SUPPLEMENTAL MATERIAL

Supplementary tables S1-S4
Supplementary figures S1-S2
MOOSE checklist for meta-analyses of observational studies
PRISMA checklist
**Supplementary Table S1:** Definition of terms

**Supplementary Table S2:** Search terms used during data searching

(CENTRAL: Cochrane Central Register of Controlled Trials; CINAHL: Cumulative Index to Nursing and Allied Health)

**Supplementary Table S3:** Summary characteristics of included studies

(AF: atrial fibrillation; CHA₂DS₂-VASc: congestive heart failure, hypertension, age >75, diabetes mellitus, prior stroke, vascular disease, age 65-74, sex; ICH: intracerebral haemorrhage; IQR: inter-quartile range; NOAC: non- vitamin K antagonist oral anticoagulant; OAC: oral anticoagulation; SD: standard deviation; VKA: vitamin-K antagonist)

**Supplementary Table S4:** Results of sub-group and sensitivity analyses

(APACHE-AF: Apixaban After Anticoagulation-associated Intracerebral Haemorrhage in Patients with Atrial Fibrillation; CI: confidence interval; ICrH: intracranial haemorrhage; RR: risk ratio; SoSTART: Start or STop Anticoagulants Randomised Trial)
**Supplementary Table S1: Definition of Terms**

| Term                                | Definition*                                                                                                                                                                                                                                                                                                                                                       |
|-------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Atrial fibrillation                 | A disease characterised by the chaotic generation of electrical impulses in the atria, leading to an irregular heart rhythm and an increased risk of thromboembolic events due to formation of blood clots.                                                                                                                                                                                                 |
| Central nervous system bleeding     | Bleeding that occurs within the brain or spinal cord.                                                                                                                                                                                                                                                                                                               |
| Cerebral infarct                    | Prolonged ischaemia that results in focal necrosis of brain tissue.                                                                                                                                                                                                                                                                                                   |
| Cerebral micro-bleed                | Small focal intracerebral haemorrhages.                                                                                                                                                                                                                                                                                                                           |
| CHA₂DS₂-VASc                        | A risk scoring tool that can be used to predict the risk of a thromboembolic event in an individual with atrial fibrillation. The tool considers the following risk factors: congestive heart failure, hypertension, age >75, diabetes mellitus, prior stroke, vascular disease, age 65-74, sex.                                                                                                               |
| Functional status                   | An individual’s ability to perform basic activities of daily living.                                                                                                                                                                                                                                                                                                   |
| International normalised ratio     | A laboratory measurement used to determine the effects of oral anticoagulants on the body’s blood clotting.                                                                                                                                                                                                                                                         |
| Intracerebral haemorrhage           | Bleeding that occurs within the brain parenchyma. Includes cerebellar, brain steam, and deep haemorrhages.                                                                                                                                                                                                                                                        |
| Intracranial haemorrhage            | Bleeding that occurs within the skull. Includes intracerebral, subdural, subarachnoid, and epidural haemorrhages.                                                                                                                                                                                                                                                    |
| Ischaemic stroke                    | A stroke caused by blockage of blood supply in the brain.                                                                                                                                                                                                                                                                                                         |
| Major vascular event                | An injury that affects the vascular system, such as ischaemic stroke, myocardial infarction, sudden cardiac death.                                                                                                                                                                                                                                                 |
| Modified Rankin scale               | A tool that assesses disability in an individual who has suffered a stroke.                                                                                                                                                                                                                                                                                      |
| Oral anticoagulation                | Oral medication that prevents coagulation of the blood.                                                                                                                                                                                                                                                                                                           |
| Systemic embolism                   | Presence of emboli (clots) in the arterial circulation.                                                                                                                                                                                                                                                                                                           |
| Thromboembolic event                | The formation of a blood clot that partially or fully obstructs venous or arterial blood flow. This includes conditions such as ischaemic stroke, systemic embolism, transient ischaemic attack).                                                                                                                                                                                  |
| Time in therapeutic range           | The percentage of time in which a patient’s international normalised ratio remains in the target range.                                                                                                                                                                                                                                                         |
| Transient ischaemic attack          | Temporary disruption of blood supply in the brain.                                                                                                                                                                                                                                                                                                               |

*Other definitions as used by the included papers were also accepted by the systematic review authors.*
## Supplementary Table S2: Search terms used during data searching

| MEDLINE and EMBASE via Ovid | CINAHL via EbscoHost | CENTRAL |
|-----------------------------|----------------------|---------|
| 1. atrial fibrillation.mp    | 1. (MM “Atrial Fibrillation”) | 1. MESH descriptor Atrial Fibrillation explode all trees |
| 2. exp atrial fibrillation/  | 2. AF or atrial fibrillation | 2. MESH descriptor Fibrinolytic Agents explode all trees |
| 3. (AF or AFib).ab           | 3. (MM “Hematologic agents”) | 3. MESH descriptor Thrombolytic Therapy explode all trees |
| 4. exp cerebral hemorrhage/  | 4. (MM “Anticoagulants”) | 4. MESH descriptor Cerebral Hemorrhage explode all trees |
| 5. cerebral hemorrhage.mp    | 5. (MM “Thrombolytic Therapy”) | 5. atrial fibrillation |
| 6. (intracerebral adj6 hemorrhage).ab | 6. antithrombotic or anticoagulant | 6. antithrombotic |
| 7. (intracerebral adj6 haemorrhage).ab | 7. Apixaban OR edoxaban OR dabigatran | 7. anticoagulant |
| 8. (cerebral adj6 bleed").ab | 8. Novel oral anticoagulant OR NOAC | 8. antiplatelet |
| 9. (intracerebral adj6 bleed").ab | 9. Non-vitamin K antagonist oral anticoagulant | 9. intracerebral hemorrhage |
| 10. (spontaneous adj6 intracerebral adj6 hemorrhage).ab | 10. Direct oral anticoagulant OR DOAC11. Factor Xa inhibitor | 10. #1 OR #5 |
| 11. (spontaneous adj6 intracerebral adj6 haemorrhage).ab | 12. antiplatelet therapy | 11. #2 OR #3 OR #6 |
| 12. (spontaneous adj6 intracerebral adj6 bleed").ab | 13. vitamin K antagonist OR VKA | 12. #6 AND #7 AND #8 |
| 13. (non-traumatic adj6 intracerebral adj6 hemorrhage).ab | 14. thrombolytic therapy in stroke | 13. #11 OR #12 |
| 14. (non-traumatic adj6 intracerebral adj6 haemorrhage).ab | 15. intracerebral hemorrhage | 14. #4 OR #5 |
| 15. (non-traumatic adj6 intracerebral adj6 bleed").ab | 16. intracerebral hemorrhage stroke | 15. #10 AND #13 AND #14 |
| 16. (hemorrhagic adj6 stroke).ab | 17. intracerebral stroke | 17. intracerebral stroke |
| 17. (haemorrhagic adj6 stroke).ab | 18. 1 OR 2 | 18. 1 OR 2 |
| 18. exp Anticoagulants/      | 19. 3 OR 4 OR 5 OR 6 | 19. 3 OR 4 OR 5 OR 6 |
| 19. anticoagulants.mp        | 20. 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 | 20. 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 |
| 20. (anticoagula$ OR oral anticoagula$).ab | 21. 15 OR 16 OR 17 | 21. 15 OR 16 OR 17 |
| 21. (direct adj6 oral adj6 anticoagula$).ab | 22. 19 OR 20 | 22. 19 OR 20 |
| 22. (novel adj6 oral adj6 anticoagula$).ab | 23 18 AND 21 AND 22 | 23 18 AND 21 AND 22 |
| 23. (non-vitamin aj6 K adj6 inhibitor adj6 oral adj6 anticoagula$).ab | 24. 23 limiters - Publication Year: 2000-2020 | 24. 23 limiters - Publication Year: 2000-2020 |
| 24. (NOAC OR DOAC).ab        | 25. (rivaroxaban OR dabigatran OR edoxaban OR apixaban).ab | 25. (rivaroxaban OR dabigatran OR edoxaban OR apixaban).ab |
| 25. (rivaroxaban OR dabigatran OR edoxaban OR apixaban).ab | 26. 1 OR 2 OR 3 | 26. 1 OR 2 OR 3 |
| 26. 1 OR 2 OR 3              | 27. 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 | 27. 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 |
| 27. 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 | 28. 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25 | 28. 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25 |
| 28. 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25 | 29. 26 AND 27 AND 28 | 29. 26 AND 27 AND 28 |
| 29. 26 AND 27 AND 28         | 30. limit 29 to yr=”2000-Current” | 30. limit 29 to yr=”2000-Current” |
| 30. limit 29 to yr=”2000-Current” | 31. limit 30 to (adaptive clinical trial or clinical study or clinical trial, all or clinical trial or comparative study or controlled clinical trial or equivalence trial or evaluation study or multicenter study or observational study or pragmatic clinical trial or randomized controlled trial) | 31. limit 30 to (adaptive clinical trial or clinical study or clinical trial, all or clinical trial or comparative study or controlled clinical trial or equivalence trial or evaluation study or multicenter study or observational study or pragmatic clinical trial or randomized controlled trial) |
### Supplementary Table S3: Summary characteristics of included studies

| First author, year, country | Study design | Key inclusion criteria | N | Female (%) | Mean age (years) [SD] | Mean CHA2DS2-VASc [SD] | Interventions | Comparison | Primary outcomes | Follow-up length | OAC at time of ICH (%) | Period of data collection |
|-----------------------------|--------------|------------------------|---|------------|-----------------------|------------------------|---------------|------------|-------------------|---------------------|--------------------------|--------------------------|
| **OAC vs no therapy**       |              |                        |   |            |                       |                        |               |            |                   |                     |                          |                          |
| Sadighi 2020, USA26         | Observational cohort | Non-traumatic intracerebral haemorrhage, non-valvular and valvular AF (incl. prosthetic heart valves) and atrial flutter | 93 | 45.7% | 76.2 [10.3] | Not reported | Warfarin or NOAC | No therapy | Rate of recurrent ICH, ischaemic stroke/systemic symbolism, death | Mean, months OAC 22.7 [22.4] No OAC 22.8 [22.0] | 100% | Patients hospitalised in the period 2010-2017 |
| Newman 2020, USA24          | Retrospective cohort | Non-valvular AF diagnosed prior to index event, OAC-associated intracranial haemorrhage, filed OAC prescription within 6 months of index event. | 1,502 | 56.3% | Not reported | Not reported | VKA or NOAC | No therapy | Composite ischaemic stroke/TIA, recurrent ICH, composite ischaemic stroke/TIA/ICH, all-cause mortality, thromboembolism | Average 780 days | 100% | 1/1/2020 – 31/10/2016 |
| Perreault 2019, Canada13    | Observational cohort | Aged ≥65, non-valvular AF, intracranial haemorrhage on or off OAC, not on antiplatelets or dual therapy | 683 | OAC 53.9% No OAC 52.7% | OAC 81.7 [5.8] No OAC 83.6 [5.8] | Not reported | VKA or NOAC | No therapy | Ischaemic stroke/systemic embolism, all-cause mortality, repeat ICH, major bleeding | Median 12 months OAC group 89.6% No treatment 69% | 1/1/1995 – 31/12/2015 |
| Sakamoto, 2019, Japan9      | Retrospective cohort | Acute spontaneous intracerebral haemorrhage, anticoagulated for AF or deep vein thrombosis, diagnosed during stroke unit stay | 236 (33 AF) | Cohort 34% AF only 24% | Median, IQR Cohort 69 [61-79] AF only 72 [65-82] | AF only 5.24 [1.62] | VKA or NOAC | No therapy | Clinical characteristics of patients in OAC-restart vs. OAC non-restart groups and in OAC-indicated and OAC non-restart groups, no. of days from ICH to OAC therapy, To hospital discharge. Median hospital stay 17 days [IQR 11-26] | OAC group 61% No treatment 50% | Consecutive patient admissions September 2014 – March 2017 |
| Kato, 2019, Japan21         | Retrospective cohort | Non-valvular AF, acute spontaneous intracerebral haemorrhage, on NOAC at time of ICH | 43 | OAC 47% No OAC 29% | OAC 74.1 No OAC 72.4 | Median [IQR] 4 [3-5] | NOAC | No therapy | Timing of NOAC resumption; factors that influence NOAC resumption | OAC 31 days No OAC 32 days | 100% | Patient admissions March 2014 – February 2018 |
| Nielsen, 2017, Denmark16    | Observational cohort | Non-traumatic or traumatic intracranial haemorrhage, prior diagnosis of AF, prior treatment with warfarin | 2,415 | 38.7% | 77.1 [9.1] | 3.9 [1.7] | Warfarin | No therapy | Composite outcome of ischaemic stroke and systemic embolism, recurrent ICH. | Median 279 days | 100% | 1/1/1998 – 28/2/2016 |
| Study                                    | Design/Loc. | Patient Source | Inclusion Criteria                                                                                                                                                                                                 | n   | Primary Endpoint/Outcome Measures                                                                                                                                                                                                 | OAC/No OAC | OAC Use/Prior Therapy | Recurrent Events | Duration | Recruitment | Study Dates |
|-----------------------------------------|-------------|----------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------|----------------------|------------------|----------|-------------|-------------|
| Park, 2016, Korea                      | Retrospective cohort | AF (incl. valvular, prosthetic valves, PE, DVT), prior intracranial haemorrhage, requiring OAC, spontaneous or traumatic ICH | 428 | OAC 62.2% No OAC 71.3% | OAC 67.9 (11.1) No OAC 69.1 [10.8] | OAC 3.35 [1.7] No OAC 3.16 [1.73] | Warfarin No therapy | Thromboembolic (incl. ischaemic stroke and systemic embolisms) and major bleeding events; composite endpoint | Mean 39.5 ± 31.9 months | OAC group 65% No OAC group 35.1% | Patient enrolment 1/1/2009 – 31/12/2013 |
| Murphy, 2018, USA/Germany              | Meta-analysis of individual-level data | Primary and first intracerebral haemorrhage, non-valvular AF requiring OAC, on OAC at time of ICH, no prior functional impairment, no ICH/ischaemic stroke at 1-year follow up | 941 | RETRACE 39% MGH 40% ERICH 32% | RETRACE 73.6 [7.8] MGH 72.1 [9.3] ERICH 71.2 [11.3] | Median [IQR RETRACE 5 [4-6] MGH 5 [4-6] ERICH 5 [4-6]] | VKA No therapy | Recovery in functional status at 1-year post index ICH | 3, 6, 12 months post index ICH | 100% Study dates RETRACE 2006 – 2010 ERICH 2011 – 2015 MGH 1994 – ongoing in 2018 |
| Biffi, 2017, USA/Germany              | Meta-analysis of individual-level data | First acute intracerebral haemorrhage, non-traumatic ICH, on OAC at time of ICH (for stroke prevention in AF, VKA with INR >1.5), potential for OAC resumption | 1,012 | RETRACE 39% MGH 40% ERICH 32% | RETRACE 73.6 [7.8] MGH 72.1 [9.3] ERICH 71.2 [11.3] | Median [IQR RETRACE 5 [4-6] MGH 5 [4-6] ERICH 5 [4-6]] | VKA No therapy | Association between OAC resumption and 90-day mortality. Functional outcomes | Median, months. Lobar ICH 48.6 [IQR 33.9-65.4] Non-lobar ICH - 46.7 [IQR 32.6 – 63.4] | 100% Study dates RETRACE 2006 – 2010 ERICH 2011 – 2015 MGH 1994 – ongoing in 2017 |
| Kuramatsu, 2015, Germany               | Retrospective cohort | Spontaneous intracerebral haemorrhage, on VKA on admission, INR on admission >1.5. | 719 | OAC (566 AF) 32.7% No OAC 39.9% | OAC 72.9 [7.7] No OAC 75.5 [7.8] | Median CHADS2 [IQR OAC 2 [1-3] No OAC 2 [2-3]] | VKA No therapy | OAC cohort: ischaemic or non-ischaemic stroke, haemorrhagic or extra-cerebral bleeding | One year | RETRACE 2006 – 2010 |

| Study                                    | Design/Loc. | Patient Source | Inclusion Criteria | n   | Primary Endpoint/Outcome Measures | OAC Use/Prior Therapy | Recurrent Events | Duration | Recruitment | Study Dates |
|-----------------------------------------|-------------|----------------|--------------------|-----|-----------------------------------|----------------------|------------------|----------|-------------|-------------|
| SoSTART Collaboration, 2021, UK         | Randomised controlled trial (pilot phase) | Diagnosed AF, survived >24 hours post spontaneous symptomatic intracranial haemorrhage, CHA2DS2-VASC ≥2. | 203 | OAC 39% No OAC 36% | Median [IQR OAC 79 [74-85] No OAC 79 [74-84]] | Median [IQR NOAC or VKA 4 [3-5]] | Antiplatelet or no therapy | Recurrent symptomatic spontaneous intracranial haemorrhage | Median 1.2 years [IQR 0.97-1.95] OAC use prior to ICH OAC 83% No OAC 84% | 29/3/2008-27/2/2020 |
| APACHE-AF Investigators, 2021, The Netherlands | Randomised controlled trial (phase 2) | Spontaneous intracerebral haemorrhage while on OAC, CHA2DS2-VASC ≥2, mRS ≤4. | 101 | 46% | Median [IQR 78 [73-83]] | Median [IQR Apixaban 4 [3-5]] | Apixaban Antiplatelet or no therapy | Non-fatal stroke (ischaemic or intracranial) or vascular death. | Median 1.9 years [IQR 1.0-3.1] | 100% | 15/01/2015-06/06/2020 |
| Chao, 2016, Taiwan                     | Nationwide cohort | Newly diagnosed AF, with or without prior intracranial | With ICH 12.917 | With ICH 43% | Median [IQR With ICH Warfarin] | Antiplatelet or no therapy | Clinical (ischaemic stroke) and safety (ICH) | Mean 3.3 ± 3.6 years | 0.5% | 1/1/1996 – 31/12/2011 |
| Reference | Design | Description | Event Rate | Median CI | OAC/NOAC | Antithrombotics | End Points | Timing | Outcome Measures |
|-----------|--------|-------------|------------|-----------|----------|----------------|------------|--------|----------------|
| Pennlert, 2015, Sweden | Observational cohort | First intracerebral haemorrhage, AF or other indication for OAC post ICH | 14,045 | 84% | Median 4 | NOAC or warfarin | Timing and predictors of, and extent to which antithrombotics are used in ICH survivors | Mean, days | 1/7/2015 – 31/12/2011 |
| Nielsen, 2015, Denmark | Observational cohort | Non-valvular AF diagnosed prior to ICH, intracranial haemorrhage requiring hospitalisation | 1,752 | 38% | Median 78.0 [IQR 71.0-83.0] | NOAC or VKA | Combined end point of Ischaemic stroke/systemic embolism and all-cause mortality | Data at 1 year | VKA 65% NOAC 2% Patients diagnosed with AF 1/1/1997 – 31/12/2013 |
| Poli, 2018, Italy | Observational cohort | Valvular AF or atrial flutter, non-traumatic intracerebral haemorrhage, on OAC at time of ICH | 244 | 41.4% | Median 76.3 [9.7] | No therapy | Composite all-cause mortality and ischaemic stroke/systemic embolism | Median, months | 100% Consecutive patient admissions 1/1/2002 – 31/7/2013 |
| Pennlert, 2017, Sweden | Observational cohort | First intracerebral haemorrhage, non-traumatic ICH, concomitant AF | 2,618 | 40.7% | 78.0 [9.1] | VKA or NOAC or antiplatelet | Thrombotic events, haemorrhagic events, thrombotic and haemorrhagic events combined | Median, years | 47.3% 1/7/2005 – 31/12/2011 |
| Lee, 2020, Korea | Retrospective cohort | Non-valvular AF, spontaneous intracranial haemorrhage, not on OAC at time of ICH | 5,712 | 43.1% | 72.4 [10.0] | NOAC | Occurrence of ischaemic stroke, ICH, and composite outcome (ICH + IS) | Median 0.6 year [IQR 0.2-1.7] | 0% January 2010 – April 2018 |
| Tsai, 2020, Taiwan | Nationwide cohort | Newly diagnosed AF, prior intracranial haemorrhage, on or off OAC at time of ICH | 4,540 | 41.6% | 76.0 [10.5] | NOAC | Annual risk of clinical (all-cause mortality, ischaemic stroke) and safety (ICH, major bleeding, adverse events) end points | Not reported | 100% 1/1/2012-31/12/2016 |
| Nielsen, 2019, Denmark | Observational cohort | Primary spontaneous intracerebral haemorrhage, non-valvular AF diagnosed prior to ICH, claimed OAC prescription during data collection period | 622 | 39.1% | 76.1 [9.2] | NOAC | Effectiveness (ischaemic stroke) and safety (intracerebral haemorrhage) outcome | 1 and 3 years | 45.2% January 2003 – April 2017 |

AF: atrial fibrillation; CHA2DS2-VASc: congestive heart failure, hypertension, age >75, diabetes mellitus, prior stroke, vascular disease, age 65-74, sex; ICH: intracerebral haemorrhage; IQR: inter-quartile range; NOAC: non- vitamin K antagonist oral anticoagulant; OAC: oral anticoagulation; SD: standard deviation; VKA: vitamin-K antagonist.
Supplementary Table S4: Results of sub-group and sensitivity analyses

| Intervention                  | Comparator                  | Outcome                              | Sub-group/sensitivity analyses | Included studies                                                                 | Participants (n) | Result                                                                 |
|-------------------------------|-----------------------------|--------------------------------------|---------------------------------|----------------------------------------------------------------------------------|------------------|----------------------------------------------------------------------|
| Oral anticoagulation          | No therapy                 | Thromboembolic events                | 1 year follow-up                | Kuramatsu (2015)\(^{22}\); Perreault (2019)\(^{13}\)                             | 633              | RR 0.34, 95% CI 0.13-0.87, p=0.03, \(I^2=0\)%                      |
| Oral anticoagulation          | No therapy                 | Thromboembolic events                | >1 year follow-up               | Park (2016)\(^{12}\); Sadighi (2020)\(^{20}\)                                  | 521              | RR 0.59, 95% CI 0.20-1.72, p=0.33, \(I^2=66\)%                    |
| Oral anticoagulation          | No therapy                 | Thromboembolic events                | Ischaemic stroke/systemic embolism only | Perreault (2019)\(^{13}\); Sadighi (2020)\(^{20}\)                            | 465              | RR 0.75, 95% CI 0.25-2.21, p=0.61, \(I^2=24\)%                   |
| Oral anticoagulation          | Antiplatelets/ no therapy  | Ischaemic stroke                     | Data from randomised controlled trials only | SoSTART, 2021\(^{8}\); APACHE-AF, 2021\(^{7}\)                             | 304              | RR 0.41, 95% CI 0.06-2.64, p=0.35, \(I^2=82\)%                   |
| Oral anticoagulation          | No therapy                 | Recurrent ICrH                       | 1 year follow-up                | Kuramatsu (2015)\(^{22}\); Perreault (2019)\(^{13}\)                             | 633              | RR 0.59, 95% CI 0.19-1.87, p=0.37, \(I^2=38\)%                   |
| Oral anticoagulation          | No therapy                 | Recurrent ICrH                       | >1 year follow-up               | Park (2016)\(^{12}\); Sadighi (2020)\(^{20}\)                                  | 521              | RR 4.97, 95% CI 0.56-44.17, p = 0.15, \(I^2 = 53\)%             |
| Oral anticoagulation          | Antiplatelets/ no therapy  | Recurrent ICrH                       | Data from randomised controlled trials only | SoSTART (2021)\(^{8}\); APACHE-AF (2021)\(^{7}\)                           | 304              | RR 2.37, 95% CI 0.85-6.62, p=0.10, \(I^2=0\)%                   |

APACHE-AF: Apixaban After Anticoagulation-associated Intracerebral Haemorrhage in Patients with Atrial Fibrillation; CI: confidence interval; ICrH: intracranial haemorrhage; RR: risk ratio; SoSTART: Start or STop Anticoagulants Randomised Trial
Supplementary Figure S1: Risk of bias assessment for the included observational studies by category (A) and by study (B)

Supplementary Figure S2: Risk of bias assessment for the included randomised controlled trial
**Supplementary Figure S1**: Risk of bias assessment for the included observational studies

A. Risk of bias assessment* by category

*BUsing Risk of Bias Assessment Tool for Non-randomized Studies (RoBANS)*

B. Risk of bias assessment* by study

*Using Cochrane Collaboration’s tool for assessing risk of bias*
Supplementary Figure S2: Risk of bias assessment for included randomised controlled trials

Al-Shahi Salman 2021

Schreuder 2021
# MOOSE Checklist for Meta-analyses of Observational Studies

| Item No | Recommendation                                                                 | Reported on Page No |
|---------|---------------------------------------------------------------------------------|---------------------|
| **Reporting of background should include** |                                                                                |                     |
| 1       | Problem definition                                                              | 4                   |
| 2       | Hypothesis statement                                                            | N/A                 |
| 3       | Description of study outcome(s)                                                 | 6                   |
| 4       | Type of exposure or intervention used                                           | 6                   |
| 5       | Type of study designs used                                                      | 8-9                 |
| 6       | Study population                                                                | 5, 8-9              |
| **Reporting of search strategy should include** |                                                                                |                     |
| 7       | Qualifications of searchers (eg, librarians and investigators)                  | 6                   |
| 8       | Search strategy, including time period included in the synthesis and key words  | 6-7                 |
| 9       | Effort to include all available studies, including contact with authors         | 7                   |
| 10      | Databases and registries searched                                               | 6                   |
| 11      | Search software used, name and version, including special features used (eg, explosion) | N/A                 |
| 12      | Use of hand searching (eg, reference lists of obtained articles)                | 8                   |
| 13      | List of citations located and those excluded, including justification           | Figure 1            |
| 14      | Method of addressing articles published in languages other than English         | N/A                 |
| 15      | Method of handling abstracts and unpublished studies                            | 6-7                 |
| 16      | Description of any contact with authors                                         | 7                   |
| **Reporting of methods should include** |                                                                                |                     |
| 17      | Description of relevance or appropriateness of studies assembled for assessing the hypothesis to be tested | Figure 1            |
| 18      | Rationale for the selection and coding of data (eg, sound clinical principles or convenience) | 6, 8                 |
| 19      | Documentation of how data were classified and coded (eg, multiple raters, blinding and interrater reliability) | 6-7                 |
| 20      | Assessment of confounding (eg, comparability of cases and controls in studies where appropriate) | 7                   |
| 21      | Assessment of study quality, including blinding of quality assessors, stratification or regression on possible predictors of study results | 7, 14               |
| 22      | Assessment of heterogeneity                                                     | 7                   |
| 23      | Description of statistical methods (eg, complete description of fixed or random effects models, justification of whether the chosen models account for predictors of study results, dose-response models, or cumulative meta-analysis) in sufficient detail to be replicated | 7                   |
| 24      | Provision of appropriate tables and graphics                                     | Tables 1, Figs 1-4  |
| **Reporting of results should include** |                                                                                |                     |
| 25      | Graphic summarizing individual study estimates and overall estimate             | Figs 2-4            |
| 26 | Table giving descriptive information for each study included | Supp. Table S2 |
| 27 | Results of sensitivity testing (eg, subgroup analysis) | 13, Supp. Table S4 |
| 28 | Indication of statistical uncertainty of findings | 9-13, Figs 2-4 |
# PRISMAL 2020 Checklist

| Section and Topic | Item # | Checklist item | Location where item is reported |
|-------------------|--------|----------------|-------------------------------|
| **TITLE**         | 1      | Identify the report as a systematic review. | Title page |
| **ABSTRACT**      | 2      | See the PRISMA 2020 for Abstracts checklist. | 2-3 |
| **INTRODUCTION**  | 3      | Describe the rationale for the review in the context of existing knowledge. | 5 |
|                   | 4      | Provide an explicit statement of the objective(s) or question(s) the review addresses. | 5 |
| **METHODS**       | 5      | Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses. | 5-6, 7 |
| Eligibility criteria | 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. | 6 |
| Information sources | 7 | Present the full search strategies for all databases, registers and websites, including any filters and limits used. | Supp. Table S2 |
| Search strategy | 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. | 6 |
| Selection 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. | 6-7 |
| Data collection process | 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. | 7, Table 1 |
|                   | 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. | 7, Supp. Table S3 |
| Data items | 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. | 7, 14 |
| Study risk of bias assessment | 12 | Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results. | 7 |
| Effect measures | 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)). | Fig 1 |
| Synthesis methods | 13b | Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions. | 7 |
|                   | 13c | Describe any methods used to tabulate or visually display results of individual studies and syntheses. | Table 1; |
| Section and Topic | Item # | Checklist item                                                                                                                                                                                                 | Location where item is reported |
|-------------------|--------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------|
|                   | 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. | Figs 2-4                        |
|                   | 13e    | Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).                                                                        | 7, 13, Supp. Table S4           |
|                   | 13f    | Describe any sensitivity analyses conducted to assess robustness of the synthesized results.                                                                                                                  | 13, Supp. Table S4              |
| Reporting bias assessment | 14    | Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).                                                                                   | 7, 13                           |
| Certainty assessment | 15    | Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.                                                                                                    | 7                               |
| 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. | 8, Fig 1                        |
|                   |        | 16b | Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.                                                                               | 8, Fig 1                        |
| Study characteristics | 17    | Cite each included study and present its characteristics.                                                                                                                                                 | 8-9, Suppl. Table S3            |
| Risk of bias in studies | 18    | Present assessments of risk of bias for each included study.                                                                                                                                              | 13, Supp. 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. | Figs 2-4                        |
| Results of syntheses | 20a   | For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.                                                                                                  | 9-13                            |
|                   | 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. | 9-13, Figs 2-4                 |
|                   | 20c    | Present results of all investigations of possible causes of heterogeneity among study results.                                                                                                            | 9-13, Figs 2-4                 |
|                   | 20d    | Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.                                                                                            | 13, Supp. Table S4              |
| Reporting biases | 21    | Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.                                                                                | -                               |
| Certainty of evidence | 22    | Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.                                                                                                    | 9-13                            |
| DISCUSSION        |        |                                                                                                                                                    |                                  |
| Section and Topic       | Item # | Checklist item                                                                 | Location where item is reported |
|-------------------------|--------|-------------------------------------------------------------------------------|--------------------------------|
| Discussion              | 23a    | Provide a general interpretation of the results in the context of other evidence. | 14-16                          |
|                         | 23b    | Discuss any limitations of the evidence included in the review.              | 16-17                          |
|                         | 23c    | Discuss any limitations of the review processes used.                        | 16-17                          |
|                         | 23d    | Discuss implications of the results for practice, policy, and future research. | 17                             |

**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. | 5                              |
|---------------------------|-----|-------------------------------------------------------------------------------------------------------------------------------|--------------------------------|
|                           | 24b | Indicate where the review protocol can be accessed, or state that a protocol was not prepared.                                  | 5                              |
|                           | 24c | Describe and explain any amendments to information provided at registration or in the protocol.                                 | N/A                            |
| Support                   | 25  | Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review. | 18                             |
| Competing interests       | 26  | Declare any competing interests of review authors.                                                                              | 18                             |
| 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. | 5                              |