

Supplemental Tables

Supplemental Table 1: ICD-10-CM diagnosis codes for hypertension.

ICD-10-CM Diagnosis Code	Description
I10	Essential (primary) hypertension
H35031	Hypertensive retinopathy, right eye
H35032	Hypertensive retinopathy, left eye
H35033	Hypertensive retinopathy, bilateral
I110	Hypertensive heart disease with heart failure
I119	Hypertensive heart disease without heart failure
I120	Hypertensive chronic kidney disease with stage 5 chronic kidney disease or end stage renal disease
I129	Hypertensive chronic kidney disease with stage 1 through stage 4 chronic kidney disease, or unspecified chronic kidney disease
I130	Hypertensive heart and chronic kidney disease with heart failure and stage 1 through stage 4 chronic kidney disease, or unspecified chronic kidney disease
I1310	Hypertensive heart and chronic kidney disease without heart failure, with stage 1 through stage 4 chronic kidney disease, or unspecified chronic kidney disease
I1311	Hypertensive heart and chronic kidney disease without heart failure, with stage 5 chronic kidney disease, or end stage renal disease
I132	Hypertensive heart and chronic kidney disease with heart failure and with stage 5 chronic kidney disease, or end stage renal disease
I150	Renovascular hypertension
I151	Hypertension secondary to other renal disorders
I152	Hypertension secondary to endocrine disorders
I158	Other secondary hypertension
I159	Secondary hypertension, unspecified
I160	Hypertensive urgency
I161	Hypertensive emergency
I169	Hypertensive crisis, unspecified
I1A0	Resistant hypertension
I674	Hypertensive encephalopathy

ICD-10-CM: International Classification of Diseases, Tenth Revision, Clinical Modification

Supplemental Table 2: Time between consecutive lines of therapy (LoTs).

	LoT1 N = 17,077,696	LoT2 N = 9,724,029	LoT3 N = 6,317,768	LoT4 N = 4,378,963
Months from diagnosis to first anti-HTN medication class, mean (SD)	1.8 (4.7)	-	-	-
Median (IQR)	0.6 (1.6)	-	-	-
Months between consecutive anti-HTN medication classes,* mean (SD)	15.0 (15.1)	9.0 (11.4)	7.3 (9.9)	6.0 (8.7)
Median (IQR)	9.0 (20.3)	3.2 (10.4)	2.6 (7.4)	2.1 (4.7)
Among patients on the 2 nd LoT				
Months between diagnosis and 1st LoT anti-HTN medication classes, mean (SD)	-	1.5 (3.7)	-	-
Median (IQR)	-	0.5 (1.4)	-	-
Months between 1 st LoT and 2 nd LoT anti-HTN medication classes, mean (SD)	-	10.0 (11.1)	-	-
Median (IQR)	-	5.2 (12.4)	-	-
Among patients on the 3 rd LoT				
Months between diagnosis and 1st LoT anti-HTN medication classes, mean (SD)	-	-	1.3 (3.1)	-
Median (IQR)	-	-	0.5 (1.3)	-
Months between 1 st LoT and 2 nd LoT anti-HTN medication classes, mean (SD)	-	-	8.2 (9.7)	-
Median (IQR)	-	-	3.6 (9.7)	-
Months between 2 nd LoT and 3 rd LoT anti-HTN medication classes, mean (SD)	-	-	5.9 (7.9)	-
Median (IQR)	-	-	2.3 (5.1)	-
Among patients on the 4 th LoT				
Months between diagnosis and 1st LoT anti-HTN medication classes, mean (SD)	-	-	-	1.2 (2.7)
Median (IQR)	-	-	-	0.5 (1.2)
Months between 1 st LoT and 2 nd LoT anti-HTN medication classes, mean (SD)	-	-	-	6.9 (8.6)
Median (IQR)	-	-	-	2.7 (7.4)
Months between 2 nd LoT and 3 rd LoT anti-HTN medication classes, mean (SD)	-	-	-	4.9 (6.8)
Median (IQR)	-	-	-	2.0 (3.4)
Months between 3 rd LoT and 4 th LoT anti-HTN medication classes, mean (SD)	-	-	-	4.7 (6.5)

Median (IQR)	-	-	-	2.0 (3.0)
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Supplemental Table 3: Demographic and baseline clinical characteristics of escalation subgroup with treatment escalation within or after 3 months.

	Patients escalating from LoT1 to LoT2 within 3 months N = 3,828,246	Patients escalating from LoT1 to LoT2 after 3 months N = 5,895,783	P value
Age, mean (SD)	70.3 (14.0)	66.2 (15.4)	< 0.001
Median (IQR)	72.0 (17.0)	68.0 (20.0)	
Age group, n (%)			< 0.001
18-29	22,737 (0.6%)	76,796 (1.3%)	
30-39	86,935 (2.3%)	267,528 (4.5%)	
40-49	204,338 (5.3%)	538,354 (9.1%)	
50-64	789,245 (20.6%)	1,555,733 (26.4%)	
65-74	1,215,466 (31.7%)	1,664,289 (28.2%)	
75-84	1,052,546 (27.5%)	1,273,994 (21.6%)	
85+	456,979 (11.9%)	519,089 (8.8%)	
Sex, n (%)			< 0.001
Male	1,706,995 (44.6%)	2,568,650 (43.6%)	
Female	2,121,251 (55.4%)	3,327,133 (56.4%)	
Race/Ethnicity, n (%)			< 0.001
White	2,584,131 (67.5%)	3,654,230 (62.0%)	
Black or African American	456,111 (11.9%)	743,038 (12.6%)	
Asian American or Pacific Islander	89,676 (2.3%)	200,851 (3.4%)	
Hispanic or Latino	178,840 (4.7%)	420,679 (7.1%)	
Unknown	519,488 (13.6%)	876,985 (14.9%)	
Payer type, n (%)			< 0.001
Medicare	2,857,584 (74.6%)	3,708,818 (62.9%)	
Commercial	572,986 (15.0%)	1,120,865 (19.0%)	
Managed Medicaid	397,676 (10.4%)	1,066,100 (18.1%)	
Census region, n (%)			< 0.001
Northeast	713,086 (18.6%)	1,099,270 (18.6%)	
Midwest	917,596 (24.0%)	1,301,715 (22.1%)	
South	1,478,301 (38.6%)	2,296,981 (39.0%)	
West	702,419 (18.3%)	1,164,826 (19.8%)	
U.S. Territory/Unknown	16,844 (0.4%)	32,991 (0.6%)	

Urbanicity, n (%)			< 0.001
Urban	2,980,063 (77.8%)	4,621,169 (78.4%)	
Rural	741,624 (19.4%)	1,058,729 (18.0%)	
Unknown	106,559 (2.8%)	215,885 (3.7%)	
Dual-eligibility status-Medicare only, n (%)			< 0.001
Yes	631,438 (22.1%)	927,649 (25.0%)	
No	2,181,597 (76.3%)	2,725,696 (73.5%)	
Unknown	44,549 (1.6%)	55,473 (1.5%)	
Low income subsidy status-Medicare only, n (%)			< 0.001
Yes	744,109 (26.0%)	1,059,650 (28.6%)	
No	2,068,926 (72.4%)	2,593,695 (69.9%)	
Unknown	44,549 (1.6%)	55,473 (1.5%)	
Area Deprivation Index, mean (SD)	50.5 (25.4)	50.3 (26.2)	< 0.001
Lowest (least deprived) quartile, n (%)	752,513 (19.7%)	1,230,299 (20.9%)	
Second quartile, n (%)	1,083,026 (28.3%)	1,612,155 (27.3%)	
Third quartile, n (%)	1,166,776 (30.5%)	1,683,580 (28.6%)	
Highest (most deprived) quartile, n (%)	733,518 (19.2%)	1,183,047 (20.1%)	
Unknown, n (%)	92,413 (2.4%)	186,702 (3.2%)	
Months of follow-up, mean (SD)	32.9 (16.6)	38.4 (14.6)	< 0.001
Median (IQR)	36.4 (29.3)	42.8 (20.6)	
Index year, n (%)			< 0.001
2019	3,037,549 (79.3%)	4,404,920 (74.7%)	
2020	328,082 (8.6%)	714,980 (12.1%)	
2021	236,392 (6.2%)	463,578 (7.9%)	
2022	153,685 (4.0%)	241,595 (4.1%)	
2023	71,280 (1.9%)	70,710 (1.2%)	
2024	1,258 (0.0%)	0 (0.0%)	

IQR: Interquartile Range; LoT: Line of Therapy; SD: Standard Deviation; U.S.: United States

Supplemental Table 4: Predictors of treatment escalation within or after 3 months (N = 9,724,029).

	Coefficient	Standard Error	Wald Chi-square	P value	Odds Ratio	95% CI- Lower	95% CI- Upper
Age group							
18-64	Reference						
65+	0.287	0.002	16364.8	< 0.001	1.333	1.327	1.338

Sex							
Male	Reference						
Female	-0.017	0.001	152.8	< 0.001	0.983	0.980	0.986
Race/Ethnicity							
White	Reference						
Black or African American	0.028	0.002	155.6	< 0.001	1.028	1.024	1.033
Asian American or Pacific Islander	-0.300	0.004	4923.9	< 0.001	0.741	0.734	0.747
Hispanic or Latino	-0.176	0.003	3080.6	< 0.001	0.839	0.833	0.844
Unknown	0.121	0.002	2459.2	< 0.001	1.128	1.123	1.134
Payer type							
Medicare	Reference						
Commercial	0.009	0.003	10.4	0.001	1.009	1.004	1.015
Managed Medicaid	-0.278	0.003	9838.1	< 0.001	0.758	0.754	0.762
Index year							
2019	Reference						
2020-2024	0.000	0.002	0.0	0.827	1.000	0.996	1.003
Comorbidities							
Hypertension complicated	0.038	0.002	268.7	< 0.001	1.039	1.034	1.043
Chronic kidney disease	0.236	0.002	11097.7	< 0.001	1.266	1.260	1.271
Primary aldosteronism	0.521	0.021	598.8	< 0.001	1.684	1.615	1.756
Renal artery stenosis	0.422	0.010	1718.7	< 0.001	1.524	1.494	1.555
Type 2 Diabetes	0.113	0.002	2428.8	< 0.001	1.120	1.115	1.125
Hyperlipidemia	-0.075	0.002	1951.5	< 0.001	0.928	0.925	0.931
Cardiovascular disease	0.366	0.002	52039.9	< 0.001	1.442	1.437	1.446
Medication classes							
Anticoagulants	0.154	0.002	6180.4	< 0.001	1.166	1.161	1.170
Antidiabetics	0.192	0.002	6396.3	< 0.001	1.212	1.206	1.218
Lipid lowering agents	0.289	0.002	30399.5	< 0.001	1.336	1.331	1.340
Anti-hypertensive medication class							
ACE inhibitors	-0.780	0.002	162199.0	< 0.001	0.458	0.457	0.460
Angiotensin receptor blockers	-0.584	0.002	81317.6	< 0.001	0.558	0.555	0.560
Beta blockers	-0.345	0.002	36217.8	< 0.001	0.708	0.706	0.711
Dihydropyridine calcium channel blockers	-0.167	0.002	7985.6	< 0.001	0.846	0.843	0.849
Non-dihydropyridine calcium channel blockers	-0.246	0.004	4428.2	< 0.001	0.782	0.776	0.787

Number of anti-hypertensive medication classes							
Monotherapy	Reference						
Combination therapy with 2+ classes	0.035	0.002	415.2	< 0.001	1.036	1.032	1.039
Combination therapy with 3+ classes	-0.036	0.003	166.2	< 0.001	0.964	0.959	0.970
Combination therapy with 4+ classes	-0.159	0.005	1100.1	< 0.001	0.853	0.845	0.861

ACE: Angiotensin Converting Enzyme; CI: Confidence Interval; IQR: Interquartile Range; LoT: Line of Therapy; SD: Standard Deviation

Supplemental Table 5: Demographic and baseline clinical characteristics of escalation subgroup with treatment escalation within or after 6 months.

	Patients escalating from LoT1 to LoT2 within 6 months N = 5,151,782	Patients escalating from LoT1 to LoT2 after 6 months N = 4,572,247	P value
Age, mean (SD)	69.3 (14.5)	66.1 (15.3)	< 0.001
Median (IQR)	71.0 (17.0)	68.0 (20.0)	
Age group, n (%)			< 0.001
18-29	40,846 (0.8%)	58,687 (1.3%)	
30-39	148,685 (2.9%)	205,778 (4.5%)	
40-49	325,064 (6.3%)	417,628 (9.1%)	
50-64	1,144,273 (22.2%)	1,200,705 (26.3%)	
65-74	1,573,599 (30.5%)	1,306,156 (28.6%)	
75-84	1,335,051 (25.9%)	991,489 (21.7%)	
85+	584,264 (11.3%)	391,804 (8.6%)	
Sex, n (%)			< 0.001
Male	2,279,036 (44.2%)	1,996,609 (43.7%)	
Female	2,872,746 (55.8%)	2,575,638 (56.3%)	
Race/Ethnicity, n (%)			< 0.001
White	3,378,396 (65.6%)	2,859,965 (62.6%)	
Black or African American	642,607 (12.5%)	556,542 (12.2%)	
Asian American or Pacific Islander	128,965 (2.5%)	161,562 (3.5%)	
Hispanic or Latino	265,716 (5.2%)	333,803 (7.3%)	
Unknown	736,098 (14.3%)	660,375 (14.4%)	
Payer type, n (%)			< 0.001

Medicare	3,683,578 (71.5%)	2,882,824 (63.1%)	
Commercial	827,863 (16.1%)	865,988 (18.9%)	
Managed Medicaid	640,341 (12.4%)	823,435 (18.0%)	
Census region, n (%)			< 0.001
Northeast	950,542 (18.5%)	861,814 (18.8%)	
Midwest	1,209,654 (23.5%)	1,009,657 (22.1%)	
South	2,006,439 (38.9%)	1,768,843 (38.7%)	
West	959,162 (18.6%)	908,083 (19.9%)	
U.S. Territory/Unknown	25,985 (0.5%)	23,850 (0.5%)	
Urbanicity, n (%)			< 0.001
Urban	4,007,595 (77.8%)	3,593,637 (78.6%)	
Rural	985,272 (19.1%)	815,081 (17.8%)	
Unknown	158,915 (3.1%)	163,529 (3.6%)	
Dual-eligibility status-Medicare only, n (%)			< 0.001
Yes	853,344 (23.2%)	705,743 (24.5%)	
No	2,770,639 (75.2%)	2,136,654 (74.1%)	
Unknown	59,595 (1.6%)	40,427 (1.4%)	
Low income subsidy status-Medicare only, n (%)			< 0.001
Yes	999,255 (27.1%)	804,504 (27.9%)	
No	2,624,728 (71.3%)	2,037,893 (70.7%)	
Unknown	59,595 (1.6%)	40,427 (1.4%)	
Area Deprivation Index, mean (SD)	50.7 (25.6)	50.0 (26.2)	< 0.001
Lowest (least deprived) quartile, n (%)	1,013,011 (19.7%)	969,801 (21.2%)	
Second quartile, n (%)	1,435,752 (27.9%)	1,259,429 (27.5%)	
Third quartile, n (%)	1,550,977 (30.1%)	1,299,379 (28.4%)	
Highest (most deprived) quartile, n (%)	1,015,486 (19.7%)	901,079 (19.7%)	
Unknown, n (%)	136,556 (2.7%)	142,559 (3.1%)	
Months of follow-up, mean (SD)	32.8 (16.6)	40.2 (13.5)	< 0.001
Median (IQR)	35.8 (29.4)	44.0 (17.4)	
Index year, n (%)			< 0.001
2019	3,991,444 (77.5%)	3,451,025 (75.5%)	
2020	472,834 (9.2%)	570,228 (12.5%)	
2021	350,601 (6.8%)	349,369 (7.6%)	
2022	229,038 (4.4%)	166,242 (3.6%)	
2023	106,607 (2.1%)	35,383 (0.8%)	
2024	1,258 (0.0%)	0 (0.0%)	

IQR: Interquartile Range; LoT: Line of Therapy; SD: Standard Deviation; U.S.: United States

Supplemental Table 6: Demographic and baseline clinical characteristics of sensitivity analysis study population with treatment escalation to combination therapy within or after 3 months.

	Patients escalating from LoT1 to LoT2 within 3 months N = 2,335,821	Patients escalating from LoT1 to LoT2 after 3 months N = 2,918,789	P value
Age, mean (SD)	69.9 (14.1)	66.6 (15.1)	< 0.001
Median (IQR)	71.0 (17.0)	68.0 (20.0)	
Age group, n (%)			< 0.001
18-29	13,462 (0.6%)	26,550 (0.9%)	
30-39	54,785 (2.3%)	113,929 (3.9%)	
40-49	133,262 (5.7%)	259,774 (8.9%)	
50-64	516,913 (22.1%)	809,637 (27.7%)	
65-74	719,049 (30.8%)	803,874 (27.5%)	
75-84	622,163 (26.6%)	629,212 (21.6%)	
85+	276,187 (11.8%)	275,813 (9.4%)	
Sex, n (%)			< 0.001
Male	1,044,691 (44.7%)	1,266,307 (43.4%)	
Female	1,291,130 (55.3%)	1,652,482 (56.6%)	
Race/Ethnicity, n (%)			< 0.001
White	1,533,821 (65.7%)	1,776,881 (60.9%)	
Black or African American	306,419 (13.1%)	408,964 (14.0%)	
Asian American or Pacific Islander	56,029 (2.4%)	99,412 (3.4%)	
Hispanic or Latino	114,976 (4.9%)	198,654 (6.8%)	
Unknown	324,576 (13.9%)	434,878 (14.9%)	
Payer type, n (%)			< 0.001
Medicare	1,701,762 (72.9%)	1,831,227 (62.7%)	
Commercial	353,067 (15.1%)	540,168 (18.5%)	
Managed Medicaid	280,992 (12.0%)	547,394 (18.8%)	
Census region, n (%)			< 0.001
Northeast	433,799 (18.6%)	543,039 (18.6%)	
Midwest	553,102 (23.7%)	651,601 (22.3%)	
South	914,907 (39.2%)	1,150,133 (39.4%)	
West	422,071 (18.1%)	555,809 (19.0%)	
U.S. Territory/Unknown	11,942 (0.5%)	18,207 (0.6%)	
Urbanicity, n (%)			< 0.001
Urban	1,804,450 (77.3%)	2,264,455 (77.6%)	
Rural	461,360 (19.8%)	543,779 (18.6%)	

Unknown	70,011 (3.0%)	110,555 (3.8%)	
Dual-eligibility status-Medicare only, n (%)			< 0.001
Yes	411,605 (24.2%)	515,739 (28.2%)	
No	1,263,018 (74.2%)	1,287,214 (70.3%)	
Unknown	27,139 (1.6%)	28,274 (1.5%)	
Low income subsidy status-Medicare only, n (%)			< 0.001
Yes	481,445 (28.3%)	584,419 (31.9%)	
No	1,193,178 (70.1%)	1,218,534 (66.5%)	
Unknown	27,139 (1.6%)	28,274 (1.5%)	
Area Deprivation Index, mean (SD)	51.3 (25.6)	51.1 (26.4)	< 0.001
Lowest (least deprived) quartile, n (%)	447,788 (19.2%)	594,628 (20.4%)	
Second quartile, n (%)	640,945 (27.4%)	771,229 (26.4%)	
Third quartile, n (%)	713,930 (30.6%)	840,483 (28.8%)	
Highest (most deprived) quartile, n (%)	474,753 (20.3%)	621,106 (21.3%)	
Unknown, n (%)	58,405 (2.5%)	91,343 (3.1%)	
Months of follow-up, mean (SD)	32.9 (16.7)	38.4 (15.0)	< 0.001
Median (IQR)	36.2 (29.7)	42.9 (21.2)	
Index year, n (%)			< 0.001
2019	1,877,763 (80.4%)	2,258,979 (77.4%)	
2020	191,238 (8.2%)	323,340 (11.1%)	
2021	135,690 (5.8%)	200,568 (6.9%)	
2022	88,226 (3.8%)	103,912 (3.6%)	
2023	42,188 (1.8%)	31,990 (1.1%)	
2024	716 (0.0%)	0 (0.0%)	

IQR: Interquartile Range; LoT: Line of Therapy; SD: Standard Deviation; U.S.: United States

Supplemental Table 7: Demographic and baseline clinical characteristics of sensitivity analysis study population with treatment escalation to combination therapy within or after 6 months.

	Patients escalating from LoT1 to LoT2 within 6 months N = 3,099,969	Patients escalating from LoT1 to LoT2 after 6 months N = 2,154,641	P value
Age, mean (SD)	69.1 (14.5)	66.7 (15.0)	< 0.001
Median (IQR)	71.0 (18.0)	68.0 (20.0)	
Age group, n (%)			< 0.001
18-29	21,654 (0.7%)	18,358 (0.9%)	
30-39	87,099 (2.8%)	81,615 (3.8%)	

40-49	202,750 (6.5%)	190,286 (8.8%)	
50-64	733,571 (23.7%)	592,979 (27.5%)	
65-74	919,462 (29.7%)	603,461 (28.0%)	
75-84	782,726 (25.2%)	468,649 (21.8%)	
85+	352,707 (11.4%)	199,293 (9.2%)	
Sex, n (%)			< 0.001
Male	1,375,859 (44.4%)	935,139 (43.4%)	
Female	1,724,110 (55.6%)	1,219,502 (56.6%)	
Race/Ethnicity, n (%)			< 0.001
White	1,981,891 (63.9%)	1,328,811 (61.7%)	
Black or African American	423,723 (13.7%)	291,660 (13.5%)	
Asian American or Pacific Islander	79,142 (2.6%)	76,299 (3.5%)	
Hispanic or Latino	165,029 (5.3%)	148,601 (6.9%)	
Unknown	450,184 (14.5%)	309,270 (14.4%)	
Payer type, n (%)			< 0.001
Medicare	2,173,004 (70.1%)	1,359,985 (63.1%)	
Commercial	497,392 (16.0%)	395,843 (18.4%)	
Managed Medicaid	429,573 (13.9%)	398,813 (18.5%)	
Census region, n (%)			< 0.001
Northeast	570,471 (18.4%)	406,367 (18.9%)	
Midwest	721,708 (23.3%)	482,995 (22.4%)	
South	1,223,712 (39.5%)	841,328 (39.0%)	
West	566,325 (18.3%)	411,555 (19.1%)	
U.S. Territory/Unknown	17,753 (0.6%)	12,396 (0.6%)	
Urbanicity, n (%)			< 0.001
Urban	2,393,355 (77.2%)	1,675,550 (77.8%)	
Rural	605,207 (19.5%)	399,932 (18.6%)	
Unknown	101,407 (3.3%)	79,159 (3.7%)	
Dual-eligibility status-Medicare only, n (%)			< 0.001
Yes	551,802 (25.4%)	375,542 (27.6%)	
No	1,585,411 (73.0%)	964,821 (70.9%)	
Unknown	35,791 (1.6%)	19,622 (1.4%)	
Low income subsidy status-Medicare only, n (%)			< 0.001
Yes	641,374 (29.5%)	424,490 (31.2%)	
No	1,495,839 (68.8%)	915,873 (67.3%)	
Unknown	35,791 (1.6%)	19,622 (1.4%)	

Area Deprivation Index, mean (SD)	51.5 (25.8)	50.7 (26.4)	< 0.001
Lowest (least deprived) quartile, n (%)	595,309 (19.2%)	447,107 (20.8%)	
Second quartile, n (%)	837,997 (27.0%)	574,177 (26.6%)	
Third quartile, n (%)	936,701 (30.2%)	617,712 (28.7%)	
Highest (most deprived) quartile, n (%)	646,301 (20.8%)	449,558 (20.9%)	
Unknown, n (%)	83,661 (2.7%)	66,087 (3.1%)	
Months of follow-up, mean (SD)	32.8 (16.7)	40.4 (13.7)	< 0.001
Median (IQR)	35.7 (29.8)	44.3 (17.3)	
Index year, n (%)			< 0.001
2019	2,447,815 (79.0%)	1,688,927 (78.4%)	
2020	269,458 (8.7%)	245,120 (11.4%)	
2021	195,218 (6.3%)	141,040 (6.5%)	
2022	126,590 (4.1%)	65,548 (3.0%)	
2023	60,172 (1.9%)	14,006 (0.7%)	
2024	716 (0.0%)	0 (0.0%)	

IQR: Interquartile Range; LoT: Line of Therapy; SD: Standard Deviation; U.S.: United States