

SUPPLEMENTARY DATA

Supplementary Table 1. Codes and medications used in study

Codes and medications used for selection of study population	
Category	Codes/Medications
Dipeptidyl-peptidase 4 inhibitors	<i>See table A4 below; Note that alogliptin and co-formulations thereof are not used for intra-class comparison</i>
Sulfonylurea	<i>See Table A4 below</i>
Type 2 diabetes mellitus	ICD-9-CM Dx: 250.x0, 250.x2
Hospitalization for heart failure	<i>See Table A2 below</i>
Pregnancy	ICD-9-CM Px: 72.xx-75.xx ICD-9-CM Dx: 630.xx-648.7x, 648.9x-679.xx, V22.xx-V23.xx, V27.xx, V28.xx, V61.6x-V61.7x, V72.42, V91.xx MS-DRG: 765-770, 774, 775, 777-779 CPT: 57022, 58605, 58611, 59000-59899, 76801-76828, 76941, 83661-83664, S0612, S0613, S2400-S2405, S2409, S2411, S8055, 01965, 01966, 0500F, 0501F, 0503F
Gestational diabetes	ICD-9-CM Dx: 648.8x
Type 1 diabetes mellitus	ICD-9-CM Dx: 250.x1, 250.x3
Codes used for measurement of outcome variables	
Category	Codes
Hospitalization for heart failure	ICD-9-CM Dx: 428.xx
Hospitalization for acute myocardial infarction	ICD-9-CM Dx: 410.xx
Hospitalization for stroke	ICD-9-CM Dx: 430.xx, 431.xx, 433.x1, 434.x1, 436.xx
Hospitalization for unstable angina	ICD-9-CM Dx: 411.1x
Coronary revascularization	ICD-9-CM Px: 00.66, 17.55, 36.06, 36.07, 36.1x CPT: 33510-33519, 33521, 33522, 33523, 33530, 33533, 33534, 33535, 33536, 92980-92984, 92920-92921, 92928, 92929, 92995, 92996, 92924, 92925, 92933, 92934, 92937, 92938, 92941, 92943, 92944 HCPCS: S2205-S2209, G0290, G0291, C9600-C9608
Codes used for measurement of baseline cardiovascular disease	
Category	Codes
Acute myocardial infarction	ICD-9-CM Dx: 410.xx
Other ischemic heart disease	ICD-9-CM Dx: 411.xx-414.xx
Other heart disease	ICD-9-CM Dx: 402.01, 402.11, 402.91, 420.xx-429.xx, 440.xx
Stroke (narrow)	ICD-9-CM Dx: 430, 431, 433.x1, 434.x1, 436
Stroke (broad)	ICD-9-CM Dx: 430, 431, 432.xx, 433.xx, 434.xx, 436

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PAD	ICD-9-CM Dx: 443.9
Coronary revascularization procedures	<i>See subcategories</i>
Coronary artery bypass graft	ICD-9-CM Px: 36.1x CPT: 33510, 33511, 33512, 33513, 33514, 33516, 33517, 33518, 33519, 33521, 33522, 33523, 33530, 33533, 33534, 33535, 33536, HCPCS: S2205-S2209
Percutaneous coronary intervention	ICD-9-CM Px: 0.66, 17.55, 36.06, 36.07 CPT: 92920, 92921, 92924, 92925, 92928, 92929, 92933, 92934, 92937, 92938, 92941, 92943, 92944, 92980, 92981, 92982, 92984, 92995, 92996 HCPCS: C9600, C9601, C9602, C9603, C9604, C9605, C9606, C9607, C9608, G0290, G0291
Carotid revascularization procedures	<i>See subcategories</i>
Carotid endarterectomy, stenting, angioplasty, or atherectomy	ICD-9-CM Px: 00.61, 00.63, 38.11, 38.12 CPT: 35301, 35390, 37215, 37216
Carotid bypass	ICD-9-CM Px: 39.28 CPT: 35501, 35601
Lower extremity revascularization procedures	<i>See subcategories</i>
Lower extremity endarterectomy, stenting, angioplasty, or atherectomy	ICD9-CM: 17.56, 38.18, 39.50, 39.90 CPT: 35302, 35303, 35304, 35305, 35306, 35351, 35355, 35361, 35363, 35371, 35372, 35454, 35456, 35458, 35459, 35460, 35470, 35473, 35474, 35475, 35476, 35482, 35483, 35484, 35485, 35492, 35493, 35494, 35495, 37205, 37206, 37207, 37208, 37220, 37221, 37222, 37223, 37224, 37225, 37226, 37227, 37228, 37229, 37230, 37231, 37232, 37233, 37234, 37235, 0237T, 0238T
Lower extremity bypass	ICD-9-CM Px: 39.25, 39.29 CPT: 34520, 34530, 35521, 35533, 35541, 35546, 35548, 35549, 35551, 35556, 35558, 35563, 35565, 35566, 35570, 35571, 35582, 35583, 35585, 35587, 35621, 35623, 35637, 35638, 35641, 35646, 35647, 35651, 35654, 35656, 35661, 35663, 35665, 35666, 35671, 35681, 35682, 35683, 35879
Lower extremity amputation	ICD-9-CM Px: 84.1x CPT: 27290, 27295, 27590, 27591, 27592, 27596, 27598, 27880, 27881, 27882, 27886, 27888, 27889, 28800, 28805, 28810, 28820, 28825
Codes and medications used for measurement of other effect modifiers and potential confounders	
Category	Codes/Medications
Lab Tests Ordered	<i>See subcategories</i>
Blood urea nitrogen	CPT: 80047, 80048, 80053, 80069, 84520, 84525, 84540, 84545
Creatinine	CPT: 80047, 80048, 80053, 80069, 82565, 82570, 82575

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HbA1c	CPT: 83036, 83037
Asthma	ICD-9-CM Dx: 493.xx
Cancer (excluding non-melanoma skin cancer)	ICD-9-CM Dx: 140.xx-172.xx, 174.xx-209.3x, 209.7x
Chronic kidney disease (excluding end stage renal disease)	ICD-9-CM Dx: 585.1-585.4 HCPCS: G0420, G0421
Chronic obstructive pulmonary disease	ICD-9-CM Dx: 491.xx, 492.xx, 496
Dementia	ICD-9-CM Dx: 290.0 , 290.1x, 290.2x, 290.3, 290.4x, 290.8, 290.9, 291.2, 292.82, 294.0, 294.1x, 294.2x, 294.8, 331.0 , 331.1x, 331.2, 331.7, 331.8x, 331.9, 797
Depression	ICD-9-CM Dx: 296.2x, 296.3x, 300.4, 311
End stage renal disease	ICD-9-CM Px: 38.95, 39.27, 39.42, 39.95, 54.98, 55.52, 55.53, 55.54, 55.69, ICD-9-CM Dx: 285.21, 403.01, 403.11, 403.91, 404.02, 404.03, 404.12, 404.13, 404.92, 404.93, 458.21, 584.5, 584.6, 584.7, 584.8, 584.9, 585.5, 585.6, 586, 792.5, 996.56, 996.68, 996.73, 996.81, V42.0, V45.1x, V56.xx, E879.1, CPT: 36145, 36800–36815, 36825–36833, 50340, 50370, 76776, 76778, 90918–90999, 93990, 99512, 0505F, 0507F, 4052F, 4053F, 4054F, 4055F HCPCS: A4690, E1510, E1590, E1592, E1594, E1630, E1632, E1635, G0257, G0320, G0321, G0322, G0323, G0324, G0325, G0326, G0327, G8075, G8076, G8081, G8082, G8085, G8488, J0636, J0881, J0882, J0885, J0886, Q4054, Q4055, S9335, S9339 UB-04: 0304, 0367, 080x, 082x, 083x, 084x, 085x, 086x, 087x, 088x
Fracture	ICD-9-CM Dx: 733.1, 733.93-733.98, 805.xx-807.4x, 808.xx-825.xx, 827.xx, V54.13, V54.23 ICD-9CM Px: 79.01,79.02, 79.05, 79.06, 79.11, 79.12, 79.15, 79.16, 79.21, 79.22, 79.25, 79.26, 79.31, 79.32, 79.35, 79.36, 79.61, 79.62, 79.65, 79.6, 81.65, 81.66
Human immunodeficiency virus/acquired immune deficiency syndrome	ICD-9-CM Dx: 042, 043, 044, 795.71, V08, 079.53
Hyperlipidemia or lipid disorder	ICD-9-CM Dx: 272.0-272.2, 272.4
Hypertension	ICD-9-CM Dx: 401.xx, 402.00, 402.1, 402.10, 402.90, 403.xx-405.xx
Hypoglycemia	ICD-9-CM Dx: 250.8x, 251.0-251.2
Liver disease	ICD-9-CM Dx: 570, 571.xx, 572.xx, 573.xx
Microvascular complications of diabetes	<i>See subcategories</i>
Nephropathy	ICD-9-CM Dx: 250.4x
Retinopathy	ICD-9-CM Dx: 250.5x, 362.0x
Peripheral neuropathy	ICD-9-CM Dx: 250.6x, 337.1, 354.xx, 355.xx, 357.2
Obesity (or weight gain)	ICD-9-CM Dx: 278.0x, 793.91, V85.3x, V85.4x, 783.1
Osteoporosis	ICD-9-CM Dx: 733.0x

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Tobacco use	ICD-9-CM Dx: 305.1, V15.82
Andiabetes medications	<i>See subcategories</i>
Alpha-glucosidase inhibitors	Acarbose, Miglitol
Amylin analogs	Pramlintide Acetate
Biguanides (metformin)	Metformin Hcl
Dipeptidyl-peptidase 4 inhibitors	Alogliptin Benzoate, Linagliptin, Saxagliptin Hcl, Sitagliptin Phosphate
Glucagon-like peptide-1 receptor agonists	Exenatide, Liraglutide
Insulin	<i>See subcategories</i>
Long-acting and combination	Insulin Aspart Protamine Human/Insulin Aspart, Insulin Detemir, Insulin Glargine, Human Recombinant Analog, Insulin Lispro Protamine & Insulin Lispro, Insulin Nph Human Semi-Syn, Insulin Nph Human Semi-Syn/Insulin Reg Human Semi-Syn, Insulin Zinc Extend Human Rec, Insulin Zinc Human Rec, Insulin Zinc Human Semi-Syn, Nph, Human Insulin Isophane, Nph, Human Insulin Isophane/Insulin Regular, Human
Short-acting	Insulin Aspart, Insulin Glulisine, Insulin Lispro, Insulin Reg Human Semi-Syn, Insulin Reg, Hum S-S Buff, Insulin Regular, Human, Insulin Regular, Human/Insulin Release Unit, Insulin Regular, Human/Insulin Release Unit/Chamber/Inhaler, Insulin Regular, Human Buffered
Meglitinides	Nateglinide, Repaglinide
Sodium- glucose cotransporter 2 inhibitors	Canagliflozin, Dapagliflozin Propanediol, Empagliflozin
Sulfonylureas	Acetohexamide, Chlorpropamide, Glimpiride, Glipizide, Glyburide, Nateglinide, Repaglinide, Tolazamide, Tolbutamide
Thiazolidinedioines	Pioglitazone Hcl, Rosiglitazone Maleate, Troglitazone
Antihypertensive medications	<i>See subcategories</i>
Angiotensin converting enzyme inhibitors	Benazepril Hcl, Captopril, Enalapril Maleate, Fosinopril Sodium, Lisinopril, Moexipril Hcl, Perindopril Erbumine, Quinapril Hcl, Ramipril, Trandolapril
Alpha-blockers	Doxazosin Mesylate, Phenoxybenzamine Hcl, Prazosin Hcl, Terazosin Hcl
Angiotensin II receptor blockers	Azilsartan Medoxomil, Candesartan Cilexetil, Eprosartan Mesylate, Irbesartan, Losartan Potassium, Olmesartan Medoxomil, Telmisartan, Valsartan
Beta-blockers	Acebutolol Hcl, Atenolol, Betaxolol Hcl, Bisoprolol Fumarate, Carteolol Hcl, Metoprolol Succinate, Metoprolol Tartrate, Nadolol, Nebivolol Hcl, Penbutolol Sulfate, Pindolol, Propranolol Hcl, Timolol Maleate
Calcium channel blockers	Amlodipine Besylate, Diltiazem Hcl, Diltiazem Malate, Felodipine, Isradipine, Mibefradil Di-Hcl, Nicardipine Hcl, Nifedipine, Nimodipine, Nisoldipine, Verapamil Hcl
Direct vasodilators	Hydralazine Hcl, Isosorbide Dinitrate/Hydralazine Hcl,

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	Minoxidil
Direct renin inhibitors	Aliskiren Hemifumarate
Diuretics	<i>See subcategories</i>
Aldosterone antagonists	Eplerenone, Spironolactone
Loop diuretics	Bumetanide, Ethacrynic Acid, Furosemide, Torsemide
Potassium sparing diuretics	Amiloride Hcl, Triamterene
Thiazide diuretics	Bendroflumethiazide, Chlorothiazide, Chlorthalidone, Hydrochlorothiazide, Hydroflumethiazide, Indapamide, Methyclothiazide, Metolazone, Polythiazide, Trichlormethiazide
Lipid lowering medications	Amlodipine Besylate/Atorvastatin Calcium, Aspirin (Calcium Carb & Magnesium Buffers)/Pravastatin, Atorvastatin Calcium, Cerivastatin Sodium, Cholestyramine (With Sugar), Cholestyramine/Aspartame, Clofibrate, Colesevelam Hcl, Colestipol Hcl, Dextrothyroxine Sodium, Docosahexanoic Acid/Eicosapentaenoic Acid, Ezetimibe, Ezetimibe/Atorvastatin Calcium, Ezetimibe/Simvastatin, Fenofibrate, Fenofibrate Nanocrystallized, Fenofibrate, Micronized, Fenofibric Acid, Fenofibric Acid (Choline), Fish Oil/Omega-3 Fatty Acids/DI-Vit E/Folic Acid/B6-B12, Fluvastatin Sodium, Gemfibrozil, Icosapent Ethyl, Inositol/Choline/Multivitamin, Lomitapide Mesylate, Lovastatin, Methionine/Inositol/Choline/Folic Acid, Mipomersen Sodium, Niacin, Niacin/Lovastatin, Niacin/Simvastatin, Omega-3 Acid Ethyl Esters, Omega-3 Fatty Acids/Dha/Epa/Other Omega-3S/Fish Oil, Omega-3/Dha/Epa/Marine Phospholipids/Astaxanthin/Krill Oil, Phytosterol/Omega-3 Fatty Acids/Dha/Epa/Fish Oil, Pitavastatin Calcium, Pravastatin Sodium, Rosuvastatin Calcium, Simvastatin
Digoxin (cardiac glycoside)	Digoxin
Anticoagulants	Anisindione, Apixaban, Dabigatran Etexilate Mesylate, Dicumarol, Rivaroxaban, Warfarin Sodium
Anti-platelets	Anagrelide Hcl, Aspirin/Dipyridamole, Cilostazol, Clopidogrel Bisulfate, Dipyridamole, Prasugrel Hcl, Ticagrelor, Ticlopidine Hcl, Vorapaxar Sulfate
Opioids	Acetaminophen With Codeine Phosphate, Aspirin/Codeine Phosphate, Buprenorphine, Butalbital/Acetaminophen/Caffeine/Codeine Phosphate, Butorphanol Tartrate, Codeine Phosphate, Codeine Phosphate/Butalbital/Aspirin/Caffeine, Codeine Phosphate/Carisoprodol/Aspirin, Codeine Sulfate, Codeine/Aspirin/Salicylamide/Acetaminophen/Caffeine, Dihydrocodeine Bitartrate/Acetaminophen/Caffeine, Dihydrocodeine Bitartrate/Aspirin/Caffeine, Dihydrocodeine/Aspirin/Caffeine, Fentanyl, Fentanyl Citrate, Hydrocodone Bitartrate, Hydrocodone Bitartrate/Acetaminophen, Hydrocodone

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	<p>Bitartrate/Acetaminophen/Dietary Supplement #11, Hydrocodone Bitartrate/Aspirin, Hydrocodone/Ibuprofen, Hydromorphone Hcl, Ibuprofen/Oxycodone Hcl, Levomethadyl Acetate Hcl, Levorphanol Tartrate, Meperidine Hcl, Meperidine Hcl/Promethazine Hcl, Methadone Hcl, Morphine Sulfate, Morphine Sulfate/Naltrexone Hcl, Oxycodone Hcl, Oxycodone Hcl/Acetaminophen, Oxycodone Hcl/Aspirin, Oxycodone Hcl/Oxycodone Terephthalate/Aspirin, Oxycodone/Aspirin, Oxymorphone Hcl, Pentazocine Hcl/Acetaminophen, Pentazocine Hcl/Aspirin, Pentazocine Hcl/Naloxone Hcl, Propoxyphene Hcl, Propoxyphene Hcl/Acetaminophen, Propoxyphene Hcl/Aspirin/Caffeine, Propoxyphene Napsylate, Propoxyphene Napsylate/Acetaminophen, Tapentadol Hcl, Tramadol Hcl, Tramadol Hcl/Acetaminophen, Tramadol Hcl/Dietary Supplement, Misc. Cb.11, Tramadol Hcl/Glucosamine Sulfate</p>
<p>Oral corticosteroids</p>	<p>Betamethasone, Cortisone Acetate, Dexamethasone, Fludrocortisone Acetate, Hydrocortisone, Hydrocortisone Cypionate, Methylprednisolone, Prednisolone, Prednisolone Acetate, Prednisolone Sod Phosphate, Prednisolone Sodium Phosphate/Peak Flow Meter, Prednisone, Triamcinolone, Triamcinolone Diacetate</p>
<p>Patients who met criteria which approximated the cardiovascular risk criteria of SAVOR-TIMI</p>	<p>Age 40+ plus one of the following conditions/procedures during the baseline period: atherosclerosis, acute myocardial infarction, stroke (based on the narrow definition), heart failure, unstable angina, percutaneous coronary intervention, or coronary artery bypass graft; or criteria below:</p> <p>Age 55+ (male) or 60+ (female) plus one of the following conditions during the baseline period: dyslipidemia, hypertension, or tobacco use disorder</p>

CPT = Current Procedural Terminology; Dx = diagnosis; HCPCS = Healthcare Common Procedure Coding System; ICD-9-CM = International Classification of Diseases, 9th Revision, Clinical Modification; MS-DRG = Medicare severity diagnosis-related group; Px = procedure; SAVOR-TIMI = Saxagliptin Assessment of Vascular Outcomes Recorded in Patients with Diabetes Mellitus (SAVOR)—Thrombolysis in Myocardial Infarction (TIMI) 53 trial

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Supplementary Table 2. Characteristics of DPP-4i and SU cohorts after propensity score matching*

	Baseline CVD		No Baseline CVD	
	DPP-4is	SUs	DPP-4is	SUs
	N=27,259	N=27,259	N=82,019	N=82,019
Age in years, mean (SD)	63.9 (11.8)	63.9 (12.0)	54.7 (10.9)	54.8 (11.1)
Age Group, %				
18-34	0.5%	0.7%	3.3%	3.5%
35-44	4.0%	4.2%	13.9%	13.9%
45-54	15.7%	15.8%	30.7%	30.3%
55-64	37.6%	37.3%	37.7%	37.8%
65-79	30.7%	30.1%	12.4%	12.2%
80+	11.4%	12.0%	2.0%	2.2%
Sex, %				
Male	60.1%	59.9%	52.9%	52.7%
Female	39.9%	40.1%	47.1%	47.3%
Insurance Plan Type, %				
Comprehensive	21.7%	21.5%	8.7%	8.8%
Exclusive provider organization	1.0%	1.0%	1.2%	1.2%
Health maintenance organization	11.6%	11.4%	13.4%	13.2%
Point of service	6.4%	6.5%	7.9%	8.0%
Preferred provider organization	51.2%	51.4%	57.5%	57.5%
Point of service with capitation	0.4%	0.4%	0.5%	0.5%
Consumer-directed health plan	2.7%	2.6%	4.6%	4.7%
High-deductible health plan	1.1%	1.0%	1.8%	1.8%
Unknown	4.0%	4.2%	4.3%	4.3%

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Payer, %				
Commercial	56.7%	56.8%	85.1%	85.0%
Medicare	43.3%	43.2%	14.9%	15.0%
Index Year, %				
2010	11.3%	11.2%	11.1%	11.1%
2011	34.9%	34.6%	35.3%	35.2%
2012	36.3%	36.5%	37.0%	36.9%
2013	17.6%	17.6%	16.7%	16.8%
Geographic Region, %				
Northeast	21.6%	21.9%	15.5%	15.6%
North Central	24.9%	25.1%	22.0%	22.2%
South	40.1%	39.7%	46.1%	46.1%
West	12.4%	12.3%	15.1%	14.9%
Unknown	1.0%	1.0%	1.3%	1.3%
Population Density, %				
Urban	82.6%	82.5%	81.9%	82.0%
Rural	16.7%	16.8%	17.2%	17.1%
Unknown	0.7%	0.7%	0.9%	0.9%
Healthcare Utilization (Baseline)				
Hospitalization in 30 days pre-index, %	8.8%	9.1%	1.4%	1.5%
Hospitalization in 31-365 days pre-index, %	23.1%	23.2%	4.2%	4.3%
Emergency room visit in 30 days pre-index, %	8.8%	9.1%	3.8%	3.8%
Emergency room visit in 31-365 days pre-index, %	32.4%	32.5%	16.2%	16.2%

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Outpatient office visits during baseline, mean (SD)	11.3 (8.1)	11.3 (8.9)	6.5 (5.0)	6.5 (5.7)
Outpatient medications during baseline, mean (SD)	16.8 (9.1)	16.8 (9.2)	11.7 (6.9)	11.8 (7.2)
Residence in nursing home or stay in other non-hospital institution during baseline, %	8.1%	8.1%	1.8%	1.8%
Cardiologist visit during baseline, %	64.3%	65.0%	9.1%	9.1%
Creatinine test ordered during baseline, %	67.1%	67.3%	73.0%	72.7%
HbA1c test ordered during baseline, %	64.5%	64.7%	79.4%	79.3%
Blood urea nitrogen test ordered during baseline, %	63.7%	64.1%	68.0%	67.9%
Comorbid Conditions (Baseline), %				
Asthma	7.3%	7.3%	4.8%	4.8%
Cancer (excluding non-melanoma skin cancer)	10.0%	10.1%	4.6%	4.6%
Chronic kidney disease (excluding ESRD)	6.8%	6.9%	1.9%	1.9%
Chronic obstructive pulmonary disease	11.0%	11.0%	2.4%	2.4%
Dementia	3.1%	3.2%	0.4%	0.4%
Depression	8.4%	8.4%	6.3%	6.3%
ESRD	7.2%	7.1%	1.2%	1.2%
Fracture	3.6%	3.7%	1.8%	1.8%
HIV/AIDS	0.1%	0.1%	0.2%	0.2%
Hyperlipidemia or lipid disorder	57.7%	58.0%	44.3%	44.2%
Hypertension	75.5%	75.5%	53.7%	53.8%
Hypoglycemia	4.1%	4.2%	1.8%	1.8%
Liver disease	3.2%	3.3%	2.4%	2.3%
Microvascular complications of diabetes				
Nephropathy	4.4%	4.5%	2.2%	2.2%
Peripheral neuropathy	14.0%	14.2%	6.9%	7.0%
Retinopathy	7.7%	7.6%	5.0%	4.9%
Obesity (or weight gain)	13.6%	13.8%	10.5%	10.5%

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Osteoporosis	2.2%	2.1%	0.9%	0.9%
Tobacco use	5.9%	5.8%	2.9%	2.9%
CVD-Related Conditions (Baseline), %				
Heart failure	13.9%	14.2%	0.0%	0.0%
Hospitalized heart failure	1.0%	1.1%	0.0%	0.0%
Acute myocardial infarction	4.8%	5.0%	0.0%	0.0%
Other ischemic heart disease	53.6%	53.6%	0.0%	0.0%
Other heart disease	59.6%	59.7%	0.0%	0.0%
Stroke (narrow)	1.7%	1.8%	0.0%	0.0%
Stroke (broad)	18.1%	18.2%	0.0%	0.0%
Peripheral artery disease	10.6%	10.7%	0.0%	0.0%
Coronary revascularization procedures				
Coronary artery bypass graft	2.1%	2.1%	0.0%	0.0%
Percutaneous coronary intervention	4.5%	4.6%	0.0%	0.0%
Carotid revascularization procedures				
Carotid endarterectomy, stenting, angioplasty, or atherectomy	0.4%	0.5%	0.0%	0.0%
Carotid bypass	0.0%	0.0%	0.0%	0.0%
Lower extremity revascularization procedures				
Lower extremity endarterectomy, stenting, angioplasty, or atherectomy	1.2%	1.2%	0.0%	0.0%
Lower extremity bypass	0.2%	0.2%	0.0%	0.0%
Lower extremity amputation	0.4%	0.5%	0.0%	0.0%
Anti-hyperglycemic Medications (180 Days Pre-Index), %				
Alpha-glucosidase inhibitors	0.3%	0.3%	0.2%	0.2%
Amylin analogs	0.1%	0.0%	0.0%	0.0%
Biguanides (metformin)	67.6%	67.3%	78.9%	78.3%

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DPP-4is	n/a	n/a	n/a	n/a
Glucagon-like peptide-1 receptor agonists	2.5%	2.7%	3.0%	3.3%
Insulin (long-acting, combination)	10.2%	10.5%	7.1%	7.1%
Insulin (short-acting)	4.4%	4.4%	2.0%	2.0%
Meglitinides	2.2%	1.9%	1.1%	1.0%
Sodium- glucose cotransporter 2 inhibitors	0.0%	0.0%	0.0%	0.0%
Sulfonylureas	n/a	n/a	n/a	n/a
Thiazolidinedioines	15.6%	15.4%	15.5%	15.5%
Any anti-hyperglycemic medication	71.2%	72.3%	75.0%	75.5%
Number of anti-hyperglycemic medication classes, mean (SD)	2.0 (0.7)	2.0 (0.8)	2.1 (0.6)	2.1 (0.7)
Anti-hyperglycemic Medications (Baseline), %				
Alpha-glucosidase inhibitors	0.3%	0.3%	0.2%	0.2%
Amylin analogs	0.1%	0.1%	0.1%	0.1%
Biguanides (metformin)	71.4%	71.3%	82.3%	81.9%
DPP-4is	n/a	n/a	n/a	n/a
Glucagon-like peptide-1 receptor agonists	3.2%	3.5%	4.0%	4.2%
Insulin (long-acting, combination)	11.3%	11.6%	7.7%	7.7%
Insulin (short-acting)	5.3%	5.2%	2.4%	2.4%
Meglitinides	2.5%	2.3%	1.2%	1.1%
Sodium- glucose cotransporter 2 inhibitors	0.0%	0.0%	0.0%	0.0%
Sulfonylureas	n/a	n/a	n/a	n/a
Thiazolidinedioines	18.7%	18.5%	18.3%	18.3%
Any anti-hyperglycemic medication	76.2%	77.2%	79.6%	80.1%
Number of anti-hyperglycemic medication classes, mean (SD)	2.1 (0.7)	2.1 (0.8)	2.1 (0.6)	2.1 (0.7)
Antihypertensive Medications (180 Days Pre-Index), %				

SUPPLEMENTARY DATA

Angiotensin-converting-enzyme inhibitors	42.2%	42.1%	38.7%	38.8%
Angiotensin II receptor blockers	27.5%	27.7%	21.8%	21.9%
Calcium channel blockers	29.4%	29.3%	17.6%	17.7%
Alpha-blockers	2.4%	2.5%	1.1%	1.1%
Beta blockers	40.7%	40.5%	15.2%	15.3%
Alpha-beta blockers	12.9%	13.3%	2.5%	2.5%
Central alpha-2 receptor agonists	3.5%	3.6%	1.5%	1.5%
Direct vasodilators	2.2%	2.2%	0.4%	0.4%
Direct renin inhibitors	0.3%	0.3%	0.2%	0.1%
Diuretics				
Loop diuretics	18.7%	18.8%	3.8%	3.9%
Potassium sparing diuretics	3.3%	3.4%	2.9%	3.0%
Thiazide diuretics	29.4%	29.6%	29.1%	29.1%
Aldosterone antagonists	4.4%	4.4%	1.2%	1.2%
Any antihypertensive medication	86.6%	86.6%	68.6%	68.8%
Antihypertensive Medications (Baseline), %				
Angiotensin-converting-enzyme inhibitors	46.3%	46.3%	41.6%	41.8%
Angiotensin II receptor blockers	29.4%	29.6%	22.8%	22.9%
Calcium channel blockers	31.9%	31.9%	18.6%	18.8%
Alpha-blockers	2.8%	2.9%	1.2%	1.2%
Beta blockers	43.7%	43.5%	16.3%	16.3%
Alpha-beta blockers	13.9%	14.4%	2.7%	2.7%
Central alpha-2 receptor agonists	4.0%	4.1%	1.7%	1.7%
Direct vasodilators	2.4%	2.5%	0.4%	0.4%
Direct renin inhibitors	0.4%	0.4%	0.2%	0.2%
Diuretics				
Loop diuretics	21.3%	21.4%	4.5%	4.6%

SUPPLEMENTARY DATA

Potassium sparing diuretics	3.9%	4.0%	3.3%	3.3%
Thiazide diuretics	32.8%	33.0%	31.1%	31.2%
Aldosterone antagonists	5.1%	5.1%	1.3%	1.4%
Any antihypertensive medication	88.9%	88.8%	71.0%	71.2%
Lipid Lowering Medications (180 Days Pre-Index), %	73.6%	73.7%	57.7%	57.9%
Lipid Lowering Medications (Baseline), %	77.5%	77.6%	61.0%	61.2%
Other Medications (180 Days Pre-Index), %				
Digoxin (cardiac glycoside)	5.5%	5.4%	0.2%	0.2%
Anticoagulants	11.9%	12.0%	0.9%	0.9%
Anti-platelets	20.4%	20.6%	1.3%	1.3%
Opioids	12.8%	12.6%	8.2%	8.3%
Oral corticosteroids	30.6%	30.6%	21.4%	21.4%
Other Medications (Baseline), %				
Digoxin (cardiac glycoside)	5.9%	5.8%	0.2%	0.2%
Anticoagulants	13.0%	13.1%	1.1%	1.2%
Anti-platelets	22.2%	22.3%	1.4%	1.4%
Opioids	18.6%	18.6%	13.1%	13.2%
Oral corticosteroids	41.8%	41.6%	31.2%	31.3%

CVD = cardiovascular disease; DPP-4is = Dipeptidyl peptidase-4 inhibitors; ESRD = end-stage renal disease; HIV/AIDS = human immunodeficiency virus/acquired immunodeficiency syndrome; SD = standard deviation; SU = sulfonyleurea

**The mean (SD, range) of the absolute value of standardized differences for all above-listed covariables was: 0.51% (0.46%, 0% to 2.30%) for patients with baseline CVD; 0.32% (0.34%, 0% to 1.60%) for patients with no baseline CVD*

SUPPLEMENTARY DATA

Supplementary Table 3. Characteristics of saxagliptin and sitagliptin cohorts after propensity score matching*

	Baseline CVD		No Baseline CVD	
	Saxagliptin	Sitagliptin	Saxagliptin	Sitagliptin
	N=13,042	N=13,042	N=43,402	N=43,402
Age in years, Mean (SD)	63.2 (11.3)	63.3 (11.4)	54.8 (10.7)	54.9 (10.8)
Age Group, %				
18-34	0.4%	0.5%	3.0%	3.0%
35-44	4.0%	4.0%	13.4%	13.3%
45-54	16.6%	16.7%	31.0%	30.8%
55-64	40.2%	39.5%	39.0%	38.8%
65-79	29.5%	29.3%	11.8%	12.1%
80+	9.3%	9.9%	1.9%	2.0%
Sex, %				
Male	61.4%	61.2%	54.1%	54.1%
Female	38.6%	38.8%	45.9%	45.9%
Insurance Plan Type, %				
Comprehensive	19.9%	19.6%	8.7%	8.9%
Exclusive provider organization	0.9%	1.0%	1.2%	1.3%
Health maintenance organization	10.9%	11.0%	11.5%	11.0%
Point of service	7.1%	7.0%	8.8%	8.6%
Preferred provider organization	52.8%	53.1%	58.7%	59.0%
Point of service with capitation	0.4%	0.4%	0.5%	0.4%
Consumer-directed health plan	2.9%	2.9%	4.8%	4.7%
High-deductible health plan	1.1%	1.1%	1.7%	1.7%
Unknown	4.0%	4.1%	4.2%	4.3%

SUPPLEMENTARY DATA

Payer, %				
Commercial	60.1%	59.8%	85.9%	85.5%
Medicare	39.9%	40.2%	14.1%	14.5%
Index Year, %				
2010	12.3%	12.4%	10.8%	11.0%
2011	39.9%	39.4%	39.7%	39.6%
2012	35.3%	35.4%	38.1%	38.2%
2013	12.5%	12.8%	11.4%	11.2%
Geographic Region, %				
Northeast	19.7%	19.8%	13.5%	13.5%
North Central	22.7%	22.9%	20.0%	20.4%
South	47.8%	47.5%	55.6%	55.5%
West	8.6%	8.7%	9.6%	9.4%
Unknown	1.2%	1.1%	1.2%	1.2%
Population Density, %				
Urban	82.3%	82.5%	81.5%	81.4%
Rural	17.1%	16.8%	17.7%	17.9%
Unknown	0.7%	0.7%	0.8%	0.7%
Healthcare Utilization (Baseline)				
Hospitalization in 30 days pre-index, %	3.9%	3.6%	0.7%	0.6%
Hospitalization in 31-365 days pre-index, %	20.7%	20.1%	3.9%	3.9%
Emergency room visit in 30 days pre-index, %	6.3%	6.3%	2.9%	2.9%
Emergency room visit in 31-365 days pre-index, %	30.5%	29.8%	15.5%	15.5%

SUPPLEMENTARY DATA

Outpatient office visits during baseline, mean (SD)	11.3 (7.7)	11.2 (8.0)	6.6 (5.0)	6.6 (5.0)
Outpatient medications during baseline, mean (SD)	17.4 (8.7)	17.4 (8.7)	12.4 (6.9)	12.5 (6.9)
Residence in nursing home or stay in other non-hospital institution during baseline, %	5.5%	5.4%	1.6%	1.6%
Cardiologist visit during baseline, %	64.1%	64.4%	8.5%	8.5%
Creatinine test ordered during baseline, %	69.4%	69.2%	74.5%	74.3%
HbA1c test ordered during baseline, %	69.1%	68.7%	82.1%	81.9%
Blood urea nitrogen test ordered during baseline, %	65.9%	65.7%	69.9%	69.7%
Comorbid Conditions (Baseline), %				
Asthma	6.2%	6.2%	4.4%	4.4%
Cancer (excluding non-melanoma skin cancer)	9.0%	9.0%	4.2%	4.1%
Chronic kidney disease (excluding ESRD)	6.2%	6.4%	1.9%	1.9%
Chronic obstructive pulmonary disease	9.6%	9.4%	2.3%	2.4%
Dementia	2.1%	2.0%	0.3%	0.3%
Depression	7.1%	7.1%	5.2%	5.2%
ESRD	5.2%	5.2%	0.9%	0.9%
Fracture	3.1%	3.0%	1.6%	1.5%
HIV/AIDS	0.1%	0.1%	0.1%	0.1%
Hyperlipidemia or lipid disorder	58.1%	57.8%	45.4%	45.3%
Hypertension	75.9%	76.2%	55.9%	55.7%
Hypoglycemia	4.4%	4.4%	1.9%	1.8%
Liver disease	2.7%	2.7%	2.2%	2.2%
Microvascular complications of diabetes				
Nephropathy	4.4%	4.4%	2.2%	2.2%
Peripheral neuropathy	14.5%	14.1%	7.2%	7.3%
Retinopathy	9.5%	9.2%	6.2%	6.2%
Obesity (or weight gain)	12.7%	12.4%	9.4%	9.5%

SUPPLEMENTARY DATA

Osteoporosis	1.6%	1.7%	0.9%	0.9%
Tobacco use	5.6%	5.6%	2.7%	2.7%
CVD-Related Conditions (Baseline), %				
Heart failure	12.0%	11.9%	0.0%	0.0%
Hospitalized heart failure	1.0%	1.1%	0.0%	0.0%
Acute myocardial infarction	3.6%	3.5%	0.0%	0.0%
Other ischemic heart disease	54.3%	54.6%	0.0%	0.0%
Other heart disease	57.2%	57.5%	0.0%	0.0%
Stroke (narrow)	1.2%	1.1%	0.0%	0.0%
Stroke (broad)	16.9%	16.5%	0.0%	0.0%
Peripheral artery disease	10.5%	10.5%	0.0%	0.0%
Coronary revascularization procedures				
Coronary artery bypass graft	1.3%	1.2%	0.0%	0.0%
Percutaneous coronary intervention	4.3%	4.2%	0.0%	0.0%
Carotid revascularization procedures				
Carotid endarterectomy, stenting, angioplasty, or atherectomy	0.5%	0.5%	0.0%	0.0%
Carotid bypass	0.0%	0.0%	0.0%	0.0%
Lower extremity revascularization procedures				
Lower extremity endarterectomy, stenting, angioplasty, or atherectomy	1.0%	1.1%	0.0%	0.0%
Lower extremity bypass	0.2%	0.1%	0.0%	0.0%
Lower extremity amputation	0.3%	0.2%	0.0%	0.0%
Anti-hyperglycemic Medications (180 Days Pre-Index), %				
Alpha-glucosidase inhibitors	0.5%	0.6%	0.3%	0.3%
Amylin analogs	0.1%	0.1%	0.0%	0.0%
Biguanides (metformin)	72.8%	72.9%	81.4%	81.1%

SUPPLEMENTARY DATA

DPP-4is	n/a	n/a	n/a	n/a
Glucagon-like peptide-1 receptor agonists	2.9%	3.0%	3.5%	3.5%
Insulin (long-acting, combination)	9.9%	10.3%	7.2%	7.1%
Insulin (short-acting)	3.2%	3.0%	1.7%	1.8%
Meglitinides	2.3%	2.3%	1.2%	1.2%
Sodium- glucose cotransporter 2 inhibitors	0.0%	0.0%	0.0%	0.0%
Sulfonylureas	40.3%	40.7%	35.5%	35.8%
Thiazolidinedioines	21.8%	21.5%	20.8%	20.9%
Any anti-hyperglycemic medication	83.6%	83.7%	81.6%	81.4%
Number of anti-hyperglycemic medication classes, mean (SD)	2.5 (0.9)	2.5 (0.9)	2.5 (0.8)	2.5 (0.8)
Anti-hyperglycemic Medications (Baseline), %				
Alpha-glucosidase inhibitors	0.6%	0.6%	0.3%	0.3%
Amylin analogs	0.1%	0.1%	0.1%	0.0%
Biguanides (metformin)	76.9%	76.9%	84.7%	84.5%
DPP-4is	n/a	n/a	n/a	n/a
Glucagon-like peptide-1 receptor agonists	3.9%	4.1%	4.7%	4.6%
Insulin (long-acting, combination)	11.0%	11.2%	7.8%	7.7%
Insulin (short-acting)	3.9%	3.8%	2.1%	2.2%
Meglitinides	2.7%	2.7%	1.4%	1.4%
Sodium- glucose cotransporter 2 inhibitors	0.0%	0.0%	0.0%	0.0%
Sulfonylureas	43.8%	44.4%	38.5%	38.9%
Thiazolidinedioines	26.3%	26.2%	25.0%	25.2%
Any anti-hyperglycemic medication	87.7%	88.0%	86.1%	86.1%
Number of anti-hyperglycemic medication classes, mean (SD)	2.7 (0.9)	2.7 (0.9)	2.6 (0.9)	2.6 (0.9)
Antihypertensive Medications (180 Days Pre-Index), %				

SUPPLEMENTARY DATA

Angiotensin-converting-enzyme inhibitors	44.8%	44.7%	41.0%	41.2%
Angiotensin II receptor blockers	29.2%	29.3%	23.8%	23.8%
Calcium channel blockers	29.5%	29.5%	18.9%	18.7%
Alpha-blockers	2.5%	2.6%	1.1%	1.0%
Beta blockers	40.7%	40.6%	15.2%	15.3%
Alpha-beta blockers	13.4%	13.4%	2.8%	2.9%
Central alpha-2 receptor agonists	3.5%	3.5%	1.6%	1.6%
Direct vasodilators	1.8%	1.7%	0.4%	0.4%
Direct renin inhibitors	0.4%	0.4%	0.3%	0.3%
Diuretics				
Loop diuretics	18.0%	17.8%	4.1%	4.1%
Potassium sparing diuretics	3.3%	3.1%	2.7%	2.7%
Thiazide diuretics	31.3%	31.0%	30.5%	30.5%
Aldosterone antagonists	3.9%	4.0%	1.1%	1.1%
Any antihypertensive medication	88.1%	88.1%	71.4%	71.8%
Antihypertensive Medications (Baseline), %				
Angiotensin-converting-enzyme inhibitors	49.4%	49.3%	44.2%	44.5%
Angiotensin II receptor blockers	31.3%	31.4%	25.0%	25.0%
Calcium channel blockers	32.0%	32.1%	20.0%	19.9%
Alpha-blockers	2.9%	2.9%	1.2%	1.2%
Beta blockers	43.6%	43.5%	16.3%	16.5%
Alpha-beta blockers	14.5%	14.5%	3.0%	3.1%
Central alpha-2 receptor agonists	4.1%	4.1%	1.8%	1.8%
Direct vasodilators	2.1%	2.0%	0.5%	0.5%
Direct renin inhibitors	0.5%	0.4%	0.3%	0.3%
Diuretics				
Loop diuretics	20.5%	20.4%	4.9%	5.0%

SUPPLEMENTARY DATA

Potassium sparing diuretics	3.9%	3.8%	3.1%	3.1%
Thiazide diuretics	35.0%	34.8%	32.7%	32.8%
Aldosterone antagonists	4.5%	4.7%	1.3%	1.3%
Any antihypertensive medication	90.1%	90.1%	74.1%	74.4%
Lipid Lowering Medications (180 Days Pre-Index), %	76.5%	76.6%	60.7%	60.7%
Lipid Lowering Medications (Baseline), %	80.3%	80.3%	64.5%	64.5%
Other Medications (180 Days Pre-Index), %				
Digoxin (cardiac glycoside)	5.0%	5.2%	0.3%	0.3%
Anticoagulants	10.8%	10.8%	1.0%	0.9%
Anti-platelets	21.5%	21.8%	1.5%	1.5%
Opioids	10.5%	10.3%	7.4%	7.6%
Oral corticosteroids	30.1%	29.9%	21.2%	21.4%
Other Medications (Baseline), %				
Digoxin (cardiac glycoside)	5.4%	5.6%	0.3%	0.3%
Anticoagulants	11.9%	11.8%	1.2%	1.1%
Anti-platelets	23.5%	23.7%	1.6%	1.6%
Opioids	16.4%	16.2%	12.2%	12.4%
Oral corticosteroids	41.8%	41.4%	31.5%	31.5%

CVD = cardiovascular disease; DPP-4is = Dipeptidyl peptidase-4 inhibitors; ESRD = end-stage renal disease; HIV/AIDS = human immunodeficiency virus/acquired immunodeficiency syndrome; SD = standard deviation; SU = sulfonylurea

**The mean (SD, range) of the absolute value of standardized differences for all above-listed covariables was: 0.48% (0.36%, 0% to 1.50%) for patients with baseline CVD; 0.32% 0.34% (0.26%, 0% to 1.20%) for patients with no baseline CVD*

SUPPLEMENTARY DATA

Supplementary Table 4. Loss of sample associated with the application of each of the study's patient selection criteria: DPP-4i vs. SU comparison

	DPP-4is	SUs
≥1 outpatient prescription claim for a DPP-4i (saxagliptin, saxagliptin/metformin, sitagliptin, sitagliptin/metformin, sitagliptin/simvastatin, linagliptin, or linagliptin/metformin)* or a SU [†] between 8/1/2010 - 8/30/2013. The date of the first of such claims is the index date.	496,297	1,123,602
≥18 years of age on the index date	496,081	1,123,151
≥365 days of continuous enrollment (no gaps >31 days) in medical and pharmacy benefits before the index date (baseline period)	291,276	657,648
≥1 outpatient prescription claim for an anti-hyperglycemic medication or ≥1 medical claim with a diagnosis of type 2 diabetes during the baseline period	281,417	624,333
Does not have more than one type of DPP-4i, more than one type of SU, or a DPP-4i and an SU on the index date	258,017	600,473
No outpatient prescription claims for DPP-4i [‡] (including alogliptin) or an SU [‡] during the baseline period	140,323	224,503
No hospitalization for heart failure in the 60-day period before the index date	139,938	223,659
No pregnancy or gestational diabetes during the baseline or follow-up periods [§]	137,339	218,104
No type 1 diabetes during the baseline or follow-up periods [§]	121,492	194,704
Total patients qualified for DPP-4i vs. SU comparison	121,492	194,704
CVD stratification:		
Patients with baseline CVD	29,545	49,419
Patients with no baseline CVD	91,947	145,285

CVD = cardiovascular disease; DPP-4i = dipeptidyl peptidase-4 inhibitor; SU = sulfonylurea

* Patients initiating treatment with alogliptin were not considered

† Patients using sulfonylureas co-formulated with metformin or a TZD will be included in the sample.

‡ Single and co-formulations

§ For the pregnancy, gestational diabetes, and type 1 diabetes exclusions, the follow-up period was defined as the index date through the earliest of the end of continuous enrollment or the end of available data

SUPPLEMENTARY DATA

Supplementary Table 5. Loss of sample associated with the application of each of the study's patient selection criteria: Saxagliptin vs. sitagliptin comparison

	Saxagliptin	Sitagliptin
≥1 outpatient prescription claim for saxagliptin (saxagliptin, saxagliptin/metformin) or sitagliptin (sitagliptin, sitagliptin/metformin, sitagliptin/simvastatin) between 8/1/2010 - 8/30/2013. The date of the first of such claims is the index date.	120,736	517,373
≥18 years of age on the index date	120,695	517,188
≥365 days of continuous enrollment (no gaps >31 days) in medical and pharmacy benefits before the index date (baseline period)	77,026	318,690
≥1 outpatient prescription claim for an anti-hyperglycemic medication or ≥1 medical claim with a diagnosis of type 2 diabetes during the baseline period	74,448	311,808
Does not have more than one type of DPP-4i [†] (including linagliptin and alogliptin) on the index date	74,349	311,657
No outpatient prescription claims for DPP-4i [†] (including linagliptin and alogliptin) during the baseline period	65,075	173,477
No hospitalization for heart failure in the 60-day period before the index date	65,004	172,808
No pregnancy or gestational diabetes during the baseline or follow-up periods [‡]	64,002	169,920
No Type 1 diabetes during the baseline or follow-up periods [‡]	56,452	148,233
Total patients qualified for saxagliptin vs. sitagliptin comparison	56,452	148,233
CVD stratification:		
Patients with baseline CVD	13,049	39,598
Patients with no baseline CVD	43,403	108,635

CVD = cardiovascular disease; DPP-4i = dipeptidyl peptidase-4 inhibitor; SU = sulfonylurea

* Patients initiating treatment with alogliptin were not considered

† Single and co-formulations

‡ For the pregnancy, gestational diabetes, and type 1 diabetes exclusions, the follow-up period was defined as the index date through the earliest of the end of continuous enrollment or the end of available data

SUPPLEMENTARY DATA

Supplementary Table 6. Summary of study follow-up duration

	Baseline CVD		No Baseline CVD		Baseline CVD		No Baseline CVD	
	DPP-4is	SUs	DPP-4is	SUs	Saxagliptin	Sitagliptin	Saxagliptin	Sitagliptin
	N=27,259	N=27,259	N=82,019	N=82,019	N=13,042	N=13,042	N=43,402	N=43,402
<i>Primary analysis follow-up</i>								
Days, mean (SD)	188 (215)	178 (208)	171 (203)	164 (198)	207 (227)	207 (228)	181 (210)	187 (218)
Minimum	1	1	1	1	1	1	1	1
Median	90	90	90	90	99	97	90	90
Maximum	1,126	1,125	1,126	1,126	1,126	1,124	1,126	1,126
Reason for end of follow-up, %								
Inpatient death	0.3%	0.4%	0.0%	0.1%	0.3%	0.3%	0.0%	0.0%
Switch from index treatment	7.6%	5.2%	7.1%	4.6%	4.0%	1.2%	3.8%	1.1%
Cessation of therapy*	57.7%	60.3%	62.2%	64.2%	62.1%	63.8%	67.3%	67.8%
End of continuous enrollment	13.5%	13.4%	12.8%	12.8%	15.5%	14.5%	14.3%	14.2%
End of study period (8/30/2013)	21.0%	20.8%	17.9%	18.3%	18.1%	20.2%	14.5%	16.8%
<i>30-day extension follow-up</i>								
Days, mean (SD)	208 (210)	198 (203)	191 (199)	185 (193)	227 (222)	227 (223)	203 (206)	208 (212)
Minimum	1	1	1	1	1	1	1	1
Median	120	120	120	120	122	121	120	120
Maximum	1,126	1,125	1,127	1,126	1,126	1,124	1,126	1,127
<i>45-day gap allowance follow-up</i>								
Days, mean (SD)	239 (238)	222 (231)	234 (236)	215 (226)	270 (251)	265 (250)	257 (242)	254 (247)
Minimum	1	1	1	1	1	1	1	1
Median	150	128	146	121	182	180	176	162
Maximum	1,126	1,125	1,126	1,126	1,126	1,124	1,126	1,126

SD = standard deviation

SUPPLEMENTARY DATA

* Cessation of index therapy was defined as a gap in days' supply for the index therapy that is equal to 1/3 of the days' supply of the most recent prescription of the index therapy. For example, if the days' supply of the most recent prescription of the index therapy was 45 days, the allowable gap would have been 15 days and the patient would be censored on the 16th day after exhaustion of the 45 days' supply from the most recent prescription. Gaps in days' supply of less than 10 days were not considered cessation regardless of the days' supply of the most recent prescription of the index therapy. In calculating days' supply of the index therapy, "stockpiling" (wherein a given prescription is filled "early" [i.e., before exhaustion of the previous prescription's days' supply]) was accounted for by adding any remaining days' supply from the previous prescription to the days supply of the "early" prescription. The maximum number of allowable "stockpiled" days' supply was 120. Hospitalized person-times during the follow-up were not removed from the analyses. For the DPP-4i versus SU comparison only, individual agents within the index therapy's class were considered interchangeable, thus within-class switches did not terminate follow-up.

SUPPLEMENTARY DATA

Supplementary Table 7. Summary of results for post-hoc analyses stratifying patients by presence vs. absence of baseline heart failure

				Sample N	Schoenfeld test	N of events	Hazard ratio	Lower 95% CI	Upper 95% CI	P-Value
DPP-4is vs. SUs	No baseline heart failure	Primary and secondary analyses	Hospitalization for heart failure	210,842	0.014	250	0.792	0.617	1.016	0.067
			Coronary artery bypass graft	210,842	0.210	312	0.733	0.586	0.917	0.007
			Hospitalization for AMI	210,842	0.104	408	0.812	0.668	0.987	0.036
			Hospitalization for stroke	210,842	0.676	280	0.671	0.528	0.851	0.001
			Hospitalization for UA	210,842	0.025	17	2.279	0.795	6.535	0.125
			Coronary revascularization	210,842	0.686	1195	0.846	0.755	0.948	0.004
			Composite endpoint	210,842	0.081	1814	0.820	0.747	0.899	0.000
	Baseline heart failure	Primary and secondary analyses	Hospitalization for heart failure	7,678	0.887	236	1.003	0.777	1.294	0.983
			Coronary artery bypass graft	7,678	0.812	25	1.226	0.557	2.698	0.613
			Hospitalization for AMI	7,678	0.505	53	0.783	0.456	1.343	0.374
			Hospitalization for stroke	7,678	0.011	42	1.042	0.569	1.908	0.893
			Hospitalization for UA	7,678	n/a	0	n/a	n/a	n/a	n/a
			Coronary revascularization	7,678	0.631	108	0.822	0.563	1.199	0.309
			Composite endpoint	7,678	0.618	400	0.954	0.784	1.161	0.638
Saxagliptin vs. sitagliptin	No baseline heart failure	Primary and secondary analyses	Hospitalization for heart failure	109,778	0.825	130	0.986	0.699	1.391	0.937
			Coronary artery bypass graft	109,778	0.080	160	1.019	0.747	1.389	0.908
			Hospitalization for AMI	109,778	0.857	201	0.947	0.718	1.250	0.702
			Hospitalization for stroke	109,778	0.675	136	0.849	0.606	1.189	0.340
			Hospitalization for UA	109,778	0.225	10	1.017	0.296	3.490	0.979
			Coronary revascularization	109,778	0.287	687	0.970	0.835	1.127	0.693
			Composite endpoint	109,778	0.319	988	0.953	0.841	1.080	0.452
	Baseline heart failure	Primary and secondary analyses	Hospitalization for heart failure	3,116	0.132	96	0.783	0.522	1.175	0.238
			Coronary artery bypass graft	3,116	0.644	13	0.889	0.300	2.633	0.832
			Hospitalization for AMI	3,116	0.969	24	1.232	0.554	2.739	0.610
			Hospitalization for stroke	3,116	0.842	15	1.295	0.478	3.513	0.611
			Hospitalization for UA	3,116	n/a	0	n/a	n/a	n/a	n/a
			Coronary revascularization	3,116	0.114	52	1.035	0.599	1.788	0.902
			Composite endpoint	3,116	0.046	163	0.874	0.641	1.190	0.391

AMI = acute myocardial infarction; CVD = cardiovascular disease; DPP-4is = Dipeptidyl peptidase-4 inhibitors; SU = sulfonylurea; UA = unstable angina