SUPPLEMENTARY MATERIAL – TABLES, FIGURES & LEGENDS

Supplementary Table 1: Search strategy MEDLINE (OVID)– this search strategy was also adapted for EMBASE, Web of Science and CINAHL	
1	exp Atrial Fibrillation/
2	(atrial adj3 firbillation).tw.
3	1 or 2
4	exp stroke/
5	exp Brain Ischemia/
6	exp Cerebral Hemorrhage/ or exp Intracranial Hemorrhages/
7	(stroke* adj3 (acute or cerebral or cerebrovascular)).tw.
8	"cerebrovascular apoplexy".tw.
9	((brain or cerebral) adj3 ischemi*).tw.
10	((brain or cerebral) adj3 ischaemi*).tw.
11	(accident adj3 (cerebrovascular or cerebral)).tw.
12	4 or 5 or 6 or 7 or 8 or 9 or 10 or 11
13	"thromboembolic event".tw.
14	*hemorrhage/ or *ecchymosis/ or *epistaxis/ or *exsanguination/ or *eye hemorrhage/ or *gastrointestinal hemorrhage/ or *hemarthrosis/ or *hematocele/ or *hematoma/ or *hematuria/ or *hemobilia/ or *hemoperitoneum/ or *hemoptysis/ or *hemothorax/ or *intracranial hemorrhage/ or *oral hemorrhage/ or *postoperative hemorrhage/ or *pupura/ or *retrobulbar hemorrhage/ or *shock, hemorrhagic/ or *uterine hemorrhage/
15	exp thromboembolism/
16	Hospital mortality/ or mortality/
17	mortality.tw.
18	(major adj3 hemorrhage).tw.
19	(major adj3 haemorrhage).tw.
20	(stroke* adj3 (acute or cerebral or cerebrovascular)).tw.
21	exp stroke/
22	exp Cerebral Hemorrhage/ or exp Intracranial Hemorrhage/
23	exp Brain Ischemia/
24	"cerebrovascular apoplexy".tw.
25	((brain or cerebral) adj3 ischaemi*).tw.
26	((brain or cerebral) adj3 ischemi*).tw.
27	13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26
28	3 and 12 and 27
29	Limit 28 to (("all adult (19 plus years) or "young adult (19 to 24 years)" or "adult (19 to 44 years)" or "young adult and adult (19-24 and 19-44)" or "middle age (45 to 64 years)" or "middle aged (45 plus years)" or "all aged (65 and over)" or "aged (80 and over)" and (adaptive clinical trial or clinical study or clinical trial, all or clinical trial, phase i or clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iv or comparative study or multicentre study or observational study or pragmatic clinical trial))

Supplementary Table 2: Risk of bias Assessment of all studies using the ROBINS-E tool.						
Author name and date	**Bias due to confounding**	**Selection bias**	**Bias in classification of exposures**	**Bias in outcome measurement**	**Missing data/ bias in reporting of outcome**	**Overall risk of bias**
Al-Khalili 2016 [15]	Low	Moderate*	Moderate	Moderate	Low	Moderate
Aronow 1999 [16]	Low	Moderate*	Moderate	Low	Low	Low
Azoulay 2012 [17]	Low	Moderate*	Moderate	Low	Low	Low
Baturova 2017 [18]	Low	Low	Moderate	Moderate	Low	Low
Britton 1984 [19]	Low	Low	Moderate	Low	Low	Low
Christensen 2014 [20]	Low	Moderate*	Low	Low	Low	Low
Friberg 2010 [21]	Moderate†	Moderate*	Low	Low	Low	Moderate†
Grond 2013 [22]	Low	Moderate*	Low	Moderate	Low	Low
Koga 2016 [23]	Low	Low	Low	Low	Low	Low
Levy 1999 [24]	Moderate†	Low	Moderate	Low	Low	Moderate†
Liantinioti 2017 [25]	Low	Moderate*	Low	Low	Low	Low
Marini 2005 [26]	Moderate†	Low	Low	Low	Low	Moderate†
Ntaios 2013 [27]	Low	Low	Low	Moderate‡	Moderate	Low
Önundarson 1987 [28]	Low	Low	Low	Moderate	Low	Low
Paciaroni 2018 [29]	Low	Low	Low	Low	Low	Low
Palomäki 2017 [30]	Low	Low	Low	Low	Moderate	Low
Petty 1998 [31]	Moderate†	Low	Low	Moderate‡	Serious	Moderate†
Rietbrock 2008 [32]	Low	Moderate*	Low	Low	Low	Low
Staszewski 2009 [33]	Moderate†	Moderate*	Low	Low	Low	Moderate†
Tanaka 2016 [34]	Moderate†	Low	Low	Low	Low	Moderate†
Tsivgoulis 2005 [35]	Moderate†	Moderate*	Low	Low	Low	Moderate†
Wolf 1978 [36]	Moderate†	Moderate	Low	Moderate‡	Low	Moderate†
Yamanouchi 1988 [37]	Moderate†	Low	Moderate	Low	Low	Moderate†
Yanagisawa 2016 [38]	Low	Moderate*	Low	Moderate	Low	Low
Yu 2018 [39]	Moderate†	Moderate*	Low	Moderate	Low	Moderate†
Zolotovskaya 2018 [40]	Moderate†	Moderate*	Moderate	Moderate	Low	Moderate†

*studies only included patients that survived their index stroke event
†potential difference in baseline characteristics between the two groups which was not adjusted may have lead to moderate RoB
‡risk of bias caused by missing information on follow-up length

Supplementary Table 3: GRADE criteria evidence and summary of findings table of the studies included in the analyses

Author(s): Antonia Mentel, Terence J. Quinn, Alan C. Cameron, Kennedy R. Lees, Azmil H. Abdul-Rahim
Question: The Impact of Atrial Fibrillation Type on the Risks of Thrombembolic Recurrence, Mortality, and Major Haemorrhage in Patients with Previous Stroke: A Systematic Review and Meta-analysis
Setting: Hospital

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	NPAF	PAF	Relative (95% CI)	Absolute (95% CI)		
Stroke recurrence in NPAF vs PAF (follow up: range 10 days to 7.4 years; assessed with: no of events)												
18	observational studies	serious [a]	not serious	not serious	not serious	all plausible residual confounding would reduce the demonstrated effect	4130/15286 (27.0%)	163/2341 (7.0%)	OR 1.47 (1.08 to 1.99)	**29 more per 1.000** (from 5 more to 60 more)	⨁⨁◯◯ LOW	IMPORTANT
Mortality in NPAF vs PAF (assessed with: no of deaths)												
18	observational studies	serious [b]	not serious	not serious	not serious	all plausible residual confounding would reduce the demonstrated effect	1514/4990 (30.3%)	457/2938 (15.6%)	OR 1.90 (1.43 to 2.52)	**104 more per 1.000** (from 53 more to 161 more)	⨁⨁◯◯ LOW	IMPORTANT
Intracranial Haemorrrhage in NPAF vs PAF (assessed with: no of events)												
8	observational studies	not serious	not serious	not serious	not serious	none	117/1426 (8.2%)	25/646 (3.9%)	OR 1.01 (0.61 to 1.69)	**0 fewer per 1.000** (from 15 fewer to 25 more)	⨁⨁◯◯ LOW	IMPORTANT

CI: Confidence interval; **OR:** Odds ratio

Explanations

a. 11/18 studies only included patients that survived their hospital stay with index stroke. 1 study only followed up patients for the length of their hospital stay. 1 study had reporting errors and several studies failed to report follow up lengths. Overall, only 3 studies adjusted their calculated RR for confounding factors. Some studies had unbalanced baseline characteristics.
b. 7/18 studies only included patients that survived their hospital stay with index stroke. 1 study only followed up patients for the length of their hospital stay. Some studies failed to report follow up. Some studies had unbalanced baseline characteristics.

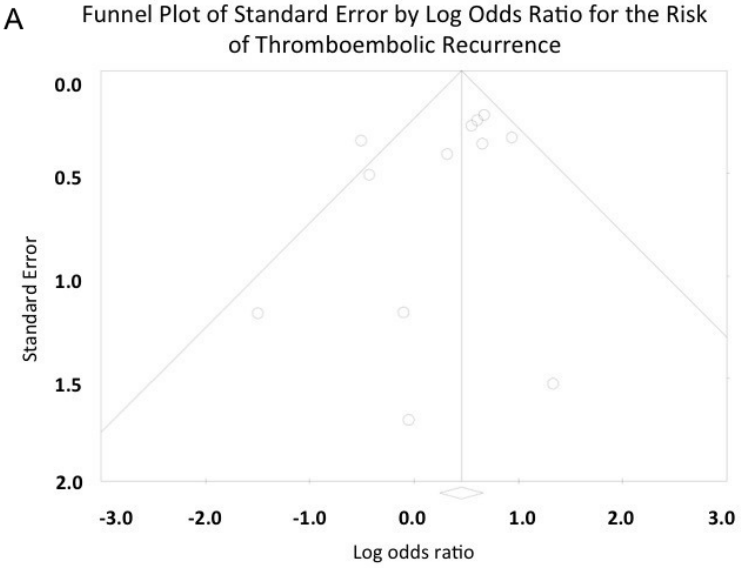
Supplementary Table 4: Baseline characteristics of patients in all included non-randomised observational studies

Author name and date	Average Age		% of Females		Diabetes (%)		Hypertension (%)		Ischaemic heart disease (%)		Congestive Heart failure (%)		Median CHA_2DS_2VASC		Median HAS BLED score		Median NIHSS score at baseline	
	PAF	NPAF	PAF	NPAF	PAF	NPAF	PAF	NPAF	PAF	NPAF	PAF	NPAF	PAF	NPAF	PAF	NPAF	PAF	NPAF
Al-Khalili 2016 [15]	72	74	54%	32%	11%	25%	72%	75%	29%	29%	7%	20%	5	5	2	2	-	-
Aronow 1999 [16]	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Azoulay 2012 [17]	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Baturova 2017 [18]	80	84	40%	41%	25%	27%	57%	64%	-	-	19%	21%	6	6	-	-	5	4
Britton 1984 [19]	76	77	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Christensen 2014 [20]	70	-	56%	-	11%	-	61%	-	-	-	-	-	4	-	-	-	1	-
Friberg 2010 [21]	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Grond 2013 [22]	76	-	55%	-	29%	-	-	-	9%	-	4%	-	-	-	-	-	-	-
Koga 2016 [23]	77	78	44%	44%	20%	21%	72%	74%	10%	9%	16%	24%	-	-	3	3	7	8
Levy 1999 [24]	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Liantinioti 2017 [25]	64	-	57%	-	-	-	-	-	-	-	-	-	-	-	-	-	5	-
Marini 2005 [26]	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Ntaios 2013 [27]	74	77	46%	55%	24%	23%	69%	75%	20%	18%	8%	12%	-	-	-	-	11	13
Önundarson 1987 [28]	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Paciaroni 2018 [29]	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

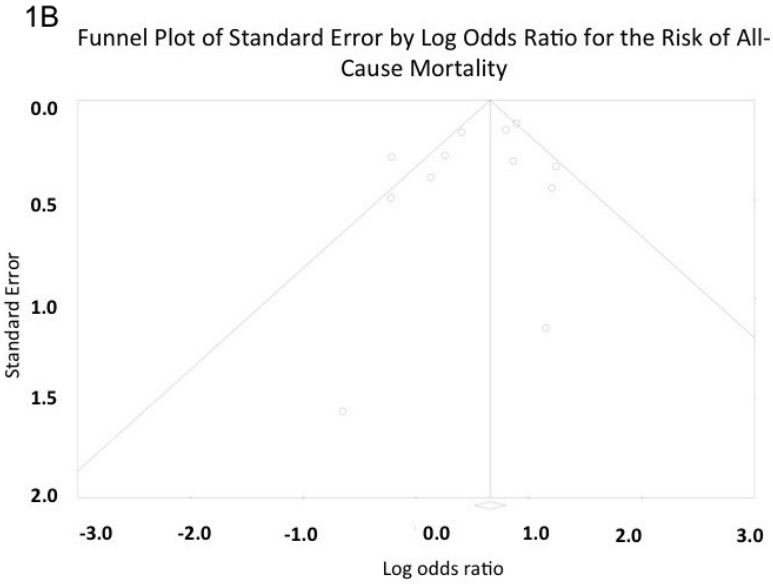
Palomäki 2017 [30]	75	80	58%	55%	19%	24%	66%	67%	16%	15%	13%	30%	4	4	2	2	-	-
Petty 1998 [31]	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Rietbrock 2008 [32]	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Staszewski 2009 [33]	76	77	66%	65%	20%	40%	93%	94%	57%	68%	36%	61%	-	-	-	-	5	12
Tanaka 2016 [34]	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Tsivgoulis 2005 [35]	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Wolf 1978 [36]	-	50	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Yamanouchi 1988 [37]	67	72	20%	44%	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Yanagisawa 2016 [38]	78	78	26%	50%	26%	27%	67%	68%	22%	14%	4%	35%	5	6	-	-	-	-
Yu 2018 [39]	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Zolotovskaya 2018 [40]	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

Supplementary Figure 1: Funnel plots for the reported incidences of recurrent thromboembolic events (A), all-cause mortality (B) and major haemorrhage (C) in paroxysmal and non-paroxysmal atrial fibrillation.

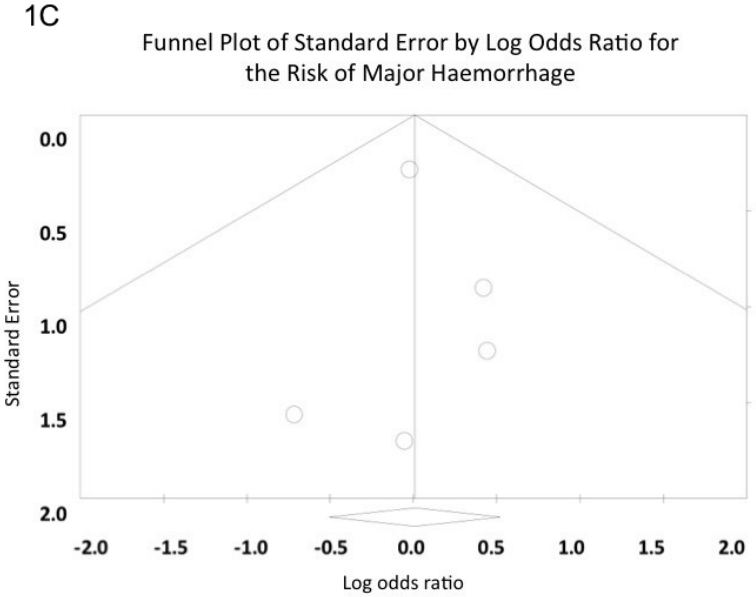
1A


Funnel Plot of Standard Error by Log Odds Ratio for the Risk of Thromboembolic Recurrence
Standard Error
0.0
0.5
1.0
1.5
2.0
-3.0
-2.0
-1.0
0.0
1.0
2.0
3.0
Log odds ratio

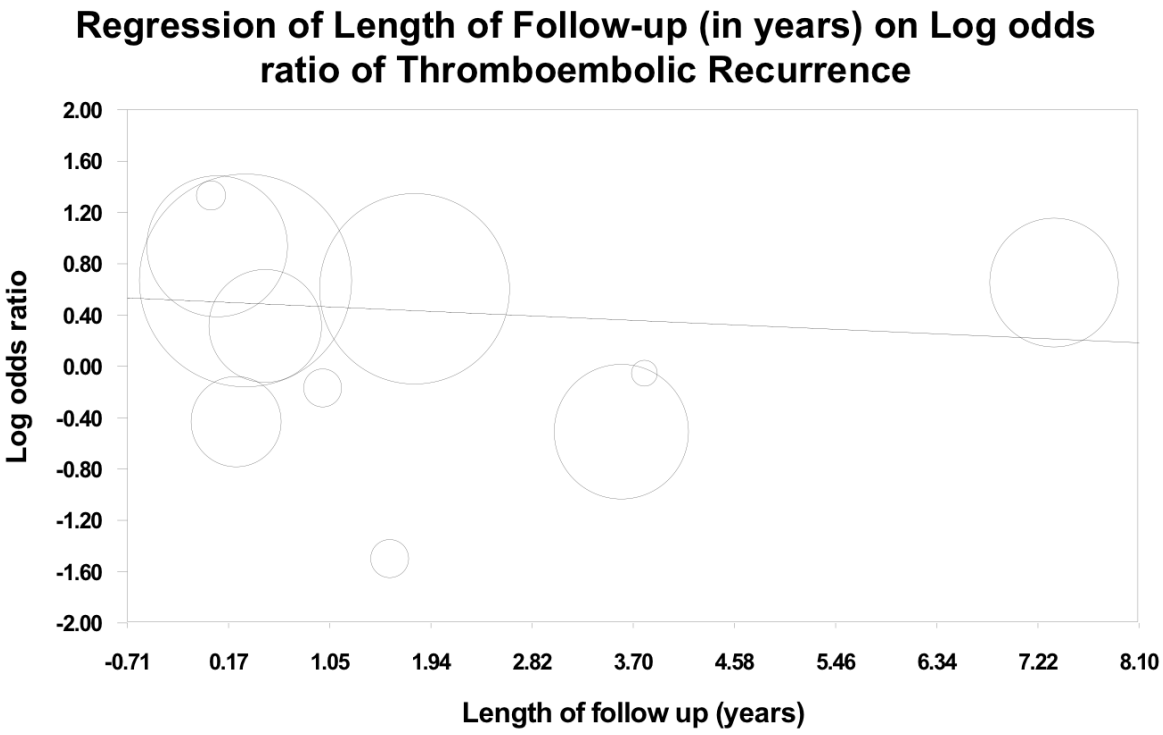
1B


Funnel Plot of Standard Error by Log Odds Ratio for the Risk of All-Cause Mortality
Standard Error
0.0
0.5
1.0
1.5
2.0
-3.0
-2.0
-1.0
0.0
1.0
2.0
3.0
Log odds ratio

1C


Funnel Plot of Standard Error by Log Odds Ratio for the Risk of Major Haemorrhage
Standard Error
0.0
0.5
1.0
1.5
2.0
-2.0
-1.5
-1.0
-0.5
0.0
0.5
1.0
1.5
2.0
Log odds ratio

Supplementary Figure 2: Meta-regression of the length of follow-up on the log odds ratio of thromboembolic recurrence.


Regression of Length of Follow-up (in years) on Log odds ratio of Thromboembolic Recurrence
Log odds ratio
2.00
1.60
1.20
0.80
0.40
0.00
-0.40
-0.80
-1.20
-1.60
-2.00
-0.71
0.17
1.05
1.94
2.82
3.70
4.58
5.46
6.34
7.22
8.10
Length of follow up (years)

Supplementary Figure 3: Sensitivity analysis comparing the thromboembolic recurrence rates of studies with low and high proportions of patients on oral anti-coagulant (OAC) for non-paroxysmal (NPAF) and paroxysmal atrial fibrillation (PAF).

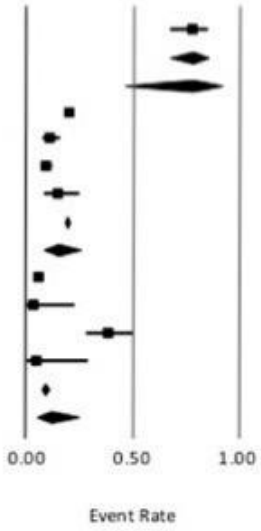
Group 0.00: 0% of patients on OAC

Group 1.00: less than 50% of patients on OAC

Group 2.00: more than 50% of patients on OAC

3A Sensitivity Analysis for the Effect of Oral-Anticoagulation use on the Incidence of Thromboembolic Recurrence in Non-Paroxysmal Atrial Fibrillation

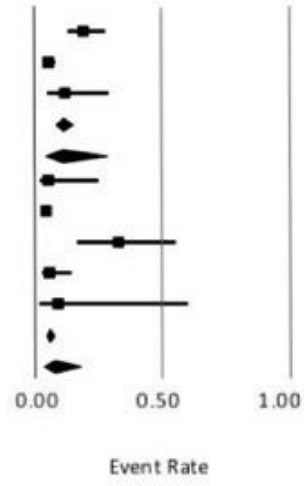
Model	Study name	Event rate	Lower limit	Upper limit	Z-Value	p-Value	Group by OAC Level	OAC%
	Aronow-noOAC 1999	0.812	0.702	0.887	4.744	0.000	0.00	0
Fixed		0.812	0.702	0.887	4.744	0.000	0.00	
Random		0.812	0.483	0.952	1.872	0.061	0.00	
	Azoulay 2012	0.215	0.203	0.228	-34.325	0.000	1.00	23
	Friberg 2010	0.121	0.083	0.173	-9.307	0.000	1.00	38
	Ntaios 2013	0.103	0.080	0.132	-15.202	0.000	1.00	39
	Yu 2018	0.159	0.091	0.265	-5.055	0.000	1.00	41
Fixed		0.203	0.192	0.214	-38.714	0.000	1.00	
Random		0.159	0.090	0.268	-4.967	0.000	1.00	
	Paciaroni 2018	0.066	0.053	0.082	-22.346	0.000	2.00	80
	Al-Khalili 2016	0.042	0.006	0.244	-3.069	0.002	2.00	100
	Aronow-OAC 1999	0.403	0.293	0.524	-1.578	0.115	2.00	100
	Yamanouchi 1988	0.056	0.008	0.307	-2.753	0.006	2.00	100
Fixed		0.095	0.079	0.115	-21.230	0.000	2.00	
Random		0.126	0.056	0.258	-4.297	0.000	2.00	



3B

Sensitivity Analysis for the Effect of Oral-Anticoagulation use on the Incidence of Thromboembolic Recurrence in Paroxysmal Atrial Fibrillation

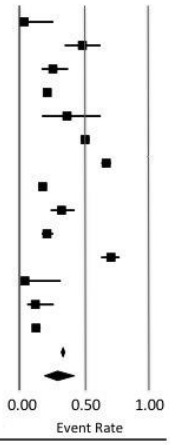
Model	Study name	Event rate	Lower limit	Upper limit	Z-Value	p-Value	Group by OAC level	OAC %
	Friberg 2010	0.187	0.119	0.280	-5.469	0.000	1.00	32
	Ntaios 2013	0.043	0.025	0.075	-10.486	0.000	1.00	33.9
	Yanagisawa 2016	0.111	0.036	0.293	-3.396	0.001	1.00	41.1
Fixed		0.100	0.071	0.139	-11.611	0.000	1.00	
Random		0.098	0.029	0.281	-3.398	0.001	1.00	
	Liantinioti 2017	0.043	0.006	0.252	-3.023	0.003	2.00	87
	Paciaroni 2018	0.035	0.025	0.049	-18.143	0.000	2.00	87.3
	Christensen 2014	0.333	0.158	0.571	-1.386	0.166	2.00	94.9
	Al-Khalili 2016	0.049	0.016	0.142	-5.002	0.000	2.00	100
	Yamanouchi 1988	0.083	0.005	0.622	-1.623	0.105	2.00	100
Fixed		0.047	0.035	0.063	-18.741	0.000	2.00	
Random		0.067	0.024	0.172	-4.841	0.000	2.00	



Supplementary Figure 4: Sensitivity analysis of the all-cause mortality risks in non-paroxysmal (NPAF) and paroxysmal atrial fibrillation (PAF), by using the outcome data of Baturova 2017 at 3-years.

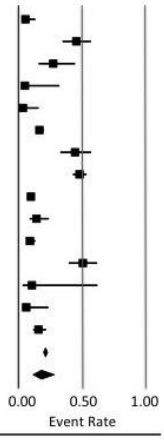
4A Sensitivity Analysis of All-Cause Mortality Rate in Non-Paroxysmal Atrial Fibrillation

Model	Study name	Event rate	Lower limit	Upper limit	Z-Value	p-Value
	Al-Khalili 2016	0.020	0.001	0.251	-2.724	0.006
	Baturova2017	0.477	0.336	0.623	-0.301	0.763
	Britton 1984	0.246	0.154	0.369	-3.769	0.000
	Koga 2016	0.202	0.175	0.232	-15.192	0.000
	Levy 1999	0.357	0.157	0.624	-1.054	0.292
	Marini 2005	0.499	0.464	0.533	-0.070	0.944
	Ntaios 2013	0.665	0.624	0.704	7.469	0.000
	Palomaki 2017	0.165	0.148	0.183	-25.601	0.000
	Straszewski 2009	0.314	0.225	0.419	-3.364	0.001
	Tanaka 2016	0.199	0.156	0.251	-9.146	0.000
	Tsivgoulis 2005	0.702	0.622	0.772	4.656	0.000
	Yamanouchi 1988	0.026	0.002	0.310	-2.519	0.012
	Yanagisawa 2016	0.108	0.041	0.255	-3.986	0.000
	Zolotovskaya 2018	0.113	0.084	0.150	-12.274	0.000
Fixed		0.320	0.306	0.335	-21.965	0.000
Random		0.277	0.175	0.410	-3.160	0.002



4B Sensitivity Analysis of All-Cause Mortality Rate in Paroxysmal Atrial Fibrillation

Model	Study name	Event rate	Lower limit	Upper limit	Z-Value	p-Value
	Al-Khalili 2016	0.031	0.008	0.115	-4.803	0.000
	Baturova2017	0.446	0.331	0.568	-0.867	0.386
	Britton 1984	0.258	0.135	0.437	-2.573	0.010
	Christensen 2014	0.026	0.002	0.310	-2.519	0.012
	Grond 2013	0.010	0.001	0.141	-3.233	0.001
	Koga 2016	0.145	0.115	0.182	-13.012	0.000
	Marini 2005	0.436	0.312	0.569	-0.941	0.347
	Ntaios 2013	0.473	0.415	0.532	-0.901	0.368
	Palomaki 2017	0.075	0.063	0.090	-25.183	0.000
	Straszewski 2009	0.121	0.062	0.224	-5.253	0.000
	Tanaka 2016	0.067	0.039	0.115	-8.788	0.000
	Tsivgoulis 2005	0.500	0.382	0.618	0.000	1.000
	Yamanouchi 1988	0.083	0.005	0.622	-1.623	0.105
	Yanagisawa 2016	0.037	0.005	0.221	-3.197	0.001
	Zolotovskaya 2018	0.137	0.091	0.201	-7.825	0.000
Fixed		0.189	0.173	0.207	-25.894	0.000
Random		0.155	0.087	0.262	-5.036	0.000



4C Sensitivity Analysis All-Cause Mortality Risk in Non-Paroxysmal versus Paroxysmal Atrial Fibrillation

Model	Study name	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
	Al-Khalili 2016	0.518	0.024	11.188	-0.419	0.675
	Baturova2017	1.133	0.526	2.442	0.320	0.749
	Britton 1984	0.938	0.347	2.532	-0.127	0.899
	Koga 2016	1.489	1.081	2.052	2.435	0.015
	Levy 1999	0.193	0.007	5.603	-0.957	0.338
	Marini 2005	1.285	0.741	2.229	0.894	0.371
	Ntaios 2013	2.210	1.643	2.973	5.243	0.000
	Palomaki 2017	2.424	1.924	3.056	7.501	0.000
	Straszewski 2009	3.318	1.392	7.905	2.707	0.007
	Tanaka 2016	3.442	1.784	6.643	3.686	0.000
	Tsivgoulis 2005	2.357	1.290	4.306	2.789	0.005
	Yanagisawa 2016	3.152	0.332	29.924	1.000	0.318
	Zolotovskaya 2018	0.801	0.455	1.410	-0.770	0.442
Fixed		1.927	1.685	2.203	9.596	0.000
Random		1.752	1.348	2.277	4.191	0.000