

Replication of the DAPA-CKD (Chronic Kidney Disease) Trial in Healthcare Claims Data

DUPLICATE DAPA-CKD

September 14, 2021

NCT04882813

1. RCT Details

This section provides a high-level overview of an 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

Dapagliflozin in Patients with Chronic Kidney Disease ([DAPA-CKD trial](#))

1.2 Intended aim(s)

The objective of the study is to assess the long-term efficacy and safety of dapagliflozin, a sodium-glucose cotransporter 2 (SGLT2) inhibitor in patients with chronic kidney disease, with or without type 2 diabetes

1.3 Primary endpoint for replication and RCT finding

Composite of a sustained decline in the estimated glomerular filtration rate (GFR) of at least 50%, end-stage kidney disease, or death from renal or cardiovascular causes.

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

With the recruitment of at least 4000 patients, the trial will have 90% power to detect a relative risk reduction of 22% in the primary endpoint based on primary events being observed in 681 patients and a two-sided P-value of 0.05.

1.5 Trial estimate

HR = 0.64 (95% CI 0.52–0.79) comparing dapagliflozin to placebo among patients with Type 2 DM and HR = 0.61 (95% CI 0.51-0.75) among patients with and without Type 2 DM (Heerspink et al., 2020, NEJM)

2. Person responsible for implementation of replication in Aetion

Helen Tesfaye, Pharm.D, ScM implemented the study design in the Aetion Evidence Platform. She is not responsible for the validity of design and analytic choices. All implementation steps are recorded, and implementation history is archived in the platform.

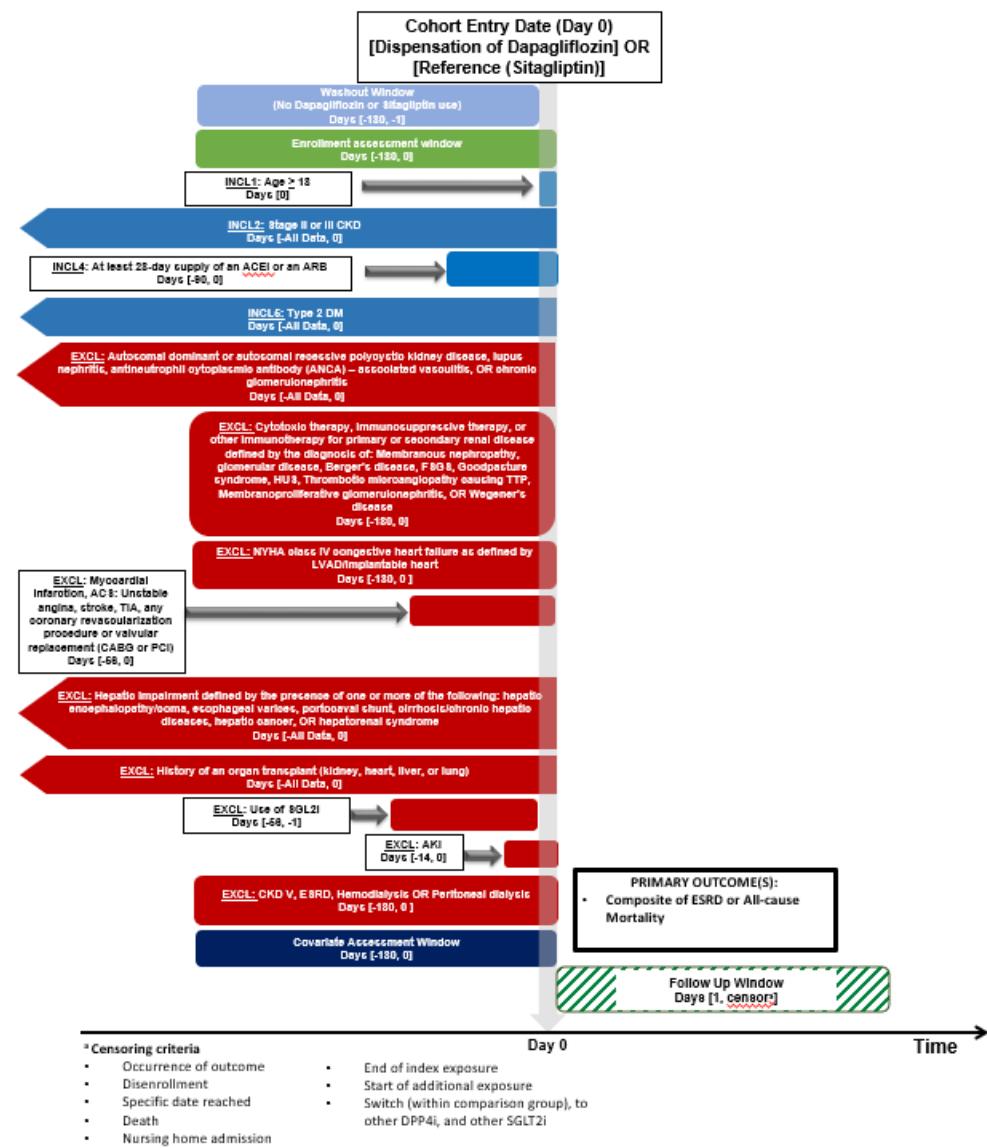
3. Data Source(s)

Optum Clininformatics Data Mart, IBM MarketScan, Medicare

4. Study Design Diagram

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

Design Diagram – DAPA-CKD TRIAL REPLICATION



5. Cohort Identification

5.1 Cohort Summary

This study will involve a new user, parallel group retrospective cohort study design comparing dapagliflozin to sitagliptin.

Although the trial compared dapagliflozin to placebo, for the current emulation we used an active comparator, sitagliptin, which is a dipeptidyl peptidase-4 (DPP-4) inhibitor. This is because both dapagliflozin and sitagliptin are guideline recommended as second to third line therapies used for the treatment of type 2 diabetes at the same stage of the disease and sitagliptin is not expected to have an effect on the primary outcome.

The patients will be required to have continuous enrollment during baseline period of 180 days before initiation of dapagliflozin or sitagliptin (cohort entry).

5.2 Important steps for cohort formation

New users (defined as no use in 180 days prior to index date) of an exposure, dapagliflozin and a comparator, sitagliptin, will be identified.

5.2.1 Eligible cohort entry date

Dapagliflozin was approved by FDA for market availability on January 8, 2014.

- Optum: January 8, 2014 – March 31, 2020 (end of data availability)
- Marketscan: January 8, 2014 – December 31, 2018 (end of data availability)
- Medicare: January 8, 2014 – December 31, 2017 (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		Marketscan		Medicare	
	Less Excluded Patients	Remaining Patients	Less Excluded Patients	Remaining Patients	Less Excluded Patients	Remaining Patients
All patients		78,202,636		200,203,908		23,466,175
Did not meet cohort entry criteria	-77,797,182	405,454	-199,563,302	640,606	-22,268,953	1,197,222
Excluded due to insufficient enrollment	-66,483	338,971	-58,936	581,670	-333,159	864,063
Excluded due to prior use of referent	-245,915	93,056	-397,135	184,535	-679,548	184,515
Excluded due to prior use of exposure	-21,695	71,361	-95,936	88,599	-27,223	157,292
Excluded because patient qualified in >1 exposure category	-36	71,325	-346	88,253	-108	157,184
Excluded based on Age	0	71,325	0	88,253	-28	157,156
Excluded based on Gender	-7	71,318	0	88,253	0	157,156
Excluded based on Inclusion #1 - Age ≥ 18 years or older	-7	71,311	-54	88,199	-692	156,464
Excluded based on Inclusion #2 - eGFR ≥30 and ≤75 mL/min/1.73 m ² (CKD-EPI formula)_ONLY STAGE II & III	-41,866	29,445	-73,659	14,540	-82,143	74,321
Excluded based on Inclusion #4 - Treatment with ACEi or ARB for at least 4 weeks, if not medically contraindicated	-4,797	24,648	-2,385	12,155	-12,272	62,049
Excluded based on Inclusion #5 - Type 2 DM	-32	24,616	-29	12,126	-45	62,004
Excluded based on Exclusion #2 - Autosomal dominant or autosomal recessive polycystic kidney disease, lupus nephritis or Antineutrophil cytoplasmic antibody (ANCA)	-1,060	23,556	-650	11,476	-3,273	58,731
Excluded based on Exclusion #3 - Receiving cytotoxic therapy, immunosuppressive therapy or other immunotherapy	-65	23,491	-15	11,461	-97	58,634
Excluded based on Exclusion #4 - NYHA class IV CHF - measured as LVAD/Implantable heart	-1	23,490	-1	11,460	-14	58,620
Excluded based on Exclusion #5 - MI, Unstable angina, Stroke, Transient Ischemic Attack	-248	23,242	-151	11,309	-1,427	57,193
Excluded based on Exclusion #6-Coronary revascularization (PCI or CABG) or valvular repair/replacement	-18	23,224	-7	11,302	-58	57,135
Excluded based on Exclusion #8 - Presence of hepatic impairment	-195	23,029	-65	11,237	-472	56,663

Excluded based on Exclusion #9 - History of Organ Transplant	-33	22,996	-14	11,223	-98	56,565
Excluded based on Exclusion #10 - Receiving therapy with SGLT2 inhibitor	-170	22,826	-83	11,140	-219	56,346
Excluded based on Exclusion #11a - Acute kidney injury (AKI)	-327	22,499	-82	11,058	-798	55,548
Excluded based on Exclusion #11b - Baseline CKD IV & V, ESRD, HD/PD	-360	22,139	-118	10,940	-949	54,599
Final cohort		22,139		10,940		54,599

6 Variables

6.1 Exposure-related variables:

Study drug:

The study exposure of interest is initiation of dapagliflozin (SGLT2i at any dose and frequency. Initiation will be defined by no use of dapagliflozin during the prior 180 days before treatment initiation (washout period). Patients are required to be incident users with respect both exposure groups.

Comparator agents:

Initiators of sitagliptin, any dose and frequency.

6.2 Preliminary Covariates:

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

Covariates listed above are a small subset of covariates that will ultimately be controlled in the design and analysis phase of the study. They are included in the preliminary assessment to determine the presence of adequate overlap between the two population of patients to proceed to the next phase of the study. Remaining covariates are defined only after the study has passed the initial feasibility analysis and initial power assessment and are listed in Table 1 (**Appendix B**).

6.3 Outcome variables and study follow-up:

6.3.1 Outcome variables

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

- **Primary outcome:** Composite of end stage renal disease (ESRD) or all-cause mortality
- Secondary outcomes:
 - ESRD
 - All-cause death

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

Control outcome definitions

- Genital infections

6.3.2 Study follow-up

Both as-treated (AT) and intention-to-treat (ITT) analysis 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 analysis, the follow-up will start the day after the initiation of dapagliflozin or sitagliptin and will continue until the earliest date of the following events:

- The first occurrence of the outcome of interest,
- The date of end of continue registration in the database,
- End of the study period,
- Death (for ESRD outcome only),
- 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 (dapagliflozin or sitagliptin) + a 30-day grace period,
- The date of switching from an exposure to comparator and vice versa,
- The date of switching to or initiation of other SGLT2i (excluding dapagliflozin) and other DPP4i (excluding sitagliptin).

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

7 Initial Feasibility Analysis

Action report name:

Optum- <https://bwh-dope.aetion.com/projects/details/1379/results/66309/result/0>

Marketscan- <https://bwh-dope.aetion.com/projects/details/1400/results/66311/result/0>

Medicare - <https://bwh-dope.aetion.com/projects/details/1377/results/66055/result/0>

Date conducted: 2/25/2021

8 Initial Power Assessment

Action report name:

Optum- <https://bwh-dope.aetion.com/projects/details/1379/results/66310/result/0>

Marketscan- <https://bwh-dope.aetion.com/projects/details/1400/results/66312/result/0>

Medicare- <https://bwh-dope.aetion.com/projects/details/1377/results/66056/result/0>

Date conducted: 2/25/2021

- Stop analyses until feasibility and power are reviewed by primary investigators, FDA, and assigned members of advisory board.

Reviewed by PI:	Shirley Wang	Date reviewed:	2/26/2021
Reviewed by FDA:	Kenneth Quinto	Date reviewed:	3/16/2021
Reasons for stopping analysis (if required):			

9. Balance Assessment

Optum- <https://bwh-dope.aetion.com/projects/details/1379/rwrs/68008>

Marketscan- <https://bwh-dope.aetion.com/projects/details/1400/rwrs/68510>

Medicare- <https://bwh-dope.aetion.com/projects/details/1377/rwrs/68010>

Date conducted: 4/02/2021, 4/16/2021 (Enrollment corrected for Marketscan)

After review of initial feasibility and power analyses, complete creation of the remaining covariates from Section 6.2. 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.

- 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%)	0 (0%)	0 (0%)
Death	64 (0.62%)	44 (0.86%)	20 (0.39%)
Start of an additional exposure	638 (6.20%)	41 (0.80%)	597 (11.60%)
End of Index Exposure	4,738 (46.04%)	2,567 (49.89%)	2,171 (42.20%)
Specified date reached	2,374 (23.07%)	1,323 (25.71%)	1,051 (20.43%)
End of patient enrollment	913 (8.87%)	479 (9.31%)	434 (8.44%)
Switch to other SGLT-2i + Switch to other DPP-4i + Nursing Home admission occurred	1,563 (15.19%)	691 (13.43%)	872 (16.95%)

- Report follow-up time by treatment group.

Patient Group	Optum Median Follow-Up Time (Days) [IQR]	MarketScan Median Follow-Up Time (Days) [IQR]	Medicare Median Follow-Up Time (Days) [IQR]
Overall Patient Population	113 [58, 221]	118 [58, 267]	118 [58, 220]
Referent - Sitagliptin	118 [58, 254]	127 [69, 285]	118 [58, 257]
Exposure - Dapagliflozin	79 [52, 183]	118 [58, 240]	88 [55, 181]

- Report overall risk of the primary outcome.

	Optum	MarketScan	Medicare	Pooled
Risk per 1,000 patients	15.6	3.3	25.5	20.2

10. Final Power Assessment

Date conducted: 4/02/2021, 4/16/2021 (MarketScan only)

- 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.

Superiority Analysis (Pooled)	
Number of patients matched	
Reference	5145.0
Exposed	5145.0
Risk per 1,000 patients	20.22
Desired HR from RCT	0.64
Alpha (2-sided)	0.05
Number of events expected	208.0638
Power	0.90

Superiority Analysis (Optum)	
Number of patients matched	
Reference	828
Exposed	828
Risk per 1,000 patients	15.60
Desired HR from RCT	0.64
Alpha (2-sided)	0.05
Number of events expected	25.8336
Power	0.205446437

Superiority Analysis (MarketScan)	
Number of patients matched	
Reference	1,687
Exposed	1,687
Risk per 1,000 patients	3.30
Desired HR from RCT	0.64
Alpha (2-sided)	0.05
Number of events expected	11.1342
Power	0.115530515

Superiority Analysis (Medicare)	
Number of patients matched	
Reference	2,630
Exposed	2,630
Risk per 1,000 patients	25.50
Desired HR from RCT	0.64
Alpha (2-sided)	0.05
Number of events expected	134.13
Power	0.733807835

- Stop analyses until balance and final power assessment are reviewed by primary investigators, FDA, and assigned members of advisory board.

Reviewed by PI:		Date reviewed:	
Reviewed by FDA:		Date reviewed:	
Reasons for stopping analysis (if required):			

Appendix A: Composite of ESRD or all-cause mortality

Measured **1 day after drug initiation** in diagnosis position specified below and inpatient and outpatient care setting -

Composite of ESRD or All-Cause Mortality

ESRD

ICD-9 diagnosis: 585.5, 585.6

ICD-10 diagnosis: N18.5, N18.6

AND

Dialysis

ICD-9 diagnosis: V45.1x, V56.0x, V56.1, V56.8x

ICD-10 diagnosis: Z49.01, Z49.31, Z49.32, Z99.2

ICD-9 procedure: 39.95, 54.98

ICD-10 procedure: 3E1M39z, 5A1D00z, 5A1D60Z

CPT: S9339, 90945, 90947, 90999

OR

CV death

Inpatient mortality - renal or CV causes --

Mortality- Dependent on data source.

1. CV mortality

Information on CV mortality through data linkage with the National Death Index (NDI) will be available for Medicare and Optum Clininformatics.

2. All-cause inpatient mortality

Identified using the discharge status codes-

Optum-

- 20 = EXPIRED
- 21 = EXPIRED TO BE DEFINED AT STATE LEVEL
- 22 = EXPIRED TO BE DEFINED AT STATE LEVEL
- 23 = EXPIRED TO BE DEFINED AT STATE LEVEL
- 24 = EXPIRED TO BE DEFINED AT STATE LEVEL
- 25 = EXPIRED TO BE DEFINED AT STATE LEVEL
- 26 = EXPIRED TO BE DEFINED AT STATE LEVEL

- 27 = EXPIRED TO BE DEFINED AT STATE LEVEL
- 28 = EXPIRED TO BE DEFINED AT STATE LEVEL
- 29 = EXPIRED TO BE DEFINED AT STATE LEVEL
- 40 = EXPIRED AT HOME (HOSPICE)
- 41 = EXPIRED IN A MEDICAL FACILITY (HOSPICE)
- 42 = EXPIRED - PLACE UNKNOWN (HOSPICE)

Truven-

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

Appendix A

#	DAPA-CKD trial definitions	Implementation in routine care	References/Rationale	Color coding
	<p>Trial details - Intended S with label change - 2 weeks run-in</p>		<p>Please see the following Google Drive for further details or any missing information: https://drive.google.com/open?id=1WD618wrywYIeaXrl1suK-VCcnb6b-eV</p>	Criteria
	<p>EXPOSURE vs. COMPARISON</p>		<p>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.ncbi.nlm.nih.gov/pmc/articles/PMC5300000/</p>	Adequate mapping in claims
	<p>Dapagliflozin 10 mg or 5 mg tablets once daily vs. placebo matching dapagliflozin 10 mg or 5 mg</p> <p>Aim: To evaluate the effect of dapagliflozin on renal outcomes and CV mortality in patients with CKD</p>	<p>Dapagliflozin 10 mg or 5 mg vs. Sitagliptin (any dose)</p> <p>Exposure: new-use dapagliflozin Reference: Sitagliptin</p>		Intermediate mapping in claims
	<p>PRIMARY OUTCOME</p>			Poor mapping or cannot be measured in claims
	<p>Primary endpoint: A composite of sustained decline in eGFR of $\geq 50\%$, ESRD, renal death or CV death</p> <p>1) time to $\geq 50\%$ eGFR decline from baseline (confirmed by ≥ 28-day SCR)</p> <p>2) time to ESRD defined as eGFR $< 15 \text{ ml/min/1.73 m}^2$, need for chronic dialysis (both confirmed after ≥ 28 days) and renal transplantation</p> <p>3) time to renal or CV death</p>	<p>Measured 1 day after drug initiation in any diagnosis position in inpatient and outpatient care setting:</p> <p><u>Composite of ESRD or All-Cause Mortality</u></p> <p><u>ESRD</u> ICD-9 diagnosis: 585.5, 585.6 ICD-10 diagnosis: N18.5, N18.6</p> <p><u>AND</u></p> <p><u>Dialysis</u> ICD-9 diagnosis: V45.1x, V56.0x, V56.1, V56.8x ICD-10 diagnosis: Z49.01, Z49.31, Z49.32, Z99.2 ICD-9 procedure: 39.95, 54.98 ICD-10 procedure: 3E1M39z, 5A1D00z, 5A1D60Z CPT: S9339, 90945, 90947, 90999</p> <p><u>OR</u></p> <p><u>CV death</u> Inpatient mortality - renal or CV causes --</p> <p><u>Mortality</u> - Dependent on data source.</p>		Can't be measured in claims but not important for the analysis
	<p>Dapagliflozin 10 mg or 5 mg tablets once daily vs. placebo matching dapagliflozin 10 mg or 5 mg</p> <p>Aim: To evaluate the effect of dapagliflozin on renal outcomes and CV mortality in patients with CKD</p>			
1	18 years of age	<p>Measured on the day of drug initiation</p> <p>Age ≥ 18</p>		

Appendix A

		Measured any time prior to and including the day of drug initiation in any diagnosis position and inpatient and outpatient care setting: <u>CKD Stage II</u> (eGFR 60 - 89 mL/min/1.73 m ²) ICD-9 diagnosis: 585.2 ICD-10 diagnosis: N18.2 <u>CKD Stage IIIa&b</u> (eGFR 30 - 59 mL/min/1.73 m ²) ICD-9 diagnosis: 585.3 ICD-10 diagnosis: N18.3 <u>CKD Stage IV</u> (eGFR 15 - 29 mL/min/1.73 m ²) ICD-9 diagnosis: 585.4 ICD-10 diagnosis: N18.4	
2	eGFR \geq 25 and \leq 75 mL/min/1.73 m ² (CKD-EPI formula) at visit 1		
3	Evidence of increased albuminuria for 3 months or more before visit 1 and UACR \geq 200 and \leq 5000 mg/g at visit 1	Measured from the start of all available data until 90 days prior to the date of drug initiation in any diagnosis position and inpatient and outpatient care setting: <u>Proteinuria</u> ICD-9 diagnosis: 791.0 ICD-10 diagnosis: R80.x	
4	Stable, and for the patient maximum tolerated labelled daily dose, treatment with ACEi or ARB for at least 4 weeks before visit 1, if not medically contraindicated	Measured 45 days prior to index drug initiation in prescription claims requiring 28 days supply of ACEi or ARB: <u>ACE inhibitors' generic names for prescription claims:</u> Enalapril, Captopril, Clazapril, Fosinopril, Lisinopril, Moexipril, Perindopril, Quinapril, Ramipril, Trandolapril, Zofenopril, Benazepril OR <u>ARBs generic names for prescription claims:</u> Candesartan, Eprosartan, Irbesartan, Losartan, Olmesartan, Telmisartan, Valsartan, Azilsartan	
EXCLUSION CRITERIA			
1	Type I diabetes mellitus	Measured from the start of all available data to and including the day of drug initiation in any diagnosis position and inpatient and outpatient care setting: <u>Type I DM</u> ICD-9 diagnosis: 250.01, 250.03, 250.11, 250.13, 250.21, 250.23, 250.31, 250.33, 250.41, 250.43, 250.51, 250.53, 250.61, 250.63, 250.71, 250.73, 250.91, 250.93 ICD-10 diagnosis: E10.x	
2	Autosomal dominant or autosomal recessive polycystic kidney disease, lupus nephritis or Antineutrophil cytoplasmic antibody (ANCA) -associated vasculitis	Measured from the start of all available data to and including the day of drug initiation in any diagnosis position and inpatient and outpatient care setting: <u>Autosomal dominant or recessive PKD</u> ICD-9 diagnosis: 753.12, 753.13, 753.14 ICD-10 diagnosis: Q61.3, Q61.2, Q61.19 <u>Lupus nephritis</u> ICD-9 diagnosis: 710.0, 583.x ICD-10 diagnosis: N05.2, N05.5, N05.9 <u>ANCA-associated vasculitis</u> ICD-9 diagnosis: 446.0, 446.4, 447.6, 446.7 ICD-10 diagnosis: M30.3, M31.30, M31.4, I77.6	Sreih AG, Annareddy N, Springer J, et al. Development and validation of case-finding algorithms for the identification of patients with anti-neutrophil cytoplasmic antibody-associated vasculitis in large healthcare administrative databases. <i>Pharmacoepidemiol Drug Saf.</i> 2016;25(12):1368–1374. doi:10.1002/pds.4116 Chibnik LB, Massarotti EM, Costenbader KH. Identification and validation of lupus nephritis cases using administrative data. <i>Lupus</i> . 2010;19(6):741–743. doi:10.1177/0961203309356289

Appendix A

3	Receiving cytotoxic therapy, immunosuppressive therapy or other immunotherapy for primary or secondary renal disease within 6 months prior to enrollment	<p>Measured 180 days prior to and including the day of drug initiation in prescription claims:</p> <p><u>Membranous nephropathy</u> ICD-9 diagnosis: 583.1, 583.2 ICD-10 diagnosis: N05.2, N05.5</p> <p><u>Glomerular disease (except chronic glomerulonephritis)</u> ICD-9 diagnosis: 580.x ICD-10 diagnosis: N00.x, N01.x, N02.x, N03.x, N04.x, N05.x, N06.x, N07.x, N08.x</p> <p><u>Immunoglobulin A nephropathy (Berger's disease)</u> ICD-9 diagnosis: 583.9 ICD-10 diagnosis: N02.8</p> <p><u>Focal segmental glomerulosclerosis (FSGS)</u> ICD-9 diagnosis: 581.1 ICD-10 diagnosis: N02.2</p> <p><u>Goodpasture syndrome</u> ICD-9 diagnosis: 446.2x ICD-10 diagnosis: M31.0</p> <p><u>Hemolytic uremic syndrome (HUS)</u> ICD-9 diagnosis: 283.11 ICD-10 diagnosis: D59.3</p>	
4	NYHA class IV congestive heart failure at the time of enrollment	<p>Measured 180 days prior to and including the day of drug initiation in any diagnosis position and inpatient and outpatient care setting:</p> <p><u>LVAD/Implantable Heart</u> ICD-9 diagnosis: V43.2x ICD-10 diagnosis: Z95.811, Z95.812 ICD-9 procedure: 37.60, 37.66 ICD-10 procedure: 02HA0RS, 02HA3RS, 02HA4RS, 5A02116, 5A02216, 02HA0QZ, 02HA3QZ, 02HA4QZ CPT-4 code: 33975, 33976, 33979, 33981 - 33983, 33977, 33978, 33980</p>	
5	MI, unstable angina, stroke, transient ischemic attack within 8 weeks prior to enrollment	<p>Measured 56 days prior to including the day of drug initiation in any diagnosis position and inpatient and ED care setting:</p> <p><u>Myocardial Infarction/STEMI</u> ICD-9 diagnosis: 410.xx (exclude 410.x2), 411.0 ICD-10 diagnosis: I21.xx, I22.xx, I23.xx</p> <p><u>ACS: Unstable Angina</u> ICD-9 diagnosis: 413.xx (exclude 413.1), 411.1, 411.8, 411.81, 411.89 ICD-10 diagnosis: I20.xx (exclude I20.1), I24.xx (exclude I24.1)</p> <p><u>Stroke</u> ICD-9 diagnosis: 430.xx, 431.xx, 433.x1, 434.xx (excluding 434.x0), 436.x, 997.02 ICD-10 diagnosis: G97.3x, I60.xx, I61.xx, I62.xx, I63.xx, I97.81x, I97.82x</p> <p><u>TIA</u> ICD-9 diagnosis: 435.xx ICD-10 diagnosis: G45.xx</p>	

Appendix A

<p>6 Coronary revascularization (percutaneous coronary intervention or coronary artery bypass grafting) or valvular repair/replacement within 8 weeks prior to enrolment</p>	<p>Measured 56 days prior to including the day of drug initiation in any diagnosis position and inpatient care setting:</p> <p><u>CABG / Transmyocardial Revascularization</u> ICD-9 procedure: 36.1x, 36.2, 36.3x ICD-10 procedure: Refer to "CABG & Revascularization" tab within this spreadsheet for complete list of procedure codes CPT-4 code: 33140, 33141, 33510 – 33548, 33572, 92937, 92938</p> <p><u>PCI (PTCA)</u> ICD-9 procedure: 36.0x, 00.66 ICD-10 procedure: 02700Z, 02710Z, 02720Z, 02730Z, 02C00Z, 02C10Z, 02C20Z, 02C30Z, 3E07017, 3E070P2, 3E07317, 3E073P2, 02C03Z, 02C04Z, 02C13Z, 02C14Z, 02C23Z, 02C24Z, 02C33Z, 02C34Z CPT-4 code: 92920, 92921, 92924, 92925, 92928, 92929, 92933, 92934, 92980, 92981, 92982, 92984</p> <p><u>Valvular repair/replacement</u> ICD-9 procedure: 35.01, 35.02, 35.05, 35.06, 35.11, 35.12, 35.21, 35.22, 35.23, 35.24, 35.97 ICD-10 procedure: 02NF3Z, 02NF4Z, 02NG3Z, 02NG4Z, 02RF3Z, 02RF38Z, 02RF3JZ, 02RF3KZ, 02RF33Z, 02RF37H, 02RF38H, 02RF3JH, 02RF3KH, 027F04Z, 027FDZ, 027FOZ, 027FOZ, 02QFOZ, 02QFOZ, 027G04Z, 027G0DZ, 027G0Z, 02NG0Z, 02QG0Z, 02VG0Z, 02RF07Z, 02RF08Z, 02RF0KZ, 02RF47Z, 02RF48Z, 02RF4KZ, 02RF03Z, 02RF43Z, 02RF01Z, 02RF4JZ, 02RG07Z, 02RG08Z, 02RG0KZ, 02RG37Z, 02RG38Z, 02RG3KZ, 02RG47Z, 02RG48Z, 02RG4KZ, 02RG01Z, 02RG31Z, 02RG41Z 02UG31Z</p> <p><u>CPT-4 codes: 22400, 22402, 2240E, 2240F, 22420, 22421, 02E71, 02E9T, 02E0T</u></p>	
<p>7 Any condition outside the renal and cardiovascular study area with a life expectancy of <2 years based on investigator's clinical judgement</p>	<p>Measured from the start of all available data of drug initiation in any diagnosis position and inpatient and outpatient care setting:</p>	
<p>8 Hepatic impairment [aspartate transaminase or alanine transaminase >3 times the upper limit of normal (ULN) or total bilirubin >2 times the ULN at the time of enrolment]</p>	<p><u>Hepatic Encephalopathy/Coma</u> ICD-9 diagnosis: 070.0, 070.2x, 070.4x, 070.6, 070.71, 572.2 ICD-10 diagnosis: B15.0, B16.0, B16.2, B17.11, B19.0, B19.11, B19.21, K72.90, K72.91</p> <p><u>Esophageal Varices</u> ICD-9 diagnosis: 456.0, 456.1, 456.2x, 572.3 ICD-10 diagnosis: I85.xx, K76.6</p> <p><u>Porto-Caval Shunt</u> ICD-9 procedure: 39.1, 42.91 ICD-10 procedure: Refer to the 'PCShunt' sheet for list of procedures CPT-4 code: 37182, 37183, 37241</p> <p><u>Cirrhosis/Chronic Hepatic Diseases</u> ICD-9 diagnosis: 571.0, 571.2, 571.3, 571.4, 571.5, 571.6</p>	
<p>9 History of organ transplantation</p>	<p>Measured from the start of all available data to and including the day of drug initiation in any diagnosis position and inpatient and outpatient care setting:</p> <p><u>Kidney Transplant</u> ICD-9 diagnosis: V42.0, 996.81 ICD-10 diagnosis: Z94.0, T86.10, T86.11, T86.12 ICD-9 procedure: 00.91, 00.92, 00.93, 55.53, 55.6, 55.61, 55.69 ICD-10 procedure: OTT00Z, OTT04Z, OTT10Z, OTT14Z, OTS00Z, OTS10Z, OTY00Z, OTY00Z1, OTY00Z2, OTY10Z, OTY10Z1, OTY10Z2 CPT-4 code: 00868, 50360, 50365, 50370, 50380</p> <p><u>Heart transplantation</u> ICD-9 diagnosis: V42.1, V49.83, 996.83 ICD-10 diagnosis: Z94.1, Z76.82, T86.20, T86.21, T86.22 ICD-9 procedure: 33.6, 37.51 ICD-10 procedure: 02YA020, 02YA021, 02YA022 CPT-4 code: 33935, 33945</p>	

Appendix A

10	<p>Receiving therapy with SGLT2 inhibitor within 8 weeks prior to enrollment or previous intolerance of an SGLT2 inhibitor</p>	<p>Measured from 56 days prior to 1 day prior to drug initiation in prescription claims:</p> <p>SGLT2 Inhibitors (including combination products containing any of the following)</p> <ul style="list-style-type: none"> - Canagliflozin (INVOKANA®) - Canagliflozin/metformin (INVOKAMET®, INVOKAMET® XR) - Empagliflozin (JARDIANCE®) - Empagliflozin/metformin (SYNJARDY®, SYNJARDY® XR) - Empagliflozin/ linagliptin/ metformin (TRIJARDY® XR) - Empagliflozin/linagliptin (GLYXAMBII®) - Dapagliflozin (FARXIGA®) - Dapagliflozin/metformin (XIGDUO® XR) - Dapagliflozin/saxagliptin (QTERN®) - Dapagliflozin/saxagliptin/metformin (QTERNMET® XR) - Ertugliflozin (STEGLATRO®) - Ertugliflozin/metformin (SEGLUROMET®) - Ertugliflozin/sitagliptin (STEGLUJAN®) 	
11a	<p>Exclude patients that have AKI during the baseline period</p>	<p>Measured from 14 days prior to and including the day of drug initiation in any diagnosis position and any care setting:</p> <p>Acute kidney injury (AKI)</p> <p>ICD-9 diagnosis: 584.xx, 586 ICD-10 diagnosis: N17.x, N19</p>	
11b	<p>Exclude patients that have CKD-V, ESRD and are on HD/PD during the baseline period</p>	<p>Measured from 180 days prior to and including the day of drug initiation in any diagnosis position and any care setting:</p> <p>Chronic Kidney Disease (CKD)-V</p> <p>ICD-9 diagnosis: 585.5 ICD-10 diagnosis: N18.5</p> <p>ESRD</p> <p>ICD-9 diagnosis: 403.01, 403.11, 403.91, 404.03, 404.13, 585.6 ICD-10 diagnosis: I12.0, N18.6</p> <p>Hemodialysis/Peritoneal Dialysis</p> <p>ICD-9 diagnosis: V45.1x, V56.xx, 996.56, 996.68, 996.73 ICD-10 diagnosis: Z49.xx, Z91.15, Z99.2, T85.611x, T85.621x, T85.631x, T85.691x, T85.71x ICD-9 procedure: 39.95, 54.98 ICD-10 procedure: 5A1D70Z, 5A1D80Z, 5A1D90Z, 3E1M39Z CPT-4 code: 90935, 90937, 90939</p>	

Appendix A

Mortality- Dependent on data source.

1. All-cause mortality / inpatient mortality

Identified using the vital status file-

Medicare

Identified using the discharge status codes-

Optum-

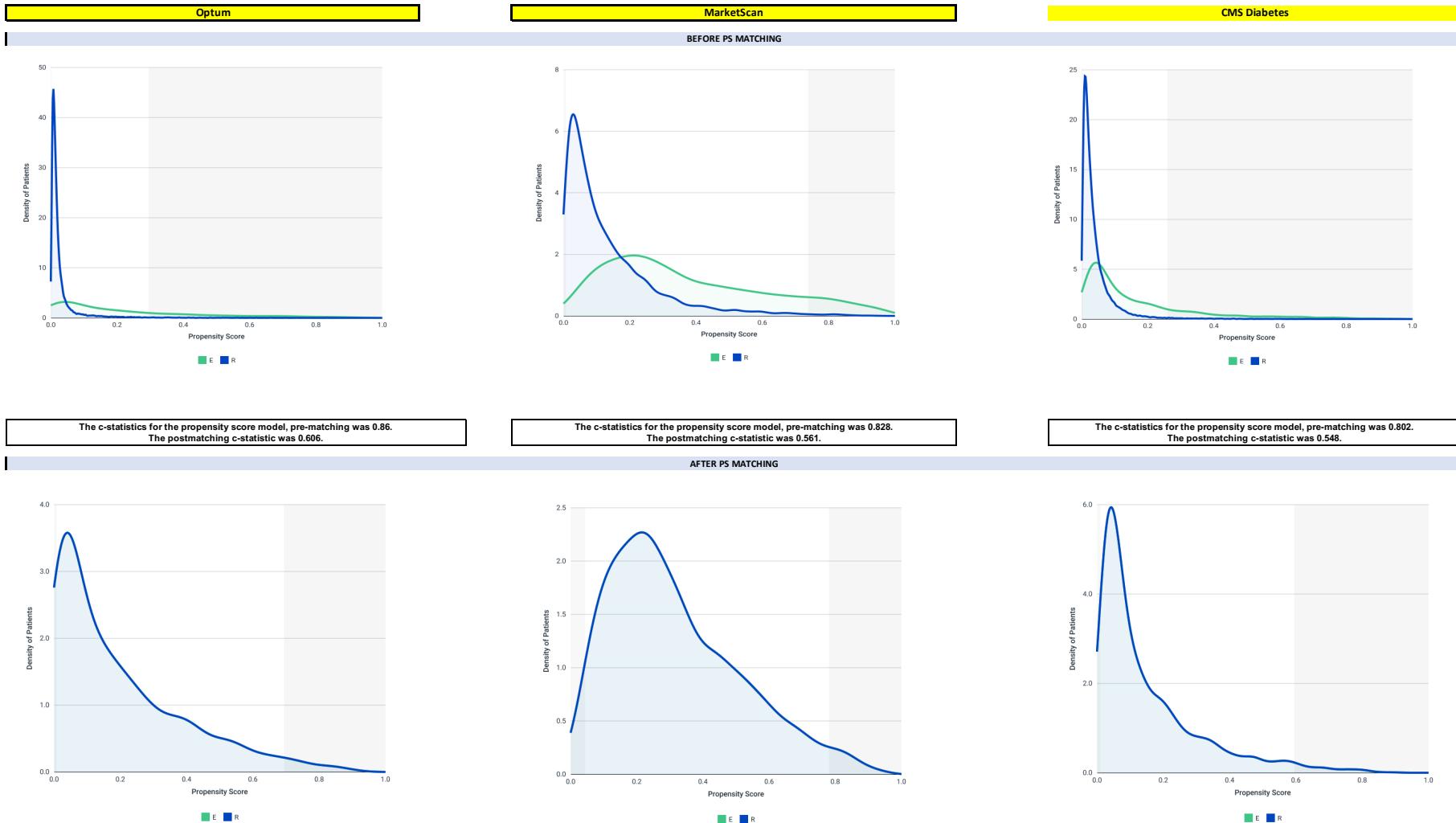
- 20 = EXPIRED
- 21 = EXPIRED TO BE DEFINED AT STATE LEVEL
- 22 = EXPIRED TO BE DEFINED AT STATE LEVEL
- 23 = EXPIRED TO BE DEFINED AT STATE LEVEL
- 24 = EXPIRED TO BE DEFINED AT STATE LEVEL
- 25 = EXPIRED TO BE DEFINED AT STATE LEVEL
- 26 = EXPIRED TO BE DEFINED AT STATE LEVEL
- 27 = EXPIRED TO BE DEFINED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

Truven-

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

Appendix A

Appendix B: Dapagliflozin vs. Sitagliptin



Appendix B: Dapagliflozin vs. Sitagliptin

Variable	BEFORE MATCHING											
	OPTUM			MARKETSCAN			MEDICARE			POOLED		
Variable	Reference - Sitagliptin	Exposure - Dapagliflozin	St. Diff.	Reference - Sitagliptin	Exposure - Dapagliflozin	St. Diff.	Reference - Sitagliptin	Exposure - Dapagliflozin	St. Diff.	Reference - Sitagliptin	Exposure - Dapagliflozin	St. Diff.
Number of patients	21,224	871		9,009	1,931		51,898	2,701		82,131	5,503	
Age - Continuous...mean (sd)	73.04 (8.33)	64.74 (10.17)	0.8929	66.93 (11.32)	59.00 (8.67)	0.7865	76.27 (7.02)	73.23 (6.25)	0.4574	74.41 (7.95)	66.89 (7.87)	0.9507
Age Categories												
...18 - 54; n (%)	564 (2.7%)	155 (17.8%)	-0.5140	1,146 (12.7%)	508 (26.3%)	-0.3484	0 (0%)	0 (0%)	#DIV/0!	1,710 (2.1%)	663 (12.0%)	-0.3942
...55 - 64; n (%)	1,973 (9.3%)	238 (27.3%)	-0.4787	3,167 (35.2%)	1,093 (56.6%)	-0.4397	0 (0%)	0 (0%)	#DIV/0!	5,140 (6.3%)	1,331 (24.2%)	-0.5141
...65 - 74; n (%)	9,500 (44.8%)	339 (38.9%)	0.1198	2,238 (24.8%)	241 (12.5%)	0.3198	23,338 (45.0%)	1,723 (6.8%)	-0.3844	32,838 (40.0%)	2,062 (37.5%)	0.0513
...>=75; n (%)	9,187 (43.3%)	139 (16.0%)	0.6264	2,458 (27.3%)	89 (4.6%)	0.6521	28,560 (55.0%)	978 (36.2%)	0.3844	37,747 (46.0%)	1,117 (20.3%)	0.5675
Gender												
...Male; n (%)	10,060 (47.4%)	487 (55.9%)	-0.1707	5,120 (56.8%)	1,212 (62.8%)	-0.1226	24,233 (46.7%)	1,385 (51.3%)	-0.0921	34,293 (41.8%)	1,872 (34.0%)	0.1613
...Female; n (%)	11,164 (52.6%)	384 (44.1%)	0.1707	3,889 (43.2%)	719 (37.2%)	0.1226	27,665 (53.3%)	1,316 (48.7%)	0.0921	38,829 (47.3%)	1,700 (30.9%)	0.3409
Geographic Region												
...Northeast; n (%)	1,916 (9.0%)	71 (8.2%)	0.0285	1,605 (17.8%)	214 (11.1%)	0.1914	9,276 (17.9%)	422 (15.6%)	0.0616	11,192 (13.6%)	493 (9.0%)	0.1457
...South; n (%)	10,975 (51.7%)	486 (55.8%)	-0.0823	4,157 (46.1%)	1,168 (60.5%)	-0.2917	22,230 (42.8%)	1,231 (45.6%)	-0.0564	33,205 (40.4%)	1,717 (31.2%)	0.1928
...Midwest; n (%)	2,594 (12.2%)	129 (14.8%)	-0.0761	2,159 (24.0%)	288 (14.9%)	0.2314	10,763 (20.7%)	389 (14.4%)	0.1662	13,357 (16.3%)	518 (9.4%)	0.2073
...West; n (%)	5,730 (27.0%)	185 (21.2%)	0.1359	1,039 (11.5%)	254 (13.2%)	-0.0517	9,502 (18.3%)	655 (24.3%)	-0.1469	15,232 (18.5%)	840 (15.3%)	0.0855
...Unknown/missing; n (%)	9 (0.0%)	0 (0.0%)	#DIV/0!	49 (0.5%)	7 (0.4%)	0.0149	127 (0.2%)	**	-	136 (0.2%)	-	#VALUE!
Calendar Time - Year of initiation (2014/15 - 2020)												
...2014-2015; n (%)	4,202 (19.8%)	294 (33.8%)	-0.3201	3,943 (43.8%)	576 (29.8%)	0.2934	24,357 (46.9%)	799 (29.6%)	0.3617	28,559 (34.8%)	1,093 (19.9%)	0.3390
...2016; n (%)	2,845 (13.4%)	78 (9.0%)	0.1399	2,048 (22.7%)	473 (24.5%)	-0.0424	13,886 (26.8%)	673 (24.9%)	0.0434			
...2017; n (%)	3,840 (18.1%)	135 (15.5%)	0.0696	1,743 (19.3%)	375 (19.4%)	-0.0025	13,655 (26.3%)	1,229 (45.5%)	-0.4085	17,495 (21.3%)	1,364 (24.8%)	-0.0832
...2018; n (%)	4,202 (19.8%)	130 (14.9%)	0.1297	1,275 (14.2%)	507 (26.3%)	-0.3046	0 (0%)	0 (0%)	#DIV/0!	4,202 (5.1%)	130 (2.4%)	0.1425
...2019 - March 2020; n (%)	6,135 (28.9%)	234 (26.9%)	0.0446	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	6,135 (7.5%)	234 (4.3%)	0.1361
Combined comorbidity score, 180 days ...mean (sd)	3.29 (2.46)	2.52 (2.23)	0.3280	2.30 (2.23)	1.62 (1.81)	0.3348	2.47 (2.48)	2.02 (2.13)	0.1947	2.66 (2.45)	1.96 (2.04)	0.3105
Futility Score: Empirical Version, 180 days ...mean (sd)	0.17 (0.05)	0.16 (0.04)	0.2209	0.16 (0.04)	0.15 (0.03)	0.2828	0.20 (0.06)	0.19 (0.05)	0.1811	0.19 (0.06)	0.17 (0.04)	0.3922
DiabRen - CKD II; n (%)	3,872 (18.2%)	191 (21.9%)	-0.0925	1,306 (14.5%)	391 (20.2%)	-0.1510	6,955 (13.4%)	497 (18.4%)	-0.1371	10,827 (13.2%)	688 (12.5%)	0.0209
DiabRen - CKD III; n (%)	11,801 (55.6%)	359 (41.2%)	0.2912	4,193 (46.5%)	563 (29.2%)	0.3625	27,504 (53.0%)	1,109 (41.1%)	0.2401	39,305 (47.9%)	1,468 (26.7%)	0.4493
DiabRen - Occurrence of Diabetic Nephropathy; n (%)	11,450 (53.9%)	398 (45.7%)	-0.1646	3,050 (33.9%)	669 (34.6%)	-0.0148	16,224 (31.3%)	906 (33.5%)	-0.0470	27,674 (33.7%)	1,304 (23.7%)	0.2224
DiabRen - Occurrence of Diabetic Neuropathy; n (%)	6,254 (29.5%)	253 (29.0%)	0.0110	1,659 (18.4%)	392 (20.3%)	-0.0481	13,517 (26.0%)	847 (31.4%)	-0.1196	19,771 (24.1%)	1,100 (20.0%)	0.0990
DiabRen - Diabetic retinopathy; n (%)	2,260 (10.6%)	95 (10.9%)	-0.0097	577 (6.4%)	113 (5.9%)	0.0208	4,571 (8.8%)	327 (12.1%)	-0.1080	6,831 (8.3%)	422 (7.7%)	0.0221
DiabRen - Diabetic foot; n (%)	713 (3.4%)	27 (3.1%)	0.0169	274 (3.0%)	52 (2.7%)	0.0180	2,084 (4.0%)	94 (3.5%)	0.0263	2,797 (3.4%)	121 (2.2%)	0.0728
DiabRen - Diabetes with peripheral circulatory disorders; n (%)	3,190 (15.0%)	90 (10.3%)	0.1417	617 (6.8%)	95 (4.9%)	0.0810	5,924 (11.4%)	343 (12.7%)	-0.0399	9,114 (11.1%)	433 (7.9%)	0.1093
DiabRen - Hypertensive nephropathy; n (%)	6,719 (31.7%)	227 (26.1%)	0.1238	1,940 (21.5%)	363 (18.8%)	0.0673	8,934 (17.2%)	477 (17.7%)	-0.0132	15,653 (19.1%)	704 (12.8%)	0.1727
DiabRen - Hypertension; n (%)	19,413 (91.5%)	786 (90.2%)	0.0451	7,700 (85.5%)	1,635 (84.7%)	0.0225	48,556 (93.6%)	5,239 (94.0%)	-0.0166	67,969 (82.8%)	3,325 (60.4%)	0.5128
DiabRen - Hypotension; n (%)	616 (2.9%)	20 (2.3%)	0.0377	181 (2.0%)	28 (1.5%)	0.0381	1,813 (3.5%)	72 (2.7%)	0.0462	2,429 (3.0%)	092 (1.7%)	0.0859
DiabRen - Gout (acute/chronic); n (%)	430 (2.0%)	15 (1.7%)	0.0223	237 (2.6%)	43 (2.2%)	0.0261	1,334 (2.6%)	44 (1.6%)	0.0698	1,764 (2.1%)	059 (1.1%)	0.0796
DiabRen - Nephrolithiasis; n (%)	362 (1.7%)	17 (2.0%)	-0.0223	223 (2.5%)	35 (1.8%)	0.0483	1,137 (2.2%)	49 (1.8%)	0.0286	1,499 (1.8%)	066 (1.2%)	0.0494
DiabRen - Proteinuria; n (%)	1,863 (8.8%)	80 (9.2%)	-0.0140	328 (3.6%)	44 (2.3%)	0.0769	4,437 (8.5%)	253 (9.4%)	-0.0315	6,300 (7.7%)	333 (6.1%)	0.0632
DiabRen - Urinary tract infections (UTIs); n (%)	2,823 (13.3%)	80 (9.2%)	0.1300	705 (7.8%)	95 (4.9%)	0.1191	9,351 (18.0%)	408 (15.1%)	0.0781	12,174 (14.8%)	488 (8.9%)	0.1833
DiabRen - Genital infections; n (%)	302 (1.4%)	9 (1.0%)	0.0367	123 (1.4%)	28 (1.5%)	-0.0084	800 (1.5%)	47 (1.7%)	-0.0159	1,102 (1.3%)	056 (1.0%)	0.2821
DiabRen - Hypoglycemia v2; n (%)	3,543 (16.7%)	121 (13.9%)	0.0778	651 (7.2%)	175 (9.1%)	-0.0695	4,291 (8.3%)	292 (10.8%)	-0.0851	7,834 (9.5%)	413 (7.5%)	0.0718
DiabRen - Hyperglycemia; n (%)	1,039 (4.9%)	32 (3.7%)	0.0592	311 (3.5%)	70 (3.6%)	-0.0054	2,817 (5.4%)	148 (5.5%)	-0.0044	3,856 (4.7%)	180 (3.3%)	0.0715
DiabRen - Hyperkalemia; n (%)	975 (4.6%)	33 (3.8%)	0.0399	312 (3.5%)	41 (2.1%)	0.0849	2,589 (5.0%)	87 (3.2%)	0.0909	3,564 (4.3%)	120 (2.2%)	0.1186
DiabRen - Hypovolemia/volume depletion; n (%)	834 (3.9%)	28 (3.2%)	0.0378	263 (2.9%)	44 (2.1%)	0.0377	2,569 (5.0%)	90 (3.3%)	0.0853	3,403 (4.1%)	118 (2.1%)	0.1156
NephroTox - ACE inhibitors; n (%)	11,816 (55.7%)	458 (52.6%)	0.0622	4,903 (54.4%)	1,056 (54.7%)	-0.0060	28,838 (55.6%)	1,361 (50.4%)	0.1043	40,654 (49.5%)	1,819 (33.1%)	0.3378
NephroTox - ARBs; n (%)	10,050 (47.4%)	451 (51.8%)	-0.0881	4,429 (49.2%)	956 (49.5%)	-0.0060	24,917 (48.0%)	1,439 (53.3%)	-0.1062	34,967 (42.6%)	1,890 (34.3%)	0.1712
NephroTox - Loop diuretics; n (%)	4,691 (22.1%)	186 (19.1%)	0.0742	1,928 (21.4%)	272 (14.1%)	0.1939	15,531 (29.9%)	647 (24.0%)	0.1333	20,222 (24.6%)	813 (14.8%)	0.2483
NephroTox - Thiazide diuretics; n (%)	4,144 (19.5%)	165 (18.9%)	0.0152	1,823 (20.2%)	333 (17.2%)	0.0770	10,001 (19.3%)	484 (17.9%)	0.0360	14,145 (17.2%)	649 (11.8%)	0.1538
NephroTox - Mineralocorticoid receptor antagonist; n (%)	1,024 (4.8%)	50 (5.7%)	-0.0404	590 (6.5%)	97 (5.0%)	0.0645	2,969 (5.7%)	128 (4.7%)	0.0451	3,993 (4.9%)	178 (3.2%)	0.0863
NephroTox - NSAIDs; n (%)	2,651 (12.5%)	140 (16.1%)	-0.1030	1,182 (13.1%)	339 (17.6%)	-0.1251	5,826 (11.2%)	427 (15.8%)	-0.1349	8,477 (10.3%)	567 (10.3%)	0.0000
NephroTox - PPIs; n (%)	5,417 (25.5%)	201 (23.1%)	0.0560	1,895 (21.0%)	380 (19.7%)	0.0323	14,510 (28.0%)	688 (25.5%)	0.0565	19,927 (24.3%)	889 (16.2%)	0.2026
NephroTox - H2RAs; n (%)	1,622 (7.6%)	40 (4.6%)	0.1256	377 (4.2%)	67 (3.5%)	0.0364	3,801 (7.3%)	217 (8.0%)	-0.0263	5,423 (6.6%)	257 (4.7%)	0.0824
NephroTox - Antivirals/Antiretrovirals/Antimicrobials; n (%)	200 (0.9%)	14 (1.6%)	-0.0630	85 (0.9%)	19 (1.0%)	-0.0103	517 (1.0%)	33 (1.2%)	-0.0192	717 (0.9%)	047 (0.9%)	0.0000
DM Medications - 1st and 2nd Generation SUs; n (%)	9,808 (46.2%)	380 (43.6%)	0.0523	3,893 (43.2%)	708 (36.7%)	0.1330	24,534 (47.3%)	1,180 (43.7%)	0.0723	34,342 (41.8%)	1,560 (28.3%)	0.2858
DM Medications - AGL & Meglitinides; n (%)	487 (2.3%)	17 (2.0%)	0.0207	246 (2.7%)	35 (1.8%)	0.0607	1,767 (3.4%)	136 (5.0%)	-0.0798	2,254 (2.7%)	153 (2.8%)	-0.0061
DM Medications - DPP-4 Inhibitors(excluding sitagliptin); n (%)	1,253 (5.9%)	134 (15.4%)	-0.3117	675 (7.5%)	172 (9.9%)	-0.0510	4,025 (7.8%)	426 (15.8%)	-0.2499	5,278 (6.4%)	560 (10.2%)	-0.1381
DM Medications - Glitazones; n (%)	1,969 (9.3%)	106 (12.2%)	-0.0937	771 (8.6%)	242 (12.5%)	-0.1272	4,266 (8.2%)	320 (11.8%)	-0.1202	6,235 (7.6%)	426 (7.7%)	0.0038
DM Medications - GLP-1 RA; n (%)	888 (4.2%)	228 (26.2%)	-0.6437	469 (5.2%)	515 (26.7%)	-0.6143	1,519 (2.9%)	515 (19.1%)	-0.5360	2,407 (2.9%)	743 (13.5%)	-0.3938
DM Medications - Insulins; n (%)	4,954 (23.3%)	291 (33.4%)	-0.2255	1,997 (22.2%)	633 (32.8%)	-0.2391	12,291 (23.7%)	1,005 (37.2%)	-0.2966	17,245 (21.0%)	1,296 (23.6%)	-0.0625
DM Medications - Metformin; n (%)	11,179 (52.7%)	529 (60.7%)	-0.1620	4,464 (49.6%)	1,188 (61.5%)	-0.2412	24,769 (47.7%)	1,510 (55.9%)	-0.1647	35,948 (43.8%)	2,039 (37.1%)	0.1368
DM Medications - SGLT-2 Inhibitors(excluding dapagliflozin); n (%)	443 (2.1%)	60 (6.9%)	-0.2331	181 (2.0%)	269 (13.9%)	-0.4509	473 (0.9%)	181 (6.7%)	-0.3069	916 (1.1%)	241 (4.4%)	-0.2028
DM Medications - Number of antIDM medications at index date ...mean (sd)	2.28 (0.84)	2.84 (0.97)	-0.6172	2.25								

Appendix B: Dapagliflozin vs. Sitagliptin

CV Comorbidity - Hyperlipidemia; n (%)	16,913 (79.7%)	726 (83.4%)	0.0955	6,345 (70.4%)	1,483 (76.8%)	-0.1456	41,955 (80.8%)	2,257 (83.6%)	-0.0732	58,868 (71.7%)	2,983 (54.2%)	0.3685
CV Comorbidity - Stable Angina; n (%)	1,232 (5.8%)	33 (3.8%)	0.0937	216 (2.4%)	42 (2.2%)	0.0133	1,933 (3.7%)	137 (5.1%)	-0.0683	3,165 (3.9%)	170 (3.1%)	0.0435
CV Comorbidity - Unstable Angina ; n (%)	331 (1.6%)	18 (2.1%)	-0.0371	93 (1.0%)	15 (0.8%)	0.0212	846 (1.6%)	38 (1.4%)	0.0165	1,177 (1.4%)	056 (1.0%)	0.0367
CV Comorbidity - Peripheral Vascular Disease (PVD) or PVD Surgery ; n (%)	2,604 (12.3%)	91 (10.4%)	0.0599	651 (7.2%)	77 (4.0%)	0.1395	8,166 (15.7%)	421 (15.6%)	0.0028	10,770 (13.1%)	512 (9.3%)	0.1207
CV Comorbidity - Stroke/TIA; n (%)	927 (4.4%)	25 (2.9%)	0.0801	183 (2.0%)	19 (1.0%)	0.0823	2,043 (3.9%)	84 (3.1%)	0.0435	2,970 (3.6%)	109 (2.0%)	0.0971
CV Comorbidity - Pulmonary hypertension/Other pulmonary heart disease ; n (%)	637 (3.0%)	19 (2.2%)	0.0503	179 (2.0%)	18 (0.9%)	0.0921	1,876 (3.6%)	64 (2.4%)	0.0704	2,513 (3.1%)	083 (1.5%)	0.1069
CV Medication - Beta-blockers; n (%)	10,748 (50.6%)	438 (50.3%)	0.0060	4,664 (51.8%)	823 (42.6%)	0.1851	29,658 (57.1%)	1,486 (55.0%)	0.0423	40,406 (49.2%)	1,924 (35.0%)	0.2906
CV Medication - CCB; n (%)	8,243 (38.3%)	274 (31.5%)	0.1533	3,256 (36.1%)	544 (28.2%)	0.1698	20,572 (39.6%)	987 (36.5%)	0.0639	28,815 (35.1%)	1,261 (22.9%)	0.2713
CV Medication - Digoxin ; n (%)	473 (2.2%)	15 (1.7%)	0.0362	198 (2.2%)	17 (0.9%)	0.1054	2,016 (3.9%)	87 (3.2%)	0.0378	2,489 (3.0%)	102 (1.9%)	0.0712
CV Medication - Nitrates; n (%)	1,651 (7.8%)	74 (8.5%)	-0.0256	564 (6.3%)	74 (3.8%)	0.1144	5,317 (10.2%)	255 (9.4%)	0.0269	6,968 (8.5%)	329 (6.0%)	0.0965
CV Medication - Use of Statins; n (%)	17,126 (80.7%)	717 (82.3%)	-0.0412	6,804 (75.5%)	1,470 (76.1%)	-0.0140	40,441 (77.9%)	2,195 (81.3%)	-0.0844	57,567 (70.1%)	2,912 (52.9%)	0.3591
CV Medication - Use of other lipid-lowering drugs; n (%)	2,741 (12.9%)	161 (18.5%)	-0.1544	1,615 (17.9%)	398 (20.6%)	-0.0685	8,062 (15.5%)	497 (18.4%)	-0.0774	10,803 (13.2%)	658 (12.0%)	0.0362
CV Medication - Use of other hypertension drugs; n (%)	2,587 (12.2%)	82 (9.4%)	0.0903	1,156 (12.8%)	181 (9.4%)	0.1084	6,811 (13.1%)	350 (13.0%)	0.0030	9,398 (11.4%)	432 (7.9%)	0.1187
Other Comorbidity - Anemia ; n (%)	4,602 (21.7%)	131 (15.0%)	0.1737	1,550 (17.2%)	240 (12.4%)	0.1355	16,274 (31.4%)	720 (26.7%)	0.1037	20,876 (25.4%)	851 (15.5%)	0.2473
Other Comorbidity - Cancer ; n (%)	2,602 (12.3%)	93 (10.7%)	0.0502	1,053 (11.7%)	128 (6.6%)	0.1776	8,190 (15.8%)	345 (12.8%)	0.0858	10,792 (13.1%)	438 (8.0%)	0.1666
Other Comorbidity - COPD ; n (%)	2,845 (13.4%)	87 (10.0%)	0.1059	667 (7.4%)	60 (3.1%)	0.1937	7,771 (15.0%)	364 (13.5%)	0.0429	10,616 (12.9%)	451 (8.2%)	0.1534
Other Comorbidity - Dementia ; n (%)	1,453 (6.8%)	28 (3.2%)	0.1657	314 (3.5%)	9 (0.5%)	0.2155	5,494 (10.5%)	167 (6.2%)	0.1591	6,947 (8.5%)	195 (3.5%)	0.2117
Other Comorbidity - Depression ; n (%)	3,072 (14.5%)	104 (11.9%)	0.0769	701 (7.8%)	137 (7.1%)	0.0267	6,957 (13.4%)	350 (13.0%)	0.0118	10,029 (12.2%)	454 (8.3%)	0.1289
Other Comorbidity - Fractures ; n (%)	772 (3.6%)	24 (2.8%)	0.0455	284 (3.2%)	36 (1.9%)	0.0825	2,685 (5.2%)	101 (3.7%)	0.0728	3,457 (4.2%)	125 (2.3%)	0.1073
Other Comorbidity - Hypothyroidism ; n (%)	1,505 (7.1%)	74 (8.5%)	-0.0522	711 (7.9%)	152 (7.9%)	0.0000	7,204 (13.9%)	330 (12.2%)	0.0505	8,709 (10.6%)	404 (7.3%)	0.1158
Other Comorbidity - Osteoporosis; n (%)	1,618 (7.6%)	47 (5.4%)	0.0893	282 (3.1%)	29 (1.5%)	0.1069	4,961 (9.6%)	304 (11.3%)	-0.0556	6,579 (8.0%)	351 (6.4%)	0.0619
Other Comorbidity - Pneumonia; n (%)	825 (3.9%)	21 (2.4%)	0.0860	315 (3.5%)	28 (1.5%)	0.1284	2,793 (5.4%)	96 (3.6%)	0.0869	3,618 (4.4%)	117 (2.1%)	0.1300
Other Comorbidity - Sleep apnea; n (%)	2,555 (12.0%)	148 (17.0%)	-0.1424	1,255 (13.9%)	329 (17.0%)	-0.0859	5,931 (11.4%)	400 (14.8%)	-0.1009	8,486 (10.3%)	548 (10.0%)	0.0099
Other Medication - Use of anticonvulsants; n (%)	4,685 (22.1%)	187 (21.5%)	0.0145	1,476 (16.4%)	312 (16.2%)	0.0054	11,018 (21.2%)	708 (26.2%)	-0.1178	15,703 (19.1%)	895 (16.3%)	0.0734
Other Medication - Use of antidepressants ; n (%)	5,538 (26.1%)	228 (26.2%)	-0.0023	2,124 (23.6%)	451 (24.3%)	0.0047	14,254 (27.5%)	799 (29.6%)	-0.0465	19,792 (24.1%)	1,027 (18.7%)	0.1320
Other Medication - Use of anti-parkinsonian meds; n (%)	668 (3.1%)	25 (2.9%)	0.0117	229 (2.5%)	40 (2.1%)	0.0267	2,031 (3.9%)	118 (4.4%)	-0.0251	2,699 (3.3%)	143 (2.6%)	0.0414
Other Medication - Use of dementia meds; n (%)	924 (4.4%)	16 (1.8%)	0.1504	217 (2.4%)	3 (0.2%)	0.1951	3,463 (6.7%)	133 (4.9%)	0.0771	4,387 (5.3%)	149 (2.7%)	0.1330
Other Medication - Use of antipsychotics ; n (%)	672 (3.2%)	24 (2.8%)	0.0235	200 (2.2%)	25 (1.3%)	0.0687	2,140 (4.1%)	93 (3.4%)	0.0369	2,812 (3.4%)	117 (2.1%)	0.0796
Other Medication - Use of anxiolytics/hypnotics; n (%)	1,093 (5.1%)	55 (6.3%)	-0.0518	534 (5.9%)	130 (6.7%)	-0.0329	3,233 (6.2%)	204 (7.6%)	-0.0553	4,326 (5.3%)	259 (4.7%)	0.0275
Other Medication - Use of Benzodiazepines; n (%)	2,322 (10.9%)	100 (11.5%)	-0.0190	920 (10.2%)	197 (10.2%)	0.0000	6,616 (12.7%)	344 (12.7%)	0.0000	8,938 (10.9%)	444 (8.1%)	0.0956
Other Medication - Use of COPD/asthma meds; n (%)	4,164 (19.6%)	175 (20.1%)	-0.0125	1,578 (17.5%)	310 (16.1%)	0.0375	10,663 (20.5%)	601 (22.3%)	-0.0439	14,827 (18.1%)	776 (14.1%)	0.1090
Other Medication - Use of anti-platelet agents; n (%)	2,950 (13.9%)	108 (12.4%)	0.0444	1,478 (16.4%)	271 (14.0%)	0.0669	8,311 (16.0%)	447 (16.5%)	-0.0136	11,261 (13.7%)	555 (10.1%)	0.1114
Other Medication - Use of oral anti-coagulants; n (%)	2,259 (10.6%)	72 (8.3%)	0.0787	875 (9.7%)	101 (5.2%)	0.1720	7,187 (13.8%)	346 (12.8%)	0.0295	9,446 (11.5%)	418 (7.6%)	0.1330
Other Medication - Use of opioids; n (%)	5,237 (24.7%)	194 (22.3%)	0.0566	2,318 (25.7%)	461 (23.9%)	0.0417	14,731 (28.4%)	737 (27.3%)	0.0245	19,968 (24.3%)	931 (16.9%)	0.1837
Lifestyle - Alcohol/Drug Abuse or Dependence; n (%)	616 (2.9%)	16 (1.8%)	0.0727	110 (1.2%)	18 (0.9%)	0.0294	870 (1.7%)	45 (1.7%)	0.0000	1,486 (1.8%)	661 (1.1%)	0.0586
Lifestyle - Obesity; n (%)	4,620 (21.8%)	273 (31.3%)	-0.2164	1,702 (18.9%)	481 (24.9%)	-0.1455	10,685 (20.6%)	795 (29.4%)	-0.2043	15,305 (18.6%)	1,068 (19.4%)	-0.0204
Lifestyle - Smoking; n (%)	2,862 (13.5%)	94 (10.8%)	0.0827	508 (5.6%)	93 (4.8%)	0.0360	8,159 (15.7%)	395 (14.6%)	0.0307	11,021 (13.4%)	489 (8.9%)	0.1433
HU - Number of Cardiologist visits ...mean (sd)	1.78 (4.22)	1.67 (4.25)	0.0260	1.10 (3.36)	0.88 (2.46)	0.0747	2.45 (5.55)	2.07 (5.07)	0.0715	2.13 (5.03)	1.59 (4.20)	0.1165
HU - Number of Nephrologist visit ...mean (sd)	0.60 (2.24)	0.48 (1.72)	0.0601	0.49 (1.99)	0.38 (1.68)	0.0597	0.74 (2.77)	0.69 (3.95)	0.0147	0.68 (2.57)	0.55 (3.02)	0.0464
HU - Number of Endocrinologist visits ...mean (sd)	0.45 (2.10)	1.18 (3.73)	-0.2412	0.49 (2.28)	0.98 (2.96)	-0.1855	0.79 (3.61)	1.32 (4.52)	-0.1296	1.18 (3.91)	1.04 (3.14)	0.1436
HU - Number of Internal Medicine/Family Medicine Visits ...mean (sd)	15.91 (18.92)	11.70 (15.83)	0.2413	9.07 (12.72)	7.67 (8.79)	0.1281	10.09 (12.96)	10.75 (14.87)	-0.0473	11.48 (14.71)	9.82 (13.24)	0.1186
HU - Number of Emergency Department (ED) visits ...mean (sd)	0.59 (1.60)	0.52 (1.83)	0.0407	0.27 (1.51)	0.18 (1.53)	0.0592	0.75 (2.06)	0.55 (1.36)	0.1146	0.66 (1.90)	0.42 (1.50)	0.1402
HU - Number of Distinct Medication Prescriptions (not generalized to generics) ...mean (sd)	28.51 (19.80)	33.44 (20.23)	-0.2463	25.94 (16.29)	27.51 (16.84)	-0.0948	31.26 (22.25)	36.01 (26.11)	-0.1958	29.97 (21.05)	32.62 (22.34)	-0.1221
HU - Number of Echocardiogram ...mean (sd)	0.28 (1.42)	0.30 (1.55)	-0.0135	0.22 (0.69)	0.13 (0.46)	0.1535	0.28 (0.70)	0.23 (0.65)	0.0740	0.27 (0.94)	0.21 (0.81)	0.0684
HU - Number of Electrocardiogram Performed ...mean (sd)	0.83 (1.83)	0.75 (1.82)	0.0438	0.68 (1.43)	0.47 (1.00)	0.1702	0.98 (1.80)	0.85 (1.58)	0.0768	0.91 (1.77)	0.70 (1.45)	0.1298
HU - Number of HbA1c tests ordered ...mean (sd)	1.50 (0.97)	1.52 (0.91)	-0.0213	0.96 (0.98)	1.39 (0.95)	-0.4455	1.53 (0.93)	1.72 (0.98)	-0.1989	1.46 (0.95)	1.57 (0.96)	-0.1152
HU - Number of Hospitalizations during CAP ...mean (sd)	0.15 (0.50)	0.12 (0.44)	0.0637	0.14 (0.44)	0.08 (0.31)	0.1576	0.25 (0.65)	0.13 (0.44)	0.2162	0.21 (0.59)	0.11 (0.40)	0.1984
HU - Recent hospitalization (-30 days to Index Rx date); n (%)	617 (2.9%)	13 (1.5%)	0.0956	254 (2.8%)	18 (0.9%)	0.1414	2,465 (4.7%)	36 (1.3%)	0.2003	3,082 (3.8%)	049 (0.9%)	0.1923
HU - Old hospitalizations (-180 to -31 days); n (%)	2,008 (9.5%)	76 (8.7%)	0.0278	841 (9.3%)	110 (5.7%)	0.1370	7,233 (13.9%)	245 (9.1%)	0.1509	9,241 (11.3%)	321 (5.8%)	0.1977
HU - Mammogram; n (%)	2,561 (12.1%)	108 (12.4%)	-0.0092	754 (8.4%)	181 (9.4%)	-0.0351	5,207 (10.0%)	293 (10.8%)	-0.0262	7,768 (9.5%)	401 (7.3%)	0.0794
HU - Pap smear; n (%)	380 (18.3%)	19 (2.2%)	-0.0286	261 (2.9%)	84 (4.4%)	-0.0801	918 (1.8%)	47 (1.7%)	0.0076	1,296 (1.6%)	066 (1.2%)	0.0341
HU - Prostate exam for DRE; n (%)	1,007 (4.7%)	38 (4.4%)	0.0144	315 (3.5%)	88 (4.6%)	-0.0558	2,664 (5.1%)	182 (6.7%)	-0.0679	3,671 (4.5%)	220 (4.0%)	0.0248
HU - Flexible Sigmoidoscopy or colonoscopy or CT virtual colonoscopy; n (%)	987 (4.7%)	33 (3.8%)	0.0446	497 (5.5%)	104 (5.4%)	0.0044	2,514 (4.8%)	134 (5.0%)	-0.0093	3,501 (4.3%)	167 (3.0%)	0.0694
HU - Bone mineral density; n (%)	1,026 (4.8%)	38 (4.4%)	0.0191	196 (2.2%)	39 (2.0%)	0.0139	2,214 (4.3%)	133 (4.9%)	-0.0286	3,240 (3.9%)	171 (3.1%)	0.0435
HU - Flu vaccine; n (%)	4,955 (23.3%)	197 (22.6%)	0.0166	1,562 (17.3%)	355 (18.4%)	-0.0287	18,258 (35.2%)	935 (34.6%)	0.0126	23,213 (28.3%)	1,132 (20.6%)	0.1799
HU - Pneumococcal vaccine; n (%)	5,388 (25.4%)	196 (22.5%)	0.0680	1,246 (13.8%)	289 (15.0%)	-0.0342	14,318 (27.6%)	856 (31.7%)	-0.0899	19,706 (24.0%)	1,052 (19.1%)	0.1194
Lab - Occurrence of 24-hour urine test; n (%)	8,939 (42.1%)	370 (42.5%)	-0.0081	2,455 (27.3%)	755 (39.1%)	-0.2526	19,220 (37.0%)	1,105 (40.9%)	-0.0800	28,159 (34.3%)	1,475 (26.8%)	0.1634
Lab - Occurrence of creatinine tests ordered; n (%)	1,202 (5.7%)	53 (6.1%)	-0.0170	466 (5.2%)	80 (4.1%)	0.0523	4,261 (8.2%)	195 (7.2%)	0.0375	5,463 (6.7%)	248 (4.5%)	0.0958
Lab - Occurrence of urine albumin test ordered; n (%)	11,839 (54.8%)	467 (53.6%)	0.0241	2,611 (29.0%)	862 (44.6%)	-0.3278	21,500 (41.4%)	1,277 (47.3%)	-0.1190	33,139 (40.3%)	1,744 (31.7%)	0.1799
Lab - Occurrence of HbA1c test; n (%)	11,207 (52.8%)	394 (45.2%)	0.1525	724 (8.0%)	149 (7.7%)	0.0112	46,435 (89.5%)					

Appendix B: Dapagliflozin vs. Sitagliptin

Variable	AFTER MATCHING											
	OPTUM			MARKETSCAN			MEDICARE			POOLED		
	Reference - Sitagliptin	Exposure - Dapagliflozin	St. Diff	Reference - Sitagliptin	Exposure - Dapagliflozin	St. Diff	Reference - Sitagliptin	Exposure - Dapagliflozin	St. Diff	Reference - Sitagliptin	Exposure - Dapagliflozin	St. Diff
Number of patients	828	828		1,687	1,687		2,630	2,630		5,145	5,145	
Age - Continuous; n; mean (sd)	65.33 (9.96)	65.27 (9.97)	0.0060	59.19 (9.34)	59.52 (8.66)	-0.0366	73.17 (5.93)	73.25 (6.25)	-0.0131	67.32 (7.91)	67.46 (7.78)	-0.0178
Age Categories												
...18 - 54; n (%)	119 (14.4%)	130 (15.7%)	-0.0364	489 (29.0%)	413 (24.5%)	0.1018	0 (0.0%)	0 (0.0%)	#DIV/0!	608 (11.8%)	543 (10.6%)	0.0381
...55 - 64; n (%)	232 (28.0%)	224 (27.1%)	0.0201	836 (49.6%)	958 (56.8%)	-0.1447	0 (0.0%)	0 (0.0%)	#DIV/0!	1,068 (20.8%)	1,182 (23.0%)	-0.0532
...65 - 74; n (%)	327 (39.5%)	336 (40.6%)	-0.0225	262 (15.5%)	228 (13.5%)	0.0568	1,686 (64.1%)	1,674 (63.7%)	0.0083	2,013 (39.1%)	2,010 (39.1%)	0.0000
...>=75; n (%)	150 (18.1%)	138 (16.7%)	0.0369	100 (5.9%)	88 (5.2%)	0.0306	944 (35.9%)	956 (36.3%)	-0.0083	1,094 (21.3%)	1,094 (21.3%)	0.0000
Gender												
...Male; n (%)	440 (53.1%)	452 (54.6%)	-0.0301	1,042 (61.8%)	1,051 (62.3%)	-0.0103	1,371 (52.1%)	1,349 (51.3%)	0.0160	1,811 (35.2%)	1,801 (35.0%)	0.0042
...Female; n (%)	388 (46.9%)	376 (45.4%)	0.0301	645 (38.2%)	636 (37.7%)	0.0103	1,259 (47.9%)	1,281 (48.7%)	-0.0160	1,647 (32.0%)	1,657 (32.2%)	-0.0043
Geographic Region												
...Northeast; n (%)	77 (9.3%)	71 (8.6%)	0.0245	197 (11.7%)	192 (11.4%)	0.0094	400 (15.2%)	412 (15.7%)	-0.0138	477 (9.3%)	483 (9.4%)	-0.0034
...South; n (%)	463 (55.9%)	460 (55.6%)	0.0060	1,024 (60.7%)	1,100 (59.9%)	-0.0164	1,189 (45.2%)	1,208 (45.9%)	-0.0141	1,652 (32.1%)	1,668 (32.4%)	-0.0064
...Midwest; n (%)	99 (12.0%)	119 (14.4%)	-0.0709	252 (14.9%)	259 (15.4%)	-0.0139	422 (16.0%)	379 (14.4%)	0.0446	521 (10.1%)	498 (9.7%)	0.0134
...West; n (%)	189 (22.8%)	178 (21.5%)	0.0313	206 (12.2%)	219 (13.0%)	-0.0241	619 (23.5%)	631 (24.0%)	-0.0117	808 (15.7%)	809 (15.7%)	0.0000
Calendar Time - Year of Initiation (2014/15 - 2020)												
...2014-2015; n (%)	257 (31.0%)	270 (32.6%)	-0.0344	531 (31.5%)	539 (32.0%)	-0.0107	755 (28.7%)	790 (30.0%)	-0.0286	1,012 (19.7%)	1,060 (20.6%)	-0.0224
...2016; n (%)	67 (8.1%)	75 (9.1%)	-0.0357	399 (23.7%)	408 (24.2%)	-0.0117	682 (25.9%)	659 (25.1%)	0.0184			
...2017; n (%)	119 (14.4%)	131 (15.8%)	-0.0391	364 (21.6%)	343 (20.3%)	0.0319	1,193 (45.4%)	1,181 (44.9%)	0.0100	1,312 (25.5%)	1,312 (25.5%)	0.0000
...2018; n (%)	140 (16.9%)	125 (15.1%)	0.0491	393 (23.3%)	397 (23.5%)	-0.0047	0 (0.0%)	0 (0.0%)	#DIV/0!	140 (2.7%)	125 (2.4%)	0.0190
...2019 - March 2020; n (%)	245 (29.6%)	227 (27.4%)	0.0488	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	245 (4.8%)	227 (4.4%)	0.0191
Combined comorbidity score, 180 days ...mean (sd)	2.54 (2.24)	2.57 (2.25)	-0.0134	1.64 (1.78)	1.63 (1.82)	0.0056	2.07 (2.19)	2.02 (2.14)	0.0231	2.00 (2.07)	1.98 (2.06)	0.0097
Frailty Score: Empirical Version, 180 days ...mean (sd)	0.16 (0.05)	0.16 (0.05)	0.0000	0.15 (0.03)	0.15 (0.03)	0.0000	0.19 (0.06)	0.19 (0.05)	0.0000	0.17 (0.05)	0.17 (0.04)	0.0000
DiabRen - CKD II; n (%)	162 (19.6%)	181 (21.9%)	-0.0567	339 (20.1%)	341 (20.2%)	-0.0025	513 (19.5%)	482 (18.3%)	0.0307	675 (13.1%)	663 (12.9%)	0.0059
DiabRen - CKD III; n (%)	351 (42.4%)	350 (42.3%)	0.0020	492 (29.2%)	508 (30.1%)	-0.0197	1,107 (42.1%)	1,090 (41.4%)	0.0142	1,458 (28.3%)	1,440 (28.0%)	0.0067
DiabRen - Occurrence of Diabetic Nephropathy; n (%)	371 (44.8%)	381 (46.0%)	-0.0241	558 (33.1%)	570 (33.8%)	-0.0148	907 (34.5%)	883 (33.6%)	0.0190	1,278 (24.8%)	1,264 (24.6%)	0.0046
DiabRen - Occurrence of Diabetic Neuropathy; n (%)	252 (30.4%)	242 (29.2%)	0.0262	357 (21.2%)	328 (19.4%)	0.0448	869 (33.0%)	821 (31.2%)	0.0386	1,121 (21.8%)	1,063 (20.7%)	0.0269
DiabRen - Diabetic retinopathy; n (%)	99 (12.0%)	90 (10.9%)	0.0346	118 (7.0%)	102 (6.0%)	0.0406	285 (10.8%)	309 (11.7%)	-0.0285	384 (7.5%)	399 (7.8%)	-0.0113
DiabRen - Diabetic foot; n (%)	18 (2.2%)	26 (3.1%)	-0.0561	33 (2.0%)	42 (2.5%)	-0.0337	92 (3.5%)	88 (3.3%)	0.0110	110 (2.1%)	114 (2.2%)	-0.0069
DiabRen - Diabetes with peripheral circulatory disorders; n (%)	74 (8.9%)	86 (10.4%)	-0.0508	86 (5.1%)	86 (5.1%)	0.0000	335 (12.7%)	328 (12.5%)	0.0060	409 (7.9%)	414 (8.0%)	-0.0037
DiabRen - Hypertensive nephropathy; n (%)	204 (24.6%)	221 (26.7%)	-0.0481	316 (18.7%)	318 (18.9%)	-0.0051	496 (18.9%)	465 (17.7%)	0.0310	700 (13.6%)	686 (13.3%)	0.0088
DiabRen - Hypertension; n (%)	750 (90.6%)	749 (90.5%)	0.0034	1,442 (85.5%)	1,429 (84.7%)	0.0225	2,483 (94.4%)	2,474 (94.1%)	0.0129	3,233 (62.8%)	3,223 (62.6%)	0.0041
DiabRen - Hypotension; n (%)	27 (3.3%)	20 (2.4%)	0.0541	21 (1.2%)	23 (1.4%)	-0.0177	77 (2.9%)	70 (2.7%)	0.0121	104 (2.0%)	90 (1.7%)	0.0223
DiabRen - Gout (acute/chronic); n (%)	14 (1.7%)	14 (1.7%)	0.0000	31 (1.8%)	38 (2.3%)	-0.0353	49 (1.9%)	44 (1.7%)	0.0150	663 (1.2%)	658 (1.1%)	0.0094
DiabRen - Neuropathiasis; n (%)	20 (2.4%)	17 (2.1%)	0.0202	29 (1.7%)	34 (2.0%)	-0.0223	54 (2.1%)	49 (1.9%)	0.0143	74 (1.4%)	666 (1.3%)	0.0087
DiabRen - Proteinuria; n (%)	72 (8.7%)	75 (9.1%)	-0.0140	40 (2.4%)	42 (2.5%)	-0.0065	251 (9.5%)	244 (9.3%)	0.0069	323 (6.3%)	319 (6.2%)	0.0041
DiabRen - Urinary tract infections (UTIs); n (%)	78 (9.4%)	79 (9.5%)	-0.0034	92 (5.5%)	83 (4.9%)	0.0270	405 (15.4%)	396 (15.1%)	0.0083	483 (9.4%)	475 (9.2%)	0.0069
DiabRen - Genital infections; n (%)	10 (1.2%)	9 (1.1%)	0.0094	25 (1.5%)	26 (1.5%)	0.0000	39 (1.5%)	44 (1.7%)	-0.0159	049 (1.0%)	053 (1.0%)	0.0000
DiabRen - Hypoglycemia v2; n (%)	132 (15.9%)	117 (14.1%)	0.0504	155 (9.2%)	145 (8.6%)	0.0211	284 (10.8%)	278 (10.6%)	0.0065	416 (8.1%)	395 (7.7%)	0.0148
DiabRen - Hyperglycemia; n (%)	31 (3.7%)	30 (3.6%)	0.0053	70 (4.1%)	59 (3.5%)	0.0314	130 (4.9%)	144 (5.5%)	-0.0270	161 (3.1%)	174 (3.4%)	-0.0169
DiabRen - Hyperkalemia; n (%)	22 (2.7%)	33 (4.0%)	-0.0723	36 (2.1%)	37 (2.2%)	-0.0069	78 (3.0%)	87 (3.3%)	-0.0172	100 (1.9%)	120 (2.3%)	-0.0279
DiabRen - Hypovolemia/volume depletion; n (%)	22 (2.7%)	27 (3.3%)	-0.0352	44 (2.6%)	39 (2.3%)	0.0194	96 (3.7%)	88 (3.3%)	0.0218	118 (2.3%)	115 (2.2%)	0.0067
NephroTox - ACE Inhibitors; n (%)	443 (53.5%)	433 (52.3%)	0.0240	899 (53.3%)	905 (53.6%)	-0.0060	1,366 (51.9%)	1,327 (50.5%)	0.0280	1,809 (35.2%)	1,760 (34.2%)	0.0210
NephroTox - ARBs; n (%)	428 (51.7%)	430 (51.9%)	-0.0040	852 (50.5%)	848 (50.3%)	0.0040	1,371 (52.1%)	1,400 (53.2%)	-0.0220	1,799 (35.0%)	1,830 (35.6%)	-0.0126
NephroTox - Loop Diuretics; n (%)	153 (18.5%)	159 (19.2%)	-0.0179	222 (13.2%)	241 (14.3%)	-0.0319	653 (24.8%)	634 (24.1%)	0.0163	806 (15.7%)	793 (15.4%)	0.0083
NephroTox - Thiazide diuretics; n (%)	169 (20.4%)	159 (19.2%)	0.0301	293 (17.4%)	300 (17.8%)	-0.0105	474 (18.0%)	476 (18.1%)	-0.0026	643 (12.5%)	635 (12.3%)	0.0061
NephroTox - Mineralocorticoid receptor antagonist; n (%)	42 (5.1%)	49 (5.9%)	-0.0351	83 (4.9%)	89 (5.3%)	-0.0182	129 (4.9%)	126 (4.8%)	0.0047	171 (3.3%)	175 (3.4%)	-0.0056
NephroTox - NSAIDs; n (%)	142 (17.1%)	133 (16.1%)	0.0269	299 (17.7%)	288 (17.1%)	0.0158	439 (16.7%)	411 (15.6%)	0.0299	581 (11.3%)	544 (10.6%)	0.0224
NephroTox - PPIs; n (%)	202 (24.4%)	193 (23.3%)	0.0258	318 (18.9%)	329 (19.5%)	-0.0152	671 (25.5%)	676 (25.7%)	-0.0046	873 (17.0%)	869 (16.9%)	0.0027
NephroTox - H2RAs; n (%)	51 (6.2%)	40 (4.8%)	0.0614	58 (3.4%)	59 (3.5%)	-0.0055	195 (7.4%)	205 (7.8%)	-0.0151	246 (4.8%)	245 (4.8%)	0.0000
NephroTox - Antivirals/Antiretrovirals/Antimicrobials; n (%)	12 (1.4%)	13 (1.6%)	-0.0165	14 (0.8%)	17 (1.0%)	-0.0212	28 (1.1%)	32 (1.2%)	-0.0094	040 (0.8%)	045 (0.9%)	-0.0109
DM Medications - 1st and 2nd Generation SUs; n (%)	362 (43.7%)	366 (44.2%)	-0.0101	641 (38.0%)	630 (37.3%)	0.0144	1,144 (43.5%)	1,160 (44.1%)	-0.0121	1,506 (29.3%)	1,526 (29.7%)	-0.0088
DM Medications - AGI & Meglitinides; n (%)	17 (2.1%)	17 (2.1%)	0.0000	34 (2.0%)	30 (1.8%)	0.0146	126 (4.8%)	131 (5.0%)	-0.0093	143 (2.8%)	148 (2.9%)	-0.0060
DM Medications - DPP-4 Inhibitors (excluding sitagliptin); n (%)	113 (13.6%)	120 (14.5%)	-0.0259	148 (8.8%)	154 (9.1%)	-0.0105	372 (4.1%)	404 (4.5%)	-0.0367	485 (9.4%)	524 (10.2%)	-0.0269
DM Medications - Glitazones; n (%)	98 (11.8%)	101 (12.2%)	-0.0123	198 (11.7%)	203 (12.0%)	-0.0093	318 (12.1%)	307 (11.7%)	0.0124	416 (8.1%)	408 (7.9%)	0.0074
DM Medications - GLP-1 RA; n (%)	207 (25.0%)	198 (23.9%)	0.0256	312 (18.5%)	332 (19.7%)	-0.0303	497 (18.9%)	460 (17.5%)	0.0363	704 (13.7%)	658 (12.8%)	0.0265
DM Medications - Insulins; n (%)	268 (32.4%)	276 (33.3%)	-0.0192	529 (31.4%)	507 (30.1%)	0.0282	994 (37.8%)	966 (36.7%)	0.0228	1,262 (24.5%)	1,242 (24.1%)	0.0093
DM Medications - Metformin; n (%)	487 (58.8%)	497 (60.0%)	-0.0244	1,019 (60.4%)	1,020 (60.5%)	-0.0020	1,447 (55.0%)	1,468 (55.8%)	-0.0161	1,934 (37.6%)	1,965 (38.2%)	-0.0124
DM Medications - SGLT-2 Inhibitors (excluding dapagliflozin); n (%)	58 (7.0%)	55 (6.6%)	0.0159	138 (8.1%)	158 (9.4%)	-0.0460	161 (6.1%)	158 (6.0%)	0.0042	219 (4.3%)	213 (4.1%)	0.0100
DM Medications - Number of antiDM medications at index date ...mean (sd)	2.80 (0.96)	2.80 (0.96)	0.0000	2.69 (0.87)	2.70 (0.93)	-0.0111	2.82 (0.94)	2.83 (0.99)	-0.0104	2.77 (0.92)	2.78 (0.97)	-0.0106
CV Comorbidity - Acute and Old MI; n (%)	26 (3.1%)	28 (3.4%)	-0.0169	20 (1.2%)	25 (1.5%)	-0.0260	126 (4.8%)	124 (4.7%)	0.0047	152 (3.0%)	152 (3.0%)	0.0000
CV Comorbidity - Any heart failure (HF); n (%)	85 (10.3%)	90 (10.9%)	-0.0195	82 (4.9%)	86 (5.1%)	-0.0092	419 (15.9%)	379 (14.4%)	0.0418	504 (9.8%)	469 (9.1%)	0.0239
CV Comorbidity - Hospitalization for CHF; n (%)	2											

Appendix B: Dapagliflozin vs. Sitagliptin

CV Comorbidity - Implantable cardioverter defibrillator ; n (%)	9 (1.1%)	10 (1.2%)	-0.0094	9 (0.5%)	10 (0.6%)	-0.0135	47 (1.8%)	47 (1.8%)	0.0000	056 (1.1%)	057 (1.1%)	0.0000
CV Comorbidity - CABG/PCI ; n (%)	63 (7.6%)	58 (7.0%)	0.0231	39 (2.3%)	38 (2.3%)	0.0000	268 (10.2%)	260 (9.9%)	0.0100	331 (6.4%)	318 (6.2%)	0.0082
CV Comorbidity - Coronary atherosclerosis and other forms of chronic ischemic heart disease ; n (%)	201 (24.3%)	0.0354	189 (22.8%)	268 (15.9%)	0.0138	260 (15.4%)	912 (34.7%)	865 (32.9%)	0.0381	1,113 (21.6%)	1,054 (20.5%)	0.0270
CV Comorbidity - Hyperlipidemia ; n (%)	690 (83.3%)	686 (82.9%)	0.0107	1,299 (77.0%)	1,281 (75.9%)	0.0259	2,212 (84.1%)	2,200 (83.7%)	0.0109	2,902 (56.4%)	2,886 (56.1%)	0.0060
CV Comorbidity - Stable Angina ; n (%)	35 (4.2%)	33 (4.0%)	0.0101	34 (2.0%)	37 (2.2%)	-0.0139	143 (5.4%)	132 (5.0%)	0.0180	178 (3.5%)	165 (3.2%)	0.0167
CV Comorbidity - Unstable Angina ; n (%)	24 (2.9%)	17 (2.1%)	0.0513	14 (0.8%)	12 (0.7%)	0.0116	42 (1.6%)	37 (1.4%)	0.0165	066 (1.3%)	054 (1.0%)	0.0281
CV Comorbidity - Peripheral Vascular Disease (PVD) or PVD Surgery ; n (%)	76 (9.2%)	89 (10.7%)	-0.0501	62 (3.7%)	72 (4.3%)	-0.0306	415 (15.8%)	405 (15.4%)	0.0110	491 (9.5%)	494 (9.6%)	-0.0034
CV Comorbidity - Stroke/TIA ; n (%)	23 (2.8%)	25 (3.0%)	-0.0119	20 (1.2%)	17 (1.0%)	0.0192	84 (3.2%)	82 (3.1%)	0.0057	107 (2.1%)	107 (2.1%)	0.0000
CV Comorbidity - Pulmonary hypertension/Other pulmonary heart disease ; n (%)	20 (2.4%)	19 (2.3%)	0.0066	16 (0.9%)	16 (0.9%)	0.0000	81 (3.1%)	63 (2.4%)	0.0428	101 (2.0%)	082 (1.6%)	0.0301
CV Medication - Beta blockers ; n (%)	408 (49.3%)	419 (50.6%)	-0.0260	719 (42.6%)	731 (43.3%)	-0.0141	1,478 (56.2%)	1,452 (55.2%)	0.0201	1,886 (36.7%)	1,871 (36.4%)	0.0062
CV Medication - CCBs ; n (%)	243 (29.3%)	267 (32.2%)	-0.0629	500 (29.6%)	484 (28.7%)	0.0198	964 (36.7%)	959 (36.5%)	0.0042	1,207 (23.5%)	1,226 (23.8%)	-0.0071
CV Medication - Digoxin ; n (%)	7 (0.8%)	14 (1.7%)	-0.0811	19 (1.1%)	17 (1.0%)	0.0098	87 (3.3%)	82 (3.1%)	0.0114	094 (1.8%)	096 (1.9%)	-0.0074
CV Medication - Nitrates ; n (%)	68 (8.2%)	72 (8.7%)	-0.0180	65 (3.9%)	67 (4.0%)	-0.0051	266 (10.1%)	246 (9.4%)	0.0236	334 (6.5%)	318 (6.2%)	0.0123
CV Medication - Use of Statins ; n (%)	688 (83.1%)	677 (81.8%)	0.0342	1,240 (73.5%)	1,275 (75.6%)	-0.0482	2,163 (82.2%)	2,135 (81.2%)	0.0259	2,851 (55.4%)	2,812 (54.7%)	0.0141
CV Medication - Use of other lipid-lowering drugs ; n (%)	148 (17.9%)	146 (17.6%)	0.0079	330 (19.6%)	345 (20.5%)	-0.0225	474 (18.0%)	479 (18.2%)	-0.0052	622 (12.1%)	625 (12.1%)	0.0000
CV Medication - Use of other hypertension drugs ; n (%)	75 (9.1%)	79 (9.5%)	-0.0138	156 (9.2%)	167 (9.9%)	-0.0238	372 (14.1%)	341 (13.0%)	0.0321	447 (8.7%)	420 (8.2%)	0.0180
Other Comorbidity - Anemia ; n (%)	150 (18.1%)	127 (15.3%)	0.0751	211 (12.5%)	217 (12.9%)	-0.0120	695 (26.4%)	705 (26.8%)	-0.0091	845 (16.4%)	832 (16.2%)	0.0054
Other Comorbidity - Cancer ; n (%)	78 (9.4%)	91 (11.0%)	-0.0529	106 (6.3%)	116 (6.9%)	-0.0242	346 (13.2%)	341 (13.0%)	0.0059	424 (8.2%)	432 (8.4%)	-0.0072
Other Comorbidity - COPD ; n (%)	86 (10.4%)	85 (10.3%)	0.0033	56 (3.3%)	58 (3.4%)	-0.0056	339 (12.9%)	354 (13.5%)	-0.0177	425 (8.3%)	439 (8.5%)	-0.0072
Other Comorbidity - Dementia ; n (%)	27 (3.3%)	28 (3.4%)	-0.0056	7 (0.4%)	9 (0.5%)	-0.0149	170 (6.5%)	161 (6.1%)	0.0165	197 (3.8%)	189 (3.7%)	0.0053
Other Comorbidity - Depression ; n (%)	105 (12.7%)	100 (12.1%)	0.0182	131 (7.8%)	118 (7.0%)	0.0306	344 (13.1%)	339 (12.9%)	0.0059	449 (8.7%)	439 (8.5%)	0.0071
Other Comorbidity - Fractures ; n (%)	19 (2.3%)	21 (2.5%)	-0.0131	33 (2.0%)	34 (2.0%)	0.0000	108 (4.1%)	99 (3.8%)	0.0154	127 (2.5%)	120 (2.3%)	0.0131
Other Comorbidity - Hypothyroidism ; n (%)	65 (7.9%)	69 (8.3%)	-0.0147	131 (7.8%)	133 (7.9%)	-0.0037	313 (11.9%)	322 (12.2%)	-0.0092	378 (7.3%)	391 (7.6%)	-0.0114
Other Comorbidity - Osteoporosis ; n (%)	45 (5.4%)	46 (5.6%)	-0.0088	18 (1.1%)	25 (1.5%)	0.0353	277 (10.5%)	291 (11.1%)	-0.0193	322 (6.3%)	337 (6.6%)	-0.0122
Other Comorbidity - Pneumonia ; n (%)	19 (2.3%)	21 (2.5%)	-0.0131	33 (2.0%)	27 (1.6%)	0.0301	109 (4.1%)	96 (3.7%)	0.0207	128 (2.5%)	117 (2.3%)	0.0131
Other Comorbidity - Sleep apnea ; n (%)	141 (17.0%)	137 (16.5%)	0.0134	313 (18.6%)	287 (17.0%)	0.0418	409 (15.6%)	389 (14.8%)	0.0223	550 (10.7%)	526 (10.2%)	0.0163
Other Medication - Use of anticonvulsants ; n (%)	171 (20.7%)	178 (21.5%)	-0.0196	279 (16.5%)	262 (15.5%)	0.0273	729 (27.7%)	681 (25.9%)	0.0406	900 (17.5%)	859 (16.7%)	0.0212
Other Medication - Use of antidepressants ; n (%)	219 (26.4%)	214 (25.8%)	0.0137	415 (24.6%)	390 (23.1%)	0.0352	804 (30.6%)	778 (29.6%)	0.0218	1,023 (19.9%)	992 (19.3%)	0.0151
Other Medication - Use of antiparkinsonian meds ; n (%)	25 (3.0%)	24 (2.9%)	0.0059	32 (1.9%)	38 (2.3%)	-0.0279	118 (4.5%)	115 (4.4%)	0.0048	143 (2.8%)	139 (2.7%)	0.0061
Other Medication - Use of dementia meds ; n (%)	21 (2.5%)	16 (1.9%)	0.0409	0 (0.0%)	3 (0.2%)	-0.0633	124 (4.7%)	125 (4.8%)	-0.0047	145 (2.8%)	141 (2.7%)	0.0061
Other Medication - Use of antipsychotics ; n (%)	22 (2.7%)	22 (2.7%)	0.0000	21 (1.2%)	22 (1.3%)	-0.0090	87 (3.3%)	89 (3.4%)	-0.0056	109 (2.1%)	111 (2.2%)	-0.0069
Other Medication - Use of anxiolytics/hypnotics ; n (%)	52 (6.3%)	51 (6.2%)	0.0041	122 (7.2%)	111 (6.6%)	0.0237	207 (7.9%)	197 (7.5%)	0.0150	259 (5.0%)	248 (4.8%)	0.0093
Other Medication - Use of Benzodiazepines ; n (%)	79 (9.5%)	98 (11.8%)	-0.0746	167 (9.9%)	167 (9.9%)	0.0000	340 (12.9%)	334 (12.7%)	0.0060	419 (8.1%)	432 (8.4%)	-0.0109
Other Medication - Use of COPD/asthma meds ; n (%)	166 (20.0%)	169 (20.4%)	-0.0100	277 (16.4%)	268 (15.9%)	0.0136	590 (22.4%)	581 (22.1%)	0.0072	756 (14.7%)	750 (14.6%)	0.0028
Other Medication - Use of antiplatelet agents ; n (%)	94 (11.4%)	104 (12.6%)	-0.0369	238 (14.1%)	234 (13.9%)	0.0058	446 (16.9%)	434 (16.5%)	0.0107	538 (10.5%)	538 (10.5%)	0.0000
Other Medication - Use of oral anticoagulants ; n (%)	77 (9.3%)	68 (8.2%)	0.0389	81 (4.8%)	93 (5.5%)	-0.0317	346 (13.2%)	338 (12.9%)	0.0089	423 (8.2%)	406 (7.9%)	0.0110
Other Medication - Use of opioids ; n (%)	190 (22.9%)	188 (22.7%)	0.0048	419 (24.8%)	410 (24.3%)	0.0116	708 (26.9%)	717 (27.3%)	-0.0090	898 (17.5%)	905 (17.6%)	-0.0026
Lifestyle - Alcohol/Drug Abuse or Dependence ; n (%)	22 (2.7%)	15 (1.8%)	0.0607	18 (1.1%)	17 (1.0%)	0.0098	40 (1.5%)	43 (1.6%)	-0.0081	662 (1.2%)	658 (1.1%)	0.0094
Lifestyle - Obesity ; n (%)	267 (32.2%)	255 (30.8%)	0.0301	383 (22.7%)	393 (23.3%)	-0.0143	830 (31.6%)	771 (29.3%)	0.0500	1,097 (21.3%)	1,026 (19.9%)	0.0346
Lifestyle - Smoking ; n (%)	88 (10.6%)	92 (11.1%)	-0.0161	88 (5.2%)	77 (4.6%)	0.0278	390 (14.8%)	388 (14.8%)	0.0000	478 (9.3%)	480 (9.3%)	0.0000
HU - Number of Cardiologist visits ...mean (sd)	1.74 (4.42)	1.67 (4.26)	0.0161	0.90 (3.32)	0.86 (2.40)	0.0138	2.18 (5.13)	2.06 (5.04)	0.0236	1.69 (4.50)	1.60 (4.22)	0.0206
HU - Number of Nephrologist visit ...mean (sd)	0.56 (2.07)	0.49 (1.76)	0.0364	0.36 (2.09)	0.39 (1.74)	-0.0156	0.70 (2.81)	0.68 (3.92)	0.0059	0.57 (2.48)	0.55 (3.06)	0.0072
HU - Number of Endocrinologist visits ...mean (sd)	0.90 (3.46)	1.04 (3.30)	-0.0414	0.86 (3.63)	0.88 (2.85)	-0.0061	1.50 (5.97)	1.31 (4.51)	0.0359	1.19 (4.95)	1.13 (4.95)	0.0135
HU - Number of Internal Medicine/Family Medicine Visits ...mean (sd)	13.24 (19.07)	12.07 (16.06)	0.0664	7.27 (7.85)	7.76 (8.89)	-0.0584	10.39 (14.68)	10.73 (14.87)	-0.0230	9.83 (13.74)	9.97 (13.43)	-0.0103
HU - Number of Emergency Department (ED) visits ...mean (sd)	0.56 (1.88)	0.54 (1.87)	0.0107	0.20 (1.55)	0.19 (1.62)	0.0063	0.60 (1.52)	0.55 (1.35)	0.0348	0.46 (1.59)	0.43 (1.53)	0.0192
HU - Number of Distinct Medication Prescriptions (not generalized to generics) ...mean (sd)	33.68 (29.55)	33.35 (20.44)	0.0130	26.94 (17.22)	26.88 (16.42)	0.0036	35.51 (26.27)	35.61 (25.53)	-0.0039	32.41 (24.30)	32.38 (22.11)	0.0013
HU - Number of Echocardiogram ...mean (sd)	0.29 (1.50)	0.31 (1.59)	-0.0129	0.13 (0.52)	0.12 (0.42)	0.0212	0.22 (0.60)	0.23 (0.65)	-0.0160	0.20 (0.80)	0.21 (0.82)	-0.0123
HU - Number of ECG performed ...mean (sd)	0.77 (1.86)	0.77 (1.85)	0.0000	0.51 (1.17)	0.47 (0.96)	0.0374	0.87 (1.61)	0.85 (1.59)	0.0125	0.74 (1.53)	0.71 (1.46)	0.0201
HU - Number of hbA1c tests ordered ...mean (sd)	1.55 (1.11)	1.50 (0.92)	0.0490	1.36 (0.96)	1.36 (0.93)	0.0000	1.70 (0.98)	1.71 (0.97)	-0.0103	1.56 (1.00)	1.56 (0.95)	0.0000
HU - Number of Hospitalizations during CAP ...mean (sd)	0.12 (0.44)	0.12 (0.44)	0.0000	0.08 (0.33)	0.08 (0.32)	0.0000	0.14 (0.47)	0.13 (0.44)	0.0220	0.12 (0.42)	0.11 (0.40)	0.0244
HU - Recent hospitalizations (>30 days to Index Rx date) ; n (%)	9 (1.1%)	13 (1.6%)	-0.0433	19 (1.1%)	18 (1.1%)	0.0000	38 (1.4%)	35 (1.3%)	0.0087	047 (0.9%)	048 (0.9%)	0.0000
HU - Old hospitalizations (>180 to <31 days) ; n (%)	69 (8.3%)	72 (8.7%)	-0.0143	99 (5.9%)	99 (5.9%)	0.0000	240 (9.1%)	243 (9.2%)	-0.0035	309 (6.0%)	315 (6.1%)	-0.0042
HU - Mammogram ; n (%)	92 (11.1%)	104 (12.6%)	-0.0464	164 (9.7%)	154 (9.1%)	0.0206	284 (10.8%)	285 (10.8%)	0.0000	376 (7.3%)	389 (7.6%)	-0.0114
HU - Pap smear ; n (%)	15 (1.8%)	18 (2.2%)	-0.0286	67 (4.0%)	71 (4.2%)	-0.0101	49 (1.9%)	46 (1.7%)	0.0150	064 (1.2%)	064 (1.2%)	0.0000
HU - Prostate exam for DRE ; n (%)	41 (5.0%)	37 (4.5%)	0.0235	80 (4.7%)	76 (4.5%)	0.0095	171 (6.5%)	178 (6.8%)	-0.0120	212 (4.1%)	215 (4.2%)	-0.0050
HU - Flexible Sigmoidoscopy or colonoscopy or CT virtual colonoscopy ; n (%)	29 (3.5%)	32 (3.9%)	-0.0212	90 (5.3%)	92 (5.5%)	-0.0088	109 (4.1%)	128 (4.9%)	-0.0386	138 (2.7%)	160 (3.1%)	-0.0238
HU - Bone mineral density ; n (%)	33 (4.0%)	37 (4.5%)	-0.0248	32 (1.9%)	37 (2.2%)	-0.0212	124 (4.7%)	130 (4.9%)	-0.0094	157 (3.1%)	167 (3.2%)	-0.0057
HU - Flu vaccine ; n (%)	191 (23.1%)	186 (22.5%)	0.0143	307 (18.2%)	305 (18.1%)	0.0026	925 (35.2%)	906 (34.4%)	0.0168	1,116 (21.7%)	1,092 (21.2%)	0.0122
HU - Pneumococcal vaccine ; n (%)	192 (23.2%)	185 (22.3%)	0.0215	227 (13.5%)	244 (14.5%)	-0.0288	838 (31.9%)	831 (31.6%)	0.0064	1,030 (20.0%)	1,016 (19.7%)	0.0075
Lab - Occurrence of 24-hour urine test ; n (%)	331 (40.0%)	347 (41.9%)	-0.0386	653 (38.7%)	648 (38.4%)	0.0062	1,085 (41.3%)	1,076 (40.9%)	0.0081	1,416 (27.5%)	1,423 (27.7%)	-0.0045
Lab - Occurrence of creatinine test ordered ; n (%)	48 (5.8%)	50 (6.0%)	-0.0085	71 (4.2%)	70 (4.1%)	0.0050	203 (7.7%)	188 (7.1%)	0.0229	251 (4.9%)	238 (4.6%)	0.0141
Lab - Occurrence of urine albumin test ordered ; n (%)	412 (49.8%)	445 (53.7%)	-0.0781	748 (44.3%)	739 (43.8%)	0.0101	1,222 (46.5%)	1,242 (47.2%)	-0.0140	1,634 (31.8%)	1,687 (32.8%)	-0.0214
Lab - Occurrence of HgA1c test ; n (%)	3											

Appendix B: Dapagliflozin vs. Sitagliptin

SES Proxy - Insurance Plan type												
...Comprehensive; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	117 (6.9%)	132 (7.8%)	-0.0345	0 (0.0%)	0 (0.0%)	#DIV/0!	117 (2.3%)	132 (2.6%)	-0.0194
...HMO; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	161 (9.5%)	176 (10.4%)	-0.0301	0 (0.0%)	0 (0.0%)	#DIV/0!	161 (3.1%)	176 (3.4%)	-0.0169
...PPO; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	924 (54.8%)	918 (54.4%)	0.0080	0 (0.0%)	0 (0.0%)	#DIV/0!	924 (18.0%)	918 (17.8%)	0.0052
...Others; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	485 (28.7%)	461 (27.3%)	0.0312	0 (0.0%)	0 (0.0%)	#DIV/0!	485 (9.4%)	461 (9.0%)	0.0138
SES Proxy - Dual status code (with Medicaid); n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	778 (29.6%)	817 (31.1%)	-0.0326	778 (15.1%)	817 (15.9%)	-0.0221