	N/A	94,637 (13.9%)	7,196 (14.4%)	-0.01
Lab values- HbA1c (%) (within 6 months) ; n (%)	100,016 (30.7%)	7,392 (35.6%)	21,446 (6.1%)	1,595 (5.5%)	N/A	N/A	121,462 (17.8%)	8,987 (18.0%)	-0.01
Lab values- BNP; n (%)	1,893 (0.6%)	97 (0.5%)	259 (0.1%)	19 (0.1%)	N/A	N/A	2,152 (0.3%)	116 (0.2%)	0.02

Table 1: Saxagliptin vs 2nd Generation Sulfonylureas

Lab values- BNP (within 3 months); n (%)	1,190 (0.4%)	60 (0.3%)	174 (0.0%)	10 (0.0%)	N/A	N/A	1,364 (0.2%)	070 (0.1%)	0.03
Lab values- BNP (within 6 months); n (%)	1,893 (0.6%)	97 (0.5%)	259 (0.1%)	19 (0.1%)	N/A	N/A	2,152 (0.3%)	116 (0.2%)	0.02
Lab values- BUN (mg/dl); n (%)	102,893 (31.5%)	7,740 (37.2%)	15,379 (4.3%)	1,670 (5.7%)	N/A	N/A	118,272 (17.4%)	9,410 (18.8%)	-0.04
Lab values- BUN (mg/dl) (within 3 months); n (%)	79,292 (24.3%)	6,146 (29.6%)	11,735 (3.3%)	1,300 (4.5%)	N/A	N/A	91,027 (13.4%)	7,446 (14.9%)	-0.04
Lab values- BUN (mg/dl) (within 6 months); n (%)	102,893 (31.5%)	7,740 (37.2%)	15,379 (4.3%)	1,670 (5.7%)	N/A	N/A	118,272 (17.4%)	9,410 (18.8%)	-0.04
Lab values- Creatinine (mg/dl) ; n (%)	105,172 (32.2%)	7,907 (38.1%)	16,016 (4.5%)	1,728 (5.9%)	N/A	N/A	121,188 (17.8%)	9,635 (19.3%)	-0.04
Lab values- Creatinine (mg/dl) (within 3 months) ; n (%)	81,025 (24.8%)	6,286 (30.3%)	12,246 (3.5%)	1,342 (4.6%)	N/A	N/A	93,271 (13.7%)	7,628 (15.3%)	-0.05
Lab values- Creatinine (mg/dl) (within 6 months) ; n (%)	105,172 (32.2%)	7,907 (38.1%)	16,016 (4.5%)	1,728 (5.9%)	N/A	N/A	121,188 (17.8%)	9,635 (19.3%)	-0.04
Lab values- HDL level (mg/dl); n (%)	84,638 (25.9%)	6,626 (31.9%)	18,060 (5.1%)	1,484 (5.1%)	N/A	N/A	102,698 (15.1%)	8,110 (16.2%)	-0.03
Lab values- HDL level (mg/dl) (within 3 months); n (%)	61,783 (18.9%)	5,027 (24.2%)	13,316 (3.8%)	1,117 (3.8%)	N/A	N/A	75,099 (11.0%)	6,144 (12.3%)	-0.04
Lab values- HDL level (mg/dl) (within 6 months); n (%)	84,638 (25.9%)	6,626 (31.9%)	18,060 (5.1%)	1,484 (5.1%)	N/A	N/A	102,698 (15.1%)	8,110 (16.2%)	-0.03
Lab values- LDL level (mg/dl) ; n (%)	87,126 (26.7%)	6,698 (32.2%)	19,684 (5.6%)	1,508 (5.2%)	N/A	N/A	106,810 (15.7%)	8,206 (16.4%)	-0.02
Lab values- LDL level (mg/dl) (within 3 months) ; n (%)	63,562 (19.5%)	5,094 (24.5%)	14,509 (4.1%)	1,133 (3.9%)	N/A	N/A	78,071 (11.5%)	6,227 (12.5%)	-0.03
Lab values- LDL level (mg/dl) (within 6 months) ; n (%)	87,126 (26.7%)	6,698 (32.2%)	19,684 (5.6%)	1,508 (5.2%)	N/A	N/A	106,810 (15.7%)	8,206 (16.4%)	-0.02
Lab values- NT-proBNP; n (%)	260 (0.1%)	18 (0.1%)	20 (0.0%)	1 (0.0%)	N/A	N/A	280 (0.0%)	19 (0.0%)	#DIV/0!
Lab values- NT-proBNP (within 3 months); n (%)	161 (0.0%)	13 (0.1%)	12 (0.0%)	1 (0.0%)	N/A	N/A	173 (0.0%)	14 (0.0%)	-
Lab values- NT-proBNP (within 6 months); n (%)	260 (0.1%)	18 (0.1%)	20 (0.0%)	1 (0.0%)	N/A	N/A	280 (0.0%)	19 (0.0%)	-
Lab values- Total cholesterol (mg/dl) ; n (%)	85,810 (26.3%)	6,733 (32.4%)	18,318 (5.2%)	1,521 (5.2%)	N/A	N/A	104,128 (15.3%)	8,254 (16.5%)	-0.03
Lab values- Total cholesterol (mg/dl) (within 3 months) ; n (	62,648 (19.2%)	5,117 (24.6%)	13,460 (3.8%)	1,147 (3.9%)	N/A	N/A	76,108 (11.2%)	6,264 (12.5%)	-0.04
Lab values- Total cholesterol (mg/dl) (within 6 months) ; n (	85,810 (26.3%)	6,733 (32.4%)	18,318 (5.2%)	1,521 (5.2%)	N/A	N/A	104,128 (15.3%)	8,254 (16.5%)	-0.03
Lab values- Triglyceride level (mg/dl); n (%)	85,006 (26.1%)	6,707 (32.3%)	17,930 (5.1%)	1,485 (5.1%)	N/A	N/A	102,936 (15.1%)	8,192 (16.4%)	-0.04
Lab values- Triglyceride level (mg/dl) (within 3 months); n ('	62,117 (19.0%)	5,102 (24.6%)	13,198 (3.7%)	1,118 (3.8%)	N/A	N/A	75,315 (11.1%)	6,220 (12.5%)	-0.04
Lab values- Triglyceride level (mg/dl) (within 6 months); n ('	85,006 (26.1%)	6,707 (32.3%)	17,930 (5.1%)	1,485 (5.1%)	N/A	N/A	102,936 (15.1%)	8,192 (16.4%)	-0.04
Lab result number- HbA1c (%) mean (only 2 to 20 included)	99,508	7,371	16,692	1,504	N/A	N/A	116,200	8,875	
...mean (sd)	8.02 (1.79)	7.95 (1.71)	8.15 (1.89)	8.03 (1.81)	N/A	N/A	8.04 (1.80)	7.96 (1.73)	0.05
...median [IQR]	7.60 [6.80, 8.80]	7.50 [6.80, 8.65]	7.65 [6.90, 9.00]	7.50 [6.80, 8.70]	N/A	N/A	7.61 (1.80)	7.50 (1.73)	0.06
...Missing; n (%)	226,748 (69.5%)	13,408 (64.5%)	337,527 (95.3%)	27,655 (94.8%)	N/A	N/A	564,275 (82.9%)	41,063 (82.2%)	0.02
Lab result number- BNP mean	1,893	97	259	19	N/A	N/A	2,152	116	
...mean (sd)	225.59 (409.79)	152.44 (201.22)	261.61 (540.42)	238.55 (559.75)	N/A	N/A	229.93 (427.68)	166.54 (290.36)	0.17
...median [IQR]	90.90 [34.30, 241.75]	85.00 [32.40, 195.85]	74.00 [26.00, 230.00]	30.00 [17.00, 112.00]	N/A	N/A	#VALUE!	#VALUE!	#VALUE!
...Missing; n (%)	324,363 (99.4%)	20,682 (99.5%)	353,960 (99.9%)	29,140 (99.9%)	N/A	N/A	678,323 (99.7%)	49,822 (99.8%)	-0.02
Lab result number- BUN (mg/dl) mean	102,893	7,740	15,379	1,670	N/A	N/A	118,272	9,410	
...mean (sd)	19.15 (8.38)	18.03 (7.12)	586.28 (9,772.52)	373.82 (7,794.27)	N/A	N/A	92.89 (3523.89)	81.17 (3283.06)	0.00
...median [IQR]	17.00 [14.00, 22.00]	16.50 [13.50, 21.00]	17.00 [14.00, 21.00]	17.00 [13.00, 20.00]	N/A	N/A	#VALUE!	#VALUE!	#VALUE!
...Missing; n (%)	223,363 (68.5%)	13,039 (62.8%)	338,840 (95.7%)	27,489 (94.3%)	N/A	N/A	562,203 (82.6%)	40,528 (81.2%)	0.04
Lab result number- Creatinine (mg/dl) mean (only 0.1 to 15	104,570	7,870	15,098	1,683	N/A	N/A	119,668	9,553	
...mean (sd)	1.06 (0.42)	1.01 (0.35)	1.03 (0.38)	0.99 (0.33)	N/A	N/A	1.06 (0.42)	1.01 (0.35)	0.13
...median [IQR]	0.97 [0.81, 1.20]	0.95 [0.80, 1.13]	0.97 [0.81, 1.14]	0.93 [0.80, 1.10]	N/A	N/A	0.97 (0.42)	0.95 (0.35)	0.05
...Missing; n (%)	221,686 (67.9%)	12,909 (62.1%)	339,121 (95.7%)	27,476 (94.2%)	N/A	N/A	560,807 (82.4%)	40,385 (80.9%)	0.04
Lab result number- HDL level (mg/dl) mean (only =<5000 in	84,638	6,626	18,017	1,481	N/A	N/A	102,655	8,107	
...mean (sd)	46.33 (13.72)	46.38 (13.32)	44.68 (13.73)	45.39 (13.98)	N/A	N/A	46.04 (13.72)	46.20 (13.44)	-0.01
...median [IQR]	44.00 [37.00, 53.50]	44.00 [37.00, 53.00]	43.00 [36.00, 52.00]	44.00 [37.00, 52.50]	N/A	N/A	43.82 (13.72)	44.00 (13.44)	-0.01
...Missing; n (%)	241,618 (74.1%)	14,153 (68.1%)	336,202 (94.9%)	27,678 (94.9%)	N/A	N/A	577,820 (84.9%)	41,831 (83.8%)	0.03
Lab result number- LDL level (mg/dl) mean (only =<5000 in	85,353	6,598	17,773	1,436	N/A	N/A	103,126	8,034	
...mean (sd)	88.53 (39.92)	87.43 (38.51)	88.95 (41.17)	89.25 (40.99)	N/A	N/A	88.60 (40.14)	87.76 (38.97)	0.02
...median [IQR]	85.00 [64.00, 111.50]	84.00 [64.00, 109.00]	86.00 [65.00, 112.00]	87.00 [65.00, 112.38]	N/A	N/A	85.17 (40.14)	84.54 (38.97)	0.02
...Missing; n (%)	240,903 (73.8%)	14,181 (68.2%)	336,446 (95.0%)	27,723 (95.1%)	N/A	N/A	577,349 (84.8%)	41,904 (83.9%)	0.02
Lab result number- Total cholesterol (mg/dl) mean (only =<	85,752	6,730	18,262	1,515	N/A	N/A	104,014	8,245	
...mean (sd)	174.39 (46.55)	172.96 (46.08)	174.81 (49.91)	174.96 (49.83)	N/A	N/A	174.46 (47.16)	173.33 (46.79)	0.02
...median [IQR]	168.00 [143.00, 199.00]	166.00 [143.00, 197.00]	169.50 [144.00, 201.00]	169.50 [145.50, 201.00]	N/A	N/A	168.26 (47.16)	166.64 (46.79)	0.03
...Missing; n (%)	240,504 (73.7%)	14,049 (67.6%)	335,957 (94.8%)	27,644 (94.8%)	N/A	N/A	576,461 (84.7%)	41,693 (83.5%)	0.03
Lab result number- Triglyceride level (mg/dl) mean (only =<	85,000	6,706	17,886	1,482	N/A	N/A	102,886	8,188	

Table 1: Saxagliptin vs 2nd Generation Sulfonylureas

...mean (sd)	182.88 (149.01)	179.77 (153.27)	191.33 (174.74)	188.19 (193.76)	N/A	N/A	184.35 (153.79)	181.29 (161.36)	0.02
...median [IQR]	150.00 [107.00, 214.33]	147.50 [105.00, 210.00]	153.00 [107.00, 222.00]	150.00 [103.00, 221.00]	N/A	N/A	150.52 (153.79)	147.95 (161.36)	0.02
...Missing; n (%)	241,256 (73.9%)	14,073 (67.7%)	336,333 (95.0%)	27,677 (94.9%)	N/A	N/A	577,589 (84.9%)	41,750 (83.6%)	0.04
Lab result number- Hemoglobin mean (only >0 included)	72,386	5,292	9,854	1,027	N/A	N/A	82,240	6,319	
...mean (sd)	13.46 (1.73)	13.72 (1.69)	4,136.65 (181,794.60)	522.41 (8,421.85)	N/A	N/A	507.50 (62926.21)	96.40 (3394.38)	0.01
...median [IQR]	13.50 [12.30, 14.60]	13.80 [12.60, 14.90]	13.80 [12.60, 14.90]	14.00 [12.90, 15.00]	N/A	N/A	#VALUE!	#VALUE!	#VALUE!
...Missing; n (%)	253,870 (77.8%)	15,487 (74.5%)	344,365 (97.2%)	28,132 (96.5%)	N/A	N/A	598,235 (87.9%)	43,619 (87.3%)	0.02
Lab result number- Serum sodium mean (only >90 and <19	102,168	7,735	14,001	1,597	N/A	N/A	116,169	9,332	
...mean (sd)	139.32 (2.84)	139.38 (2.70)	138.77 (2.75)	138.94 (2.61)	N/A	N/A	139.25 (2.83)	139.30 (2.68)	-0.02
...median [IQR]	139.50 [138.00, 141.00]	139.50 [138.00, 141.00]	139.00 [137.00, 140.50]	139.00 [137.50, 141.00]	N/A	N/A	139.44 (2.83)	139.41 (2.68)	0.01
...Missing; n (%)	224,088 (68.7%)	13,044 (62.8%)	340,218 (96.0%)	27,562 (94.5%)	N/A	N/A	564,306 (82.9%)	40,606 (81.3%)	0.04
Lab result number- Albumin mean (only >0 and <=10 includ	94,681	7,310	12,437	1,463	N/A	N/A	107,118	8,773	
...mean (sd)	4.23 (0.33)	4.28 (0.32)	4.18 (0.57)	4.24 (0.58)	N/A	N/A	4.22 (0.37)	4.27 (0.38)	-0.13
...median [IQR]	4.25 [4.03, 4.45]	4.30 [4.10, 4.50]	4.25 [4.00, 4.50]	4.30 [4.10, 4.50]	N/A	N/A	4.25 (0.37)	4.30 (0.38)	-0.13
...Missing; n (%)	231,575 (71.0%)	13,469 (64.8%)	341,782 (96.5%)	27,696 (95.0%)	N/A	N/A	573,357 (84.3%)	41,165 (82.4%)	0.05
Lab result number- Glucose (fasting or random) mean (only	102,043	7,747	13,741	1,522	N/A	N/A	115,784	9,269	
...mean (sd)	168.63 (71.80)	163.00 (65.86)	176.14 (76.75)	164.90 (65.90)	N/A	N/A	169.52 (72.41)	163.31 (65.87)	0.09
...median [IQR]	151.00 [122.00, 195.00]	146.00 [120.00, 185.00]	156.00 [125.00, 206.83]	148.00 [121.38, 192.00]	N/A	N/A	151.59 (72.41)	146.33 (65.87)	0.08
...Missing; n (%)	224,213 (68.7%)	13,032 (62.7%)	340,478 (96.1%)	27,637 (94.8%)	N/A	N/A	564,691 (83.0%)	40,669 (81.4%)	0.04
Lab result number- Potassium mean (only 1-7 included)	104,247	7,831	15,120	1,636	N/A	N/A	119,367	9,467	
...mean (sd)	4.44 (0.44)	4.40 (0.42)	4.37 (0.44)	4.39 (0.41)	N/A	N/A	4.43 (0.44)	4.40 (0.42)	0.07
...median [IQR]	4.40 [4.15, 4.70]	4.40 [4.10, 4.65]	4.35 [4.10, 4.62]	4.40 [4.10, 4.60]	N/A	N/A	4.39 (0.44)	4.40 (0.42)	-0.02
...Missing; n (%)	222,009 (68.0%)	12,948 (62.3%)	339,099 (95.7%)	27,523 (94.4%)	N/A	N/A	561,108 (82.5%)	40,471 (81.0%)	0.04
Comorbidity Scores									
CCI (180 days)- ICD9 and ICD10									
...mean (sd)	2.64 (2.03)	2.24 (1.79)	1.89 (1.77)	1.62 (1.50)	3.05 (2.19)	2.88 (2.07)	2.69 (2.06)	2.33 (1.84)	0.18
...median [IQR]	2.00 [1.00, 4.00]	2.00 [1.00, 3.00]	1.00 [1.00, 3.00]	1.00 [1.00, 2.00]	2.00 [1.00, 4.00]	2.00 [1.00, 4.00]	1.77 (2.06)	1.68 (1.84)	0.05
Frailty Score: Qualitative Version 365 days as Categories,									
...0; n (%)	144,570 (44.3%)	8,405 (40.4%)	130,992 (37.0%)	10,100 (34.6%)	243,493 (29.2%)	8,951 (21.8%)	519,055 (34.3%)	27,456 (30.1%)	0.09
...1 to 2; n (%)	109,279 (33.5%)	7,860 (37.8%)	142,156 (40.1%)	13,184 (45.2%)	280,929 (33.7%)	14,929 (36.3%)	532,364 (35.2%)	35,973 (39.5%)	-0.09
...3 or more; n (%)	72,407 (22.2%)	4,514 (21.7%)	81,071 (22.9%)	5,875 (20.1%)	309,408 (37.1%)	17,264 (42.0%)	462,886 (30.6%)	27,653 (30.4%)	0.00
Frailty Score: Empirical Version 365 days as Categories,									
...<0.12908; n (%)	79,447 (24.4%)	6,187 (29.8%)	93,169 (26.3%)	8,684 (29.8%)	94,495 (11.3%)	4,810 (11.7%)	267,111 (17.6%)	19,681 (21.6%)	-0.10
...0.12908 - 0.1631167; n (%)	101,582 (31.1%)	6,793 (32.7%)	113,888 (32.2%)	9,961 (34.2%)	194,372 (23.3%)	9,685 (23.5%)	409,842 (27.1%)	26,439 (29.0%)	-0.04
...>= 0.1631167; n (%)	145,227 (44.5%)	7,799 (37.5%)	147,162 (41.5%)	10,514 (36.1%)	544,963 (65.4%)	26,649 (64.8%)	837,352 (55.3%)	44,962 (49.4%)	0.12
Non-Frailty; n (%)	182,262 (55.9%)	11,848 (57.0%)	175,584 (49.6%)	15,199 (52.1%)	37,855 (4.5%)	1,488 (3.6%)	395,701 (26.1%)	28,535 (31.3%)	-0.12
Frailty Score (mean): Qualitative Version 365 days,									
...mean (sd)	1.52 (2.10)	1.49 (1.90)	1.59 (1.95)	1.46 (1.68)	2.34 (2.51)	2.53 (2.36)	1.99 (2.30)	1.95 (2.06)	0.02
...median [IQR]	1.00 [0.00, 2.00]	1.00 [0.00, 2.00]	1.00 [0.00, 2.00]	1.00 [0.00, 2.00]	2.00 [0.00, 4.00]	2.00 [1.00, 4.00]	1.55 (2.30)	1.45 (2.06)	0.05
Frailty Score (mean): Empirical Version 365 days,									
...mean (sd)	0.15 (0.06)	0.15 (0.05)	0.16 (0.05)	0.15 (0.05)	0.20 (0.07)	0.19 (0.07)	0.18 (0.06)	0.17 (0.06)	0.17
...median [IQR]	0.13 [0.10, 0.17]	0.13 [0.11, 0.17]	0.15 [0.12, 0.18]	0.14 [0.12, 0.17]	0.18 [0.15, 0.23]	0.18 [0.15, 0.23]	0.16 (0.06)	0.16 (0.06)	0.00
Healthcare Utilization									
Any hospitalization; n (%)	35,287 (10.8%)	1,425 (6.9%)	43,063 (12.2%)	2,073 (7.1%)	115,570 (13.9%)	3,921 (9.5%)	193,920 (12.8%)	7,419 (8.1%)	0.15
Any hospitalization within prior 30 days; n (%)	14,867 (4.6%)	352 (1.7%)	16,930 (4.8%)	428 (1.5%)	42,910 (5.1%)	1,044 (2.5%)	74,707 (4.9%)	1,824 (2.0%)	0.16
Any hospitalization during prior 31-180 days; n (%)	22,672 (6.9%)	1,121 (5.4%)	28,419 (8.0%)	1,706 (5.9%)	80,929 (9.7%)	3,095 (7.5%)	132,020 (8.7%)	5,922 (6.5%)	0.08
Endocrinologist Visit; n (%)	18,976 (5.8%)	1,974 (9.5%)	20,447 (5.8%)	2,685 (9.2%)	64,972 (7.8%)	4,910 (11.9%)	104,395 (6.9%)	9,569 (10.5%)	-0.13
Endocrinologist Visit (30 days prior); n (%)	10,972 (3.4%)	1,271 (6.1%)	12,019 (3.4%)	1,888 (6.5%)	36,189 (4.3%)	3,019 (7.3%)	59,180 (3.9%)	6,178 (6.8%)	-0.13
Endocrinologist Visit (31 to 180 days prior); n (%)	13,157 (4.0%)	1,382 (6.7%)	14,187 (4.0%)	1,815 (6.2%)	48,466 (5.8%)	3,711 (9.0%)	75,810 (5.0%)	6,908 (7.6%)	-0.11
Internal medicine/family medicine visits; n (%)	279,476 (85.7%)	16,015 (77.1%)	290,157 (81.9%)	25,344 (86.9%)	698,850 (83.8%)	34,934 (84.9%)	1,268,483 (83.8%)	76,293 (83.8%)	0.00
Internal medicine/family medicine visits (30 days prior) ; n	209,246 (64.1%)	11,953 (57.5%)	213,564 (60.3%)	19,663 (67.4%)	497,741 (59.7%)	25,429 (61.8%)	920,551 (60.8%)	57,045 (62.6%)	-0.04
Internal medicine/family medicine visits (31 to 180 days pr	238,305 (73.0%)	13,787 (66.4%)	238,819 (67.4%)	21,573 (74.0%)	601,665 (72.2%)	31,272 (76.0%)	1,078,789 (71.2%)	66,632 (73.2%)	-0.04
Cardiologist visit; n (%)	88,147 (27.0%)	5,475 (26.3%)	77,765 (22.0%)	6,761 (23.2%)	288,718 (34.6%)	14,709 (35.8%)	454,630 (30.0%)	26,945 (29.6%)	0.01
Number of Cardiologist visits (30 days prior); n (%)	34,095 (10.5%)	1,954 (9.4%)	28,267 (8.0%)	2,434 (8.3%)	106,572 (12.8%)	5,200 (12.6%)	168,934 (11.2%)	9,588 (10.5%)	0.02
Number of Cardiologist visits (31 to 180 days prior); n (%)	71,893 (22.0%)	4,633 (22.3%)	64,786 (18.3%)	5,657 (19.4%)	245,011 (29.4%)	12,880 (31.3%)	381,690 (25.2%)	23,170 (25.4%)	0.00
Electrocardiogram ; n (%)	100,694 (30.9%)	6,409 (30.8%)	106,524 (30.1%)	9,248 (31.7%)	297,892 (35.7%)	15,158 (36.8%)	505,110 (33.4%)	30,815 (33.8%)	-0.01

Table 1: Saxagliptin vs 2nd Generation Sulfonylureas

Use of glucose test strips; n (%)	11,797 (3.6%)	853 (4.1%)	12,023 (3.4%)	1,275 (4.4%)	29,191 (3.5%)	1,529 (3.7%)	53,011 (3.5%)	3,657 (4.0%)	-0.03
Dialysis; n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	000 (0.0%)	000 (0.0%)	#DIV/0!
Naive new user ; n (%)	100,125 (30.7%)	6,035 (29.0%)	104,280 (29.4%)	7,406 (25.4%)	215,694 (25.9%)	9,800 (23.8%)	420,099 (27.7%)	23,241 (25.5%)	0.05
N antidiabetic drugs at index date									
...mean (sd)	1.71 (0.63)	1.84 (0.66)	1.75 (0.65)	1.87 (0.67)	1.69 (0.63)	1.81 (0.66)	1.71 (0.63)	1.84 (0.66)	-0.20
...median [IQR]	2.00 [1.00, 2.00]	2.00 [1.00, 2.00]	2.00 [1.00, 2.00]	2.00 [1.00, 2.00]	2.00 [1.00, 2.00]	2.00 [1.00, 2.00]	2.00 (0.63)	2.00 (0.66)	0.00
number of different/distinct medication prescriptions									
...mean (sd)	9.04 (4.55)	9.01 (4.67)	8.91 (4.49)	9.01 (4.53)	9.48 (4.52)	10.14 (5.03)	9.25 (4.52)	9.52 (4.79)	-0.06
...median [IQR]	8.00 [6.00, 12.00]	8.00 [6.00, 12.00]	8.00 [6.00, 11.00]	8.00 [6.00, 11.00]	9.00 [6.00, 12.00]	9.00 [7.00, 13.00]	8.55 (4.52)	8.45 (4.79)	0.02
Number of Hospitalizations									
...mean (sd)	0.13 (0.43)	0.08 (0.33)	0.14 (0.43)	0.08 (0.32)	0.18 (0.52)	0.12 (0.42)	0.16 (0.48)	0.10 (0.37)	0.14
...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]	0.00 [0.00, 0.00]	0.00 (0.48)	0.00 (0.37)	0.00
Number of hospital days									
...mean (sd)	0.78 (3.52)	0.44 (2.26)	0.87 (3.92)	0.43 (2.33)	1.16 (4.59)	0.72 (3.58)	1.01 (4.23)	0.56 (2.95)	0.12
...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]	0.00 [0.00, 0.00]	0.00 (4.23)	0.00 (2.95)	0.00
Number of Emergency Department (ED) visits									
...mean (sd)	0.42 (1.21)	0.28 (0.89)	0.21 (1.40)	0.11 (1.03)	0.61 (1.48)	0.48 (1.27)	0.48 (1.41)	0.32 (1.12)	0.13
...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]	0.00 [0.00, 0.00]	0.00 (1.41)	0.00 (1.12)	0.00
Number of Office visits									
...mean (sd)	4.66 (3.91)	4.93 (3.87)	4.65 (4.13)	5.03 (3.99)	5.42 (4.50)	6.30 (4.81)	5.08 (4.29)	5.58 (4.35)	-0.12
...median [IQR]	4.00 [2.00, 6.00]	4.00 [2.00, 6.00]	4.00 [2.00, 6.00]	4.00 [2.00, 7.00]	4.00 [2.00, 7.00]	5.00 [3.00, 8.00]	4.00 (4.29)	4.45 (4.35)	-0.10
Number of Endocrinologist visits									
...mean (sd)	0.26 (1.68)	0.49 (2.47)	0.25 (1.62)	0.52 (2.67)	0.43 (2.50)	0.81 (3.84)	0.35 (2.16)	0.64 (3.21)	-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]	0.00 [0.00, 0.00]	0.00 (2.16)	0.00 (3.21)	0.00
Number of internal medicine/family medicine visits									
...mean (sd)	9.90 (13.97)	7.91 (12.17)	6.53 (9.66)	7.35 (9.32)	8.17 (10.66)	9.17 (11.81)	8.16 (11.24)	8.30 (11.16)	-0.01
...median [IQR]	6.00 [2.00, 13.00]	5.00 [1.00, 11.00]	4.00 [1.00, 8.00]	5.00 [2.00, 10.00]	5.00 [2.00, 11.00]	6.00 [2.00, 12.00]	4.98 (11.24)	5.45 (11.16)	-0.04
Number of Cardiologist visits									
...mean (sd)	1.38 (3.89)	1.35 (3.98)	0.98 (3.06)	1.07 (3.34)	1.85 (4.67)	2.03 (4.87)	1.55 (4.18)	1.57 (4.23)	0.00
...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, 2.00]	0.00 [0.00, 2.00]	0.00 (4.18)	0.00 (4.23)	0.00
Number electrocardiograms received									
...mean (sd)	0.63 (1.46)	0.53 (1.15)	0.55 (1.21)	0.53 (1.08)	0.76 (1.46)	0.73 (1.35)	0.68 (1.41)	0.62 (1.22)	0.05
...median [IQR]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00 (1.41)	0.00 (1.22)	0.00
Number of HbA1c tests ordered									
...mean (sd)	1.14 (0.89)	1.25 (0.87)	0.84 (0.86)	1.03 (0.90)	1.28 (0.88)	1.42 (0.90)	1.15 (0.88)	1.26 (0.89)	-0.12
...median [IQR]	1.00 [1.00, 2.00]	1.00 [1.00, 2.00]	1.00 [0.00, 1.00]	1.00 [0.00, 2.00]	1.00 [1.00, 2.00]	1.00 [1.00, 2.00]	1.00 (0.88)	1.00 (0.89)	0.00
Number of glucose tests ordered									
...mean (sd)	0.48 (2.98)	0.48 (1.61)	0.36 (1.34)	0.41 (1.05)	0.40 (1.06)	0.51 (1.25)	0.41 (1.72)	0.47 (1.28)	-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]	0.00 [0.00, 1.00]	0.00 (1.72)	0.00 (1.28)	0.00
Number of lipid tests ordered									
...mean (sd)	0.91 (0.93)	1.09 (1.00)	0.72 (1.13)	0.97 (1.33)	0.93 (0.82)	1.14 (0.90)	0.88 (0.92)	1.07 (1.08)	-0.19
...median [IQR]	1.00 [0.00, 1.00]	1.00 [0.00, 2.00]	0.00 [0.00, 1.00]	1.00 [0.00, 1.00]	1.00 [0.00, 1.00]	1.00 [1.00, 2.00]	0.77 (0.92)	1.00 (1.08)	-0.23
Number of creatinine tests ordered									
...mean (sd)	0.07 (0.37)	0.06 (0.33)	0.11 (0.51)	0.06 (0.32)	0.10 (0.44)	0.10 (0.41)	0.10 (0.44)	0.08 (0.37)	0.05
...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]	0.00 [0.00, 0.00]	0.00 (0.44)	0.00 (0.37)	0.00
Number of BUN tests ordered									
...mean (sd)	0.04 (0.30)	0.04 (0.27)	0.06 (0.41)	0.04 (0.28)	0.06 (0.35)	0.06 (0.33)	0.06 (0.36)	0.05 (0.30)	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]	0.00 [0.00, 0.00]	0.00 (0.36)	0.00 (0.30)	0.00
Number of tests for microalbuminuria									
...mean (sd)	0.67 (1.10)	0.72 (1.12)	0.44 (0.89)	0.53 (0.98)	0.41 (0.69)	0.48 (0.75)	0.47 (0.84)	0.55 (0.92)	-0.09
...median [IQR]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00 [0.00, 0.00]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00 (0.84)	0.00 (0.92)	0.00
Total N distinct ICD9/ICD10 diagnoses at the 3rd digit level									
...mean (sd)	4.73 (7.18)	3.43 (5.80)	1.90 (4.73)	1.08 (3.22)	5.66 (8.51)	4.01 (6.97)	4.58 (7.50)	2.94 (5.74)	0.25
...median [IQR]	1.00 [0.00, 7.00]	0.00 [0.00, 5.00]	0.00 [0.00, 2.00]	0.00 [0.00, 0.00]	2.00 [0.00, 8.00]	0.00 [0.00, 6.00]	1.32 (7.50)	0.00 (5.74)	0.20
Use of thiazide; n (%)	40,916 (12.5%)	2,098 (10.1%)	42,866 (12.1%)	2,950 (10.1%)	117,483 (14.1%)	4,979 (12.1%)	201,265 (13.3%)	10,027 (11.0%)	0.07
Use of beta blockers; n (%)	126,828 (38.9%)	7,225 (34.8%)	138,568 (39.1%)	10,503 (36.0%)	390,039 (46.8%)	18,959 (46.1%)	655,435 (43.3%)	36,687 (40.3%)	0.06
Use of calcium channel blockers; n (%)	94,025 (28.8%)	5,575 (26.8%)	99,484 (28.1%)	7,927 (27.2%)	273,482 (32.8%)	13,549 (32.9%)	466,991 (30.8%)	27,051 (29.7%)	0.02

Table 1: Saxagliptin vs 2nd Generation Sulfonylureas

PS-matched									
	Optum		MarketScan		Medicare		POOLED		
Variable	Reference- 2nd Generation SUs	Exposure- Saxagliptin	Reference- 2nd Generation SUs	Exposure- Saxagliptin	Reference- 2nd Generation SUs	Exposure- Saxagliptin	Reference- 2nd Generation SUs	Exposure- Saxagliptin	St. Diff.
Number of patients	**20772**	**20772**	**29150**	**29150**	**41141**	**41141**	**91,063**	**91,063**	
Age									
...mean (sd)	65.97 (8.35)	66.00 (8.42)	64.00 (8.47)	64.01 (8.25)	73.91 (6.97)	73.88 (6.93)	68.93 (7.80)	68.92 (7.72)	0.00
...median [IQR]	66.00 [60.00, 71.00]	65.00 [60.00, 71.00]	62.00 [59.00, 68.00]	62.00 [59.00, 68.00]	73.00 [68.00, 78.00]	73.00 [68.00, 78.00]	67.88 (7.80)	67.65 (7.72)	0.03
Age categories									
...18 - 54; n (%)	1,121 (5.4%)	921 (4.4%)	1,719 (5.9%)	1,526 (5.2%)	0 (0.0%)	0 (0.0%)	2,840 (3.1%)	2,447 (2.7%)	0.02
...55 - 64; n (%)	7,765 (37.4%)	8,841 (42.6%)	17,220 (59.1%)	17,419 (59.8%)	868 (2.1%)	757 (1.8%)	25,853 (28.4%)	27,017 (29.7%)	-0.03
...65 - 74; n (%)	8,652 (41.7%)	7,471 (36.0%)	6,470 (22.2%)	6,582 (22.6%)	23,506 (57.1%)	23,714 (57.6%)	38,628 (42.4%)	37,767 (41.5%)	0.02
...>= 75; n (%)	3,234 (15.6%)	3,539 (17.0%)	3,741 (12.8%)	3,623 (12.4%)	16,767 (40.8%)	16,670 (40.5%)	23,742 (26.1%)	23,832 (26.2%)	0.00
Gender									
...Males; n (%)	12,157 (58.5%)	12,147 (58.5%)	17,924 (61.5%)	18,048 (61.9%)	18,432 (44.8%)	18,280 (44.4%)	48,513 (53.3%)	48,475 (53.2%)	0.00
...Females; n (%)	8,615 (41.5%)	8,625 (41.5%)	11,226 (38.5%)	11,102 (38.1%)	22,709 (55.2%)	22,861 (55.6%)	42,550 (46.7%)	42,588 (46.8%)	0.00
Race									
...White; n (%)	N/A	N/A	N/A	N/A	30,779 (74.8%)	30,782 (74.8%)	30,779 (74.8%)	30,782 (74.8%)	0.00
...Black; n (%)	N/A	N/A	N/A	N/A	4,533 (11.0%)	4,513 (11.0%)	4,533 (11.0%)	4,513 (11.0%)	0.00
...Asian; n (%)	N/A	N/A	N/A	N/A	1,883 (4.6%)	1,951 (4.7%)	1,883 (4.6%)	1,951 (4.7%)	0.00
...Hispanic; n (%)	N/A	N/A	N/A	N/A	1,960 (4.8%)	1,895 (4.6%)	1,960 (4.8%)	1,895 (4.6%)	0.01
...North American Native; n (%)	N/A	N/A	N/A	N/A	575 (1.4%)	540 (1.3%)	575 (1.4%)	540 (1.3%)	0.01
...Other/Unknown; n (%)	N/A	N/A	N/A	N/A	1,411 (3.4%)	1,460 (3.5%)	1,411 (3.4%)	1,460 (3.5%)	-0.01
Region (lumping missing&other category with West)									
...Northeast; n (%)	2,316 (11.1%)	2,359 (11.4%)	6,104 (20.9%)	5,957 (20.4%)	8,132 (19.8%)	8,083 (19.6%)	16,552 (18.2%)	16,399 (18.0%)	0.01
...South; n (%)	11,440 (55.1%)	11,446 (55.1%)	5,868 (20.1%)	6,007 (20.6%)	19,036 (46.3%)	18,936 (46.0%)	36,344 (39.9%)	36,389 (40.0%)	0.00
...Midwest; n (%)	3,778 (18.2%)	3,701 (17.8%)	14,089 (48.3%)	14,091 (48.3%)	7,077 (17.2%)	7,132 (17.3%)	24,944 (27.4%)	24,924 (27.4%)	0.00
...West; n (%)	3,238 (15.6%)	3,266 (15.7%)	2,716 (9.3%)	2,738 (9.4%)	6,896 (16.8%)	6,990 (17.0%)	12,850 (14.1%)	12,994 (14.3%)	-0.01
...Unknown+missing; n (%)	N/A	N/A	373 (1.3%)	357 (1.2%)	N/A	N/A	373 (1.3%)	357 (1.2%)	0.01
CV Covariates									
Ischemic heart disease; n (%)	4,667 (22.5%)	4,615 (22.2%)	6,088 (20.9%)	6,045 (20.7%)	12,003 (29.2%)	11,984 (29.1%)	22,758 (25.0%)	22,644 (24.9%)	0.00
Acute MI; n (%)	233 (1.1%)	244 (1.2%)	282 (1.0%)	300 (1.0%)	483 (1.2%)	471 (1.1%)	998 (1.1%)	1,015 (1.1%)	0.00
ACS/unstable angina; n (%)	320 (1.5%)	311 (1.5%)	384 (1.3%)	374 (1.3%)	626 (1.5%)	589 (1.4%)	1,330 (1.5%)	1,274 (1.4%)	0.01
Old MI; n (%)	514 (2.5%)	524 (2.5%)	443 (1.5%)	415 (1.4%)	1,241 (3.0%)	1,318 (3.2%)	2,198 (2.4%)	2,257 (2.5%)	-0.01
Stable angina; n (%)	691 (3.3%)	662 (3.2%)	739 (2.5%)	729 (2.5%)	1,473 (3.6%)	1,494 (3.6%)	2,903 (3.2%)	2,885 (3.2%)	0.00
Coronary atherosclerosis and other forms of chronic ischemic heart disease; n (%)	4,278 (20.6%)	4,251 (20.5%)	5,578 (19.1%)	5,543 (19.0%)	11,376 (27.7%)	11,360 (27.6%)	21,232 (23.3%)	21,154 (23.2%)	0.00
Other atherosclerosis with ICD10 ; n (%)	222 (1.1%)	253 (1.2%)	319 (1.1%)	366 (1.3%)	835 (2.0%)	937 (2.3%)	1,376 (1.5%)	1,556 (1.7%)	-0.02
Previous cardiac procedure (CABG or PTCA or Stent) ; n (%)	157 (0.8%)	166 (0.8%)	201 (0.7%)	199 (0.7%)	244 (0.6%)	233 (0.6%)	602 (0.7%)	598 (0.7%)	0.00
History of CABG or PTCA; n (%)	942 (4.5%)	932 (4.5%)	665 (2.3%)	693 (2.4%)	2,928 (7.1%)	2,852 (6.9%)	4,535 (5.0%)	4,477 (4.9%)	0.00
Any stroke; n (%)	1,315 (6.3%)	1,284 (6.2%)	1,559 (5.3%)	1,582 (5.4%)	3,796 (9.2%)	3,882 (9.4%)	6,670 (7.3%)	6,748 (7.4%)	0.00
Ischemic stroke (w and w/o mention of cerebral infarction); n (%)	1,300 (6.3%)	1,269 (6.1%)	1,551 (5.3%)	1,568 (5.4%)	3,760 (9.1%)	3,839 (9.3%)	6,611 (7.3%)	6,676 (7.3%)	0.00
Hemorrhagic stroke; n (%)	31 (0.1%)	30 (0.1%)	22 (0.1%)	33 (0.1%)	65 (0.2%)	90 (0.2%)	118 (0.1%)	153 (0.2%)	-0.03
TIA; n (%)	312 (1.5%)	289 (1.4%)	346 (1.2%)	335 (1.1%)	872 (2.1%)	873 (2.1%)	1,530 (1.7%)	1,497 (1.6%)	0.01
Other cerebrovascular disease; n (%)	300 (1.4%)	298 (1.4%)	299 (1.0%)	289 (1.0%)	994 (2.4%)	984 (2.4%)	1,593 (1.7%)	1,571 (1.7%)	0.00
Late effects of cerebrovascular disease; n (%)	305 (1.5%)	291 (1.4%)	225 (0.8%)	220 (0.8%)	837 (2.0%)	826 (2.0%)	1,367 (1.5%)	1,337 (1.5%)	0.00
Cerebrovascular procedure; n (%)	18 (0.1%)	15 (0.1%)	28 (0.1%)	29 (0.1%)	40 (0.1%)	26 (0.1%)	086 (0.1%)	070 (0.1%)	0.00
Heart failure (CHF); n (%)	1,274 (6.1%)	1,229 (5.9%)	1,275 (4.4%)	1,274 (4.4%)	4,225 (10.3%)	4,239 (10.3%)	6,774 (7.4%)	6,742 (7.4%)	0.00
Peripheral Vascular Disease (PVD) or PVD Surgery ; n (%)	1,525 (7.3%)	1,479 (7.1%)	1,776 (6.1%)	1,702 (5.8%)	4,754 (11.6%)	4,859 (11.8%)	8,055 (8.8%)	8,040 (8.8%)	0.00
Atrial fibrillation; n (%)	1,271 (6.1%)	1,217 (5.9%)	1,377 (4.7%)	1,393 (4.8%)	4,481 (10.9%)	4,452 (10.8%)	7,129 (7.8%)	7,062 (7.8%)	0.00
Other cardiac dysrhythmia; n (%)	1,384 (6.7%)	1,327 (6.4%)	1,407 (4.8%)	1,413 (4.8%)	4,462 (10.8%)	4,442 (10.8%)	7,253 (8.0%)	7,182 (7.9%)	0.00
Cardiac conduction disorders; n (%)	415 (2.0%)	406 (2.0%)	431 (1.5%)	396 (1.4%)	1,446 (3.5%)	1,404 (3.4%)	2,292 (2.5%)	2,206 (2.4%)	0.01
Other CVD; n (%)	2,080 (10.0%)	1,991 (9.6%)	2,434 (8.3%)	2,357 (8.1%)	6,289 (15.3%)	6,323 (15.4%)	10,803 (11.9%)	10,671 (11.7%)	0.01
Diabetes-related complications									
Diabetic retinopathy; n (%)	1,011 (4.9%)	1,005 (4.8%)	1,031 (3.5%)	1,018 (3.5%)	2,947 (7.2%)	2,806 (6.8%)	4,989 (5.5%)	4,829 (5.3%)	0.01
Diabetes with other ophthalmic manifestations; n (%)	82 (0.4%)	75 (0.4%)	921 (3.2%)	927 (3.2%)	1,297 (3.2%)	1,319 (3.2%)	2,300 (2.5%)	2,321 (2.5%)	0.00
Retinal detachment, vitreous hemorrhage, vitrectomy; n (%)	66 (0.3%)	81 (0.4%)	63 (0.2%)	86 (0.3%)	159 (0.4%)	146 (0.4%)	288 (0.3%)	313 (0.3%)	0.00
Retinal laser coagulation therapy; n (%)	112 (0.5%)	105 (0.5%)	154 (0.5%)	164 (0.6%)	261 (0.6%)	275 (0.7%)	527 (0.6%)	544 (0.6%)	0.00
Occurrence of Diabetic Neuropathy ; n (%)	2,892 (13.9%)	2,857 (13.8%)	2,320 (8.0%)	2,352 (8.1%)	7,189 (17.5%)	7,056 (17.2%)	12,401 (13.6%)	12,265 (13.5%)	0.00
Occurrence of diabetic nephropathy with ICD10; n (%)	1,950 (9.4%)	1,930 (9.3%)	1,006 (3.5%)	1,037 (3.6%)	3,194 (7.8%)	3,131 (7.6%)	6,150 (6.8%)	6,098 (6.7%)	0.00

Table 1: Saxagliptin vs 2nd Generation Sulfonylureas

Hypoglycemia ; n (%)	534 (2.6%)	520 (2.5%)	708 (2.4%)	710 (2.4%)	1,293 (3.1%)	1,309 (3.2%)	2,535 (2.8%)	2,539 (2.8%)	0.00
Hyperglycemia; n (%)	913 (4.4%)	914 (4.4%)	950 (3.3%)	933 (3.2%)	1,892 (4.6%)	1,907 (4.6%)	3,755 (4.1%)	3,754 (4.1%)	0.00
Disorders of fluid electrolyte and acid-base balance; n (%)	1,200 (5.8%)	1,202 (5.8%)	1,102 (3.8%)	1,090 (3.7%)	3,357 (8.2%)	3,443 (8.4%)	5,659 (6.2%)	5,735 (6.3%)	0.00
Diabetic ketoacidosis; n (%)	88 (0.4%)	80 (0.4%)	128 (0.4%)	97 (0.3%)	178 (0.4%)	185 (0.4%)	394 (0.4%)	362 (0.4%)	0.00
Hyperosmolar hyperglycemic nonketotic syndrome (HONK); n (%)	84 (0.4%)	98 (0.5%)	85 (0.3%)	88 (0.3%)	199 (0.5%)	190 (0.5%)	368 (0.4%)	376 (0.4%)	0.00
Diabetes with peripheral circulatory disorders with ICD-10 ; n (%)	1,044 (5.0%)	1,120 (5.4%)	865 (3.0%)	836 (2.9%)	2,944 (7.2%)	2,985 (7.3%)	4,853 (5.3%)	4,941 (5.4%)	0.00
Diabetic Foot; n (%)	335 (1.6%)	325 (1.6%)	428 (1.5%)	424 (1.5%)	1,008 (2.5%)	1,019 (2.5%)	1,771 (1.9%)	1,768 (1.9%)	0.00
Gangrene ; n (%)	44 (0.2%)	38 (0.2%)	45 (0.2%)	41 (0.1%)	52 (0.1%)	65 (0.2%)	141 (0.2%)	144 (0.2%)	0.00
Lower extremity amputation; n (%)	71 (0.3%)	72 (0.3%)	57 (0.2%)	53 (0.2%)	192 (0.5%)	177 (0.4%)	320 (0.4%)	302 (0.3%)	0.02
Osteomyelitis; n (%)	92 (0.4%)	90 (0.4%)	129 (0.4%)	123 (0.4%)	201 (0.5%)	192 (0.5%)	422 (0.5%)	405 (0.4%)	0.01
Skin infections ; n (%)	989 (4.8%)	971 (4.7%)	1,415 (4.9%)	1,382 (4.7%)	2,761 (6.7%)	2,771 (6.7%)	5,165 (5.7%)	5,124 (5.6%)	0.00
Erectile dysfunction; n (%)	787 (3.8%)	765 (3.7%)	710 (2.4%)	705 (2.4%)	1,077 (2.6%)	1,044 (2.5%)	2,574 (2.8%)	2,514 (2.8%)	0.00
Diabetes with unspecified complication; n (%)	806 (3.9%)	811 (3.9%)	803 (2.8%)	799 (2.7%)	1,639 (4.0%)	1,619 (3.9%)	3,248 (3.6%)	3,229 (3.5%)	0.01
Diabetes mellitus without mention of complications; n (%)	19,200 (92.4%)	19,171 (92.3%)	28,205 (96.8%)	28,166 (96.6%)	39,638 (96.3%)	39,582 (96.2%)	87,043 (95.6%)	86,919 (95.4%)	0.01
Hypertension: 1 inpatient or 2 outpatient claims within 365 days; n (%)	17,011 (81.9%)	16,976 (81.7%)	19,581 (67.2%)	19,540 (67.0%)	36,783 (89.4%)	36,792 (89.4%)	73,375 (80.6%)	73,308 (80.5%)	0.00
Hyperlipidemia ; n (%)	16,365 (78.8%)	16,344 (78.7%)	18,229 (62.5%)	18,157 (62.3%)	33,577 (81.6%)	33,568 (81.6%)	68,171 (74.9%)	68,069 (74.7%)	0.00
Edema; n (%)	1,188 (5.7%)	1,153 (5.6%)	1,155 (4.0%)	1,142 (3.9%)	3,729 (9.1%)	3,622 (8.8%)	6,072 (6.7%)	5,917 (6.5%)	0.01
Renal Dysfunction (non-diabetic) ; n (%)	3,426 (16.5%)	3,335 (16.1%)	2,700 (9.3%)	2,665 (9.1%)	8,387 (20.4%)	8,461 (20.6%)	14,513 (15.9%)	14,461 (15.9%)	0.00
Occurrence of acute renal disease ; n (%)	517 (2.5%)	473 (2.3%)	477 (1.6%)	435 (1.5%)	1,256 (3.1%)	1,234 (3.0%)	2,250 (2.5%)	2,142 (2.4%)	0.01
Occurrence of chronic renal insufficiency; n (%)	2,611 (12.6%)	2,601 (12.5%)	1,723 (5.9%)	1,713 (5.9%)	6,558 (15.9%)	6,642 (16.1%)	10,892 (12.0%)	10,956 (12.0%)	0.00
Chronic kidney disease ; n (%)	2,470 (11.9%)	2,480 (11.9%)	1,614 (5.5%)	1,643 (5.6%)	6,118 (14.9%)	6,213 (15.1%)	10,202 (11.2%)	10,336 (11.4%)	-0.01
CKD Stage 3-4; n (%)	1,612 (7.8%)	1,589 (7.6%)	995 (3.4%)	993 (3.4%)	4,059 (9.9%)	4,042 (9.8%)	6,666 (7.3%)	6,624 (7.3%)	0.00
Occurrence of hypertensive nephropathy; n (%)	1,054 (5.1%)	1,007 (4.8%)	637 (2.2%)	634 (2.2%)	2,624 (6.4%)	2,658 (6.5%)	4,315 (4.7%)	4,299 (4.7%)	0.00
Occurrence of miscellaneous renal insufficiency ; n (%)	1,124 (5.4%)	1,039 (5.0%)	1,050 (3.6%)	974 (3.3%)	3,066 (7.5%)	3,095 (7.5%)	5,240 (5.8%)	5,108 (5.6%)	0.01
Glaucoma or cataracts ; n (%)	3,957 (19.0%)	3,868 (18.6%)	4,501 (15.4%)	4,474 (15.3%)	11,477 (27.9%)	11,808 (28.7%)	19,935 (21.9%)	20,150 (22.1%)	0.00
Cellulitis or abscess of toe; n (%)	192 (0.9%)	184 (0.9%)	183 (0.6%)	184 (0.6%)	387 (0.9%)	352 (0.9%)	762 (0.8%)	720 (0.8%)	0.00
Foot ulcer; n (%)	332 (1.6%)	320 (1.5%)	444 (1.5%)	438 (1.5%)	1,033 (2.5%)	1,031 (2.5%)	1,809 (2.0%)	1,789 (2.0%)	0.00
Bladder stones; n (%)	37 (0.2%)	33 (0.2%)	32 (0.1%)	33 (0.1%)	97 (0.2%)	75 (0.2%)	166 (0.2%)	141 (0.2%)	0.00
Kidney stones; n (%)	557 (2.7%)	502 (2.4%)	689 (2.4%)	627 (2.2%)	1,207 (2.9%)	1,198 (2.9%)	2,453 (2.7%)	2,327 (2.6%)	0.01
Urinary tract infections (UTIs); n (%)	1,686 (8.1%)	1,703 (8.2%)	1,779 (6.1%)	1,725 (5.9%)	6,277 (15.3%)	6,276 (15.3%)	9,742 (10.7%)	9,704 (10.7%)	0.00
Dipstick urinalysis; n (%)	7,535 (36.3%)	7,904 (38.1%)	9,562 (32.8%)	9,919 (34.0%)	17,882 (43.5%)	18,912 (46.0%)	34,979 (38.4%)	36,735 (40.3%)	-0.04
Non-dipstick urinalysis; n (%)	8,224 (39.6%)	8,380 (40.3%)	9,173 (31.5%)	9,298 (31.9%)	16,448 (40.0%)	16,601 (40.4%)	33,845 (37.2%)	34,279 (37.6%)	-0.01
Urine function test; n (%)	541 (2.6%)	522 (2.5%)	797 (2.7%)	798 (2.7%)	1,782 (4.3%)	1,710 (4.2%)	3,120 (3.4%)	3,030 (3.3%)	0.01
Cytology; n (%)	227 (1.1%)	221 (1.1%)	393 (1.3%)	393 (1.3%)	740 (1.8%)	757 (1.8%)	1,360 (1.5%)	1,371 (1.5%)	0.00
Cystos; n (%)	350 (1.7%)	351 (1.7%)	516 (1.8%)	535 (1.8%)	969 (2.4%)	979 (2.4%)	1,835 (2.0%)	1,865 (2.0%)	0.00
Other Covariates									
Liver disease; n (%)	1,041 (5.0%)	1,007 (4.8%)	964 (3.3%)	951 (3.3%)	2,109 (5.1%)	2,120 (5.2%)	4,114 (4.5%)	4,078 (4.5%)	0.00
Osteoarthritis; n (%)	2,964 (14.3%)	2,939 (14.1%)	3,120 (10.7%)	3,066 (10.5%)	9,491 (23.1%)	9,594 (23.3%)	15,575 (17.1%)	15,599 (17.1%)	0.00
Other arthritis, arthropathies and musculoskeletal pain; n (%)	6,815 (32.8%)	6,756 (32.5%)	8,386 (28.8%)	8,254 (28.3%)	18,345 (44.6%)	18,289 (44.5%)	33,546 (36.8%)	33,299 (36.6%)	0.00
Dorsopathies; n (%)	4,125 (19.9%)	4,111 (19.8%)	5,015 (17.2%)	4,993 (17.1%)	11,187 (27.2%)	11,235 (27.3%)	20,327 (22.3%)	20,339 (22.3%)	0.00
Fractures; n (%)	473 (2.3%)	464 (2.2%)	630 (2.2%)	623 (2.1%)	1,539 (3.7%)	1,478 (3.6%)	2,642 (2.9%)	2,565 (2.8%)	0.01
Falls ; n (%)	400 (1.9%)	421 (2.0%)	175 (0.6%)	172 (0.6%)	1,378 (3.3%)	1,361 (3.3%)	1,953 (2.1%)	1,954 (2.1%)	0.00
Osteoporosis; n (%)	1,213 (5.8%)	1,166 (5.6%)	1,066 (3.7%)	1,105 (3.8%)	4,387 (10.7%)	4,452 (10.8%)	6,666 (7.3%)	6,723 (7.4%)	0.00
Hyperthyroidism; n (%)	141 (0.7%)	142 (0.7%)	154 (0.5%)	145 (0.5%)	484 (1.2%)	456 (1.1%)	779 (0.9%)	743 (0.8%)	0.01
Hypothyroidism ; n (%)	3,175 (15.3%)	3,119 (15.0%)	3,017 (10.3%)	2,931 (10.1%)	8,320 (20.2%)	8,090 (19.7%)	14,512 (15.9%)	14,140 (15.5%)	0.01
Other disorders of thyroid gland ; n (%)	691 (3.3%)	730 (3.5%)	868 (3.0%)	889 (3.0%)	2,014 (4.9%)	2,248 (5.5%)	3,573 (3.9%)	3,867 (4.2%)	-0.02
Depression; n (%)	1,417 (6.8%)	1,395 (6.7%)	1,524 (5.2%)	1,455 (5.0%)	4,115 (10.0%)	4,149 (10.1%)	7,056 (7.7%)	6,999 (7.7%)	0.00
Anxiety; n (%)	1,150 (5.5%)	1,110 (5.3%)	1,033 (3.5%)	976 (3.3%)	3,117 (7.6%)	3,190 (7.8%)	5,300 (5.8%)	5,276 (5.8%)	0.00
Sleep_Disorder; n (%)	1,846 (8.9%)	1,817 (8.7%)	2,953 (10.1%)	2,943 (10.1%)	3,774 (9.2%)	3,794 (9.2%)	8,573 (9.4%)	8,554 (9.4%)	0.00
Dementia; n (%)	520 (2.5%)	513 (2.5%)	436 (1.5%)	417 (1.4%)	2,620 (6.4%)	2,659 (6.5%)	3,576 (3.9%)	3,589 (3.9%)	0.00
Delirium; n (%)	139 (0.7%)	127 (0.6%)	150 (0.5%)	136 (0.5%)	569 (1.4%)	577 (1.4%)	858 (0.9%)	840 (0.9%)	0.00
Psychosis; n (%)	116 (0.6%)	125 (0.6%)	149 (0.5%)	139 (0.5%)	704 (1.7%)	696 (1.7%)	969 (1.1%)	960 (1.1%)	0.00
Obesity; n (%)	2,583 (12.4%)	2,589 (12.5%)	1,765 (6.1%)	1,801 (6.2%)	4,272 (10.4%)	4,255 (10.3%)	8,620 (9.5%)	8,645 (9.5%)	0.00
Overweight; n (%)	752 (3.6%)	748 (3.6%)	279 (1.0%)	279 (1.0%)	1,140 (2.8%)	1,164 (2.8%)	2,171 (2.4%)	2,191 (2.4%)	0.00
Smoking; n (%)	1,718 (8.3%)	1,667 (8.0%)	1,199 (4.1%)	1,207 (4.1%)	4,251 (10.3%)	4,199 (10.2%)	7,168 (7.9%)	7,073 (7.8%)	0.00
Alcohol abuse or dependence; n (%)	155 (0.7%)	152 (0.7%)	157 (0.5%)	134 (0.5%)	244 (0.6%)	249 (0.6%)	556 (0.6%)	535 (0.6%)	0.00
Drug abuse or dependence; n (%)	169 (0.8%)	169 (0.8%)	102 (0.3%)	101 (0.3%)	287 (0.7%)	280 (0.7%)	558 (0.6%)	550 (0.6%)	0.00
COPD; n (%)	1,529 (7.4%)	1,480 (7.1%)	1,507 (5.2%)	1,500 (5.1%)	4,727 (11.5%)	4,617 (11.2%)	7,763 (8.5%)	7,597 (8.3%)	0.01
Asthma; n (%)	979 (4.7%)	1,013 (4.9%)	1,122 (3.8%)	1,110 (3.8%)	2,606 (6.3%)	2,618 (6.4%)	4,707 (5.2%)	4,741 (5.2%)	0.00
Obstructive sleep apnea; n (%)	1,620 (7.8%)	1,611 (7.8%)	2,321 (8.0%)	2,286 (7.8%)	2,171 (5.3%)	2,191 (5.3%)	6,112 (6.7%)	6,088 (6.7%)	0.00

Table 1: Saxagliptin vs 2nd Generation Sulfonylureas

Pneumonia; n (%)	379 (1.8%)	378 (1.8%)	460 (1.6%)	466 (1.6%)	1,272 (3.1%)	1,258 (3.1%)	2,111 (2.3%)	2,102 (2.3%)	0.00
Imaging; n (%)	34 (0.2%)	19 (0.1%)	16 (0.1%)	17 (0.1%)	54 (0.1%)	51 (0.1%)	104 (0.1%)	87 (0.1%)	0.00
Diabetes Medications									
DM Medications - AGIs; n (%)	63 (0.3%)	65 (0.3%)	93 (0.3%)	80 (0.3%)	179 (0.4%)	192 (0.5%)	335 (0.4%)	337 (0.4%)	0.00
DM Medications - Glitazones; n (%)	2,628 (12.7%)	2,617 (12.6%)	5,543 (19.0%)	5,541 (19.0%)	4,414 (10.7%)	4,429 (10.8%)	12,585 (13.8%)	12,587 (13.8%)	0.00
DM Medications - GLP-1 RA; n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	#VALUE!	#VALUE!	#VALUE!
DM Medications - Insulin; n (%)	3,259 (15.7%)	3,169 (15.3%)	3,930 (13.5%)	3,878 (13.3%)	7,703 (18.7%)	7,651 (18.6%)	14,892 (16.4%)	14,698 (16.1%)	0.01
DM Medications - Meglitinides; n (%)	334 (1.6%)	334 (1.6%)	752 (2.6%)	774 (2.7%)	1,119 (2.7%)	1,129 (2.7%)	2,205 (2.4%)	2,237 (2.5%)	-0.01
DM Medications - Metformin; n (%)	14,469 (69.7%)	14,670 (70.6%)	21,163 (72.6%)	21,117 (72.4%)	27,388 (66.6%)	27,400 (66.6%)	63,020 (69.2%)	63,187 (69.4%)	0.00
Concomitant initiation or current use of SGLT2i; n (%)	569 (2.7%)	540 (2.6%)	344 (1.2%)	349 (1.2%)	508 (1.2%)	516 (1.3%)	1,421 (1.6%)	1,405 (1.5%)	0.01
Concomitant initiation or current use of AGIs; n (%)	55 (0.3%)	45 (0.2%)	64 (0.2%)	49 (0.2%)	121 (0.3%)	125 (0.3%)	240 (0.3%)	219 (0.2%)	0.02
Concomitant initiation or current use of Glitazones; n (%)	1,515 (7.3%)	1,495 (7.2%)	3,216 (11.0%)	3,195 (11.0%)	2,710 (6.6%)	2,669 (6.5%)	7,441 (8.2%)	7,359 (8.1%)	0.00
Concomitant initiation or current use of GLP-1 RA; n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	000 (0.0%)	000 (0.0%)	#DIV/0!
Concomitant initiation or current use of Insulin; n (%)	2,393 (11.5%)	2,338 (11.3%)	2,955 (10.1%)	2,911 (10.0%)	5,862 (14.2%)	5,819 (14.1%)	11,210 (12.3%)	11,068 (12.2%)	0.00
Concomitant initiation or current use of Meglitinides; n (%)	234 (1.1%)	236 (1.1%)	501 (1.7%)	559 (1.9%)	790 (1.9%)	800 (1.9%)	1,525 (1.7%)	1,595 (1.8%)	-0.01
Concomitant initiation or current use of Metformin; n (%)	12,550 (60.4%)	12,734 (61.3%)	18,351 (63.0%)	18,424 (63.2%)	23,232 (56.5%)	23,281 (56.6%)	54,133 (59.4%)	54,439 (59.8%)	-0.01
Past use of SGLT2i; n (%)	232 (1.1%)	234 (1.1%)	108 (0.4%)	119 (0.4%)	203 (0.5%)	197 (0.5%)	543 (0.6%)	550 (0.6%)	0.00
Past use of AGIs; n (%)	8 (0.0%)	20 (0.1%)	29 (0.1%)	31 (0.1%)	58 (0.1%)	67 (0.2%)	095 (0.1%)	118 (0.1%)	0.00
Past use of Glitazones; n (%)	1,113 (5.4%)	1,122 (5.4%)	2,328 (8.0%)	2,346 (8.0%)	1,704 (4.1%)	1,760 (4.3%)	5,145 (5.6%)	5,228 (5.7%)	0.00
Past use of GLP-1 RA; n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	000 (0.0%)	000 (0.0%)	#DIV/0!
Past use of Insulin; n (%)	866 (4.2%)	831 (4.0%)	975 (3.3%)	967 (3.3%)	1,841 (4.5%)	1,832 (4.5%)	3,682 (4.0%)	3,630 (4.0%)	0.00
Past use of Meglitinides; n (%)	100 (0.5%)	98 (0.5%)	251 (0.9%)	215 (0.7%)	329 (0.8%)	329 (0.8%)	680 (0.7%)	642 (0.7%)	0.00
Past use of metformin (final); n (%)	1,919 (9.2%)	1,936 (9.3%)	2,812 (9.6%)	2,693 (9.2%)	4,156 (10.1%)	4,119 (10.0%)	8,887 (9.8%)	8,748 (9.6%)	0.01
Other Medications									
Use of ACE inhibitors; n (%)	8,548 (41.2%)	8,588 (41.3%)	12,091 (41.5%)	12,183 (41.8%)	16,283 (39.6%)	16,298 (39.6%)	36,922 (40.5%)	37,069 (40.7%)	0.00
Use of ARBs; n (%)	6,027 (29.0%)	6,014 (29.0%)	9,104 (31.2%)	9,054 (31.1%)	13,919 (33.8%)	13,948 (33.9%)	29,050 (31.9%)	29,016 (31.9%)	0.00
Use of Loop Diuretics ; n (%)	2,050 (9.9%)	2,094 (10.1%)	3,016 (10.3%)	2,970 (10.2%)	7,243 (17.6%)	7,190 (17.5%)	12,309 (13.5%)	12,254 (13.5%)	0.00
Use of other diuretics; n (%)	487 (2.3%)	491 (2.4%)	679 (2.3%)	707 (2.4%)	1,337 (3.2%)	1,357 (3.3%)	2,503 (2.7%)	2,555 (2.8%)	-0.01
Use of nitrates-United; n (%)	972 (4.7%)	970 (4.7%)	1,432 (4.9%)	1,429 (4.9%)	3,294 (8.0%)	3,287 (8.0%)	5,698 (6.3%)	5,686 (6.2%)	0.00
Use of other hypertension drugs; n (%)	1,261 (6.1%)	1,250 (6.0%)	1,563 (5.4%)	1,535 (5.3%)	3,298 (8.0%)	3,334 (8.1%)	6,122 (6.7%)	6,119 (6.7%)	0.00
Use of digoxin; n (%)	412 (2.0%)	368 (1.8%)	600 (2.1%)	605 (2.1%)	1,533 (3.7%)	1,512 (3.7%)	2,545 (2.8%)	2,485 (2.7%)	0.01
Use of Anti-arrhythmics; n (%)	213 (1.0%)	211 (1.0%)	332 (1.1%)	348 (1.2%)	836 (2.0%)	819 (2.0%)	1,381 (1.5%)	1,378 (1.5%)	0.00
Use of COPD/asthma meds; n (%)	2,785 (13.4%)	2,794 (13.5%)	4,169 (14.3%)	4,167 (14.3%)	7,710 (18.7%)	7,674 (18.7%)	14,664 (16.1%)	14,635 (16.1%)	0.00
Use of statins; n (%)	13,588 (65.4%)	13,603 (65.5%)	19,039 (65.3%)	18,973 (65.1%)	28,374 (69.0%)	28,291 (68.8%)	61,001 (67.0%)	60,867 (66.8%)	0.00
Use of other lipid-lowering drugs; n (%)	3,030 (14.6%)	2,944 (14.2%)	5,019 (17.2%)	4,897 (16.8%)	5,994 (14.6%)	5,973 (14.5%)	14,043 (15.4%)	13,814 (15.2%)	0.01
Use of antiplatelet agents; n (%)	2,640 (12.7%)	2,605 (12.5%)	4,128 (14.2%)	4,089 (14.0%)	6,851 (16.7%)	6,953 (16.9%)	13,619 (15.0%)	13,647 (15.0%)	0.00
Use of oral anticoagulants (Dabigatran, Rivaroxaban, Apixaban, Warfarin); n (%)	1,112 (5.4%)	1,077 (5.2%)	1,464 (5.0%)	1,445 (5.0%)	3,637 (8.8%)	3,537 (8.6%)	6,213 (6.8%)	6,059 (6.7%)	0.00
Use of heparin and other low-molecular weight heparins; n (%)	94 (0.5%)	90 (0.4%)	0 (0.0%)	1 (0.0%)	177 (0.4%)	169 (0.4%)	271 (0.3%)	260 (0.3%)	0.00
Use of NSAIDs; n (%)	3,123 (15.0%)	3,100 (14.9%)	4,272 (14.7%)	4,343 (14.9%)	7,170 (17.4%)	7,301 (17.7%)	14,565 (16.0%)	14,744 (16.2%)	-0.01
Use of oral corticosteroids; n (%)	2,722 (13.1%)	2,663 (12.8%)	3,635 (12.5%)	3,677 (12.6%)	6,754 (16.4%)	6,571 (16.0%)	13,111 (14.4%)	12,911 (14.2%)	0.01
Use of bisphosphonate (United); n (%)	628 (3.0%)	603 (2.9%)	612 (2.1%)	637 (2.2%)	1,921 (4.7%)	1,970 (4.8%)	3,161 (3.5%)	3,210 (3.5%)	0.00
Use of opioids; n (%)	4,763 (22.9%)	4,735 (22.8%)	7,046 (24.2%)	6,977 (23.9%)	10,491 (25.5%)	10,563 (25.7%)	22,300 (24.5%)	22,275 (24.5%)	0.00
Use of antidepressants; n (%)	4,125 (19.9%)	4,035 (19.4%)	5,686 (19.5%)	5,621 (19.3%)	10,351 (25.2%)	10,384 (25.2%)	20,162 (22.1%)	20,040 (22.0%)	0.00
Use of antipsychotics; n (%)	358 (1.7%)	369 (1.8%)	454 (1.6%)	432 (1.5%)	1,440 (3.5%)	1,456 (3.5%)	2,252 (2.5%)	2,257 (2.5%)	0.00
Use of anticonvulsants; n (%)	2,400 (11.6%)	2,374 (11.4%)	2,784 (9.6%)	2,730 (9.4%)	6,445 (15.7%)	6,460 (15.7%)	11,629 (12.8%)	11,564 (12.7%)	0.00
Use of lithium; n (%)	22 (0.1%)	23 (0.1%)	45 (0.2%)	26 (0.1%)	66 (0.2%)	43 (0.1%)	133 (0.1%)	092 (0.1%)	0.00
Use of Benzos; n (%)	1,724 (8.3%)	1,648 (7.9%)	2,989 (10.3%)	2,963 (10.2%)	3,802 (9.2%)	3,787 (9.2%)	8,515 (9.4%)	8,398 (9.2%)	0.01
Use of anxiolytics/hypnotics; n (%)	1,306 (6.3%)	1,300 (6.3%)	2,107 (7.2%)	1,988 (6.8%)	3,334 (8.1%)	3,334 (8.1%)	6,747 (7.4%)	6,622 (7.3%)	0.00
Use of dementia meds; n (%)	360 (1.7%)	361 (1.7%)	378 (1.3%)	365 (1.3%)	2,292 (5.6%)	2,350 (5.7%)	3,030 (3.3%)	3,076 (3.4%)	-0.01
Use of antiparkinsonian meds; n (%)	401 (1.9%)	410 (2.0%)	571 (2.0%)	556 (1.9%)	1,325 (3.2%)	1,332 (3.2%)	2,297 (2.5%)	2,298 (2.5%)	0.00
Any use of pramlintide; n (%)	8 (0.0%)	11 (0.1%)	20 (0.1%)	38 (0.1%)	5 (0.0%)	12 (0.0%)	033 (0.0%)	061 (0.1%)	-0.04
Any use of 1st generation sulfonylureas; n (%)	3 (0.0%)	5 (0.0%)	21 (0.1%)	8 (0.0%)	31 (0.1%)	19 (0.0%)	055 (0.1%)	032 (0.0%)	0.00
Entresto (sacubitril/valsartan); n (%)	9 (0.0%)	16 (0.1%)	1 (0.0%)	1 (0.0%)	6 (0.0%)	11 (0.0%)	016 (0.0%)	028 (0.0%)	0.00
Initiation as monotherapy ; n (%)	4,379 (21.1%)	4,352 (21.0%)	5,359 (18.4%)	5,432 (18.6%)	6,352 (15.4%)	6,427 (15.6%)	16,090 (17.7%)	16,211 (17.8%)	0.00
Labs							49,922	49,922	
Lab values- HbA1c (%) ; n (%)	6,855 (33.0%)	7,389 (35.6%)	1,708 (5.9%)	1,595 (5.5%)	N/A	N/A	8,563 (17.2%)	8,984 (18.0%)	-0.02
Lab values- HbA1c (%) (within 3 months) ; n (%)	5,387 (25.9%)	5,927 (28.5%)	1,324 (4.5%)	1,266 (4.3%)	N/A	N/A	6,711 (13.4%)	7,193 (14.4%)	-0.03
Lab values- HbA1c (%) (within 6 months) ; n (%)	6,855 (33.0%)	7,389 (35.6%)	1,708 (5.9%)	1,595 (5.5%)	N/A	N/A	8,563 (17.2%)	8,984 (18.0%)	-0.02
Lab values- BNP; n (%)	95 (0.5%)	97 (0.5%)	13 (0.0%)	19 (0.1%)	N/A	N/A	108 (0.2%)	116 (0.2%)	0.00

Table 1: Saxagliptin vs 2nd Generation Sulfonylureas

Lab values- BNP (within 3 months); n (%)	54 (0.3%)	60 (0.3%)	5 (0.0%)	10 (0.0%)	N/A	N/A	059 (0.1%)	070 (0.1%)	0.00
Lab values- BNP (within 6 months); n (%)	95 (0.5%)	97 (0.5%)	13 (0.0%)	19 (0.1%)	N/A	N/A	108 (0.2%)	116 (0.2%)	0.00
Lab values- BUN (mg/dl); n (%)	7,159 (34.5%)	7,737 (37.2%)	1,493 (5.1%)	1,670 (5.7%)	N/A	N/A	8,652 (17.3%)	9,407 (18.8%)	-0.04
Lab values- BUN (mg/dl) (within 3 months); n (%)	5,533 (26.6%)	6,143 (29.6%)	1,160 (4.0%)	1,300 (4.5%)	N/A	N/A	6,693 (13.4%)	7,443 (14.9%)	-0.04
Lab values- BUN (mg/dl) (within 6 months); n (%)	7,159 (34.5%)	7,737 (37.2%)	1,493 (5.1%)	1,670 (5.7%)	N/A	N/A	8,652 (17.3%)	9,407 (18.8%)	-0.04
Lab values- Creatinine (mg/dl) ; n (%)	7,273 (35.0%)	7,904 (38.1%)	1,541 (5.3%)	1,728 (5.9%)	N/A	N/A	8,814 (17.7%)	9,632 (19.3%)	-0.04
Lab values- Creatinine (mg/dl) (within 3 months) ; n (%)	5,629 (27.1%)	6,283 (30.2%)	1,192 (4.1%)	1,342 (4.6%)	N/A	N/A	6,821 (13.7%)	7,625 (15.3%)	-0.05
Lab values- Creatinine (mg/dl) (within 6 months) ; n (%)	7,273 (35.0%)	7,904 (38.1%)	1,541 (5.3%)	1,728 (5.9%)	N/A	N/A	8,814 (17.7%)	9,632 (19.3%)	-0.04
Lab values- HDL level (mg/dl); n (%)	6,230 (30.0%)	6,623 (31.9%)	1,540 (5.3%)	1,484 (5.1%)	N/A	N/A	7,770 (15.6%)	8,107 (16.2%)	-0.02
Lab values- HDL level (mg/dl) (within 3 months); n (%)	4,634 (22.3%)	5,024 (24.2%)	1,143 (3.9%)	1,117 (3.8%)	N/A	N/A	5,777 (11.6%)	6,141 (12.3%)	-0.02
Lab values- HDL level (mg/dl) (within 6 months); n (%)	6,230 (30.0%)	6,623 (31.9%)	1,540 (5.3%)	1,484 (5.1%)	N/A	N/A	7,770 (15.6%)	8,107 (16.2%)	-0.02
Lab values- LDL level (mg/dl) ; n (%)	6,312 (30.4%)	6,695 (32.2%)	1,631 (5.6%)	1,508 (5.2%)	N/A	N/A	7,943 (15.9%)	8,203 (16.4%)	-0.01
Lab values- LDL level (mg/dl) (within 3 months) ; n (%)	4,683 (22.5%)	5,091 (24.5%)	1,211 (4.2%)	1,133 (3.9%)	N/A	N/A	5,894 (11.8%)	6,224 (12.5%)	-0.02
Lab values- LDL level (mg/dl) (within 6 months) ; n (%)	6,312 (30.4%)	6,695 (32.2%)	1,631 (5.6%)	1,508 (5.2%)	N/A	N/A	7,943 (15.9%)	8,203 (16.4%)	-0.01
Lab values- NT-proBNP; n (%)	6 (0.0%)	18 (0.1%)	0 (0.0%)	1 (0.0%)	N/A	N/A	06 (0.0%)	0 (0.0%)	-
Lab values- NT-proBNP (within 3 months); n (%)	5 (0.0%)	13 (0.1%)	0 (0.0%)	1 (0.0%)	N/A	N/A	05 (0.0%)	0 (0.0%)	-
Lab values- NT-proBNP (within 6 months); n (%)	6 (0.0%)	18 (0.1%)	0 (0.0%)	1 (0.0%)	N/A	N/A	06 (0.0%)	19 (0.0%)	-
Lab values- Total cholesterol (mg/dl) ; n (%)	6,283 (30.2%)	6,730 (32.4%)	1,564 (5.4%)	1,521 (5.2%)	N/A	N/A	7,847 (15.7%)	8,251 (16.5%)	-0.02
Lab values- Total cholesterol (mg/dl) (within 3 months) ; n (%)	4,661 (22.4%)	5,114 (24.6%)	1,155 (4.0%)	1,147 (3.9%)	N/A	N/A	5,816 (11.7%)	6,261 (12.5%)	-0.02
Lab values- Total cholesterol (mg/dl) (within 6 months) ; n (%)	6,283 (30.2%)	6,730 (32.4%)	1,564 (5.4%)	1,521 (5.2%)	N/A	N/A	7,847 (15.7%)	8,251 (16.5%)	-0.02
Lab values- Triglyceride level (mg/dl); n (%)	6,237 (30.0%)	6,704 (32.3%)	1,531 (5.3%)	1,485 (5.1%)	N/A	N/A	7,768 (15.6%)	8,189 (16.4%)	-0.02
Lab values- Triglyceride level (mg/dl) (within 3 months); n (%)	4,640 (22.3%)	5,099 (24.5%)	1,134 (3.9%)	1,118 (3.8%)	N/A	N/A	5,774 (11.6%)	6,217 (12.5%)	-0.03
Lab values- Triglyceride level (mg/dl) (within 6 months); n (%)	6,237 (30.0%)	6,704 (32.3%)	1,531 (5.3%)	1,485 (5.1%)	N/A	N/A	7,768 (15.6%)	8,189 (16.4%)	-0.02
Lab result number- HbA1c (%) mean (only 2 to 20 included)	6,825	7,368	1,534	1,504	N/A	N/A	8,359	8,872	
...mean (sd)	8.18 (1.81)	7.95 (1.71)	8.20 (1.81)	8.03 (1.81)	N/A	N/A	8.18 (1.81)	7.96 (1.73)	0.12
...median [IQR]	7.70 [6.95, 9.00]	7.50 [6.80, 8.65]	7.70 [7.00, 9.00]	7.50 [6.80, 8.70]	N/A	N/A	7.70 (1.81)	7.50 (1.73)	0.11
...Missing; n (%)	13,947 (67.1%)	13,404 (64.5%)	27,616 (94.7%)	27,646 (94.8%)	N/A	N/A	41,563 (83.3%)	41,050 (82.2%)	0.03
Lab result number- BNP mean	95	97	13	19	N/A	N/A	108	116	
...mean (sd)	164.54 (440.30)	152.44 (201.22)	116.99 (165.82)	238.55 (559.75)	N/A	N/A	158.82 (420.35)	166.54 (290.36)	-0.02
...median [IQR]	72.10 [21.70, 154.80]	85.00 [32.40, 195.85]	46.40 [21.45, 142.90]	30.00 [17.00, 112.00]	N/A	N/A	#VALUE!	#VALUE!	#VALUE!
...Missing; n (%)	20,677 (99.5%)	20,675 (99.5%)	29,137 (100.0%)	29,131 (99.9%)	N/A	N/A	49,814 (99.8%)	49,806 (99.8%)	0.00
Lab result number- BUN (mg/dl) mean	7,159	7,737	1,493	1,670	N/A	N/A	8,652	9,407	
...mean (sd)	18.18 (7.32)	18.03 (7.12)	472.97 (9,177.52)	373.82 (7,794.27)	N/A	N/A	96.66 (3811.78)	81.19 (3283.58)	0.00
...median [IQR]	17.00 [13.50, 21.00]	16.50 [13.50, 21.00]	17.00 [14.00, 20.50]	17.00 [13.00, 20.00]	N/A	N/A	#VALUE!	#VALUE!	#VALUE!
...Missing; n (%)	13,613 (65.5%)	13,035 (62.8%)	27,657 (94.9%)	27,480 (94.3%)	N/A	N/A	41,270 (82.7%)	40,515 (81.2%)	0.04
Lab result number- Creatinine (mg/dl) mean (only 0.1 to 15 included)	7,235	7,867	1,505	1,683	N/A	N/A	8,740	9,550	
...mean (sd)	1.01 (0.36)	1.01 (0.35)	0.97 (0.29)	0.99 (0.33)	N/A	N/A	1.00 (0.35)	1.01 (0.35)	-0.03
...median [IQR]	0.94 [0.79, 1.14]	0.95 [0.80, 1.13]	0.93 [0.79, 1.09]	0.93 [0.80, 1.10]	N/A	N/A	0.94 (0.35)	0.95 (0.35)	-0.03
...Missing; n (%)	13,537 (65.2%)	12,905 (62.1%)	27,645 (94.8%)	27,467 (94.2%)	N/A	N/A	41,182 (82.5%)	40,372 (80.9%)	0.04
Lab result number- HDL level (mg/dl) mean (only =<5000 included)	6,230	6,623	1,539	1,481	N/A	N/A	7,769	8,104	
...mean (sd)	45.66 (13.30)	46.38 (13.32)	44.68 (13.91)	45.39 (13.98)	N/A	N/A	45.47 (13.42)	46.20 (13.44)	-0.05
...median [IQR]	44.00 [37.00, 53.00]	44.00 [37.00, 53.00]	43.00 [36.00, 52.00]	44.00 [37.00, 52.50]	N/A	N/A	43.80 (13.42)	44.00 (13.44)	-0.01
...Missing; n (%)	14,542 (70.0%)	14,149 (68.1%)	27,611 (94.7%)	27,669 (94.9%)	N/A	N/A	42,153 (84.4%)	41,818 (83.8%)	0.02
Lab result number- LDL level (mg/dl) mean (only =<5000 included)	6,194	6,595	1,490	1,436	N/A	N/A	7,684	8,031	
...mean (sd)	87.61 (40.85)	87.44 (38.52)	87.29 (41.68)	89.25 (40.99)	N/A	N/A	87.55 (41.01)	87.76 (38.98)	-0.01
...median [IQR]	85.00 [63.00, 112.00]	84.00 [64.00, 109.00]	86.00 [63.44, 113.00]	87.00 [65.00, 112.38]	N/A	N/A	85.19 (41.01)	84.54 (38.98)	0.02
...Missing; n (%)	14,578 (70.2%)	14,177 (68.3%)	27,660 (94.9%)	27,714 (95.1%)	N/A	N/A	42,238 (84.6%)	41,891 (83.9%)	0.02
Lab result number- Total cholesterol (mg/dl) mean (only =<5000 included)	6,281	6,727	1,562	1,515	N/A	N/A	7,843	8,242	
...mean (sd)	176.40 (48.75)	172.97 (46.09)	176.21 (49.12)	174.96 (49.83)	N/A	N/A	176.36 (48.83)	173.34 (46.80)	0.06
...median [IQR]	170.00 [144.00, 201.00]	166.00 [143.00, 197.00]	172.00 [145.50, 203.00]	169.50 [145.50, 201.00]	N/A	N/A	170.40 (48.83)	166.64 (46.80)	0.08
...Missing; n (%)	14,491 (69.8%)	14,045 (67.6%)	27,588 (94.6%)	27,635 (94.8%)	N/A	N/A	42,079 (84.3%)	41,680 (83.5%)	0.02
Lab result number- Triglyceride level (mg/dl) mean (only =<5000 included)	6,236	6,703	1,530	1,482	N/A	N/A	7,766	8,185	

Table 1: Saxagliptin vs 2nd Generation Sulfonylureas

...mean (sd)	198.52 (201.95)	179.80 (153.29)	201.91 (196.77)	188.19 (193.76)	N/A	N/A	199.19 (200.95)	181.32 (161.38)	0.10
...median [IQR]	155.00 [109.00, 225.88]	147.50 [105.00, 210.00]	157.00 [109.00, 231.00]	150.00 [103.00, 221.00]	N/A	N/A	155.39 (200.95)	147.95 (161.38)	0.04
...Missing; n (%)	14,536 (70.0%)	14,069 (67.7%)	27,620 (94.8%)	27,668 (94.9%)	N/A	N/A	42,156 (84.4%)	41,737 (83.6%)	0.02
Lab result number- Hemoglobin mean (only >0 included)	5,023	5,290	944	1,027	N/A	N/A	5,967	6,317	
...mean (sd)	13.70 (1.67)	13.72 (1.69)	11,075.13 (325,562.43)	522.41 (8,421.85)	N/A	N/A	1763.66 (129455.74)	96.42 (3394.92)	0.02
...median [IQR]	13.80 [12.60, 14.80]	13.80 [12.60, 14.90]	13.90 [12.80, 15.00]	14.00 [12.90, 15.00]	N/A	N/A	#VALUE!	#VALUE!	#VALUE!
...Missing; n (%)	15,749 (75.8%)	15,482 (74.5%)	28,206 (96.8%)	28,123 (96.5%)	N/A	N/A	43,955 (88.0%)	43,605 (87.3%)	0.02
Lab result number- Serum sodium mean (only > 90 and < 190 included)	7,115	7,732	1,415	1,597	N/A	N/A	8,530	9,329	
...mean (sd)	139.13 (2.80)	139.38 (2.70)	138.84 (2.60)	138.94 (2.61)	N/A	N/A	139.08 (2.77)	139.30 (2.68)	-0.08
...median [IQR]	139.00 [137.67, 141.00]	139.50 [138.00, 141.00]	139.00 [137.00, 140.50]	139.00 [137.50, 141.00]	N/A	N/A	139.00 (2.77)	139.41 (2.68)	-0.15
...Missing; n (%)	13,657 (65.7%)	13,040 (62.8%)	27,735 (95.1%)	27,553 (94.5%)	N/A	N/A	41,392 (82.9%)	40,593 (81.3%)	0.04
Lab result number- Albumin mean (only >0 and <=10 included)	6,700	7,308	1,299	1,463	N/A	N/A	7,999	8,771	
...mean (sd)	4.27 (0.32)	4.28 (0.32)	4.25 (0.46)	4.24 (0.58)	N/A	N/A	4.27 (0.35)	4.27 (0.38)	0.00
...median [IQR]	4.30 [4.10, 4.50]	4.30 [4.10, 4.50]	4.30 [4.10, 4.50]	4.30 [4.10, 4.50]	N/A	N/A	4.30 (0.35)	4.30 (0.38)	0.00
...Missing; n (%)	14,072 (67.7%)	13,464 (64.8%)	27,851 (95.5%)	27,687 (95.0%)	N/A	N/A	41,923 (84.0%)	41,151 (82.4%)	0.04
Lab result number- Glucose (fasting or random) mean (only 10-1000 included)	7,121	7,744	1,371	1,522	N/A	N/A	8,492	9,266	
...mean (sd)	170.54 (71.23)	163.02 (65.86)	172.40 (71.73)	164.90 (65.90)	N/A	N/A	170.84 (71.32)	163.33 (65.87)	0.11
...median [IQR]	152.00 [123.75, 198.33]	146.00 [120.00, 185.00]	156.00 [125.00, 200.50]	148.00 [121.38, 192.00]	N/A	N/A	152.65 (71.32)	146.33 (65.87)	0.09
...Missing; n (%)	13,651 (65.7%)	13,028 (62.7%)	27,779 (95.3%)	27,628 (94.8%)	N/A	N/A	41,430 (83.0%)	40,656 (81.4%)	0.04
Lab result number- Potassium mean (only 1-7 included)	7,219	7,828	1,482	1,636	N/A	N/A	8,701	9,464	
...mean (sd)	4.42 (0.43)	4.40 (0.42)	4.38 (0.40)	4.39 (0.41)	N/A	N/A	4.41 (0.43)	4.40 (0.42)	0.02
...median [IQR]	4.40 [4.13, 4.70]	4.40 [4.10, 4.65]	4.40 [4.10, 4.60]	4.40 [4.10, 4.60]	N/A	N/A	4.40 (0.43)	4.40 (0.42)	0.00
...Missing; n (%)	13,553 (65.2%)	12,944 (62.3%)	27,668 (94.9%)	27,514 (94.4%)	N/A	N/A	41,221 (82.6%)	40,458 (81.0%)	0.04
Comorbidity Scores									
CCI (180 days)- ICD9 and ICD10									
...mean (sd)	2.25 (1.79)	2.24 (1.79)	1.62 (1.51)	1.62 (1.50)	2.87 (2.04)	2.88 (2.07)	2.33 (1.83)	2.33 (1.84)	0.00
...median [IQR]	2.00 [1.00, 3.00]	2.00 [1.00, 3.00]	1.00 [1.00, 2.00]	1.00 [1.00, 2.00]	2.00 [1.00, 4.00]	2.00 [1.00, 4.00]	1.68 (1.83)	1.68 (1.84)	0.00
Frailty Score: Qualitative Version 365 days as Categories,									
...0; n (%)	8,392 (40.4%)	8,404 (40.5%)	10,050 (34.5%)	10,096 (34.6%)	9,086 (22.1%)	8,951 (21.8%)	27,528 (30.2%)	27,451 (30.1%)	0.00
...1 to 2; n (%)	7,972 (38.4%)	7,860 (37.8%)	13,116 (45.0%)	13,180 (45.2%)	15,015 (36.5%)	14,927 (36.3%)	36,103 (39.6%)	35,967 (39.5%)	0.00
...3 or more; n (%)	4,408 (21.2%)	4,508 (21.7%)	5,984 (20.5%)	5,874 (20.2%)	17,040 (41.4%)	17,263 (42.0%)	27,432 (30.1%)	27,645 (30.4%)	-0.01
Frailty Score: Empirical Version 365 days as Categories,									
...< 0.12908; n (%)	5,862 (28.2%)	6,186 (29.8%)	8,421 (28.9%)	8,678 (29.8%)	4,443 (10.8%)	4,810 (11.7%)	18,726 (20.6%)	19,674 (21.6%)	-0.02
...0.12908 - 0.1631167; n (%)	6,990 (33.7%)	6,791 (32.7%)	10,018 (34.4%)	9,960 (34.2%)	9,817 (23.9%)	9,685 (23.5%)	26,825 (29.5%)	26,436 (29.0%)	0.01
...>= 0.1631167; n (%)	7,920 (38.1%)	7,795 (37.5%)	10,711 (36.7%)	10,512 (36.1%)	26,881 (65.3%)	26,646 (64.8%)	45,512 (50.0%)	44,953 (49.4%)	0.01
Non-Frailty; n (%)	11,629 (56.0%)	11,843 (57.0%)	15,184 (52.1%)	15,193 (52.1%)	1,784 (4.3%)	1,488 (3.6%)	28,597 (31.4%)	28,524 (31.3%)	0.00
Frailty Score (mean): Qualitative Version 365 days,									
...mean (sd)	1.47 (1.87)	1.49 (1.90)	1.48 (1.71)	1.47 (1.68)	2.50 (2.34)	2.53 (2.36)	1.94 (2.05)	1.95 (2.06)	0.00
...median [IQR]	1.00 [0.00, 2.00]	1.00 [0.00, 2.00]	1.00 [0.00, 2.00]	1.00 [0.00, 2.00]	2.00 [1.00, 4.00]	2.00 [1.00, 4.00]	1.45 (2.05)	1.45 (2.06)	0.00
Frailty Score (mean): Empirical Version 365 days,									
...mean (sd)	0.15 (0.05)	0.15 (0.05)	0.15 (0.05)	0.15 (0.05)	0.19 (0.07)	0.19 (0.07)	0.17 (0.06)	0.17 (0.06)	0.00
...median [IQR]	0.14 [0.11, 0.17]	0.13 [0.11, 0.17]	0.14 [0.12, 0.17]	0.14 [0.12, 0.17]	0.18 [0.15, 0.23]	0.18 [0.15, 0.23]	0.16 (0.06)	0.16 (0.06)	0.00
Healthcare Utilization									
Any hospitalization; n (%)	1,502 (7.2%)	1,425 (6.9%)	2,187 (7.5%)	2,073 (7.1%)	3,930 (9.6%)	3,921 (9.5%)	7,619 (8.4%)	7,419 (8.1%)	0.01
Any hospitalization within prior 30 days; n (%)	374 (1.8%)	352 (1.7%)	471 (1.6%)	428 (1.5%)	1,064 (2.6%)	1,044 (2.5%)	1,909 (2.1%)	1,824 (2.0%)	0.01
Any hospitalization during prior 31-180 days; n (%)	1,167 (5.6%)	1,121 (5.4%)	1,765 (6.1%)	1,706 (5.9%)	3,034 (7.4%)	3,095 (7.5%)	5,966 (6.6%)	5,922 (6.5%)	0.00
Endocrinologist Visit; n (%)	2,056 (9.9%)	1,969 (9.5%)	2,764 (9.5%)	2,681 (9.2%)	4,912 (11.9%)	4,908 (11.9%)	9,732 (10.7%)	9,558 (10.5%)	0.01
Endocrinologist Visit (30 days prior); n (%)	1,317 (6.3%)	1,266 (6.1%)	1,957 (6.7%)	1,885 (6.5%)	3,127 (7.6%)	3,017 (7.3%)	6,401 (7.0%)	6,168 (6.8%)	0.01
Endocrinologist Visit (31 to 180 days prior); n (%)	1,458 (7.0%)	1,377 (6.6%)	1,868 (6.4%)	1,813 (6.2%)	3,777 (9.2%)	3,709 (9.0%)	7,103 (7.8%)	6,899 (7.6%)	0.01
Internal medicine/family medicine visits; n (%)	16,288 (78.4%)	16,010 (77.1%)	25,399 (87.1%)	25,335 (86.9%)	35,174 (85.5%)	34,931 (84.9%)	76,861 (84.4%)	76,276 (83.8%)	0.02
Internal medicine/family medicine visits (30 days prior) ; n (%)	11,885 (57.2%)	11,951 (57.5%)	19,584 (67.2%)	19,656 (67.4%)	25,464 (61.9%)	25,427 (61.8%)	56,933 (62.5%)	57,034 (62.6%)	0.00
Internal medicine/family medicine visits (31 to 180 days prior) ; n (%)	13,833 (66.6%)	13,782 (66.3%)	21,677 (74.4%)	21,565 (74.0%)	31,293 (76.1%)	31,269 (76.0%)	66,803 (73.4%)	66,616 (73.2%)	0.00
Cardiologist visit; n (%)	5,579 (26.9%)	5,471 (26.3%)	6,873 (23.6%)	6,760 (23.2%)	14,871 (36.1%)	14,709 (35.8%)	27,323 (30.0%)	26,940 (29.6%)	0.01
Number of Cardiologist visits (30 days prior); n (%)	1,938 (9.3%)	1,952 (9.4%)	2,477 (8.5%)	2,433 (8.3%)	5,195 (12.6%)	5,200 (12.6%)	9,610 (10.6%)	9,585 (10.5%)	0.00
Number of Cardiologist visits (31 to 180 days prior); n (%)	4,732 (22.8%)	4,630 (22.3%)	5,725 (19.6%)	5,657 (19.4%)	12,978 (31.5%)	12,880 (31.3%)	23,435 (25.7%)	23,167 (25.4%)	0.01
Electrocardiogram ; n (%)	6,245 (30.1%)	6,406 (30.8%)	8,940 (30.7%)	9,246 (31.7%)	14,823 (36.0%)	15,158 (36.8%)	30,008 (33.0%)	30,810 (33.8%)	-0.02

Table 1: Saxagliptin vs 2nd Generation Sulfonylureas

Use of glucose test strips; n (%)	876 (4.2%)	852 (4.1%)	1,297 (4.4%)	1,275 (4.4%)	1,535 (3.7%)	1,529 (3.7%)	3,708 (4.1%)	3,656 (4.0%)	0.01
Dialysis; n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	000 (0.0%)	000 (0.0%)	#DIV/0!
Naive new user ; n (%)	6,124 (29.5%)	6,035 (29.1%)	7,314 (25.1%)	7,406 (25.4%)	9,743 (23.7%)	9,800 (23.8%)	23,181 (25.5%)	23,241 (25.5%)	0.00
N antidiabetic drugs at index date									
...mean (sd)	1.83 (0.69)	1.84 (0.66)	1.87 (0.70)	1.87 (0.67)	1.81 (0.69)	1.81 (0.66)	1.83 (0.69)	1.84 (0.66)	-0.01
...median [IQR]	2.00 [1.00, 2.00]	2.00 [1.00, 2.00]	2.00 [1.00, 2.00]	2.00 [1.00, 2.00]	2.00 [1.00, 2.00]	2.00 [1.00, 2.00]	2.00 (0.69)	2.00 (0.66)	0.00
number of different/distinct medication prescriptions									
...mean (sd)	9.09 (4.65)	9.01 (4.67)	9.07 (4.49)	9.01 (4.54)	10.17 (4.92)	10.14 (5.03)	9.57 (4.72)	9.52 (4.80)	0.01
...median [IQR]	8.00 [6.00, 12.00]	8.00 [6.00, 12.00]	8.00 [6.00, 11.00]	8.00 [6.00, 11.00]	9.00 [7.00, 13.00]	9.00 [7.00, 13.00]	8.45 (4.72)	8.45 (4.80)	0.00
Number of Hospitalizations									
...mean (sd)	0.08 (0.33)	0.08 (0.33)	0.09 (0.33)	0.08 (0.32)	0.12 (0.43)	0.12 (0.42)	0.10 (0.38)	0.10 (0.37)	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]	0.00 [0.00, 0.00]	0.00 (0.38)	0.00 (0.37)	0.00
Number of hospital days									
...mean (sd)	0.44 (2.40)	0.44 (2.26)	0.45 (2.24)	0.43 (2.33)	0.74 (3.54)	0.72 (3.58)	0.58 (2.93)	0.56 (2.95)	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]	0.00 [0.00, 0.00]	0.00 (2.93)	0.00 (2.95)	0.00
Number of Emergency Department (ED) visits									
...mean (sd)	0.30 (0.92)	0.28 (0.89)	0.12 (1.08)	0.11 (1.03)	0.49 (1.25)	0.48 (1.27)	0.33 (1.13)	0.32 (1.12)	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]	0.00 [0.00, 0.00]	0.00 (1.13)	0.00 (1.12)	0.00
Number of Office visits									
...mean (sd)	5.00 (4.34)	4.92 (3.86)	5.09 (4.75)	5.03 (3.99)	6.36 (5.21)	6.30 (4.81)	5.64 (4.88)	5.58 (4.35)	0.01
...median [IQR]	4.00 [2.00, 7.00]	4.00 [2.00, 6.00]	4.00 [2.00, 7.00]	4.00 [2.00, 6.25]	5.00 [3.00, 8.00]	5.00 [3.00, 8.00]	4.45 (4.88)	4.45 (4.35)	0.00
Number of Endocrinologist visits									
...mean (sd)	0.52 (2.53)	0.49 (2.46)	0.47 (2.21)	0.52 (2.67)	0.76 (3.62)	0.81 (3.84)	0.61 (2.99)	0.64 (3.21)	-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]	0.00 [0.00, 0.00]	0.00 (2.99)	0.00 (3.21)	0.00
Number of internal medicine/family medicine visits									
...mean (sd)	8.48 (13.64)	7.91 (12.09)	7.23 (9.90)	7.35 (9.32)	8.91 (11.47)	9.17 (11.81)	8.27 (11.54)	8.30 (11.14)	0.00
...median [IQR]	5.00 [1.00, 11.00]	5.00 [1.00, 11.00]	5.00 [2.00, 9.00]	5.00 [2.00, 10.00]	5.00 [2.00, 12.00]	6.00 [2.00, 12.00]	5.00 (11.54)	5.45 (11.14)	-0.04
Number of Cardiologist visits									
...mean (sd)	1.35 (3.78)	1.35 (3.98)	1.07 (3.16)	1.07 (3.34)	2.05 (5.09)	2.03 (4.87)	1.58 (4.26)	1.57 (4.23)	0.00
...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, 2.00]	0.00 [0.00, 2.00]	0.00 (4.26)	0.00 (4.23)	0.00
Number electrocardiograms received									
...mean (sd)	0.54 (1.19)	0.53 (1.15)	0.53 (1.12)	0.53 (1.08)	0.72 (1.37)	0.73 (1.35)	0.62 (1.25)	0.62 (1.22)	0.00
...median [IQR]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00 (1.25)	0.00 (1.22)	0.00
Number of HbA1c tests ordered									
...mean (sd)	1.26 (0.93)	1.25 (0.87)	1.04 (0.93)	1.03 (0.90)	1.43 (0.97)	1.42 (0.90)	1.27 (0.95)	1.26 (0.89)	0.01
...median [IQR]	1.00 [1.00, 2.00]	1.00 [1.00, 2.00]	1.00 [0.00, 2.00]	1.00 [0.00, 2.00]	1.00 [1.00, 2.00]	1.00 [1.00, 2.00]	1.00 (0.95)	1.00 (0.89)	0.00
Number of glucose tests ordered									
...mean (sd)	0.49 (2.88)	0.48 (1.61)	0.42 (1.29)	0.41 (1.05)	0.51 (1.40)	0.51 (1.25)	0.48 (1.82)	0.47 (1.28)	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, 1.00]	0.00 [0.00, 1.00]	0.00 (1.82)	0.00 (1.28)	0.00
Number of lipid tests ordered									
...mean (sd)	1.09 (1.05)	1.09 (1.00)	0.98 (1.50)	0.97 (1.33)	1.13 (0.92)	1.14 (0.90)	1.07 (1.16)	1.07 (1.08)	0.00
...median [IQR]	1.00 [0.00, 2.00]	1.00 [0.00, 2.00]	1.00 [0.00, 1.00]	1.00 [0.00, 1.00]	1.00 [1.00, 2.00]	1.00 [1.00, 2.00]	1.00 (1.16)	1.00 (1.08)	0.00
Number of creatinine tests ordered									
...mean (sd)	0.06 (0.37)	0.06 (0.33)	0.06 (0.39)	0.06 (0.33)	0.10 (0.43)	0.10 (0.41)	0.08 (0.40)	0.08 (0.37)	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]	0.00 [0.00, 0.00]	0.00 (0.40)	0.00 (0.37)	0.00
Number of BUN tests ordered									
...mean (sd)	0.03 (0.29)	0.04 (0.27)	0.03 (0.29)	0.04 (0.28)	0.06 (0.34)	0.06 (0.33)	0.04 (0.31)	0.05 (0.30)	-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]	0.00 [0.00, 0.00]	0.00 (0.31)	0.00 (0.30)	0.00
Number of tests for microalbuminuria									
...mean (sd)	0.71 (1.13)	0.72 (1.12)	0.53 (0.97)	0.53 (0.98)	0.48 (0.77)	0.48 (0.75)	0.55 (0.93)	0.55 (0.92)	0.00
...median [IQR]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00 (0.93)	0.00 (0.92)	0.00
Total N distinct ICD9/ICD10 diagnoses at the 3rd digit level									
...mean (sd)	3.44 (5.93)	3.43 (5.80)	1.11 (3.31)	1.08 (3.22)	4.03 (6.95)	4.01 (6.97)	2.96 (5.78)	2.94 (5.74)	0.00
...median [IQR]	0.00 [0.00, 5.00]	0.00 [0.00, 5.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 6.00]	0.00 [0.00, 6.00]	0.00 (5.78)	0.00 (5.74)	0.00
Use of thiazide; n (%)	2,083 (10.0%)	2,098 (10.1%)	2,947 (10.1%)	2,950 (10.1%)	5,096 (12.4%)	4,979 (12.1%)	10,126 (11.1%)	10,027 (11.0%)	0.00
Use of beta blockers; n (%)	7,279 (35.0%)	7,224 (34.8%)	10,647 (36.5%)	10,502 (36.0%)	19,033 (46.3%)	18,957 (46.1%)	36,959 (40.6%)	36,683 (40.3%)	0.01
Use of calcium channel blockers; n (%)	5,503 (26.5%)	5,572 (26.8%)	8,041 (27.6%)	7,927 (27.2%)	13,451 (32.7%)	13,548 (32.9%)	26,995 (29.6%)	27,047 (29.7%)	0.00