SUPPLEMENTAL MATERIAL
Table S1. Summary of strategies for emulating target trial.

| Components       | Target trial (EAST-AFNET4)                                                                 | This study                                                                 |
|------------------|------------------------------------------------------------------------------------------|----------------------------------------------------------------------------|
| Inclusion period | July 28, 2011 – December 31, 2016                                                       | July 28, 2011 – December 31, 2015                                         |
| Eligibility criteria | 1) Adults (≥18 years of age) who were older than 75 years of age, had a previous transient ischemic attack or stroke, or met two of the following criteria: age greater than 65 years, female sex, heart failure, hypertension, diabetes mellitus, severe coronary artery disease, chronic kidney disease, and left ventricular hypertrophy 2) Early AF (diagnosed ≤12 months before enrolment) | 1) Selected adults (≥18 years of age) that received a rhythm-control or rate-control treatments and have no prior history of prescriptions and no records of ablation in the database who were older than 75 years of age, had a previous transient ischemic attack or stroke, or met two of the following criteria: age greater than 65 years, female sex, heart failure, hypertension, diabetes mellitus, myocardial infarction, and chronic kidney disease 2) Undergoing oral anticoagulation (>90 days of supply within 180 days after their first recorded prescription of rhythm- or rate-control medications or ablation procedure) |
| Exposed group    | Rhythm control: AADs, AF ablation, cardioversion of persistent AF, to be initiated early after randomization | Rhythm control: a prescription of more than a 90-day supply of any rhythm-control drugs in the 180-day period since the first prescription or the performance of an ablation procedure for AF. |
| Unexposed group  | Usual care: initially treated with rate-control therapy without rhythm-control therapy | Rate control: a prescription of more than a 90-day supply of any rate-control drugs in the 180-day period since the first prescription and with no prescription of rhythm-control drug and no ablation within this period. Patients prescribed rhythm-control drugs for more than 90 days or who underwent ablation within the 180-day period since the initiation of rate-control drugs were classified as intention-to-treat with rhythm control. |
| Outcome          | 1) A composite of death from cardiovascular causes, stroke, or hospitalization with worsening of heart failure or acute coronary syndrome 2) The number of nights spent in the hospital per year. 3) Each component of the primary composite outcome, rhythm, left ventricular function, quality of life, AF-related symptom | 1) Ischemic stroke 2) Hospitalization for heart failure 3) Acute myocardial infarction 4) Cardiovascular death |
| Follow-up        | From randomization until the end of the trial, death, or withdrawal from the trial.      | From 180 days after their first recorded prescription or procedure to avoid immortal time bias until the end of follow-up of the database (December 31, 2016) or death. |
| Medical conditions                                    | Definitions                                                                 | Codes or conditions                                                                 |
|------------------------------------------------------|------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|
| Atrial fibrillation                                  | Defined from diagnosis*                                                      | I48                                                                                  |
| Heart failure                                        | Defined from diagnosis*                                                      | ICD-10: I11.0, I50, I97.1                                                           |
| Heart failure admission history                      | Defined if fulfilling both diagnosis* and treatment within 90 days prior to the first recorded prescription or procedure for rhythm or rate control | ICD-10: I11.0, I50, I97.1                                                           |
| Hypertension                                         | Defined if fulfilling both diagnosis* and treatment within 90 days prior to the first recorded prescription or procedure for rhythm or rate control | ICD-10: 110, 111, 112, 113, 115 Treatment: prescription for at least one of all kinds of antihypertensive medication |
| Diabetes mellitus                                    | Defined if fulfilling both diagnosis* and treatment within 90 days prior to the first recorded prescription or procedure for rhythm or rate control | ICD-10: E10, E11, E12, E13, E14 Treatment: prescription for at least one of all kinds of oral antidiabetics or insulin |
| Dyslipidemia                                         | Defined from diagnosis*                                                      | ICD-10: E78                                                                          |
| Ischemic stroke                                       | Defined from diagnosis*                                                      | ICD-10: I63, I64                                                                     |
| Transient ischemic attack                            | Defined from diagnosis*                                                      | ICD-10: G45                                                                          |
| Intracranial bleeding                                | Defined from diagnosis*                                                      | ICD-10: I60, I61, I62                                                                |
| Myocardial infarction                                | Defined from diagnosis*                                                      | ICD-10: I21, I22, I25.2                                                             |
| Peripheral arterial disease                          | Defined from diagnosis*                                                      | ICD-10: I70.0, I70.1, I70.2, I70.8, I70.9                                           |
| Valvular heart disease                               | Defined from diagnoses* mitral stenosis or claims for heart valve surgery    | ICD-10: I05.0, I05.2, I34.2, Z95.2-4 Claim for valve replacement or valvuloplasty: O1781, O1782, O1783, O1791, O1792, O1793, O1797, O1794, O1795, O1796, O1798 |
| Chronic kidney disease                               | Defined from eGFR or diagnosis* (if laboratory value was not available, diagnosis code was used) | eGFR <60mL/min per 1.73 m² ICD-10: N18, N19                                           |
| Proteinuria                                          | Defined from laboratory data (if laboratory value was not available, diagnosis code* was used) | Urine dipstick proteinuria 1+ or higher (ICD-10: N06, N391, N392, R80)                |
| Hyperthyroidism                                      | Defined from diagnosis*                                                      | ICD-10: E05                                                                          |
| Hypothyroidism                                       | Defined from diagnosis*                                                      | ICD-10: E03                                                                          |
| Malignancy                                           | Defined from diagnoses* of cancer (non-benign)                               | ICD-10: C00-C97                                                                     |
| Chronic obstructive pulmonary disease                | Defined if fulfilling both diagnosis* and treatment within 90 days prior to the first recorded prescription or procedure for rhythm or rate control | ICD-10: J42, J43(except J43.0), J44 Treatment: SABA, SAM, LABA, LAMA, ICS, ICS+LABA, or methylxanthine (>1 months). |
| Chronic liver disease                                | Defined from diagnosis* of chronic liver disease, cirrhosis, and hepatitis   | ICD-10: B18, K70, K71, K72, K73, K74, K76.1                                         |
| Hypertrophic cardiomyopathy                          | Defined from at least one records of either inpatient or                     | ICD-10: I42.1, I42.2                                                                 |
| Outpatient Diagnoses | ICD-10 | Notes |
|----------------------|--------|-------|
| Osteoporosis         | M80, M81, M82 (except M82.0) | Defined from diagnosis* |
| Sleep apnea          | G47.3 | Defined from diagnosis* |

**Drug treatment for atrial fibrillation (available in South Korea)**

| Anti-arrhythmic drug | Available in South Korea |
|----------------------|--------------------------|
| Class Ic             | flecainide, pilsicainide, propafenone |
| Class III            | amiodarone, dronedarone, sotalol |

| Rate control drugs | Available in South Korea |
|--------------------|--------------------------|
| Beta-blocker       | atenolol, bisoprolol, carvedilol, metoprol, nebivolol, propranolol, labetalol |
| Calcium channel blocker | diltiazem, verapamil |
| Cardiac glycosides | digoxin |

**Procedures for atrial fibrillation**

| Procedure | Defined from admission | ICD-10 | Claim codes |
|-----------|-------------------------|--------|-------------|
| Catheter ablation for AF | diagnosis of AF plus claims for ablation procedures | I48 | M6542 (Conventional Radiofrequency Ablation of Atrial fibrillation) or M6547 (Radiofrequency Ablation of Atrial fibrillation Through Intracardiac Electrophysiologic 3-Dimensional Mapping) |
| Cardioversion | Defined from diagnosis of AF plus claims for cardioversion | I48 | M5880 |

*For greater accuracy, either one diagnosis during hospitalization or more than twice at outpatient clinics was required for the diagnosis.
Table S3. Definitions and codes used for study outcomes.

| Outcomes                        | Definitions                                                                 | Codes or conditions | PPV    |
|---------------------------------|-----------------------------------------------------------------------------|---------------------|--------|
| Ischemic stroke                 | Defined from admission diagnosis with concomitant imaging studies of the brain or related death | ICD-10: I63, I64   | 90.6%* (2347/2591) |
| Hospitalization owing to heart failure | Defined from principal or first secondary admission diagnoses of heart failure | ICD-10: I11.0, I50, I97.1 | 82.1%* (110/134) |
| Acute myocardial infarction     | Defined from admission diagnosis of acute myocardial infarction concurrently with coronary angiography or related death | ICD-10: I21, I22   | 86.5%† (4054/4688) |

PPV was represented as % (number of true positive cases / number of examined cases).
*We conducted a validation study using hospital administrative data from two tertiary hospitals.
†Validated in a study by Lee, HY. et al. (Atrial fibrillation and the risk of myocardial infarction: a nation-wide propensity-matched study. Sci Rep 2017;7(1):12716).
ICD-10, International Classification of Diseases-10th Revision; PPV, positive predictive value.
Table S4. Baseline characteristics after propensity score matching.

| Variables                                      | Rhythm Control (N=5183) | Rate Control (N=5183) | ASD  |
|------------------------------------------------|-------------------------|-----------------------|------|
| **Sociodemographic**                           |                         |                       |      |
| Age, years                                     | 70 (62.76)              | 70 (62.76)            | <0.1%|
| <65 years                                      | 1592 (30.7)             | 1587 (30.6)           | 0.2% |
| 65-74 year                                     | 1921 (37.1)             | 1940 (37.4)           | 0.8% |
| ≥75 years                                      | 1670 (32.2)             | 1656 (32.0)           | 0.6% |
| Male                                           | 2862 (55.2)             | 2894 (55.8)           | 1.2% |
| AF duration, months                            | 0.5 (0.0-10.4)          | 0.1 (0.0-13.1)        | 2.1% |
| **Enroll year**                                |                         |                       |      |
| 2011                                           | 342 (6.6)               | 341 (6.6)             | 0.1% |
| 2012                                           | 935 (18.0)              | 950 (18.3)            | 0.8% |
| 2013                                           | 1118 (21.6)             | 1095 (21.1)           | 1.1% |
| 2014                                           | 1215 (23.4)             | 1205 (23.2)           | 0.5% |
| 2015                                           | 1573 (30.3)             | 1592 (30.7)           | 0.8% |
| High tertile of income                         | 2250 (43.4)             | 2277 (43.9)           | 0.1% |
| Number of OPD visits ≥12/year                  | 4224 (81.5)             | 4232 (81.7)           | 0.4% |
| Living in metropolitan areas                   | 2322 (44.8)             | 2306 (44.5)           | 0.6% |
| Level of care initiating treatment             |                         |                       |      |
| Tertiary                                       | 2544 (49.1)             | 2503 (48.3)           | 1.6% |
| Secondary                                      | 2361 (45.6)             | 2373 (45.8)           | 0.5% |
| Primary                                        | 278 (5.4)               | 307 (5.9)             | 2.4% |
| **Risk scores**                                |                         |                       |      |
| CHA2DS2-VASc score                             | 4 (3-5)                 | 4 (3-5)               | 0.9% |
| mHAS-BLED score*                              | 2 (2-3)                 | 2 (2-3)               | 0.2% |
| Charlson comorbidity index                     | 4 (2-5)                 | 4 (2-5)               | 0.3% |
| Hospital Frailty Risk score                    | 2.9 (0.3-6.6)           | 2.6 (0.0-6.7)         | 0.4% |
| **Medical history**                            |                         |                       |      |
| Heart failure                                  | 2817 (54.4)             | 2815 (54.3)           | 0.1% |
| Previous hospitalisation for heart failure     | 748 (14.4)              | 750 (14.5)            | 0.1% |
| Hypertension                                  | 4123 (79.5)             | 4086 (78.8)           | 1.8% |
| Diabetes                                       | 1502 (29.0)             | 1480 (28.6)           | 0.9% |
| Dyslipidemia                                   | 4287 (82.7)             | 4258 (82.2)           | 1.5% |
| Intracranial haemorrhage                       | 1777 (34.3)             | 1779 (34.3)           | 0.1% |
| Transient ischaemic attack                     | 496 (9.6)               | 504 (9.7)             | 0.5% |
| Haemorrhagic stroke                            | 132 (2.5)               | 133 (2.6)             | 0.1% |
| Myocardial infarction                          | 421 (8.1)               | 415 (8.0)             | 0.4% |
| Peripheral arterial disease                    | 744 (14.4)              | 715 (13.8)            | 1.6% |
| Valvular heart disease                         | 609 (11.7)              | 607 (11.7)            | 0.1% |
| Chronic kidney disease                         | 289 (5.6)               | 295 (5.7)             | 0.5% |
| Proteinuria                                    | 386 (7.4)               | 369 (7.1)             | 1.3% |
| Hyperthyroidism                                | 502 (9.7)               | 528 (10.2)            | 1.7% |
| Hypothyroidism                                 | 589 (11.4)              | 612 (11.8)            | 1.4% |
| Malignancy                                     | 1241 (23.9)             | 1229 (23.7)           | 0.5% |
| COPD                                           | 1617 (31.2)             | 1635 (31.5)           | 0.7% |
| Chronic liver disease                          | 2123 (41.0)             | 2167 (41.8)           | 1.7% |
| Hypertrophic cardiomyopathy                    | 68 (1.3)                | 71 (1.4)              | 0.5% |
| Osteoporosis                                   | 1796 (34.7)             | 1779 (34.3)           | 0.7% |
| Sleep apnea                                    | 29 (0.6)                | 22 (0.4)              | 1.9% |
| **Concurrent medication†**                     |                         |                       |      |
| Oral anticoagulant                             | 5183 (100.0)            | 5183 (100.0)          | <0.1%|
| Warfarin                                       | 4301 (83.0)             | 4276 (82.5)           | 1.3% |
| DOAC                                           | 1155 (22.3)             | 1199 (23.1)           | 2.0% |
| Beta-blocker                                   | 3797 (73.3)             | 3644 (70.3)           | 6.6% |
| Non-DHP CCB | 849 (16.4) | 818 (15.8) | 1.6% |
|------------|------------|------------|------|
| Digoxin    | 893 (17.2) | 1001 (19.3)| 5.4% |
| Aspirin    | 1051 (20.3)| 1010 (19.5)| 2.0% |
| P2Y₁₂ inhibitor | 468 (9.0) | 478 (9.2) | 0.7% |
| Statin     | 2394 (46.2)| 2355 (45.4)| 1.5% |
| DHP CCB    | 816 (15.7) | 837 (16.1) | 1.1% |
| ACEI/ARB   | 2790 (53.8)| 2806 (54.1)| 0.6% |
| Loop/thiazide diuretics | 2455 (47.4) | 2467 (47.6) | 0.5% |
| K⁺ sparing diuretics | 983 (19.0) | 997 (19.2) | 0.7% |
| Alpha-blocker | 79 (1.5)  | 105 (2.0)  | 3.8% |

Values are presented as median (interquartile range) or n (%).

*Modified HAS-BLED = hypertension, 1 point: >65 years old, 1 point: stroke history, 1 point: bleeding history or predisposition, 1 point: liable international normalised ratio, not assessed: ethanol or drug abuse, 1 point: drug predisposing to bleeding, 1 point.

†Defined as a prescription fill of >90 days within the 180-day after the first prescription for rhythm- or rate-control drugs or the performance of an ablation procedure for AF.

AAD, antiarrhythmic drug; ACEI, angiotensin converting enzyme inhibitor; AF, atrial fibrillation; ARB, angiotensin II receptor blocker; ASD, absolute standardised difference; COPD, chronic obstructive pulmonary disease; DHP, dihydropyridine; DOAC, direct oral anticoagulant; OPD, outpatient department.
| Falsification endpoints                      | Definitions                                                                 | ICD-10 codes / other conditions                          |
|---------------------------------------------|-----------------------------------------------------------------------------|----------------------------------------------------------|
| Influenza                                   | Defined from diagnosis plus treatment                                       | J09, J10, J11 / Treatment: Oseltamivir                   |
| Major fracture                              | Defined from diagnosis on inpatient or emergency department record           | S72, S72.0, S72.1, S72.2, S12.0, S12.1, S12.2, S12.7, S12.9, S22.0, S22.1, S32.0, S32     |
| Urinary tract infection                      | Defined from diagnosis*                                                      | N30, N300, N309, N341, N342, N390                        |
| Fall accident                               | Defined from diagnosis on inpatient or emergency department record           | W00-W19                                                 |
| Tuberculosis                                | Defined from diagnosis*                                                      | A15, A16, A17, A18, A19                                 |
| Syphilis                                    | Defined from diagnosis*                                                      | A50, A51, A52, A53                                      |
| Viral enteritis                             | Defined from diagnosis*                                                      | A08                                                     |
| Warts                                       | Defined from diagnosis*                                                      | B07                                                     |
| Acute hepatitis A                           | Defined from diagnosis*                                                      | B15                                                     |
| Bone malignancy                             | Defined from diagnosis*                                                      | C40, C41, C90, C795                                     |
| Lymphoma                                    | Defined from diagnosis*                                                      | C81, C82, C83, C84, C85                                 |
| Benign neoplasm of colon, rectum            | Defined from diagnosis*                                                      | D12                                                     |
| Lipoma                                      | Defined from diagnosis*                                                      | D17                                                     |
| Sleep apnea                                 | Defined from diagnosis*                                                      | G473                                                    |
| Carpal tunnel syndrome                      | Defined from diagnosis*                                                      | G560                                                    |
| Hordeolum / chalazion                       | Defined from diagnosis*                                                      | H00                                                     |
| Pterygium                                   | Defined from diagnosis*                                                      | H110                                                    |
| Glucoma                                     | Defined from diagnosis*                                                      | H40, H42                                                |
| Otitis media                                | Defined from diagnosis*                                                      | H65, H66, H67                                           |
| Meniere's disease                           | Defined from diagnosis*                                                      | H810                                                    |
| Benign paroxysmal positional vertigo        | Defined from diagnosis*                                                      | H811                                                    |
| Varicose veins of lower extremities         | Defined from diagnosis*                                                      | I83                                                     |
| Chronic sinusitis                           | Defined from diagnosis*                                                      | J32                                                     |
| Nasal polyp                                 | Defined from diagnosis*                                                      | J33                                                     |
| Acute appendicitis                          | Defined from diagnosis on inpatient or emergency department record           | K35                                                     |
| Inguinal hernia                             | Defined from diagnosis*                                                      | K40                                                     |
| Diverticulitis of intestine                 | Defined from diagnosis*                                                      | K57                                                     |
| Cholecystitis                               | Defined from diagnosis*                                                      | K81                                                     |
| Cellulitis                                  | Defined from diagnosis*                                                      | L03                                                     |
| Allergic contact dermatitis                 | Defined from diagnosis*                                                      | L23                                                     |
| Urticaria                                   | Defined from diagnosis*                                                      | L50                                                     |
| Ingrowing nail                              | Defined from diagnosis*                                                      | L600                                                    |
| Seropositive rheumatoid arthritis           | Defined from diagnosis*                                                      | M05                                                     |
| Spinal stenosis                             | Defined from diagnosis*                                                      | M480                                                    |
| Frozen shoulder                             | Defined from diagnosis*                                                      | M750                                                    |
| Osteomyelitis                               | Defined from diagnosis*                                                      | M86                                                     |
| Nausea and vomiting                         | Defined from diagnosis*                                                      | R11                                                     |
| Dysuria                                     | Defined from diagnosis*                                                      | R30                                                     |
| Voice disturbances                          | Defined from diagnosis*                                                      | R49                                                     |
| Gout                                        | Defined from diagnosis*                                                      | M10                                                     |
| Burns                                       | Defined from diagnosis*                                                      | T20-T32                                                 |
| Anaphylaxis/Allergic reaction               | Defined from diagnosis*                                                      | T78                                                     |
| Traffic accident                            | Defined from diagnosis*                                                      | V01-V99                                                 |

*To ensure accuracy, diagnosis was established based on one inpatient or two outpatient records of ICD-10 codes in the database. ICD-10, International Classification of Diseases, Tenth Revision.
Table S6. Stratified analyses according to the initial choice of rhythm-control treatments: cardiovascular outcomes in weighted patients undergoing rhythm or rate control.

| Outcome                      | Number of events | Person-years | Event rate | Number of events | Person-years | Event rate | Absolute rate difference per 100 person-years (95% CI) | Hazard ratio (95% CI) | P value |
|------------------------------|------------------|--------------|------------|------------------|--------------|------------|------------------------------------------------------|------------------------|---------|
|                              | AAD (N=12869)    |              |            | Rate control (N=8982) |              |            |                                                     |                        |         |
| Ischemic stroke              | 695              | 28142        | 2.84       | 704              | 19379        | 3.66       | -0.82 (-1.38 to -0.25)                               | 0.78 (0.66–0.93)        | 0.006   |
| Hospitalization for HF       | 901              | 27875        | 3.67       | 856              | 19098        | 4.22       | -0.55 (-1.18 to 0.08)                               | 0.88 (0.75–1.03)         | 0.116   |
| Acute myocardial infarction  | 74               | 28958        | 0.23       | 64               | 20172        | 0.37       | -0.14 (-0.31 to 0.03)                               | 0.63 (0.35–1.13)         | 0.118   |
| Cardiovascular death         | 517              | 29035        | 2.25       | 532              | 20253        | 2.44       | -0.19 (-0.66 to 0.28)                               | 0.93 (0.76–1.14)         | 0.472   |
|                              |                  |              |            |                  |              |            |                                                     |                        |         |
|                              | Ablation (N=784) |              |            | Rate control (N=8982) |              |            |                                                     |                        |         |
| Ischemic stroke              | 20               | 2086         | 0.75       | 704              | 19379        | 2.68       | -1.93 (-3.40 to -0.47)                               | 0.29 (0.11–0.80)         | 0.017   |
| Hospitalization for HF       | 20               | 2081         | 1.53       | 856              | 19098        | 3.16       | -1.63 (-3.35 to 0.09)                               | 0.51 (0.23–1.10)         | 0.085   |
| Acute myocardial infarction  | 4                | 2109         | 0.23       | 64               | 20172        | 0.29       | -0.06 (-0.62 to 0.50)                               | 0.83 (0.10–7.11)         | 0.867   |
| Cardiovascular death         | 6                | 2114         | 0.69       | 532              | 20253        | 1.50       | -0.81 (-1.96 to 0.34)                               | 0.48 (0.16–1.45)         | 0.193   |

Event rates (per 100 person-years) and hazard ratios are overlap weighted.
AAD, antiarrhythmic drug; CI, confidence interval; HF, heart failure.
Table S7. Cardiovascular outcomes in rhythm- and rate-controlled patients taking oral anticoagulants ≥80% of time at risk.

| Outcome                        | Number of events | Person-years | Event rate | Number of events | Person-years | Event rate | Absolute rate difference per 100 person-years (95% CI) | Weighted hazard ratio (95% CI) | P value |
|--------------------------------|------------------|--------------|------------|------------------|--------------|------------|------------------------------------------------------|--------------------------------|--------|
| **Propensity overlap weighting** |                  |              |            |                  |              |            |                                                      |                                |        |
| **Intention to treat**         |                  |              |            |                  |              |            |                                                      |                                |        |
| Ischemic stroke                | 429              | 18302        | 2.52       | 426              | 13863        | 3.17       | -0.65 (-1.30 to -0.00)                                | 0.79 (0.63–1.00)                | 0.048  |
| Hospitalization for HF         | 571              | 18132        | 3.50       | 532              | 13673        | 3.71       | -0.21 (-0.94 to 0.52)                                | 0.95 (0.77–1.16)                | 0.594  |
| Acute myocardial infarction    | 40               | 18810        | 0.20       | 26               | 14357        | 0.22       | -0.02 (-0.19 to 0.15)                                | 0.92 (0.40–2.11)                | 0.849  |
| Cardiovascular death           | 291              | 18848        | 1.90       | 296              | 14383        | 2.06       | -0.16 (-0.69 to 0.37)                                | 0.92 (0.71–1.20)                | 0.547  |

Event rates (per 100 person-years) and hazard ratios are overlap weighted.
CI, confidence interval; HF, heart failure.
| Endpoints                              | HR (95% CI)       | P value |
|---------------------------------------|-------------------|---------|
| Influenza                             | 0.89 (0.62-1.28)  | 0.532   |
| Major fracture                        | 1.12 (0.90-1.38)  | 0.316   |
| Urinary tract infection               | 1.07 (0.97-1.19)  | 0.183   |
| Fall accident                         | 1.01 (0.39-2.63)  | 0.982   |
| Tuberculosis                          | 0.91 (0.72-1.15)  | 0.415   |
| Syphilis                              | 0.67 (0.35-1.25)  | 0.208   |
| Viral enteritis                       | 1.35 (0.79-2.32)  | 0.275   |
| Warts                                 | 0.79 (0.41-1.54)  | 0.488   |
| Acute hepatitis A                     | 0.88 (0.37-2.05)  | 0.761   |
| Viral conjunctivitis                  | 1.20 (0.75-1.93)  | 0.444   |
| Stomach cancer                        | 0.87 (0.63-1.19)  | 0.375   |
| Bone malignancy                       | 0.74 (0.44-1.26)  | 0.265   |
| Lymphoma                              | 0.70 (0.30-1.66)  | 0.418   |
| Benign neoplasm of colon, rectum      | 1.32 (1.01-1.72)  | 0.039   |
| Lipoma                                | 1.72 (0.96-3.06)  | 0.067   |
| Sleep apnea                           | 1.51 (0.71-3.21)  | 0.281   |
| Carpal tunnel syndrome                | 0.64 (0.39-1.04)  | 0.069   |
| Hordeolum                             | 1.10 (0.86-1.40)  | 0.468   |
| Pterygium                             | 1.17 (0.78-1.76)  | 0.447   |
| Glaucoma                              | 1.05 (0.95-1.16)  | 0.363   |
| Otitis media                          | 1.05 (0.87-1.26)  | 0.614   |
| Meniere's disease                     | 1.11 (0.83-1.49)  | 0.489   |
| Benign paroxysmal positional vertigo  | 1.05 (0.82-1.35)  | 0.682   |
| Varicose veins of lower extremities   | 0.94 (0.60-1.47)  | 0.784   |
| Chronic sinusitis                     | 1.11 (0.94-1.30)  | 0.213   |
| Nasal polyp                           | 1.50 (0.78-2.90)  | 0.225   |
| Acute appendicitis                    | 1.40 (0.75-2.62)  | 0.286   |
| Inguinal hernia                       | 1.11 (0.68-1.80)  | 0.671   |
| Diverticulitis of intestine           | 1.47 (0.83-2.62)  | 0.187   |
| Cholecystitis                         | 0.91 (0.61-1.36)  | 0.640   |
| Cellulitis                            | 1.09 (0.95-1.24)  | 0.234   |
| Allergic contact dermatitis           | 1.07 (0.98-1.17)  | 0.153   |
| Urticaria                             | 1.07 (0.95-1.19)  | 0.262   |
| Ingrowing nail                        | 1.06 (0.70-1.60)  | 0.781   |
| Seropositive rheumatoid arthritis     | 1.00 (0.85-1.17)  | 0.970   |
| Spinal stenosis                       | 1.07 (0.97-1.18)  | 0.206   |
| Frozen shoulder                       | 0.91 (0.79-1.06)  | 0.226   |
| Osteomyelitis                         | 1.01 (0.44-2.31)  | 0.975   |
| Nausea and vomiting                   | 1.10 (0.99-1.21)  | 0.064   |
| Dysuria                               | 0.93 (0.75-1.16)  | 0.533   |
| Voice disturbance                     | 1.32 (0.48-3.69)  | 0.591   |
| Gout                                  | 0.88 (0.67-1.17)  | 0.367   |
| Burns                                 | 1.24 (0.89-1.71)  | 0.201   |
| Anaphylaxis/Allergic reaction         | 0.99 (0.67-1.47)  | 0.957   |
| Traffic accident                      | 0.83 (0.07-10.2)  | 0.886   |

CI, confidence interval; HR, hazard ratio.
Figure S1. Distributions of the propensity scores before and after overlap weighting.
Figure S2. Relation between treatment timing and risk of ischemic stroke (A) and hospitalization owing to heart failure (B) for rhythm control or rate control in on treatment analyses (overlap weighting) and propensity score matched analyses.

A. Ischemic stroke

The x axis shows the timing of treatment initiation since the first diagnosis of atrial fibrillation; the y axis, hazard ratios (HRs) associated with rhythm control compared with rate control. The skyblue horizontal lines indicate HR=1, which corresponds to an equal risk of outcomes in patients treated with rhythm and rate control. Dashed black lines show the 95% confidence interval (CI).
Figure S3. Stratified analyses according to the initial choice of rhythm-control treatments: relation between treatment timing and risk of cardiovascular outcomes for rhythm control or rate control.

**A. AAD vs. Rate control**

- Ischemic stroke:
  - Lower With Rhythm Control
  - Lower With Rate Control
  - No Difference

- Hospitalization for HF:
  - Lower With Rhythm Control
  - Lower With Rate Control
  - No Difference

- Acute MI:
  - Lower With Rhythm Control
  - Lower With Rate Control
  - No Difference

- Cardiovascular death:
  - Lower With Rhythm Control
  - Lower With Rate Control
  - No Difference

**B. Ablation vs. Rate control**

- Ischemic stroke:
  - Lower With Rhythm Control
  - Lower With Rate Control
  - No Difference

- Hospitalization for HF:
  - Lower With Rhythm Control
  - Lower With Rate Control
  - No Difference

- Acute MI:
  - Lower With Rhythm Control
  - Lower With Rate Control
  - No Difference

- Cardiovascular death:
  - Lower With Rhythm Control
  - Lower With Rate Control
  - No Difference

AAD, anti-arrhythmic drug; AF, atrial fibrillation; CI, confidence interval; HF, heart failure, HR, hazard ratio; MI, myocardial infarction.
Figure S4. Relation between treatment timing and risk of cardiovascular outcomes for rhythm control or rate control among patients taking oral anticoagulants ≥80% of time at risk.

AF, atrial fibrillation; CI, confidence interval; HF, heart failure, HR, hazard ratio; MI, myocardial infarction.