SUPPLEMENTARY APPENDIX

1. Methods for study selection, data synthesis and statistical analysis
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Appendix 1 - Methods for study selection, data synthesis and statistical analysis

We sought to determine the treatment effect of anticoagulation on all-cause mortality, (re)hospitalisation for heart failure, non-fatal stroke, non-fatal MI, and major haemorrhage, in patients with chronic HFrEF who were in sinus rhythm. Our overall search strategy is presented in the main manuscript, and model search strategies presented within this supplementary appendix. Restrictions were imposed to limit the search to randomised controlled trials (RCTs) enrolling human subjects that were reported in English. To be eligible for inclusion in our meta-analysis, trials had to include randomisation to oral anticoagulation compared to ATT and/or placebo and/or no therapy. Trial titles and abstracts were initially screened, with potentially eligible trials subsequently undergoing more detailed analysis of the primary and relevant secondary results papers. The risk of bias of individual studies – and across studies - was assessed using the Cochrane Collaboration's tool for assessing risk of bias in RCTs. All individual trials were deemed either of low or unclear risk, with none deemed high risk; bias across studies was deemed either low or unclear risk. Our analysis was not stratified further according to potential bias. This approach was agreed by all authors.

Data sought are presented in Table 1 of the main manuscript, with the exception of RRs and 95%CIs, which are presented for individual trials in Figures 2 to 6 of the main manuscript.

All analyses were conducted using STATA version 14.0 (StataCorp, College Station, TX). This work was not funded and there was no role of any funding source in the conception, data synthesis, analysis, interpretation, or in drafting of the manuscript.

Appendix 2 – Assessment of bias among trials included in meta-analysis using the Cochrane Risk of Bias Tool

	WASH	HELAS	WATCH	WARCEF	COMMANDER-HF
Random sequence generation (selection bias)	Low	Low	Low	Low	Low
Allocation concealment (selection bias)	Low	Low	Low	Low	Low
Blinding of participants and researchers (performance bias)	High	Low	High	Low	Low
Blinding of outcome assessment (detection bias)	Low	Unclear	Low	Low	Low
Incomplete outcome data (attrition bias)	Unclear	Unclear	Low	Low	Low
Selective reporting (reporting bias)	Low	Unclear	Unclear	Low	Low
Overall bias within trial	Unclear	Unclear	Unclear	Low	Low

Appendix 3 - Search strategy for MedLine (via PubMed)

The following search strategy was employed to perform a search of PubMed:

(((((((anticoagulants[MeSH Terms]) OR anticoagulants)) OR ((rivaroxaban[MeSH Terms]) OR rivaroxaban)) OR ((apixaban[MeSH Terms]) OR apixaban)) OR ((dabigatran[MeSH Terms]) OR dabigatran)) OR ((edoxaban[MeSH Terms]) OR edoxaban)) OR ((warfarin[MeSH Terms]) OR warfarin)) AND ((heart failure[MeSH Terms]) OR heart failure)

Restrictions were subsequently applied to filter for randomized controlled trial and for trials enrolling adult patients only.

Appendix 4 - Search strategy for the Cochrane Central Register of Controlled Trials (CENTRAL)

The following search strategy was employed to perform a search of CENTRAL:

ID	Search
#1	Randomised controlled trial
#2	RCT
#3	controlled trial
#4	anticoagulant
#5	anticoagulants
#6	warfarin
#7	apixaban
#8	rivaroxaban
#9	dabigatran
#10	edoxaban
#11	heart failure
#12	left ventricular dysfunction
#13	(#1 OR #2 OR #3) AND (#4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10) AND (#11 OR #12)

Appendix 5 – Results of fixed-effects and random-effects models

	Fixed-effects model			Random-effects model		
	Effect size	Lower 95% CI	Upper 95% CI	Effect size	Lower 95% CI	Upper 95% CI
Outcome measure						
All-cause mortality	0.99	0.90	1.08	0.99	0.90	1.08
HF readmission	0.98	0.91	1.07	0.97	0.82	1.13
Non-fatal stroke	0.63	0.49	0.81	0.63	0.49	0.81
Non-fatal MI	0.92	0.75	1.13	0.97	0.70	1.34
Major haemorrhage	1.88	1.49	2.38	1.91	1.45	2.52