

Supplemental Materials:

Table S1. Antihypertensive Medication Classes and Common Generic and Brand Names

#	Antihypertensive medication classes FDA Chronic Antihypertensive Treatment Classes	Generic Name (GNN)	Brand Name (BN)*
Category-1: Angiotensin II <u>Stimulating</u> drugs			
1	Angiotensin II receptor blockers (ARB)	Azilsartan Candesartan Eprosartan Irbesartan Losartan Olmesartan Telmisartan Valsartan	Edarbi, Edarbychlor [†] Atacand, Atacand HCT [†] Teveten, Teveten HCT [†] , Teveten Plus [†] Avapro, Avalide [†] Cozaar, Hyzaar [†] Benicar, Azor [†] , Benicar HCT [†] , Tribenzor [†] Micardis, Micardis HCT [†] , Micardis Plus [†] , Twynsta [†] Diovan, Prexxartan [§] , Byvalson [†] , Diovan HCT [†] , Exforge HCT [†] , Entresto [†] , Valtuna [†]
2	Calcium channel blocker (CCB)- dihydropyridine	Amlodipine Felodipine Isradipine Nicardipine Nifedipine Nimodipine Nisoldipine	Norvasc, Amturnide [†] , Azor [†] , Exforge HCT [†] , Lotrel [†] , Prestalia [†] , Tekamlo [†] , Tribenzor [†] , Twynsta [†] Cabren, Cardioplen XL, Felendil XL, Felogen XL, Felotens XL, Keloc SR, Neofel XL, Plendil, Renedil, Vascalpha, Lexxel ^{†§} Cardene, Cardene SR Adalat, Adalat CC, Afeditab CR, Nifediac CC, Nifedical XL, Procardia, Procardia XL, Sular
3	Diuretics: thiazide	Bendroflumethiazide Chlorothiazide Hydrochlorothiazide Hydroflumethiazide Polythiazide Trichlormethiazide	Naturetin [§] , NeoNaClex [§] , Urizide [§] , Corzide [†] Diuril, Tekturina HCT [†] Microzide, Accuretic [†] , Aldactazide [†] , Atacand HCT [†] , Avalide [†] , Benicar HCT [†] , Capozide [†] , Corzide [†] , Dutoprol [†] , Exforge HCT [†] , Hydra-zide [†] , Hyzaar [†] , Inderide [†] , Lopressor HCT [†] , Lotensin HCT [†] , Maxide [†] , Micardis HCT [†] , Micardis Plus [†] , Moduretic [†] , Teveten HCT [†] , Teveten Plus [†] , Tribenzor [†] , Uniretic [†] , Vaseretic [†] , Zestoretic [†] , Ziac [†] , Diucardin; Renese; Achletin, Diu-Hydrin and Triflumen
4	Diuretics: thiazide-type	Chlorthalidone Indapamide Metolazone	Hygroton, Thalitone, Chlorthalid, Clorpres [†] , Edarbychlor [†] , Tenoretic [†] Zaroxolyn
Category-2: Angiotensin II <u>Inhibiting</u> drugs			
5	Angiotensin-converting enzyme (ACE) inhibitor	Benazepril Captopril Enalapril Fosinopril Lisinopril Moexipril Perindopril Quinapril Ramipril Trandolapril	Lotensin, Lotensin HCT [†] , Lotrel [†] Capoten, Captoril, Capozide [†] Vasotec, Enalaprilat, Epaned, Lexxel ^{†§} , Vaseretic [†] Monopril Prinivil, Qbrelis, Zestril, Zestoretic [†] Univasc, Uniretic [†] Aceon, Prestalia [†] Accupril, Accuretic [†] Altace Mavik, Tarka [†]
6	Beta adrenergic blockers (β-blockers)	Acebutolol Atenolol Betaxolol Bisoprolol	Sectral Tenormin, Tenoretic [†] Kerlone Monocor, Zebeta, Ziac [†] Coreg, Coreg CR

		Carvedilol {also with $\alpha 1$ properties} Esmolol [¶] Labetalol {also with $\alpha 1$ properties} Metoprolol Nadolol Nebivolol Penbutolol Propranolol Sotalol Carteolol Pindolol Timolol	Brevibloc Trandate Kaspargo Sprinkle, Lopressor, Toprol XL, Dutoprol [‡] , Lopressor HCT [‡] Corgard, Corzide [‡] Bystolic, Byvalson [‡] Levatol Inderal, Inderal LA, InnoPran XL, Inderide [‡] Betapace, Sorine [¶] Ocupress; Visken; Blocadren, Timoptic-xe, Istalol, Timoptic, Betimol, and Timoptic Ocudose (PF)
7	Calcium channel blocker – non-dihydropyridine	Diltiazem Verapamil	Cardizem, Cardizem CD, Cardizem LA, Dilacor, Dilacor XR, Dilatrate, Diltazem, Diltazem CD, Diltiaz, Diltiaz CD, Diltiaz SR, Tiazac Calan, Calan HS, Calan SR, Covera HS, Isoptin, Isoptin SR, Verelan, Verelan PM, Tarka [‡]
Category-3: Other types of anti-hypertensive drugs			
8	Aldosterone antagonists [†]	Eplerenone Spironolactone	Inspra Aldactone, Carospir, Aldactazide [‡]
9	Alpha 1 adrenergic receptor agonist (selective; α-blocker)	Doxazosin Prazosin Terazosin	Cardura (XL) Minipress, Prazin, Prazo Hytrin
10	Arteriolar vasodilators	Hydralazine Minoxidil	-, Hydra-zide [‡] Loniten, Minodyl, Minoxidil HTN
11	Autonomic ganglionic vasodilators	Mecamylamine	-
12	Central alpha 2 adrenergic agonists	Clonidine Guanabenz [§] Guanfacine Methyldopa	Catapres, Jenloga, Kapvay, Nexiclon XR, Clorpres [‡] Wytensin [§] Intuniv, Tenex Aldomet
13	Diuretics: loop	Bumetanide Ethacrynic acid Furosemide Torsemide	Bumex, Burinex Edecrin [¶] Lasix Demadex
14	Diuretics: potassium-sparing [†]	Amiloride Triamterene	Midamor, Moduretic [‡] Dyrenium, Maxide [‡]
15	Peripheral adrenergic neuron antagonist [†]	Reserpine	Serpasil
16	Renin inhibitors	Aliskiren	Tekturna, Tekturna HCT [‡] , Teklamo [‡] , Amturnide [‡] , Valturna [‡]

*Part-D data appear to have generic name (GNN) only because BN has the same info as GNN in the dataset (so far as noted).

[†]Not used alone/used in combination for chronic hypertension treatment

[‡]Combination medication also listed in another class

[§]Currently discontinued in the US

Source in part from:

Healthline: A List of Blood Pressure Medications. <https://www.healthline.com/health/high-blood-pressure-hypertension-medication#overview>, accessed July 19, 2022.

Table S2. ICD-9 and ICD-10 codes for Alzheimer's Disease and related Dementia (ADRD)

ICD-9	Description for ICD-9 codes	ICD-10	Description for ICD-10 codes
290.0	Senile dementia, uncomplicated	F03.90	Unspecified dementia without behavioral disturbance
290.1	Presenile dementia, uncomplicated	F03.90	Unspecified dementia without behavioral disturbance
290.2	Senile dementia with delusional or depressive features	F03.90	Unspecified dementia without behavioral disturbance
290.3	Senile dementia with delirium (acute confusional state)	F03.90	Unspecified dementia without behavioral disturbance
290.40	Vascular dementia	F01.50	Vascular dementia
290.41	Vascular dementia, with delirium	F01.51	Vascular dementia with behavioral disturbance
290.42	Vascular dementia, with delusions		
290.43	Vascular dementia, with depressed mood		
290.8	Other specified senile psychotic conditions	F03.90	Unspecified dementia without behavioral disturbance
290.9	Unspecified senile psychotic condition	F03.90	Unspecified dementia without behavioral disturbance
291.2	Alcohol-induced persisting dementia	F10.27	Alcohol-induced dementia
292.82	Drug-induced persisting dementia	F19.97	Other-psychoactive substance use/unspecified with psychoactive substance induced persisting dementia
294.10	Dementia in conditions classified elsewhere without behavioral disturbance	F02.80	Dementia in other diseases classified elsewhere without behavioral disturbance
294.11	Dementia in conditions classified elsewhere with behavioral disturbance	F02.81	Dementia in other diseases classified elsewhere with behavioral disturbance
294.20	Dementia, unspecified, without behavioral disturbance	F03.90	Unspecified dementia without behavioral disturbance
294.21	Dementia, unspecified, with behavioral disturbance	F03.91	Unspecified dementia with behavioral disturbance
294.8	Other persistent mental disorders due to conditions classified elsewhere	F06.0	Psychotic disorder with hallucinations due to known physiological condition
294.9	Unspecified persistent mental disorders due to conditions classified elsewhere	F06.8	Other specified mental disorders due to known physiological condition
331.0	Alzheimer's disease	G30	Alzheimer's disease
		G30.0	Alzheimer's disease with early onset
		G30.1	Alzheimer's disease with late onset
		G30.8	Other Alzheimer's disease
		G30.9	Alzheimer's disease, unspecified
331.11	Frontotemporal dementia, Pick's disease	G31.01	Frontotemporal dementia, Pick's disease
331.19	Other frontotemporal dementia	G31.09	Other frontotemporal dementia
331.2	Senile degeneration of brain	G31.1	Senile degeneration of brain, not elsewhere classified
331.7	Cerebral degeneration in dis. classified elsewhere	G94	Other disorders of brain in dis. classified elsewhere
331.82	Dementia with Lewy bodies	G31.83	Dementia with Lewy bodies
331.83	Mild cognitive impairment, so stated	G31.84	Mild cognitive impairment, so stated
331.89	Other cerebral degeneration	G31.89	Other specified degenerative dis. of nervous system
331.9	Cerebral degeneration, unspecified	G31.9	Degenerative disease of nervous system, unspecified
797	Senility without mention of psychosis	R41.81	Age-related cognitive decline

Table S3. Incidence-density of dementia (ADRD*) by antihypertensive drug types

	Incidence-density of ADRD (per 1,000 person-years)						
Characteristics	AD*	Vascular	DLB*	FTD*	MCI*	Others	Total ADRD
Antihypertensive drug types							
Angiotensin-II stimulating drugs	12.5	6.1	0.9	0.4	4.2	66.2	71.8
Angiotensin-II inhibiting drugs	13.3	7.5	1.2	0.4	5.4	79.6	85.5
Angiotensin-II stimulating + inhibiting drugs	14.4	7.5	0.9	0.4	4.8	70.7	76.2
Other antihypertensive drugs	16.3	10.6	1.2	0.3	6.6	111.9	120.3
Did not receive any antihypertensive drugs	11.0	6.4	1.1	0.2	5.0	87.2	93.8
Did not have hypertension	6.7	2.3	0.8	0.2	3.1	39.3	42.3
Age (years)							
65-69	4.2	2.8	0.4	0.1	2.3	29.0	31.8
70-74	7.5	4.1	0.8	0.3	3.3	46.5	50.6
75-79	13.4	7.2	1.4	0.4	5.0	72.7	79.0
80-84	20.6	10.3	1.4	0.4	6.7	112.7	120.0
85 or older	28.4	14.1	1.6	0.6	10.1	189.9	204.1
Gender							
Men	10.3	5.8	1.3	0.4	4.4	66.0	71.3
Women	14.1	7.3	0.8	0.3	5.1	78.1	83.9
Race/ethnicity							
NH-Whites	12.5	6.4	1.1	0.4	5.3	73.3	78.9
NH-Blacks	14.9	11.1	0.7	0.2	4.9	90.4	97.7
NH-Asians/Pacific Islanders	9.9	4.6	0.9	0.1	2.5	59.6	63.7
Hispanics	12.6	5.9	1.0	0.3	2.9	65.0	70.3
Others	2.7	4.1	0	1.3	4.1	54.2	56.0
Unknown/missing	5.0	3.0	0	1.0	3.0	31.4	33.8
Marital status							
Married	10.0	4.8	1.0	0.3	4.1	54.1	58.7
Unmarried	15.1	8.7	1.0	0.3	5.4	93.7	100.5
Unknown	12.7	6.0	1.0	0.4	5.0	70.0	75.3
Tumor stage							
In-situ/local stage	13.6	6.6	1.2	0.3	4.8	64.4	69.7
Regional	11.9	6.4	1.0	0.3	4.8	70.5	76.1
Distant	5.1	5.6	0.2	0.1	4.1	107.6	112.9
Unknown/Missing	19.3	12.3	1.0	1.5	7.1	169.8	180.0
Tumor grade							
Well-differentiated	12.4	5.6	0.9	0.5	4.7	62.6	68.0
Moderately-differentiated	12.6	6.4	1.1	0.3	4.5	69.8	74.8
Poorly-differentiated	12.0	7.1	0.6	0.3	6.2	82.0	88.7
Unknown/Missing	12.4	7.9	1.2	0.4	4.5	82.8	89.5
Tumor site							
Colon	13.2	7.2	1.0	0.3	5.1	76.1	82.1
Rectal	10.1	4.9	1.0	0.5	3.8	62.6	67.1
Chemotherapy							
No	14.4	7.8	1.2	0.4	5.3	81.1	87.3
Yes	7.1	3.4	0.6	0.3	3.5	50.4	54.5
Radiotherapy							
No	12.8	6.9	1.0	0.3	4.9	74.3	79.9
Yes	9.1	4.0	0.6	0.3	3.2	56.5	61.5
Comorbidity Scores							
0	10.4	5.0	1.0	0.3	4.3	53.8	58.3
1	13.9	7.5	1.1	0.4	4.9	79.6	85.4
≥2	16.4	10.2	0.9	0.5	6.1	127.5	136.8
SEER Areas							
Connecticut	16.6	15.0	1.6	0.6	7.0	85.0	93.1
Detroit	18.0	11.9	0.9	0.3	5.3	90.4	96.6
Hawaii	7.9	6.3	1.6	0	1.6	54.8	55.6
Iowa	11.3	4.9	0.8	0.1	4.9	66.1	69.6
New Mexico	6.9	4.3	0.8	0.3	4.0	54.2	58.0
Seattle	8.0	5.6	1.1	1.0	3.9	59.1	63.1
Utah	9.1	3.9	0	0	3.6	60.8	64.0
Georgia	10.7	4.4	0.6	0.2	3.5	64.2	68.7
Kentucky	14.1	5.4	0.8	0.1	2.9	78.3	82.4
Louisiana	12.6	6.6	0.8	0.4	3.7	77.5	81.9
New Jersey	17.3	8.9	1.4	0.4	6.0	82.7	90.9
California	10.4	5.3	1.0	0.3	5.2	69.8	75.8
Total	12.5	6.6	1.0	0.3	4.8	72.7	78.3

* ADRD (Alzheimer's disease and related dementia), AD (Alzheimer's disease), Vascular (vascular dementia), DLB (dementia with Lewy bodies), FTD (Frontotemporal degeneration and dementia), MCI (Mild cognitive impairment), others (other dementia), and total (any of above ADRD).

Table S4. Adjusted hazard ratio of developing dementia by antihypertensive drug types by excluding dementia cases that occurred within 3 and 5 years from the baseline

Characteristics	Hazard ratio (95% CI)* of ADRD by excluding dementia cases that occurred within 3 years from baseline			Hazard ratio (95% CI)* of ADRD by excluding dementia cases that occurred within 5 years from baseline		
	AD**	Vascular	Total ADRD**	AD**	Vascular	Total ADRD**
Antihypertensive drug types						
Angiotensin-II stimulating drugs	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
Angiotensin-II inhibiting drugs	1.26 (1.04-1.52)	1.35 (1.01-1.81)	1.25 (1.12-1.41)	1.20 (0.92-1.57)	1.34 (0.87-2.05)	1.22 (1.02-1.45)
Angiotensin -II stimulating + inhibiting drugs	1.09 (0.91-1.31)	1.26 (0.95-1.66)	1.23 (1.10-1.37)	1.03 (0.8-1.33)	1.37 (0.93-2.03)	1.14 (0.97-1.34)
Other antihypertensive drugs	1.36 (1.05-1.78)	1.72 (1.17-2.53)	1.31 (1.11-1.55)	1.07 (0.7-1.63)	1.88 (1.06-3.33)	1.17 (0.89-1.55)
Did not receive any antihypertensive drugs	1.19 (0.95-1.49)	0.82 (0.56-1.21)	1.01 (0.87-1.16)	1.03 (0.74-1.45)	0.63 (0.34-1.18)	0.93 (0.74-1.16)
Did not have hypertension	1.05 (0.82-1.34)	0.50 (0.31-0.81)	0.87 (0.75-1.01)	1.15 (0.83-1.59)	0.47 (0.24-0.92)	0.87 (0.70-1.08)
Age (years)						
65-69	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
70-74	1.60 (1.28-2.01)	1.70 (1.22-2.36)	1.58 (1.41-1.78)	1.79 (1.31-2.46)	2.01 (1.28-3.17)	1.44 (1.22-1.70)
75-79	3.16 (2.56-3.89)	2.83 (2.07-3.87)	2.45 (2.19-2.75)	3.93 (2.93-5.27)	3.17 (2.05-4.92)	2.39 (2.03-2.81)
80-84	4.77 (3.86-5.89)	3.09 (2.23-4.28)	3.24 (2.88-3.65)	5.43 (4.02-7.33)	3.26 (2.05-5.20)	3.12 (2.63-3.71)
85 or older	6.28 (5.04-7.83)	4.03 (2.87-5.67)	4.68 (4.12-5.31)	6.62 (4.77-9.17)	4.38 (2.67-7.18)	4.43 (3.66-5.38)
Gender						
Men	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
Women	1.01 (0.89-1.15)	0.91 (0.75-1.11)	0.91 (0.84-0.98)	0.98 (0.82-1.18)	0.91 (0.69-1.21)	0.97 (0.86-1.09)
Race/ethnicity						
NH-Whites	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
NH-Blacks	1.26 (1.03-1.54)	1.38 (1.03-1.86)	1.09 (0.96-1.24)	1.12 (0.84-1.51)	1.19 (0.77-1.85)	1.18 (0.97-1.42)
NH-Asians/Pacific Islanders	0.74 (0.55-0.98)	0.61 (0.38-0.98)	0.77 (0.66-0.90)	0.59 (0.39-0.90)	0.51 (0.24-1.09)	0.73 (0.58-0.92)
Hispanics	1.26 (1.01-1.57)	1.06 (0.75-1.51)	0.99 (0.87-1.14)	0.91 (0.65-1.28)	1.27 (0.80-2.02)	1.01 (0.82-1.23)
Others	0.33 (0.05-2.37)	0.70 (0.10-5.00)	0.79 (0.41-1.53)	- ^T	-	0.37 (0.09-1.51)
Unknown/missing	0.77 (0.29-2.09)	1.39 (0.44-4.43)	0.96 (0.58-1.59)	0.60 (0.15-2.45)	3.40 (1.04-11.14)	0.78 (0.35-1.79)
Marital status						
Married	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
Unmarried	1.03 (0.90-1.17)	1.11 (0.91-1.36)	1.14 (1.05-1.23)	1.01 (0.84-1.21)	1.00 (0.76-1.33)	1.04 (0.92-1.17)
Unknown	0.89 (0.69-1.16)	0.95 (0.64-1.40)	1.02 (0.87-1.19)	0.95 (0.66-1.36)	0.65 (0.35-1.20)	1.00 (0.79-1.27)
Tumor stage						
Local	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
Regional	0.97 (0.85-1.11)	1.05 (0.85-1.29)	1.02 (0.94-1.11)	0.89 (0.73-1.08)	1.25 (0.93-1.67)	1.02 (0.90-1.15)
Distant	0.80 (0.54-1.18)	1.12 (0.65-1.91)	1.00 (0.82-1.23)	0.79 (0.42-1.45)	1.50 (0.68-3.28)	1.21 (0.89-1.66)
Unknown/Missing	0.98 (0.66-1.47)	1.30 (0.74-2.29)	1.38 (1.10-1.73)	1.31 (0.77-2.21)	1.78 (0.85-3.71)	1.08 (0.73-1.60)
Tumor grade						
Well-differentiated	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
Moderately-differentiated	0.96 (0.80-1.17)	1.09 (0.80-1.48)	1.05 (0.93-1.19)	0.84 (0.65-1.08)	1.23 (0.79-1.91)	0.99 (0.83-1.17)
Poorly-differentiated	0.99 (0.79-1.25)	1.12 (0.77-1.61)	1.10 (0.96-1.28)	0.84 (0.60-1.15)	1.04 (0.60-1.79)	1.01 (0.82-1.25)
Unknown/Missing	1.03 (0.81-1.30)	1.07 (0.74-1.56)	1.00 (0.86-1.16)	0.96 (0.70-1.32)	1.12 (0.65-1.93)	1.01 (0.82-1.26)
Tumor site						
Colon	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
Rectal	0.81 (0.69-0.96)	0.84 (0.65-1.09)	0.95 (0.86-1.05)	0.84 (0.66-1.06)	0.83 (0.57-1.20)	0.95 (0.82-1.10)

Chemotherapy						
No	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
Yes	0.76 (0.64-0.91)	0.73 (0.56-0.97)	0.94 (0.85-1.04)	0.83 (0.64-1.07)	0.68 (0.46-0.99)	0.90 (0.77-1.05)
Radiotherapy						
No	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
Yes	1.11 (0.83-1.49)	0.83 (0.51-1.35)	0.94 (0.80-1.11)	0.97 (0.63-1.49)	1.06 (0.56-1.99)	0.97 (0.76-1.24)
Comorbidity Scores						
0	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
1	1.20 (1.05-1.35)	1.27 (1.04-1.54)	1.27 (1.17-1.37)	1.26 (1.05-1.50)	1.05 (0.80-1.38)	1.24 (1.10-1.39)
≥2	1.45 (1.23-1.71)	1.22 (0.94-1.59)	1.65 (1.50-1.83)	1.44 (1.13-1.83)	1.14 (0.78-1.66)	1.80 (1.55-2.09)

* Hazard ratios adjusted for the following variables: age, gender, race/ethnicity, marital status, tumor stage, tumor grade, tumor site, comorbidity score, chemotherapy, radiation therapy, year of diagnosis, and SEER areas.

** AD (Alzheimer's disease), Vascular (vascular dementia), total ADRD (Alzheimer's disease and related dementia) included AD, vascular dementia, DLB (dementia with Lewy bodies), FTD (Frontotemporal degeneration and dementia), MCI (Mild cognitive impairment), and other dementia.

[†] no cases.

Figure S1. Forest Plot on the hazard ratio of developing AD in patients receiving angiotensin II–inhibiting vs stimulating antihypertensive medications

[AD (Alzheimer’s disease), Vascular (vascular dementia), DLB (dementia with Lewy bodies), FTD (Frontotemporal degeneration and dementia), MCI (Mild cognitive impairment), others (other dementia), and total ADRD (Alzheimer’s disease and related dementia)]

