

Appendix 1: Search Terms

Medication Adherence

Adherence OR Compliance OR Concordance OR Persistence OR nonadherence OR non-adherence OR non-compliance OR noncompliance OR dosage adherence OR dosage compliance OR dose adherence OR dose compliance OR dosing adherence OR dosing compliance OR drug adherence OR drug compliance OR drug intake compliance OR drug regimen adherence OR drug regimen compliance OR medication adherence OR medication compliance OR medication intake adherence OR medication non adherence OR medication non compliance OR medication nonadherence OR medication non-adherence OR medication noncompliance OR medication non-compliance OR medication persistence OR nonadherence patient OR noncompliance patient OR patient adherence OR patient adherence OR patient compliance OR patient cooperation OR patient non adherence OR patient non compliance OR patient nonadherence OR patient non-adherence OR patient noncompliance OR patient non-compliance OR therapy adherence OR therapy compliance OR treatment adherence OR treatment compliance

Stroke

ACA Infarction OR acute cerebrovascular accident OR acute cerebrovascular lesion OR acute focal cerebral vasculopathy OR acute ischemic stroke OR acute stroke OR Anoxic Brain Damage OR Anoxic Encephalopathy OR Anoxic-Ischemic Encephalopathy OR Anterior Cerebral Artery Infarction OR Anterior Cerebral Artery Stroke OR Anterior Cerebral Artery Syndrome OR anterior cerebral circulation infarction OR anterior choroidal artery infarction OR anterior circulation brain infarction OR Anterior Circulation Transient Ischemic Attack OR apoplectic stroke OR apoplexia OR apoplexy OR Basal Ganglionic Hemorrhage OR Basilar Artery Insufficiency OR Basilar Artery Ischemia OR Basilar Artery Stenosis OR Basilar Insufficiency OR Benedict Syndrome OR brain accident OR Brain Anoxia OR Brain Anoxia-Ischemia OR brain arterial insufficiency OR brain attack OR brain blood flow disturbance OR brain circulation disorder OR Brain Hemorrhage OR Brain Hypoxia OR Brain Hypoxia-Ischemia OR brain infarct OR brain infarction OR brain insult OR brain ischaemia OR brain ischemic attack OR brain stem infarction OR Brain Stem Transient Ischemic Attack OR Brain TIA OR brain transient ischemic attack OR brain vascular accident OR brain venous infarction OR brainstem infarction OR Brainstem Stroke OR Brainstem Transient Ischemic Attack OR Carotid Circulation Transient Ischemic Attack OR cerebellar infarction OR cerebellum infarction OR Cerebral Anoxia OR Cerebral Anoxia-Ischemia OR cerebral apoplexia OR cerebral blood circulation disorder OR cerebral blood flow disorder OR Cerebral Brain Hemorrhage OR cerebral circulation disorder OR cerebral circulatory disorder OR Cerebral Hemorrhage OR Cerebral Hypoxia OR Cerebral Hypoxia-Ischemia OR cerebral infarct OR cerebral infarction OR cerebral insult OR cerebral ischaemia OR cerebral ischemia OR

Cerebral Parenchymal Hemorrhage OR cerebral stroke OR cerebral vascular accident OR cerebral vascular insufficiency OR cerebrovascular accident OR cerebrovascular apoplexy OR cerebrovascular arrest OR cerebrovascular circulation disorder OR cerebrovascular failure OR cerebrovascular infarction OR cerebrovascular injury OR cerebrovascular insufficiency OR cerebrovascular insult OR cerebrovascular ischaemia OR cerebrovascular ischemia OR cerebrovascular stroke OR cerebrovascular trauma OR Cerebrum Hemorrhage OR cerebrum vascular accident OR chronic ischemic stroke OR circulatory epilepsy OR Claude Syndrome OR cortical infarction OR Crescendo Transient Ischemic Attacks OR cryptogenic stroke OR CVA OR cvas OR Foville Syndrome OR Hematoma, Basal Ganglia OR hemisphere infarct OR hemisphere infarction OR hemispheric infarct OR hemispheric infarction OR Hemorrhage, Basal Ganglia OR Heubner Artery Infarction OR Heubner's Artery Infarction OR Hypoxic Brain Damage OR Hypoxic Encephalopathy OR Hypoxic-Ischemic Encephalopathy OR Infarction, Anterior Cerebral Artery Circulation OR Infarction Anterior Cerebral Artery Distribution OR infarctions lacunar OR Intracerebral Hemorrhage OR Intracranial Hemorrhage OR ischaemic attack OR ischaemic brain disease OR ischaemic seizure OR ischaemic stroke OR ischemia cerebri OR ischemic attack OR ischemic brain disease OR ischemic cerebral attack OR ischemic encephalopathy OR ischemic seizure OR ischemic stroke OR lacunar infarct OR lacunar infarction OR lacunar stroke OR lacunar syndrome OR left hemisphere infarction cerebral OR Left Middle Cerebral Artery Infarction OR MCA Infarction OR Middle Cerebral Artery Circulation Infarction OR Middle Cerebral Artery Embolic Infarction OR Middle Cerebral Artery Embolus OR Middle Cerebral Artery Infarction OR Middle Cerebral Artery Occlusion OR Middle Cerebral Artery Stroke OR Middle Cerebral Artery Syndrome OR Middle Cerebral Artery Thrombosis OR Middle Cerebral Artery Thrombotic Infarction OR Millard-Gublar Syndrome OR neural ischemia OR PCA Infarction OR Perinatal Subarachnoid Hemorrhage OR Posterior Cerebral Artery Embolic Infarction OR Posterior Cerebral Artery Infarction OR Posterior Cerebral Artery Stroke OR Posterior Cerebral Artery Syndrome OR Posterior Cerebral Artery Thrombotic Infarction OR posterior choroidal artery infarction OR posterior circulation brain infarction OR Posterior Circulation Transient Ischemic Attack OR Posterior Fossa Hemorrhage OR right hemisphere cerebral infarction OR Right Middle Cerebral Artery Infarction OR SAH OR silent brain infarction OR stroke OR subarachnoid hemorrhage OR Subarachnoid Hemorrhage Aneurysmal OR Subarachnoid Hemorrhage Intracranial OR Subarachnoid Hemorrhage Spontaneous OR subcortical infarction OR TIA OR Top of the Basilar Syndrome OR transient brain ischemia OR Transient Brain Stem Ischemia OR Transient Brainstem Ischemia OR Transient Cerebral Ischemia OR Transient Ischemic Attack OR transient ischemic seizure OR Vertebral Artery Insufficiency OR Vertebral Artery Ischemia OR Vertebral Artery Stenosis OR Vertebrobasilar Circulation Transient Ischemic Attack OR Vertebrobasilar Dolichoectasia OR Vertebro-Basilar Insufficiency OR Vertebrobasilar Ischemia OR Vertebro-Basilar Ischemia OR Weber Syndrome.

Appendix 2: PRISMA Checklist

| Section/topic | # | Checklist item | Reported on page # |
|---------------------------|----|---|--------------------|
| TITLE | | | |
| Title | 1 | Identify the report as a systematic review, meta-analysis, or both. | 1 |
| ABSTRACT | | | |
| Structured summary | 2 | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. | 2 & 3 |
| INTRODUCTION | | | |
| Rationale | 3 | Describe the rationale for the review in the context of what is already known. | 4 |
| Objectives | 4 | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). | 4 |
| METHODS | | | |
| Protocol and registration | 5 | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number. | 5 |
| Eligibility criteria | 6 | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. | 5 |
| Information sources | 7 | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched. | 5 |
| Search | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated. | 5 & Appendix |
| Study selection | 9 | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis). | 5 & 6 |
| Data collection process | 10 | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators. | 6 |
| Section/topic | # | Checklist item | Reported on page # |

| Data items | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. | 6 |
|------------------------------------|----|--|--------------------|
| Risk of bias in individual studies | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis. | Appendix |
| Summary measures | 13 | State the principal summary measures (e.g., risk ratio, difference in means). | - |
| Synthesis of results | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis. | 6 |
| Risk of bias across studies | 15 | Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies). | 6 |
| Additional analyses | 16 | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified. | 7 |
| RESULTS | | | |
| Study selection | 17 | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram. | 7 & figure 1 |
| Study characteristics | 18 | For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations. | 8 – 9 & table 1 |
| Risk of bias within studies | 19 | Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12). | 7 & appendix |
| Results of individual studies | 20 | For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot. | 8 – 11 & appendix |
| Synthesis of results | 21 | Present results of each meta-analysis done, including confidence intervals and measures of consistency. | 11 |
| Risk of bias across studies | 22 | Present results of any assessment of risk of bias across studies (see Item 15). | 7 & appendix |
| Additional analysis | 23 | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]). | N/A |
| DISCUSSION | | | |
| Section/topic | # | Checklist item | Reported on page # |
| Summary of evidence | 24 | Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers). | 12 & 13 |

| | | | |
|----------------|----|---|----|
| Limitations | 25 | Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias). | 13 |
| Conclusions | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research. | 14 |
| FUNDING | | | |
| Funding | 27 | Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. | 15 |

Table 1: Significance of Predictive Factors

| Study author, year & direction of effect | Analysis used | Medication classes studied | N | Overall non-adherence (%) | Predictive factor | Significance | | | | |
|--|---|--|------|---------------------------|---|---|--|---|--|--|
| | | | | | | p-Value | OR | HR | 95% CI Lower | 95% CI Upper |
| Arif et al, 2007 Improved adherence | Multivariable analysis with forward conditional logistic regression | Antiplatelets Antihypertensives Lipid-lowering drugs | 298 | 119 (40) | School education (minimum) Dyslipidaemia (not with other co-morbidities) | 0.004 0.018 | 2.1 0.5 | --- --- | 1.3 0.3 | 3.5 0.9 |
| Burke et al, 2010 Worsened adherence | Cox proportional hazard | Antiplatelets | 1413 | 633 (44.8) | Higher medication co-payment > \$40 (relative to co-payment of ≤ \$20) | 0.0042 | --- | 1.32 | 1.091 | 1.596 |
| Bushnell et al, 2010 Improved adherence | Multivariable logistic regression analyses | Antiplatelets Warfarin Antihypertensives Lipid-lowering drugs Diabetes medications | 2598 | N/A | Fewer prescribed medication classes Increasing age No history of atrial fibrillation History of hypertension History of diabetes mellitus History of dyslipidaemia History of CAD/prior MI Less severe stroke disability (mRS < 3) | <0.001 0.005 0.007 <0.001 0.008 <0.001 0.02 <0.001 | 1.85 1.11 1.48 1.47 1.39 1.46 1.32 1.54 | --- 1.03 1.11 1.17 1.09 1.20 1.05 1.24 | 1.61 1.03 1.20 1.11 1.09 1.20 1.05 1.90 | 2.11 1.20 1.96 1.84 1.78 1.79 1.68 1.90 |

| | | | | | | | | | | |
|---|--|--|------------------------|---|---|--|------|--|--|------|
| | | | | | Working status: Home not by choice vs home by choice | 0.06 | 1.61 | | 1.08 | 2.42 |
| | | | | | Home not by choice vs working | --- | 1.47 | | 1.00 | 2.15 |
| | | | | | Understanding why medications are prescribed | 0.006 | 1.81 | | 1.19 | 2.76 |
| | | | | | Understanding how to refill medication | 0.03 | 1.64 | | 1.04 | 2.58 |
| | | | | | Increased quality of life (EuroQol-5D, per 10% increase) | 0.009 | 2.33 | | 1.24 | 4.38 |
| | | | | | Financial hardship | 0.002 | 1.38 | | 1.12 | 1.69 |
| | | | | | Hospital size (per 100-bed increase) | 0.052 | 1.04 | | 1.02 | 1.09 |
| Bushnell et al, 2011 Improved adherence & persistence | Multivariable logistic regression | Warfarin Antiplatelets Antihypertensives Lipid-lowering drugs Diabetic drugs | 2457 837 (34.1) | Fewer medications at discharge Adequate income Appointment with a primary care provider Appointment with neurologist Lower mRS score (≤ 3) | 0.001 0.003 0.027 0.023 0.006 | 1.04 1.30 1.47 1.20 1.33 | --- | 1.02 1.10 1.05 1.03 1.09 | 1.06 1.55 2.07 1.41 1.61 | |

| | | | | | | | | | | |
|--|------------------------------|-------------------|-----|---------|--|--------|------------------------------|-----|-------|-------|
| | | | | | Understanding of medications rational & side effects | 0.003 | 1.43 | | 1.13 | 1.81 |
| | | | | | Used compliance aid (pillbox) | 0.001 | 1.89 | | 1.48 | 2.41 |
| Chambers et al, 2011 (subgroup analysis from O'Carroll <i>et al</i> , 2008) Improved adherence | Qualitative analysis | Not specified | 26 | 13 (50) | Medication routine Positive beliefs about medication and treatment Knowledge about the medication rationale or intentions Support from family and health professionals Realistic understanding of the consequences of non- adherence Not forgetting to take medication | --- | --- | --- | --- | --- |
| Choi-Kwon et al, 2005 Worsened adherence | Multiple logistic regression | Antihypertensives | 256 | N/A | Early-onset patients (younger age) Lack of insurance | <0.001 | --- | | --- | --- |
| | | | | | | <0.05 | Mean difference = -4.4 | | -7.6 | -1.2 |
| | | | | | | <0.05 | Mean difference = 24.6 | 0.5 | 48.7 | |
| | | | | | | | 0.096 | | 0.008 | 0.976 |

| | | | | | | | | | | | | |
|---|--|--|------|------------|---|--------------------------------------|----------------------|--------------|----------------------|----------------------|--------------|------------------------------|
| Coetzee et al, 2008 Worsened adherence | Regression analysis | All preventative classes plus other classes | 26 | N/A | Cognitive dysfunction Emotional dysfunction Misbeliefs about medication Less support with medication intake at home | <0.001 <0.001 <0.001 <0.001 | --- | --- | --- | --- | --- | |
| De Schryver et al, 2005 | Cox proportional hazard | Aspirin Oral anticoagulants | 4447 | 832 (18.7) | <u>Aspirin (worst):</u> Age ≥ 65 years Higher doses (300 mg instead of 30 mg) <u>Aspirin (better):</u> Diastolic blood pressure of ≥ 90 mmHg Dizziness <u>Oral anti-coagulant:</u> None identified | --- | --- | 1.31 1.30 | 1.04 1.03 | 1.64 1.62 | 0.74 0.54 | 0.59 0.33 0.93 0.89 |
| Edmondson et al, 2013 Worsened adherence | Multivariable logistic regression analysis | Antithrombotics Antihypertensives Lipid-lowering drugs Diabetes medications | 535 | 218 (40.8) | Symptoms of PTSD Concerns about medications Years since last stroke | --- | 1.02 1.17 1.17 | --- | 1.00 1.10 1.02 | 1.05 1.25 1.34 | | |

| | | | | | | | | | | |
|--------------------|---|---|-------|-----|---|---|--|-----|--|---|
| Glader et al, 2010 | Multiple logistic regression with stepwise backward variable removal ($P > 0.10$ as removal criterion) | Anti-hypertensives Statins Antiplatelet drugs Warfarin | 21077 | N/A | <u>Anti-hypertensives:</u> Female gender Haemorrhagic stroke History of diabetes History of AF Previous treatment Institutional living Low mood Poor self-perceived health Lack of support <u>Statins:</u> Recurrent stroke No acute treatment in stroke unit Previous treatment Institutional living Poor self-perceived health No outpatient follow-up <u>Antiplatelet drugs:</u> Female gender | <0.001 0.004 0.01 <0.001 <0.001 <0.001 0.001 0.02 0.001 NS? 0.001 <0.001 0.05 0.04 | 0.81 1.24 1.17 1.24 2.07 1.47 0.88 0.86 1.13 0.77 1.25 1.28 1.64 0.69 1.04 0.92 | --- | 0.75 1.07 1.06 1.12 1.89 1.27 0.79 0.76 1.02 0.68 1.06 1.15 1.32 0.59 0.93 0.85 | 0.89 1.4 1.30 1.38 2.27 1.70 0.98 0.98 1.25 0.88 1.46 1.42 2.04 0.80 1.17 0.99 |
|--------------------|---|---|-------|-----|---|---|--|-----|--|---|

| | | | | | | | | | | |
|--|--|--|-------|-------------|---|---|--|-----|--|--|
| | | | | | Advanced age (>85) Absent history of AF Institutional living Low mood Poor self-perceived health <u>Warfarin:</u> Advanced age (>85) Recurrent stroke Institutional living Lack of support | <0.001 <0.001 <0.001 0.04 <0.001 0.01 0.04 0.004 0.05 | 1.37 0.78 1.78 0.92 0.79 0.57 0.70 0.45 0.98 | | 1.20 0.70 1.55 0.83 0.70 0.34 0.53 0.27 0.76 | 1.57 0.87 2.05 1.02 0.89 0.94 0.93 0.76 1.26 |
| Huang et al, 2013 | Multivariable logistic regression | Antihypertensives Antithrombotics Lipid-lowering drugs | 11050 | N/A | There was no difference across income quintiles in the use of post discharge medications | --- | --- | --- | --- | --- |
| Ji et al, 2013 Improved adherence | Univariate and multivariate logistic regression (stepwise backward method with likelihood ratio test) | Antiplatelets Warfarin Antihypertensives Statins Diabetic agents | 9998 | 3635 (36.4) | Univariate (+Multivariate): <u>Younger age (≤75)</u> <u>Male gender</u> Race (Hans) Married <u>History of hypertension</u> Absent history of diabetes | 0.05 0.003 0.003 0.05 0.05 | 1.11 1.14 1.40 1.15 1.09 | --- | 1.00 1.05 1.23 1.00 1.00 | 1.23 1.24 1.75 1.32 1.19 |

| | | | | | | | | | | |
|---|----------------------------------|---------------|-----|------------|---|--|--|-----|--|--|
| | | | | | <u>Absent history of atrial fibrillation</u> <u>Pre-stroke independence</u> <u>Acute ischaemic stroke vs TIA</u> <u>Treated in an academic hospital</u> <u>Longer hospital stay</u> <u>Fewer number of medications</u> | 0.01 0.04 0.005 0.003 0.005 0.001 | 0.73 1.17 1.22 1.13 1.01 1.78 | | 0.61 1.01 1.06 1.04 1.00 1.63 | 0.87 1.37 1.39 1.23 1.01 1.93 |
| Ke et al, 2009 Worsened adherence | Only reported count & percentage | Aspirin | 367 | 166 (45.2) | Concerns about side effects Inadequate communication with prescriber | --- | --- | --- | --- | --- |
| Kronish et al, 2012 Worsened adherence | Logistic regression | Not specified | 535 | 218 (40.8) | PTSD (post-traumatic stress disorder) | --- | Relativ e risk: 2.90 | --- | 1.92 | 4.42 |
| Kronish et al, 2013 Worsened adherence | Logistic regression | Not specified | 600 | 242 (40.3) | Increased concerns about medications Low trust in doctor Language barrier Perceived discrimination Difficulty accessing healthcare | <0.001 0.001 0.02 <0.001 0.002 | --- | --- | --- | --- |

| | | | | | | | | | | |
|--|---|--|------|-----|---|---------------------------------|--|-----|--|---|
| | | | | | Inadequate continuity of care <u>Adjusted model:</u> Increased concerns about medication Perceived discrimination | 0.05 <0.001 0.008 | 5.02 1.85 1.18 | | 2.76 2.90 | 9.11 |
| Levine et al, 2013 Worsened adherence | Multivariable logistic regression analyses | Not specified | 8673 | N/A | Cost-related non-adherence (Self-reported): Aged 45 – 64 Aged ≥ 65 | 0.01 0.21 | --- | --- | --- | --- |
| Lopes et al, 2011 Improved adherence | Multivariate logistic regression | Warfarin | 291 | N/A | Male gender | 0.01 | 2.27 | --- | 1.22 | 4.35 |
| Lummis et al, 2008 | Multivariable analysis (for each medication class separately) | Anti-thrombotics Anti-hypertensives Lipid-lowering drugs Diabetes medications | 420 | N/A | <u>Anti-hypertensives:</u> Age between (65 – 79) Number of medication prescribed Monthly drug cost: < \$90 \$90 - \$199 <u>Anti-thrombotics:</u> Age between (65 – 79) | --- | 0.11 0.80 7.05 5.76 0.23 | --- | 0.03 0.65 1.43 1.27 0.06 | 0.39 0.995 34.81 26.18 0.81 |

| | | | | | | | | | | |
|---|---|---|-----|----------|---|---------------------------------|--|-----|------|-------|
| | | | | | Disability before stroke | | 7.01 | | 1.66 | 29.58 |
| | | | | | Disability after stroke | | 3.22 | | 1.29 | 8.04 |
| | | | | | <u>Lipid-lowering drugs:</u> | | | | | |
| | | | | | Smoking | | 4.35 | | 1.44 | 13.13 |
| | | | | | History of previous stroke | | 0.13 | | 0.02 | 1.004 |
| O'Carroll et al, 2011 Worsened adherence | Multivariable- Hierarchical linear regression | Antihypertensives Aspirin Statins | 180 | N/A | <u>Time 1:</u> Younger age Concerns about medications Reduced cognitive functioning (MMSE score) Low perceived benefit of medication. | <0.001 0.01 0.043 | 0.371 0.355 0.201 0.159 | --- | --- | --- |
| Østergaard et al, 2012 Worsened | Univariate and multivariate analysis (cox regression) | Antiplatelets | 503 | 181 (36) | <u>Univariate:</u> Younger age Severe stroke | 0.005 <0.001 | --- | --- | --- | --- |

| | | | | | | | | | | | |
|--|--|--|------|------------|---|---|------------------|-----|----------------------------|----------------------------|----------------------------|
| persistence | | | | | History of MI <u>Multivariate:</u> Stroke severity | 0.03 --- | --- | --- | --- | --- | |
| Østergaard et al, 2014 Worsened persistence | Cox proportional hazards model (univariate) then unconditional logistic regression for multivariate | Antiplatelets | 594 | 140 (23.6) | <u>Univariate:</u> Younger age (<55 years) Current smoking status High alcohol intake History of hypertension <u>Multivariate:</u> Younger age (<54) Delay between TIA onset and neurological evaluation (7+ days) | <0.001 0.05 0.03 0.002 1.9 2.0 | --- | --- | 0.47 1.9 2.0 | 0.30 1.3 1.0 | 0.74 2.8 4.1 |
| Rodriguez et al, 2011 | Multivariate logistic model | Antiplatelets Warfarin Antihypertensives Lipid-lowering agents Diabetic agents | 2720 | 734 (27) | No differences between rural & urban residence in medication persistence post discharge | --- | --- | --- | --- | --- | |
| Sappok et al, 2001 Worsened | Stepwise backward logistic regression | Antithrombotics | 386 | N/A | Higher age Stroke Severity on admission | --- | 1.03 1.09 | --- | 1.00 1.00 | 1.06 1.20 | |

| adherence | | | | | Cardio-embolic cause | | 4.13 | | 1.23 | 13.83 |
|---|--|---|-------|------------|--|--|-------|-----|-------|-------|
| Sjölander et al, 2012 Improved adherence | Multiple log-linear Poisson regression | Antihypertensives | 18349 | N/A | Previous treatment with antihypertensive drug: Men (Prevalence ratio, PR) Women (PR) | --- | 1.15 | --- | 1.06 | 1.25 |
| Sjölander et al, 2013 Worsened adherence | Multivariable logistic regression models | Not specified | 578 | 72 (12.5) | Negative beliefs about medicines Male gender Not treated in stroke units Dependent on the help and support from relatives History of stroke Self-reported memory difficulties | 0.042 0.016 0.015 0.01 0.014 | 1.12 | --- | 1.05 | 1.21 |
| Thrift et al, 2014 Improved adherence | Logistic regression | Antihypertensives Antithrombotics Statins | 256 | 88 (34.4) | Prescription of medications at hospital discharge | --- | 2.62 | --- | 1.19 | 5.77 |
| Wang et al, 2006. | Univariate odds ratio (OR) values | Antithrombotics | 472 | 146 (19.7) | <u>Improved adherence:</u> Medical insurance or free medical care | --- | 1.624 | --- | 1.004 | 2.626 |

| | | | | | | | | | |
|---|--|---------------------|------|-------------|--|--------|-------|-----|-------------|
| | | | | | <u>Worst adherence:</u> | | | | |
| | | | | | Non-aspirin based regimen | --- | 0.465 | | 0.238 0.908 |
| | | | | | Poor quality of daily life (BI) | 0.01 | --- | | --- |
| Weimar et al, 2008 Worsened adherence | Stepwise logistic regression analysis | Oral anticoagulants | 293 | 33 (11.3) | Higher age | <0.001 | 0.944 | --- | 0.930 0.957 |
| | | | | | Greater baseline stroke severity on the NIHSS | <0.001 | 0.943 | | 0.918 0.969 |
| | | | | | Discharge to another institution than home | 0.003 | 1.599 | | 1.175 2.176 |
| | | | | | Higher disability on the mRS at discharge | <0.001 | 0.808 | | 0.727 0.898 |
| Xu et al, 2013 | Multivariate logistic regression | Antihypertensives | 4458 | 1531 (34.3) | <u>Worst adherence:</u> | | | | |
| | | | | | Older age (>/= 76) | --- | 1.45 | --- | 1.14 1.84 |
| | | | | | History of AF | | 1.25 | | 1.04 1.15 |
| | | | | | History of drinking | | 1.19 | | 1.01 1.41 |
| | | | | | Higher NIHSS (≥ 15) | | 1.41 | | 1.14 1.74 |
| | | | | | <u>Improved adherence:</u> | | | | |
| | | | | | Higher level of education | | 0.75 | | 0.66 0.85 |
| | | | | | History of hyperlipidaemia | | 0.90 | | 0.81 0.99 |
| | | | | | History of CAD | | 0.87 | | 0.76 0.99 |
| | | | | | Previous treatment with anti- | | 0.69 | | 0.62 0.76 |

AF: Atrial fibrillation, AH: Antihypertensive drugs, AT: Anti-thrombotic drugs, BI: Barthel Index, CAD: Coronary artery disease, LL: Lipid-lowering drugs, MI: Myocardial infarction, mRS: modified Rankin Scale, N/A: Not available, NIHSS: National Institute of Health Stroke Scale, TIA: Transient ischaemic attack

Table 2: Classification of Predictive Factors of Adherence to Secondary Preventative Medication after Stroke

| Factors Predicted Better Adherence | |
|---|--|
| Factor | Studies reported |
| Education | Arif et al, 2007 Xu et al, 2013 |
| Working status | Bushnell et al, 2010 |
| Presence of carer or supporter | Glader et al, 2010 Chambers et al, 2011 Coetze et al, 2008 Ji et al, 2013 |
| Positive beliefs about medication | Chambers et al, 2011 Coetze et al, 2008 Sjölander et al, 2013 |
| Awareness of consequence of not taking medication | Chambers et al, 2011 |
| History of hypertension | Bushnell et al, 2010 Ji et al, 2013 Østergaard et al, 2014 |
| History of diabetes | Glader et al, 2010 Bushnell et al, 2010 |
| History of dyslipidaemia | Bushnell et al, 2010 Arif et al, 2007 Xu et al, 2013 |
| History of coronary artery disease | Bushnell et al, 2010 Xu et al, 2013 |
| History of myocardial infarction | Bushnell et al, 2010 Østergaard et al, 2012 |

| | |
|---|--|
| Absent history of atrial fibrillation | Glader et al, 2010 Bushnell et al, 2010 Ji et al, 2013 Sappok et al, 2001 Xu et al, 2013 |
| Understanding of medication rationale | Bushnell et al, 2011 Bushnell et al, 2010 Chambers et al, 2011 Ke et al, 2009 |
| Awareness of duration of treatment | Ke et al, 2009 |
| Knowledge of how to refill prescription | Bushnell et al, 2010 |
| Previous treatment by the same medication class | Glader et al, 2010 Sjölander et al, 2012 Xu et al, 2013 |
| Prescription and education at discharge | Thrift et al, 2014 |
| Development of medication routine | Chambers et al, 2011 |
| Use of compliance aid | Bushnell et al, 2011 |
| Prescriber speciality (e.g. neurologist) | Bushnell et al, 2011 |
| Treatment in stroke unit | Glader et al, 2010 Sjölander et al, 2013 |
| Treatment in academic hospital | Ji et al, 2013 |
| Hospital size | Bushnell et al, 2010 |
| Medical insurance | Wang et al, 2006 Choi-Kwon et al, 2005 |
| Accessible healthcare facility | Glader et al, 2010 Kronish et al, 2013 |

| <i>Factors Predicted Worst Adherence</i> | |
|---|---|
| Having concerns about medication | O'Carroll et al, 2011 Kronish et al, 2013 Edmondson et al, 2013 Ke et al, 2009 |
| No perceived benefit of treatment | O'Carroll et al, 2011 |
| Living at care institution other than home | Glader et al, 2010 Weimar et al, 2008 |
| Disability | Bushnell et al, 2011 Lummis et al, 2008 Bushnell et al, 2010 Ji et al, 2013 Sjölander et al, 2013 Weimar et al, 2008 |
| Reduced cognition function | O'Carroll et al, 2011 Chambers et al, 2011 Coetzee et al, 2008 Sjölander et al, 2013 |
| Poor quality of life | Glader et al, 2010 Wang et al, 2006 Bushnell et al, 2010 |
| Low mood | Glader et al, 2010 Coetzee et al, 2008 |
| Smoking | Lummis et al, 2008 Østergaard et al, 2014 |
| Alcohol consumption | Østergaard et al, 2014 Xu et al, 2013 |

| | |
|--|--|
| Cost of medication | Lummis et al, 2008 Levine et al, 2013 Burke et al, 2010 |
| Number and frequency of prescribed drugs | Bushnell et al, 2011 Lummis et al, 2008 Bushnell et al, 2010 Ji et al, 2013 |
| Higher dose (of aspirin) | De Schryver et al, 2005 |
| Non-aspirin based regimen (for Anti-platelet drugs) | Wang et al, 2006 |
| Language barrier | Bushnell et al, 2011 |
| Low trust in healthcare provider | Bushnell et al, 2011 |
| Perceived discrimination (e.g. minorities) | Bushnell et al, 2011 |
| Inadequate continuity of care | Bushnell et al, 2011 |
| Inadequate communication of information regarding prescribed regimen | Ke et al, 2009 |
| delay from onset of symptoms to evaluation | Østergaard et al, 2014 |
| Post-traumatic stress disorder (PTSD) | Edmondson et al, 2013 Kronish et al, 2012 |
| More severe stroke | Østergaard et al, 2012 Sappok et al, 2001 Weimar et al, 2008 Xu et al, 2013 |
| Previous stroke incidence | Glader et al, 2010 Lummis et al, 2008 Sjölander et al, 2013 |
| Time from stroke onset | Edmondson et al, 2013 |
| Ischaemic stroke vs. TIA | Ji et al, 2013 |

| | |
|-----------------------------------|---|
| Cardio-embolic cause | Sappok et al, 2001 |
| Haemorrhagic stroke | Glader et al, 2010 |
| Contradictory Factors | |
| Age: Younger age better adherence | Glader et al, 2010 Ji et al, 2013 Sappok et al, 2001 Weimar et al, 2008 Xu et al, 2013 |
| Age: Younger age worst adherence | Lummis et al, 2008 O'Carroll et al, 2011 Bushnell et al, 2010 Choi-Kwon et al, 2005 De Schryver et al, 2005 Østergaard et al, 2012 Østergaard et al, 2014 |
| Gender: Women adhere better | Sjölander et al, 2013 |
| Gender: Women adhere worst | Glader et al, 2010 Ji et al, 2013 Lopes et al, 2011 |

Table 3: Quality Assessment of Included Studies

| | | | | | | | | |
|--------------------|---------------|---------------|----------|---------------|---------------|---------------|---------------|------------|
| | No Unclear | No Unclear | No NA | No Unclear | No Unclear | No Unclear | No Unclear | No High |
| Thrift et al, 2014 | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Low |
| | No | No | No | No | No | No | No | High |
| | Unclear | Unclear | NA | Unclear | Unclear | Unclear | Unclear | |
| Wang et al, 2006 | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Low |
| | No | No | No | No | No | No | No | High |
| | Unclear | Unclear | NA | Unclear | Unclear | Unclear | Unclear | |
| Weimar et al, 2008 | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Low |
| | No | No | No | No | No | No | No | High |
| | Unclear | Unclear | NA | Unclear | Unclear | Unclear | Unclear | |
| Xu et al, 2013 | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Low |
| | No | No | No | No | No | No | No | High |
| | Unclear | Unclear | NA | Unclear | Unclear | Unclear | Unclear | |