

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Centre for Clinical Practice – Surveillance Programme

Clinical guideline

[CG 68 Stroke](#): Diagnosis and initial management of acute stroke and transient ischaemic attack (TIA)

Publication date

2008

Surveillance report for GE

May 2014

Key findings

			Potential impact on guidance	
			Yes	No
Evidence from evidence update				✓
Feedback from Guideline Development Group Chair				✓
Anti-discrimination and equalities considerations				✓
No update	Rapid update	Standard update	Transfer to static list	Change review cycle
✓				

Surveillance recommendation

GE is asked to consider the following proposals and the attached paper:

- CG68 stroke: diagnosis and initial management of acute stroke and TIA guidance should not be considered for an update at this time.
- The guideline [recommendation 1.4.1.1](#) incorporated from TA122 should be stood down and should cross refer to the technology appraisal which replaces TA122.

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Centre for Clinical Practice – Surveillance Programme

Surveillance review of CG 68 Stroke: Diagnosis and initial management of acute stroke and transient ischaemic attack (TIA)

Background information

Guideline issue date: 2008
3 year review: 2011 (no update)
NCC: NCGC

Main conclusions from previous surveillance review

1. CG68 previously underwent a surveillance review in 2011 when the review recommendation was that the guideline should not be considered for an update.

Current six year surveillance review

2. A literature search for systematic reviews was carried out between August 2011 (the end of the search period for the last review) and January 2014 and relevant abstracts were assessed. Clinical feedback on the guideline was obtained from 4 members of the GDG through a questionnaire.
3. No new evidence that may impact on existing recommendations was identified relating to any of the clinical areas within the guideline.

4. Half of the GDG that responded to the questionnaire felt that the guideline does not require an update at this time. The remaining GDG, including the Chair, stated the guideline should be updated due to its age. However, no specific evidence applicable to this review time point was provided that would indicate an impact on guideline recommendations.
5. A GDG member indicated that they thought the scope of the guideline should be extended to include guidance on what 'high quality stroke services' should provide, including topics such as staffing and consultant availability, scanning availability and access to thrombolysis. The 6 year process does not allow for areas outside the original guideline scope to be considered. Hence these areas will be considered again at the 8 year review.

On-going Research

6. A number of ongoing trials within the scope of the guideline have been identified these include: A NIHR funded trial to look at inter-professional team-work across stroke care pathways in two centres in UK, (due to complete in 2015), the AVERT3 trial on early mobilisation which is still recruiting, STASH trial on statin use in acute stroke which is still recruiting, and the NIHR STICH3 on early surgery.

Anti-discrimination and equalities considerations

7. None identified

Implications for other NICE programmes

8. None identified

Conclusion

9. Through the surveillance review of CG68, no new evidence which may potentially change the direction of guideline recommendations was identified.
10. NICE Technology Appraisal TA246 replaced TA122 which was incorporated within this guideline.
11. The guideline [recommendation 1.4.1.1](#) incorporated which was incorporated from TA122 should be stood down and replaced by cross referral to the new TA (TA246).

12. Due to ongoing research identified above this guideline should remain on the active surveillance list.

Surveillance recommendation

13. GE is asked to consider the proposal to not update the guideline at this time. GE are asked to note that as a 6 year surveillance review this 'no to update' proposal will not be consulted on.

Mark Baker – Centre Director

Sarah Willett – Associate Director

Katy Harrison– Technical Analyst

Centre for Clinical Practice

April2014

Appendix- Decision Matrix

Conclusions from previous review (3 year)	Impact at 3 years	Evidence summary of clinical area at 6 year and GDG/clinical perspective	Impact
5. The rapid recognition of symptoms and diagnosis 1.1.1.1-1.1.2.5			
68-01 Are emergency health professionals able to use a clinical assessment tool to accurately identify patients who have a suspected stroke or TIA?			
3 year review One RCT that agreed with recommendations was identified ¹ .	No new evidence was identified which would invalidate current guideline recommendations.		
68-02 Can scoring systems accurately predict those patients with suspected TIA who need urgent referral for specialist assessment, and whether this early (immediate) assessment improves outcome?			
3 year review Early versus late assessment of people with TIA, and identifying those at high risk of stroke One RCT that agreed with recommendations was identified ² . Scoring Systems Two systematic reviews that agreed with recommendations were identified ^{3, 4} .	No new evidence was identified which would invalidate current guideline recommendations.	Scoring systems Two systematic reviews were identified that support current recommendations ^{4,5}	New evidence is consistent with guideline recommendations.
6. Imaging in TIA and non-disabling stroke 1.2.1.1-1.2.4.3			
68-03 Which patients with suspected TIA should undergo brain imaging?			
No new evidence identified		No new evidence identified	
68-04 Does MR or CT provides the most information to guide treatment in those patients with TIA who require brain imaging?			
3 year review One systematic review and a cost-	No new evidence was identified which would invalidate current	No new evidence identified	

Conclusions from previous review (3 year)	Impact at 3 years	Evidence summary of clinical area at 6 year and GDG/clinical perspective	Impact
effectiveness analysis which were in line with recommendations were identified ^{6 7} .	guideline recommendations		
68-05 In which patients with suspected stroke/TIA should be referred for urgent carotid imaging?			
3 year review A Cochrane systematic review ⁸ , a systematic review, ⁹ a post hoc analysis ¹⁰ and a meta-analysis ¹¹ that support guideline recommendations were identified	No new evidence was identified which would invalidate current guideline recommendations.	No new evidence identified	
68-06 In which patients with symptomatic carotid stenosis should be referred for early interventional procedures?			
No new evidence identified		One systematic review was identified that supports current recommendations ¹² .	New evidence is consistent with guideline recommendations.
7. Specialist care in acute stroke 1.3.1.1-1.3.2.2			
68-07 Do patients who are rapidly admitted to a specialist stroke unit have better clinical outcomes than those admitted through a general ward?			
3 year review Two systematic reviews and three RCTs were identified that have addressed service delivery for patients with acute stroke ^{13 14 1,15 16} . All agreed with recommendations	No new evidence was identified which would invalidate current guideline recommendations.	One Cochrane systematic reviews and 2 systemic reviews were identified that supported guideline recommendations ¹⁷⁻¹⁹ . Clinical feedback indicated that the reorganisation of stroke services since the publication of the guideline means that services are provided in different ways across the NHS, and some services inevitably are more advanced than others. The GDG	New evidence is consistent with guideline recommendations.

Conclusions from previous review (3 year)	Impact at 3 years	Evidence summary of clinical area at 6 year and GDG/clinical perspective	Impact
		requested that recommendations about the principles underlying high quality stroke services (e.g. 24 hour specialist availability, availability of scanning out of hours, access to thrombolysis) should be made and indicated that there is a growing body of published evidence to support this. This is currently not covered by the guideline and hence is beyond the scope of this current 6 year review. This area will be looked at in the next surveillance review.	
68-08 How quickly brain imaging should be performed following an acute stroke?			
<p>3 year review</p> <p>A systematic review which compared the diagnostic accuracy of diffusion-weighted MRI (DWI) and CT scans for acute ischaemic stroke and estimated the diagnostic accuracy of MRI for acute haemorrhagic stroke was identified. ⁶ The authors concluded that DWI appeared to be more sensitive than CT for the early detection of ischaemic stroke in highly selected patients. However, the variability in the quality of included studies and the</p>	<p>No new evidence was identified which would invalidate current guideline recommendations.</p> <p>It is recommended that brain imaging should be performed immediately in patients with stroke that meet specific indications and as soon as possible in those who do not meet these criteria. Currently scan type is not detailed in the guideline for acute ischaemic stroke, but MRI (DWI) is</p>	No new evidence identified	

Conclusions from previous review (3 year)	Impact at 3 years	Evidence summary of clinical area at 6 year and GDG/clinical perspective	Impact
presence of spectrum and incorporation biases render the reliability and generalisability of observed results questionable.	recommended for TIA and non-disabling stroke (Section 6, R12). Limited evidence, which had methodological issues associated with it, was identified that indicated that MRI (DWI) was more sensitive than CT scans for acute ischaemic stroke. As such, there is currently insufficient consistent new evidence in this area of the guideline.		
8. Pharmacological treatments for people with acute stroke 1.4.1.1-1.4.4.2			
68-09 TA 122 Alteplase			
<u>3 year review</u> The pharmacological treatment of acute stroke by thrombolysis (TA122) was noted to be in need of update as various trials (including CLOTs2, AVERT3 and IST3) had published new relevant data that may result in changes to current recommendations. NICE technology appraisal (TA), guidance 122. There were 52 studies identified ²⁰⁻⁷¹ .		1 Cochrane and 4 systematic reviews ⁷²⁻⁷⁶ were identified that relate to thrombolysis (TA264).	The GDG highlighted the recent publication of the IST-3 trial which sought to determine whether a wider range of patients might benefit up from the use of tissue plasminogen activator to 6 h from stroke onset. The authors concluded that for the types of patient recruited in IST-3, despite the early hazards, thrombolysis within 6 h improved functional outcome. Benefit did not seem to be diminished in elderly patients. This trial could potentially impact on the TA264.
68-10 How safe and effective are antiplatelet agents and anticoagulants after an acute ischaemic stroke?			
Clinical effectiveness of clopidogrel and modified-release dipyridamole.	No new evidence that was not related to TA210 or TA210 was	Two systematic reviews related TA 210 were identified ^{90,91} .	New evidence not relating to TA210 or TA264 is consistent with guideline

Conclusions from previous review (3 year)	Impact at 3 years	Evidence summary of clinical area at 6 year and GDG/clinical perspective	Impact
<p>NICE technology appraisal guidance 210. There were 7 studies^{77,78-83} identified.</p> <p>Thrombolysis One RCT was identified that agreed with guideline recommendations⁸⁴.</p> <p>Aspirin and anticoagulant treatment A Cochrane systematic review and 3 RCTs that supported current recommendations were identified^{85,86,77, 87}.</p> <p>Anticoagulants Two Cochrane systematic reviews were identified that agreed with current recommendations^{88, 89}.</p>	<p>identified which would invalidate current guideline recommendations.</p> <p>The use of new anticoagulants (such as rivaroxaban or dabigatran by patients with atrial fibrillation (TAs are currently in development, publication expected early 2012) was noted as having a potential impact on the use of thrombolysis drugs in patients with acute stroke or on reversal of anticoagulation treatment in people with ICH.</p>	<p>Clinical feedback- Clopidogrel no longer under patent and price fallen dramatically; there therefore might be a difference in the antiplatelet recommendations- these are covered by the TA and hence will not impact the surveillance review decision.</p> <p>Antiplatelet treatment</p> <p>A systematic review and meta-analysis of 4 RCTs comparing the off label use of cilostazol with aspirin was identified⁹². Cilostazol was associated with a reduction in hemorrhagic stroke, a reduction in the composite end point of stroke, myocardial infarction, or vascular death and reduction in total haemorrhagic events in comparison to aspirin. However, there is no mention of reduction in ischaemic stroke, DVT or death or dependence at 1 month which are the primary outcomes for this question in the</p>	<p>recommendations.</p> <p>One GDG member indicated that there is new data on anticoagulation, (particularly new anticoagulants). However these were not named and have not been identified as part of the search.</p> <p>Clinical feedback indicated that there was new data on IA and clot retrieval use however this has not been identified in the current search and insufficient information was provided to identify these studies.</p>

Conclusions from previous review (3 year)	Impact at 3 years	Evidence summary of clinical area at 6 year and GDG/clinical perspective	Impact
		<p>guideline.</p> <p>Anticoagulant treatment One Cochrane systematic review and one systematic review were identified that were in line with current recommendations^{93,94}.</p> <p>Fibrinogen depleting agents An update of a Cochrane systematic review which looked at the use of two fibrinogen depleting agents (one off label and the other unlicensed in the UK) was identified that was in line with current guideline recommendations⁹⁵.</p> <p>Sonothrombosis Two studies on the use of sonothrombosis, an intervention currently not within CG68, were identified. The first a Cochrane systematic review found that patients treated with sonothrombolysis were less likely to be dead or disabled at</p>	

Conclusions from previous review (3 year)	Impact at 3 years	Evidence summary of clinical area at 6 year and GDG/clinical perspective	Impact
		<p>three months however the CI were wide and it is not clear if comparison was made to any other intervention⁹⁶. The second systematic review which included a heterogeneous mix of methods for sonothrombolysis found that, there was some evidence that sonothrombolysis associated with alteplase is safe and results in an increased rate of recanalization⁹⁷. This evidence base appears to be at an early stage with trials looking more at safety than efficacy. This area should be looked at again at the next review period but does not impact at present on guideline recommendations.</p>	
68-11 Should patients with acute venous stroke receive antiplatelet or anticoagulant treatment acutely?			
No new evidence identified		No new evidence identified	
68-12 Should patients with acute arterial dissection be treated with antiplatelets or anticoagulants?			
68-13 Should patients with acute stroke should be anticoagulated immediately or treated with antiplatelet agents?			
No new evidence identified		No new evidence identified	
68-14 How is it best to reverse anticoagulation in patients with haemorrhagic stroke?			
No new evidence identified		One systematic review which was in line with current recommendations was identified	New evidence is consistent with guideline recommendations.

Conclusions from previous review (3 year)	Impact at 3 years	Evidence summary of clinical area at 6 year and GDG/clinical perspective	Impact
98			
68-15 Is it safe to give anticoagulants to patients with acute stroke who have other comorbidities and who would normally require anticoagulation? What is the safety and efficacy of caval filters for deep vein thrombosis or pulmonary embolism?			
<p>3 year review A systematic review which agreed with current recommendations was identified⁹⁹. In addition the CLOTs RCT trial which investigated preventive options for DVT indicated that low dose low molecular weight heparin and long compression stockings were equally effective in preventing haematoma growth but that asymptomatic DVT was more common in patients who received the low molecular weight heparin in comparison to stockings¹⁰⁰.</p>	No new evidence was identified which would invalidate current guideline recommendations.	The GDG identified the recent CLOTS-3 on IPC to prevent DVT following stroke. This has already been reviewed for the VTE guideline CG92 which is to be updated to include this evidence.	No new evidence that would invalidate recommendation was identified.
68-16 Should patients with acute stroke should be give early treatment with statins?			
<p>3 year review A Cochrane systematic review and 2 RCTs , that were line with current guideline recommendations were identified^{101 102 103}.</p>		One Cochrane systematic review which was in line with current recommendations was identified ¹⁰⁴ .	New evidence is consistent with guideline recommendations.
9 Maintenance or restoration of homeostasis 1.5.1.1-1.5.3.2			
68-17			
<p>3 year review 2 systematic reviews and 2 RCTs that were in line with recommendations</p>	No new evidence was identified which would invalidate current guideline	None	Clinical feedback indicated that there may be trials relating to blood pressure particularly after haemorrhage. However

Conclusions from previous review (3 year)	Impact at 3 years	Evidence summary of clinical area at 6 year and GDG/clinical perspective	Impact
were identified ^{13 14 105 106}			insufficient information was provided to enable identification of these studies.
68-18 Should patients who are not hypoxic should be treated with oxygen supplementation?			
<p>3 year review One Cochrane systematic review and two RCTs were identified ^{107 108 109}. On the whole, the new information identified does not provide sufficient evidence that supplemental oxygen therapy has beneficial effects on clinical outcomes of patients with acute stroke. Therefore, the identified new evidence appears to support the current guideline recommendations that agreed with guideline recommendations.</p>	Overall, however, new evidence appears to support the current guideline recommendation	No new evidence identified	
68-19 Should patients with acute stroke who have mildly elevated blood glucose levels should have treatment with insulin?			
<p>3 year review Four RCTs were identified ^{110 111 112 113} that overall support the current guideline recommendations.</p>	Overall, however, new evidence appears to support the current guideline recommendation	One Cochrane systematic review and 1 systematic review were identified ^{114,115} . These both provided evidence that was in line with the evidence within CG68. Hence the new evidence is unlikely to impact recommendations.	New evidence is consistent with guideline recommendations.
68-20 Is manipulation of blood pressure safe or improves outcome in acute stroke?			
<p>3 year review Two Cochrane reviews, 2 systematic reviews and 6 RCTs were identified ^{116, 117 118 119 120 121 122 123 124, 125 126}</p>	New evidence supports guideline recommendations.	No new evidence identified	

Conclusions from previous review (3 year)	Impact at 3 years	Evidence summary of clinical area at 6 year and GDG/clinical perspective	Impact
<p>¹²⁷. The new evidence indicated that although these agents are effective at lowering blood pressure they do not effect clinical outcomes relating to stroke . This supports current guideline recommendations for antihypertensive treatment in people with acute stroke only if there is a hypertensive emergency due to a serious concomitant medical condition.</p>			
<p>10 Nutrition and hydration 1.6.1.1-1.6.1.4</p>			
<p>68-21 What is the best way to assess the presence and severity of swallowing difficulties after stroke?</p>			
<p>No new evidence identified</p>		<p>No new evidence identified</p>	
<p>68-22 When is the most appropriate time to initiate tube feeding in patients with acute stroke who cannot swallow safely?</p>			
<p>3 year review One RCT that agreed with recommendations was identified¹²⁸.</p>	<p>No new evidence was identified which would invalidate current guideline recommendations.</p>	<p>No new evidence identified</p>	
<p>68-23 Should patients who are not identified as being malnourished receive nutritional supplementation after stroke?</p>			
<p>3 year review A systematic review that agreed with recommendations was identified¹²⁹.</p>	<p>No new evidence was identified which would invalidate current guideline recommendations.</p>	<p>No new evidence identified</p>	
<p>11 Early mobilisation and optimum positioning of people with acute stroke 1.7.1.1.-1.7.1.2</p>			
<p>68-24 Should patients with acute stroke be mobilised early and whether there is any benefit in placing them in specific positions?</p>			
<p>3 year review A Cochrane systematic review and 6 studies^{130, 131, 132, 133, 134, 135, 136, 137, 138, 139} were identified that support current</p>	<p>No new evidence was identified which would invalidate current guideline recommendations.</p>	<p>No new evidence identified</p>	

Conclusions from previous review (3 year)	Impact at 3 years	Evidence summary of clinical area at 6 year and GDG/clinical perspective	Impact
guidance.			
12 Avoidance of aspiration pneumonia 1.8.1.1.			
68-25 How is it best to reduce the likelihood of patients with acute stroke developing aspiration pneumonia?			
No new evidence identified		No new evidence identified	
13 Surgery for people with acute stroke 1.9.1.1.-1.9.2.2			
68-26 Which patients with primary intracerebral haemorrhage should be referred for surgical evacuation?			
<p>3 year review</p> <p>Surgical referral for decompressive hemicraniectomy Two RCTs that support recommendations were identified^{140 141}.</p> <p>Other non-pharmacological methods for clot removal</p> <p>Percutaneous vascular interventions A Cochrane systematic review was identified which assessed the safety and efficacy of percutaneous vascular interventions in patients with acute ischaemic stroke. The review identified 4 trials all of which tested intra-arterial thrombolytic drugs and one trial used guidewire-mediated clot disruption in some patients randomised to the intervention group. The authors concluded that intervention results in a significant</p>	<p>No new evidence was identified which would invalidate current guideline recommendations.</p> <p>Other methods of non-pharmacological methods for clot removal in ischaemic stroke including percutaneous vascular interventions (mechanical endovascular therapy, intra-arterial thrombolytic drugs, guidewire-mediated clot disruption, transcranial laser therapy) and neurothrombectomy were not specifically reviewed in CG68. The current evidence is on the whole insufficient to establish the role of percutaneous vascular interventions for acute ischemic stroke in clinical practice. Some of the procedures still requiring RCT based evidence whilst others are</p>	<p>One update of a Cochrane systematic review and a systematic review were identified^{151,152}. These both supported guideline recommendations.</p>	<p>New evidence is consistent with guideline recommendations.</p>

Conclusions from previous review (3 year)	Impact at 3 years	Evidence summary of clinical area at 6 year and GDG/clinical perspective	Impact
<p>increase in the proportion of patients with a favourable outcome, despite a significant increase in intracranial haemorrhage. However, current data was insufficient to establish the role of percutaneous vascular intervention for acute ischemic stroke in clinical practice ¹⁴².</p> <p>Two systematic review and meta-analyses were identified. The first estimated the efficacy and safety of mechanical endovascular therapy and the meta-analysis of clinical outcomes showed a pooled estimate of 40% for a favourable outcome, 28% for mortality, and 8% for symptomatic intracranial haemorrhage. This was stated to be acceptable in regards to safety and efficacy in stroke patients ¹⁴³. The second review and meta-analysis for mechanical thrombectomy in the treatment of ischemic stroke indicated that percutaneous mechanical embolectomy for treatment of acute ischemic stroke was feasible and provides an option for some patients seen after the interval for administration of intravenous tissue plasminogen activator therapy has</p>	<p>equivocal to their effectiveness.</p>		

Conclusions from previous review (3 year)	Impact at 3 years	Evidence summary of clinical area at 6 year and GDG/clinical perspective	Impact
<p>elapsed¹⁴⁴.</p> <p>Two RCTs of transcranial laser therapy for acute ischemic stroke within 24 hours of onset were identified^{145, 146}. The first RCT indicated that the technique was safe but did not show significant efficacy whereas the second smaller RCT indicated that this technique was effective.</p> <p>A novel catheter treatment (NeuroFlo) did not show efficacy at the end point of the study in comparison to standard care in patients with acute ischaemic stroke in one RCT¹⁴⁷.</p> <p>Two cost–effectiveness studies for mechanical clot removal or disruption compared to standard therapy in patients who were ineligible for tissue plasminogen activator were identified^{148, 149}. A cost utility analysis which examined mechanical clot removal or disruption with angioplasty for acute ischemic stroke concluded that on the basis of available data (no RCTs), mechanical therapies in qualified patients with acute stroke beyond the window for i.v. alteplase appear to be</p>			

Conclusions from previous review (3 year)	Impact at 3 years	Evidence summary of clinical area at 6 year and GDG/clinical perspective	Impact
<p>cost-effective however the results were sensitive to several assumptions¹⁴⁸. A Markov cost-effectiveness model which compared the health benefits and costs associated with mechanical thrombectomy compared with standard medical therapy indicated that this treatment was cost-effective however the results require validation with RCT data¹⁴⁹.</p> <p>Neurothrombectomy</p> <p>A review was identified that investigated the evidence for the use of neurothrombectomy in patients with acute ischemic stroke¹⁵⁰. Successful recanalization, rates of harm, intracranial haemorrhage, vessel perforation or dissection showed wide variation by device (MERCI Retriever or the Penumbra System) and between trials. As most available data are from single-group or non-comparative studies the routine use of these devices still requires further investigation.</p>			
Research Recommendations			

Conclusions from previous review (3 year)	Impact at 3 years	Evidence summary of clinical area at 6 year and GDG/clinical perspective	Impact
<u>Safety and efficacy of carotid stenting:- What is the safety and efficacy of carotid stenting compared with carotid endarterectomy when these procedures are carried out within 2 weeks of [transient ischaemic attack] (TIA) or recovered stroke?</u>			
No new evidence		No new evidence	
<u>Blood pressure control:- How safe and effective is the early manipulation of blood pressure after stroke?</u>			
No new evidence		No new evidence	
<u>Early mobilisation and optimum positioning of people with acute stroke:- How safe and effective is very early mobilisation delivered by appropriately trained healthcare professionals after stroke?</u>			
See section 68-24 above		No new evidence	
<u>Aspirin treatment in acute ischaemic stroke:- Should a person who has a stroke or a TIA and is already taking aspirin be prescribed the same or an increased dose of aspirin after the stroke?</u>			
No new evidence		No new evidence	
<u>Aspirin and anticoagulant treatment for acute ischaemic stroke:- Does modified-release dipyridamole or clopidogrel with aspirin improve outcome compared with aspirin alone when administered early after acute ischaemic stroke?</u>			
Covered by TA210			
<u>Avoidance of aspiration pneumonia:- Does the withdrawal of oral liquids or the use of modified (thickened) oral fluids prevent the development of aspiration pneumonia after an acute stroke?</u>			
No new evidence		No new evidence	

References

1. De LA, Toni D, Lauria L et al. (2009) An emergency clinical pathway for stroke patients--results of a cluster randomised trial (isrctn41456865). BMC Health Services Research 9:14.

2. Ross MA, Compton S, Medado P et al. (2007) An emergency department diagnostic protocol for patients with transient ischemic attack: a randomized controlled trial. *Annals of Emergency Medicine* 50:109-119.
3. Giles MF and Rothwell PM. (2010) Systematic review and pooled analysis of published and unpublished validations of the ABCD and ABCD2 transient ischemic attack risk scores. *Stroke* 41:667-673.
4. Galvin R, Geraghty C, Motterlini N et al. (2011) Prognostic value of the ABCD2 clinical prediction rule: A systematic review and meta-analysis. *Family Practice* 28:366-376.
5. Sanders LM, Srikanth VK, Blacker DJ et al. (4-9-2012) Performance of the ABCD2 score for stroke risk post TIA: meta-analysis and probability modeling. *Neurology* 79:971-980.
6. Brazzelli M, Sandercock PA, Chappell FM et al. (2009) Magnetic resonance imaging versus computed tomography for detection of acute vascular lesions in patients presenting with stroke symptoms. [Review] [155 refs]. *Cochrane Database of Systematic Reviews* CD007424.
7. Tholen AT, de MC, Genders TS et al. (2010) Suspected carotid artery stenosis: cost-effectiveness of CT angiography in work-up of patients with recent TIA or minor ischemic stroke. *Radiology* 256:585-597.
8. Rerkasem K and Rothwell PM. (2011) Carotid endarterectomy for symptomatic carotid stenosis. *Cochrane database of systematic reviews (Online)* 4.
9. Rerkasem K and Rothwell PM. (2009) Systematic review of the operative risks of carotid endarterectomy for recently symptomatic stenosis in relation to the timing of surgery. *Stroke* 40:e564-e572.
10. Stingele R, Berger J, Alfke K et al. (2008) Clinical and angiographic risk factors for stroke and death within 30 days after carotid endarterectomy and stent-protected angioplasty: a subanalysis of the SPACE study. *Lancet Neurology* 7:216-222.
11. Carotid Stenting TC, Bonati LH, Dobson J et al. (25-9-2010) Short-term outcome after stenting versus endarterectomy for symptomatic carotid stenosis: a preplanned meta-analysis of individual patient data. *Lancet* 376:1062-1073.

12. Gulli G, Marquardt L, Rothwell PM et al. (2013) Stroke risk after posterior circulation stroke/transient ischemic attack and its relationship to site of vertebrobasilar stenosis: pooled data analysis from prospective studies. [Review]. *Stroke* 44:598-604.
13. Govan L, Langhorne P, Weir CJ et al. (2007) Does the prevention of complications explain the survival benefit of organized inpatient (stroke unit) care?: further analysis of a systematic review. *Stroke* 38:2536-2540.
14. Middleton S, McElduff P, Ward J et al. (12-11-2011) Implementation of evidence-based treatment protocols to manage fever, hyperglycaemia, and swallowing dysfunction in acute stroke (QASC): a cluster randomised controlled trial. *Lancet* 378:1699-1706.
15. Wang ZM, Wang P, Chen J et al. (2008) [Application of stroke rehabilitation unit in municipal hospitals during the acute phase of cerebral infarction]. *Zhonghua liu xing bing xue za zhi = Zhonghua liuxingbingxue zazhi* 29:724-725.
16. Price CI, Clement F, Gray J et al. (2009) Systematic review of stroke thrombolysis service configuration. [Review] [79 refs]. *Expert Review of Neurotherapeutics* 9:211-233.
17. Organised inpatient (stroke unit) care for stroke [Systematic Review]. *Cochrane Database of Systematic Reviews* 2013;(9) .
18. Chan DK, Cordato D, O'Rourke F et al. (2013) Comprehensive stroke units: a review of comparative evidence and experience. [Review]. *International Journal of Stroke* 8:260-264.
19. Langhorne P, Fearon P, Ronning OM et al. (2013) Stroke unit care benefits patients with intracerebral hemorrhage: systematic review and meta-analysis. [Review]. *Stroke* 44:3044-3049.
20. Ahmed N, Wahlgren N, Grond M et al. (2010) Implementation and outcome of thrombolysis with alteplase 3-4.5 h after an acute stroke: an updated analysis from SITS-ISTR. *Lancet Neurology* 9:866-874.
21. Alexandrov AV, Mikulik R, Ribo M et al. (2008) A pilot randomized clinical safety study of sonothrombolysis augmentation with ultrasound-activated perflutren-lipid microspheres for acute ischemic stroke. *Stroke* 39:1464-1469.

22. Bhatnagar P, Sinha D, Parker RA et al. (2011) Intravenous thrombolysis in acute ischaemic stroke: a systematic review and meta-analysis to aid decision making in patients over 80 years of age. *Journal of Neurology, Neurosurgery & Psychiatry* 82:712-717.
23. Bluhmki E, Chamorro A, Davalos A et al. (2009) Stroke treatment with alteplase given 3.0-4.5 h after onset of acute ischaemic stroke (ECASS III): additional outcomes and subgroup analysis of a randomised controlled trial. *Lancet Neurology* 8:1095-1102.
24. Carpenter CR, Keim SM, Milne WK et al. (2011) Thrombolytic therapy for acute ischemic stroke beyond three hours. *Journal of Emergency Medicine* 40:82-92.
25. Chao A-C, Hsu H-Y, Chung C-P et al. (2010) Outcomes of thrombolytic therapy for acute ischemic stroke in Chinese patients: The Taiwan thrombolytic therapy for acute ischemic stroke (TTT-AIS) study. *Stroke* 41:885-890.
26. Cronin CA. (2010) Intravenous tissue plasminogen activator for stroke: a review of the ECASS III results in relation to prior clinical trials. [Review] [28 refs]. *Journal of Emergency Medicine* 38:99-105.
27. Davis SM, Donnan GA, Parsons MW et al. (2008) Effects of alteplase beyond 3 h after stroke in the Echoplanar Imaging Thrombolytic Evaluation Trial (EPITHET): a placebo-controlled randomised trial. *Lancet Neurology* 7:299-309.
28. De Silva DA, Fink JN, Christensen S et al. (2009) Assessing reperfusion and recanalization as markers of clinical outcomes after intravenous thrombolysis in the echoplanar imaging thrombolytic evaluation trial (EPITHET). *Stroke; a journal of cerebral circulation* 40:2872-2874.
29. De Silva DA, Brekenfeld C, Ebinger M et al. (2010) The benefits of intravenous thrombolysis relate to the site of baseline arterial occlusion in the echoplanar imaging thrombolytic evaluation trial (EPITHET). *Stroke* 41:295-299.
30. De Silva DA, Ebinger M, Christensen S et al. (2010) Baseline diabetic status and admission blood glucose were poor prognostic factors in the EPITHET trial. *Cerebrovascular Diseases* 29:14-21.

31. Demaerschak BM, Hwang H-M, and Leung G. (2010) Cost analysis review of stroke centers, telestroke, and rt-PA. *American Journal of Managed Care* 16:537-544.
32. Demchuk AM, Khan F, Hill MD et al. (2008) Importance of leukoaraiosis on CT for tissue plasminogen activator decision making: Evaluation of the NINDS rt-PA stroke study. *Cerebrovascular Diseases* 26:120-125.
33. Dharmasaroja PA and Pattaraarchachai J. (2011) Low vs standard dose of recombinant tissue plasminogen activator in treating East Asian patients with acute ischemic stroke. *Neurology India* 59:180-184.
34. Ebinger M, Iwanaga T, Prosser JF et al. (2009) Clinical-diffusion mismatch and benefit from thrombolysis 3 to 6 hours after acute stroke. *Stroke* 40:2572-2574.
35. Eggers J, Konig IR, Koch B et al. (2008) Sonothrombolysis with transcranial color-coded sonography and recombinant tissue-type plasminogen activator in acute middle cerebral artery main stem occlusion: results from a randomized study. *Stroke* 39:1470-1475.
36. Ehlers L, Muskens WM, Jensen LG et al. (2008) National use of thrombolysis with alteplase for acute ischaemic stroke via telemedicine in Denmark: a model of budgetary impact and cost effectiveness. *CNS Drugs* 22:73-81.
37. Elkind MS, Prabhakaran S, Pittman J et al. (2007) Sex as a predictor of outcomes in patients treated with thrombolysis for acute stroke. *Neurology* 68:842-848.
38. Georgiadis AL, Memon MZ, Shah QA et al. (2011) Comparison of partial (.6 mg/kg) versus full-dose (.9 mg/kg) intravenous recombinant tissue plasminogen activator followed by endovascular treatment for acute ischemic stroke: a meta-analysis. *Journal of Neuroimaging* 21:113-120.
39. Hacke W, Kaste M, Bluhmki E et al. (25-9-2008) Thrombolysis with alteplase 3 to 4.5 hours after acute ischemic stroke. *New England Journal of Medicine* 359:1317-1329.
40. Haley EC, Jr., Thompson JL, Grotta JC et al. (2010) Phase IIB/III trial of tenecteplase in acute ischemic stroke: results of a prematurely terminated randomized clinical trial. *Stroke* 41:707-711.

41. Johnston SC. (2010) The economic case for new stroke thrombolytics. [Review]. *Stroke* 41:Suppl-62.
42. Jovanovic DR, Beslac-Bumbasirevic L, Budimkic M et al. (2009) Do women benefit more from systemic thrombolysis in acute ischemic stroke? A Serbian experience with thrombolysis in ischemic stroke (SETIS) study. *Clinical Neurology & Neurosurgery* 111:729-732.
43. Jung KT, Shin DW, Lee KJ et al. (2010) Cost-effectiveness of recombinant tissue plasminogen activator in the management of acute ischemic stroke: a systematic review. *Journal of Clinical Neurology* 6:117-126.
44. Kent DM, Buchan AM, and Hill MD. (30-9-2008) The gender effect in stroke thrombolysis: of CASES, controls, and treatment-effect modification. *Neurology* 71:1080-1083.
45. Kim AS, Nguyen-Huynh M, and Johnston SC. (2011) A cost-utility analysis of mechanical thrombectomy as an adjunct to intravenous tissue-type plasminogen activator for acute large-vessel ischemic stroke. *Stroke* 42:2013-2018.
46. Lansberg MG, Bluhmki E, and Thijs VN. (2009) Efficacy and safety of tissue plasminogen activator 3 to 4.5 hours after acute ischemic stroke: a metaanalysis. *Stroke* 40:2438-2441.
47. Lee M, Hong KS, and Saver JL. (2010) Efficacy of intra-arterial fibrinolysis for acute ischemic stroke: meta-analysis of randomized controlled trials. *Stroke* 41:932-937.
48. Lees KR, Bluhmki E, von KR et al. (15-5-2010) Time to treatment with intravenous alteplase and outcome in stroke: an updated pooled analysis of ECASS, ATLANTIS, NINDS, and EPITHET trials. *Lancet* 375:1695-1703.
49. Lou M and Selim M. (2009) Does body weight influence the response to intravenous tissue plasminogen activator in stroke patients? *Cerebrovascular Diseases* 27:84-90.
50. Maiser SJ, Georgiadis AL, Suri MF et al. (2011) Intravenous recombinant tissue plasminogen activator administered after 3 h following onset of ischaemic stroke: a metaanalysis. [Review]. *International Journal of Stroke* 6:25-32.

51. Mikulik R, Dusek L, Hill MD et al. (2010) Pattern of response of National Institutes of Health Stroke Scale components to early recanalization in the CLOTBUST trial. *Stroke* 41:466-470.
52. Molina CA, Barreto AD, Tsivgoulis G et al. (2009) Transcranial ultrasound in clinical sonothrombolysis (TUCSON) trial. *Annals of Neurology* 66:28-38.
53. Nichols C, Khoury J, Brott T et al. (2008) Intravenous recombinant tissue plasminogen activator improves arterial recanalization rates and reduces infarct volumes in patients with hyperdense artery sign on baseline computed tomography. *Journal of Stroke & Cerebrovascular Diseases* 17:64-68.
54. Pancioli AM, Broderick J, Brott T et al. (2008) The combined approach to lysis utilizing eptifibatid and rt-PA in acute ischemic stroke: the CLEAR stroke trial. *Stroke* 39:3268-3276.
55. Parsons MW, Christensen S, McElduff P et al. (2010) Pretreatment diffusion- and perfusion-MR lesion volumes have a crucial influence on clinical response to stroke thrombolysis. *Journal of Cerebral Blood Flow & Metabolism* 30:1214-1225.
56. Poncyłjusz W, Falkowski A, Kojder I et al. (2007) Treatment of acute ischemic brain infarction with the assistance of local intraarterial thrombolysis with recombinant tissue-type plasminogen activator. *Acta radiologica (Stockholm, Sweden : 1987)* 48:774-780.
57. Reeves M, Bhatt A, Jajou P et al. (2009) Sex differences in the use of intravenous rt-PA thrombolysis treatment for acute ischemic stroke: a meta-analysis. [Review] [42 refs]. *Stroke* 40:1743-1749.
58. Rhoney DH, Coplin WM, Lin Y et al. (2010) Time of day, outcome, and response to thrombolytic therapy: the National Institute of Neurological Disorders and Stroke Recombinant Tissue Plasminogen Activator Stroke Trial experience. *Journal of Stroke & Cerebrovascular Diseases* 19:40-48.
59. Sen S, Huang DY, Akhavan O et al. (2009) IV vs. IA TPA in acute ischemic stroke with CT angiographic evidence of major vessel occlusion: a feasibility study. *Neurocritical Care* 11:76-81.

60. Sena ES, Briscoe CL, Howells DW et al. (2010) Factors affecting the apparent efficacy and safety of tissue plasminogen activator in thrombotic occlusion models of stroke: systematic review and meta-analysis. [Review]. *Journal of Cerebral Blood Flow & Metabolism* 30:1905-1913.
61. Skoloudik D, Fadrna T, Roubec M et al. (2010) Changes in hemocoagulation in acute stroke patients after one-hour sonothrombolysis using a diagnostic probe. *Ultrasound in Medicine & Biology* 36:1052-1059.
62. Tiraboschi P, Candelise L, del ZG et al. (2010) Intra-arterial or intravenous thrombolysis for acute ischemic stroke? The SYNTHESIS pilot trial. *Journal of NeuroInterventional Surgery* 2:74-79.
63. Tsivgoulis G, Eggers J, Ribo M et al. (2010) Safety and efficacy of ultrasound-enhanced thrombolysis: A comprehensive review and meta-analysis of randomized and nonrandomized studies. *Stroke* 41:280-287.
64. Wahlgren N, Ahmed N, Eriksson N et al. (2008) Multivariable analysis of outcome predictors and adjustment of main outcome results to baseline data profile in randomized controlled trials: Safe Implementation of Thrombolysis in Stroke-MOnitoring Study (SITS-MOST). *Stroke* 39:3316-3322.
65. Wahlgren N, Ahmed N, Davalos A et al. (11-10-2008) Thrombolysis with alteplase 3-4.5 h after acute ischaemic stroke (SITS-ISTR): an observational study. *Lancet* 372:1303-1309.
66. Wardlaw JM, Murray V, Berge E et al. (2009) Thrombolysis for acute ischaemic stroke. [Review] [148 refs][Update of *Cochrane Database Syst Rev.* 2003;(3):CD000213; PMID: 12917889]. *Cochrane Database of Systematic Reviews* CD000213.
67. Wolfe T, Suarez JI, Tarr RW et al. (2008) Comparison of Combined Venous and Arterial Thrombolysis with Primary Arterial Therapy Using Recombinant Tissue Plasminogen Activator in Acute Ischemic Stroke. *Journal of Stroke and Cerebrovascular Diseases* 17:121-128.
68. Yong M, Diener HC, Kaste M et al. (2007) Long-term outcome as function of blood pressure in acute ischemic stroke and effects of thrombolysis. *Cerebrovascular Diseases* 24:349-354.

69. Yong M and Kaste M. (2008) Association of characteristics of blood pressure profiles and stroke outcomes in the ECASS-II trial. *Stroke* 39:366-372.
70. Fields JD, Khatri P, Nesbit GM et al. (2011) Meta-analysis of randomized intra-arterial thrombolytic trials for the treatment of acute stroke due to middle cerebral artery occlusion. *Journal of NeuroInterventional Surgery* 3:151-155.
71. Dentali F, Squizzato A, Gianni M et al. (3-11-2010) Safety of thrombolysis in cerebral venous thrombosis. A systematic review of the literature. [Review]. *Thrombosis & Haemostasis* 104:1055-1062.
72. Li B-HD, X. (2013) Meta-analysis of clinical outcomes of intravenous recombinant tissue plasminogen activator for acute ischemic stroke: Within 3 hours versus 3-4.5 hours. *Current Medical Research and Opinion* 29:1105-1114.
73. Mazighi M, Meseguer E, Labreuche J et al. (2012) Bridging therapy in acute ischemic stroke: a systematic review and meta-analysis. [Review]. *Stroke* 43:1302-1308.
74. Wardlaw JM, Murray V, Berge E et al. (23-6-2012) Recombinant tissue plasminogen activator for acute ischaemic stroke: an updated systematic review and meta-analysis. [Review]. *Lancet* 379:2364-2372.
75. Wardlaw JM, Koumellis P, and Liu M. Thrombolysis (different doses, routes of administration and agents) for acute ischaemic stroke [Systematic Review]. *Cochrane Database of Systematic Reviews* 2013;(5) .
76. Whiteley WN, Slot KB, Fernandes P et al. (2012) Risk factors for intracranial hemorrhage in acute ischemic stroke patients treated with recombinant tissue plasminogen activator: a systematic review and meta-analysis of 55 studies. [Review]. *Stroke* 43:2904-2909.
77. King A, Bath PM, and Markus HS. (2011) Clopidogrel versus dipyridamole in addition to aspirin in reducing embolization detected with ambulatory transcranial Doppler: a randomized trial. *Stroke* 42:650-655.
78. Halkes PH, Gray LJ, Bath PM et al. (2008) Dipyridamole plus aspirin versus aspirin alone in secondary prevention after TIA or stroke: a meta-analysis by risk. *Journal of Neurology, Neurosurgery & Psychiatry* 79:1218-1223.

79. Greenhalgh J, Bagust A, Boland A et al. (2011) Clopidogrel and modified-release dipyridamole for the prevention of occlusive vascular events (review of Technology Appraisal No. 90): a systematic review and economic analysis. *Health Technology Assessment (Winchester, England)* 15:1-178.
80. Dengler R, Diener HC, Schwartz A et al. (2010) Early treatment with aspirin plus extended-release dipyridamole for transient ischaemic attack or ischaemic stroke within 24 h of symptom onset (EARLY trial): a randomised, open-label, blinded-endpoint trial. *Lancet Neurology* 9:159-166.
81. Tsai NW, Chang WN, Shaw CF et al. (2010) Serial change in platelet activation markers with aspirin and clopidogrel after acute ischemic stroke. *Clinical Neuropharmacology* 33:40-45.
82. Wong KS, Chen C, Fu J et al. (2010) Clopidogrel plus aspirin versus aspirin alone for reducing embolisation in patients with acute symptomatic cerebral or carotid artery stenosis (CLAIR study): a randomised, open-label, blinded-endpoint trial. *Lancet Neurology* 9:489-497.
83. Bath PM, Cotton D, Martin RH et al. (2010) Effect of combined aspirin and extended-release dipyridamole versus clopidogrel on functional outcome and recurrence in acute, mild ischemic stroke: PROFESS subgroup analysis. *Stroke* 41:732-738.
84. Hacke W, Furlan AJ, Al-Rawi Y et al. (2009) Intravenous desmoteplase in patients with acute ischaemic stroke selected by MRI perfusion-diffusion weighted imaging or perfusion CT (DIAS-2): a prospective, randomised, double-blind, placebo-controlled study. *Lancet Neurology* 8:141-150.
85. Sandercock PA, Counsell C, Gubitz GJ et al. (2008) Antiplatelet therapy for acute ischaemic stroke. [Review] [77 refs][Update of Cochrane Database Syst Rev. 2003;(2):CD000029; PMID: 12804384]. *Cochrane Database of Systematic Reviews* CD000029.
86. Lee Y-S, Bae H-J, Kang D-W et al. (2011) Cilostazol in acute ischemic stroke treatment (CAIST Trial): A randomized double-blind non-inferiority trial. *Cerebrovascular Diseases* 32:65-71.
87. Adams HP, Jr., Leira EC, Torner JC et al. (2008) Treating patients with 'wake-up' stroke: the experience of the AbESTT-II trial. *Stroke* 39:3277-3282.

88. Sandercock PA, Counsell C, and Kamal AK. (2008) Anticoagulants for acute ischaemic stroke. [Review] [74 refs][Update of Cochrane Database Syst Rev. 2004;(3):CD000024; PMID: 15266421]. Cochrane Database of Systematic Reviews CD000024.
89. Sandercock PA, Counsell C, and Tseng MC. (2008) Low-molecular-weight heparins or heparinoids versus standard unfractionated heparin for acute ischaemic stroke. Cochrane database of systematic reviews (Online) CD000119.
90. Wong KS, Wang Y, Leng X et al. (8-10-2013) Early dual versus mono antiplatelet therapy for acute non-cardioembolic ischemic stroke or transient ischemic attack: an updated systematic review and meta-analysis. [Review]. Circulation 128:1656-1666.
91. Dewilde S and Hawkins N. (2012) Investigating incoherence gives insight: clopidogrel is equivalent to extended-release dipyridamole plus aspirin in secondary stroke prevention. [Review]. Journal of Clinical Epidemiology 65:835-845.
92. Dinicolantonio JJ, Lavie CJ, Fares H et al. (15-10-2013) Meta-analysis of cilostazol versus aspirin for the secondary prevention of stroke. [Review]. American Journal of Cardiology 112:1230-1234.
93. Miedema I, Lujckx GJ, De KJ et al. (2012) Thrombolytic therapy for ischaemic stroke in patients using warfarin: a systematic review and meta-analysis. [Review]. Journal of Neurology, Neurosurgery & Psychiatry 83:537-540.
94. De Schryver EL, Algra A, Kappelle LJ et al. (2012) Vitamin K antagonists versus antiplatelet therapy after transient ischaemic attack or minor ischaemic stroke of presumed arterial origin. [Review][Update of Cochrane Database Syst Rev. 2006;(3):CD001342; PMID: 16855967]. Cochrane Database of Systematic Reviews 9:CD001342.
95. Hao Z, Liu M, Counsell C et al. (2012) Fibrinogen depleting agents for acute ischaemic stroke. [Review][Update of Cochrane Database Syst Rev. 2003;(3):CD000091; PMID: 12917882]. Cochrane Database of Systematic Reviews 3:CD000091.
96. Ricci S, Dinia L, Del Sette M et al. Sonothrombolysis for acute ischaemic stroke [Systematic Review]. Cochrane Database of Systematic Reviews 2012;(10) .

97. Bor-Seng-Shu E, Nogueira RC, Figueiredo EG et al. (2012) Sonothrombolysis for acute ischemic stroke: a systematic review of randomized controlled trials. [Review]. *Neurosurgical Focus* 32:E5.
98. Dentali FM. (2011) Safety of prothrombin complex concentrates for rapid anticoagulation reversal of vitamin K antagonists. *Thrombosis and Haemostasis* 106:429-438.
99. Beri A and Punnam SR. (2008) Anticoagulation in patients with acute ischemic stroke and atrial fibrillation--a balance of risks and benefits. [Review] [56 refs]. *Cardiovascular Drugs & Therapy* 22:419-425.
100. Orken DN, Kenangil G, Ozkurt H et al. (2009) Prevention of deep venous thrombosis and pulmonary embolism in patients with acute intracerebral hemorrhage. *Neurologist* 15:329-331.
101. Squizzato A, Romualdi E, Dentali F et al. (2011) Statins for acute ischemic stroke. *Cochrane Database of Systematic Reviews* CD007551.
102. Montaner J, Chacon P, Krupinski J et al. (2008) Simvastatin in the acute phase of ischemic stroke: a safety and efficacy pilot trial. *European Journal of Neurology* 15:82-90.
103. Muscari A, Puddu GM, Santoro N et al. (2011) The atorvastatin during ischemic stroke study: a pilot randomized controlled trial. *Clinical Neuropharmacology* 34:141-147.
104. Squizzato A, Romualdi E, Dentali F et al. (2011) Statins for acute ischemic stroke. [Review]. *Cochrane Database of Systematic Reviews* CD007551.
105. den Hertog HM, van der Worp HB, Tseng MC et al. (2009) Cooling therapy for acute stroke. [Review] [56 refs][Update of *Cochrane Database Syst Rev.* 2000;(2):CD001247; PMID: 10796427]. *Cochrane Database of Systematic Reviews* CD001247.
106. den Hertog HM, van der Worp HB, van Gemert HM et al. (2009) The Paracetamol (Acetaminophen) In Stroke (PAIS) trial: a multicentre, randomised, placebo-controlled, phase III trial. *Lancet Neurology* 8:434-440.

107. Bennett MH, Wasiak J, Schnabel A et al. (2009) Hyperbaric oxygen therapy for acute ischaemic stroke. Cochrane Database of Systematic Reviews .
108. Padma MV, Bhasin A, Bhatia R et al. (2010) Normobaric oxygen therapy in acute ischemic stroke: A pilot study in Indian patients. *Annals of Indian Academy of Neurology* 13:284-288.
109. Roffe C, Ali K, Warusevitane A et al. (2011) The SOS pilot study: a RCT of routine oxygen supplementation early after acute stroke--effect on recovery of neurological function at one week. *PLoS ONE [Electronic Resource]* 6:e19113.
110. Staszewski J, Brodacki B, Kotowicz J et al. (2011) Intravenous insulin therapy in the maintenance of strict glycaemic control in nondiabetic acute stroke patients with mild hyperglycemia. *Journal of Stroke & Cerebrovascular Diseases* 20:150-154.
111. Vriesendorp TM, Roos YB, Kruijff ND et al. (2009) Efficacy and safety of two 5 day insulin dosing regimens to achieve strict glycaemic control in patients with acute ischaemic stroke. *Journal of Neurology, Neurosurgery & Psychiatry* 80:1040-1043.
112. Bruno A, Kent TA, Coull BM et al. (2008) Treatment of hyperglycemia in ischemic stroke (THIS): a randomized pilot trial. *Stroke* 39:384-389.
113. McCormick M, Hadley D, McLean JR et al. (2010) Randomized, controlled trial of insulin for acute poststroke hyperglycemia. *Annals of Neurology* 67:570-578.
114. Bellolio MF, Gilmore RM, and Stead LG. (2011) Insulin for glycaemic control in acute ischaemic stroke. [Review]. *Cochrane Database of Systematic Reviews* CD005346.
115. Laird EA and Coates V. (2013) Systematic review of randomized controlled trials to regulate glycaemia after stroke. [Review]. *Journal of Advanced Nursing* 69:263-277.
116. Geeganage C and Bath PM. (2008) Interventions for deliberately altering blood pressure in acute stroke. [Review] [92 refs][Update of *Cochrane Database Syst Rev.* 2001;(3):CD000039; PMID: 11686949]. *Cochrane Database of Systematic Reviews* CD000039.

117. Geeganage C and Bath PM. (2010) Vasoactive drugs for acute stroke. [Review] [183 refs][Update of Cochrane Database Syst Rev. 2000;(4):CD002839; PMID: 11034772]. Cochrane Database of Systematic Reviews CD002839.
118. Geeganage C and Bath-Philip MW. (2010) Vasoactive drugs for acute stroke. Cochrane Database of Systematic Reviews .
119. Sare GM, Gray LJ, and Bath PM. (2008) Effect of antihypertensive agents on cerebral blood flow and flow velocity in acute ischaemic stroke: systematic review of controlled studies. *Journal of Hypertension* 26:1058-1064.
120. Nakamura T, Tsutsumi Y, Shimizu Y et al. (2010) Renin-angiotensin system blockade safely reduces blood pressure in patients with minor ischemic stroke during the acute phase. *Journal of Stroke & Cerebrovascular Diseases* 19:435-440.
121. Potter J, Mistri A, Brodie F et al. (2009) Controlling hypertension and hypotension immediately post stroke (CHHIPS)--a randomised controlled trial. *Health Technology Assessment (Winchester, England)* 13:iii-ixi.
122. Wilson EC, Ford GA, Robinson T et al. (2010) Controlling hypertension immediately post stroke: a cost utility analysis of a pilot randomised controlled trial. *Cost Effectiveness & Resource Allocation* 8:3.
123. Eveson DJ, Robinson TG, and Potter JF. (2007) Lisinopril for the treatment of hypertension within the first 24 hours of acute ischemic stroke and follow-up. *American Journal of Hypertension* 20:270-277.
124. Anderson CS, Huang Y, Wang JG et al. (2008) Intensive blood pressure reduction in acute cerebral haemorrhage trial (INTERACT): a randomised pilot trial. *Lancet Neurology* 7:391-399.
125. Anderson CS, Huang Y, Arima H et al. (2010) Effects of early intensive blood pressure-lowering treatment on the growth of hematoma and perihematomal edema in acute intracerebral hemorrhage: the Intensive Blood Pressure Reduction in Acute Cerebral Haemorrhage Trial (INTERACT). *Stroke* 41:307-312.
126. Koch S, Romano JG, Forteza AM et al. (2008) Rapid blood pressure reduction in acute intracerebral hemorrhage: feasibility and safety. *Neurocritical Care* 8:316-321.

127. Robinson TG, Potter JF, Ford GA et al. (2010) Effects of antihypertensive treatment after acute stroke in the Continue or Stop Post-Stroke Antihypertensives Collaborative Study (COSSACS): a prospective, randomised, open, blinded-endpoint trial. *Lancet Neurology* 9:767-775.
128. Beavan J, Conroy SP, Harwood R et al. (2010) Does looped nasogastric tube feeding improve nutritional delivery for patients with dysphagia after acute stroke? A randomised controlled trial. *Age & Ageing* 39:624-630.
129. Foley NC, Martin RE, Salter KL et al. (2009) A review of the relationship between dysphagia and malnutrition following stroke. [Review] [38 refs]. *Journal of Rehabilitation Medicine* 41:707-713.
130. Bernhardt J, Thuy MN, Collier JM et al. (2009) Very early versus delayed mobilisation after stroke. [Review] [56 refs]. *Cochrane Database of Systematic Reviews* CD006187.
131. Bernhardt J, Dewey H, Thrift A et al. (2008) A very early rehabilitation trial for stroke (AVERT): phase II safety and feasibility. *Stroke* 39:390-396.
132. Sorbello D, Dewey HM, Churilov L et al. (2009) Very early mobilisation and complications in the first 3 months after stroke: further results from phase II of A Very Early Rehabilitation Trial (AVERT). *Cerebrovascular Diseases* 28:378-383.
133. Tyedin K, Cumming TB, and Bernhardt J. (2010) Quality of life: an important outcome measure in a trial of very early mobilisation after stroke. *Disability & Rehabilitation* 32:875-884.
134. Tay-Teo K, Moodie M, Bernhardt J et al. (2008) Economic evaluation alongside a phase II, multi-centre, randomised controlled trial of very early rehabilitation after stroke (AVERT). *Cerebrovascular Diseases* 26:475-481.
135. Cumming TB, Collier J, Thrift AG et al. (2008) The effect of very early mobilisation after stroke on psychological well-being. *Journal of Rehabilitation Medicine* 40:609-614.
136. Cumming TB, Thrift AG, Collier JM et al. (2011) Very early mobilization after stroke fast-tracks return to walking: further results from the phase II AVERT randomized controlled trial. *Stroke* 42:153-158.

137. Craig LE, Bernhardt J, Langhorne P et al. (2010) Early mobilization after stroke: an example of an individual patient data meta-analysis of a complex intervention. *Stroke* 41:2632-2636.
138. Cuesy PG, Sotomayor PL, and Pina JO. (2010) Reduction in the incidence of poststroke nosocomial pneumonia by using the "turn-mob" program. *Journal of Stroke & Cerebrovascular Diseases* 19:23-28.
139. CLOTS TC, Dennis M, Sandercock PA et al. (6-6-2009) Effectiveness of thigh-length graduated compression stockings to reduce the risk of deep vein thrombosis after stroke (CLOTS trial 1): a multicentre, randomised controlled trial. *Lancet* 373:1958-1965.
140. Hofmeijer J, Kappelle LJ, Algra A et al. (2009) Surgical decompression for space-occupying cerebral infarction (the Hemicraniectomy After Middle Cerebral Artery infarction with Life-threatening Edema Trial [HAMLET]): a multicentre, open, randomised trial. *Lancet Neurology* 8:326-333.
141. Juttler E, Schwab S, Schmiedek P et al. (2007) Decompressive Surgery for the Treatment of Malignant Infarction of the Middle Cerebral Artery (DESTINY): a randomized, controlled trial. *Stroke* 38:2518-2525.
142. O'Rourke K, Berge E, Walsh CD et al. (2010) Percutaneous vascular interventions for acute ischaemic stroke. [Review]. *Cochrane Database of Systematic Reviews* CD007574.
143. Rouchaud A, Mazighi M, Labreuche J et al. (2011) Outcomes of mechanical endovascular therapy for acute ischemic stroke: a clinical registry study and systematic review. [Review]. *Stroke* 42:1289-1294.
144. Stead LG, Gilmore RM, Bellolio MF et al. (2008) Percutaneous clot removal devices in acute ischemic stroke: a systematic review and meta-analysis. [Review] [38 refs]. *Archives of Neurology* 65:1024-1030.
145. Lampl Y, Zivin JA, Fisher M et al. (2007) Infrared laser therapy for ischemic stroke: a new treatment strategy: results of the NeuroThera Effectiveness and Safety Trial-1 (NEST-1). *Stroke; a journal of cerebral circulation* 38:1843-1849.
146. Zivin JA, Albers GW, Bornstein N et al. (2009) Effectiveness and safety of transcranial laser therapy for acute ischemic stroke. *Stroke* 40:1359-1364.

147. Shuaib A, Bornstein NM, Diener H-C et al. (2011) Partial aortic occlusion for cerebral perfusion augmentation: Safety and efficacy of neuroflo in acute ischemic stroke trial. *Stroke* 42:1680-1690.
148. Nguyen-Huynh MN and Johnston SC. (2011) Is mechanical clot removal or disruption a cost-effective treatment for acute stroke? *Ajnr: American Journal of Neuroradiology* 32:244-249.
149. Patil CG, Long EF, and Lansberg MG. (2009) Cost-effectiveness analysis of mechanical thrombectomy in acute ischemic stroke. *Journal of Neurosurgery* 110:508-513.
150. Baker WL, Colby JA, Tongbram V et al. (15-2-2011) Neurothrombectomy devices for the treatment of acute ischemic stroke: state of the evidence. [Review]. *Annals of Internal Medicine* 154:243-252.
151. Cruz-Flores S, Berge E, and Whittle IR. (2012) Surgical decompression for cerebral oedema in acute ischaemic stroke. [Review][Update of Cochrane Database Syst Rev. 2002;(3):CD003435; PMID: 12137695]. *Cochrane Database of Systematic Reviews* 1:CD003435.
152. Gregson BA, Broderick JP, Auer LM et al. (2012) Individual patient data subgroup meta-analysis of surgery for spontaneous supratentorial intracerebral hemorrhage.[Erratum appears in *Stroke*. 2013 Jul;44(7):e82]. *Stroke* 43:1496-1504.