

SUPPLEMENTARY MATERIALS

Title: Cost offset of Dapagliflozin in the US Medicare population with Cardio-Kidney Metabolic Syndrome

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Table S1. Definition of historical standard of care (hSoC)

Clinical trial	SoC
DECLARE TIMI 58[1]	Use of other glucose-lowering agents at the discretion of the treating physician (excluding open-label SGLT2 inhibitors, pioglitazone, or rosiglitazone). Anti-hyperglycemic medications, lipid lowering therapy could be prescribed by a physician for hypercholesterolemia
DAPA-HF[2]	Standard heart-failure device therapy (an implantable cardioverter–defibrillator and/or cardiac resynchronization therapy) and standard drug therapy (ACE inhibitors, ARBs, or sacubitril–valsartan plus a beta-blocker unless contraindicated), a MRA, and continued use of glucose-lowering therapies for patients with T2D
DELIVER[3]	Treated according to regional standard of care of HFpEF and existing comorbidities, excluding other SGLT2 inhibitors. Standard of care typically comprised of beta-blockers (83%) and/or loop diuretics (77%), sometimes MRAs (43%), ACE inhibitors (37%), ARBs (36%), and sacubitril–valsartan (5%)
DAPA-CKD[4]	Receiving a stable dose of an ACE inhibitor or ARB $\geq$ 4 weeks before screening, unless contraindicated

Abbreviations: ARB: angiotensin-receptor blocker; ACE: angiotensin-converting enzyme; HFpEF: heart failure with preserved ejection fraction; hSoC: historical standard of care; MRA: mineralocorticoid receptor antagonist; SGLT2: sodium-glucose co-transport protein 2; SoC: standard of care; T2D: type 2 diabetes

Table S2. Key safety outcomes reported in the pivotal dapagliflozin trials

Event	DECLARE TIMI 58[1]		DAPA-HF[2]		DELIVER[3]		DAPA-CKD[4]	
	Dapagliflozin + hSoC	hSoC	Dapagliflozin + hSoC	hSoC	Dapagliflozin + hSoC	hSoC	Dapagliflozin + hSoC	hSoC
	N=8574	N=8569	N=2368	N=2368	N=3126	N=3127	N=2149	N=2149
Serious adverse event	2925 (34.1%)	3100 (36.2%)	846 (35.7%)	951 (40.2%)	1361 (43.5%)	1423 (45.5%)	633 (29.5%)	729 (33.9%)
Adverse event leading to discontinuation	693 (8.1%)	592 (6.9%)	111 (4.7%)	116 (4.9%)	182 (5.8%)	181 (5.8%)	118 (5.5%)	123 (5.7%)
Adverse events of special interest								
Renal-related adverse event*	125 (1.5%)	175 (2.0%)	153 (6.5%)	170 (7.2%)	73 (2.3%)	79 (2.5%)	155 (7.2%)	188 (8.7%)
Amputation	123 (1.4%)	113 (1.3%)	13 (0.5%)	12 (0.5%)	19 (0.6%)	25 (0.8%)	35 (1.6%)	39 (1.8%)
Diabetic ketoacidosis	27 (0.3%)	12 (0.1%)	3 (0.1%)	0 (0.0%)	2 (0.1%)	0 (0.0%)	0 (0.0%)	2 (<0.1%)
Fournier's gangrene	1 (<0.1%)	5 (0.1%)	0	1 (<0.1%)	0	0	0	1 (<0.1%)
Fracture	457 (5.3%)	440 (5.1%)	49 (2.1%)	50 (2.1%)	NR	NR	85 (4.0%)	69 (3.2%)
Major hypoglycemic event	58 (0.7%)	83 (1.0%)	4 (0.2%)	4 (0.2%)	6 (0.2%)	7 (0.2%)	14 (0.7%)	28 (1.3%)
Volume depletion	213 (2.5%)	207 (2.4%)	178 (7.5%)	162 (6.8%)	42 (1.3%)	32 (1.0%)	127 (5.9%)	90 (4.2%)
Abbreviations: hSoC: historical standard of care; NR: not reported.								
*DECLARE-TIMI 58 reported only acute kidney injury and therefore reflects the values presented here.								

Table S3. Diagnosis codes from International Classification of Diseases, Tenth Revision (ICD-10) for estimation of prevalence of CKM syndrome population

Code Type	Code	Description
Heart failure		
ICD-10-CM	I0981	Rheumatic heart failure
ICD-10-CM	I110	Hypertensive heart disease with heart failure
ICD-10-CM	I130	Hypertensive heart and chronic kidney disease with heart failure and stage 1 through stage 4 chronic kidney disease, or unspecified chronic kidney disease
ICD-10-CM	I501	Left ventricular failure, unspecified
ICD-10-CM	I5020	Unspecified systolic (congestive) heart failure
ICD-10-CM	I5021	Acute systolic (congestive) heart failure
ICD-10-CM	I5022	Chronic systolic (congestive) heart failure
ICD-10-CM	I5023	Acute on chronic systolic (congestive) heart failure
ICD-10-CM	I5030	Unspecified diastolic (congestive) heart failure
ICD-10-CM	I5031	Acute diastolic (congestive) heart failure
ICD-10-CM	I5032	Chronic diastolic (congestive) heart failure
ICD-10-CM	I5033	Acute on chronic diastolic (congestive) heart failure
ICD-10-CM	I5040	Unspecified combined systolic (congestive) and diastolic (congestive) heart failure
ICD-10-CM	I5041	Acute combined systolic (congestive) and diastolic (congestive) heart failure
ICD-10-CM	I5042	Chronic combined systolic (congestive) and diastolic (congestive) heart failure
ICD-10-CM	I5043	Acute on chronic combined systolic (congestive) and diastolic (congestive) heart failure
ICD-10-CM	I50810	Right heart failure, unspecified
ICD-10-CM	I50811	Acute right heart failure
ICD-10-CM	I50812	Chronic right heart failure
ICD-10-CM	I50813	Acute on chronic right heart failure
ICD-10-CM	I50814	Right heart failure due to left heart failure
ICD-10-CM	I5082	Biventricular heart failure
ICD-10-CM	I5083	High output heart failure
ICD-10-CM	I5084	End stage heart failure
ICD-10-CM	I5089	Other heart failure
ICD-10-CM	I509	Heart failure, unspecified
Chronic kidney disease		
ICD-10-CM	A1811	Tuberculosis Of Kidney And Ureter
ICD-10-CM	A5275	Syphilis Of Kidney And Ureter
ICD-10-CM	B520	Plasmodium Malariae Malaria With Nephropathy
ICD-10-CM	D593	Hemolytic-Uremic Syndrome
ICD-10-CM	E0821	Diabetes Mellitus Due To Underlying Condition With Diabetic Nephropathy
ICD-10-CM	E0822	Diabetes Mellitus Due To Underlying Condition With Diabetic Chronic Kidney Disease
ICD-10-CM	E0829	Diabetes Mellitus Due To Underlying Condition With Other Diabetic Kidney Complication
ICD-10-CM	E0921	Drug Or Chemical Induced Diabetes Mellitus With Diabetic Nephropathy
ICD-10-CM	E0922	Drug Or Chemical Induced Diabetes Mellitus With Diabetic Chronic Kidney Disease
ICD-10-CM	E0929	Drug Or Chemical Induced Diabetes Mellitus With Other Diabetic Kidney Complication
ICD-10-CM	E1021	Type 1 Diabetes Mellitus With Diabetic Nephropathy
ICD-10-CM	E1022	Type 1 Diabetes Mellitus With Diabetic Chronic Kidney Disease
ICD-10-CM	E1029	Type 1 Diabetes Mellitus With Other Diabetic Kidney Complication
ICD-10-CM	E1121	Type 2 Diabetes Mellitus With Diabetic Nephropathy
ICD-10-CM	E1122	Type 2 Diabetes Mellitus With Diabetic Chronic Kidney Disease
ICD-10-CM	E1129	Type 2 Diabetes Mellitus With Other Diabetic Kidney Complication
ICD-10-CM	E1321	Other Specified Diabetes Mellitus With Diabetic Nephropathy
ICD-10-CM	E1322	Other Specified Diabetes Mellitus With Diabetic Chronic Kidney Disease
ICD-10-CM	E1329	Other Specified Diabetes Mellitus With Other Diabetic Kidney Complication
ICD-10-CM	I129	Hypertensive Chronic Kidney Disease With Stage 1 Through Stage 4 Chronic Kidney Disease, Or Unspecified Chronic Kidney Disease
ICD-10-CM	I130	Hypertensive Heart And Chronic Kidney Disease With Heart Failure And Stage 1 Through Stage 4 Chronic Kidney Disease, Or Unspecified Chronic Kidney Disease
ICD-10-CM	I1310	Hypertensive Heart And Chronic Kidney Disease Without Heart Failure, With Stage 1 Through Stage 4 Chronic Kidney Disease, Or Unspecified Chronic Kidney Disease
ICD-10-CM	K767	Hepatorenal Syndrome
ICD-10-CM	M1030	Gout Due To Renal Impairment, Unspecified Site
ICD-10-CM	M10311	Gout Due To Renal Impairment, Right Shoulder
ICD-10-CM	M10312	Gout Due To Renal Impairment, Left Shoulder
ICD-10-CM	M10319	Gout Due To Renal Impairment, Unspecified Shoulder
ICD-10-CM	M10321	Gout Due To Renal Impairment, Right Elbow

ICD-10-CM	M10322	Gout Due To Renal Impairment, Left Elbow
ICD-10-CM	M10329	Gout Due To Renal Impairment, Unspecified Elbow
ICD-10-CM	M10331	Gout Due To Renal Impairment, Right Wrist
ICD-10-CM	M10332	Gout Due To Renal Impairment, Left Wrist
ICD-10-CM	M10339	Gout Due To Renal Impairment, Unspecified Wrist
ICD-10-CM	M10341	Gout Due To Renal Impairment, Right Hand
ICD-10-CM	M10342	Gout Due To Renal Impairment, Left Hand
ICD-10-CM	M10349	Gout Due To Renal Impairment, Unspecified Hand
ICD-10-CM	M10351	Gout Due To Renal Impairment, Right Hip
ICD-10-CM	M10352	Gout Due To Renal Impairment, Left Hip
ICD-10-CM	M10359	Gout Due To Renal Impairment, Unspecified Hip
ICD-10-CM	M10361	Gout Due To Renal Impairment, Right Knee
ICD-10-CM	M10362	Gout Due To Renal Impairment, Left Knee
ICD-10-CM	M10369	Gout Due To Renal Impairment, Unspecified Knee
ICD-10-CM	M10371	Gout Due To Renal Impairment, Right Ankle And Foot
ICD-10-CM	M10372	Gout Due To Renal Impairment, Left Ankle And Foot
ICD-10-CM	M10379	Gout Due To Renal Impairment, Unspecified Ankle And Foot
ICD-10-CM	M1038	Gout Due To Renal Impairment, Vertebrae
ICD-10-CM	M1039	Gout Due To Renal Impairment, Multiple Sites
ICD-10-CM	M3214	Glomerular Disease In Systemic Lupus Erythematosus
ICD-10-CM	M3215	Tubulo-Interstitial Nephropathy In Systemic Lupus Erythematosus
ICD-10-CM	M3504	Sicca Syndrome With Tubulo-Interstitial Nephropathy
ICD-10-CM	N010	Rapidly Progressive Nephritic Syndrome With Minor Glomerular Abnormality
ICD-10-CM	N011	Rapidly Progressive Nephritic Syndrome With Focal And Segmental Glomerular Lesions
ICD-10-CM	N012	Rapidly Progressive Nephritic Syndrome With Diffuse Membranous Glomerulonephritis
ICD-10-CM	N013	Rapidly Progressive Nephritic Syndrome With Diffuse Mesangial Proliferative Glomerulonephritis
ICD-10-CM	N014	Rapidly Progressive Nephritic Syndrome With Diffuse Endocapillary Proliferative Glomerulonephritis
ICD-10-CM	N015	Rapidly Progressive Nephritic Syndrome With Diffuse Mesangiocapillary Glomerulonephritis
ICD-10-CM	N016	Rapidly Progressive Nephritic Syndrome With Dense Deposit Disease
ICD-10-CM	N017	Rapidly Progressive Nephritic Syndrome With Diffuse Crescentic Glomerulonephritis
ICD-10-CM	N018	Rapidly Progressive Nephritic Syndrome With Other Morphologic Changes
ICD-10-CM	N019	Rapidly Progressive Nephritic Syndrome With Unspecified Morphologic Changes
ICD-10-CM	N020	Recurrent And Persistent Hematuria With Minor Glomerular Abnormality
ICD-10-CM	N021	Recurrent And Persistent Hematuria With Focal And Segmental Glomerular Lesions
ICD-10-CM	N022	Recurrent And Persistent Hematuria With Diffuse Membranous Glomerulonephritis
ICD-10-CM	N023	Recurrent And Persistent Hematuria With Diffuse Mesangial Proliferative Glomerulonephritis
ICD-10-CM	N024	Recurrent And Persistent Hematuria With Diffuse Endocapillary Proliferative Glomerulonephritis
ICD-10-CM	N025	Recurrent And Persistent Hematuria With Diffuse Mesangiocapillary Glomerulonephritis
ICD-10-CM	N026	Recurrent And Persistent Hematuria With Dense Deposit Disease
ICD-10-CM	N027	Recurrent And Persistent Hematuria With Diffuse Crescentic Glomerulonephritis
ICD-10-CM	N028	Recurrent And Persistent Hematuria With Other Morphologic Changes
ICD-10-CM	N029	Recurrent And Persistent Hematuria With Unspecified Morphologic Changes
ICD-10-CM	N030	Chronic Nephritic Syndrome With Minor Glomerular Abnormality
ICD-10-CM	N031	Chronic Nephritic Syndrome With Focal And Segmental Glomerular Lesions
ICD-10-CM	N032	Chronic Nephritic Syndrome With Diffuse Membranous Glomerulonephritis
ICD-10-CM	N033	Chronic Nephritic Syndrome With Diffuse Mesangial Proliferative Glomerulonephritis
ICD-10-CM	N034	Chronic Nephritic Syndrome With Diffuse Endocapillary Proliferative Glomerulonephritis
ICD-10-CM	N035	Chronic Nephritic Syndrome With Diffuse Mesangiocapillary Glomerulonephritis
ICD-10-CM	N036	Chronic Nephritic Syndrome With Dense Deposit Disease
ICD-10-CM	N037	Chronic Nephritic Syndrome With Diffuse Crescentic Glomerulonephritis
ICD-10-CM	N038	Chronic Nephritic Syndrome With Other Morphologic Changes
ICD-10-CM	N039	Chronic Nephritic Syndrome With Unspecified Morphologic Changes
ICD-10-CM	N040	Nephrotic Syndrome With Minor Glomerular Abnormality
ICD-10-CM	N041	Nephrotic Syndrome With Focal And Segmental Glomerular Lesions
ICD-10-CM	N042	Nephrotic Syndrome With Diffuse Membranous Glomerulonephritis
ICD-10-CM	N043	Nephrotic Syndrome With Diffuse Mesangial Proliferative Glomerulonephritis
ICD-10-CM	N044	Nephrotic Syndrome With Diffuse Endocapillary Proliferative Glomerulonephritis
ICD-10-CM	N045	Nephrotic Syndrome With Diffuse Mesangiocapillary Glomerulonephritis
ICD-10-CM	N046	Nephrotic Syndrome With Dense Deposit Disease

ICD-10-CM	N047	Nephrotic Syndrome With Diffuse Crescentic Glomerulonephritis
ICD-10-CM	N048	Nephrotic Syndrome With Other Morphologic Changes
ICD-10-CM	N049	Nephrotic Syndrome With Unspecified Morphologic Changes
ICD-10-CM	N050	Unspecified Nephritic Syndrome With Minor Glomerular Abnormality
ICD-10-CM	N051	Unspecified Nephritic Syndrome With Focal And Segmental Glomerular Lesions
ICD-10-CM	N052	Unspecified Nephritic Syndrome With Diffuse Membranous Glomerulonephritis
ICD-10-CM	N053	Unspecified Nephritic Syndrome With Diffuse Mesangial Proliferative Glomerulonephritis
ICD-10-CM	N054	Unspecified Nephritic Syndrome With Diffuse Endocapillary Proliferative Glomerulonephritis
ICD-10-CM	N055	Unspecified Nephritic Syndrome With Diffuse Mesangiocapillary Glomerulonephritis
ICD-10-CM	N056	Unspecified Nephritic Syndrome With Dense Deposit Disease
ICD-10-CM	N057	Unspecified Nephritic Syndrome With Diffuse Crescentic Glomerulonephritis
ICD-10-CM	N058	Unspecified Nephritic Syndrome With Other Morphologic Changes
ICD-10-CM	N059	Unspecified Nephritic Syndrome With Unspecified Morphologic Changes
ICD-10-CM	N060	Isolated Proteinuria With Minor Glomerular Abnormality
ICD-10-CM	N061	Isolated Proteinuria With Focal And Segmental Glomerular Lesions
ICD-10-CM	N062	Isolated Proteinuria With Diffuse Membranous Glomerulonephritis
ICD-10-CM	N063	Isolated Proteinuria With Diffuse Mesangial Proliferative Glomerulonephritis
ICD-10-CM	N064	Isolated Proteinuria With Diffuse Endocapillary Proliferative Glomerulonephritis
ICD-10-CM	N065	Isolated Proteinuria With Diffuse Mesangiocapillary Glomerulonephritis
ICD-10-CM	N066	Isolated Proteinuria With Dense Deposit Disease
ICD-10-CM	N067	Isolated Proteinuria With Diffuse Crescentic Glomerulonephritis
ICD-10-CM	N068	Isolated Proteinuria With Other Morphologic Lesion
ICD-10-CM	N069	Isolated Proteinuria With Unspecified Morphologic Lesion
ICD-10-CM	N070	Hereditary Nephropathy, Not Elsewhere Classified With Minor Glomerular Abnormality
ICD-10-CM	N071	Hereditary Nephropathy, Not Elsewhere Classified With Focal And Segmental Glomerular Lesions
ICD-10-CM	N072	Hereditary Nephropathy, Not Elsewhere Classified With Diffuse Membranous Glomerulonephritis
ICD-10-CM	N073	Hereditary Nephropathy, Not Elsewhere Classified With Diffuse Mesangial Proliferative Glomerulonephritis
ICD-10-CM	N074	Hereditary Nephropathy, Not Elsewhere Classified With Diffuse Endocapillary Proliferative Glomerulonephritis
ICD-10-CM	N075	Hereditary Nephropathy, Not Elsewhere Classified With Diffuse Mesangiocapillary Glomerulonephritis
ICD-10-CM	N076	Hereditary Nephropathy, Not Elsewhere Classified With Dense Deposit Disease
ICD-10-CM	N077	Hereditary Nephropathy, Not Elsewhere Classified With Diffuse Crescentic Glomerulonephritis
ICD-10-CM	N078	Hereditary Nephropathy, Not Elsewhere Classified With Other Morphologic Lesions
ICD-10-CM	N079	Hereditary Nephropathy, Not Elsewhere Classified With Unspecified Morphologic Lesions
ICD-10-CM	N08	Glomerular Disorders In Diseases Classified Elsewhere
ICD-10-CM	N131	Hydronephrosis With Ureteral Stricture, Not Elsewhere Classified
ICD-10-CM	N132	Hydronephrosis With Renal And Ureteral Calculous Obstruction
ICD-10-CM	N1330	Unspecified Hydronephrosis
ICD-10-CM	N1339	Other Hydronephrosis
ICD-10-CM	N140	Analgesic Nephropathy
ICD-10-CM	N141	Nephropathy Induced By Other Drugs, Medicaments And Biological Substances
ICD-10-CM	N142	Nephropathy Induced By Unspecified Drug, Medicament Or Biological Substance
ICD-10-CM	N143	Nephropathy Induced By Heavy Metals
ICD-10-CM	N144	Toxic Nephropathy, Not Elsewhere Classified
ICD-10-CM	N150	Balkan Nephropathy
ICD-10-CM	N158	Other Specified Renal Tubulo-Interstitial Diseases
ICD-10-CM	N159	Renal Tubulo-Interstitial Disease, Unspecified
ICD-10-CM	N16	Renal Tubulo-Interstitial Disorders In Diseases Classified Elsewhere
ICD-10-CM	N181	Chronic Kidney Disease, Stage 1
ICD-10-CM	N182	Chronic Kidney Disease, Stage 2 (Mild)
ICD-10-CM	N183	Chronic Kidney Disease, Stage 3 (Moderate)
ICD-10-CM	N1830	Chronic kidney disease, stage 3 unspecified
ICD-10-CM	N1831	Chronic kidney disease, stage 3a
ICD-10-CM	N1832	Chronic kidney disease, stage 3b
ICD-10-CM	N184	Chronic Kidney Disease, Stage 4 (Severe)
ICD-10-CM	N189	Chronic Kidney Disease, Unspecified
ICD-10-CM	N250	Renal Osteodystrophy
ICD-10-CM	N251	Nephrogenic Diabetes Insipidus

ICD-10-CM	N2581	Secondary Hyperparathyroidism Of Renal Origin
ICD-10-CM	N2589	Other Disorders Resulting From Impaired Renal Tubular Function
ICD-10-CM	N259	Disorder Resulting From Impaired Renal Tubular Function, Unspecified
ICD-10-CM	N261	Atrophy Of Kidney (Terminal)
ICD-10-CM	N269	Renal Sclerosis, Unspecified
ICD-10-CM	Q6102	Congenital Multiple Renal Cysts
ICD-10-CM	Q6111	Cystic Dilatation Of Collecting Ducts
ICD-10-CM	Q6119	Other Polycystic Kidney, Infantile Type
ICD-10-CM	Q612	Polycystic Kidney, Adult Type
ICD-10-CM	Q613	Polycystic Kidney, Unspecified
ICD-10-CM	Q614	Renal Dysplasia
ICD-10-CM	Q615	Medullary Cystic Kidney
ICD-10-CM	Q618	Other Cystic Kidney Diseases
ICD-10-CM	Q620	Congenital Hydronephrosis
ICD-10-CM	Q622	Congenital Megaureter
ICD-10-CM	Q6210	Congenital Occlusion Of Ureter, Unspecified
ICD-10-CM	Q6211	Congenital Occlusion Of Ureteropelvic Junction
ICD-10-CM	Q6212	Congenital Occlusion Of Ureterovesical Orifice
ICD-10-CM	Q6231	Congenital Ureterocele, Orthotopic
ICD-10-CM	Q6232	Cecoureterocele
ICD-10-CM	Q6239	Other Obstructive Defects Of Renal Pelvis And Ureter
ICD-10-CM	R944	Abnormal Results Of Kidney Function Studies
Type 2 diabetes		
ICD-10-CM	E11.00	Type 2 diabetes mellitus with hyperosmolarity without nonketotic hyperglycemic-hyperosmolar coma (NKHHC)
ICD-10-CM	E11.01	Type 2 diabetes mellitus with hyperosmolarity with coma
ICD-10-CM	E11.10	Type 2 diabetes mellitus with ketoacidosis without coma
ICD-10-CM	E11.11	Type 2 diabetes mellitus with ketoacidosis with coma
ICD-10-CM	E11.21	Type 2 diabetes mellitus with diabetic nephropathy
ICD-10-CM	E11.22	Type 2 diabetes mellitus with diabetic chronic kidney disease
ICD-10-CM	E11.29	Type 2 diabetes mellitus with other diabetic kidney complication
ICD-10-CM	E11.311	Type 2 diabetes mellitus with unspecified diabetic retinopathy with macular edema
ICD-10-CM	E11.319	Type 2 diabetes mellitus with unspecified diabetic retinopathy without macular edema
ICD-10-CM	E11.321	Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema
ICD-10-CM	E11.3211	Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, right eye
ICD-10-CM	E11.3212	Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, left eye
ICD-10-CM	E11.3213	Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, bilateral
ICD-10-CM	E11.3219	Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, unspecified eye
ICD-10-CM	E11.329	Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy without macular edema
ICD-10-CM	E11.3291	Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy without macular edema, right eye
ICD-10-CM	E11.3292	Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy without macular edema, left eye
ICD-10-CM	E11.3293	Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy without macular edema, bilateral
ICD-10-CM	E11.3299	Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy without macular edema, unspecified eye
ICD-10-CM	E11.331	Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema
ICD-10-CM	E11.3311	Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, right eye
ICD-10-CM	E11.3312	Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, left eye
ICD-10-CM	E11.3313	Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, bilateral
ICD-10-CM	E11.3319	Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, unspecified eye
ICD-10-CM	E11.339	Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema

ICD-10-CM	E11.3391	Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema, right eye
ICD-10-CM	E11.3392	Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema, left eye
ICD-10-CM	E11.3393	Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema, bilateral
ICD-10-CM	E11.3399	Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema, unspecified eye
ICD-10-CM	E11.341	Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema
ICD-10-CM	E11.3411	Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, right eye
ICD-10-CM	E11.3412	Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, left eye
ICD-10-CM	E11.3413	Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, bilateral
ICD-10-CM	E11.3419	Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, unspecified eye
ICD-10-CM	E11.349	Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema
ICD-10-CM	E11.3491	Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema, right eye
ICD-10-CM	E11.3492	Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema, left eye
ICD-10-CM	E11.3493	Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema, bilateral
ICD-10-CM	E11.3499	Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema, unspecified eye
ICD-10-CM	E11.351	Type 2 diabetes mellitus with proliferative diabetic retinopathy with macular edema
ICD-10-CM	E11.3511	Type 2 diabetes mellitus with proliferative diabetic retinopathy with macular edema, right eye
ICD-10-CM	E11.3512	Type 2 diabetes mellitus with proliferative diabetic retinopathy with macular edema, left eye
ICD-10-CM	E11.3513	Type 2 diabetes mellitus with proliferative diabetic retinopathy with macular edema, bilateral
ICD-10-CM	E11.3519	Type 2 diabetes mellitus with proliferative diabetic retinopathy with macular edema, unspecified eye
ICD-10-CM	E11.3521	Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, right eye
ICD-10-CM	E11.3522	Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, left eye
ICD-10-CM	E11.3523	Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, bilateral
ICD-10-CM	E11.3529	Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, unspecified eye
ICD-10-CM	E11.3531	Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, right eye
ICD-10-CM	E11.3532	Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, left eye
ICD-10-CM	E11.3533	Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, bilateral
ICD-10-CM	E11.3539	Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, unspecified eye
ICD-10-CM	E11.3541	Type 2 diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, right eye
ICD-10-CM	E11.3542	Type 2 diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, left eye
ICD-10-CM	E11.3543	Type 2 diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, bilateral
ICD-10-CM	E11.3549	Type 2 diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, unspecified eye
ICD-10-CM	E11.3551	Type 2 diabetes mellitus with stable proliferative diabetic retinopathy, right eye
ICD-10-CM	E11.3552	Type 2 diabetes mellitus with stable proliferative diabetic retinopathy, left eye
ICD-10-CM	E11.3553	Type 2 diabetes mellitus with stable proliferative diabetic retinopathy, bilateral
ICD-10-CM	E11.3559	Type 2 diabetes mellitus with stable proliferative diabetic retinopathy, unspecified eye
ICD-10-CM	E11.359	Type 2 diabetes mellitus with proliferative diabetic retinopathy without macular edema

ICD-10-CM	E11.3591	Type 2 diabetes mellitus with proliferative diabetic retinopathy without macular edema, right eye
ICD-10-CM	E11.3592	Type 2 diabetes mellitus with proliferative diabetic retinopathy without macular edema, left eye
ICD-10-CM	E11.3593	Type 2 diabetes mellitus with proliferative diabetic retinopathy without macular edema, bilateral
ICD-10-CM	E11.3599	Type 2 diabetes mellitus with proliferative diabetic retinopathy without macular edema, unspecified eye
ICD-10-CM	E11.36	Type 2 diabetes mellitus with diabetic cataract
ICD-10-CM	E11.37X1	Type 2 diabetes mellitus with diabetic macular edema, resolved following treatment, right eye
ICD-10-CM	E11.37X2	Type 2 diabetes mellitus with diabetic macular edema, resolved following treatment, left eye
ICD-10-CM	E11.37X3	Type 2 diabetes mellitus with diabetic macular edema, resolved following treatment, bilateral
ICD-10-CM	E11.37X9	Type 2 diabetes mellitus with diabetic macular edema, resolved following treatment, unspecified eye
ICD-10-CM	E11.39	Type 2 diabetes mellitus with other diabetic ophthalmic complication
ICD-10-CM	E11.40	Type 2 diabetes mellitus with diabetic neuropathy, unspecified
ICD-10-CM	E11.41	Type 2 diabetes mellitus with diabetic mononeuropathy
ICD-10-CM	E11.42	Type 2 diabetes mellitus with diabetic polyneuropathy
ICD-10-CM	E11.43	Type 2 diabetes mellitus with diabetic autonomic (poly)neuropathy
ICD-10-CM	E11.44	Type 2 diabetes mellitus with diabetic amyotrophy
ICD-10-CM	E11.49	Type 2 diabetes mellitus with other diabetic neurological complication
ICD-10-CM	E11.51	Type 2 diabetes mellitus with diabetic peripheral angiopathy without gangrene
ICD-10-CM	E11.52	Type 2 diabetes mellitus with diabetic peripheral angiopathy with gangrene
ICD-10-CM	E11.59	Type 2 diabetes mellitus with other circulatory complications
ICD-10-CM	E11.610	Type 2 diabetes mellitus with diabetic neuropathic arthropathy
ICD-10-CM	E11.618	Type 2 diabetes mellitus with other diabetic arthropathy
ICD-10-CM	E11.620	Type 2 diabetes mellitus with diabetic dermatitis
ICD-10-CM	E11.621	Type 2 diabetes mellitus with foot ulcer
ICD-10-CM	E11.622	Type 2 diabetes mellitus with other skin ulcer
ICD-10-CM	E11.628	Type 2 diabetes mellitus with other skin complications
ICD-10-CM	E11.630	Type 2 diabetes mellitus with periodontal disease
ICD-10-CM	E11.638	Type 2 diabetes mellitus with other oral complications
ICD-10-CM	E11.641	Type 2 diabetes mellitus with hypoglycemia with coma
ICD-10-CM	E11.649	Type 2 diabetes mellitus with hypoglycemia without coma
ICD-10-CM	E11.65	Type 2 diabetes mellitus with hyperglycemia
ICD-10-CM	E11.69	Type 2 diabetes mellitus with other specified complication
ICD-10-CM	E11.8	Type 2 diabetes mellitus with unspecified complications
ICD-10-CM	E11.9	Type 2 diabetes mellitus without complications
ICD-10-CM	O24.111	Pre-existing Type 2 diabetes mellitus, in pregnancy, first trimester
ICD-10-CM	O24.112	Pre-existing Type 2 diabetes mellitus, in pregnancy, second trimester
ICD-10-CM	O24.113	Pre-existing Type 2 diabetes mellitus, in pregnancy, third trimester
ICD-10-CM	O24.119	Pre-existing Type 2 diabetes mellitus, in pregnancy, unspecified trimester
ICD-10-CM	O24.12	Pre-existing Type 2 diabetes mellitus, in childbirth
ICD-10-CM	O24.13	Pre-existing Type 2 diabetes mellitus, in the puerperium

Table S4. Clinical trials used to inform event rates for each subpopulation

Population	DECLARE-TIMI 58	DAPA-HF + DELIVER (pooled)	DAPA-CKD	Justification
T2D	✓			T2D only population
HF		✓		HF only population
CKD			✓	CKD only population
T2D + CKD			✓	68% of the DAPA-CKD population have T2D
HF + CKD			✓	Most representative of CKD population
T2D + HF		✓		42% of the DAPA-HF and 45% of the DELIVER populations have T2D
T2D + HF + CKD			✓	DAPA-CKD population reflects a larger proportion of patients with CKD, HF and T2D than other studies

Abbreviations: CKD: chronic kidney disease; HF: heart failure; T2D: type 2 diabetes

*Weighted averages based on age and sex. †Assumed to relate to fatal

Table S5. Event rates applied to modelled subpopulations

Event	Dapagliflozin + hSoC	hSoC	Source
CKD only			
≥ 50% sustained eGFR decline	10.60	19.57	DAPA-CKD; McMurray et al. (2021)[5]
Onset of kidney failure	10.19	15.49	
Hospitalization for HF (initial)	3.23	6.45	
Death (renal)	0.19	0.48	
Death (cardiovascular)	5.71	6.93	
Death (other causes)	14.39	20.28	
CKD + HF			
≥ 50% sustained eGFR decline	24.98	46.11	DAPA-CKD; McMurray et al. (2021)[5]
Onset of kidney failure	24.02	36.50	
Hospitalization for HF (initial)	7.60	15.21	
Death (renal)	0.45	1.13	
Death (cardiovascular)	13.45	16.33	
Death (other causes)	33.91	47.78	
CKD + T2D			
≥ 50% sustained eGFR decline	19.63	36.23	DAPA-CKD; McMurray et al. (2021)[5]
Onset of kidney failure	18.87	28.69	
Hospitalization for HF (initial)	25.77	51.55	
Death (renal)	0.35	0.89	
Death (cardiovascular)	10.57	12.83	
Death (other causes)	43.71	61.59	
CKD + HF + T2D			
≥ 50% sustained eGFR decline	46.25	85.39	DAPA-CKD; McMurray et al. (2021)[5]
Onset of kidney failure	44.47	67.60	
Hospitalization for HF (initial)	60.74	121.47	
Death (renal)	0.84	2.09	
Death (cardiovascular)	24.90	30.24	
Death (other causes)	103.00	145.14	
HF only			
≥ 50% sustained eGFR decline	1.78	1.84	DAPA-HF; McCausland et al. (2023)[6]; Inzucchi et al. (2022)[7]
Onset of kidney failure	0.00	3.27	
Hospitalization for HF (initial)	40.27	54.34	DAPA-HF; DELIVER; Jhund et al. (2022)[8]; Inzucchi et al. (2022)[7]
Hospitalization for HF (recurrent)	57.60	81.30	DAPA-HF; DELIVER; and Inzucchi et al. (2022)[7]
Urgent HF visit	2.26	11.05	ACMP poster,[9] DAPA-HF, DELIVER, and Inzucchi et al. (2022)[7]
Death (renal)	0.00	0.00	Assumed nil
Death (cardiovascular)	28.80	40.83	Jhund et al. (2022)[8]
Death (other causes)	58.49	68.84	DAPA-HF; DELIVER; Jhund et al. (2022)[8]; and Inzucchi et al. (2022)[7]
HF + T2D			
≥ 50% sustained eGFR decline	3.65	6.63	DAPA-HF; McCausland et al. (2023)[6]; Inzucchi et al. (2022)[7]
Onset of kidney failure	0.00	5.35	

Event	Dapagliflozin + hSoC	hSoC	Source
Hospitalization for HF (initial)	58.84	63.05	DAPA-HF; DELIVER; Jhund et al. (2022)[8] and Inzucchi et al. (2022)[7]
Hospitalization for HF (recurrent)	79.28	91.11	DAPA-HF; DELIVER; and Inzucchi et al. (2022)[7]
Urgent HF visit	8.50	10.99	Booth et al. (2023)[9], DAPA-HF; DELIVER; and Inzucchi et al. (2022)[7]
Death (renal)	0.00	0.00	Assume 0 based on overall event rates
Death (cardiovascular)	35.20	46.23	Jhund et al. (2022)[8]
Death (other causes)	61.95	75.71	DAPA-HF; DELIVER; Jhund et al. (2022)[8]; Inzucchi et al. (2022)[7]
T2D only			
Hospitalization for HF (initial)	0.79	1.09	DECLARE-TIMI 58
Urgent HF visit	0.00	0.00	
Death (renal)	0.00	0.00	
Death (cardiovascular)	2.00	2.03	
Death (other causes)	4.22	4.59	

Abbreviations: eGFR: estimated glomerular filtration rate; HF: heart failure; hSoC: historical standard of care; T2D: type 2 diabetes

Table S6. Scenario 1: Effect of event rate increases in the dapagliflozin arm

Event rates increase, dapagliflozin arm	Dapagliflozin plus hSoC	hSoC	Incremental
Increase of 5%	\$219,771,111,826	\$310,258,780,205	-\$90,487,668,379
Increase of 10%	\$228,393,415,460	\$310,258,780,205	-\$81,865,364,745
Increase of 15%	\$236,872,762,858	\$310,258,780,205	-\$73,386,017,347
Increase of 20%	\$245,211,943,407	\$310,258,780,205	-\$65,046,836,798

Abbreviations: hSoC: historical standard of care

Table S7. Scenario 2: Effect of changes in disease prevalence ($\pm 5\%$) by subpopulation

Subpopulation	Dapagliflozin plus hSoC	hSoC	Incremental
T2D, total	\$211,078,798,024	\$310,346,506,656	-\$99,267,708,632
HF, total	\$212,623,792,951	\$312,685,193,497	-\$100,061,400,545
CKD, total	\$212,408,008,708	\$312,412,652,600	-\$100,004,643,892
T2D + CKD	\$213,331,424,466	\$313,815,772,976	-\$100,484,348,510
HF + CKD	\$211,890,704,947	\$311,581,918,087	-\$99,691,213,140
T2D + HF	\$212,774,057,930	\$312,726,190,676	-\$99,952,132,745
T2D + HF + CKD	\$213,464,360,257	\$313,756,165,954	-\$100,291,805,697

Abbreviations: CKD, chronic kidney disease; HF: heart failure; hSoC: historical standard of care; T2D: type 2 diabetes

Table S8. Scenario 3: Effect of changing definition of cost for death by other causes

Subpopulation	Dapagliflozin plus hSoC	hSoC	Incremental
Base-case (Event cost: \$13,697)			
Other deaths (non-renal/CV)	\$13,244,084,764	\$16,045,934,851	-\$2,801,850,087
Total	\$211,002,999,615	\$310,258,780,205	-\$99,255,780,590
Scenario (Event cost: \$12,712)			
Other deaths (non-renal/CV)	\$12,291,304,770	\$14,891,589,648	-\$2,600,284,878
Total	\$210,050,219,621	\$309,104,435,003	-\$99,054,215,382

Abbreviations: CV: cardiovascular; hSoC: historical standard of care

Table S9. Deterministic sensitivity analyses

Subpopulation	Lower	Upper
Event costs		
Hospitalization for HF, initial	-\$96,602,443,925	-\$101,909,117,256
Hospitalization for HF, recurrent	-\$98,738,201,952	-\$99,773,359,229
Urgent HF visit	-\$99,203,164,488	-\$99,308,396,692
Death, other causes	-\$98,415,225,564	-\$100,096,335,616
Death, cardiovascular	-\$97,297,085,387	-\$101,214,475,793
Death, renal	-\$98,967,359,283	-\$99,544,201,898
Maintenance costs		
Hospitalization for HF, initial	-\$95,530,002,806	-\$102,981,558,374
Hospitalization for heart failure, recurrent	-\$98,421,563,533	-\$100,089,997,647
≥ 50% sustained eGFR decline	-\$96,346,406,336	-\$102,165,154,845
Kidney failure	-\$83,259,618,452	-\$115,251,942,729
All costs		
Hospitalization for heart failure, initial	-\$92,876,666,141	-\$105,634,895,040
Hospitalization for heart failure, recurrent	-\$97,903,984,894	-\$100,607,576,286
Urgent HF visit	-\$99,203,164,488	-\$99,308,396,692
≥ 50% sustained eGFR decline	-\$96,346,406,336	-\$102,165,154,845
Kidney failure	-\$83,259,618,452	-\$115,251,942,729
Death, other causes	-\$98,415,225,564	-\$100,096,335,616
Death, cardiovascular	-\$97,297,085,387	-\$101,214,475,793
Death, renal	-\$98,967,359,283	-\$99,544,201,898

Abbreviations: CV: cardiovascular; eGFR: estimated glomerular filtration rate; HF: heart failure

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