SUPPLEMENTAL MATERIAL

Data S1. Literature search terms:

The following search terms used were in the Medline database:

(adherence [All Fields] OR medication adherence [Mesh] OR patient compliance [Mesh] OR persistence [All Fields])

AND (hypertension [Mesh] OR antihypertensive agents [Mesh] OR angiotensin-converting enzyme inhibitors [Mesh] OR calcium channel blockers [Mesh] OR angiotensin receptor antagonists [Mesh] OR adrenergic beta-antagonists [Mesh] OR diuretics [Mesh] OR antihypertensive medications [All Fields])

AND (stroke [Mesh] OR cerebrovascular disorders [Mesh] OR cardiovascular diseases [Mesh]).

The search strategy for the Embase database was similar to that used for the Medline database.

Table S1 The data source and diseases classification in each included study

First author (year of publication)	Data source	Diseases classification
Yang 2016 [1]	MarketScan Medicaid database from 11 geographically dispersed states in the USA	ICD-9
Kim 2016 [2]	Korea National Health Insurance program in Korea	ICD-10
Herttua 2016 [3]	The Statistics Finland Labor Market database; National Death Register in Finland; National Drug Reimbursement Register in Finland; the Drug Prescription Register by the Social Insurance Institution of Finland; National Institute for Health and Welfare in Finland	ICD-10
Krousel–Wood 2015 [4]	The Cohort Study of Medication Adherence in Older Adults (CoSMO) in the southeastern Louisiana, USA	ICD-9
Gosmanova 2015 [5]	Racial and Cardiovascular Risk Anomalies in CKD (RCAV) study examining risk factors of incident CKD in USA veterans	ICD-9
Xu 2013 [6]	The China National Stroke Registry database	Self-reported
Wong 2013 [7]	A territorywide database in Hong Kong	ICD-9
Shin 2013 [8]	Korean National Health Insurance Claims Database	ICD-10
Herttua 2013 [9]	The Statistics Finland Labor Market database; National Drug Reimbursement Register in Finland; the Drug Prescription Register by the Social Insurance Institution of Finland; National Institute for Health and Welfare in Finland	ICD-10
Perreault 2012 [10]	A linked administrative health database from the RAMQ (Régie Assurance Maladie Québec) in	ICD-9

	Quebec, Canada	
Degli 2011 [11]	Medications Prescription Database maintained by the Local Health Unit of Florence, Italy	ICD-9
Corrao 2011[12]	The health service databases of Lombardy in Italy	Self-reported
Khan 2010[13]	The Registry of the Canadian Stroke Network	Self-reported
Bailey 2010[14]	Tennessee's Medicaid program in USA	ICD-9
Mazzaglia 2009[15]	The Health Search/Thales Database in Italy	ICD-9
Liu 2009 [16]	NHI Research Database in Taiwan	ICD-9
Kettani 2009 [17]	A linked administrative health database from the RAMQ (Régie Assurance Maladie Québec) in Quebec, Canada; Med-Echo databases in Canada	ICD-9
Breekveldt–Postma 2008[18]	PHARMO Record Linkage System in Netherlands	ATC codes

ICD, International Classification of Diseases; CKD, chronic kidney disease; ATC, Anatomical Therapeutic Chemical.

Table S2 The confounders adjusted for the multivariate analysis in each included study.

First author (year of publication)	Adjustment for confounders
Yang 2016 [1]	Age, sex, race, previous CVD, and comorbidities (dyslipidemia, diabetes, chronic respiratory disease, chronic kidney disease, depression)
Kim 2016 [2]	Age, sex, income, residential regions, comorbidities (diabetes, dyslipidemia, and CCI), and the number of AHM
Herttua 2016 [3]	Age, sex, education, comorbidity (diabetes), and a history of cancer
Krousel–Wood 2015 [4]	Age, sex, race, marital status, education, comorbidities (depressive symptoms and CCI), the number of AHM, BMI, and lifestyle behaviors
Gosmanova 2015 [5]	Age, sex, race, marital status, income, public service, baseline glomerular filtration rate, BMI, SBP and DBP, and comorbidities (diabetes, CAD, PAD, chronic respiratory disease, dementia, liver disease, cancers, HIV/AIDS, and depression)
Xu 2013 [6]	Age, education, income, marital status, a history of stroke, comorbidities (myocardial infarction, atrial fibrillation, and diabetes), AHM history, the class of AHM at discharge, severity of stroke, dysphagia, co-medication at discharge (antiplatelet agents, anticoagulants, lipid-lowering agents, and antidiabetic agents)
Wong 2013 [7]	Age, sex, public service, and the class of first AHM
Shin 2013 [8]	Age, sex, type of health insurance, cardiovascular risk at baseline, comorbidities (diabetes, dyslipidemia, and CCI), and the number and class of AHM
Herttua 2013 [9]	Age, sex, length of AHM, education, income, comorbidity (diabetes), and a history of cancer
Perreault 2012 [10]	Age, sex, adherence to other medications (e.g. statins, antidiabetic agents, proton pump inhibitors, and antiresorptive agents for osteoporosis)

Degli 2011 [11]	Age, sex, comorbidities (diabetes, dyslipidemia, heart disease, and atherosclerotic disease), and use of antidiabetic agents, lipid-lowering agents, cardiac therapy, and antiplatelet agents
Corrao 2011[12]	Sex, age, the number of AHM, comorbidity (CCI), and drugs prescribed for heart failure or coronary heart disease
Khan 2010[13]	Age, AHM history, comorbidities (depression and other conditions), total number of baseline drugs used, socioeconomic status, and severity and type of previous stroke
Bailey 2010[14]	Age, sex, race, income, residential regions, type of health insurance, comorbidities (obesity, diabetes, dyslipidemia, CHF, myocardial infarction, atrial fibrillation, TIA, and CCI), history of substance abuse, the class of AHM
Mazzaglia 2009[15]	Age, sex, use of antithrombotics, ≥ 5 concurrent medications, and comorbidities (diabetes, dyslipidemia, and PAD), prior hospitalization, and the number of AHM
Liu 2009 [16]	Age, sex, the number of AHM, and comorbidities (diabetes, CAD, other heart, dyslipidemia, and renal diseases)
Kettani 2009 [17]	Sex , public assistance, comorbidities (CAD, CHF, PAD, other CVD, diabetes, and dyslipidemia), antiplatelet agents, antidiabetic agents, and lipid-lowering agents
Breekveldt–Postma 2008[18]	Sex, age, type of prescriber, cardiovascular co-medication, initial AHM and number of AHM classes, and comorbidity (myocardial infarction)

AHM, antihypertensive medication; CVD, cardiovascular disease; CCI, Charlson Comorbidity Index; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HIV, human immunodeficiency virus; AIDS, acquired immune deficiency syndrome; CHF, congestive heart failure; PAD, peripheral artery diseases; CAD, coronary artery disease.

Table S3 Quality assessment of the included studies*

Reference	Is the exposed cohort representative?	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of important factors†	Assessment of outcome	Follow up period	Adequacy of follow up of cohorts	Total quality scores
Yang 2016 [1]	☆	☆	☆	☆	☆☆	—	☆	☆	8
Kim 2016 [2]	☆	☆	☆	☆	☆☆	☆	☆	☆	9
Herttua 2016 [3]	☆	☆	☆	☆	☆☆	☆	☆	☆	9
Krousel–Wood 2015 [4]	☆	☆	☆	☆	☆☆	☆	☆	☆	9
Gosmanova 2015 [5]	☆	☆	☆	☆	☆☆	☆	☆	☆	9
Xu 2013 [6]	☆	☆	☆	☆	☆	☆	—	—	6
Wong 2013 [7]	☆	☆	☆	☆	—	☆	☆	☆	7
Shin 2013 [8]	☆	☆	☆	☆	☆☆	☆	—	—	7
Herttua 2013 [9]	☆	☆	☆	☆	☆☆	☆	☆	☆	9
Perreault 2012 [10]	☆	☆	☆	☆	☆☆	☆	☆	☆	9
Degli 2011 [11]	☆	☆	☆	☆	☆	☆	☆	☆	8
Corrao 2011[12]	☆	☆	☆	☆	☆	☆	☆	☆	8
Khan 2010[13]	☆	☆	☆	☆	—	☆	—	☆	6
Bailey 2010[14]	☆	☆	☆	☆	—	☆	☆	☆	7
Mazzaglia 2009[15]	☆	☆	☆	☆	☆	☆	☆	☆	8
Liu 2009 [16]	☆	☆	☆	☆	☆☆	☆	☆	☆	9
Kettani 2009 [17]	☆	☆	☆	☆	☆	☆	☆	☆	8

Breekveldt–Postma 2008[18]	☆	☆	☆	☆	☆☆	☆	☆	☆	9

*Newcastle-Ottawa Scale was used to assess the study quality in this meta-analysis. The full score was 9 stars, and the high-quality study was defined as a study with 8 awarded stars.

† A maximum of two stars could be awarded for this item. One star with adjustment for age and sex, two stars if there was additional comorbidity.

Table S4 Sensitivity analysis for the main confounders*

Group	No. of studies	RR	95% CI	I^2,%	PI
Adjusted for the number of AHM					0.188
Yes	7	0.69	0.62-0.76	64.0	
No	11	0.76	0.68-0.84	86.4	
Adjusted for the class of AHM					0.020
Yes	5	0.82	0.74-0.91	83.0	
No	13	0.69	0.64-0.74	55.9	
Adjusted for other co-medications†					
Yes	6	0.73	0.65-0.81	68.3	0.997
No	12	0.72	0.65-0.81	87.9	

AHM, antihypertensive medication; RR, relative risk; CI, confidence interval; PI, P interaction.

* Pooled RRs and 95% CIs were estimated using a random-effects model.

†Other co-medications included antiplatelet agents, antidiabetic agents, lipid-lowering agents, and anticoagulants.

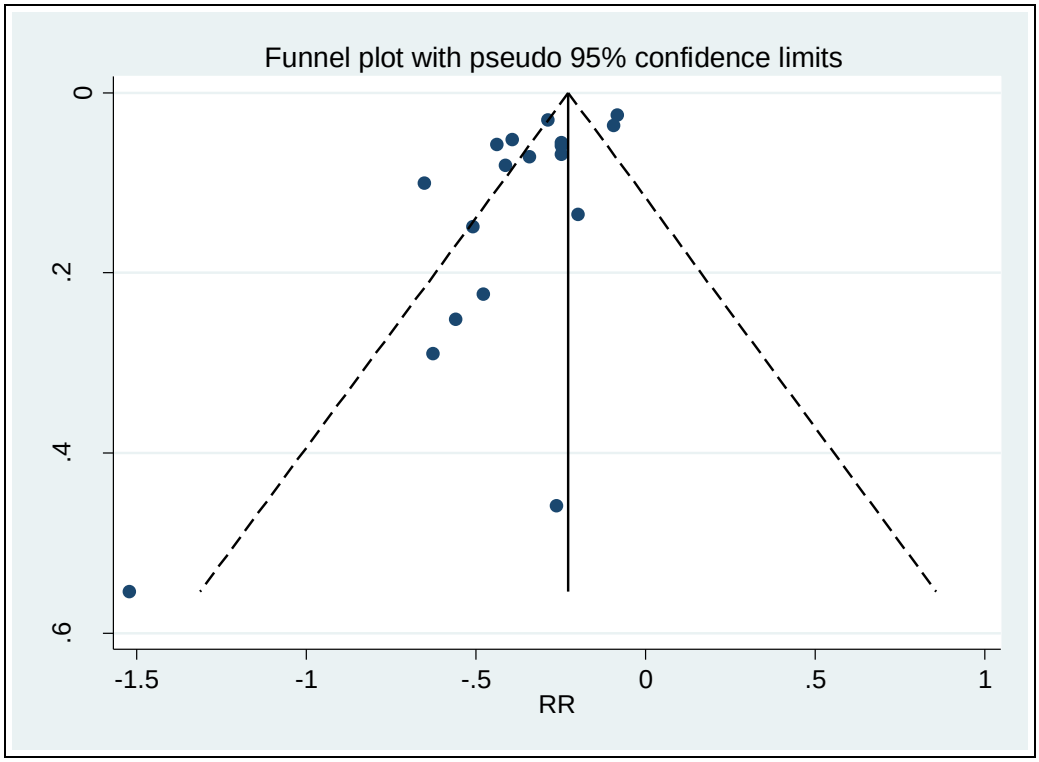

Figure S1. Funnel plot for publication bias test.

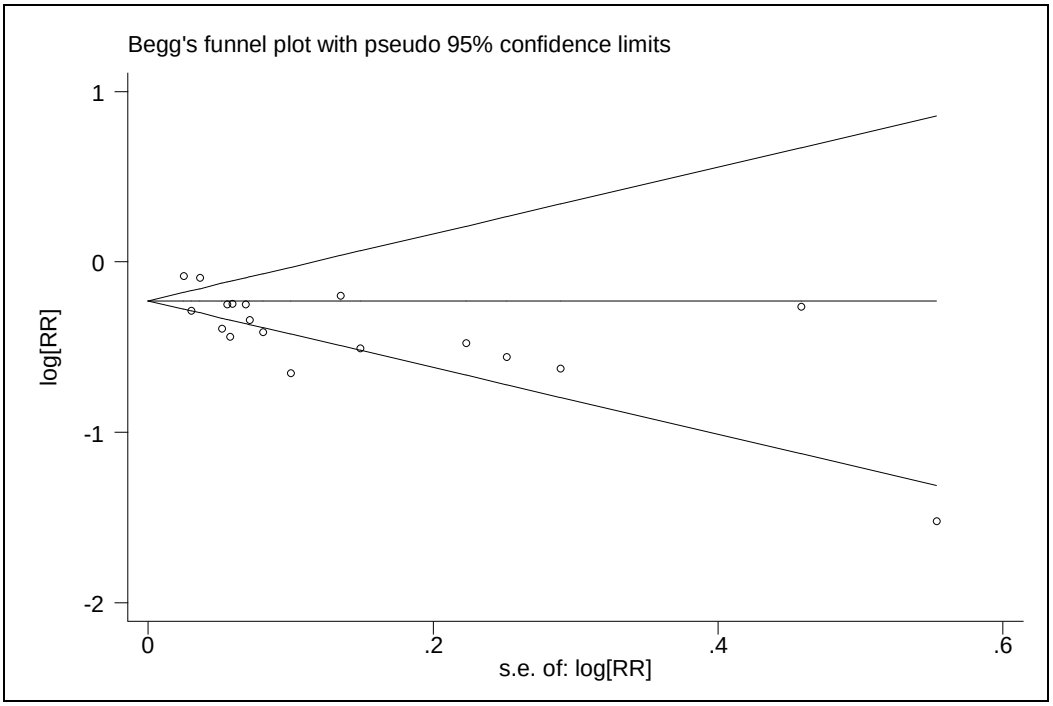

Figure S2. Publication bias test for the association between antihypertensive agents adherence and stroke risk. Begg's test, z = 0.680 (continuity corrected); $p > |z| = 0.495$ (continuity corrected).

Supplemental References

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