### Supplemental Table S1. Components of the cumulative deficit frailty index.

| Deficit            | Score                                                                 |
|--------------------|-----------------------------------------------------------------------|
| BMI                | 18.5 – 30kg/m² = 0; Otherwise = 1                                     |
| Sitting            | Calculated ratio of sitting minutes to the total of physically active minutes (estimated by self-report using the International Physical Activity Questionnaire) and sitting minutes (estimated by self-report of the number of minutes spend sitting in the previous seven days) |
|                    | The highest quarter of the ratio = 1                                  |
|                    | The lowest three quarters of the ratio = 0                           |
| Current Smoking    | No = 0; Yes = 1                                                      |
| Diabetes           | No = 0; Yes = 1                                                      |
| Renal function     | 0 for eGFR >60ml/min; 1 for eGFR 15-60ml/min; 2 for eGFR <15ml/min   |
| Hypertension       | No = 0; Yes = 1                                                      |
| Condition                                | Code |
|------------------------------------------|------|
| Aortic aneurysm                          | No = 0; Yes = 1 |
| Heart failure                            | No = 0; Yes = 1 |
| Limb or foot amputation                  | No = 0; Yes = 1 |
| Transient ischemic attack or stroke      | No = 0; Yes = 1 |
| Cancer                                   | No = 0; Yes = 1 |
| Liver disease                            | No = 0; Yes = 1 |
| Peptic ulcer disease                     | No = 0; Yes = 1 |
| Inflammatory bowel disease               | No = 0; Yes = 1 |
| Gastrointestinal surgery                 | No = 0; Yes = 1 |
| Diverticulitis                           | No = 0; Yes = 1 |
| **EQ5D questionnaire**                   |      |
| Mobility                                 | No problems = 0; some problems = 0.5; confined to bed = 1 |
| Self-care                                | No problems = 0; some problems = 0.5; unable to wash or dress = 1 |
| Usual activities                         | No problems = 0; some problems = 0.5; unable to perform usual activities = 1 |
| Pain or discomfort                       | None = 0; moderate = 0.5; extreme = 1 |
| Anxiety or depression | None = 0; moderate = 0.5; extreme = 1 |
|-----------------------|-------------------------------------|
| **SAGE questionnaire**|                                     |
| Maintaining attention | No problems = 0; mild difficulty = 0.33; moderate difficulty = 0.67; severe difficulty = 1 |
| Memory                | No problems = 0; mild difficulty = 0.33; moderate difficulty = 0.67; severe difficulty = 1 |
| Switching between activities | No problems = 0; mild difficulty = 0.33; moderate difficulty = 0.67; severe difficulty = 1 |
| Concentration         | No problems = 0; mild difficulty = 0.33; moderate difficulty = 0.67; severe difficulty = 1 |
| Orientation in a new building | No problems = 0; mild difficulty = 0.33; moderate difficulty = 0.67; severe difficulty = 1 |
| Organizing a trip or social activities | No problems = 0; mild difficulty = 0.33; moderate difficulty = 0.67; severe difficulty = 1 |
| Finances or shopping  | No problems = 0; mild difficulty = 0.33; moderate difficulty = 0.67; severe difficulty = 1 |
| Meal or laundry       | No problems = 0; mild difficulty = 0.33; moderate difficulty = 0.67; severe difficulty = 1 |
| Organizing or taking medications | No problems = 0; mild difficulty = 0.33; moderate difficulty = 0.67; severe difficulty = 1 |
| Driving               | No problems = 0; mild difficulty = 0.33; moderate difficulty = 0.67; severe difficulty = 1 |
| **Using public transport** | No problems = 0; mild difficulty = 0.33; moderate difficulty = 0.67; severe difficulty = 1 |
| Using stairs          | No problems = 0; mild difficulty = 0.33; moderate difficulty = 0.67; severe difficulty = 1 |
| Walking 10m           | No problems = 0; mild difficulty = 0.33; moderate difficulty = 0.67; severe difficulty = 1 |
| Dressing | No problems = 0; mild difficulty = 0.33; moderate difficulty = 0.67; severe difficulty = 1 |
|----------|-------------------------------------------------------------------------------------|
| Transferring from bed to chair | No problems = 0; mild difficulty = 0.33; moderate difficulty = 0.67; severe difficulty = 1 |
| Bathing or toileting | No problems = 0; mild difficulty = 0.33; moderate difficulty = 0.67; severe difficulty = 1 |

Have any of the following limited your abilities to perform activities of daily living?

- Memory problems; physical injury; loss of vision; arthritis; stroke/transient ischemic attack; unsteadiness; shortness of breath; chronic pain; chest pain; heart failure—any one of these was awarded 1 point.

The score for this item = sum of the points divided by 10

| Total | 37 |

Supplemental Table S2. The effects of rivaroxaban 2.5mg twice daily in addition to aspirin 100mg once daily stratified by the presence of non-cardiovascular frailty (non-CV frailty index >0.2) versus absence of non-cardiovascular frailty (non-CV frailty index ≤0.2) of frailty. CI = confidence interval; CV = cardiovascular; HR = hazard ratio; MI = myocardial infarction.

| Outcome | Non-frail | Frail | Interaction p-value |
|---------|-----------|-------|---------------------|


|                          | Aspirin alone N=6837 | Rivaroxaban and aspirin N=6868 | HR (95% CI) for rivaroxaban and aspirin | Aspirin alone N=2289 | Rivaroxaban and aspirin N=2284 | HR (95% CI) for rivaroxaban and aspirin |
|--------------------------|----------------------|----------------------------------|------------------------------------------|----------------------|----------------------------------|------------------------------------------|
| **Primary efficacy**     | 333 (4.9)            | 228 (3.3)                        | 0.68 (0.57-0.80)                         | 163 (7.1)            | 151 (6.6)                        | 0.90 (0.72-1.13)                         | 0.045                                  |
| **Mortality**            | 235 (3.4)            | 178 (2.6)                        | 0.76 (0.62-0.92)                         | 143 (6.2)            | 135 (5.9)                        | 0.93 (0.73-1.17)                         | 0.21                                   |
| **CV death**             | 124 (1.8)            | 82 (1.2)                         | 0.66 (0.50-0.87)                         | 79 (3.5)             | 78 (3.4)                         | 0.97 (0.71-1.33)                         | 0.073                                  |
| **Non-CV death**         | 111 (1.6)            | 96 (1.4)                         | 0.87 (0.66-1.14)                         | 64 (2.8)             | 57 (2.5)                         | 0.87 (0.61-1.24)                         | 1.00                                   |
| **MI**                   | 153 (2.2)            | 117 (1.7)                        | 0.76 (0.60-0.97)                         | 52 (2.3)             | 61 (2.7)                         | 1.15 (0.79-1.66)                         | 0.066                                  |
| **Stroke**               | 94 (1.4)             | 49 (0.7)                         | 0.52 (0.37-0.73)                         | 48 (2.1)             | 34 (1.5)                         | 0.69 (0.45-1.07)                         | 0.32                                   |
| **Major bleeding**       | 113 (1.7)            | 209 (3.0)                        | 1.86 (1.48-2.34)                         | 57 (2.5)             | 79 (3.5)                         | 1.37 (0.97-1.92)                         | 0.14                                   |
| **Intracranial bleeding**| 19 (0.3)             | 16 (0.2)                         | 0.84 (0.43-1.63)                         | 5 (0.2)              | 12 (0.5)                         | 2.37 (0.83-6.72)                         | 0.10                                   |
Supplemental Figure S1. Study Flow Diagram

Participants may have had more than one reason for exclusion after run-in. Major bleeding occurred in 25 participants who entered the run in and in 3 participants this was identified as the reason for exclusion.

Vital status was ascertained at the end of follow-up in 99.8% of randomized participants.
Supplemental Figure S2. Histogram of frailty scores.

Supplemental Figure S3. Forest plot illustrating the relationship between the non-cardiovascular frailty index (i.e. that did not include any recognized cardiovascular risk factors) by quartile and the outcomes of 1) the composite of cardiovascular death, myocardial infarction and stroke (Primary efficacy); 2) mortality; and 3) cardiovascular (CV) death. Models adjusted for age, sex, race and treatment allocation group. CI = confidence interval; HR = hazard ratio.
Supplemental Figure S4. Forest plot illustrating the relationship between the non-cardiovascular frailty index (i.e. that did not include any recognized cardiovascular risk factors) by quartile and the outcomes of 1) myocardial infarction (MI); 2) stroke; 3) major bleeding; and 4) intracranial (IC) bleeding. Models adjusted for age, sex, race and treatment allocation group.
## CONSORT 2010 checklist of information to include when reporting a randomised trial*

| Section/Topic | Item No | Checklist item | Reported on page No |
|---------------|---------|----------------|---------------------|
| **Title and abstract** | | | |
| | 1a | Identification as a randomised trial in the title | 1 |
| | 1b | Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts) | 3 |
| **Introduction** | | | |
| Background and objectives | 2a | Scientific background and explanation of rationale | 5 |
| | 2b | Specific objectives or hypotheses | 5 |
| **Methods** | | | |
| Trial design | 3a | Description of trial design (such as parallel, factorial) including allocation ratio | 6 |
| | 3b | Important changes to methods after trial commencement (such as eligibility criteria), with reasons | Not applicable |
| Participants | 4a | Eligibility criteria for participants | 6 |
| | 4b | Settings and locations where the data were collected | 6 |
| Interventions | 5 | The interventions for each group with sufficient details to allow replication, including how and when they were actually administered | 6 |
| Outcomes | 6a | Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed | 7 |
| | 6b | Any changes to trial outcomes after the trial commenced, with reasons | Not applicable |
| Sample size | 7a | How sample size was determined | Not applicable |
| | 7b | When applicable, explanation of any interim analyses and stopping guidelines | Not applicable |
| Randomisation: Sequence generation | 8a | Method used to generate the random allocation sequence | 6 |
| | 8b | Type of randomisation; details of any restriction (such as blocking and block size) | 6 |
| Allocation concealment mechanism | 9 | Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned | 6 |
| Implementation | 10 | Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions | 6 |
| Blinding | 11a | If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how | 6 |
| | 11b | If relevant, description of the similarity of interventions | Not applicable |
| Statistical methods | 12a | Statistical methods used to compare groups for primary and secondary outcomes | 7 |
| | 12b | Methods for additional analyses, such as subgroup analyses and adjusted analyses | 7 |
### Results

| Item | Description |
|------|-------------|
| 13a  | For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome |
| 13b  | For each group, losses and exclusions after randomisation, together with reasons |
| 14a  | Dates defining the periods of recruitment and follow-up |
| 14b  | Why the trial ended or was stopped |
| 15   | A table showing baseline demographic and clinical characteristics for each group |
| 16   | For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups |
| 17a  | For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval) |
| 17b  | For binary outcomes, presentation of both absolute and relative effect sizes is recommended |
| 18   | Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory |
| 19   | All important harms or unintended effects in each group (for specific guidance see CONSORT for harms) |

### Discussion

| Item | Description |
|------|-------------|
| 20   | Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses |
| 21   | Generalisability (external validity, applicability) of the trial findings |
| 22   | Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence |

### Other information

| Item | Description |
|------|-------------|
| 23   | Registration number and name of trial registry |
| 24   | Where the full trial protocol can be accessed, if available |
| 25   | Sources of funding and other support (such as supply of drugs), role of funders |

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Citation: Schulz KF, Altman DG, Moher D, for the CONSORT Group. CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials. BMC Medicine. 2010;8:18. © 2010 Schulz et al. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/2.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up-to-date references relevant to this checklist, see www.consort-statement.org.*