Canadian Stroke Best Practices

CANADIAN STROKE BEST PRACTICE RECOMMENDATIONS

Acute Stroke Management Evidence Tables
Outpatient Management of Transient Ischemic Attack and Non-Disabling Stroke

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on Behalf of the Canadian Stroke Best Practice Recommendations
ACUTE STROKE MANAGEMENT Best Practice Writing Group

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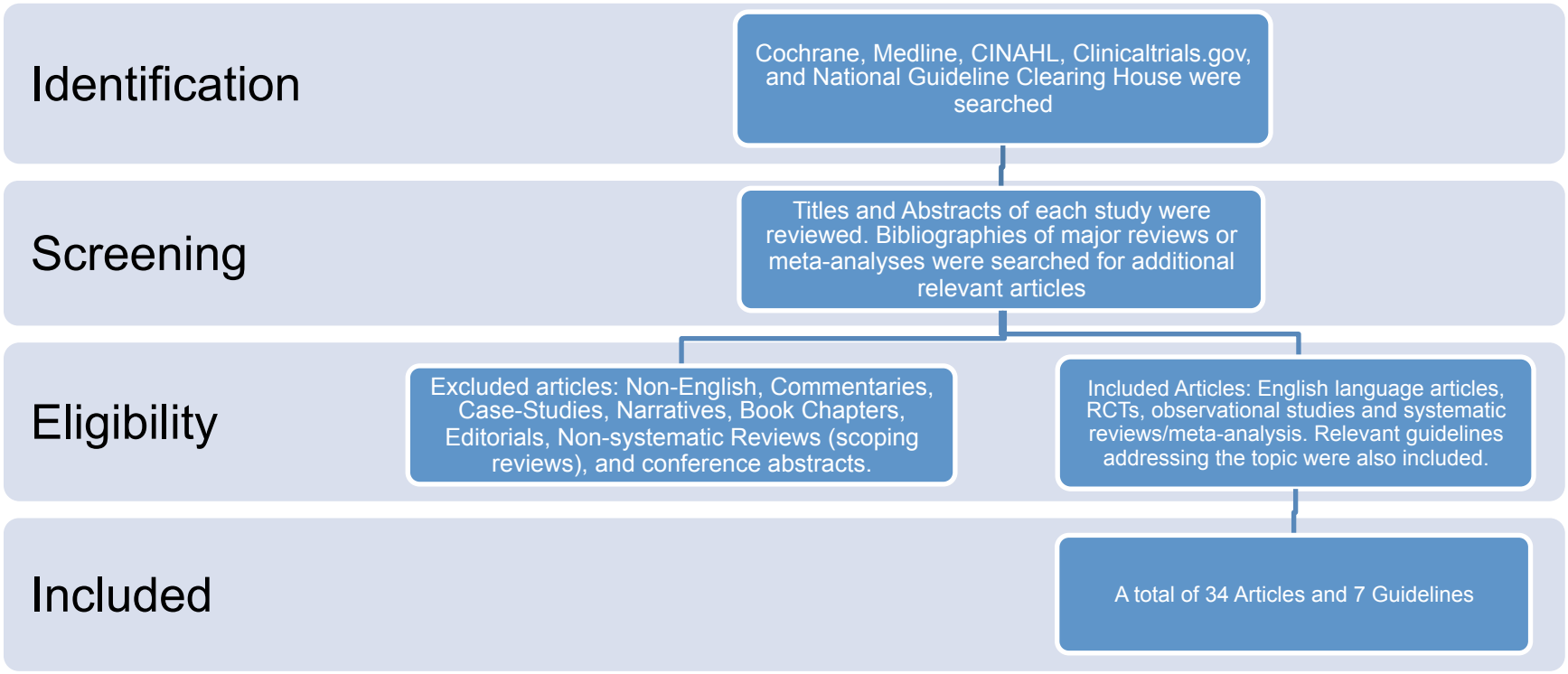
Search Strategy



Cochrane, Medline, CINAHL, National Guideline Clearing House and clinicaltrials.gov were search using the terms (“minor stroke” OR “TIA” OR “transient ischemic attack”) AND (“outpatient” OR “rapid access” OR “TIA clinic”). Titles and abstract of each article were reviewed for relevance. Bibliographies were reviewed to find additional relevant articles. Articles were excluded if they were: non-English, commentaries, case-studies, narrative, book chapters, editorials, or conference abstracts. Additional searches for relevant best practice guidelines were completed and included in a separate section of the review. A total of 34 articles and 7 guidelines were included and were separated into separate categories designed to answer specific questions.

Published Guidelines

Guideline	Recommendations
Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, Biller J, Brown M, Demaerschalk BM, Hoh B, Jauch EC, Kidwell CS, Leslie-Mazwi TM, Ovbiagele B, Scott PA, Sheth KN, Southerland AM, Summers DV, Tirschwell DL; on behalf of the American Heart Association Stroke Council. **2018 Guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association.** ***Stroke.* 2018; Mar;49(3):e46-e110**	**6.3. Cardiac Evaluation** 1. Cardiac monitoring is recommended to screen for atrial fibrillation and other potentially serious cardiac arrhythmias that would necessitate emergency cardiac interventions. Cardiac monitoring should be performed for at least the first 24 hours. Class I; LOE B-NR. 2. The clinical benefit of prolonged cardiac monitoring to detect atrial fibrillation after AIS is uncertain. Class I; LOEIb B-R. 3. In some patients with AIS, prolonged cardiac monitoring to provide additional information to plan subsequent secondary preventive treatment may be reasonable, although the effect on outcomes is uncertain. Class IIb; LOE C-EO. 4. Routine use of echocardiography in all patients with AIS to plan subsequent secondary preventive treatment is not cost-effective and is not recommended. Class III: No Benefit; LOE B-NR. 5. In selected patients with AIS, echocardiography to provide additional information to plan subsequent secondary preventive treatment may be reasonable. Class IIb; LOE B-R.
Clinical Guidelines for Stroke Management 2017. Melbourne (Australia): National Stroke Foundation.	**Early assessment and diagnosis of TIA** Strong recommendation Updated • All patients with suspected transient ischaemic attack (TIA), i.e. focal neurological symptoms due to focal ischaemia that have fully resolved, should have urgent clinical assessment. • Patients with symptoms that are present or fluctuating at time of initial assessment should be treated as having a stroke and be immediately referred for emergency department and stroke specialist assessment, investigation and reperfusion therapy where appropriate. • In pre-hospital settings, high risk indicators (e.g. crescendo TIA, current or suspected AF, current use of anticoagulants, carotid stenosis or high $ABCD^2$ score) can be used to identify patients for urgent specialist assessment. Strong recommendation New When TIA patients present to primary care, the use of TIA electronic decision support, when available, is recommended to improve diagnostic and triage decisions. Weak recommendation AGAINST New In TIA patients, use of the ABCD2 risk score in isolation to determine the urgency of investigation may delay recognition of atrial fibrillation and symptomatic carotid stenosis in some patients and should be avoided.

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	Strong recommendation Updated All TIA patients with anterior circulation symptoms should undergo early carotid imaging with CT angiography (aortic arch to cerebral vertex), carotid Doppler ultrasound or MR angiography. Carotid imaging should preferably be done during the initial assessment but should not be delayed more than 2 days. Weak recommendation Updated Patients with TIA should routinely undergo brain imaging to exclude stroke mimics and intracranial haemorrhage. MRI, when available, is recommended to improve diagnostic accuracy. Strong recommendation New Patients with suspected TIA should commence secondary prevention therapy urgently. Strong recommendation New • All patients with TIA should be investigated for atrial fibrillation with ECG during initial assessment and referred for possible prolonged cardiac monitoring as required. • TIA patients with atrial fibrillation should commence anticoagulation therapy early after brain imaging has excluded haemorrhage, unless contraindicated.
Intercollegiate Stroke Working Party. Royal College of Physicians. National Clinical guidelines for stroke. 5th Edition 2016, Edinburgh, Scotland	**Management of TIA – assessment and diagnosis** A- Patients with acute neurological symptoms that resolve completely within 24 hours (i.e. suspected TIA) should be given aspirin 300 mg immediately and assessed urgently within 24 hours by a specialist physician in a neurovascular clinic or an acute stroke unit. B- Patients with suspected TIA that occurred more than a week previously should be assessed by a specialist physician as soon as possible within 7 days. C- Patients with suspected TIA and their family/carers should receive information about the recognition of stroke symptoms and the action to be taken if they occur. D- Patients with suspected TIA should be assessed by a specialist physician before a decision on brain imaging is made, except when haemorrhage requires exclusion in patients taking an anticoagulant or with a bleeding disorder when unenhanced CT should be performed urgently. E- For patients with suspected TIA in whom brain imaging cannot be undertaken within 7 days of symptoms, T2* MRI imaging should be the preferred means of excluding haemorrhage. F- Patients with a confirmed diagnosis of TIA should receive clopidogrel (300 mg loading dose and 75 mg daily thereafter) and high intensity statin therapy (e.g. atorvastatin 20-80 mg daily) started immediately. **Management of TIA – treatment and vascular prevention** A-Patients with non-disabling stroke or TIA should receive treatment for secondary prevention introduced as soon as the diagnosis is confirmed, including: – discussion of individual lifestyle factors (smoking, alcohol excess, diet, exercise);

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	– clopidogrel 300 mg loading dose followed by 75 mg daily; – high intensity statin therapy with atorvastatin 20-80 mg daily; – blood pressure-lowering therapy with a thiazide-like diuretic, long-acting calcium channel blocker or angiotensin-converting enzyme inhibitor. B- Patients with non-disabling stroke or TIA in atrial fibrillation should be anticoagulated as soon as intracranial bleeding has been excluded and with an anticoagulant that has rapid onset, provided there are no other contraindications. C-Patients with non-disabling stroke or TIA who after specialist assessment are considered candidates for carotid intervention should have carotid imaging performed urgently within 24 hours. D- The degree of carotid artery stenosis should be reported using the North American Symptomatic Carotid Endarterectomy Trial (NASCET) method. E- Patients with TIA or an acute non-disabling stroke with stable neurological symptoms who have symptomatic severe carotid stenosis of 50–99% (NASCET method) should: – be assessed and referred for carotid endarterectomy to be performed as soon as possible within 7 days of the onset of symptoms in a vascular surgical centre routinely participating in national audit; – receive optimal medical treatment: control of blood pressure, antiplatelet treatment, cholesterol reduction through diet and drugs, and lifestyle advice including smoking cessation. F- Patients with TIA or an acute non-disabling stroke who have mild or moderate carotid stenosis of less than 50% (NASCET method) should: – not undergo carotid intervention; – receive optimal medical treatment: control of blood pressure, antiplatelet treatment, cholesterol reduction through diet and drugs, and lifestyle advice including smoking cessation. G-Patients with recurrent attacks of transient neurological symptoms despite optimal medical treatment, in whom an embolic source has been excluded, should be reassessed for an alternative neurological diagnosis. H- Patients who meet the criteria for carotid intervention but who are unsuitable for open surgery (e.g. inaccessible carotid bifurcation, re-stenosis following endarterectomy, radiotherapy-associated carotid stenosis) should be considered for carotid angioplasty and stenting. I- People who have undergone carotid revascularisation should be reviewed post-operatively by a stroke physician to optimise medical aspects of vascular secondary prevention.
New Zealand guideline for the assessment and management of people with recent transient ischaemic attack (TIA) **Stroke Foundation of New**	Recommendations – location of initial assessment and management • Most people at high risk of stroke following TIA should be transferred urgently to hospital to facilitate rapid specialist assessment and treatment. (European Grade B) • Most people identified at low risk may initially be managed in the community by a general practitioner and should be referred to a specialist clinic and seen within 7 days. • If the treating doctor is confident about the diagnosis, can implement recommended treatments, and has access to brain and

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Zealand **2010**	carotid imaging within 7 days, then specialist review of people at low risk may not be necessary. Assessment of stroke risk after TIA • All people with suspected TIA should have an assessment of stroke risk using the ABCD2 tool at the initial point of health care contact whether first seen in primary or secondary care. (Australian Grade B, English/Welsh, RCP) • HIGH risk is indicated by any of the following: o Active TIA – All people who have symptoms at the time of first contact. (European Grade B) o ABCD2 score of 4 or more (English/Welsh, RCP) o Other high-risk factors – all people with crescendo TIAs, atrial fibrillation or who are already on anticoagulation, should be managed as high risk regardless of their ABCD2 scores. (NZ TIA) • LOW risk is indicated by any of the following: o ABCD2 score of 3 or less – these people are at low risk of early stroke, about one in a hundred by one week and one in thirty by 90 days. (RCP) o People who present late (after one week) – after their TIA are at lower risk, as two thirds of early strokes will have already occurred by this period. (RCP) Clinical Assessment and Blood Tests • In patients with TIA, early clinical evaluation, including physiological parameters and routine blood tests (Full blood count, electrolytes, glucose, lipids and creatinine, and in selected patients CRP or ESR) are recommended (European Grade A) Electrocardiography (ECG) • All TIA patients should have a 12-lead electrocardiograph (ECG). (European Grade A) • In TIA patients seen after the acute phase, 24-hour Holter ECG monitoring should be performed when arrhythmias are suspected and no other causes of TIA are found (European Grade A) Brain Imaging • Patients classified as high risk should have an urgent MRI or CT brain ('urgent' is considered as soon as possible, but certainly within 24 hours). (European Grade A) • Patients classified as low risk should have a MRI or CT brain as soon as possible, but certainly within 7 days. (Australian Grade B) • If MRI is used, the inclusion of DWI and T2* weighted gradient echo sequences is recommended (European Level A) Carotid Imaging

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	• All patients with TIA who are candidates for carotid intervention should have carotid imaging within one week of symptom onset (RCP), and within one working day if at high risk. (English/Welsh, NZ TIA) Cardiac imaging • Echocardiography is recommended in selected patients (European Grade B) Recommendations - for District Health Boards providing TIA Services • A TIA service should be provided by an appropriately resourced, open-access daily specialist outpatient clinic, an inpatient short-stay facility or a combination of these services. In smaller District Health Boards with insufficient population to warrant specialised TIA services this should be by general medical services, using agreed protocols. Recommendations – initial management • All people with TIA who attend emergency departments, out-of-hours medical centres or similar providers soon after TIA must be treated and must not be sent home and simply told to see their GP in due course. (English/Welsh • Clinicians should establish all people with TIA on measures for secondary prevention as soon as the diagnosis is confirmed, including discussion of individual risk factors. (RCP) This should consist of an appropriate individual combination of: o Anti-platelet agent(s) such as aspirin, aspirin plus dipyridamole or clopidogrel o Blood pressure lowering therapy o Statin o Warfarin - if atrial fibrillation or other cardiac source of emboli o Nicotine replacement therapy or other smoking cessation aid. Treatment must be initiated at first contact. (RCP, English/Welsh)
National Clinical Guidelines and Recommendations for the Care of People with Stroke and Transient Ischaemic Attack **Irish Heart Foundation: Council for Stroke** **March 2010**	Assessment • All patients with probable TIA should be assessed by a physician who has received specialist training in stroke and TIA management. (I) • Patients with TIA should be referred to a hospital with a specialist stroke service for immediate assessment, investigation, and treatment. (I) • Non-randomised studies suggest that stroke risk is substantially reduced in patients with TIA who are immediately assessed and treated by a specialist stroke service in outpatient, day care, and stroke unit settings. As available data do not indicate that any one of these service models is superior to another, all are acceptable provided that access is available to appropriate early diagnostic investigations. (I) • When combined with clinical assessment by a trained physician, clinical prediction scores for stroke risk after TIA such as ABCD2 may be valuable aids, particularly for identification of patients at highest stroke risk. Their role in the identification of

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	low-risk patients requires further study before being considered as the sole basis for non-urgent assessment of individual patients with TIA. (I) Imaging • Brain imaging is clinically useful in the management of individual patients and should be performed following TIA. Either MRI with diffusion-weighted imaging and T2* (time constant, gradient Echo) or CT is reasonable, although evidence indicates higher sensitivity of MRI for focal cerebral pathology. (I) • Vascular imaging of the carotid arteries should be performed urgently (as soon as possible and no later than 72 hours) following confirmed TIA, using carotid ultrasound and/or MR, CT or invasive angiography. (I) Investigation • All patients with TIA should have 12-lead ECG. 24-hour Holter ECG monitoring should be performed when arrhythmias are suspected and no other causes of stroke are found. Echocardiography is recommended in selected patients (evidence of cardiac disease, suspected cardiac, aortic, or paradoxical embolism). (I) All patients with TIA should have a general medical assessment, including fasting lipid profile, full blood count and electrolytes, and investigation for diabetes (fasting glucose and/or oral glucose tolerance test, as appropriate). (I)
Easton et al., 2009 **Definition and Evaluation of Transient Ischemic Attack: A Scientific Statement for Healthcare Professionals from the American Heart Association/American Stroke Association Stroke Council; Council on Cardiovascular Surgery and Anesthesia; Council on Cardiovascular Radiology and Intervention; Council on Peripheral Vascular Disease:** ***Stroke 2009*;40:2276-2293.**	Class I Recommendations 1. Patients with TIA should preferably undergo neuroimaging evaluation within 24 hours of symptom onset. MRI, including DWI, is the preferred brain diagnostic imaging modality. If MRI is not available, head CT should be performed (Class I, Level of Evidence B). 2. Noninvasive imaging of the cervicocephalic vessels should be performed routinely as part of the evaluation of patients with suspected TIAs (Class I, Level of Evidence A). 3. Noninvasive testing of the intracranial vasculature reliably excludes the presence of intracranial stenosis (Class I, Level of Evidence A) and is reasonable to obtain when knowledge of intracranial steno-occlusive disease will alter management. Reliable diagnosis of the presence and degree of intracranial stenosis requires the performance of catheter angiography to confirm abnormalities detected with noninvasive testing. 4. Patients with suspected TIA should be evaluated as soon as possible after an event (Class I, Level of Evidence B). Class II Recommendations 1. Initial assessment of the extracranial vasculature may involve any of the following: CUS/TCD, MRA, or CTA, depending on local availability and expertise, and characteristics of the patient (Class IIa, Level of Evidence B). 2. If only noninvasive testing is performed before endarterectomy, it is reasonable to pursue 2 concordant noninvasive findings; otherwise, catheter angiography should be considered (Class IIa, Level of Evidence B). 3. The role of plaque characteristics and detection of MESs is not yet defined (Class IIb, Level of Evidence B).

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	4. ECG should occur as soon as possible after TIA (Class I, Level of Evidence B). Prolonged cardiac monitoring (inpatient telemetry or Holter monitor) is useful in patients with an unclear origin after initial brain imaging and electrocardiography (Class IIa, Level of Evidence B). 5. Echocardiography (at least TTE) is reasonable in the evaluation of patients with suspected TIAs, especially 6. In patients in whom no cause has been identified by other elements of the workup (Class IIa, Level of Evidence B). TEE is useful in identifying PFO, aortic arch atherosclerosis, and valvular disease and is reasonable when identification of these conditions will alter management (Class IIa, Level of Evidence B). 7. Routine blood tests (complete blood count, chemistry panel, prothrombin time and partial thromboplastin time, and fasting lipid panel) are reasonable in the evaluation of patients with suspected TIAs (Class IIa, Level of Evidence B). 8. It is reasonable to hospitalize patients with TIA if they present within 72 hours of the event and any of the following criteria are present: a. ABCD2 score of ≥3 (Class IIa, Level of Evidence C). b. ABCD2 score of 0 to 2 and uncertainty that diagnostic workup can be completed within 2 days as an outpatient (Class IIa, Level of Evidence C). c. ABCD2 score of 0 to 2 and other evidence that indicates the patient's event was caused by focal ischemia (Class IIa, Level of Evidence C).
Management of patients with stroke or TIA: assessment, investigation, immediate management and secondary prevention. A national clinical guideline December 2008 **(Scottish Intercollegiate Guidelines Network)**	2.3 Assessment, diagnosis and investigation 2.3.1 Brain imaging for suspected acute stroke or TIA • All patients with suspected stroke should have brain imaging immediately on presentation (Grade A) 2.3.2 Carotid Evaluation • All patients with non-disabling acute stroke syndrome/TIA in the carotid territory who are potential candidates for carotid surgery should have carotid imaging. (Grade A) • The ABcd2 score should be used to identify patients who are at highest risk of recurrent stroke to allow very rapid investigation and treatment. (Grade C) 4.2.3 Modality of Imaging • CT scanning is recommended for most patients in the acute phase of stroke. (Grade B) • MRI with diffusion weighted and gradient echo sequences is recommended (where available and practical) for the diagnosis of acute stroke syndromes in patients who: (Grade B) ○ are not severely ill, especially where either neurological deficit is mild and the clinical likelihood is that the lesion is

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	small or lies in the posterior fossa or ○ present late (after one week). 4.3 Carotid Evaluation • All patients with non-disabling acute stroke syndrome/TIA in the carotid territory who are potential candidates for carotid surgery should have carotid imaging. (Grade A) • Initial carotid imaging with duplex ultrasound or alternative should be performed rapidly once a diagnosis of ischaemic stroke or TIA in the carotid territory is made. (Grade C) • Initial carotid imaging should be performed within 48 hours of presentation. (GPP) • Corroborative imaging is recommended to confirm and more accurately grade carotid disease if duplex carotid ultrasound is abnormal. (Grade C) • Non-invasive angiographic carotid imaging (CE-MRA) should be performed and interpreted by radiologists specifically trained and with specialist interest in vascular imaging. (Grade C) • Duplex ultrasound criteria for grading of carotid disease should be standardised and regularly audited against another modalities and surgical findings. (GPP) 4.4 Cardiac Imaging • The routine use of echocardiography with contrast media for evaluation of patients with stroke is not recommended. (Grade b) • Echocardiography should be considered in patients with: (Grade B) ○ clinical findings and/or baseline investigations suggesting cardiac disease ○ cryptogenic stroke. 4.5 Diagnostic Tests • The routine requesting of thrombophilia screens, antiphospholipid antibodies, other auto-antibodies or homocysteine levels is not recommended (Grade C)

Evidence Tables

Estimates of Risk of Stroke Recurrence

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings
Estimates of Stroke Following First or Recurrent Stroke					
Callaly et al. 2016 **UK** **Prospective study**	NA	567 patients ≥18 years who were participants in the North Dublin Population Stroke Study. Mean age was 71 years, 49% were male. 484 patients (85.4%) had suffered a first-ever stroke, while 83 (14.6%) were recurrent stroke, of which 80.1% were ischemic stroke, 10.7% were ICH, 5.1% were SAH and 4.1% were unconfirmed.	Participants, residing in the community or in institutions, who had suffered a new (first-ever or recurrent) stroke during a one-year period (2006) were identified.	**Primary outcome:** Recurrent stroke up to 2 years post event	At 2 years, data were available for 91.4% of participants. Recurrent stroke occurred in 46 patients. The cumulative rate of recurrence was: 5.4% (95% CI 3.7%-7.9%) at 90 days 8.5% (95% CI 6.2%-11.5%) at 1 year 10.8% (95% CI 8.2-14.2%) at 2 years. Recurrence rates were highest for patients with ischemic stroke (11.5%, 95% CI 8.6%-15.3%) at 2 years. 2-year case fatality was 38.6%.
Mohan et al. 2011 **UK** **Systematic review & meta-analysis**	NA	13 studies (n=9,115) from hospital and community-based stroke registries reporting on stroke recurrence following first-ever stroke.	Cumulative risk of reported stroke recurrence was pooled across studies.	**Primary outcome:** Stroke recurrence up to 10 years	The pooled cumulative risk of stroke recurrence after initial stroke was: 3.1% (95% CI, 1.7%- 4.4%) at 30 days (n=8) 11.1% (95% CI, 9.0% -13.3%) at 1 year (n=12) 26.4% (95% CI, 20.1%-32.8%) at 5 years (n=7) 39.2% (95% CI, 27.2%-51.2%) at 10 years (n=4)
Hankey et al. 1998 **Australia** **Prospective study**	NA	351 patients with first-ever stroke who had survived for >2 days following hospitalization (1989-1990) participating in the Perth Community Stroke Study. 73% of	Patients were assessed at baseline, 4 months, 12 months and 5 years. Outcome ascertainment was through administrative databases.	**Primary outcome:** Stroke recurrence at 5 years	Follow-up data were available at 5 years for 343 patients (98%). During follow-up, 199 patients (58%) had died, 52 (15%) suffered a first recurrent stroke, of which 12 (28%) were fatal within 28 days. Of the recurrent strokes, 37 (71%) were ischemic, 4

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		strokes were ischemic, 10.5% were ICH, 3.8% were SAH and 12.7% of strokes were of undetermined etiology. Mean age was 73 years, 53% were male.			(7.7%) were ICH and 11 (21.1%) were of undetermined etiology. 89% of recurrent ischemic strokes occurred in patients with an index event that was ischemic. The 5-year cumulative risk of recurrent stroke was 22.4% (95% CI16.8%-28.1%), with the highest risk (8.8%) during the first 6 months.
Estimates of Stroke Following TIA					
Montassier et al. 2013 **France** **Prospective cohort study**	NA	60 patients were referred to the outpatient TIA clinic from the emergency department (ED). Mean age: 73.1 years	The outpatient clinic offered patients referred from the ED, access to Doppler ultrasound (within 8-15 days) following a battery of assessments in the ED (blood tests, ECG, CT). Patients were also started on antiplatelet therapy in the ED.	**Primary Outcome:** Occurrence of stroke within 90 days. **Secondary Outcomes**: Occurrence of TIA within 90 days, presence of stenosis (>70% symptomatic carotid), hospitalization (for cardiovascular event), death.	Occurrence of stroke within 90 days: 1.7% Occurrence of TIA within 90 days: 5% Presence of carotid stenosis: 1.7% There were no cases of hospitalization as a result of a cardiovascular event or death. The rate of stroke predicted using the ABCD2 scoring algorithm was 9.7%, higher than the rate experienced in the present study.
Giles & Rothwell 2007 **UK** **Systematic Review and meta-analysis**	N/A	18 studies, including 10,126 patients diagnosed with TIA, and recruited within 7 days of symptom onset. Mean age: 61 years-73 years.	Recurrent stroke risk was first determined for each study individually and then pooled.	**Primary Outcome**: Risk of stroke at days 2 and 7	Overall risk of stroke was 3.1% at day 2 and 5.2% at day 7. Pooled risk of stroke varied across studies from 0.6% at Day 2 to 10.4% at Day 7. **Outpatient studies:** Risk of stroke was 1.7% at day 2 and 3.3% at day 7. **Population based with face to face follow-up**: Risk of stroke was 6.7% at day 2 and 10.4% at day 7. **Specialized stroke service:** Risk of stroke was 0.6% at day 2 and 0.9% at day 7.

Predictors of Stroke Recurrence

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings
Amarenco et al. 2016 **France** **Prospective study**	NA	4,583 patients ≥18 years recruited from 61 sites in 21 countries from 1997-2003 with TIA or minor stroke that occurred within the previous 7 days and who were evaluated by a stroke specialist at a high-volume stroke facility. Mean age was 66.1 years, 60.2% were male. 17.6% had previous stroke or TIA	Data pertaining to the qualifying event were collected at baseline. Thereafter, data related to the occurrence of clinical events, vascular risk factors and medical treatments were collected prospectively at 1,3, and 12 months after stroke and annually for up to 5 years.	**Primary outcome:** Composite of death from cardiovascular causes, nonfatal stroke and nonfatal acute coronary syndrome (MI +/- ST-segment elevation or unstable angina followed by urgent catheterization). **Secondary outcomes** Individual components of the primary outcome, TIA recurrence, death from any cause, and bleeding.	Median duration of follow-up was 27.2 months. 87.6% of patients sought treatment within 24 hours of symptom onset. 78.4% of patients were seen by a stroke specialist within 24 hours of symptom onset. 5.0% of the patients received a new diagnosis of atrial fibrillation, of which 66.8% (n=133) received anticoagulant therapy before discharge. A carotid stenosis of ≥50% was found in 15.5% of patients, of which 26.9% (n=166) underwent carotid revascularization before discharge. The primary outcome occurred 274 times. Event rate was 6.2%, 95% CI 5.5-7.0%. Estimates of the stroke rate at days 2, 7, 30, 90, and 365 were 1.5%, 2.1%, 2.8%, 3.7%, and 5.1%, respectively. Independent predictors of stroke recurrence were: Cerebral infarctions on brain imaging vs. no infarction: HR=2.16; 95% CI, 1.46-3.21, p<0.001 $ABCD^2$ score of 6-7 vs. 0-3: HR=2.20, 95% CI 1.41-3.42, p<0.001), and large-artery atherosclerosis vs. undetermined cause: HR=2.01, 95% CI 1.29- 3.13; p= 0.002)
Wardlaw et al. 2015 **UK** **Systematic review & meta-analysis**	NA	29 studies (n=13,766), published in 31 reports, including 15 prospective and 14 retrospective cohort studies, of persons suffering from suspected minor stroke or TIA, and where an ABCD2 score had been	The ability of ABCD2 clinical risk score to was used to: 1) Predict stroke recurrence in patients at high (≥4) and low (<4) risk of stroke; 2) Differentiate patients with mimics from true stroke/TIA, 3) Identify carotid stenosis or AF and 4) Estimate its effect on proportions of patients entering fast- or slow-track assessment in stroke prevention service.	**Primary outcome:** Proportion of recurrent stroke patients (per 1,000 patients)	Timing of assessment ranged from <24 hours to a median of 15 days, post event. Using data from 17 studies, the pooled percentage of patients with recurrent stroke at day 7 was higher in persons with an ABCD2 score of ≥4 (7.7%, 95% CI 5.0%-11.6%) compared with persons with a score <4 (2.3%, 95% CI 1.3%-4.1%). Using data from 22 studies, the pooled percentage of patients with recurrent stroke at

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings
		calculated. Both population and hospital-based studies were included. Sample sizes ranged from 69 to 1,679 patients.			day 90 was higher in persons with an ABCD2 score of ≥4 (7.2%, 95% CI 4.8%-10.8%) compared with persons with a score <4 (2.4%, 95% CI 1.1%-5.4%). Using the results from 10 studies that assessed recurrent stroke at both 7 and 90 days, the sensitivity of ABCD2 score ≥4 to predict stroke was: 86.7 (95% CI: 81 to 90.7) at 7 days and 85.4 (95% CI: 81.1 to 88.9) at 90 days. The associated sensitivities were 35.4 (95% CI: 33.3 to 38.3) at 7 days and 36.2 (95% CI: 34.0 to 37.6) at 90 days. Using hypothetical cohort of 1,000 referrals to a stroke prevention clinic, it was estimated that 52% of patients would have ABCD2 score ≥4, and would require fast-track assessment. In this group there would be 16 recurrent strokes at day 7 and 27 at day 90, but 32% would be stroke mimics. Among persons with ABCD2 scores <4, requiring slow-tract assessment, there would be 5 recurrent stroke at day 7 and 5 at day 90, with 58% stroke mimics.
Perry et al. 2014 **Canada** **Observational**	NA	3,906 patients admitted to 8 ER departments over a 5-year period (2006-2011) ≥18 years diagnosed with TIA. Mean age was 68 years, 49.4% were male. Exclusion criteria: Confirmed stroke, admission to ER>7days following onset of symptoms, documented cause that was not TIA, treatment with t-PA	Standardized data collection of 49 clinical variables. The characteristics of patients who developed subsequent stroke and those who did not were compared and independent predictors of subsequent stroke were identified.	**Primary outcome:** Subsequent stroke within 7 days of TIA **Secondary outcomes:** Subsequent stroke within 2, 30 and 90 days	86 patients (2.2%) developed subsequent stroke within 7 days, 132 (3.4%) at 90 days. 12 variables were independently associated with subsequent stroke. 1 variable (history of vertigo) was significant associated with no progression to stroke. The adj ORs for each of the predictors ranged from 1.6 to 4.5. The area under ROC curve for the model was 0.77, 95% CI 0.73-0.82. The performance of the models was similar for risk of 2 and 90-day stroke. From these models, the Canadian TIA score was developed, and its performance was assessed using the same groups of patients. Items include: first TIA, symptoms persisting for ≥10 min. Hx of carotid stenosis, on antiplatelet therapy, Hx of gait disturbance, Hx of unilateral leg weakness, DBP

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings
					≥110 mmHg, dysarthria or aphasia, investigations in ER, AF on ECG, infarction on CT, elevated platelet count ≥400x10^9/L and blood glucose≥15 mmol/L. Total TIA scores range from -3 to 23. Using the TIA score, the estimated probabilities of having a subsequent stroke (within the range of scores -3 to 14, since no patients had a score >14) ranged from 0.01% to 27.6%
Coutts et al. 2012 **Canada** **Prospective cohort study**	N/A	510 patients (174 CT positive; 336 CT negative), mean age= 69 years, ≥18 years, with suspected focal TIA or symptoms lasting at least 5 minutes, and CT scan conducted within 24 hours. Exclusion criteria: low premorbid functioning (mRS≥2), thrombolytic treatment, and severe comorbidity that is likely to result in death.	Variables for prediction of recurrent stroke were derived from previous literature. Imaging outcomes were classified as CT/CTA positive or negative indicating a high risk and low risk phenotype respectively. Secondary analysis involved a comparison of CT to MRI. Imputation methods were used to account for missing MRI results (some patients had missing MRI) (n=90).	**Primary outcome**: Recurrent stroke. **Other outcomes:** Sensitivity and specificity of CT and MRI. Assessment time points: 90 days (recurrent stroke)	**Recurrent stroke**: 7.1% **Predictors of recurrent stroke:** Positive CT/CTA scan was the only predictive variable of recurrent stroke in the multivariate model. CT and MRI were found to be equal in their ability to predict recurrent stroke (P=0.09). **CT/CTA** Sensitivity: 67% (95% CI 49% to 81%) Specificity: 68% (95% CI 64% to 72%) **MRI/DWI** Sensitivity: 75% (95% CI 57% to 88%) Specificity: 43% (95% CI 39% to 48%) Immediate CT/CTA imaging findings (within 24 hours) were found to be predictive of recurrent stroke at 90 days.
Purroy et al. 2012 **Spain** **Prospective cohort study**	N/A	1137 patients from 30 centers admitted with TIA, with mRS score ≤2. Mean age was 68.6 years	Patients were prospectively scored on the clinical variables included in the following tools: 1. ABCD 2. $ABCD^2$ 3. $ABCD^2I$ 4. ABCD (+brain infarction) 5. $ABCD^3$ 6. ESRS 7. SPI-II 8. California Scale Each of these tools are used to	**Primary outcome:** Stroke within 7 and 90 days **Secondary outcomes:** Detection of large artery atherosclerosis on imaging	**Prevalence of recurrent stroke:** 2.6% of patients had a recurrent stroke within 7 days; 3.9% within 90 days. **Stroke within 7 days of index TIA**: The ABCD3 and ABCD3V offered the ability to predict stroke within 7 days of TIA (P=0.004; P<0.001), all others were unable to predict stroke risk beyond chance alone. **Stroke within 90 days of index TIA**: The ABCD3 and ABCD3V offered the ability to predict stroke within 90 days of TIA (P=0.015; P=0.003). All

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings
			assess the likelihood of recurrent stroke in patients diagnosed with TIA.		others were unable to predict stroke risk beyond chance alone (P>0.05). **Clinical predictors of stroke within 7 days**: Prior TIA (P<0.001) and large artery atherosclerosis (P=0.003). **Clinical predictors of stroke within 90 days**: Prior TIA (P=0.006), large artery atherosclerosis (P=0.018), and motor weakness (P=0.035).
Ferrari et al. 2010 **Austria** **Prospective study**	N/A	8,291 patients admitted with TIA or minor stroke and NIHSS score <4, included in the Austrian Stroke Unit registry Median age: 70 years (no deterioration group); 73 years (deterioration group).	Predictors of deterioration were assessed for patients registered in the Austrian stroke unit registry. Predictors included: age, sex, delay in seeking medical attention, risk factors (hypertension, diabetes, hyperlipidemia, smoking status), treatment regime (heparin, platelet inhibitors), complications (acute infection, cardiac decompensation, seizure, hemorrhaging, pulmonary embolism, DVT), etiology.	**Primary outcome**: Patient deterioration (≥2-point increase in NIHSS score). **Other outcomes**: Patient deterioration (≥4-point increase in NIHSS score). Assessment time points: admission to stroke unit, discharge from stroke unit (with 3-month follow-up phone call when necessary).	**Predictors of patient deterioration:** Hypertension: OR=1.5 (95% CI 1.1-2.1; P=0.005). Diabetes Mellitus: OR=1.5 (95% CI 1.2 to 2.0; P<0.001). Etiology: Cardioembolic stroke (OR=1.5 95% CI 1.1-2.2; P=0.014), Macroangiopathy (OR=2.0, 95% CI 1.4 to 2.7; P<0.001), Other known causes (OR=2.4; 95% CI 3.5 to 7.3). Acute infection: OR=5.1 (95% CI 3.5 to 7.3; P<0.001). Cardiac decompensation: OR=4.4 (95% CI 2.3 to 8.4). **Predictors of patient deterioration (≥4 point increase in NIHSS score):** The same predictors were identified as above. Cardioembolism became not significant – OR= 1.6 (95% CI 1.0 to 2.7; P=0.057).

Investigations/Monitoring for TIA and Non-Disabling Stroke

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings
Detection of Atrial Fibrillation					
Wachter et al. 2016 **Germany** **RCT**	CA: ☑ Blinding: Patient ☒ Assessor ☒	398 patients, >60 years admitted with acute ischemic stroke within 7 days of symptom onset, in sinus rhythm at	Patients were randomized to receive prolonged Holter ECG monitoring (10-days) and repeated at 3 and 6 months (n=200) vs. standard care (minimum of 24 hours of cardiac monitoring, n=198)	**Primary outcome:** Detection of newly diagnosed AF/flutter (≥30 sec) within 6 months and before stroke recurrence	Results from ISC 2016 presentation At 6 months, detection of AF was significantly higher in the prolonged monitoring group (13.5% vs. 4.5%; absolute difference 9%, 95% CI 3.5-14.6, p=0.002; NNS=11).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings
Finding Atrial Fibrillation in Stroke - Evaluation of Enhanced and Prolonged Holter Monitoring (FIND-AF)	ITT: ☑	admission and without history of AF, and a premorbid mRS score ≤2. Mean age was 73 years, 40.2% were female.		**Secondary outcomes:** Detection of newly diagnosed AF/flutter within 12 months, recurrent stroke or systemic embolism, and death	At 12 months, detection of AF was significantly higher in the prolonged monitoring group (13.5% vs. 6.1%; absolute difference 7.4%, 95% CI 1.6-13.2; p=0.02; NNS=13). There were no differences between groups in stroke recurrence (2.5 vs. 4.5%, p=0.28) or death (3.0 vs. 4.5%, p=0.45). There were no interactions based on sub group analyses based on age, sex, baseline NIHSS, CHADS-2 score, symptoms at admission and imaging (lacunar vs. non-lacunar)
Edwards et al. 2016 **Canada** **Retrospective study**	NA	17,398 consecutive patients presenting with first-ever stroke or TIA with motor or speech deficits to the ED of 12 designated stroke centres from 2003-2013 without a known history of AF in sinus rhythm. Mean age was 69 years, 54% were male, 75% of patients presented with a stroke, 25%, a TIA. 79% of patients hospitalized had a mRS score of 0-3.	The use of ambulatory ECG (Holter monitoring and 14-day loop recorders) to detect episodes of AF, was assessed.	**Primary outcome:** The number of patients who received a minimum of 24-hour Holter monitoring within 30 days of index event **Secondary outcomes:** The number of patients receiving single or multiple Holter studies for a maximum cumulative ECG monitoring duration of 24, 48, or >60 hours within 7, 30, or 90 days after index event, the number of patients receiving prolonged ECG monitoring with an event loop recorder within 7, 30, or 90 days after index event	5,318 patients (30.6%, 95% CI 29.8-31.4%) received at least 24-hour Holter monitoring within 30 days of the index event. 2,253 patients (12.9%, 95% CI 12.4-13.5%) underwent 48-hr Holter monitoring within 90 days of the index event. 25 patients (0.1%, 95% CI 0.0-0.3%) underwent >60-hr Holter monitoring within 90 days of the index event. 139 patients (0.8%, 95% CI 0.0-0.0%) underwent monitoring with event loop recording within 90 days of the index event. Factors associated with lower odds of undergoing Holter monitoring within 30 days of index event were: age <75 years, rural residence, moderately disabling stroke (mRS 4-5) and TIA as index event Factors associated with increased odds of undergoing Holter monitoring within 30 days of index event were: pre-morbid independence and admission to a registry hospital
Sposato et al. 2015	NA	50 studies, estimating the	Sub groups of studies were formed based on 4 phases of cardiac	**Primary outcome:** Proportion of patients	The results from the 11 studies (n=2,896) that initiated investigations during the Emergency

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings
Canada **Systematic review & meta-analysis**		proportion of patients diagnosed with atrial fibrillation following stroke or TIA, using 8 diagnostic methods: admission ECG, serial ECG, continuous inpatient ECG monitoring, continuous inpatient cardiac telemetry, Holter monitoring, mobile cardiac outpatient telemetry, external loop recording, and implantable loop recording. Mean age of included patients was 67 years, 57% were men.	monitoring: emergency room, in-hospital, first ambulatory period and second ambulatory period.	diagnosed with post-stroke AF	room (phase 1), which an ECG, reported an estimated 7.7% (95% CI 5.0-10.8%) of patients were diagnosed with AF.
Gladstone et al. 2014 **Canada** **RCT** ***Event Monitor Belt for Recording Atrial Fibrillation after a Cerebral Ischemic Event (EMBRACE)***	CA: ☑ Blinding: Patient ☒ Assessor ☒ ITT: ☑	572 patients ≥55 years without known atrial fibrillation (AF), who had sustained a cryptogenic ischemic stroke or TIA of undetermined cause following standardized testing (including 24-hr ECG), within the previous 6 months.	Patients were randomized (1:1) to undergo ambulatory ECG monitoring with a 30-day event-triggered loop recorder or one additional round of 24-hour Holter monitoring (control group).	**Primary outcome:** Occurrences of AF or atrial flutter ≥30 seconds in duration, detected during 90-day follow-up. **Secondary outcomes:** Anticoagulant use at 90 days, AF ≥30 seconds and ≥2.5 minutes in duration, and any AF	Patients were randomized an average of 75 days following qualifying event. The primary outcome was detected more frequently in patients in the enhanced monitoring group (16.1% vs. 3.2%, absolute difference =12.9%, 95% CI 8.0-17.6%, p<0.001, number need to screen [NNS] 8). AF ≥30 seconds was detected more frequently in patients in the enhanced monitoring group (15.5% vs. 2.5%, absolute difference =13.0%, 95% CI 8.4-17.6%, p<0.001, NNS=8). AF ≥2.5 minutes was detected more frequently in patients in the enhanced monitoring group (9.9%

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings
		Mean age: 73 yrs. 56% male, 63% of patients sustained an ischemic stroke, 37%, a TIA.			vs. 2.5%, absolute difference =7.4%, 95% CI 3.4-11.3%, p<0.001, NNS=14). A higher number of patients in the enhanced monitoring group were treated with anticoagulants (18.6% vs. 11.1%) and switched from antiplatelet to anticoagulant therapy (13.6% vs. 4.7%).
Sanna et al. 2014 **International** **RCT** ***Cryptogenic Stroke and Underlying AF (CRYSTAL-AF)***	CA: ☑ Blinding: Patient ☒ Assessor ☒ ITT: ☑	441 patients >40 years with no evidence of atrial fibrillation during at least 24 hours of ECG monitoring associated with a cryptogenic symptomatic TIA or cryptogenic ischemic stroke, sustained within 90 days of the event. Mean age: 61 yrs. 63% male	Patients were randomized (1:1) to received ECG monitoring on a schedule at the discretion of their treating physician or long-term monitoring with an insertable cardiac monitor (ICM) using the Reveal® XT device, inserted within 10 days of the event.	**Primary outcome:** Time to first detection of atrial fibrillation (lasting >30 seconds) within 6 months **Secondary outcome:** Time to first detection of atrial fibrillation at 12 months of follow-up, recurrent stroke or TIA, and the change in use of oral anticoagulant drugs For patients for patients in both groups were scheduled at 1, 6, and 12 months.	The mean time between the index event and randomization was 38 days. The majority of patients completed 18 months of follow-up. Maximum duration of follow-up was 36 months (n=48). At 6 months, the rate of detection of AF was significantly higher among patients assigned to the ICM group (8.9% vs. 1.4%, HR=6.4, 95% CI 1.9- 21.7, p<0.001). At 12 months, the rate of detection of AF was significantly higher among patients assigned to the ICM group (12.4% vs. 2.0%, HR=7.3, 95% CI 2.6- 20.8, p<0.001). The majority of patients completed 18 months of follow-up. Maximum duration of follow-up was 36 months (n=48). There were no significant interactions observed in subgroup analysis (age, sex, race or ethnic group, type of index event, presence or absence of patent foramen ovale, and $CHADS_2$. 2.4% of devices were removed due to infection at the insertion site or pocket erosion
Higgins et al. 2013 **UK** **RCT**	CA: ☑ Blinding: Patient ☒ Assessor ☑	100 patients admitted within 7 days of ischemic stroke, from 2 centres with no history of AF, presenting in sinus	Patients were randomized to receive standard practice (SP) investigations or SP + additional investigations, which included 7 days of additional non-invasive cardiac event monitoring. Patients in the SP group received standard practice cardiac	**Primary outcome:** Detection of paroxysmal atrial fibrillation (PAF) at 14 and 90 days	The detection of sustained PAF at 14 days was significantly higher in the group that received additional investigations (44% vs. 4%, p<0.001). The detection of any PAF at 14 days was significantly higher in the group that received additional investigations (18% vs. 2%, p<0.05)

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings
	ITT: ☑	rhythm. Mean age was 65.8 years, 56% were male	investigations for the detection of AF, at the discretion of the local physician.		The detection of sustained PAF at 90 days was not significantly higher in the group that received additional investigations (22% vs. 8%, p<0.09). The detection of any PAF at 90 days was higher in the group that received additional investigations (48% vs. 10%, p<0.001). Significantly more patients that received additional monitoring were started on anticoagulants for AF associated thromboembolic prophylaxis at day 14 (16% vs. 0%, p<0.01) and at day 90 (22% vs. 6%, p<0.05).
Flint et al. 2012 **Prospective cohort study** **US**	NA	239 patients referred for cardiac monitoring, a median of 29 days following ischemic stroke of unknown cause stroke. Mean age: 64.6 years Exclusion criteria: lacunar/small vessel syndrome, and/or stenosis of greater than 70%.	Cardiac monitoring involved the use of a 30-day electrocardiographic loop recorder (CardioPAL SAVI) that was mailed to patients for self-setup with guidance over the phone.	**Primary outcome:** Number of patients with paroxysmal atrial fibrillation (PAF) detection. **Secondary outcome**: Number of patients with a PAF event >30 seconds.	**PAF detection:** 26 patients (11.0%; 95% CI: 7.6% to 15.7%) experienced previously undiagnosed PAF during the 30-day monitoring. 45% of patients had PAF detection within the first 10 days, 31% from day 11 to 20 and 24% from Day 21 to 30. **Length of PAF:** 16 patients (6.7%) experienced PAF episodes of greater than 30 seconds in duration.
Douen et al. 2008 **Canada** **Prospective cohort study**	NA	144 patients were included (143 patients had serial ECGs completed; 126 patients had Holter monitoring).	Rates of AF detection were compared between the use of serial ECGs (up to 72 hours after admission) and a Holter monitor in an inpatient stroke unit setting.	**Primary outcome**: Detection of AF	No statistically significant difference in detection of AF was found between Holter and serial ECG monitoring. (P=0.25). **Detection of AF**: AF was identified in 15 new patients using serial ECG compared to baseline; a statistically significantly greater rate of diagnosis compared to baseline ECG findings (P=0.001). AF was identified in 9 new patients from baseline assessment using a Holter monitor.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings
					Together, serial ECG's and Holter monitoring identified 18 new cases of AF after baseline ECG assessment. The majority of these cases were identified within 72 hours (83%).
Transesophageal echocardiography (TEE)					
Katsanos et al. 2015 **Greece** **Systematic review & meta-analysis**	NA	35 studies including 5,772 participants with cryptogenic ischemic stroke or TIA who had undergone TEE investigations. Mean age was 54 years, 57% were male.	Cardiac conditions known to be associated with cerebral ischemia were identified using ASCOD criteria, including atherosclerosis, small-vessel disease, cardiac pathology, other causes and dissection	**Primary outcome:** Prevalence of cardioembolic causes	The most common TEE findings were: Atheromatosis in the ascending aorta/aortic arch (51.2%) PFO (43.2%) Complex aortic plaques (14%) Large PFO (19.5%) Atrial septal aneurysm (12.3%) ASA +PFO (14.5%) Conditions associated with cryptogenic ischemia were low including left atrial thrombus (3.0%), spontaneous echo contrast (3.8%) and intracardiac tumors (0.2%).
de Bruijn et al. 2006 **Netherlands** **Prospective cohort study**	NA	231 patients with recent stroke (all types) or TIA of unknown cause. Age: 192 patients were greater than 45 years; 39 patients were less than or equal to 45 years. Exclusion criteria: patients with contraindication to anticoagulation therapy.	All patients had a transesophageal echocardiography (TEE) followed by a transthoracic echocardiography (TTE). Identification of major and minor cardiac sources of embolism were compared between the two diagnostic tools. Subgroup analysis: Analysis also performed separately for patients older than 45 years and younger than 45 years of age.	**Outcomes**: Major (left atrium (LA) cavity thrombus, LA appendage thrombus, left ventrical (LV) thrombus, aortic thrombus, dilated cardiomyopathy, mitral valve stenosis) and minor (mitral valve prolapse, mitral annular calcification, calcified aortic stenosis, patent foramen ovale, spontaneous echo contrast, atrial septal aneurysms, LV aneurysm, aortic aneurysm, false tendon, aortic plaques, other) risk factors for cardiac embolism.	**Prevalence of potential sources of embolism**: 55% (127/231); 20% (46/231) of patients were assessed as having a major risk factor. **Comparison of TTE and TEE:** The detection of possible cardiac sources of embolism was significantly greater using TEE compared to TTE in both age groups (≤45 years; 10/39; P=0.002) (>45 years; 80/192; P<0.004).
Metabolic Monitoring					
Kisialiou et al. 2012	N/A	105 patients Mean age: 63.3	Patients were assessed for biomarkers on admission: glucose, albumin, TG, TC, LDL, HDL, INR,	**Primary outcomes**: Size of ischemic lesion (D1 - <1.5cm; D2 – 1.5 to 3cm;	*Results of the multivariate analysis adjusted for age and sex.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings
Italy **Prospective cohort study**		years Inclusion criteria: diagnosis of ischemic stroke within 24 hours. Exclusion criteria: other conditions (heart, kidney etc.), non-ischemic strokes, missing data.	PTT, platelets, fibrinogen, and erythrocyte sedimentation rate (ESR).	D3 - >3cm; D4 – non-confluent dimensions), location (anterior or posterior), stroke severity (NIHSS). Assessment time points: at admission (imaging), 7 days (NIHSS).	**Size of ischemic lesion:** **D1**: Greater odds of having a D1 lesion with a blood Albumin level of 3.4-3.8 compared to less than 2.9 (OR 5.250; 95% CI 1.351 to 20.396) and a triglyceride level of 111-162 compared to less than 78 (OR 9.000; 95% CI 2.487 to 32.567). **D2**: Lower odds of having a D2 lesion with blood albumin levels of 2.9-3.4, 3.4-3.8 and greater than 3.8 compared to a blood albumin level of less than 2.9 (OR 0.227; 0.164; 0.205). **D3**: Greater odds of having a D3 lesion when an ESR of greater than 30 compared to an ESR of less than 10 (OR 5.250), and a fibrinogen level of 368-462 compared to less than 303 (OR 5.500). Lower odds of having a D3 lesion with a platelet value of 256-323 compared to a platelet value of less than 189 (OR 0.059). **D4**: there was no statistically significant association between any of the blood biomarkers and a D4 lesion. **Location of stroke lesion**: No significant association with blood markers. **Stroke Severity**: high values for INR and PTT were associated with worse outcomes on the NIHSS (≥14; ≥7) (P=0.01; P=0.001). Better outcomes on the NIHSS were found when blood albumin levels were higher (P=0.006). Key Points: Select routine blood biomarkers were found to be associated with lesion size on admission to hospital and stroke severity at 7 days in the population under study. These values may be useful in patent management plans such as the administration of thrombolysis and predicting outcome.

Rapid Evaluation of TIA and Non-Disabling Stroke

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Paul et al. 2013 **UK** **Prospective Cohort Study**	NA	411 patients with first-ever minor stroke (NIHSS score ≤3 at assessment) who accessed either the stroke clinic (n=250) or acute hospital (n=161) were included. Mean age: Stroke clinic – 72.7 years, Acute hospital – 74.8 years.	Based on data from the Oxford vascular (OXVASC) study. The risk of recurrent stroke was compared between care locations. Regression analysis was used to determine if care location was a significant predictor of care costs at 30 days.	**Primary Outcome:** Risk of recurrent stroke and risk of hospitalization. **Secondary Outcomes**: Length of stay, resource costs. Assessment time points: 1 month, 6 months, 1 year and 5-year follow-up.	Risk of recurrent stroke: There were no significant differences in rates of recurrent stroke between patients seen in hospital compared to the clinic (p=0.61). Risk of hospitalization: There were no significant differences in risk of hospitalization between patients seen in hospital compared to the clinic (p=0.83). Costs of care (based on length of stay) were significantly lower for patients seen in the clinic compared to patients assessed in acute hospital.
Martinez-Martinez et al. 2013 **Spain** **Prospective Cohort Study**	NA	282 patients with low-moderate risk TIA (ABCD2 score ≤5) were managed either in-hospital (n=86) or in a TIA clinic (n=125). Mean age: 67.91 years – in-hospital, 65.73 years – TIA clinic.	In hospital evaluation and management included brain imaging, EKG, chest x-ray, echocardiography etc. and subsequent admission to the stroke unit (if TIA suspected) or neurology ward. Patients receiving evaluation and management at the TIA clinic received a referral from the hospital for next day assessment. A stroke neurologist reassessed patients including imaging, EKG, echocardiography, etc. Patients were admitted to hospital if there were any abnormal findings.	**Primary Outcome:** Risk of recurrent stroke at 7 days and 90 days. **Secondary Outcome:** Cost of hospital stay	Recurrence of stroke at 90 days: there were no significant differences in the 90-day risk of stroke or TIA recurrence between the in-hospital group and the in-clinic group (p=0.69, p=0.65). Costs: the cost of in-hospital management of TIA was close to 5 times higher than the TIA clinic costs (note: the costs of diagnostic and laboratory tests were not included in cost estimates.)
Luengo-Fernandez et al. 2009 **UK** **Prospective**	N/A	310 patients with TIA or non-disabling stroke accessed the EXPRESS clinic during phase I; 281 in phase II. Mean Age: 67% of	Two prospective cohorts of patients with suspected TIA who were referred (by family doctors) to the EXPRESS TIA clinic during either Phase I or Phase II were included.	**Primary Outcome:** Rate of stroke at 90 days. **Secondary Outcomes**: Hospital admissions, length of stay, hospital costs, patient disability, death.	90-day risk of stroke: There was a statistically significant reduction in risk of stroke at 90 days during Phase 2 vs. Phase 1 (8% vs. 2%, p=0.001) There were no significant differences in the number of hospital admissions between the two

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
cohort study		patients in both cohorts were <80 years old. .	Phase I of EXPRESS was a weekday only, appointment-based TIA clinic. Phase II of EXPRESS was implemented 30 months later with no appointments necessary – assessment was immediate.		groups (p=0.11). Length of stay in hospital and hospital costs were significantly lower in the Phase 2 group compared to the Phase 1 group (p=0.02, p=0.03). The odds of new death or disability and overall disability or death was significantly lower in the Phase 2 group (p=0.03, p=0.04).
Wu et al. 2009 **Canada** **Retrospective Case-Control Study**	N/A	189 patients who attended the rapid evaluation unit with TIA, admitted within 24 hours of symptom onset, between March 2002-April 2003 (intervention group) and 392 patients with a discharge diagnosis of TIA who were admitted to the Emergency Room in 2000 (control group) were included. Mean age: Intervention group – 67.5 years, control group – 71.0 years.	Logistic regression analysis was used to determine if being part of the intervention or control group predicted the odds of having a stroke within 90 days.	**Primary outcome**: Occurrence of stroke within 90 days of a TIA.	Occurrence of stroke: there was a significant reduction in the odds of stroke occurrence for patients in the intervention group (OR 0.43, p=0.029). Resource use and costs: Patients in the intervention group used significantly more resources than the control group within 30 days of admission (e.g. ECG, MRI, Echocardiogram, new statin drug, etc.) (p<0.05). The cost of managing patients was also significantly higher for the intervention group compared to the control group (p<0.001). (Note: These analyses do not control for differences in patient baseline characteristics between the groups.)
Lavallée et al. 2007 **France** **Prospective study**	NA	1,085 patients admitted between January 2003 and December 2005 to a newly formed rapid TIA assessment clinic for evaluation. 68% of patients had a history of hypertension, 58% had hypercholesterolaemia, and 87% had at least 1 vascular risk factor.	The SOS-TIA clinic accepted referrals by telephoned 24hr/7 day. Patients who had been seen by their physician or local ER, who were presumed to have had a minor stroke or TIA, with full recovery, were considered for admission. The clinic was designed to conduct standardized assessments within 4 hours of admission. Following assessments, patients were discharged home and the referring physician was	**Primary outcome:** Risk of stroke at 90 days, risks of stroke, myocardial infarction and vascular death at 1-year	87% of patients were seen by a neurologist within 24 hours of initial telephone call and 53% were seen within 24 hours of symptoms onset by a neurologist. 64% of patients had a confirmed TIA or minor stroke, 13% had possible TIA, and 22% had other diagnoses. Of those with confirmed or possible TIA, all patients started a stroke prevention program, 5% had urgent carotid revascularisation and 5% were treated for AF with anticoagulants

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			contacted to discuss diagnosis/treatments. The clinic was staffed with a stroke-prevention nurse. A vascular neurologist was available to discuss symptoms with the nurse; and was responsible for the decision to exclude patients who were judged to have non-ischaemic neurological transient symptoms (e.g. migraines)		74% of patients were sent home on the same day. The 90-day risk of stroke for all patients seen was 1.24%, (95% CI 0.72-2.12%), which was lower than predicted by their $ABCD^2$ score (5.96%). Among those seen within 24 hours of symptoms onset (n=552), the frequency of 90-day recurrent stroke was lower than that predicted by their $ABCD^2$ score (1.63%, 95% CI 0.85-3.12 vs. 6.49%). Among those with definite or possible TIA or minor stroke who had been seen within 24 hours of symptom onset (n=434), the 90-day stroke rate was 2.08%, (95% CI 1.09-3.96). The one-year risk of stroke for all patients was 1.95%; 95% CI: 1.26 to 3.00. The highest risk was among persons with TIA (new lesions 4.76%, 95% CI: 2.01 to 11.06). No persons with other diagnoses, sustained a stroke. The one-year risk of stroke, MI and vascular death for all patients was 2.54% (95% CI: 1.74 to 3.72), and was highest for those with TIA (new lesion (5.74%; 95% CI: 2.62 to 12.34).
Rothwell et al. 2007 **UK** **Prospective non-randomized controlled study (based on patients from the Oxford Vascular Study)**	N/A	591 patients were referred to the EXPRESS clinic with TIA or minor stroke. (310 in Phase 1 and 281 in phase 2). Patient age: 33% of patients were ≥ 80 years (Phase 1); 33% ≥ 80 years (Phase 2). Patients were identified	The EXPRESS clinic offered patients more timely access to outpatient services. The clinic required no appointments and treatment was initiated by the patients GP immediately (aspirin and clopidogrel) when possible. Outcomes were compared between phase 1 (non-immediate access) and phase	**Primary outcome**: Recurrent stroke within 90 days, risk of adverse event.	**Recurrent stroke**: The risk of recurrent stroke was significantly lower in patients who were referred to the clinic during Phase 2 (2.1% vs.10.3%, p=0.0001). **Adverse events (non-fatal stroke, MI, death):** The risk of adverse events was significantly lower in Phase 2 (3.6% vs. 11.9%, p=0.0002). **Time to prescribing treatment:** Significantly shorter delay in initiating a treatment prescription for patients referred to the clinic in phase 1

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
		from the Oxford Vascular study which recruits patients who have experienced a vascular event and who are registered with one of 63 general practitioners in the UK.	2 (immediate access) to the EXPRESS clinic.		(median 20 days) vs. phase 2 (median 1 day).

Components of Care for Outpatient Management of TIA and Non-Disabling Stroke

Study	Referral Source/Hours/Location/Staffing	Assessments				Follow-up
		Imaging	ECG	Echocardiography	Blood Tests	
Benavente et al. 2013 **Spain** **TIA Unit**	1. Urgent care physician 2. 24 hours/day 3. Emergency department of hospital 4. Not specified	☑ (CT – right away) (Transcranial Doppler imaging of brain arteries – if applicable – within one week)	☑ (right away)	☑ (Trans-esophageal ultrasound – if applicable – within one week)	☑ (right away)	Treatment started immediately: 1. Low Molecular weight heparin – 0.1mL/10kg/day 2. Anti-platelets (Aspirin – 100mg, subsequently changed thereafter) 3. Enalapril when blood pressure ≥220/120mmHg 4. Patients with 70-99% stenosis were referred immediately to a surgeon to assess stenting. Follow-up visit scheduled with a neurovascular specialist within 15 days, and after 6 and 12 months.
Van Rooij et al. 2012 **The Netherlands** **24/7 TIA-**	1. General practitioners 2. 24 hours/7 days per week 3. Acute day ward 4. Specialized nurse (for secondary prevention and education), neurology resident under supervision of	☑ (Brain Imaging - MRI or CT - within half day) (Cervical and intracranial arteries - within half day)	☑ (Within half day)	☒ (Not specified)	☑ (Within half day)	Treatment started immediately: 1. Antithrombotic or anticoagulant therapy, antihypertensive and lipid-lowering drugs where applicable. 2. Carotid surgery (>70% stenosis) –

Service	a neurologist					within 14 days. 3. Lifestyle modification (smoking, exercise, nutrition) Patients are contacted 2 weeks after initial visit, asked to attend the outpatient clinic after 4 weeks, and consultations are continued as needed. Involvement of the GP is facilitated through written correspondence and active engagement in the patient's treatment plan.
Banerjee et al. 2009 **United Kingdom** **FAST-TIA Clinic**	1. Primary care and in-hospital 2. Weekday only 3. Neurovascular clinic 4. Specialist nurse under the supervision of a neurologist	☑ (CT – same day)	☑ (Same day)	☑ (Trans-thoracic echocardiography – same day when possible)	☑ (Same day)	Treatment started immediately: 1. Lifestyle modification and driving advice provided 2. Anti-platelets (Aspirin – 300mg, subsequently changed thereafter) 3. Patients with 70-99% stenosis were referred immediately to a surgeon to assess stenting. Follow-up visits were scheduled for a week after admission and 3 months later.
Lavallee et al. 2007 **France** **SOS-TIA Clinic**	1. Family physicians, cardiologists, neurology, ophthalmology, emergency departments 2. 24 hours/7 days per week 3. Neurology department of hospital 4. Nurse (9am-5pm), On duty Neurologist (5pm-9am)	☑ (Brain Imaging - MRI or CT - within 4 hours) (Duplex ultrasonography – within 4 hours) (Transcranial Doppler imaging of brain arteries – within 4 hours)	☑ (Within 4 hours)	☑ (If cardiac source suspected – complete within 4 hours, otherwise not urgent)	☑ (Not urgent)	Referring physician contacted by neurologist to discuss diagnosis and treatment. Summary sent to family doctor with recommended management targets: 1. Blood Pressure (140/90mm Hg, 130/85mm Hg for patients with diabetes) 2. LDL 2.56mmol/L 3. Antithrombotic treatment (300-500mg Aspirin) Patient discharged home.
Rothwell et al. 2007 **United Kingdom**	1. Primary Care referral *(Appointment only)* 2. Weekday only 3. Hospital outpatient clinic 4. Not specified	☑ (Brain Imaging – CT – same day)	☑ (Same day)	☑ (Trans-thoracic/trans-oesophageal echocardiography –	☒ (Not stated)	Report sent to primary care physician and patients told to follow-up with them. Included: 1. Aspirin, or clopidogrel (both if within 48 hours or if at high risk)

EXPRESS – Phase I		(Carotid Ultrasound – within week)		when necessary – within week)		2. Simvastatin 3. Anticoagulation therapy
Rothwell et al. 2007 **United Kingdom** **EXPRESS – Phase II**	1. Primary Care referral *(No Appointment necessary)* 2. Weekday only 3. Hospital outpatient clinic 4. Not specified	☑ (Brain Imaging – CT – same day) (Carotid Ultrasound – within week)	☑ (Same day)	☑ (Trans-thoracic/trans-oesophageal echocardiography – when necessary – within week)	☒ (Not stated)	Treatment started immediately: 1. Aspirin (300mg in the clinic): For patients with tiA or stroke 2. Clopidogrel (300mg) *Plus other medication as necessary (based on the protocol above) with a 4-week prescription Report sent to primary care physician.

Tools for Assessing the Risk of Recurrent Stroke or TIA

Author/ Assessment Tool	Purpose of the tool Details of the validation study	Items and Scoring		Results of validation study
Rothwell et al. 2005 **ABCD Score**	**Purpose**: To determine the 7-day risk of stroke in patients with suspected or definitive TIA. **Sample**: 188 patients from the Oxford Vascular Study (OXVASC), a cohort of individuals who had experienced an initial or recurrent stroke or TIA.	1) **Age** (>60 years old)	1 point	Diagnostic standard: Occurrence of stroke or TIA within 7 days of index event. <u>Patients with suspected TIA:</u> ROC curve 0.91 (0.86-0.95) <u>Patients with probable or definitive TIA</u>: ROC curve 0.85 (0.78-0.91) <u>Patients with suspected TIA (not from the OXVASC study):</u> ROC curve 0.80 (0.72-0.89) Note: Sensitivity and Specificity not reported.
		2) **Blood Pressure** (Systolic >140mm Hg and/or Diastolic ≥90mm Hg)	1 point	
		3) **Clinical Features** (weakness, speech, or other)	1 point (2 points for unilateral weakness)	
		4) **Duration of symptoms** between 10-59min	1 point (2 points if ≥ 60min)	
			Total Possible Score: 6	
Perry et al. 2011 **ABCD^2 Score**	**Purpose**: To determine the 7 and 90-day risk of stroke in patients with suspected or definitive TIA. **Sample**: 2056 patients from the emergency department diagnosed as having a TIA.	1) **Age** (>60 years old)	1 point	Diagnostic standard: Occurrence of stroke or TIA within 7 or 90 days of index event. **Predicting stroke** <u>Patients with Score of **>2**</u> (designated high risk by the American Heart Association): Sensitivity **(7 days)**: 94.7% (82.7-98.5) Specificity **(7 days):** 12.5% (11.2-14.1)
		2) **Blood Pressure** (Systolic >140mm Hg and/or Diastolic ≥90mm Hg)	1 point	
		3) **Clinical Features** (weakness, speech, or other)	1 point (2 points for unilateral weakness)	

		4) **Duration of symptoms** between 10-59min	1 point (2 points if ≥ 60min)	Patients with Score of **>5** (designated high risk by original ABCD2 score): Sensitivity **(7 days)**: 31.6% (19.1-47.5) Specificity **(7 days):** 86.9% (85.3-88.3) Patients with Score of **>2** (designated high risk by the American Heart Association): Sensitivity **(90 days)**: 96.9% (89.3-99.1) Specificity (**90 days)**: 12.7% (11.3-14.3) Patients with Score of **>5** (designated high risk by original ABCD2 score): Sensitivity **(90 days)**: 29.2% (19.6-41.2) Specificity **(90 days):** 79.7% (77.9-81.4)
		5) **Diabetes**	1 point	
			Total Possible Score: 7	
Meng et al. 2011 **ABCD^2-I Score**	**Purpose**: To determine the 1-year risk of stroke in patients with TIA. **Sample**: 410 patients admitted to hospital with TIA.	1) **Age** (>60 years old)	1 point	Diagnostic standard: Occurrence of stroke or TIA within 1 year of index event. Risk of stroke or TIA: 27.07% **ABCD^2 Score** Patients with high risk of stroke (Score 6-7): ROC Curve 0.59 (0.53 – 0.65) **ABCD^2-I Score** Patients with high risk of stroke (Score 6-7): ROC Curve 0.77 (0.72-0.82) Note: Sensitivity and Specificity not reported.
		2) **Blood Pressure** (Systolic >140mm Hg and/or Diastolic ≥90mm Hg)	1 point	
		3) **Clinical Features** (weakness, speech, or other)	1 point (2 points for unilateral weakness)	
		4) **Duration of symptoms** between 10-59min	1 point (2 points if ≥ 60min)	
		5) **Diabetes**	1 point	
		6) **Imaging** (acute DWI hyperintensity)	3 points	
			Total Possible Score: 10	
Song et al. 2013 **ABCD^3-I Score**	**Purpose**: To determine the 90-day risk of stroke in patients with TIA.	1) **Age** (>60 years old)	1 point	Diagnostic standard: Occurrence of stroke within 90 days of index event. Risk of stroke or TIA: 12.1% **ABCD^2 Score** ROC Curve 0.694 (0.601 – 0.786)
		2) **Blood Pressure** (Systolic >140mm Hg and/or Diastolic ≥90mm Hg)	1 point	
		3) **Clinical Features** (weakness, speech, or other)	1 point (2 points for unilateral weakness)	
		4) **Duration of symptoms** between 10-59min	1 point (2 points if ≥ 60min)	

	Sample: 239 patients presenting to hospital with TIA.	5) **Diabetes**	1 point	**ABCD^3-I Score** ROC Curve 0.825 (0.752 – 0.898) Note: Sensitivity and Specificity not reported.
		6) **Imaging** (acute DWI hyperintensity)	3 points	
		7) **Dual TIA** (earlier TIA within 7 days)	2 points	
		8) **Stenosis** of internal carotid artery (ipsilateral **≥50%**)	2 points	
			Total Possible Score: 14	
Fitzek et al. 2011 **Essen Stroke Risk Score (ESRS)**	**Purpose**: To determine the 1-year risk of stroke in patients with acute ischemic stroke. **Sample**: 730 patients presenting to hospital with acute ischemic stroke.	1) **Age** ≥65 years	1 point (2 points if >75 years)	Diagnostic standard: Occurrence of stroke within 1 year of index event. Risk of stroke or TIA: 10.4% Patients with high risk of stroke (Score >2): ROC Curve 0.59 Note: Sensitivity and Specificity not reported.
		2) Arterial **Hypertension**	1 point	
		3) **Diabetes** Mellitus	1 point	
		4) Previous **Myocardial Infarction**	1 point	
		5) Other **cardiovascular diseases** (not atrial fibrillation)	1 point	
		6) **Peripheral arterial disease**	1 point	
		7) **Smoking** within 5 years	1 point	
		8) Previous **TIA or ischemic stroke**	1 point	
			Total Possible Score: 9	
Kernan et al. 2000 **Stroke Prognosis Instrument SPI-II**	**Purpose**: To determine the 2-year risk of stroke in patients with TIA or ischemic stroke **Sample**: Consisted of participants from 4 independent cohorts (current or former trials – WEST, UK-TIA, CAPRIE and NoMaSS)	1) **Congestive heart failure**	3 points	Diagnostic standard: Occurrence of stroke within 2 year of index event. Pooled risk of stroke or death from all 4 cohorts: Low Risk (Score 0-3) 10%; Middle Risk Group (Score 4-7) 19%; High Risk Group (Score 8-15) 315. **SPI-I Score** ROC Curve 0.59 (0.57-0.60) **SPI-II Score** ROC Curve 0.63 (0.62-0.65) Note: Sensitivity and Specificity not reported.
		2) **Diabetes**	3 points	
		3) **Prior Stroke**	3 points	
		4) **Age** >70 years	2 points	
		5) **Stroke** (vs. TIA for index event)	2 points	
		6) Severe **hypertension**	1 point	
		7) **Coronary Artery Disease**	1 point	
			Total Possible Score: 15	

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