

Appendix 4. Results of Individual studies

Author	Publication Year	AD Diagnostic Tool	Hypertension Definition	Intervention	Comparator	No. AD Events	Unadjusted Effect estimate [95% CI]	Adjusted Effect estimate [95% CI]	Confounders	ROBINS-I
<b>Barthold et al.</b>	2018	ICD-9	Hypertension diagnosis (ICD9)	ACEI	Non-RAS AHA users	ACEI: 5895/640,715	NR	ACEI: OR 1.009 [0.989-1.031] †	Age, age squared, sex, race, education, income quartiles by zip code, statin use, years since hypertension diagnosis, number of physicians visits, comorbidity index, atrial fibrillation, acute myocardial infarction, stroke and hyperlipidaemia	Moderate
				ARB		ARB: 3083/380,606	ARB: OR 0.916 [0.893-0.940] ††			
						Non-RAS AHA: 6889/615,116				
<b>Chiu et al.</b>	2014	ICD-9 or AChEI	Hypertension diagnosis (ICD9)	ARB	Non-ARB AHA users	ARB: 184/24,531	NR	HR 0.53 [0.43-0.64] †	Adjusted for ACEI, BB, CCB and diuretics. Cohorts matched 1:1 based on: age, sex, income, urbanization, hypertension, coronary heart disease, kidney disease, diabetes mellitus, hypercholesterolaemia and depressive disorder	Moderate
						Non-ARB AHA: 350/24,531				
<b>Davies et al.</b>	2011	Diagnostic codes (UK)	Systolic BP ≥140 mmHg	ACEI	Non-ACEI AHA users	ACEI: Cases 734/2227	ACEI: OR 0.77 [0.71-0.85] *	ACEI: OR 0.76 [0.69–0.84] †	Age, gender, geographical region, number of GP consultations, index of multiple deprivation, blood pressure, diabetes mellitus, stroke, coronary artery disease and smoking	Serious
						Controls 14,794/39166				
				ARB	Non-ARB AHA users	ARB: Cases 89/2227	ARB: OR 0.49 [0.39–0.61] *	ARB: OR 0.47 [0.37–0.58] †		
						Controls 2741/39166				
<b>Haag et al.</b>	2009	NINCDS-ADRDA	Systolic BP ≥140 mm/Hg	Any AHA	Non-AHA users	AHA: 218/6249	NR	HR 0.94 [0.90-0.99]	Age, sex, education, blood pressure, smoking, total serum cholesterol, body mass index, diabetes mellitus, cardiovascular and cerebrovascular disease.	Serious
						Non-AHA: 214/6249				
<b>Hsu et al.</b>	2013	ICD-9	Hypertension diagnosis (ICD9)	ARB	Non-ARB AHA users	ARB: 488/16426	HR 1.08 [0.96-1.22]	HR 1.0 [0.88-1.13]	Age, sex, history of hypertension, diabetes mellitus, coronary artery	Serious

						Non-ARB: 543/16485			disease, hyperlipidaemia, and arrhythmias	
<b>Hwang et al.</b>	2016	Diagnostic codes (S. Korea)	Hypertension diagnosis (Diagnostic codes)	<b>Part 1:</b> - ACEI - ARB - CCB - Diuretics	<b>Part 1:</b> - BB	<b>Part 1 :</b> 6360/50755 §	NR	<b>Part 1:</b> ACEI HR 0.98 [0.91-1.05]  ARB HR 0.90 [0.86-0.94]  CCB HR 0.87 [0.83-0.90]  Diuretics HR 0.96 [0.92-1.00]	Age, sex, blood pressure, body mass index, income, urbanization, smoking status, alcohol intake, coronary artery disease, hypercholesterolemia, diabetes mellitus and number of hypertensive drugs	Moderate
				<b>Part 2:</b> - CCB	<b>Part 2:</b> Non-CCB AHA users	<b>Part 2 :</b> CCB 1421/13692  Non-CCB 566/4731		<b>Part 2:</b> HR 0.80 [0.72 -0.88] †		
<b>In't Veld et al.</b>	2001	NINCDS-ADRDA	Systolic BP ≥140 mm/Hg	Any AHA	Non-AHA users	NR	NR	RR 0.77 [0.49–1.24]	Age, sex, blood pressure, history of stroke and diabetes mellitus. Body mass index, smoking status, education, living situation (independent, home for the elderly), baseline MMSE and peripheral arterial disease.	Serious
<b>Kuan et al.</b>	2016	ICD-9 +/- AChEi + memantine	Hypertension diagnosis (ICD9)	ACEI	Non-ACEI AHA users	ACEI: 18/2377  Non-ACEI: 11/2377	ACEI: HR 1.44 [0.68-3.04]	ACEI: HR 1.43 [0.67-3.04]	Age, sex, chronic kidney disease, hyperlipidaemia, COPD, asthma, stroke, head injury, coronary artery disease and the following medications used before type 2 DM diagnosis: α-blockers, β-blockers, potassium-sparing diuretics, thiazides, loop diuretics, and calcium channel blockers	Moderate
				ARB	Non-ARB AHA users	ARB: 8/1780  Non-ARB: 8/1780	ARB: HR 0.73 [0.31-2.22]	ARB: HR 0.80 [0.29-2.17]		
<b>Tully et al.</b>	2016	NINCDS-ADRDA	Systolic BP ≥140 mm/Hg	BB	Non-AHA users	NR	NR	HR 1.022 [0.8-1.306] †	Sex, study centre, education, BMI, cardiovascular disease, hypercholesterolemia, arrhythmia, diabetes mellitus, chronic kidney	Moderate

disease, depressive  
symptoms, APOE  
genotype and mean  
blood pressure quartiles

ACEI, angiotensin converting enzyme inhibitor; AChEI, anticholinesterase inhibitors; AHA, antihypertensive agent; ARB, angiotensin II receptor blocker; BB, beta blocker; CCB, calcium channel blocker; HR, hazard ratio; ICD-9, *International Classification of Diseases and Related Health Problems, Ninth Edition*; MMSE, Mini-Mental State Examination; NINCDS-ADRDA, *the National Institute of Neurological and Communicative Disorders and Stroke Alzheimer's Disease and Related Disorders Association*; Non-RAS AHA, Non-renin angiotensin system antihypertensive agent; NR, Not reported; OR, odds ratio; RR, risk ratio.

† Not published – obtained direct from author

‡ Statistically significant *p*-value

§ Cumulative total