

Supplementary I: Literature search

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('cerebrovascular accident'/mj/exp OR (stroke* OR ((cerebrovascular OR 'brain vascular' OR 'cerebral vascular' OR ischemic* OR ischaemic* OR lacunar) NEAR/3 (accident* OR lesion* OR injur* OR attack* OR infarct*)) OR apoplex* OR CVA):ab,ti) **AND** ('biological marker'/de OR 'cell marker'/exp OR 'molecular marker'/de OR 'biological factor'/exp OR 'blood clotting factor'/exp OR 'fibrinogen gamma'/de OR 'fibrinogen gamma chain'/de OR 'phospholipid antibody'/de OR 'cardiolipin antibody'/de OR 'antithrombin III'/de OR 'thrombin antithrombin complex'/de OR 'fibrinopeptide A'/de OR 'thrombomodulin'/de OR 'tissue plasminogen activator'/de OR 'plasminogen activator inhibitor'/exp OR 'C reactive protein'/de OR 'fibrinolytic factor'/exp OR 'prothrombin fragment 1'/de OR 'prothrombin fragment 2'/de OR 'prothrombin fragment'/de OR 'prothrombin fragment 1.2'/de OR 'membrane microparticle'/exp OR 'extracellular trap'/de OR 'metalloproteinase'/exp OR 'circulating endothelial cell'/de OR 'histidine rich glycoprotein'/de OR (biomarker* OR ((bio OR biological OR cell* OR molecular* OR blood OR serum OR plasma OR hemosta* OR haemosta* OR coagulat*) NEAR/3 (marker* OR indicator* OR factor*)) OR ((clotting OR Willebrand OR fibrinolytic OR tissue) NEXT/1 (factor*)) OR fibrin* OR 'protein C' OR 'protein S' OR 'C reactive protein' OR CRP OR 'D-dimer' OR 'D-dimers' OR ((membrane OR endothelial OR leukocyte OR platelet OR 'cell derived' OR circulating OR procoagulant) NEXT/1 (microparticle*)) OR ((extracellular) NEXT/1 (trap*)) OR metalloproteinase* OR 'ADAMTS 13' OR ADAMTS13 OR ((neutrophil* OR antiphospholipid* OR phospholipid* OR anticardiolipin* OR cardiolipin*) NEAR/3 (antibod*)) OR uPA OR uPAR OR PAP OR 'scu-PA' OR 'tc-tPA' OR antithrombin* OR thrombomodulin* OR thromboplastin* OR ((plasminogen) NEXT/1 (activator*)) OR 'factor 1' OR 'factor 5' OR 'factor V' OR 'factor 7' OR 'factor VII' OR 'factor 8' OR 'factor VIII' OR 'factor 9' OR 'factor IX' OR 'factor 10' OR 'factor X' OR 'factor 11' OR 'factor XI' OR 'factor 12' OR 'factor XII' OR 'factor 13' OR 'factor XIII' OR ((alpha2 OR 'alpha 2') NEAR/3 (antiplasmin* OR plasmin*)) OR prothrombin* OR microRNA* OR 'micro RNA' OR miRNA* OR thromboglobulin* OR PolyP OR ((circulating) NEXT/1 (endothel*)) OR TAFI OR ((histidine) NEXT/1 (rich) NEXT/1 (glycoprotein* OR protein*)) OR HRGP):ab,ti) **AND** ('activity of daily living assessment'/exp OR 'Barthel index'/de OR 'severity of illness index'/de OR 'performance'/de OR 'performance status'/de OR 'eq 5d questionnaire'/de OR 'motor dysfunction assessment'/exp OR (Rankin OR (mRS AND (scale* OR score*))) OR Barthel OR ((ADL OR 'daily living' OR motor) NEAR/3 (assess* OR scale* OR score* OR measur*)) OR performance* OR ((severity) NEAR/3 (index)) OR 'eq 5d' OR NIHSS OR 'NIH Stroke Scale'):ab,ti) **AND** ('prediction'/de OR 'predictive value'/de OR 'prognosis'/de OR 'predictors'/de OR (predict* OR prognos*):ab,ti) **NOT** ([animals]/lim NOT [humans]/lim) **NOT** ('Conference abstract' OR 'editorial')/it

Medline Epub:

(exp "Stroke"/ OR (stroke* OR ((cerebrovascular OR "brain vascular" OR "cerebral vascular" OR ischemic* OR ischaemic* OR lacunar) ADJ3 (accident* OR lesion* OR injur* OR attack* OR infarct*)) OR apoplex* OR CVA).ab,ti.) **AND** (exp "Biological Factors"/ OR exp "Blood Coagulation Factors"/ OR exp "Blood Coagulation Factor Inhibitors"/ OR exp "Fibrinogen"/ OR exp "Antibodies, Antiphospholipid"/ OR "Antibodies, Anticardiolipin"/ OR "Thrombomodulin"/ OR "C-Reactive Protein"/ OR "Cell-Derived Microparticles"/ OR "Extracellular Traps"/ OR exp "Matrix Metalloproteinases"/ OR exp "Matrix Metalloproteinase Inhibitors"/ OR "Histidine-rich proteins".mp. OR (biomarker* OR ((bio OR biological OR cell* OR molecular* OR blood OR serum OR plasma OR hemosta* OR haemosta* OR coagulat*) ADJ3 (marker* OR indicator* OR factor*)) OR ((clotting OR Willebrand OR fibrinolytic OR tissue) ADJ1 (factor*)) OR fibrin* OR "protein C" OR "protein S" OR "C reactive protein" OR CRP OR "D-dimer" OR "D-dimers" OR ((membrane OR endothelial OR leukocyte OR platelet OR "cell derived" OR circulating OR procoagulant) ADJ1 (microparticle*)) OR ((extracellular) ADJ1 (trap*)) OR metalloproteinase* OR "ADAMTS 13" OR ADAMTS13 OR ((neutrophil* OR antiphospholipid* OR phospholipid* OR anticardiolipin* OR cardiolipin*) ADJ3 (antibod*)) OR

uPA OR uPAR OR PAP OR "scu-PA" OR "tc-tPA" OR antithrombin* OR thrombomodulin* OR thromboplastin* OR ((plasminogen) ADJ1 (activator*)) OR "factor 5" OR "factor V" OR "factor 7" OR "factor VII" OR "factor 8" OR "factor VIII" OR "factor 9" OR "factor IX" OR "factor 10" OR "factor X" OR "factor 11" OR "factor XI" OR "factor 12" OR "factor XII" OR "factor 13" OR "factor XIII" OR ((alpha2 OR "alpha 2") ADJ3 (antiplasmin* OR plasmin*)) OR prothrombin* OR microRNA* OR "micro RNA" OR miRNA* OR thromboglobulin* OR PolyP OR ((circulating) ADJ1 (endothel*)) OR TAFI OR HRGP).ab,ti.) **AND** (exp "Severity of Illness Index"/ OR (Rankin OR (mRS AND (scale* OR score*)) OR Barthel OR ((ADL OR "daily living" OR motor) ADJ3 (assess* OR scale* OR score* OR measur*)) OR performance* OR ((severity) ADJ3 (index)) OR "eq 5d").ab,ti.) **AND** ("Predictive Value of Tests"/ OR exp "Prognosis"/ OR (predict* OR prognos*).ab,ti.) **NOT** (exp animals/ NOT humans/) **NOT** ("congresses" OR "editorial").pt.

Cochrane Central (trials):

((stroke* OR ((cerebrovascular OR 'brain vascular' OR 'cerebral vascular' OR ischemic* OR ischaemic* OR lacunar) NEAR/3 (accident* OR lesion* OR injur* OR attack* OR infarct*)) OR apoplex* OR CVA):ab,ti) **AND** ((biomarker* OR ((bio OR biological OR cell* OR molecular* OR blood OR serum OR plasma OR hemosta* OR haemosta* OR coagulat*) NEAR/3 (marker* OR indicator* OR factor*)) OR ((clotting OR Willebrand OR fibrinolytic OR tissue) NEXT/1 (factor*)) OR fibrin* OR 'protein C' OR 'protein S' OR 'C reactive protein' OR CRP OR 'D-dimer' OR 'D-dimers' OR ((membrane OR endothelial OR leukocyte OR platelet OR 'cell derived' OR circulating OR procoagulant) NEXT/1 (microparticle*)) OR ((extracellular) NEXT/1 (trap*)) OR metalloproteinase* OR 'ADAMTS 13' OR ADAMTS13 OR ((neutrophil* OR antiphospholipid* OR phospholipid* OR anticardiolipin* OR cardiolipin*) NEAR/3 (antibod*)) OR uPA OR uPAR OR PAP OR 'scu-PA' OR 'tc-tPA' OR antithrombin* OR thrombomodulin* OR thromboplastin* OR ((plasminogen) NEXT/1 (activator*)) OR 'factor 1' OR 'factor 5' OR 'factor V' OR 'factor 7' OR 'factor VII' OR 'factor 8' OR 'factor VIII' OR 'factor 9' OR 'factor IX' OR 'factor 10' OR 'factor X' OR 'factor 11' OR 'factor XI' OR 'factor 12' OR 'factor XII' OR 'factor 13' OR 'factor XIII' OR ((alpha2 OR 'alpha 2') NEAR/3 (antiplasmin* OR plasmin*)) OR prothrombin* OR microRNA* OR 'micro RNA' OR miRNA* OR thromboglobulin* OR PolyP OR ((circulating) NEXT/1 (endothel*)) OR TAFI OR ((histidine) NEXT/1 (rich) NEXT/1 (glycoprotein* OR protein*)) OR HRGP):ab,ti) **AND** ((Rankin OR (mRS AND (scale* OR score*)) OR Barthel OR ((ADL OR 'daily living' OR motor) NEAR/3 (assess* OR scale* OR score* OR measur*)) OR performance* OR ((severity) NEAR/3 (index)) OR 'eq 5d' OR NIHSS OR 'NIH Stroke Scale'):ab,ti) **AND** ((predict* OR prognos*):ab,ti)

Web of Science:

TS=((stroke* OR ((cerebrovascular OR "brain vascular" OR "cerebral vascular" OR ischemic* OR ischaemic* OR lacunar) NEAR/2 (accident* OR lesion* OR injur* OR attack* OR infarct*)) OR apoplex* OR CVA) **AND** ((biomarker* OR ((bio OR biological OR cell* OR molecular* OR blood OR serum OR plasma OR hemosta* OR haemosta* OR coagulat*) NEAR/2 (marker* OR indicator* OR factor*)) OR ((clotting OR Willebrand OR fibrinolytic OR tissue) NEAR/1 (factor*)) OR fibrin* OR "protein C" OR "protein S" OR "C reactive protein" OR CRP OR "D-dimer" OR "D-dimers" OR ((membrane OR endothelial OR leukocyte OR platelet OR "cell derived" OR circulating OR procoagulant) NEAR/1 (microparticle*)) OR ((extracellular) NEAR/1 (trap*)) OR metalloproteinase* OR "ADAMTS 13" OR ADAMTS13 OR ((neutrophil* OR antiphospholipid* OR phospholipid* OR anticardiolipin* OR cardiolipin*) NEAR/2 (antibod*)) OR uPA OR uPAR OR PAP OR "scu-PA" OR "tc-tPA" OR antithrombin* OR thrombomodulin* OR thromboplastin* OR ((plasminogen) NEAR/1 (activator*)) OR "factor 1" OR "factor 5" OR "factor V" OR "factor 7" OR "factor VII" OR "factor 8" OR "factor VIII" OR "factor 9" OR "factor IX" OR "factor 10" OR "factor X" OR "factor 11" OR "factor XI" OR "factor 12" OR "factor XII" OR "factor 13" OR "factor XIII" OR ((alpha2 OR "alpha 2") NEAR/2 (antiplasmin* OR plasmin*)) OR prothrombin* OR microRNA* OR "micro RNA" OR miRNA* OR thromboglobulin* OR PolyP OR ((circulating) NEAR/1 (endothel*)) OR TAFI OR

((histidine) NEAR/1 (rich) NEAR/1 (glycoprotein* OR protein*)) OR HRGP)) **AND** ((Rankin OR (mRS AND (scale* OR score*)) OR Barthel OR ((ADL OR "daily living" OR motor) NEAR/2 (assess* OR scale* OR score* OR measur*)) OR performance* OR ((severity) NEAR/2 (index)) OR "eq 5d" OR NIHSS OR "NIH StrokeScale")) **AND** ((predict* OR prognos*)) **NOT** ((animal* OR mouse OR mice OR rat OR rats) NOT (human* OR patient*)) **AND DT=Article**

Google Scholar:

stroke|"cerebrovascular accident"|CVA biomarker|biomarkers|"biological|bio|molecular marker"|"protein C"|"D-dimers" Rankin|mRS score|Barthel|ADL|"daily living"|"severity index|NIHSS prediction|predictive|prognosis

Supplementary II: Checklist for quality assessment⁶

1. Diagnosis of stroke is based on expert clinical opinion supported by neuroimaging.
2. All patients (including controls, in case) have expert opinion + neuroimaging.
3. The biomarker is not used to determine the end-point.
4. Specify that biomarker measurement is blinded to clinical data.
5. Specify that clinical data collection is blinded or collected before biomarker measurement.
6. All patients who entered into study complete it or withdrawals are explained.
7. Biomarker cut-off is previously established, based on literature or pilot study.
8. Specify any or none disclosure.
9. Report if the study is prospective.
10. Definition of time period, follow-up end and median follow-up time of the study (at least two items).
11. Clinical end-points to be measured are defined prior to analysis.
12. Rationale for used sample size.
13. Reporting a list of candidate variables and estimated effect (Odd Ratio/Hazard Ratio) with 95% CI for all variables in multivariate analysis.
14. Specify the assay method and provide or reference a detailed protocol.
15. Cases are not representing a selected subgroup of patients (e.g. only atrial fibrillation patients).