SUPPLEMENTAL MATERIAL

Data S1.

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	P1,P3,P6
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	See below
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	P5-6
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	P6
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	P6
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	P6
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Table S1
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	P6-7
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	P6
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	P7
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	P7
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	P7
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	P7
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	P6
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	P7
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	P7
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	P7-8
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	P7-8
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	P8
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	P6-7, Table S2
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Not assessed

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	P8
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Figure 1
Study characteristics	17	Cite each included study and present its characteristics.	P8-9, Tables 1 and S3
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Table S4
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Figures 2-4
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	P8-9, Table S4
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	P9-10, Figure 2-5
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	P9-10
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	P9-10, Fig.3-4
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Table S4
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Not reported
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	P10-11
	23b	Discuss any limitations of the evidence included in the review.	P11-12
	23c	Discuss any limitations of the review processes used.	P12
	23d	Discuss implications of the results for practice, policy, and future research.	P12
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Not registered
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Not available
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	Not applicable
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	P13
Competing interests	26	Declare any competing interests of review authors.	P13
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	P6, P8

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

PRISMA 2020 for Abstracts Checklist

Section and Topic	Item #	Checklist item	Reported (Yes/No)
TITLE			
Title	1	Identify the report as a systematic review.	yes
BACKGROUND			
Objectives	2	Provide an explicit statement of the main objective(s) or question(s) the review addresses.	yes
METHODS			
Eligibility criteria	3	Specify the inclusion and exclusion criteria for the review.	yes
Information sources	4	Specify the information sources (e.g. databases, registers) used to identify studies and the date when each was last searched.	yes
Risk of bias	5	Specify the methods used to assess risk of bias in the included studies.	no
Synthesis of results	6	Specify the methods used to present and synthesise results.	yes
RESULTS			
Included studies	7	Give the total number of included studies and participants and summarise relevant characteristics of studies.	yes
Synthesis of results	8	Present results for main outcomes, preferably indicating the number of included studies and participants for each. If meta-analysis was done, report the summary estimate and confidence/credible interval. If comparing groups, indicate the direction of the effect (i.e. which group is favoured).	yes
DISCUSSION			
Limitations of evidence	9	Provide a brief summary of the limitations of the evidence included in the review (e.g. study risk of bias, inconsistency and imprecision).	yes
Interpretation	10	Provide a general interpretation of the results and important implications.	yes
OTHER			
Funding	11	Specify the primary source of funding for the review.	no
Registration	12	Provide the register name and registration number.	no

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

For more information, visit: http://www.prisma-statement.org/

Table S1. Literature search on online databases.

Database	Search
Pubmed	(‘Atrial fibrillation [Mesh] OR ‘heart atrium arrhythmia’ OR ‘arrhythmia, atrial’ OR ‘atrial arrhythmia’ OR ‘atrium arrhythmia’ OR ‘heart atrial arrhythmia’ OR ‘heart atrium arrhythmia’ OR ‘atrial fibrillation’ OR ‘atrial fibrillation’ OR ‘atrium fibrillation’ OR ‘auricular fibrillation’ OR ‘auricular fibrillation’ OR ‘cardiac atrial fibrillation’ OR ‘cardiac atrium fibrillation’ OR ‘fibrillation, heart atrium’ OR ‘heart atrial fibrillation’ OR ‘heart atrium fibrillation’ OR ‘heart fibrillation atrium’ OR ‘non-valvular atrial fibrillation’ OR ‘nonvalvular atrial fibrillation’) AND (‘dementia’ [Mesh] OR ‘dementia’ OR ‘amentia’ OR ‘dementia’ OR ‘demention’ OR ‘Alzheimer’ OR ‘frontotemporal dementia’)
Scopus	‘Atrial fibrillation’ AND (dementia OR ‘Alzheimer Disease’ OR ‘frontotemporal dementia’)
Embase	(‘heart atrium arrhythmia’/mj OR ‘arrhythmia, atrial’ OR ‘atrial arrhythmia’ OR ‘atrium arrhythmia’ OR ‘heart atrial arrhythmia’ OR ‘heart atrium arrhythmia’ OR ‘atrial fibrillation’/mj OR ‘atrial fibrillation’ OR ‘atrium fibrillation’ OR ‘auricular fibrillation’ OR ‘auricular fibrillation’ OR ‘cardiac atrial fibrillation’ OR ‘cardiac atrium fibrillation’ OR ‘fibrillation, heart atrium’ OR ‘heart atrial fibrillation’ OR ‘heart atrium fibrillation’ OR ‘heart fibrillation atrium’ OR ‘non-valvular atrial fibrillation’ OR ‘nonvalvular atrial fibrillation’) AND (‘dementia’/mj OR ‘amentia’ OR ‘dementia’ OR ‘demention’)

Table S2. Criteria adopted for risk of bias assessment using Risk of Bias for in Non-randomized Studies of Exposures (ROBINS-E) tool.

Domains	Criteria
Bias due to confounding	Studies are considered at **moderate** risk of bias if they considered age in the confounding factors. Studies are considered at **low** risk of bias if they considered the educational attainment in the adjustment factors. Studies are considered at **high** risk of bias if adjusting factors are not reported.
Bias in selecting participants in the study	Studies are considered at **low** risk of bias if selection of eligible dementia cases was independent of the diagnosis of atrial fibrillation. Studies are considered at **moderate** risk of bias if selection of cases from a population at higher risk of dementia (e.g. mild cognitive impairment. Studies are considered at **high** risk of bias if the modality of selection of participants is not specified.
Bias in exposure classification	Studies are considered at **low** risk of bias if the assessment of atrial fibrillation was through electrocardiography (ECGs) at baseline and at each follow-up examination or through medical records, with a discharge diagnosis or at least confirmed twice. Studies are considered at **moderate** risk of bias if exposure assessment was performed relying on self-reports, but afterwards the exposure was confirmed through medical records. Studies are considered at **high** risk of bias if they relied only on self-report for exposure classification or criteria are not reported.
Bias in departure from intended exposure	This domain should not of concerns since the exposure is presence of atrial fibrillation, thus departure from the intended exposure is not an issue. As consequence, all studies are considered at low risk of bias for this domain.
Bias due to missing data	Studies are considered at **low** risk of bias if less than 10% of participants were excluded to missing data, while at **moderate** risk of bias if less than 20%. Studies with higher proportion (≥20%) are considered at **high** risk of bias.
Bias in outcome measurement	Studies are considered at **low** risk of bias if outcome assessment was based on a discharged diagnosis or at least on two consecutive diagnoses in outpatient clinic consultation. Studies are considered at **moderate** risk of bias if outcome assessment was based on the use of the Mini-Mental State Examination or the Geriatric Mental State Schedule, while they are still considered at low risk if this first diagnosis was confirmed with a subsequent clinical analysis. Studies are considered at **high** risk of bias if outcome assessment was based on self-report only without external validation or if information about outcome assessment was missing.
Bias in selection of reported results	Studies are considered at **low** risk of bias if they reported a prior publication of the protocol or data are made available in a public and accessible repository. Studies are considered at **moderate** risk of bias if they presented outcome measures and analyses consistent with a priori plan outlined in the manuscript. Studies are considered at **high** risk of bias if no protocol was available and the a priori plan was not outlined
Overall risk of bias	If at least one domain was found at **high** risk of bias, the overall risk was considered **high**. If at least one domain was found at **moderate** risk of bias, the overall risk was considered **moderate**. If all domains were at **low** risk of bias, the overall risk was considered **low**.

Table S3. Additional characteristics of the included studies.

Reference	Databases	Assessment of AF and dementia	Follow-up duration	Exclusion criteria	Types of dementia	Outcomes	Main findings	Adjustments
Bunch et al. 2010[21]	Database Registry of the Intermountain Heart Collaborative Study	(ICD-9); AF: hospital discharge or admission for AF or electrocardiographic database of all Intermountain Healthcare hospitals. Dementia: medical records (ICD9)	5 y	incomplete medical information about dementia screening or follow-up on dementia diagnosis; prevalent dementia;	VaD, Senile, Alzheimer's and non-specific dementia	incidence of dementia	AF independently associated with all types of dementia and the highest risk of AD was in the younger AF group	Age, sex, hypertension, hyperlipidemia, diabetes mellitus, renal failure, smoking, family history, MI, CVA, heart failure, statin, ACE inhibitor, ARB, beta-blockers, diuretic*
Chen et al. 2021[29]	NHIRD released by the Taiwan NHRI	(ICD-9-CM) AF and dementia: discharge diagnosis or more than two consecutive clinic visits; further analysis of AD and VaD with AD medications (i.e., donepezil, rivastigmine, memantine and galantamine) and PET/SPECT imaging	3.5 ± 3.4 y (F) 3.4 ± 3.3 (M) y	patients with incomplete demographic data, age < 20 years, rheumatic heart disease, hyperthyroidism, past valvular heart surgery, and a history of dementia.	Alzheimer's dementia, VaD	incidence of dementia stratified by age and by sex; differences between incidence of AD and VaD	higher incidence in women than in men in all groups older than 55; higher incidence in women than in men only in the age groups between 56-85 if considering only AD	Age, sex, monthly income (USD), urbanization level, hypertension, diabetes mellitus, ischemic heart disease, dyslipidemia, gout, COPD, peripheral arterial disease, renal function status, abnormal liver function, traumatic brain injury, alcohol abuse, systemic thromboembolism (excluding ischemic stroke), myocardial infarction, stroke, heart failure, history of depression or bipolar disorder, use of anticoagulant, antiplatelet, ACEi/ARB, dihydropyridine CCB, don-dihydropyridine CCB, beta-blockers, statins, DPP4 inhibitors, biguanides, sulfonylurea, thiazolidinedione, insulin
de Bruijn et al. 2015[22]	The Rotterdam Study	AF: ECGs and hospital discharges; dementia: MMSE and GMS, subsequent interview with eventually further neuropsychological testing if dementia was suspected and, if necessary, clinical neuroimaging.	Up to 20 y	preexisting AF or dementia	Alzheimer's dementia and overall dementia	incidence of dementia	atrial fibrillation is associated with an increased risk of dementia, independent of clinical stroke; association strongest in the younger	Age, sex, diabetes mellitus, smoking, total cholesterol, high density lipoprotein cholesterol levels, lipid-lowering medication, systolic and diastolic blood pressure, blood pressure-lowering medication, BMI, educational level, ever use of oral anticoagulant medication, coronary heart disease, heart failure, apolipoprotein E ε4 carrier status.

Kim et al. 2019[30]	Korean NHIS-HEALS database	(ICD-10) AF: discharge diagnosis or at least confirmed twice; dementia: ICD-10 with prescription of dementia drugs (rivastigmine, galantamine, memantine, or donepezil)	AF group 96 months, IQR 86-101 months); AF-free group 93 months, IQR 84-100 months)	valvular heart disease, TIA/stroke, hemorrhagic stroke, dementia, prevalent AF	Alzheimer's dementia, VaD	incidence of AF and dementia	after censoring for stroke, the cumulative incidence of dementia was higher in the incident-AF group	Age, sex, hypertension, diabetes mellitus, dyslipidemia, heart failure, previous myocardial infarction, peripheral artery disease, osteoporosis, chronic kidney disease, chronic obstructive pulmonary disease, malignant neoplasm, liver disease, CHA2DS2-VASc score, cardiovascular medications, economic status, alcohol consumption, smoking status, exercise habits, follow-up duration, body mass index, systolic and diastolic blood pressure, blood glucose, total cholesterol, and blood hemoglobin level.
Kim et al. 2020[31]	Korean NHIS-Senior database	(ICD-10) AF and dementia: ICD10 diagnosis confirmed if secondary to a hospital discharge or at least confirmed twice in outpatient department.	AF group 86 months, IQR 62-96 months); AF-free group 85 months, IQR 58-95 months)	valvular heart disease (mitral stenosis or prosthetic heart valves or with insurance claims for valve replacement or valvuloplasty), ischemic stroke or TIA, hemorrhagic stroke, pre-existing dementia or AF	Alzheimer's dementia, VaD	incidence of dementia	higher incidence of dementia in AF participants, independently of stroke	Age, sex, and clinical variables, including hypertension, diabetes mellitus, previous MI, heart failure, peripheral artery disease, dyslipidemia, osteoporosis, CKD, COPD, liver disease, history of malignant neoplasm, economic status, cardiovascular medications (aspirin, P2Y12 inhibitor, statin, anticoagulant, beta-blocker, ACEi or ARB, calcium channel blocker, digoxin, diuretics), body mass index, systolic and diastolic blood pressure (BP), blood glucose level, total cholesterol, and alcohol and smoking habits.
Liao et al. 2015[32]	NHIRD released by the Taiwan NHRI	(ICD-9-CM) AF: discharge diagnosis or at least confirmed twice; dementia: registered by the physicians responsible for the treatment (medical records).	NR	preexisting dementia, age <20 years old	presenile and senile dementia, VaD Alzheimer's dementia	incidence of dementia and usefulness of CHADS2 and CHA2DS2-VASc scores in predicting dementia	the cumulative incidence of dementia was higher in the incident-AF group, even in patients without comorbidities; CHADS2 and CHA2DS2-VASc scores higher in patients with dementia	Age, sex, hypertension, diabetes mellitus, heart failure, vascular diseases, dyslipidemia, CVA, ESRD, COPD, malignancy, autoimmune diseases, the use of aspirin, clopidogrel, warfarin, ACEi/ARB, statin, Charlson index, income level, and systemic diseases

Abbreviations: ACEi: angiotensin-converting enzyme inhibitor; AD: Alzheimer's dementia; AF: atrial fibrillation; ARB: angiotensin II-receptor blocker; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease; CVA: cerebral vascular accident; CHADS2: Congestive heart failure, Hypertension, Age >75 years, Diabetes mellitus, prior Stroke 2 or transient ischemic attack, or thromboembolism; ESRD: end-stage renal disease; ICD: International Classification of Diseases; MI: myocardial infarction; NHIRD: National Health Insurance Research Database; NHRI: National Health Research Institutes; NR: not reported; TIA: transient ischemic stroke; VaD: vascular dementia.

Note: *data obtained from Table 1 of the original study [20].

Table S4. Risk of bias assessment of the included studies.

Reference	Bias due to confounding	Bias in selecting participants in the study	Bias in exposure classification	Bias in departure from intended exposure	Bias due to missing data	Bias in outcome measurement	Bias in selection of reported results	Overall risk of bias
Bunch et al. 2010[21]	Moderate	Low	Low	Low	Low	Low	Low	Moderate
Chen et al. 2021[29]	Moderate	Low	Low	Low	Low	Low	Low	Moderate
de Bruijn et al. 2015[22]	Low	Low	Low	Low	Low	Low	Low	Low
Kim et al. 2019[30]	Moderate	Low	Low	Low	Low	Low	Low	Moderate
Kim et al. 2020[31]	Moderate	Low	Low	Low	Low	Low	Low	Moderate
Liao et al. 2015[32]	Moderate	Low	Low	Low	Low	Low	Low	Moderate

Figure S1. Forest plot for risk of early-onset (<70 years) dementia in association to atrial fibrillation; sensitivity analysis after exclusion of Chen et al. 2021 study.[29] AD, Alzheimer's dementia; F, female; M, male; ND, Nonspecified dementia; SDm, senile dementia; VaD, vascular dementia.

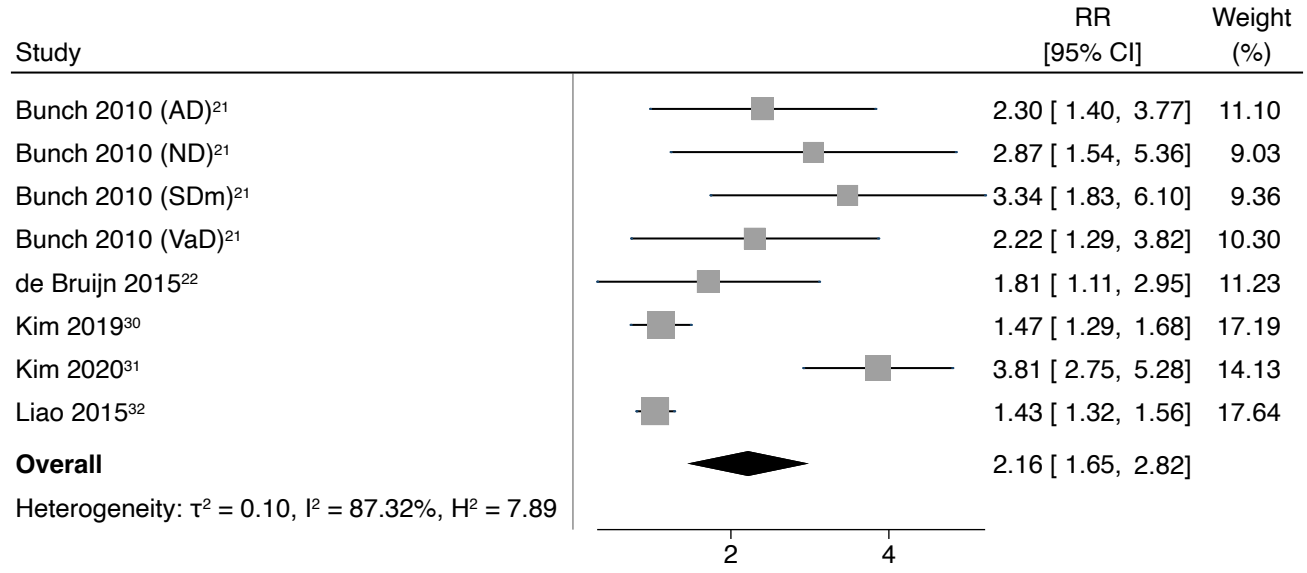
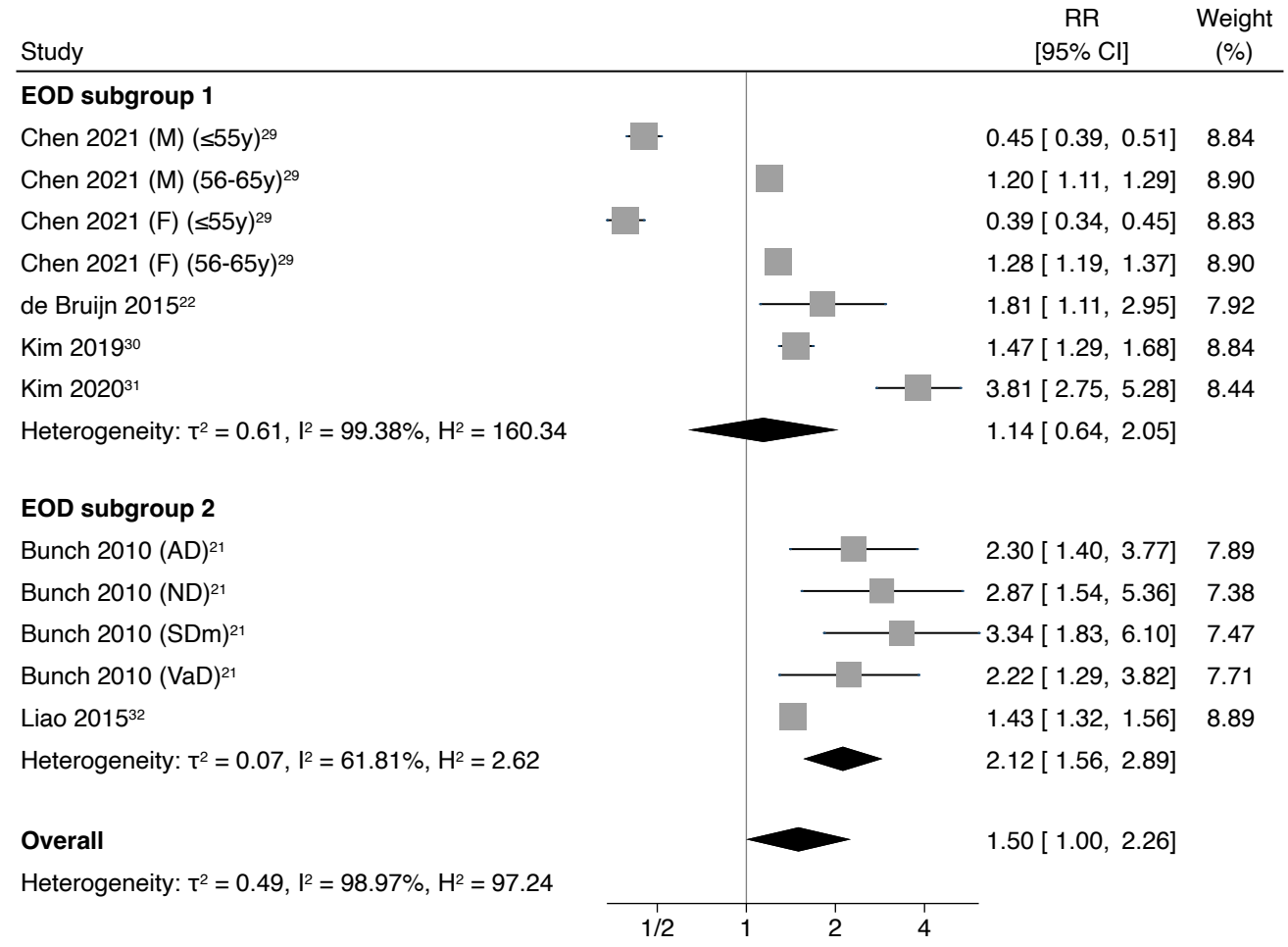


Figure S2. Forest plot for risk of early-onset (<70 years) dementia in association to atrial fibrillation; sensitivity analysis stratified by certainty of EOD diagnosis: dementia onset before 65 years (EOD subgroup 1) and unclear exact age of onset (EOD subgroup 2). AD, Alzheimer's dementia; F, female; M, male; ND, Nonspecified dementia; SDm, senile dementia; VaD, vascular dementia.



Random-effects model based on Paule and Mandel method-ebayes option