Canadian Stroke Best Practices

CANADIAN STROKE BEST PRACTICE RECOMMENDATIONS

Acute Stroke Management Evidence Tables

Preventing and Managing Complications following Acute Stroke

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ACUTE STROKE MANAGEMENT Writing Group

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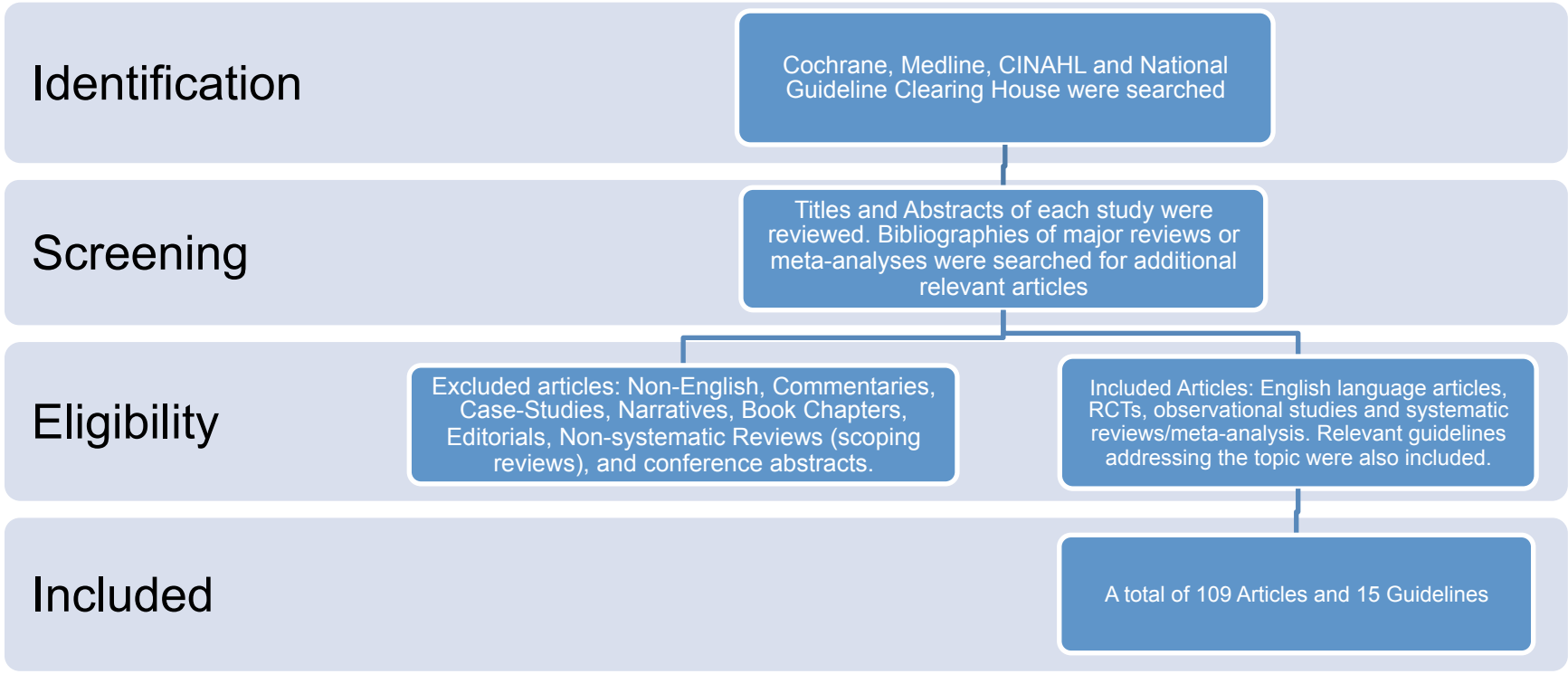
Search Strategy



Cochrane, Medline, CINAHL and National Guideline Clearing House were search using the medical subject heading (“stroke” And Venous Thromboembolism/ *Temperature/mobilization/*Fecal Incontinence/ or *Urinary Incontinence/*Nutrition Assessment/ or *Nutrition Therapy/ or *Enteral Nutrition/*Dental Care/ or *Oral Health or cardiac investigation n or electrocardiogram). 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, non-systematic review, or conference abstracts. Additional searches for relevant best practice guidelines were completed and included in a separate section of the review. A total of 109 articles and 15 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**	**4.4. Temperature** 1. Sources of hyperthermia (temperature >38°C) should be identified and treated. Antipyretic medications should be administered to lower temperature in hyperthermic patients with stroke. Class I; LOE C-EO. 2. The benefit of induced hypothermia for treating patients with ischemic stroke is not well established. Hypothermia should be offered only in the context of ongoing clinical trials. Class IIb; LOE B-R. **4.6. Dysphagia Screening** 1. Dysphagia screening before the patient begins eating, drinking, or receiving oral medications is reasonable to identify patients at increased risk for aspiration. Class IIa; LOE C-LD. 2. It is reasonable for dysphagia screening to be performed by a speech-language pathologist or other trained healthcare provider. Class IIa; C-LD. 3. An instrumental evaluation is reasonable for those patients suspected of aspiration to verify the presence/absence of aspiration and to determine the physiological reasons for the dysphagia to guide the treatment plan. Class IIa; LOE B-NR. 4. It is not well established which instrument to choose for evaluation of swallowing with sensory testing, but the choice may be based on instrument availability or other considerations (ie, fiberoptic endoscopic evaluation of swallowing, videofluoroscopy, fiberoptic endoscopic evaluation). Class IIb; LOE C-LD. **4.7. Nutrition** 1. Enteral diet should be started within 7 days of admission after an acute stroke. Class I; LOE B-R. 2. For patients with dysphagia, it is reasonable to initially use nasogastric tubes for feeding in the early phase of stroke (starting within the first 7 days) and to place percutaneous gastrostomy tubes in patients with longer anticipated persistent inability to swallow safely (>2–3 weeks). Class IIa; LOE C-EO. 3. Nutritional supplements are reasonable to consider for patients who are malnourished or at risk of malnourishment. Class IIa; LOE B-R. 4. Implementing oral hygiene protocols to reduce the risk of pneumonia after stroke may be reasonable. Class IIb; LOE B-NR. **4.8. Deep Vein Thrombosis Prophylaxis** 1. In immobile stroke patients without contraindications, intermittent pneumatic compression (IPC) in addition to routine care (aspirin and hydration) is recommended over routine care to reduce the risk of deep vein thrombosis (DVT). Class I; LOE B-R. 2. The benefit of prophylactic-dose subcutaneous heparin (unfractionated heparin [UFH] or LMWH) in immobile patients with AIS is not well established. Class IIb; LOE A. 3. When prophylactic anticoagulation is used, the benefit of prophylactic-dose LMWH over prophylactic-dose UFH is uncertain. IIb B-R. 4. In ischemic stroke, elastic compression stockings should not be used. Class III: Harm; LOE B-R. **4.10. Other** 2. Routine placement of indwelling bladder catheters should not be performed because of the associated risk of catheter-associated urinary tract infections. Class III: Harm; LOE C-LD. **4.11 Rehabilitation** 3. High-dose, very early mobilization within 24 hours of stroke onset should not be performed because it can reduce the odds of a

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	favorable outcome at 3 months. Class III: Harm; LOE B-R. 5.2. Seizures 1. Recurrent seizures after stroke should be treated in a manner similar to when they occur with other acute neurological conditions, and anti-seizure drugs should be selected based upon specific patient characteristics. Class I; LOE C-LD. 2. Prophylactic use of anti-seizure drugs is not recommended. Class III: No Benefit; LOE B-R. **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 IIb; LOE 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.
Fuentes B, Ntaios G, Putaala J, Thomas B, Turc G, Díez-Tejedor E. **European Stroke Organisation (ESO) guidelines on glycaemia management in acute stroke.** ***Eur Stroke J* 2017:2396987317742065.**	In patients with acute IS, we suggest against the routine use of IV insulin to achieve a tight glycaemic control as a means to improve functional outcome, survival or infarct growth. Quality of evidence: Low Strength of recommendation: Weak In patients with acute haemorrhagic stroke, we suggest against the routine use of IV insulin to achieve a tight glycaemic control as a means to improve functional outcome or survival. Quality of evidence: Very low Strength of recommendation: Weak
Holtkamp M, Beghi E, Benninger F, Kälviäinen R, Rocamora R, Christensen H et al. **European Stroke Organisation guidelines for the management of post-stroke seizures and epilepsy.** ***Euro Stroke J.* 2017;2(2):103-15.** **(selected)**	In the presence of only one underpowered RCT, there is no evidence if immediate primary prophylaxis with an antiepileptic drug compared to no treatment prevents occurrence of acute symptomatic seizure (ASS); in ischaemic stroke or intracranial (intracerebral or subarachnoidal) haemorrhage. Based on low incidence of ASS in observational studies, we make a weak recommendation against primary AED prophylaxis. Quality of evidence: Very low; Strength of Recommendation: Weak against strong intervention (↓?) In the absence of RCTs, we cannot make strong recommendations when and in whom to treat ASS with immediate secondary AED prophylaxis compared to no treatment for prevention of further ASS. Low incidence of ASS recurrence suggests not implementing secondary prophylaxis. Quality of evidence: Very low; Strength of Recommendation: Weak against intervention (↓?). In the absence of RCTs, we cannot make strong recommendations when to start immediate primary prophylaxis with an AED to prevent occurrence of post-stroke US. Low incidence of US occurrence suggests not implementing secondary prophylaxis. Quality of evidence: Very low; Strength of Recommendation: Weak against intervention (↓?). In the absence of RCTs but on the basis of observation study finding we cannot make strong recommendations. Due to high seizure recurrence risk, we suggest considering secondary AED prophylaxis. Quality of evidence: Very low; Strength of Recommendation: Weak against intervention (↑?)
Clinical Guidelines for Stroke Management 2017. Melbourne (Australia): National Stroke	**Nutrition and Hydration** **Strong recommendation Updated** • All stroke patients should have their hydration status assessed, monitored, and managed throughout their hospital admission. • Where fluid support is required, crystalloid solution should be used in preference to colloid solutions as the first option to treat or

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Foundation.	prevent dehydration. Strong recommendation Updated All stroke patients should be screened for malnutrition at admission and on an ongoing basis (at least weekly) while in hospital Strong recommendation For stroke patients whose nutrition status is poor or deteriorating, nutrition supplementation should be offered. Weak recommendation Updated • For stroke patients who do not recover a functional swallow, nasogastric tube feeding is the preferred method of feeding in the short term. • For stroke patients, there is no preference with regard to continuous pump (meaning using a pump for greater than or equal to 16hrs out of 24hrs for less than or equal to 80ml/hr) feeding versus intermittent bolus feeding (meaning 250-400mls/hr for 4-5times/day) therefore practical issues, cost and patient preferences should guide practice. Weak recommendation AGAINST New For stroke patients who are adequately nourished, routine oral nutrition supplements are not recommended. **Poor Oral Hygiene** Strong recommendation All stroke patients, particularly those with swallowing difficulties, should have assistance and/or education to maintain good oral and dental (including dentures) hygiene Strong recommendation Staff and carers of stroke patients (in hospital, in residential care and home settings) should be trained in assessment and management of oral hygiene. Weak recommendation New For stroke patients, chlorhexidine in combination with oral hygiene instruction, and/or assisted brushing may be used to decrease dental plaque and gingiva bleeding. Caution should be taken, however, for patients with dysphagia. **Incontinence** Weak recommendation • All stroke survivors with suspected urinary continence difficulties should be assessed by trained personnel using a structured functional assessment For stroke survivors, a portable bladder ultrasound scan should be used to assist in diagnosis and management of urinary incontinence. Weak recommendation • Stroke patients in hospital with confirmed continence difficulties, should have a structured continence management plan formulated, documented, implemented and monitored. • A community continence management plan should be developed with the stroke survivor and family/carer prior to discharge, and should include information on accessing continence resources and appropriate review in the community.

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	• If incontinence persists the stroke survivor should be re-assessed and referred for specialist review. Weak recommendation For stroke survivors with urge incontinence: • anticholinergic drugs can be tried • a prompted or scheduled voiding regime program/ bladder retraining can be trialled • if continence is unachievable, containment aids can assist with social continence. **Faecal Incontinence** Weak recommendation • All stroke survivors with suspected faecal continence difficulties should be assessed by trained personnel using a structured functional assessment. • For stroke survivors with constipation or faecal incontinence, a full assessment (including a rectal examination) should be carried out and appropriate management of constipation, faecal overflow or bowel incontinence established and targeted education provided. Weak recommendation For stroke survivors with bowel dysfunction, bowel habit retraining using type and timing of diet and exploiting the gastro-colic reflex should be used **Deep Venous Thrombosis (DVT) or Pulmonary Embolism (PE)** Early mobilisation and adequate hydration should be encouraged in all acute stroke patients to help prevent DVT and PE. (GPP) Antiplatelet therapy should be used for people with ischaemic stroke to help prevent DVT/PE. (Grade A) Low molecular weight heparin or heparin in prophylactic doses can be used with caution for selected patients with acute ischaemic stroke at high risk of DVT/PE. If low molecular weight heparin is contraindicated or not available, unfractionated heparin should be used. (Grade B) Antithrombotic therapy is NOT recommended for the prevention of DVT/PE in haemorrhagic stroke patients. (GPP) Thigh-length antithrombotic stockings are NOT recommended for the prevention of DVT/PE post-stroke. (Grade B) **Pressure Care** All stroke survivors at risk (e.g., stroke severity, reduced mobility, diabetes, incontinence and nutritional status) should have a pressure care risk assessment and regular evaluation completed by trained personnel. (GPP) All stroke survivors assessed as high risk should be provided with appropriate pressure-relieving aids and strategies, including a pressure-relieving mattress as an alternative to a standard hospital mattress. (Grade B)
Intercollegiate Stroke Working Party. National clinical guideline for stroke, 5th edition. London: Royal College of Physicians, 2016. **(selected)**	**DVT** • Patients with immobility after acute stroke should be offered intermittent pneumatic compression within 3 days of admission to hospital for the prevention of deep vein thrombosis. Treatment should be continuous for 30 days or until the patient is mobile or discharged, whichever is sooner. • Patients with immobility after acute stroke should not be routinely given low molecular weight heparin or graduated compression stockings (either full-length or below-knee) for the prevention of deep vein thrombosis. • Patients with ischaemic stroke and symptomatic deep vein thrombosis or pulmonary embolism should receive anticoagulant treatment provided there are no contraindications. D Patients with intracerebral haemorrhage and symptomatic deep vein

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	thrombosis or pulmonary embolism should receive treatment with a vena caval filter. **Mobilization** • Patients with difficulty moving after stroke should be assessed as soon as possible within the first 24 hours of onset by an appropriately trained healthcare professional to determine the most appropriate and safe methods of transfer and mobilisation. • Patients with difficulty moving early after stroke who are medically stable should be offered frequent, short daily mobilisations (sitting out of bed, standing or walking) by appropriately trained staff with access to appropriate equipment, typically beginning between 24 and 48 hours of stroke onset. Mobilisation within 24 hours of onset should only be for patients who require little or no assistance to mobilise. **Nutrition/Dysphagia** • Patients with acute stroke should have their swallowing screened, using a validated screening tool, by a trained healthcare professional within four hours of arrival at hospital and before being given any oral food, fluid or medication. • Until a safe swallowing method is established, patients with dysphagia after acute stroke should: – be immediately considered for alternative fluids; – have a comprehensive specialist assessment of their swallowing; – be considered for nasogastric tube feeding within 24 hours; – be referred to a dietitian for specialist nutritional assessment, advice and monitoring; – receive adequate hydration, nutrition and medication by alternative means. • Patients with swallowing difficulties after acute stroke should only be given food, fluids and medications in a form that can be swallowed without aspiration. • Patients with acute stroke should have their hydration assessed using multiple methods within four hours of arrival at hospital, and should be reviewed regularly and managed so that normal hydration is maintained. • Patients with acute stroke should be screened for the risk of malnutrition on admission and at least weekly thereafter. Screening should be conducted by trained staff using a structured tool. • Patients with acute stroke who are adequately nourished on admission and are able to meet their nutritional needs orally should not routinely receive oral nutritional supplements. • Patients with acute stroke who are at risk of malnutrition or who require tube feeding or dietary modification should be referred to a dietitian for specialist nutritional assessment, advice and monitoring. • Patients with stroke who are at risk of malnutrition should be offered nutritional support. This may include oral nutritional supplements, specialist dietary advice and/or tube feeding in accordance with their expressed wishes or, if the patient lacks mental capacity, in their best interests. • Patients with stroke who are unable to maintain adequate nutrition and fluids orally should be: – referred to a dietitian for specialist nutritional assessment, advice and monitoring; – be considered for nasogastric tube feeding within 24 hours of admission; – assessed for a nasal bridle if the nasogastric tube needs frequent replacement, using locally agreed protocols; – assessed for gastrostomy if they are unable to tolerate a nasogastric tube with nasal bridle. • People with stroke who require food or fluid of a modified consistency should: – be referred to a dietitian for specialist nutritional assessment, advice and monitoring; – have the texture of modified food or fluids prescribed using nationally agreed descriptors. • People with stroke should be considered for gastrostomy feeding if they: – need but are unable to tolerate nasogastric tube feeding; – are unable to swallow adequate food and fluids orally by four weeks from the onset of stroke; – are at high long-term risk of malnutrition.

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	• People with difficulties self-feeding after stroke should be assessed and provided with the appropriate equipment and assistance (including physical help and verbal encouragement) to promote independent and safe feeding. • People with stroke discharged from specialist care services with continuing problems meeting their nutritional needs should have their dietary intake and nutritional status monitored regularly. • People with stroke receiving end-of-life (palliative) care should not have burdensome restrictions imposed on oral food and/or fluid intake if those restrictions would exacerbate suffering. **Urinary/fecal incontinence** • Stroke unit staff should be trained in the use of standardised assessment and management protocols for urinary and faecal incontinence and constipation in people with stroke. • People with stroke should not have an indwelling (urethral) catheter inserted unless indicated to relieve urinary retention or when fluid balance is critical. • People with stroke who have continued loss of bladder and/or bowel control 2 weeks after onset should be reassessed to identify the cause of incontinence, and be involved in deriving a treatment plan (with their family/carers if appropriate). The treatment plan should include: – treatment of any identified cause of incontinence; – training for the person with stroke and/or their family/carers in the management of incontinence; – referral for specialist treatments and behavioural adaptations if the person is able to participate; – adequate arrangements for the continued supply of continence aids and services. • People with stroke with continued loss of urinary continence should be offered behavioural interventions and adaptations such as: – timed toileting; – prompted voiding; – review of caffeine intake; – bladder retraining; – pelvic floor exercises; – external equipment prior to considering pharmaceutical and long-term catheter options. • People with stroke with constipation should be offered: – advice on diet, fluid intake and exercise; – a regulated routine of toileting; – a prescribed drug review to minimise use of constipating drugs; – oral laxatives; – a structured bowel management programme which includes nurse-led bowel care interventions; – education and information for the person with stroke and their family/carers;

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	– rectal laxatives if severe problems persist. **Oral Care** • People with stroke, especially those who have difficulty swallowing or are tube fed, should have mouth care at least 3 times a day including: – brushing of teeth and cleaning of gums with a suitable cleaning agent (toothpaste and/or chlorhexidine dental gel), for which an electric toothbrush should be considered; – removal of excess secretions; – application of lip balm. • People with stroke who have dentures should have their dentures: – put in during the day; – cleaned regularly using a toothbrush, toothpaste and/or chlorhexidine dental gel; – checked and replaced if ill-fitting, damaged or lost. • People in hospital or living in a care home after stroke should receive mouth care from staff who have been trained in: – assessment of oral hygiene; – selection and use of appropriate oral hygiene equipment and cleaning agents; – provision of oral care routines; – awareness and recognition of swallowing difficulties. People with stroke and their family/carers should receive information and training in mouth care and maintaining good oral hygiene before transfer of their care from hospital.
Dennis M, Caso V, Kappelle J et al. For the European Stroke Organisation **European Stroke Organisation (ESO) guidelines for prophylaxis for venous thromboembolism in immobile patients with acute ischaemic stroke** ***Eur Stroke J* 2016; 1(1):6-19.**	We recommend that intermittent pneumatic compression (IPC) (thigh-length, sequential) should be used for immobile patients with ischaemic stroke. It should not be used in patients with open wounds on the legs and should be used with caution in those with existing DVT, heart failure, severe peripheral vascular disease or confusion where attempts to mobilise when unsupervised could lead to falls and injury. Quality of evidence: Moderate Strength of recommendation: Strong Prophylactic anticoagulation with unfractionated heparin (UFH) (5000U 2, or 3 daily) or low molecular weight heparin (LMWH) or heparinoid should be considered in immobile patients with ischaemic stroke in whom the benefits of reducing the risk of venous thromboembolism is high enough to offset the increased risks of intracranial and extracranial bleeding associated with their use. Quality of evidence: Moderate

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	Strength of recommendation: Weak Where a judgement has been made that prophylactic anticoagulation is indicated LMWH or heparinoid should be considered instead of UFH because of its greater reduction in risk of DVT, the greater convenience, reduced staff costs and patient comfort associated single daily dose vs. multiple daily injections but these advantages should be weighed against the higher risk of extracranial bleeding, higher drug costs and risks in elderly patients with poor renal function Quality of evidence: Moderate Strength of recommendation: Weak
Ntaios G, Dziedzic T, Michel P, et al. **European Stroke Organisation (ESO) guidelines for the management of temperature in patients with acute ischemic stroke.** ***Int J Stroke 2015*;10(6):941-949.**	**PICO1:** In hyperthermic patient with acute ischemic stroke, does treatment of hyperthermia compared with no treatment of hyperthermia improve functional outcome and/or survival? In patients with acute ischemic stroke and hyperthermia, we cannot make any recommendation for treating hyperthermia as a means to improve functional outcome and/or survival. Quality of evidence: Low/⊕⊕ Strength of recommendation: Weak **PICO2**: In normothermic patients with acute ischemic stroke, does prevention of hyperthermia with antipyretics compared with no prevention of hyperthermia improve functional outcome and/or survival? In patients with acute ischemic stroke and normothermia, we do not recommend routine prevention of hyperthermia with antipyretics as a means to improve functional outcome and/or survival. Quality of evidence: Moderate/⊕⊕⊕ Strength of recommendation: Weak/↓? **PICO3**: In patients with acute ischemic stroke, does induction of hypothermia compared with no induction of hypothermia improve functional outcome and/or survival? In patients with acute ischemic stroke, we do not recommend induction of hypothermia as a means to improve functional outcome and/or survival. Quality of evidence: Very low/⊕ Strength of recommendation: Weak/↓?
Steiner T, Al-Shahi Salman R, Beer R, et al. **European Stroke Organisation (ESO) guidelines for the management** **of spontaneous intracerebral**	12. There is insufficient evidence from RCTs to make strong recommendations on whether, when, and for whom preventive or early fever treatment should be given after acute ICH. Quality of Evidence: Low Strength of recommendation: Weak 13a. We do not recommend short or long graduated compression stockings for the prevention of DVT. We recommend intermittent

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haemorrhage. ***Int J Stroke 2014*;9:840–855.** **(selected)**	pneumatic compression to improve outcome and reduce the risk of DVT in immobile patients with ICH. Quality of Evidence: Moderate Strength of recommendation: Strong 13b. There is insufficient evidence from RCTs to make strong recommendations about how, when, and for whom anticoagulation should be given to prevent DVT or improve outcome. Quality of Evidence: Low Strength of recommendation: Weak 14a. There is insufficient evidence from RCTs to make strong recommendations on whether preventive antiepileptic treatment should be used after ICH for the prevention of seizures or improvement of outcome in the long term. Low Weak 14b. There is insufficient evidence from RCTs to make strong recommendations about how, when, and for whom AEDs should be given to reduce the risk of epilepsy after ICH. Quality of Evidence: Low Strength of recommendation: Weak
Anderson D, Larson D, Bluhm J, Charipar R, Fiscus L, Hanson M, Larson J, Rabinstein A, Wallace G, Zinkel A. Institute for Clinical Systems Improvement. Diagnosis and Initial Treatment of Ischemic Stroke. Updated July 2012.	**Initiate Deep Vein Thrombosis (DVT) Prophylaxis** Clinician should provide appropriate prophylaxis against deep vein thrombosis in immobilized patients with acute ischemic stroke, weighing risks and benefits of various options. Select the appropriate prophylaxis, such as unfractionated heparin or low-molecular-weight heparin in patients without contraindications (Strong Recommendation, Moderate Quality Evidence) See the ICSI Antithrombotic Therapy Supplement and ICSI Venous Thromboembolism Prophylaxis guideline. **Perform Swallow Evaluation** Clinician should perform a swallow screening test as soon as feasible on a patient with acute ischemic stroke and withhold oral intake of fluids, medications or food until/unless the screen is successfully passed (Strong Recommendation, Low Quality Evidence) Clinicians are encouraged to see the ICSI recommendation for swallow screens prior to administering aspirin, in Annotation #35, "Initiate Aspirin Unless Contraindicated." **Initiate Rehabilitation Early** Clinician should mobilize patients with acute ischemic stroke as soon as possible, monitoring for and avoiding postural hypotension (Strong Recommendation, Moderate Quality Evidence) **Perform Nutritional Status Assessment** Assessment of the patient's baseline nutritional status and the implementation of treatments to correct any major nutritional problems are recommended [R]. Poor nutritional status in patients admitted for stroke is associated with increased morbidity and

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	mortality [B]. However, a trial did not find benefit in administering nutritional supplementation (Food Trial Collaboration, 2005) [A]. **Treat Hyperthermia** Clinician should treat hyperthermia (i.e., temperature > 38°C) with specific measures (e.g., antibiotics targeted to discovered infections) and/or non-specific measures (e.g., cooling blankets, acetaminophen) in patients with acute ischemic stroke (Strong Recommendation, Low Quality Evidence)
Qaseem A, Chou R, Humphrey LL, Starkey M, Shekelle P, for the Clinical Guidelines Committee of the American College of Physician. **Venous thromboembolism prophylaxis in hospitalized patients: a clinical practice guideline from the American college of physicians.** ***Ann Intern Med* 2011;155:625-632.**	Recommendation 1: ACP recommends assessment of the risk for thromboembolism and bleeding in medical (including stroke) patients prior to initiation of prophylaxis of venous thromboembolism (Grade: strong recommendation, moderate-quality evidence). Recommendation 2: ACP recommends pharmacologic prophylaxis with heparin or a related drug for venous thromboembolism in medical (including stroke) patients unless the assessed risk for bleeding outweighs the likely benefits (Grade: strong recommendation, moderate-quality evidence). Recommendation 3: ACP recommends against the use of mechanical prophylaxis with graduated compression stockings for prevention of venous thromboembolism (Grade: strong recommendation, moderate-quality evidence).
Scottish Intercollegiate Guidelines Network (SIGN). Prevention and management of venous thromboembolism. A national clinical guideline. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN); 2010 Dec. 101 p.	Assessment of Risk for Venous Thromboembolism (VTE) Clinical Assessment of Venous Thrombosis Risk D - All patients admitted to hospital or presenting acutely to hospital should be individually assessed for risk of VTE and bleeding. The risks and benefits of prophylaxis must be discussed with the patient. D - The use of a risk assessment method checklist is recommended for this purpose. D - The assessment should be repeated regularly and at least every 48 hours. Guidelines for VTE Prophylaxis B - Hospitals should adopt approaches which are likely to increase compliance with thromboprophylaxis guidelines and improve patient outcomes. D - Local prophylaxis guidelines should be developed and updated for specific patient groups. Laboratory Tests in Assessment of Thrombosis Risk D - Routine laboratory screening for thrombophilias is not recommended. Thromboprophylaxis in Medical Patients Pharmacological Thromboprophylaxis to Prevent Asymptomatic and Symptomatic VTE A - When the assessment of risk favours use of thromboprophylaxis, UFH, LMWH or fondaparinux should be administered.

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	C - Aspirin is not recommended as the sole pharmacological agent for VTE prophylaxis in medical patients. Acute Stroke A - AES should not be used routinely in stroke patients. A - In patients with non-haemorrhagic stroke at high risk of VTE, LMWH can be considered.
Scottish Intercollegiate Guidelines Network (SIGN). Management of patients with stroke: rehabilitation, prevention and management of complications, and discharge planning. A national clinical guideline. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN); 2010 Jun. 101 p.	**Early Mobilization** B: Stroke patients should be mobilised as early as possible after stroke. **Nutrition and Swallowing** **Nutritional Screening and Assessment** D: Assessment of nutritional risk should be carried out within the first 48 hours with regular reassessment thereafter during the patient's recovery and be recorded prior to discharge. D: Assessment of a patient's nutritional risk should include an assessment of their ability to eat independently and a periodic record of their food consumption. D: Ongoing monitoring of nutritional status after a stroke should include a combination of the following parameters: • Biochemical measures (i.e., low prealbumin, impaired glucose metabolism) • Swallowing status • Unintentional weight loss • Eating assessment and dependence • Nutritional intake **Nutritional Interventions** C: Following nutritional screening, those identified as undernourished, and those at risk of becoming undernourished, should be referred to a dietitian and considered for prescription of oral nutritional supplements as part of their overall nutritional care plan. **Continence** **Urinary Incontinence** D: All stroke patients should be assessed, investigated and treated for urinary incontinence. D: The presence or absence of incontinence of urine should be documented for all patients after a stroke. D: Behavioural therapies for incontinence should be trialled on an individual basis after stroke. **Pressure Ulcer Prevention** D: • Hospital managers should ensure that nursing expertise, staffing and equipment levels are sufficient to prevent pressure ulcers. • Hospitals should have up-to-date policies on risk assessment, pressure ulcer prevention and treatment.

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	Venous Thromboembolism **Early Medication Treatment** A: Aspirin (300 mg/day) should be given to all patients with acute ischaemic stroke in the first two weeks following stroke onset to help prevent deep vein thrombosis and pulmonary embolism (provided there are no known contraindications to aspirin therapy). **Graduated Elastic Compression Stockings** A: Above-knee graduated elastic compression stockings to reduce the risk of deep vein thrombosis after acute stroke are not recommended.
Canadian Dental Association (2009). Optimal oral health for frail older adults: best practice along the continuum of care. Available at: http://www.cda-adc.ca/_files/dental_profession/practising/best_practices_seniors/optimal_oral_health_older_adults_2009.pdf	The authors conclude that the dentist's focus should always be on prevention of dental disease, especially in people who have progressive debilitating systemic diseases. For an oral health care program to be successful, there needs to be support at all levels within the facility and a culture that values and promotes oral health as a basic right of residents that is integral to their overall health and well-being. Champions within the facility should be identified to oversee the program and liaise with all members of the team. As part of the organization's quality assurance program, the facility should monitor and evaluate its oral care program and ensure its sustainability. An interprofessional approach should be used for the design, implementation and evaluation of the oral health care program.
Summers D, Leonard A, Wentworth D, Saver JL, Simpson J, Spilker JA, Hock N, Miller E, Mitchell PH; on behalf of the American Heart Association Council on Cardiovascular Nursing and the Stroke Council. **Comprehensive overview of nursing and interdisciplinary care of the acute ischemic stroke patient: a scientific statement from the American Heart Association.** ***Stroke 2009*;40:2911–2944.**	1. Stroke neurological assessments should be performed every 4 hours after the hyperacute phase of stroke, and then frequency should be based on the patient's stability and other comorbid conditions (Class I, Level of Evidence B). 2. Temperatures >99.6°F should be managed aggressively (Class I, Level of Evidence C). 3. Continuous cardiac monitoring of the stroke patient should be provided for at least 24 to 48 hours after stroke to detect potential cardiac problems (Class I, Level of Evidence B). 4. Careful, frequent monitoring and assessment for worsening of neurological deficits or bleeding should be performed for up to 24 hours after thrombolytic therapy (Class I, Level of Evidence B). 5. Hyperglycemia should be treated in patients with a serum glucose concentration >140 mg/dL (Class I, Level of Evidence C). 6. Management of arterial hypertension in the acute phase should be approached with caution because of the lack of data available to guide management (Class I, Level of Evidence C). 7. Oxygenation should be evaluated with an oxygen saturation monitor (Class I, Level of Evidence C). 8. To prevent aspiration pneumonia, the patient's lungs should be auscultated, and the patient should be evaluated for signs of respiratory compromise and dysphagia (Class I, Level of Evidence C). Nurses should report seizure activity, and treatment should begin immediately (Class I, Level of Evidence B). Prophylactic treatment of seizures should not be given. Class IIa 9. It is reasonable to use clinical pathways, protocols, or preprinted stroke order sets to organize care of the stroke patient (Class IIa, Level of Evidence B). 10. Infections, such as pneumonia and UTI, should be identified and treated immediately with antibiotics (Class I, Level of Evidence B). 11. Early bowel and bladder care should be instituted to prevent complications such as constipation and urinary retention or

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	infection (Class I, Level of Evidence A). Use of indwelling catheters should be avoided if possible because of the risk of UTI (Class I, Level of Evidence A). 12. Early implementation of anticoagulant therapy or physical compression modalities should be considered for all stroke patients who cannot ambulate at 2 days and who are at risk for DVT or pulmonary embolus (Class I, Level of Evidence A). 13. Early mobility should always be attempted if safe for the patient (Class I, Level of Evidence B). 14. Fall precautions should be initiated, and the stroke patient should be told not to ambulate without assistance (Class I, Level of Evidence B). 15. Frequent turning should be instituted in bedridden patients to prevent skin breakdown (Class I, Level of Evidence A). Use of the Braden Scale in nursing practice can assist in the prediction of stroke patients at high risk of developing pressure ulcers (Class I, Level of Evidence A). Range-of-motion exercises should start in the early phase of acute stroke care once risk has been assessed (Class I, Level of Evidence C). 16. A swallow screen should be performed in the first 24 hours after stroke, preferably by the speech language pathologist (Class I, Level of Evidence B). Nurses should be familiar with bedside swallow assessment if a formal evaluation cannot be done within the specified period. Stroke patients should be kept NPO until the screen has been performed (Class I, Level of Evidence B). Further studies of dysphagia in the setting of acute stroke should be performed. 17. Patients who cannot swallow should have a nasogastric tube placed, or if severity warrants, a percutaneous endoscopic gastrostomy tube should be placed (Class I, Level of Evidence B). Assessment of proper hydration is included in this recommendation. Class IIa 18. If an indwelling catheter is required, excellent pericare and prevention of infection modalities should be instituted to prevent complications (Class IIa, Level of Evidence C). 19. The stroke patient can be fed either by intravenous infusion or through nasogastric or percutaneous endoscopic gastrostomy tubes (Class IIa, Level of Evidence B). Class IIb 20. Nurses may provide passive range-of-motion exercises between physical therapy visits to help patients maintain joint mobility and prevent complications of immobility (Class IIb, Level of Evidence C).
American Association of Neuroscience Nurses. Guide to the care of the hospitalized patient with ischemic stroke. 2nd ed. Glenview (IL): American Association of Neuroscience Nurses; 2008. 38 p.	**Aspiration/Swallowing** At the time of the stroke or during the acute stages of a stroke, patients may not be able to clear secretions and could be at high risk for aspiration. Aspiration can result in respiratory compromises due to infection or pulmonary edema. Nurses must frequently auscultate lungs, evaluate for signs of respiratory compromise, and evaluate for signs of dysphagia to prevent the occurrence of aspiration pneumonia. Initial interventions may include elevating the head of the bed (HOB) or turning the patient on his or her side, monitoring the patient during oral intake, and obtaining a formal swallowing evaluation if symptoms of choking are noted. Nurses must do a bedside swallowing assessment prior to the institution of any oral intake, including medications. **Temperature Should Be Monitored** Temperature elevation has been associated with increased mortality and morbidity in an acute stroke. The fever increases metabolic demands of the brain, which can worsen the ischemia and lead to further tissue damage. Fever following an acute stroke may be due to infection or may be neurogenic. The patient should be treated with antipyretic agents and other cooling measures, evaluated for pneumonia and urinary tract infection, and treated accordingly. Research is studying the use of hypothermia for acute stroke and head injury, but data supporting its use are insufficient. The 2007 AHA guidelines recommend

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	keeping the patient normothermic (Level 2; Adams et al., 2007). Antipyretics should be used to lower body temperature in febrile patients until further studies are completed (Level 3; Adams et al., 2007). **Fluid Management** Fluid management is crucial for the patient with acute stroke; both volume overload and depletion should be avoided. As with fluid overload, dehydration is associated with a less favorable outcome and is a common problem (Mohr et al., 2004). Dehydration may be preexisting and related to the cause of the acute prothrombotic event, associated with treatment delay, or may be due to difficulties with swallowing, resulting in unbalanced hydration needs. Patients who have difficulty with communication, cognitive problems, decreased mobility, or an infection or who are receiving diuretic therapy or are hyperthermic are also at risk. Critically ill stroke patients may also suffer from more complex electrolyte disturbances, such as the syndrome of inappropriate antidiuretic hormone or cerebral salt-wasting syndrome (for a review of signs and symptoms, see Dooling & Winkelman, 2004), and, in rare cases, diabetes insipidus. Intravenous therapy with isotonic fluids, such as Ringer 's solution or normal saline, should be instituted and continued for at least the first 24 hours after the acute prothrombotic event. Fluid balance during the first 24 hours should be more or less positive, depending on the level of dehydration on admission (Mohr et al., 2004). Hydration should be assessed by clinical observation; fluid intake and output, serum hematocrit, osmolarity, and sodium, as well as urine osmolarity, should be evaluated. In critically ill patients, fluid disturbances can be further assessed with central venous pressure measurements or pulmonary capillary wedge pressure via a pulmonary catheter. **Nutrition** Nutritional compromise interferes with stroke recovery. A swallow assessment should be performed as soon as possible after admission to the hospital and no later than 48 hours after admission. Patients suspected of having swallowing problems should be given nothing by mouth until after a structured bedside swallowing assessment is performed (Level 2; Adams et al., 2007). Nutrition should be initiated within 48–72 hours after the swallowing assessment. It is suggested that enteral, rather than parenteral, nutrition be pursued in critically ill patients. The enteral route has several advantages, including simpler application, lower risk of infection, utilization of the normal physiological functions of digestion and absorption, maintenance of the intestinal mucosa, and lower cost (Mohr et al., 2004). Intestinal function and motility (as manifested by bowel sounds and aspiration of gastric residual) must be regularly monitored and, if necessary, supported by a stimulant such as metoclopramide. If motility is not restored or if dysphagia is expected to continue for more than 6–8 weeks, postpyloric feeding via a percutaneous endoscopic gastrostomy (PEG) should be considered. Parenteral nutrition is indicated in cases of imminent intubation or operation, gastrointestinal leakage, ileus, pancreatitis, and other conditions in which a patient's gastrointestinal tract is unable to tolerate oral or enteral feedings for at least 5 to 7 days (Mohr et al., 2004). **Dysphagia** Nurses must monitor patients for clinically observable signs of dysphagia that include coughing or choking on saliva or food, pocketing of food in the mouth, garbled speech, facial muscle weakness, delayed or absent swallow reflex, drooling, watery eyes after any intake, or gurgling voice. Clinically observable signs of aspiration are not always evident because stroke patients can be "silent aspirators." Patients at highest risk include those with infarctions in the brainstem, large hemispheric lesions, multiple strokes, or decreased LOC.

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	Clinical interventions after the initial nursing swallow screen include consulting the speech and language pathologist (SLP) for formal evaluation and further recommendations on diet or techniques for decreasing the risk of aspiration. Also, nurses should perform aggressive oral care. Minimizing the bacterial count in the mouth can decrease the risk of developing aspiration pneumonia if the patient aspirates (Level 2; Abe et al., 2006; Ferozali, Johnson, & Cavagnaro, 2007). When the patient is determined to be at risk for aspiration, nurses must alert the physician or nurse practitioner to request a formal dietary consultation from a registered dietitian so that the patient's metabolic and nutritional needs can be evaluated. Malnutrition has been proven to delay recovery and to increase the duration of hospital stay. However, nutritional supplements are not routinely recommended (Level 2; Adams et al., 2007). Tests to evaluate for dysphagia include bedside videofluoroscopic and endoscopic studies. Videofluoroscopic procedures include barium esophagram and modified barium swallow. The patient is asked to swallow different textures of food coated with barium, and then he or she is watched for any aspiration. These tests must be conducted with fluoroscopy in the radiology department. Endoscopic studies include flexible endoscopic evaluation of swallowing (FEES) and flexible endoscopic evaluation of swallowing with sensory testing. These tests allow direct visualization of the laryngopharyngeal structure while the patient is given a variety of dyed food textures and consistencies. Both tests are used to evaluate for pooling, spillage, endotracheal penetration, and aspiration. The FEES test is popular because of its portability for patients in the intensive care unit (Tabaee et al., 2006). After these tests, the radiologist and SLP can make recommendations for safe food and liquid consistency. Patients who are aspirating or are at risk for aspiration with all types of food and liquids should receive nutrition through a soft feeding tube until swallowing is feasible. Alternatively, nutrition can be provided via a PEG if long-term feeding is anticipated. The dietitian can help determine the exact caloric needs and the correct commercially prepared formula. The dietitian follows the patient during the rehabilitation and adjusts his or her caloric needs as necessary. Most patients can tolerate an oral diet but may need to be taught special techniques, such as specific ways of positioning the head and neck and specified swallowing maneuvers. In addition, changes in consistency of food may be necessary during the acute phase of the stroke (Level 2; Huang et al., 2006; Ramsey, Smithard, & Kalra, 2003). Weight should be monitored at least once weekly to assess for adequacy of nutrition (Level 3; CPG Panel Consensus). An SLP will develop a feeding plan to decrease the risk of aspiration. Basic principles for preventing aspiration include the following: The patient should be placed in a high Fowler's position, preferably seated in a chair, for the meal and should remain seated for at least 30 minutes after the meal. Mouth care should be performed prior to feeding because it can facilitate sensation and the production of saliva, which in turn can facilitate swallowing. Mouth care also should be performed after eating to observe whether the patient is pocketing food. Food fragments retained in the patient's mouth can lead to aspiration. The patient or care provider should be instructed to place the foods into the unaffected side of the patient's mouth. Pulmonary status should be assessed after eating. Suctioning apparatus should be kept near the patient at all times for possible use, and the patient should be monitored closely during his or her first meal. Families must be educated about the feeding plan and the required special techniques for decreasing the risk of aspiration. In addition, patients should be fed small portions and allowed ample time for chewing and swallowing. Use of the chin-tuck method can help minimize aspiration during swallowing. Avoid allowing a patient to drink thin fluid from a straw while lying flat in bed; this is a dangerous feeding practice that can increase the risk of aspiration. Straws should be removed from the room and the family

Guideline	Recommendations
	instructed not to give the patient a drink with a straw under the aforementioned circumstance. Nurses must be aware of whether the patient has a visual-field cut, because he or she may eat only the items on one side of the plate. Patients must be instructed to visually scan their meal tray and plate (Level 3; Barker, 2007). **Risk of Infection** Airway and oxygenation should be monitored closely, and a structured swallowing assessment has been shown to be the best way to decrease the incidence of pneumonia in cases of acute stroke (Level 2; Hinchey et al., 2005). Patients with suspected pneumonia or UTI should be treated with antibiotics (Level 1; Adams et al., 2007). Two additional, nurse initiated interventions that have been shown to decrease the incidence of pneumonia are (a) initiation of early mobility and (b) good pulmonary toileting (Level 2; Hilker et al., 2003). Stroke patients are at risk for a higher incidence of UTI because of changes in sphincter control and frequent use of an indwelling catheter. If at all possible, placement of indwelling catheters should be avoided because of this risk (Level 3; Adams et al., 2007). A change in a patient's LOC should lead to suspicion of a UTI if there are no other reasons for neurological deterioration. Urinalysis and cultures should be obtained if a UTI is suspected (Adams et al., 2007; Roth et al., 2001). **Bowel and Bladder Care** Bowel and bladder dysfunction can lead to skin breakdown, UTIs, decreased self-esteem, depression, and interference with the progress of rehabilitation. The nurse must be responsible for evaluating the patient's bowel and bladder routine and coordinating a retraining program that meets the needs of individual patients. Constipation is the most common bowel problem after a stroke, and to date virtually no interventional studies have been conducted in this important area. The nurse must assess for bowel sounds and abdominal distension and evaluate the patient's fluid intake and hydration status. Nurses also should assess the patient's premorbid bowel-elimination pattern. If, prior to the stroke, the patient usually had bowel movements in the morning, it would be ideal to attempt to duplicate this pattern; the use of medications may be necessary in this situation. The patient should be evaluated for impaction every 2 days. A bowel program for preventing constipation can integrate the use of stool softeners, laxatives, suppositories, digital stimulation, and enemas. Stool softeners should be given daily beginning with the acute phase. A laxative is necessary if the patient has not had a bowel movement for 2 days. At the end of the second day, it is ideal to give a laxative that requires 6–8 hours to work, after which bowel care should be attempted again in the morning. An enema should be used as a last resort if the laxative, suppository, or digital stimulation is ineffective after the third day. The nurse must assume the responsibility for requesting the medications or developing a bowel program protocol or set of orders (Level 1; Harari et al., 2004). AHA guidelines recommend avoiding indwelling catheters or, if they are medically necessary, they should be removed as soon as possible because of the increased risk of infection (see "Risk of Infection" section above). Indwelling catheters should not be placed for the convenience of nursing care. After the indwelling catheter is removed, intermittent catheterization may be necessary to retrain the bladder. A bladder scanner can be used to evaluate post-void residuals (PVRs) and determine whether catheterization is necessary. The goal is to simulate normal physiological filling and emptying. If the PVR is >100, intermittent catheterization is recommended. This should also help to decrease the incidence of UTIs (Level 3; Chan, 1997). Daily intake and output should be monitored. The patient should be offered a commode, bedpan, or urinal every 2 hours during waking hours and every 4 hours at night. The patient should be taken to the bathroom regularly during the night or be encouraged to use a bedside commode at night to decrease the risk of falling. Also, if there are fluid restrictions, the nurse may encourage greater fluid intake during the day and decreased fluid intake during the evening before bedtime (Level 3; North American Nursing Diagnosis Association, 2007).

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	Risk of Pulmonary Embolism and Deep Vein Thrombosis Following a stroke, patients are at risk for development of thrombophlebitis or DVT in the weak or paralyzed lower extremity. The DVT risk is related to both the paralysis of the leg and the immobility caused by the stroke. If the patient is unable to ambulate, passive range of motion or active range of motion can be started during the first 24 hours poststroke. Patients should be positioned to minimize the occurrence of dependent edema. Joint guidelines published by the ASA and the American Academy of Neurology recommend that subcutaneous unfractionated heparin, low-molecular-weight heparin (LMWH), and heparinoids may be considered for DVT prophylaxis for at-risk patients with acute ischemic stroke, but the guidelines also acknowledge the lack of demonstrable benefit in the treatment of pulmonary embolism (Level 1; Adams et al., 2007; Coull et al., 2002). The guidelines' authors caution that the relative benefits of these drugs must be weighed against the risk of hemorrhage. A recent meta-analysis reviewed the use of compression and pneumatic devices for DVT prevention for intensive-care patients. The conclusion of the review was that no significant difference existed among results obtained from three patient treatments: (a) no treatment, (b) treatment with LMWH, or (c) treatment with compression or mechanical devices (Level 1; Limpus et al., 2006). Compression devices should be used if anticoagulants are contraindicated (Level 2; Adams et al., 2007). If hemorrhage is a concern in the acute stroke, prophylactic prevention should include the use of bilateral-sequential compression devices. In addition, the most effective prevention of DVT is early mobilization of the patient. Early mobilization not only decreases the risk of DVT but also lessens the likelihood of major complications such as pneumonia and decubitus ulcers (Adams et al., 2007). **Mobility and Musculoskeletal System** Immobility can lead to contractures, orthopedic complications, atrophy, and nerve-pressure palsies. Nursing interventions, including range-of-motion and positioning techniques, can prevent joint contractures and atrophy. Nurses must assess for special deformities that may be found on the affected side, including shoulder adduction; flexion contractures of the hand, wrist, and elbow; external rotation of the hip; and plantar flexion of the foot. Subluxation of the affected shoulder is common. Nurses should take special care to avoid pulling on the affected arm and shoulder when repositioning patients in bed or from a lying to a sitting or standing position. Subluxation may not be preventable; however, careful positioning and movement of the affected arm may prevent the development of a painful shoulder-hand syndrome. Nurses can implement passive range-of-motion exercises during the first 24 hours or instruct patients and their families to perform active range-of-motion exercises to prevent contractures and other orthopedic complications. The rehabilitation team (i.e., physical and occupational therapists) should be consulted soon after the acute stroke to develop a plan of care for rehabilitation and to determine whether the patient has any special adaptive-equipment needs (Level 3; Adams et al., 2007). **Skin Care** Stroke patients are at risk for skin breakdown because of loss of sensation and impaired circulation. Approximately 9% of all hospitalized patients develop pressure ulcers. The stroke patient is the most at risk because of dependence in mobility and incontinence; also, many stroke patients have associated diabetes, peripheral vascular disease, and end-stage renal failure (Berlowitz et al., 2001). A reliable risk-assessment tool such as the Braden scale can be used initially to evaluate and predict the risk of pressure-ulcer development. Nursing measures include repositioning the patient, turning the patient every 2 hours, using proper transfer techniques to avoid excessive friction that can lead to skin injury or tears, using skin-care products on the patient, and keeping the patient's skin clean and dry (Level 3; Duncan, 2005).

Evidence Tables

Prevalence of In-Hospital Medical Complications

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Otite et al. 2017 **USA** **Retrospective study**	NA	575,211 patients included in the Nationwide Inpatient Sample from 2004-2013 admitted to hospital with intracerebral hemorrhage. Mean age was 68.9 years, 49.7% were women.	The frequencies of medical complications including UTI, DVT, PE, pneumonia and MI were retrieved.	In-hospital medical complications	29.3% of all patients experienced at least 1 complication. Mortality was 23.8% The most frequently reported medical complication was UTI (14.8%). Frequencies of other complications were: pneumonia 7.8%, sepsis 4.1%, DVT 2.7%, PE 0.7% and MI 2.0% Medical complications were associated with increased lengths of hospital stays and increased costs.
Ingeman et al. 2011 **Denmark** **Retrospective study**	NA	13,721 patients admitted to 10 stroke units from 2003-2009. Mean age: 72 years, 79.4% ischemic stroke, 16.6% had severe or very severe stroke, 15.5% moderate stroke and 38.9% mild (the stroke severity of the remaining patients was not assessed).	Medical complications including pneumonia, UTI, DVT, pressure ulcer, falls and severe constipation, were retrieved through chart review. Associations between complications and stroke outcome were explored using regression analysis controlling for age, sex, Scandinavian Stroke Scale score, type of stroke and processes of care received)	30 day and 1-year mortality rate and LOS	3,453 (25.2%) patients experienced at least one medical complication during hospitalization. UTI-15.4%, pneumonia-9.0%, constipation-6.8%, falls-2.1%, DVT-0.6%, pressure ulcer-1.2%. The median LOS for all patients was 13 days but was higher for patients with any complication (median=33 days). Any medical complication was associated with an increased LOS (adj relative LOS extension=2.48, 95% CI 2.01-3.06). Any complication was associated with significant increases in mortality rate ratios. Adj MMR for 1-year mortality=1.20, 95% CI 1.04-1.39. Pneumonia was associated with the highest MMR: 30-day mortality=1.59, 95% CI 1.31-1.93 1-year mortality=1.76, 95% CI 1.45-2.14
Indredavik et al. 2008	NA	256 patients admitted to a stroke unit within 24 hours of symptom onset.	The frequency of 16 complication types that developed during the first	Frequency of medical complications at 1 week and during 90 days follow-up,	63.8% of patients experienced ≥1 complication during the first week of admission.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Rohweder et al. 2015 **Norway** **Additional reporting from RCT**		Mean age was 77.2 years, 52.4% were female, 90% of strokes were ischemic.	week of admission were documented. Complications continued to be recorded in 50% patients during the next 3 months, by weekly telephone calls.	independent predictors of complications and poor outcome (mRS 3-4) at 90 days	Increased stroke severity was an independent predictor of the occurrence of complications. The 5 most frequently reported complications were diffuse pain (23.9%), fever (23.7%), stroke progression (18.4%), UTI (16.0%) and Troponin T elevation without MI (11.7%). The onset of most complications occurred during the first 24 hours of admission. During 3-month follow-up, 82.4% experienced ≥1 complication. Pain, UTIs, non-serious falls and chest infections were the most commonly reported. After controlling for age, sex, pre-stroke mRS, and Stroke severity, the odds of a poor outcome at 3 months were significantly increased given: recurrent stroke (OR=7.45, 95% CI 2.83-20.96, p<0.0001), chest infection (OR=3.28, 95% CI 1.16-9.29, p=0.025) or a fall (OR=1.43, 95% CI 1.06-1.93, p=0.021).
Roth et al. 2001 **USA** **Retrospective study**	NA	1,029 patients consecutively admitted to a single hospital for stroke rehabilitation from 1993-1997, associated with a recent (within 3 months) stroke. Mean age was 63.4 years, 53% were female, 71% ischemic stroke.	83 possible medical complications were recorded from the medical chart. Examination of clinical factors associated with the development of a medical complication and factors associated with the development of a complication requiring transfer back to acute care. Analyses were adjusted for stroke severity.	Factors associated with the development of medical complications.	Mean stroke onset to rehab admission was 17.4 days. Mean rehab LOS was 28 days. 773 patients (75%) experienced at least one medical complication. The most commonly cited were: UTI (30.5%), soft tissue pain (14.2%), depression (13.0%), falls (10.5%), and dehydration (10.0%). DVT- 4.1%, pneumonia-4.0%, seizures-1.5% and PE-1.1%. 19% of patients experienced a complication requiring transfer to an acute care facility. The presence of hypoalbuminemia, a history of HTN and moderate to severe stroke were independent predictors of the development of a medical complication.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					Elevated WBC count, low hemoglobin levels, moderate-to-severe stroke and a history of cardiac arrhythmia were independent predictors of the development of a medical complication requiring transfer to acute care. Medical complications were more prevalent among patients with increasing severity of stroke.
Langhorne et al. 2000 **UK** **Retrospective study**	NA	311 consecutive patients admitted to 3 stroke units within 7 days of stroke onset, over a 7-month period. The mean age was 76 years, 52% were male. 89% of strokes were ischemic. 74% of patients were independent prior to stroke	Complications were noted during the acute stroke admission and at 6, 18 and 30 months of stroke. Complications were classified as: neurological, infections, complications associated with immobility, thromboembolism, pain, psychological and misc.	Complications that developed during hospital stay and up to 30 months following stroke.	265 patients (85%) experienced at least 1 complication during hospital stay: UTI: 23%, chest infections: 22%, pressure sores: 21%, falls (total): 25%, DVT: 2%, PE:1%. During the acute and rehabilitation period increasing dependency was associated with an increased frequency of infections, pressure sores and anxiety. The majority of complications occurred within the first 6 weeks of stroke Of 148 patients who were alive and available for follow-up at 30 months, the number of complications reported were: UTI: 22%, chest infections: 29%, pressure sores: 11%, falls (total): 45%, DVT: 0%, PE:0%.
Johnston et al. 1998 **USA** **Additional reporting from RCT**	NA	279 patients included in the Randomized Trial of Tirilazad Meslyate in Patients with Acute Stroke (RANTTAS) study. Patients were recruited from 27 participating acute care centres from 1993-1994. The mean age was 69 years. Median admission NIHSS score was 9.0.	Data related to neurological and medical complications that occurred in patients in the placebo arm of the trial during 3 months were collected. Associations between medical complications and poor outcome were examined.	Poor outcome, defined as severe disability (Barthel Index score <60 or Glasgow Outcome Scale of severe disability or vegetative survival) or death at 3 months	32% of patients had at least one serious event. The most common medical complications were: congestive heart failure (11%), UTIs (11%), pneumonia (10%), aspiration pneumonia (6%), angina (6%) and gastrointestinal bleed (5%). 3-month mortality was 14%, 51% of which were related to medical complications. The odds of a poor outcome were increased significantly for patients with any serious medical complication (adj OR=6.4, 95% CI 2.5-15 using BI criteria and adj OR=11.6, 95% CI 4.3-30.9, using GOS criteria).

Cardiovascular Investigations

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
i) Detection of Atrial Fibrillation & Other Arrhythmias					
Sposato et al. 2015 **Canada** **Systematic review & meta-analysis**	NA	50 studies, estimating the proportion of patients diagnosed with atrial fibrillation (AF) 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.	Sub groups of studies were formed based on 4 phases of cardiac monitoring: emergency room, in-hospital, first ambulatory period and second ambulatory period.	Proportion of patients diagnosed with post-stroke AF	The detection of AF between the 4 methods used during the inpatient phase (phase 2), including serial electrocardiography, continuous inpatient electrocardiographic monitoring, continuous inpatient cardiac telemetry and In-hospital Holter monitoring did not differ. Overall the proportion of patients diagnosed with AF was 5.1%, 95% CI 3.8-6.5%
Kishore et al. 2014 **UK** **Systematic review & meta-analysis**	NA	32 studies (RCTs and prospective cohort) including the results from 5038 patients with acute ischemic stroke or TIA had undergone invasive or noninvasive cardiac monitoring for a minimum of 12 hours following event. The mean age of all patients was 68.4 years.	Forms of cardiac monitoring evaluated included inpatient cardiac monitoring (IP), 24, 48 & 72hr and 7-day Holter, external loop recorder (n=3), invasive cardiac monitoring (n=4), and mobile cardiac outpatient telemonitoring (n=1). Maximum duration of monitoring was 30days (n=1). Time of event to initiation of monitoring ranged from 0 hrs to 3 months.	**Primary outcome:** Detection of all AF (could not isolate paroxysmal AF as a separate outcome due to lack of reporting detail) **Secondary outcome:** Detection rates in subgroups including selected and unselected patients, latency between event and detection of AF and detection of AF in different stroke subtypes	The overall detection rate of AF was 11.5% (95% CI 8.9%-14.3%). The detection rate of AF in unselected patients was 6.2% (95% CI 4.4%-8.3%). The detection rate of AF in selected patients was 13.4% (95% CI 9.0%-18.4%). The detection rate of AF in cryptogenic stroke was 15.9% (95% CI 10.9%-21.6%). In unselected patients, the detection rates associated with monitoring type were: IP 5.5% (95% CI 4.2%-6.9%) n=9 24 hr Holter 5.0% (95% CI 2.0%-9.0%) n=6 >24 hr monitoring 14.1% (95% CI 1.5%-36.4%) n=3 In selected patients, the detection rates associated with monitoring type were: IP 15.0% (95% CI 7.0%-25.0%) n=3

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					24 hr Holter 10.7% (95% CI 3.4%-21.5%) n=8 >24 hr monitoring 14.7% (95% CI 10.7%-19.3%) n=12 There was insufficient data to explore AF detection rates related to latency period, or among stroke subtypes.
Ground et al. 2013 **Germany** **Prospective Cohort Study**	NA	1135 unselected patients from 9 stroke units admitted with stroke (71%) or TIA (29%) without a previous diagnosis of atrial fibrillation (AF). Mean age was 67 years, 45% women.	All patients underwent 72 hour Holter ECG monitoring using a 3-lead device.	**Primary outcome:** Detection of AF during observation period	Median time to onset of monitoring was 1 day. AF was detected in 49 new cases (4.3%, 95% CI 3.4%-5.2%). AF was detected in 29 patients within the first 24 hours of monitoring and in additional 20 patients by the end of 72 hours.
Higgins et al. 2013 **UK** **RCT**	CA: ☑ Blinding: Patient ☒ Assessor ☒ ITT: ☒	100 patients admitted from 2 acute stroke services with ischemic stroke or TIA within 7 days of onset of symptoms without a history of AF and who demonstrated a normal sinus rhythm. Mean age was 65.8 years, 56% male.	Patients were randomized to receive noninvasive investigation to detect AF in accordance with standard practice (SP, n=50), or to received SP + additional cardiac event monitoring with the Novacor R-test Evolution device.	**Primary outcome:** Detection of sustained (20 sec) and unsustained paroxysmal AF (PAF) at 14 and 90 days.	At 14 days, sustained PAF was detected in 2% (95% CI 0%-10.6%) of patients in the SP group compared with 8% (95% CI 2.2%-19.2%) of patients in the SP+AM group (p=0.36). At 90 days, sustained PAF was detected in 8% (95% CI 2.2%-19.26%) of patients in the SP group compared with 16% (95% CI 7.2%-29.1 %) of patients in the SP+AM group (p=0.36). At 14 days, PAF of any duration was detected in 4% (95% CI 0%-13.7%) of patients in the SP group compared with 12% (95% CI 4.5%-24.3%) of patients in the SP+AM group (p=0.27). At 90 days, PAF of any duration was detected in 10% (95% CI3.3%-21.8%) of patients in the SP group compared with 22% (95% CI 11.5%-36.0%) of patients in the SP+AM group (p=0.10). Anticoagulation therapy was initiated significantly more frequently among patients in the SP+AM group.
Flint et al. 2012 **USA**	NA	239 patients with cryptogenic ischemic stroke. Mean age was 64.6 years, 39.5% female	All patients underwent 30-day outpatient monitoring with an external loop recorder.	**Primary outcome:** Detection of paroxysmal AF during observation period	The average time from stroke event to initiation of monitoring was 29 days. Patients wore the monitors for an average of 24.5

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Stroke Monitoring for PAF in Real Time (SMART) **Registry**					days. PAF was detected in 26 of 236 patients (11.0%, 95% CI, 7.6%-15.7%). The first episode was detected an average of 11.4 days following the initiation of monitoring. The median number of events was 2/patient. Most PAFs were asymptomatic.
Lazzaro et al. 2012 **USA**	NA	113 consecutive patients admitted to a single institution from 2007-2008, following acute ischemic stroke or TIA, who had received cardiac investigations using continuous cardiac telemetry (CCT) and Holter monitoring. Mean age was 63.1 years, 50% were male. Patients with AF detected at baseline were excluded.	The detection of atrial fibrillation (AF) using Holter Monitoring and CCT, was compared.	**Primary outcome:** Detection of AF during observation period	Mean durations of monitoring were 29.8 hours (Holter) and 73.6 hours (CCT). Holter monitoring was initiated an average of 27.5 hours after initiation of CCT. Overall, the detection of AF was significantly higher using Holter monitoring (6.0%, 95% CI 2.9-11.6% vs. 0%, 95% CI, 0-3.4%, p=0 .008). Among 101 patients with stroke, the detection of AF was significantly higher using Holter monitoring (6.9%, 95% CI 3.2-13.9% vs. 0%, 95% CI, 0-4.4%, p=0 .016).
Rizos et al. 2012 **Germany** **Prospective Cohort Study**	NA	496 patients admitted to a single stroke unit with stroke (79%) or TIA (21%) without a previous diagnosis of atrial fibrillation (AF). Mean age was 69 years, 61.5% male. Median NIHSS score was 3.	All patients underwent both 24 hr Holter monitoring initiated within 48 hours of stroke and continuous ECG monitoring (CEM) initiated immediately following admission. CEM data were also monitored using an automated system (aCEM).	**Primary outcome:** Detection of AF and paroxysmal AF during stroke unit admission.	CEM continued for a median duration of 64 hours. Median length of time spent on stroke unit was 89 hours. AF was newly detected during stroke unit admission in 68 patients (13.7%). Of these, paroxysmal AF was identified in 41 patients. The overall rate of newly detected paroxysmal AF was 8.3%. aCEM detected significantly more cases of paroxysmal AF compared with CEM or 24 hr Holter monitoring (92.7% vs. 65.9% vs. 34.1%)
Suissa et al. 2012 **France** **Prospective cohort study**	NA	946 patients with acute ischemic stroke and previously undiagnosed with AF were included. Mean age was 62.6 years.	Patients were enrolled into either intensive stroke unit care (with continuous cardiac monitoring initiated on admission, n=592) or conventional stroke unit care (baseline ECG, 24-hour Holter	**Primary outcome:** Detection of AF	New cases of AF were found in 8 patients (2.26%) with routine cardiac monitoring while 88 (14.86%) patients were diagnosed with AF in the continuous cardiac monitoring group. In the adjusted analysis, patients in the continuous cardiac monitoring group had greater

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			monitor and additional ECGs when necessary, n=352) (admission to either unit was based on neurologist evaluation).		odds of being diagnosed with AF (OR=5.29; 95% CI 2.43 to 11.55). The odds of detection were greatest within the first 24 hours (OR=9.82; 95% CI 3.01 to 32.07).
Douen et al. 2008 **Canada** **Prospective cohort study**	NA	144 patients with acute ischemic stroke 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). 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. 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%).
Liao et al. 2007 **Canada** **Systematic Review**	NA	5 prospective cohort studies (n=736) including patients without a previous diagnosis of atrial fibrillation (AF), who were diagnosed with ischemic stroke or TIA, and received cardiac monitoring for at least 12 hours.	Evaluation of forms of non-invasive cardiac monitoring.	**Primary outcome**: Detection of AF	No RCTs were identified in the review. Cardiac monitoring was initiated at variable time points, but ranged between admission to a ward, and 55 days after admission to hospital. All cardiac monitoring involved the use of a Holter monitor. Some studies also used an event loop recorder. **Detection of AF**: Combined detection of AF in 4.6% (95% CI 0% to 12.7%) of patients. The use of a Holter monitor for variable durations following acute stroke (ischemic or hemorrhagic) appear to identify new cases of atrial fibrillation or atrial flutter even months following stroke.
ii) Use of Transesophageal Echocardiography					
Katsanos et al. 2015	NA	35 studies including 5,772 participants with cryptogenic	Cardiac conditions known to be associated with cerebral	Prevalence of cardioembolic causes	The most common TEE findings were: Atheromatosis in the ascending aorta/aortic arch

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Greece **Systematic review & meta-analysis**		ischemic stroke or TIA who had undergone TEE investigations. Mean age was 54 years, 57% were male.	ischemia were identified using ASCOD criteria, including atherosclerosis, small-vessel disease, cardiac pathology, other causes and dissection		(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%).
Marino et al. 2016 **USA** **Retrospective study**	NA	263 patients ≥50 years, consecutively admitted over a 4-year period (2009-2012) to a single institution with acute ischemic stroke, with a normal transthoracic echocardiogram (TTE), were included. Patients with pre-existing atrial fibrillation/flutter or those taking anticoagulants, were excluded. Mean age was 66.7 years, 42.5% were female.	All patients underwent transesophageal echocardiography (TEE), to detect potential sources of stroke etiology.	Cardiac abnormalities	Overall, 42.6% of patients had a TEE finding which could explain the etiology of stroke/TIA One patient (0.4%) had a finding that changed therapy. TEE findings: Atrial septal aneurysm 25 (5.3%) Patent foramen ovale 18 (2.7%) Atrial septal aneurysm and PFO 11 (4.2%) Complex aortic plaque 44 (16.7%) Spontaneous contrast 13 (4.9%) Left atrial appendage thrombus* 1 (0.4%) Total 112 (42.6%) At 6 months, follow-up was available for 85 patients, during which time 13 (15%) had developed AF.
McGrath et al. 2014 **Ireland/Canada** **Systematic review**	NA	27 studies (n=5,653) including patients who had transthoracic echocardiogram (TTE), following cryptogenic ischemic stroke, following routine investigations	TEE findings of interest (atrial septal aneurysm, ASA, patent foramen ovale PFO, left atrial thrombus, spontaneous echo contrast (SEC) and aortic arch), were grouped by age (< 55 and ≥ 55 years)	**Primary outcome:** TEE cardiac findings **Secondary outcomes:** Initiation of anticoagulation following TEE	There was significant heterogeneity among studies, with wide ranges of prevalences of cardiac disorders. Standardized definitions/criteria of cardiac abnormalities were not provided in many studies **PFO Prevalence** <55 years: 35.0%, 95% CI 28.1-42.5% (16 studies) ≥55 years: 19.3%, 95% CI 15.1-24.2% (17 studies)

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					ASA Prevalence <55 years: 12.9%, 95% CI 7.4%-21.3% (11 studies) ≥55 years: 11.2%, 95% CI 8.4%-14.8% (16 studies) **Prevalence of left atrial thrombus** <55 years: 2.5%, 95% CI 0.9%-7.0% (7 studies) ≥55 years: 4.0%, 95% CI 2.1%-7.4% (15 studies) **Prevalence of SEC** <55 years: 4.5%, 95% CI 2.1%-9.3% (7 studies) ≥55 years: 6.9%, 95% CI 4.3%-10.7%, (15 studies) **Prevalence of aortic atheroma** <55 years: (3.5%, 95% CI 1.5%-7.9% (6 studies) ≥55 years: 18.6%, 95% CI 14.1%-24.3% (13 studies) The proportion of patients who were initiated on oral anticoagulant therapy following the results of TEE, was 0%, 2.3%, 6.0%, 11.0%, and 30.7% (5 studies)
Zhang et al. 2012 **USA** **Retrospective study**	NA	186 patients admitted consecutively with ischemic stroke or TIA to a single stroke unit, previously undiagnosed with AF. Mean age was 62.9 years, 53% male.	All patients received a transthoracic echocardiography (TTE) within 48 hours of symptom onset. 30 patients also received a transthoracic echocardiography (TEE) at the discretion of the treating physician, 28 of which were conducted within 2-7 days of symptom onset.	**Primary outcome:** Identification of high and medium risk sources of cardiogenic emboli. **Secondary outcomes:** Patterns of TEE use.	Abnormal results were found in 35 (18.8%) of patients with TTEs and in 9 patients who had also received TEEs. TEEs did not identify additional major sources of cardiogenic embolism in any patient with a normal TTE but did clarify the type of atrial defect present in 3 patients. Of the 151 patients with a normal TTE, 21 also received a TEE. Of these patients, 9 had abnormal findings. TEEs did not identify additional major sources of cardiogenic embolism in any patient with a normal TTE but did detect intraarterial septal abnormality in 7 patients. Based on TTE results, patient management was changed in 10.8% of cases (5.4% long-term management). Of the 30 patients who received TEE, the results of that test alone changed

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					management in 10 patients (7 long-term management). TEE was used in patients with abnormal TTE results to: confirm TTE findings (n=4), exclude left ventricular thrombus (n=2) and evaluate atrial septal anatomy (n=3). Of the patients with normal TTEs, additional TEEs were performed in: 6 cases of young (cryptogenic) stroke, 9 with ''embolic'' imaging, 1 case suggestive of complex aortic plaque, 3 cases of illicit drug use and in 2 cases with technically inadequate TTEs.
de Bruijn et al. 2006 **Netherlands** **Prospective study**	NA	231 patients with recent stroke (all types) or TIA were enrolled. 83% of patients were aged ≥ 45 years. Only patients whose stroke etiology remained in questions following initial ECG, ultrasound assessments and blood tests were included.	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 also performed separately for patients older than 45 years and younger than 45 years of age.	**Outcomes**: Potential and major cardiac sources of embolism.	**Prevalence of potential sources of embolism**: A potential cardiac source of embolism was detected in 55% (127/ 231) of the patients. Among all patients, a potential cardiac source was identified in 16% of patients (TTE+, TEE+) and a major risk factor was identified in 3% of patients (TTE+, TEE+). Significantly more abnormalities were identified using TEE Cardiac source: 39% (90/231) where TEE +, TTE- Major risk factor: 16% (38/231) where TEE +, TTE- The detection of possible cardiac sources of embolism was statistically 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).
Harloff et al. 2006 **Germany** **Prospective study**	NA	503 admitted patients acutely to a single stroke unit following ischemic stroke.	Stroke etiology was determined in 276 cases. In the remaining 227 cases, stroke etiology was unknown following routine diagnostic procedures. Of these, 15 patients had contradictions for oral anticoagulation therapy and did	**Primary outcome:** Detection of high-risk cardiac sources (aortic thrombus, left atrial cavity/appendage thrombus, spontaneous echo contrast, LAA flow	Among patients who received a TEE, a high-risk cardiac source was identified in 42 patients (19.85), leading to oral anticoagulation therapy in 17 cases (8.1%). An additional 71 patients (33.5%) were identified with a potential risk cardiac source. Of these, 48 patients (22.6%) were discharged on some form

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			not received a TEE. The remaining 212 patients received a TEE a median of 2 days following stroke onset. These patients also received a TTE, ECG and in some cases, 24 hrs. Holter monitoring.	<30cm/sec, aortic atheroma ≥4mm) and potential sources (patent foramen ovale, atrial septal aneurysm, both PFO+ASA)	of oral anticoagulation therapy.

CA Concealed allocation; ITT intention-to-treat

Venous Thromboembolism Prophylaxis

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
i) Efficacy of Low Molecular Weight Heparin (LMWH) vs. Unfractionated Heparin (UFH) following Acute Ischemic Stroke					
Sandercock et al. 2017 **UK** **Cochrane review**	NA	9 RCTs (n= 3,137) including patients with acute ischemic stroke who were randomized within 14 days of stroke onset.	Treatment contrasts examined were LMWHs or heparinoids vs. UFH. Four trials compared a heparinoid with UFH and 5 compared LMWH with UFH. The control condition in 8 trials was heparin (5,000U sc, q 8 or 12 hours). Average duration of treatment was 10-12 days.	**Primary outcome:** The incidence of DVT during the treatment period. **Secondary outcomes:** Incidence of PE during follow-up, all-cause mortality during treatment and follow-up, vascular death during follow-up, bleeding events during follow-up. Duration of follow-up was 3 months in all trials except one, in which it was 14 days.	The odds of DVT occurrence during treatment period were lower in the LMWH/heparinoid group (OR=0.55, 95% CI 0.44 -0.70, p<0.0001). Results from 7 trials included. There was no difference between groups in the odds of death during the treatment period (OR= 1.06, 95% CI 0.78- 1.46, p=0.70) or follow-up (OR= 0.98, 95% CI 0.79-1.23, p=0.89). Results from 8 trials included. There was no difference between groups in the odds of any ICH/hemorrhagic transformation during treatment (OR= 0.75, 95% CI 0.46- 1.23, p=0.25). Results from 9 trials included There was no difference between groups in the odds of PE during follow-up (OR= 0.57, 95% CI 0.23- 1.41, p=0.23). Results from 6 trials included. The odds of major extracranial hemorrhage were lower in the UHF group (OR= 3.79,

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					95% CI 1.30-11.06, p=0.015). Results from 7 trials included.
Lederle et al. 2011 **USA** **Systematic Review & Meta-analysis**	N/A	A subset of 19 trials, which included patients with acute stroke were identified from the total pool of 40 trials. The trials evaluated treatments for the prophylaxis of VTE for all medical patients. Eligibility criteria for most trials included high risk for DVT. The mean age of patients in most of the studies was >70 years. Patients with definitive indications/contra-indications were excluded.	Treatment contrasts examined were: i) heparin vs. placebo (n=8), ii) LMWH vs. UFH (n=5) and iii) mechanical vs. no mechanical prophylaxis (n=3). Treatment periods ranged from 6-14 days for pharmacological trials and 10 & 30 days for mechanical devices. (treatment period not specified in third trial)	**Primary outcomes:** Incidence of DVT, DVT, PE, bleeding events. Outcomes were assessed at points ranging from 10 days to 6 months.	All results include only trials restricted to diagnosis of stroke. Heparin vs. no heparin: There were no significant differences between groups for any of the outcomes except an increase in the incidence of bleeding events associated with heparin use. Death: OR=0.91, 95% CI 0.70-1.18. Results from 9 trials included. Symptomatic DVT: OR=0.14, 95% CI 0.0-7.09. Results from a single trial included. Fatal PE: OR=1.25, 95% CI 0.74-2.09. Results from 2 trials included. Major bleeding events: OR=1.66, 95% CI 1.20-2.28. Results from 8 trials included. LMWH vs. UFH There were no significant differences between groups on any of the outcomes. Death: OR=1.00, 95% CI 0.81-1.22. Results from 5 trials included. Symptomatic DVT: OR=0.34, 95% CI 0.11-1.00. Results from 2 trials included. Fatal PE: OR=1.25, 95% CI 0.74-2.09. Results from 2 trials included. Major bleeding events: OR=1.49, 95% CI 0.73-3.06. Results from 5 trials included. Mechanical vs. no mechanical Death: OR=1.13, 95% CI 0.89-1.13. Results from 3 trials included. PE: OR=0.65, 95% CI 0.33-1.31. Results from 2 trials included. Skin damage: Use of mechanical devices was associated with an increase in skin breakdown. OR=4.02, 95% CI 2.34-6.91. Results from a single trial included.
Sherman et al. 2007	CA: ☑	1,762 patients who had	Patients were randomized to	**Primary outcome:**	Mean duration of treatment was 10.5 days.

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USA **RCT (PREVAIL)** **Pineo et al. 2011** **Canada** **Economic Analysis**	Blinding: Patient ☒ Assessor ☑ ITT: ☒	experienced an ischemic stroke within the previous 48 hours and who were immobile with NIHSS motor scores of ≥2 (leg).	receive 40 mg enoxaparin subcutaneously once daily (n=877) or 5000U UFH q12 hours (n=872) with UFH, for 10 days.	Cumulative incidence of VTE including symptomatic or asymptomatic DVT or symptomatic or fatal PE during the study treatment (up to day 14). **Secondary outcomes:** Incidence of symptomatic VTE or PE at 30, 60, and 90 days from randomization, stroke recurrence (up to 90 days), stroke progression during the study treatment period (≥4 points in NIHSS score), NIHSS and mRS scores up to 90 days after treatment. **Safety outcomes:** All bleeding events, thrombocytopenia, adverse events	The incidence of all VTE at 14 days was lower among patients receiving enoxaparin (10% vs. 18%, RR= 0.57, 95% CI 0.44 to 0.76, p<0.0001). The incidences of all proximal and distal DVT at 14 days were lower among patients receiving enoxaparin (5% vs. 10%, RR= 0.47, 95% CI 0.31 to 0.72, p=0.0003) and 7% vs. 13%, RR= 0.52, 95% CI 0.37 to 0.74, p=0.0002, respectively). There were no differences between groups in the incidence of symptomatic DVT or PE at 14 days (DVT: <1% vs. 1%, RR=0.29, 95% CI 0.06-1.38, p=0.096; PE: <1% vs. 1%, RR= 0.29, 95% CI 0.02-1.39, p=0.059). The protective effects were maintained at day 30, 60 and 90, p<0.0001. There were no significant differences between groups in any of the bleeding outcomes: total bleeding events, symptomatic ICH, major extracranial hemorrhage, all-cause mortality at days 14 or 90. No significant interactions were detected in subgroup analysis: time to initiation of prophylaxis, diabetes, obesity, previous stroke, stroke severity (NIHSS score ≥14 vs.< 14), gender or age. Economic evaluation: Estimated cost saving associated with use of enoxaparin (over heparin) was USD$1,096/patient.
Diener et al. 2006 **Germany** ***PROphylaxis of***	CA: ☑ Blinding: Patient ☑ Assessor ☑	545 patients aged 18-85 years with a clinical diagnosis of ischemic stroke, who could be treated within 24 hours	Patients were randomized to certoparin 3000 U anti-Xa sc once daily + 2 placebo injections (n=272) or UFH 5000 tid (n=273).	**Primary outcome:** Composite outcome of symptomatic or asymptomatic proximal DVT, symptomatic PE, or	The incidence of the primary outcome was similar between groups during the treatment period (certoparin: 6.6% vs. UHF 8.8%).

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Thromboembolic Events by Certoparin Trial (PROTECT) **RCT (non-inferiority)**	ITT: ☑	of symptom onset and who presented with paresis of the leg and a baseline NIHSS score of 4-30.	Duration of treatment was 12-16 days.	death related to VTE occurring during treatment period. **Secondary outcomes:** Bleeding complications, mortality at 3 months	During the treatment period 17 patients in the certoparin group experienced DVT compared with 24 in the UFH group (p=0.29). No patient in either group experienced a PE. Bleeding complications were similar between Groups (3.7% vs. 3.7%). At the end of 3 months there was a non-significant increase in mortality in the certoparin group (5.1% vs. 2.9%).
ii) The use of antithromboembolic agents in pregnancy					
Rodger et al. 2015/2016 **Canada** **RCT (feasibility)** ***PostpaRtum PrOphylaxiS for PE Randomized Control Trial Pilot (PROSPER)***	CA: ☑ Blinding: Patient ☑☒ Assessor ☑ ☒ ITT: ☒	Women ≥18 years, at high risk of thromboembolism (>3.0%) were recruited during the third trimester, during labour/delivery or within 36 hours of delivery at 6 centres from 2011-2012 and 2012-2013. Sample size calculation indicated that 4,000 women would need to be recruited over 3 years from 40 centres, based on an event rate of 1% in intervention arm and 3% in placebo arm.	2015 protocol: Patients were randomized to receive 5,000 U dalteparin vs. saline (placebo) injections for 3 weeks following delivery 2016 protocol: Patients were randomized to receive 5,000 U dalteparin for 10 days following delivery vs. no treatment	**Primary Outcome:** Number of patients recruited/month **Secondary Outcomes:** Venous thromboembolism (DVT, PE) within 10 days of delivery, VTE within 10-90 days of delivery	**2015 (double-blind)** 1,346 women were assessed for eligibility. Of these, 968 did not meet eligibility criteria and 353 refused. 25 women were randomized (dalteparin n=14; placebo n=11). There was 1 drop-out. Recruitment rate was 0.7 per centre, per month. Target rate was 6/centre/month 67.5% of study drugs were administered. There were no VTEs. There were no major bleeding events or adverse events. **2016 (open-label)** 2,014 women were assessed for eligibility. Of these, 1,671 did not meet eligibility criteria and 306 refused. 37 women were randomized (dalteparin n=16; no treatment n=21). There were 3 drop-outs or losses to follow-up.

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					Recruitment rate was 0.9 per centre, per month. Target rate was 6/centre/month There were no VTEs. There was one major bleeding event, 2 clinically significant bleeding events and one minor bleeding event, all which occurred in the intervention group.
Bain et al. 2014 **Australia** **Cochrane Review**	NA	16 RCTs (n=2,592) including women who were pregnant or had given birth in the previous 6 weeks and were at increased risk of VTE (women who had a caesarean section, had previously had VTE, had an acquired or inherited thrombophilia, and other risk factors for VTE)	Treatment contrasts included: LMWH or UFH vs. placebo or no treatment; LMWH vs. UFH; hydroxyethyl starch (HES) vs. UFH; and 5-day vs. 10-day LMWH. Treatment periods included antenatal, following Cesarean section and post vaginal delivery	**Primary outcomes:** Maternal death, symptomatic thromboembolic events, symptomatic PE and symptomatic DVT	LMWH or UFH was not associated with a significant reduction in the risk of antenatal symptomatic thromboembolic events compared with placebo (RR=0.33, 95% CI 0.04-2.99. Results from 2 studies. LMWH was not associated with a significant reduction in the risk of antenatal symptomatic thromboembolic events compared with UFH (RR= 0.48, 95% CI 0.09-2.49). Data from one study. LMWH was associated with significantly fewer bleeding events compared with UFH (RR=0.28, 95% CI 0.15-0.53). Results from 3 studies. LMWH or UFH was not associated with a significant reduction in the risk of symptomatic thromboembolic events following Cesarean section compared with placebo (RR= 1.30, 95% CI 0.39-4.27). Results from 4 studies. LMWH or UFH was associated with a significantly increased risk of bleeding events following Cesarean section (RR=5.03, 95% CI 2.49-10.18). LMWH was not associated with a significant reduction in the risk of symptomatic thromboembolic events

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					following Cesarean section compared with UFH (RR= 0.33, 95% CI 0.01-7.99). Data from one study.
Rodger et al. 2014 **Canada** **RCT** ***Thrombophilia in Pregnancy Prophylaxis Study (TIPPS)***	Concealed Allocation: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑	292 pregnant women recruited from 36 centres with confirmed thrombophilia at high-risk of placenta-mediated pregnancy, pregnancy loss, complications and/or DVT. Women were excluded if they were ≥21 weeks' gestation or had known contraindications to heparin. Mean maternal age was 32 years. Mean gestational age at randomization was 12 weeks. Mean of 2.2 previous pregnancies, 1.0 deliveries, with 61% of women experiencing pregnancy-related complications	Women were randomized to receive antepartum dalteparin (5,000 IU) once daily from randomization to 20 weeks' gestation and then the same dose twice daily until 37 weeks of gestation vs. no dalteparin. All women received 5,000 IU dalteparin once daily postpartum until day 42.	**Primary outcome:** Composite including any of: proximal DVT, PE or sudden maternal death, severe or early onset preeclampsia, oliguria, pulmonary edema, coagulopathy, birth of small-for-gestational-age (SGA) infant, or pregnancy loss. **Secondary outcomes:** Major and minor bleeding events.	The primary outcome occurred in 25 women in the dalteparin group and 27 women in the control group (17.1% vs. 18.9%, risk difference of -1.8%, 95% CI -10.6%-7.1%, p=0.70). There were no significant interactions for the primary outcome found for pre-planned subgroup analysis including age, previous history loss, previous preeclampsia, previous SGA infant, previous VTE, thrombophilia, and aspirin use. There was no significant differences in the incidence of any of the individual components of the primary outcome (major VTE: 0.7% vs. 1.4%, risk difference of -0.7%, 95% CI -3.1%-1.6%, p=0.62; preeclampsia: 5.5% vs. 3.3%, risk difference of 2.0%, 95% CI -2.8%-6.8%, p=0.42; severe or early onset preeclampsia: 4.8% vs. 2.8%, risk difference of 2.0%, 95% CI -2.4%-6.4%, p=0.38; SGA infant: 6.2% vs. 8.4%, risk difference of -2.2%, 95% CI -8.2%-3.8%, p=0.47; any pregnancy loss: 8.2% vs. 7.0%, 95% CI 1.2%, 95% CI-4.9%-7.3%, p=0.69). There was no significant difference in the incidence of major bleeding between groups (2.1% vs. 1.45, RD=0.7%, 95% CI -2.4%-3.7%, p=1.0), but the incidence of minor bleeding events was significantly higher in the dalteparin group (19.6% vs. 9.2%, RD=10.4%, 95% CI 2.3%-18.4%, p=0.01).
Che Yaakob et al. 2010	NA	Inclusion criteria: pregnant women with	RCTs comparing i) warfarin vs. placebo, ii) UFH vs. placebo, iii)	**Primary outcome:** Resolution of thrombosis,	No studies were found.

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Malaysia **Cochrane Review**		confirmed deep vein thrombosis	LMWH vs. placebo, iv) UFH vs. LMWH.	adverse effects, pulmonary embolism, mortality, stroke, ICH	
iii) Pharmacological Prevention of VTE in Patients with Acute ICH					
Paciaroni et al. 2011 **Italy** **Meta-analysis**	NA	4 studies (2 RCTs, 2 non RCTs) in which prophylactic treatment for venous thromboembolism, following hemorrhagic stroke was initiated within 4 days of the event	Studies compared anticoagulants (UFH, n=2 or LMWH, n=2) with alternative treatment (placebo n=1, or compression stockings n=3). Mean follow-up periods were 10 days, 21 days, 3 months and were not recorded. Mean treatment durations were 10 days and 7-14 days and were not recorded in 2 studies	Symptomatic and asymptomatic DVT, PE, hematoma enlargement or death	Treatment with heparin was associated with a non-significant reduction in the risk of DVT (RR=0.77, 95% CI 0.44-1.34) and death (RR=0.76, 95% CI 0.57-1.03) Treatment with heparin was associated with a significant reduction in the risk of PE (RR=0.37, 95% CI 0.17-0.80) Treatment with heparin was associated with a non-significant increase in the risk of hematoma expansion (RR=1.42, 95% CI 0.15-90.7)
Orken et al. 2009 **Turkey** **RCT**	CA: ☒ Blinding: Patient ☒ Assessor ☑ ITT: ☒	75 patients admitted to hospital with non-traumatic, primary ICH	Patients were randomized after the first 48 hours to receive LMWH (enoxaparin, 40 mg/d) (n=39) or to wear compression stockings (CS)(n=36). Duration of treatment was not reported.	**Primary outcome:** Significant hemorrhage enlargement (>33% or 12.5mL) assessed by CT at 24 hours, 72 hours, day 7, and day 21. **Secondary outcomes:** Incidence of symptomatic or asymptomatic DVT and PE	After 24 hours, hemorrhage enlargement was present in 9 (15.3%) patients in the LMWH group and 3 (8.3%) patients in the CS group (i.e. prior to drug administration). The difference was not statistically significant (p=0.483). There was no hematoma enlargement in any patient in either group at any of the other time points. There was a non-significant increase in the number of asymptomatic DVTs associated with LMWH (3 vs. 1, p=0.62). There were no symptomatic DVTs in either group. There was 1 asymptomatic PE in each group and 1 symptomatic PE in the CS group.
Kiphuth et al. 2009 **Germany**	NA	Chart reviews of 97 patients admitted to hospital with spontaneous ICH who	Patients received either 4,000 IU enoxaparin or 25 IU dalteparin, once daily.	**Primary outcome:** Significant hemorrhage enlargement (>33%) or moderate enlargement	No patients developed significant hematoma expansion. 2 patients had moderate increase in

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Retrospective study		had received LMWH if there was no evidence of hematoma growth 24 hours following initial CT or MRI scan.		(>20%) assessed by CT or MRI 5-11 days after LMWH administration.	hematoma expansion. 2 patients developed heparin-induced thrombocytopenia.
Tetri et al. 2008 **Finland** **Retrospective Study**	NA	407 patients admitted to a single stroke unit with spontaneous ICH who were alive 2 days after stroke onset.	232 patients with a paralyzed lower limb were treated with 20 mg daily of enoxaparin starting 24 hours following stroke onset. (24 patients received a dose of 40 mg). Mean duration of treatment was 8 days. 175 patients did not receive treatment for VTE prophylaxis. Patients in neither group used compression stockings or IPC devices.	**Primary outcomes:** 3-month outcome, assessed by Glasgow Coma Scale (GCS) score **Secondary outcomes:** Incidence of DVT, PE, significant hematoma enlargement (>33%) within 2 weeks of stroke onset	Treatment was initiated within 24, 48 and 120 hours in 23%, 61% and 16% of patients respectively. Patients who received treatment were older and had lower SSS-PRG scores. Fewer treated patients had a good recovery at 3 months (21% vs. 48%) and were more likely to be severely disabled (35% vs. 15%). After adjustment for baseline severity and age, the odds of survival with severe disability associated with treatment were not significantly increased (OR=1.06, 95% CI 0.64-1.75). There was no difference in the number of patients who experienced significant hematoma enlargement (9% vs. 7%) or any enlargement (16% vs. 10%). There was no difference in the number of symptomatic VTEs between groups (6 vs. 4). In 2/6 cases, VTE occurred following discontinuation of treatment. There were 3 fatal PEs (2 received no treatment, 1 died following d/c of treatment).
iv) Physical Methods to Prevent DVT					
Naccarato et al. 2010 **UK** **Cochrane review**	NA	4 RCTs (n= 2,792) including patients with ischemic stroke or ICH who were randomized within 7 days of stroke onset.	Treatment contrasts were: thigh-length graduated compression stockings (GCS) vs. no stockings (n=2) and pneumatic compression (IPC) + GCS vs. no IPC +GCS (n=1) and IPC vs. no IPC (n=1).	**Primary outcomes:** Deaths from any cause, DVT or fatal or non-fatal PE that occurred during the study period. **Secondary outcomes:**	Physical methods (GCS or IPC) were not associated with reductions in death during treatment period (OR= 1.12, 95% CI 0.87-1.45, p=0.38), the incidence of DVT (OR= 0.85, 95% CI 0.70-1.04, p=0.12), or death/DVT (OR= 0.94, 95% CI 0.79-1.11, p=0.48). Results from 4 trials were

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
		Patients in 3 of the trials were immobile at baseline. Patients in one of the trials included only those with traumatic or spontaneous ICH with or without SAH	Duration of treatment was 10 days (n=2), not specified (n=1) and continued until death/discharge/mobile/refused (n=1)	Deaths from any cause, DVT or fatal or non-fatal PE that occurred during the follow-up period, adverse events.	included. Physical methods were not associated with reductions in symptomatic PE during scheduled treatment period (OR=0.94, 95% CI 0.79-1.11, p=0.23). Results from a single study included. Pooled analyses of secondary outcomes not performed.
Clots in Legs Or sTockings after Stroke (CLOTS) I **2009** **UK** **RCT**	CA: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑	2,518 patients, admitted to hospital within 1 week of acute ischemic stroke or ICH and who were immobile were enrolled from 64 centres in the UK, Italy, and Australia	Patients were randomized to either routine care plus thigh-length GCS (n=1,256) or to routine care plus avoidance of GCS (n=1262). Patients wore the garments day and night until they became mobile, were discharged, or there were concerns with skin breakdown.	**Primary outcome:** Symptomatic or asymptomatic DVT detected by Doppler u/s in the popliteal or femoral veins within 30 days of randomization **Secondary outcomes:** Death, any DVT, PE, complications and compliance with treatment (2 scans were performed between days 7-10 and 25-30, when possible)	At 30 days there was no significant difference between groups in the incidence of proximal DVT (GCS 10.0% vs. avoid GCS 10.5%). GCS was associated with a non-significant absolute reduction in risk of 0.5% (95% CI -1.9% to 2.9%). There were no significant differences between groups on any of the secondary outcome. The incidence of any DVT or PE was non-significantly lower in the GCS group (17.0% vs. 18.4%, OR=0.91, 95% CI 0.74-1.11). The odds of skin ulcers or breakdown were significant higher in the GCS group (5.1% vs. 1.3%, OR=4.18, 95% CI 2.40-7.27)
Clots in Legs Or sTockings after Stroke (CLOTS) 2 **2010** **UK** **RCT**	CA: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑	3,114 patients, admitted to hospital within 1 week of acute ischemic stroke or ICH and who were immobile, were recruited from 112 centres. 100 additional patients were included in CLOTS Lite in which a single scan was performed at 7-10 days.	Patients were randomized to wear thigh-length stockings (n=1,552) or below-knee stockings (n=1,562) while they were in the hospital, in addition to routine care, which could have included early mobilization, hydration, and/or the use of anticoagulants/antiplatelets. Patients wore the garments day and night until they became mobile, were discharged, or there were concerns with skin	As per CLOTS 1 **Primary outcome:** Symptomatic or asymptomatic DVT detected by Doppler u/s in the popliteal or femoral veins within 30 days of randomization **Secondary outcomes:** Death, any DVT, PE, complications and compliance with treatment (2 scans were performed	At 30 days, there was a significant reduction in the odds of proximal DVT associated with thigh-length GCS (6.3% vs. 8.8%, adj OR=0.69, 95% CI 0.53-0.91, p=0.008). There were no significant differences between groups for the outcomes of death by 30 days, symptomatic proximal DVT, symptomatic proximal or distal DVT, any DVT, PE or any DVT or PE. The odds of asymptomatic DVT were lower in the thigh length GCS group (3.2% vs. 4.8%, adj OR=0.64, 95% CI 0.44-0.93,

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			breakdown.	between days 7-10 and 25-30, when possible)	p=0.02). The odds of any skin breakdown were significant higher in the thigh-length GCS group 9.0% vs. 6.9%, OR=1.33, 95% CI 1.031.73, p=0.03).
Clots in Legs Or sTockings after Stroke (CLOTS) 3 2013 **UK** **RCT**	CA: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑ (Primary outcome)	2,876 patients admitted to 105 hospitals in the UK within 3 days of acute stroke, who were immobile.	Patients were randomized to wear thigh length intermittent pneumatic compression (IPC) device (n=1,438) or to no IPC (n=1,438) at all times except for washing and therapy, for a minimum of 30 days, or until the patient became mobile, was discharged from hospital, or declined to continue to IPC.	As per CLOTS 1 & 2+ additional 6-months outcomes **Primary outcome:** Symptomatic or asymptomatic DVT detected by Doppler u/s in the popliteal or femoral veins within 30 days of randomization. **Secondary outcomes:** Death, any DVT, PE, complications and compliance with treatment within 30 days (2 scans were performed between days 7-10 and 25-30, when possible) 6-month outcomes: Death from any cause, any symptomatic or asymptomatic DVT or PE.	Mean duration of IPC use was 12.5 days. 100% adherence to treatment was 31% in IPC group. The incidence of proximal DVT within 30 days was lower for IPC group (8.5% vs. 12.1%, OR=0.65, 95% CI 0.51-0.84, p=0.001, ARR=3.6%, 95% CI 1.4%-5.8%). There were no significant differences between groups for the outcomes of: death at 30 days (10.8% vs. 13.1%, p=0.057), symptomatic proximal DVT (2.7% vs. 3.4%, p=0.269), or PE (2.0% vs. 2.4%, p=0.453). The incidence of any DVT (symptomatic, asymptomatic, proximal or calf) was significantly lower for IPC group (16.2% vs. 21.1%, OR=0.72, 95% CI 0.60-0.87, p=0.001). The incidence of any DVT, death or PE was significantly lower for IPC group (27.2% vs. 34.1%, OR=0.72, 95% CI 0.61-0.84, p<0.0001). Skin breakdown was more common in IPC group (3.1% vs. 1.4%, OR=2.23, 95% CI 1.31-3.81, p=0.002). At 6 months, the incidence of any DVT remained significantly lower in the IPC group (16.7% vs. 21.7%, OR=0.72, 95% CI 0.60-0.87, p=0.001). The incidence of any DVT, death or PE also remained significantly lower for IPC group (36.6% vs. 43.5%, OR=0.74, 95% CI 0.63-0.86,

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					p<0.0001). There were no significant interactions found in sub-group analyses including: time to initiation of treatment (days), concurrent use of anticoagulants, or antithrombotics, baseline prognosis, baseline risk for DVT, stroke type (ischemic vs. hemorrhagic) or type of sleeve used.

CA Concealed allocation; ITT intention-to-treat

Temperature Management

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
De Ridder et al. 2017 **Netherlands** **RCT** ***Paracetamol (Acetaminophen) in Stroke 2 (PAIS 2)***	CA: ☑ Blinding: Patient ☑ Assessor ☑ ITT: ☑	256 patients ≥18 yrs, recruited from 12 sites, with ischemic or hemorrhagic stroke, temp of ≥ 36.5^{o} C, treated within 12 hrs of symptom onset. Mean age was 69 years, 56% were male. Median NIHSS score was 5.5.	Patients were randomized to receive high-dose paracetamol (6 grams, n=136) or placebo (n=118) for 3 days.	**Primary outcome:** Shift in distribution of mRS scores at day 90. **Secondary outcomes:** Favourable outcome (mRS 0-2), Barthel index, Telephone Interview for Cognitive Status score, and Euroqol 5D at 3 months, body temperature and markers of inflammation at 24 h after start of treatment	Recruitment was stopped early due to lack of funding. Sample size of 1,500 patients was planned. There was no significant shift in mRS scores at 90 days associated with paracetamol (common adj OR=1.15, 95% CI 0.74-1.79) The odds of a favourable outcome or a BI score >100 at 90 days were not significantly increased with paracetamol (adj OR=1.01, 95% CI 0.55-1.78 and adj OR=1.02, 95% CI 0.58-1.80, respectively).
Frank et al. 2013 **Germany** **Retrospective study**	NA	6,015 ischemic stroke patients who were registered in Virtual International Stroke Trials Archive (VISTA) and who had received paracetamol for the treatment of pain or fever. Patients who were started on paracetamol 1 day before the diagnosis	Patients who received paracetamol for the management of pain (n=1626) or fever (n=809) were compared to those who had not received the medication.	**Primary outcome:** Distribution of mRS scores at day 90. **Secondary outcomes:** Pneumonia and pneumonia-related mortality, death within 30 days of admission.	The median daily dose of paracetamol was 650 mg. In patients treated with paracetamol for fever or pain, there was no difference in the distribution of mRS scores at 90 days, compared with patients who did not receive treatment. In this same group, the odds of pneumonia were significantly reduced (OR=0.73, 95% CI 0.56-0.94, p=0.017). Among patients without pain or fever who were

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
		of pneumonia were excluded. Mean age was 69 years.			treated with paracetamol, the odds of poor outcome were increased (mortality at 90 days: OR=1.59, 95% CI 1.13-2.23, p=0.008, mRS score 0-2: OR=0.55, 95% CI 0.41-0.74, p<0.001 and recurrent stroke within 7 days: OR=3.57, 95% CI 1.37-9.32, p=0.009).
Kallmunzer et al. 2011 **Germany** **Controlled trial**	NA	77 patients with acute cerebral ischemia, hemorrhage or sinus thrombosis who experienced a body temperature ≥37.5ºC during the first 6 days of admission. Mean age 70 years, 58% female. Median baseline NIHSS score was 6.5. The control group consisted of 77 patients admitted to the same unit one year previously who had developed a fever ≥37.5ºC within the first 6 days of admission and were treated without adherence to a standardized protocol	The use of a 4-step standardized antipyretic procedure, was examined by comparing the results with a historic control group that underwent conventional treatment. The protocol included sequential administration of 1g paracetamol, 1g metamizole, calf packing (if patient was non-responsive to medications), and 500 ml cooled saline (0.9% NaCl), infused over 30 minutes, if patients was not responsive to prior therapies.	**Primary outcome:** Course of body temperature, duration of fever and achievement of normothermia.	Indications for antipyretic treatment occurred 251 times. Treatments used were paracetamol (n = 219), metamizole (n = 71), calf packing (n = 24), cooled saline (n=9). The use of all sequential elements of the protocol resulted in significantly reduced temps (p<0.002) with the exception of cooled saline (p=0.062). Concomitant antibiotics were used in 74% of cases. Compared to the control group, the overall duration of body temperature ≥37.5ºC was significantly shorter in the study group during the first 4 days after admission (p≤0.001). Normothermia was achieved in more than 90% of cases within 120 minutes and 100% of patients within 30 minutes following initiation of the protocol.
Middleton et al. 2011, 2017 **Australia** **Cluster RCT** ***Quality in Acute Stroke Care (QASC)***	CA: ☑ Blinding: Patient ☑ Assessor ☑ ITT: ☑	19 large tertiary care facilities with acute stroke units. Patients were eligible if they had been admitted to one of these facilities with a diagnosis of stroke (ischemic or hemorrhagic) within 48 hours. Age was evenly distributed among 3 groups, age 65 to 85. 60% male. 41% mild	4,198 patients were randomized to receive care at institutions that had adopted nursing protocols to identify and manage 3 complications-hyperglycemia, fever and swallowing dysfunction or to a control facility. Clinicians at the participating control institutions received abridged guidelines only. The protocol for	**Primary outcome:** Death or dependency at 90 days (mRS score of ≥2), BI, SF-36 (mental component summary score), physical component summary score. **Secondary outcomes:** Mean temperature for first 72 hours, proportion of swallowing screenings completed within the first	Intervention was associated with a decreased frequency of death or dependency at 90 days (42% vs. 58%, p=0.002). The % of patients with BI scores ≥95 was non-significantly higher in the intervention group (69% vs. 60%, p=0.07). **Fever outcomes:** Mean temperature of patients in the intervention hospitals was significantly lower compared with control hospitals during the first 72 hours after admission (36.5 vs. 36.6 degrees, p=0.02, absolute difference =0.09, 95% CI 0.04-0.15).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
		stroke.	monitoring/management of temperature control included: temperature monitored and charted every 4 hours after admission to the acute stroke unit for the first 72 hours. Temperatures ≥37.5°C were treated with paracetamol (intravenous, per rectum, or oral), unless clinically contraindicated.	24 hours of admission, pneumonia diagnosis, LOS.	Significantly fewer patients at intervention hospitals had at least one temperature ≥37·5ºC in first 72 hours after admission (17% vs. 27%, p<0.001, absolute difference=16.4%, 95% CI 8.3-24.6). **Long-term follow-up** Median duration of follow-up was 4.1 years. There were 264 (24.5%) deaths during study follow-up, most of which were attributed to cardiovascular disease. There were fewer deaths in the intervention group (22.3% vs. 27.3%). In an adjusted analysis (age, sex, marital status, education, and stroke severity (Los Angeles Motor Scale), assignment to the intervention group was associated with a significantly decreased risk of death (HR=0.77; 95% CI, 0.59–0.99, p=0.045).
den Hertog et al. 2009 **Netherlands** **Cochrane review**	NA	8 RCTs (n=423 patients) including patients ≥18 years, within 24 hours of a cerebral infarction or primary intracerebral hemorrhage.	Treatment contrasts evaluated included pharmacological agents (paracetamol vs. placebo, n=3, metamizole vs. placebo, n=1, ibuprofen vs. placebo n=1). Maximum duration of treatment was 5 days. Physical methods included endovascular cooling (n=1), cooling using forced air (n=1) and a cooling blanket (n=1). All control conditions were standard care or absence of treatment condition. Duration of treatment for physical methods ranged from 6-72 hours.	**Primary outcome:** Death and dependency at follow-up of 1-3 months, defined as mRS ≥3. **Secondary outcomes:** Death from all causes, mean body temp 24 hrs following treatment	Treatment was not associated with a reduction in the odds of death or dependency at follow-up (OR= 0.92, 95% CI 0.59- 1.42, p=0.69) Treatment was not associated with a reduction in the odds of death at follow-up (OR=0.86, 95% CI 0.48-1.54, p=0.62). Pharmacological treatment significantly reduced temperature at 24 hours following treatment (MD= -0.21, 95% CI -0.28, -0.15, p<0.0001).
den Hertog et al. 2009 **Netherlands**	CA: ☑ Blinding: Patient ☑	1400 patients, previously independent, admitted to one of 60 participating centres with ischemic or hemorrhagic stroke, who	Patients were randomized to receive 1 g paracetamol, 6x daily for 3 days (n=697) or placebo (n=703).	**Primary outcome:** The odds of improvement beyond expectation at 3 months (changed from unfavourable outcome,	21 patients assigned to paracetamol and 34 assigned to placebo discontinued treatment within 24 hours. 30% of all patients did not complete the 3-day treatment.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
RCT ***Paracetamol (Acetaminophen) In Stroke (PAIS) trial***	Assessor ☑ ITT: ☑	were able to receive the study drug within 12 hours of symptom onset. Mean age was 70 years, 56% men.		defined as mRS score 3-6). **Secondary outcomes:** Improvement of 1 category in mRS score, favourable outcome (mRS ≤2 or≤3 or Barthel Index score of 20), EuroQol-5D and body temperature. Outcomes were assessed at 14 days and 3 months following enrolment.	Treatment with paracetamol was not associated with improvement beyond expectation (adjusted OR=1.20, 95% CI 0.96-1.50). No evidence of benefit was reported in any of the pre-planned sub group analyses (stroke type, time to treatment, treatment with alteplase, or baseline body temperature). Treatment with paracetamol was not associated with increased odds of a favourable outcome, and did not result in significant differences in QoL. Treatment with paracetamol did significantly lower body temperature by a mean of 0.26 °C, 95% CI 0.18-0.31). Treatment with paracetamol was associated with a decrease in 14-day mortality (OR=0.60, 95% CI 0.36-0.90), with no difference at 3 months (OR=0.90, 95% CI 0.68-1.18).
Dippel et al. 2003 **Netherlands** **RCT** ***effect of Paracetamol (acetaminophen) and Ibuprofen on body temperature in Acute ischemic Stroke PISA***	CA: ☑ Blinding: Patient ☑ Assessor ☑ ITT: ☑	75 patients with acute ischemic stroke, confined to the anterior circulation and a body temperature of 36-39^{o} C, who were able to start treatment within 24 hours of symptom onset. Mean age was 67 years, 65% were male, mean NIHSS score was 14. Mean baseline body temp was 37.2^{o} C	Patients were randomized to receive either 1,000 mg acetaminophen (n=26), 400 mg ibuprofen (n=24), or placebo (n=25), 6x/day for 5 days. Treatment was started within 24 hours from the onset of symptoms.	**Primary outcome:** Body temperature at 24 hours from start of treatment **Secondary outcomes:** Change from baseline temperature at 1 and 5 days from start of treatment, time with elevated body temperature (> 37.0°C) during the first 24 hours and the first five days, and functional outcome at 1 month (assessed using mRS and BI)	Mean changes from baseline body temp during the first 24 hours were: Acetaminophen -0.1°C, Ibuprofen 0.1°C Placebo 0.2 Compared with placebo, treatment with acetaminophen resulted in a 0.3°C (95% CI: 0.0 to 0.6°C) larger reduction in body temperature in the first 24 hours. Only about half of the patients were still taking treatment at day 5. There were no significant differences between groups in any of the secondary outcomes.
Kasner et al. 2002 **USA**	CA: ☑ Blinding: Patient ☑ ☒	39 patients admitted to one of two centres following acute ischemic or hemorrhagic stroke, within 24 hours of	Patients were randomized to receive either acetaminophen 650 mg (n=20) or a placebo (n=19) every 4 hours for the initial	**Primary outcome:** The difference in mean core body temperature (CBT) Between groups during	Mean baseline temps were similar between groups (36.96 vs. 46.95, p=0.96). During the study period, CBT was non-significantly lower in the acetaminophen group (37.13°C vs.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
RCT	Assessor ☑☒ (open-label at 1 site) ITT: ☒	symptoms onset, NIHSS score ≥5, admission body temp <38.5°C, and admission WBC< 12.6 x 10^3 cells/mm^3. Mean age was 68 years, 41% male, mean NIHSS score 12.5.	24 hours after admission (total of 7 doses, 4550 mg).	the first 24 hours. **Secondary outcomes:** The proportion of time spent hyperthermic (>37.5°C) and time spent hypothermic (<36.5°C),	37.35°C). Mean difference between groups was 0.22°C, 95% CI 0.08°C to 0.51°C, p=0.14). The effect of acetaminophen did not differ significantly by stroke type. 13 patients in each group had ≥1 hyperthermic episode. The odds of hyperthermia/hypothermia associated with acetaminophen treatment were non-significantly decreased/increased, respectively (OR=0.52, 95% CI 0.19-1.44, p=0.22 and OR=3.4, 95% CI 0.83-14.2, p=0.09).
Body Temperature Cooling					
Oversen et al. 2013 **Denmark** **RCT** **COOLAID**	CA: ☑ Blinding: Patient ☒ Assessor ☒ ITT: ☒	31 patients admitted to one of two stroke units with acute ischemic stroke within 24 hours of onset of symptoms, with NIHSS scores 6-17. 14 patients were treated with rtPA but did not show signs of improvement at 3 hrs. Mean age was 64 years.	Patients were randomized to receive therapeutic hypothermia (TH) in the ICU (n=17) using endovascular or surface methods, or standard supportive care in the stroke unit (n=14). Patients in the TH group had body temperature lowered to 33 degrees C and maintained for 24 hours. Patients in the standard care group received acetaminophen if body temp exceeded 37.5 degrees C.	**Primary outcome:** Adverse events (AE) and serious AEs within 30 days of treatment. **Secondary outcomes:** Functional outcome	Patients in the TH group had significantly more episodes of bradycardia (11 vs. 0, p<0.0001). There were no significant differences between groups in other cardiac AEs (atrial fibrillation, hypotensive episodes, MI or DVT), pulmonary AEs (pneumonia, pneumothorax, sinusitis, respiratory failure or acidosis), Hemorrhagic AEs or death. Mean duration of hospital stay was 25 days for patients in TH group and 22.5 days for patients in control group. There were no differences between groups in median baseline NIHHS scores, or at 48 hours, 7 and 90 days. There was no significant difference in median mRS score at 90 days (3 vs. 1.5, p=0.15)
Harris et al. 2012 **UK** **Health Technology Assessment**	NA	High-quality RCTs examining the use of any form of non-invasive head cooling in adults following TBI or stroke of any severity, and following cardiac arrest, were sought. 46 studies were identified, none of	Of the studies identified, 2 studies included patients with stroke were included. COOL BRAIN-stroke trial, (Wang et al. 2004) and Giada et al. 2008, (abstract). In the COOL-Brain trial (n=14), the active treatment condition was head and neck	**Primary outcomes:** Intracranial temperature, All-cause mortality by end of follow-up, functional outcome **Secondary outcomes:** Reduction in ICP, Improvement in	12 studies reported on the effect of head cooling on intracranial and/or core trunk temperature. Within this group, 99 patients with stroke/TBI were included. The most effective techniques for which there were adequate data (nasal coolant and liquid cooling helmets) indicated that intracranial temperature could be reduced by 1 °C in 1 hour.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
		which were considered to be of high quality.	cooling with water-circulating cooling helmet vs. standard care. Target temperatures were > 33 °C and > 35 °C if age > 45 years. The second study included 6 patients recovering from aneurysmal SAH who received standard treatment for elevated temps consisting of paracetamol, metamizole, alcohol washing, and ice packs plus head and neck cooling. Duration of treatment was 6 hours.	biochemical markers of injury, adverse events	No studies that included stroke/TBI patients assessed functional outcome.
Lakhan & Pamplona 2012 **USA** **Systematic review & meta-analysis**	NA	17 studies, (4 observational studies and 13 clinical trials). Patients included in these studies were admitted acutely to hospital with ischemic and hemorrhagic stroke and intracranial aneurysm. Patients in 2 trials underwent hemicraniectomy.	4 observational trials examined the relationship between body temperature and mortality following stroke. There were 5 single group intervention studies (no control). There were 8 controlled trials (3 RCTs). In these studies, mild hypothermia was induced using external cooling (n=3), endovascular devices (n=3), or both (n=2).	**Primary outcomes:** Mortality, stroke severity (assessed using NIHSS or mRS). Timing of outcome not stated	There was no significant difference in stroke severity associated with hypothermia treatment (SMD=-0.17, 955 CI -0.42-0.08, p=0.19). Hypothermia was not associated with a reduced risk of death (RR=1.6, 95% CI 0.93-2.78, p=0.09).

CA Concealed allocation; ITT intention-to-treat

Early Mobilization

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Li et al. 2018 **China** **Systematic**	NA	6 RCTs including patients admitted to hospital following acute ischemic or hemorrhagic stroke	Trials compared early mobilization (within 24 hours of stroke) vs. usual care. Trials included SEVEL, AVERT (phases II and III), Chippala &	**Primary outcomes:** mRS (0-2), mortality at 3 months **Secondary outcomes:**	There was no significant difference between groups in the proportion of patients with mRS score of 0-2 at 3 months (RR=0.80, 95% CI 0.58-1.02). The results from 5 trials were included (n=1,646).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
review & meta-analysis			Sharma 2016, and Sundseth et al. 2014, all described below)	BI scores at 3 months, LOS	Early mobilization was not associated with an increased risk of mortality (RR=1.21, 95% CI 0.76-1.75). The results from 4 trials were included. Early mobilization was associated with higher BI scores at 3 months (SMD=0.66, 95% CI 0.0-1.31). The results from 4 trials were included (n=285). Early mobilization was associated with a significantly reduced LOS (WMD=-1.97, 95% CI -2.63 to -1.32). The results from 3 trials were included (n=236).
Chippala & Sharma 2016 **India** **RCT**	CA: ☑ Blinding: Patient:☒ assessor ☑ ITT:☒	86 patients ≥18 years with acute onset of ischemic stroke who were able to react to verbal commands, had SBP 120-180 mm Hg, oxygen saturation >92%, a heart rate of 40-100 bpm and temperature <38.5°C. Mean age was 60 years, 53% were male. 52% of patients had moderately disabling strokes (NIHSS 8-16).	Within 24 hours of stroke onset, patients were randomized 1:1 to either the Very Early Mobilization group or a standard care group for 7 days or until discharge. The treatment protocol for the Early mobilization group was similar to the AVERT protocol. Patients were out of bed within 24 hours, and received passive and active mobilization. Patients in the standard care groups received routine stroke unit care.	**Primary outcome:** Barthel Index at day 7 and 3 months **Secondary outcomes:** LOS	The were 6 losses to follow-up (3 in each group). Median BI scores at baseline, discharge and 3 months were: 50, 85 and 90 (intervention) and 52.5, 70 and 75 (control). There was significantly greater improvement in median BI scores from admission to discharge (p<0.001) and from admission to 3-months in the intervention group (p<0.001) Median LOS was significantly shorter in the early mobilization group (8 vs. 10, p<0.001.
Herisson et al. 2016 **France** **RCT** ***Stroke and Early VErticaL positioning (SEVEL)***	CA: ☑ Blinding: Patient:☒ assessor ☒ ITT: ☒	167 patients ≥18 years with acute onset of ischemic stroke were recruited from 11 centres. Patients with severe stroke (NIHSS ≥22 were excluded). Mean ages were 68.1 (early group), 71.2 years (progressive group). Mean NIHSS scores were 7.2 (early) and 7.8 (progressive).	Patients were randomized 1:1 to early and progressive sitting arms. Patients in the early sitting arm were seated out of bed as soon as possible, within the first day of stroke. Patients in the progressive group sat in bed for days 1-2 post stroke, and then seating out of bed on day 3. For both protocols, Minimal duration of the first sitting was 15 minutes in both groups; maximum duration was 60 minutes. Duration of treatment	**Primary outcome:** Favourable outcome (mRS 0-2) at 3 months **Secondary outcomes:** Medical complications, LOS, tolerance at 7 days and 3 months	The study was terminated early due to slow enrollment. There were 24 losses to follow-up (17 early group, 7 progressive group). The percentage of patients with mRS scores of 0-2 at 3 months was similar (76.2% vs. 77.3%, p=0.52). There were no significant differences between groups on any of the secondary outcomes (medical infections: pulmonary infection, UTI, dysphagia, DVT, pressure ulcer). Mean LOS was 9.8 (early) vs. 10.5 (progressive)

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			was 7 days, or until discharge.		days, p=0.27. The procedure was well-tolerated in both groups. There were no significant changes in SBP, DBP or heart rate immediately after the procedure, or 5 minutes later.
Bernhardt et al. 2015, 2016 **Australia** **RCT** ***A Very Early Rehabilitation Trial for stroke (AVERT)***	CA: ☑ Blinding: Patient:☒ assessor ☑ ITT: ☑	2,104 patients ≥18 years, recruited from 56 stroke units, located in 5 countries, within 24 hours of ischemic or hemorrhagic stroke without pre-morbid disability. Mean age was 72 years, 55% of patients were admitted with mild stroke (NIHSS score 1-7)	Patients were randomized to receive usual care (n=1,050) or early mobilization (n=1,054), a task-specific intervention focused on sitting, standing, and walking activity, initiated within 24 hrs. of stroke onset. Four pre-specified levels of out-of-bed activity were used, depending on functional recovery. The duration of treatment was 14 days, or until discharge from the stroke unit.	**Primary outcome:** Favourable outcome (mRS 0-2) at 3 months **Secondary outcomes:** Shift in distribution of mRS, time to achieve assisted- free walking over 50m, proportion of patients able to walk unassisted at 3 months, death, serious adverse events	**Main Results (2015)** Significantly fewer patients in the very early mobilization group had a favourable outcome (46% vs. 50%; adjusted OR=0.73, 95% CI 0.59-0.90, p=0.004). There was no significant shift in the distribution of mRS between groups (adjusted OR=0.94, 95% CI 0.85-1.03, p=0.193). Significantly more patients in the very early mobilization group were mobilized within 12 and 24 hrs (23% vs. 14% and 92% vs. 59%, respectively). The median time to first mobilization was significant sooner in the early mobilization group (18.5 vs. 22.4 hrs, p<0.0001). Patients in the early mobilization group received significantly more out of bed sessions (median of 6.5 vs. 3, p<0.0001) and more daily therapy (31 vs. 10 min, p<0.0001). The odds of walking for 50 m independently were not significantly increased in the early mobilization group (adjusted OR=1.04, 95% CI 0.94-1.15, p=0.46). The odds of death non-serious adverse events and neurological serious adverse events were not significantly increased in the early mobilization group. **Subgroup analysis (2016)** Regardless of group assignment, keeping time to first mobilization and frequency constant, every extra 5 minutes of out-of-bed activity per day reduced the odds of a favorable outcome

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					(OR=0.94, 95% CI 0.91-0.97, p<0.001) and reduced the odds of walking unassisted for 50 m (OR=0.85, 95% CI 0.81-0.89, p<0.001), after controlling for age and stroke severity. Regardless of group assignment, increasing the frequency of out-of-bed sessions improved the odds of favorable outcome by 13% (OR for each additional session =1.13, 95% CI 1.09-1.18, p <0.001) and improved the odds of walking 50 meters unassisted by 66% (OR for each additional session =1.66, 95% CI 1.53–1.80, p< 0.001), after controlling for age and stroke severity. Increased frequency of out-of-bed sessions also reduced the odds of death and fatal and nonfatal neurological serious adverse events.
Sundseth et al. 2012 **Norway** **RCT** **Akerhus Early *Mobilization in Stroke Study (AKEMIS)***	CA: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑	65 patients admitted to a single stroke unit with ischemic stroke or ICH within 24 hours of onset of symptoms were included. Mean age was 77 years, 45% male.	Patients were randomized to a very early mobilization (VEM) group (n=32) or to a control group (n=33). Patients in both groups received standard stroke unit care. Patients in the VEM group were mobilized as soon as possible (within 24 hours post stroke). The control group were mobilized between 24 and 48 hours.	**Primary Outcomes:** Poor outcome at 3 months, defined as mRS score of 3-6. **Secondary Outcomes:** Independence (BI score of ≥18), death and number of complications at 3 months.	The median time to first mobilization from stroke onset was significantly shorter for patients in the VEM group (13.1 vs. 33.3 hrs, p<0.001). More patients in the VEM group had poorer outcomes compared with control participants, although this difference was not statistically significant (OR= 2.70, 95% CI: 0.78-9.34; p=0.12). The odds of death or dependency, or dependency at 3 months were not significantly reduced in the VEM group (OR= 5.26, 95% CI: 0.84-32.88; p=0.08; OR= 1.25; 95% CI: 0.36-4.34; p=0.73, respectively). The improvement in mean NIHSS scores from baseline to 3 months was significantly greater for patients in the VEM group (7.2-3.9 vs. 7.5-5.5, p=0.02). The proportion of patients with at least 1 complication within 3 months was the same in the 2 groups (67% vs. 66%, p=0.93).
Diserens et al.	CA: ☑	50 patients with ischemic	Participants were randomized	**Primary Outcomes:**	8 patients in the delayed group were transferred to

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
2011 **Switzerland** **RCT**	Blinding: Patient ☒ Assessor ☒ ITT: ☒	stroke admitted to a single stroke unit within 12 hours of onset of symptoms, with an NIHSS score >6. Mean age was 71.5 years.	to either an "early mobilization" group (n=25) in which they were mobilized out of bed after 52 hour or "delayed mobilization" group (n=25) where they were mobilized after 7 days.	Severe complications during hospitalization (i.e. complications having vital consequences). **Secondary Outcome:** Minor complications, differences in neurological deficits, and modifications in cerebral blood flow.	other hospitals and were not included in the analysis. There were significantly fewer severe complications among patients in the early mobilization group: 2/25 (8%) vs. 8/17 (47%) in the delayed mobilization group ($p < 0.006$). No significant differences were found in the numbers of minor complications, neurological deficits, or blood flow modifications.
Bernhardt et. al. 2010 **UK** **Cochrane Review**	N/A	1 RCT that included the results of 71 patients recovering from acute stroke (Bernhardt et. al. 2008)	RCTs examining mobilization within 48 hours of symptom onset compared with conventional care.	**Primary Outcomes:** Death or poor outcome. **Secondary Outcomes:** Death from any cause, number of days dead or dependent, institutionalization, ADL and extended ADL performance, health status/ quality of life, time to walking unassisted, adverse events, patient mood.	There was a non-significant reduction in death or poor outcome in the early mobilization vs. delayed mobilization group at three months (OR= 0.67, 95% CI: 0.25 to 1.79, p=0.42). For additional results, see below.
Bernhardt et al. 2008, Sorbello et al. 2009, Cumming et al. 2011 **Australia** **RCT** ***A Very Early Rehabilitation Trial for stroke (AVERT)***	CA: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑	71 patients with stroke admitted to hospital within 24 hours of symptom onset, who could react to verbal commands and who were independent in ADL prior to stroke. Mean age was 75 years, 46% male.	Participants were randomized to receive either very early and frequent mobilization (upright, out of bed, activity – 2x/day, for 6 days a week until discharge beginning within 24 hours of stroke (n=38), or usual multi-disciplinary stroke team care (n=33).	**Primary Outcomes:** Safety (deaths at 3 months) and feasibility (significant difference in dose of mobilization) **Secondary outcomes:** Serious adverse events at 3 months, good outcome (mRS score of 0-2) at 3, 6 and 12 months, number of days from stroke to return to unassisted	There was a non-significant increase in the number of patient deaths in the early mobilization vs. delayed mobilization group at 3 months (21% vs. 9%, absolute risk difference = 12.0%, 95% CI, 4.3% to 28.2%, p=0.20). After adjusting for age, baseline NIHSS score and premorbid mRS score, the odds of experiencing a good outcome were significantly higher at 12 months for the VEM group (OR= 8.15, 95% CI 1.61-41.2, p<0.01), although not at 3 or 6 months. There were no differences in the total number of complications, severe complications or stroke-

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
				walking (50 meters), functional outcome at 3 months, motor impairment at 3 and 12 months.	related complications between groups. Patients in the control group experienced a total of 91 complications while patients in the VEM group experienced 87. Patients in the VEM group returned to walking significantly sooner (Median of 3.5 vs. 7 days, p=0.032). There were no differences in proportions of patients who were independent on the BI (score of 20) or who had achieved a good outcome on the Rivermead Motor Assessment Scale (score of 10-13) at either 3 or 12 months. VEM group assignment was a significant, independent predictor of independence on the BI at 3 months, but not at 6 months. VEM group assignment was a significant, independent predictor of good outcome on RMA at both 3 and 12 months.
Craig et al. 2010 **UK** **Systematic Review and Meta-Analysis**	NA	103 patients included in the AVERT (n=71) and VERITAS (n=32) trials. The baseline characteristics of patients in both trials were similar. Participants with severe pre-stroke disability were excluded from both studies.	In both studies, patients were randomized to early mobilization within 24 hours of stroke onset groups or to standard care. The duration of the intervention in the AVERT study implemented was 14 days, whereas the VERITAS trials lasted 7 days.	**Primary Outcome:** Independence at 3 months, defined as mRS score of 0-2. **Secondary Outcome:** Early complications of immobility and independence in ADL s at 3 months (BI score 18-20).	The median time to first mobilization in AVERT was significantly shorter in the VEM group in the AVERT trial, but not in VERITAS (18.1 vs. 30.8 hrs, p<0.001; 27.3 vs. 31.8 hrs, p>0.05). In pooled analysis, median time to first mobilization was shorter in VEM group (21 vs. 31 hrs). The odds of independence (mRS criteria) at 3 months were significantly higher for VEM patients (adjusted OR= 3.11, 95% CI 1.03-9.33). VEM patients were more likely to be independent in ADL at 3 months (adjusted OR= 4.41, 95% CI 1.36-14.32). More standard care patients experienced at least one complication (51%) compared with the treatment group (35.3%). The risk of experiencing immobility related complications was significantly lower in VEM patients (adjusted OR= 0.20, 95%CI

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					0.10-0.70).

CA Concealed allocation; ITT intention-to-treat

Management of Bowel and Bladder Incontinence

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
i) Methods of assessment of urinary incontinence					
Martin et al. 2006 **UK** **Health Technology Assessment**	NA	121 studies that compared a diagnostic technique with multichannel urodynamics, considered the gold standard for urinary incontinence. Studies included both men and women, most frequently with symptoms of UI. No studies were stroke specific.	Quantitative comparisons between two or more methods of assessing urinary incontinence were conducted. Diagnostic techniques under study included clinical history, validated scales, pad test	Sensitivity (SN), specificity (SP)	Only a limited number of studies could be used in pooled analyses. Clinical history for diagnosing urinary incontinence in women: SN= 0.92, SP=0.56. The results from 15 studies were included. Clinical history for diagnosing detrusor over activity in women: SN=0.61, SP=0.87. The results from 8 studies were included.
ii) Management of urinary incontinence					
Thomas et al. 2014 **UK** **RCT (feasibility)** ***Identifying Continence Options after Stroke (ICONS)***	CA: ☑☒ Blinding: Patient ☒ Assessor ☒ ITT: ☑	413 patients ≥18 years, admitted to one of 12 specialized units with urinary incontinence (UI) secondary to stroke. Median age was 79 years, 46% were male, 82% of patients had mRS score of 0-2 prior to stroke	Centres were randomized to participate in a systematic voiding program (SVP; n=4 centres, 164 patients), SVP + supported implementation (n=4 centres, 125 patients) or usual care (n=4 centres, 124 patients)	**Primary outcome:** Urinary continence at 6 and 12 weeks post stroke	At 6 weeks, compared with usual care, the odds of being continent were not significantly increased with SVP (OR=0.94, 95% CI 0.46-1.94) or SVP+ supported implementation (OR=0.62, 95% CI 0.28-1.37). The response rate was 85%. At 12 weeks, compared with usual care, the odds of being continent were not significantly increased with SVP (OR=1.02, 95% CI 0.54-1.93) or SVP+ supported implementation (OR=1.06, 95% CI 0.54-2.09). The response rate was 88%.
Cournan et al. 2012 **USA** **Controlled trial**	NA	70 females with impaired bladder management admitted to a rehabilitation unit following stroke and who had been continent prior to stroke. The mean age was 72 years. Patients	The outcomes of patients who had been admitted to the unit prior to the implementation of a standardized bladder management program (n=35) were compared with those admitted	**Primary outcome:** Admission and discharge scores of the 2 FIM bladder items.	The average length of stay was 21 days. Women who received the interventions experienced a significantly greater improvement in mean FIM bladder scores (2.83±2.23 vs. 1.6±2.17, p=0.01).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
		were admitted a mean of 12 days following stroke.	following the establishment of the program (n=35) during hospital stay. Bladder management strategies included timed/prompted voiding, bathroom training, and pelvic floor exercises).		
Moon et al. 2012 **South Korea** **RCT**	CA: ☑ Blinding: Patient ☒ Assessor ☒ ITT: ☒	60 patients admitted to a stroke rehabilitation unit following ischemic (n=25) or ICH (n=35). Mean age was 63 yrs, 50% male.	Patients were randomized to 1 of 3 groups evaluating indwelling urethral catheter (IUC) clamping prior to removal: no clamping (n=20), and clamping for 4hrs followed by 5 min of urinary drainage, for 24 hrs (n=20) or 72-hrs (n=20).	**Primary outcome:** Time to first void, first voided volume, voiding method (self-voiding (SV) or intermittent catheterization (IC) and residual urine volume following first void. **Secondary outcomes:** Symptomatic urinary tract infections (UTI)	Indwelling catheters had remained in place prior to removal for an average of 33-41 days. There were no significant differences between groups on any of the outcomes. No clamping vs. clamping groups combined Mean time to first void: 308 vs. 273 min, p=0.17 Mean volume of first void: 216 vs. 239 mL, p=0.37 Mean residual volume: 79 vs. 60, p=0.26 Method of first void (SV/IC): 15/5 vs. 24/16, p=0.39 Number of UTIs: 0 vs. 3, p=0.54
Thomas et al. 2008 **UK** **Cochrane Review**	NA	12 RCTs (n=724) including participants from a mixture of settings, age groups, and phases of stroke recovery. Two trials enrolled only women, while the sex distribution was not reported in 3 trials. In 3 trials, the authors stated that patients had been incontinent prior to stroke, while continence status prior to stroke was not stated in the remaining studies. In 5 studies, care was provided in a hospital setting, including a rehabilitation unit and	Treatments evaluated included behavioral interventions (n=4), specialised professional input (n=2), complementary medicine (n=4), pharmacotherapy (n=3) and physical therapy (n=1). The control condition was usually standard care or no treatment.	**Primary outcome:** Incontinence **Secondary outcomes:** Symptom scores, physical measures, health status	In the overall analysis, treatment was associated with a decreased risk of UI (RR= 0.44, 95% CI 0.23-0.86, p=0.0017). Results from 5 trials included (complementary medicine n=3, professional input, n=2). The results from no other analyses included results from >2 studies. Evidence from a single small trial suggested that structured assessment and management of care in early rehabilitation may reduce the risk of incontinence at hospital discharge (RR= 0.06, 95% CI 0.01-0.43). Evidence from another trial suggested that assessment and management of care by continence nurse practitioners in a community setting may reduce the number of urinary symptoms (RR= 0.77, 95% CI 0.59-0.99).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
		long-stay geriatric wards. One trial was restricted to persons living in the community.			
Eustice et al 2000 **Australia** **Cochrane Review**	NA	9 RCTs (n= 674), including elderly men and women with urinary incontinence of any etiology. Setting included home (n=1), nursing home (n=7) and not stated (n=1). Patients in some of the studies were cognitively impaired. No studies were specific to stroke.	The treatment comparison under study was prompted voiding vs. no prompted voiding. Duration of treatment varied (10 days-13 weeks).	**Primary outcome:** Urinary symptoms (improvement in wet episode, number of incontinent episodes in 24 hours) and Health status (measures of ADL). Outcomes assessed before and after treatment. Maximum follow-up period was 3 months.	Prompted voiding was associated with a reduction in the number of incontinent episodes in 24 hours (MD= -0.92, 95% CI -1.32 to -0.53, p<0.0001). Results from 2 trials were included. For all other planned outcomes, results were available for 0 or 1 studies.
Chan et al. 1997 **Australia** **Single group evaluation (pre/post-test)**	NA	42 patients admitted to a single acute stroke unit between May and August 1995. 62% female.	Each patient was prescribed an individualized bladder program consisting of bladder scanning, intermittent catheterizations/ post-void residual regimen, non-invasive voiding strategies (e.g. pelvic muscle exercises) and/or drug therapy. The regimen was continued until the post-void urine residual was below 100 ml for three consecutive days	**Primary outcome:** Bladder function was assessed on admission using a 5-point Bladder score, where 1=total urinary retention to 5= residual volume of <100 ml.	37 patients participated in the bladder management program. Average duration of IMC/PVR was 8 days 84% of all stroke patients achieved urinary continence within the first month of stroke (all females became continent, while 23% of the male patients did not).
iii) Treatment of Fecal Incontinence					
Harari et al. 2004 **UK** **RCT**	CA: ☑ Blinding: Patient ☒ Assessor ☒ ITT: ☒	146 stroke patients with constipation or fecal incontinence (122 community, 24 stroke rehabilitation inpatients). Mean age was 72 years, 41% female. The average time from stroke	Patients were randomized to an intervention (n=73) or routine care group (n=73). The intervention consisted of a 1 time nursing assessment (history and rectal	**Primary outcome:** Number of bowel movements (BM)/week. **Secondary outcomes:** Percentage of BM graded as normal by the patient, episodes of fecal	The mean number of BMs/ week was significantly higher in the intervention group at 1 month (5.5 vs. 4.1, p=0.011) and 6 months (5.2 vs. 3.6, p=0.005). There were no differences between groups on any of the other outcomes, at any of the assessment points.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
		onset to study entry was 2 years.	examination), followed by patient/carer education (booklet) and provision of diagnostic summary and treatment recommendations.	incontinence. Assessments were conducted at 1, 3, 6, and 12 month, using postal prospective 7-day stool diaries.	Persons in the intervention group had an average of 5 episodes of FI at 1 and 6 months, compared with 12 and 6 episodes, respectively among persons in the control group.

CA Concealed allocation; ITT intention-to-treat

Dysphagia Screening & Assessment to Prevent Pneumonia & Management

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
i) Dysphagia Screening and Assessment					
Ho et al. 2018 **Taiwan** **Retrospective study**	NA	Patients included in a national database, ≥18 years who had been admitted from 2006-2010 for rehabilitation following first-ever stroke.	The outcomes of patients who had dysphagia (identified by the placement of ≥2 NG feeding tubes, n=5,032) were compared with those without dysphagia (n=52,323).	**Primary outcomes:** Readmission to hospital within one year for chest infection (including pneumonia) and mortality at one-year post stroke **Secondary outcomes:** Same as primary, but assessed at 5 years	The mean NG tube insertions was 2.51 vs. 0.17 in the control group. One-year post stroke: The risks of chest infection and death were significantly higher among the patients with dysphagia (adjusted HR= 1.73, 95% CI 1.61-1.85 and HR=1.61, 95% CI 1.46-1.79, respectively). Five-years post stroke: The risks of chest infection and death were significantly higher among the patients with dysphagia (adjusted HR= 1.53, 95% CI 1.45-1.62 and HR=1.54, 95% CI 1.41-1.68, respectively).
Smith et al. 2018 **Canada/US/UK** **Systematic review**	NA	3 RCTs including persons ≥18 years, hospitalized for stroke (ischemic or hemorrhagic)	Trials compared dysphagia screening protocols or quality improvement interventions designed to improve screening rates vs. no screening, alternative screening, usual care or gold standard	**Primary outcomes:** ≥1 of death, dependency, or pneumonia	3 trials (Rai et al. 2016, Miles et al. 2013 and Middleton et al. 2011), are all described below. The percentage of patients who received dysphagia screening and developed pneumonia was not significantly lower, compared with patients in a control group, in any of the trials. The authors highlight the lack of evidence from RCTs and state that *"no conclusions can be drawn about the clinical effectiveness of dysphagia screening protocols."*
Bray et al. 2017	NA	63,650 patients included	The risk of stroke-associated	**Primary outcome:**	55, 838 (87.7%) patients had a dysphagia screen,

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
UK **Retrospective study**		in a nation register, ≥16 years admitted to 199 hospitals, following an acute ischaemic stroke or primary intracerebral haemorrhage, between 2013 and 2014. Median age was 77 years, 50.4% were female, 88.2% of strokes were ischemic	pneumonia in relation to timing of dysphagia screening and comprehensive assessment was examined using multivariable models adjusted for age, sex, stroke subtype, pre-stroke functional level (mRS), place of stroke (out of hospital vs. inpatient), vascular comorbidity and either NIHSS score or level of consciousness on admission. Timing of screening and assessment was arranged into quartiles.	Stroke-associated pneumonia (SAP) **Secondary outcome:** 30-day mortality	of which 24,542 (38.6%) proceeded to a comprehensive assessment by a SLP. The overall incidence of SAP was 8.7% (13.8% for patients not screened, 8.0% for patients who were screened and 14.7% for patients who received a comprehensive assessment). The median time from admission to dysphagia screening was 2.9 hours. The median time from admission to dysphagia assessment was 22.9 hours. The odds of SAP associated with timing of screening including data from 55,838 patients were: Q1 (0-79 min): OR=1.00 (ref) Q2 (80-176 min): OR=0.92, 95% CI 0.83-1.01, p=0.08 Q3 (177-344 min): OR=0.89, 95% CI 0.81-0.99, p=0.03 Q4 (≥345 min): OR=1.14, 95% CI 1.03-1.24, p=0.008 The odds of SAP associated with timing of dysphagia assessment including data from 24,542 patients were: Q1 (0-369 min): OR=1.00 (ref) Q2 (370-1371 min): OR=1.40, 95% CI 1.22-1.06, p<0.0001 Q3 (1372-2961 min): OR=1.60, 95% CI 1.41-1.84, p<0.0001 Q4 (≥2962 min): OR=2.01, 95% CI 1.76-2.30, p<0.0001 The odds of 30-day mortality, excluding patients dying or who started palliative care in the first 72 hours after admission, were associated with increased delays in dysphagia assessment (Q1: ref, Q2 OR= 1.31, Q3 OR= 1.54, Q$4OR=1.39, all p<0.0001)

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Joundi et al. 2017 **Canada** **Retrospective study**	NA	6,677 patients ≥18 years, included in the Canadian Stroke Registry from 2010-2013 who were eligible for dysphagia screening within 72 hours of admission following acute ischemic stroke. 78.7% of patients suffered a mild stroke (CNS score >7), 9.5% had moderately severe stroke (CNS 5-7) and 6.3% had a severe stroke (CNS <5)	The association between formal dysphagia outcome and stroke outcomes was examined.	**Primary outcome:** In-hospital pneumonia within 30 days of admission, severe disability (mRS 4-5) and all-cause mortality at 1 year	19.2% of patients did not receive a dysphagia screen within 72 hours of admission. Independent predictors of receiving a dysphagia screen included older age, admission to specialized units, the presence of weakness, speech difficulties and treatment with thrombolysis. Patients with mild strokes were less likely to be screened compared with those with moderate strokes (adj OR=0.51, 95% CI 0.41-0.64). Of the patients who were screened, 47.8% failed. Compared with patients who passed the screen, those who failed were at significantly higher risk of pneumonia (adj OR=4.71, 95% CI 3.43-6.47), severe disability (adj OR=5.19, 95% CI 4.48-6.02) and death (adj OR=2.42, 95% CI 2.09-2.80)
Al-Khaled et al. 2016 **Germany** **Retrospective study**	NA	12,276 patients, ≥18 years recruited from 15 hospitals from 2007-2012 following admission for acute ischemic stroke. Mean age was 73 years, 49% were women.	The association between dysphagia, assessed shortly after admission to hospital, and clinical outcomes was examined.	**Primary outcomes:** Stroke-related pneumonia during hospitalization **Secondary outcomes:** 30-day mortality, disability (mRS ≥2) at discharge and 30 days	9,164 patients were screened for dysphagia. 94% of patients were screened within 24 hours of admission. 3,083 patients had dysphagia. Mean LOS was 9 days. During this time, 1,271 patients (10.3%) developed pneumonia. Pneumonia incidence was significantly higher in patients with dysphagia (29.7% vs. 3.75, p<0.001). Dysphagia was an independent predictor of pneumonia (OR=3.4, 95% CI 2.8-4.2). Early dysphagia screening within 24 hours was protective (OR=0.68, 95% CI 0.52-0.89). Dysphagia was also a significant, independent predictor of case fatality (OR=2.8, 95% CI 2.1-3.7), disability at discharge (OR=2.0, 95% CI 1.6-2.3), 3-month mortality (OR=3.2, 95% CI 2.4-4.2) and 3-month disability (OR=2.3, 95% CI 1.8-3.0)
Rai et al. 2016 **India**	CA: ☑ Blinding: Patient ☒	162 patients, ≥18 years admitted to 2 wards within 72 hours of stroke onset. Mean age was	Patients were randomized by ward to an intervention (n=77) or control group (n=85). Patients in the intervention	**Primary outcome:** Aspiration pneumonia **Secondary outcomes:**	Non-significantly fewer patients in the intervention group developed aspiration pneumonia during hospitalization (6.5% vs. 15.3%, RR = 0.42, 95% CI 0.16-1.14, *p*= 0.062).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Cluster RCT	Assessor ☒ ITT: ☒	55.7 years, 73.5% were men. Median NIHSS score was 6	group were managed by a stroke care pathway consisting of nurse education, care checklist, swallow assessment flowchart, swallow screen conducted by a physician, and patient and caregiver education. Patients in the control group were treated with conventional care. There was no dysphagia assessment, and feeding was started by the resident doctor based on clinical judgment.	3-month mortality, BI and mRS at 3 months	Fewer patients in the intervention group required mechanical ventilation during hospital stay (7.8% vs. 17.6%, p=0.05). There were significantly fewer deaths in the intervention group at 90 days (7.8% vs. 20%, p=0.02). There were no significant differences between groups in median mRS or BI scores at discharge or 3 months.
Hoffmeister et al. 2013 **Chili** **Retrospective study**	NA	Records of 677 patients, aged ≥15 years admitted acutely following ischemic stroke from 7 public hospitals in Santiago, Chile, from 2007 to 2009, were reviewed. Mean age was 70 Years, 52% male. Intravenous thrombolysis was used in 1.7% of patients.	Patients were identified and classified according to dysphagia screening status: unscreened; or screened (using a valid screen within 48 hr. of admission) and associations between screening status and incidence of pneumonia and 30-day mortality were explored.	**Primary outcomes:** Pneumonia, 30-day mortality.	The majority of patients were unscreened, n=595 (87.9%) vs. screened n=82 (12.1%) There was no significant reduction in the development of or post-stroke pneumonia, (adjusted OR= 0.52, 95% CI 0.26-1.04, p= 0.07) or 30-day mortality (adjusted OR=1.58, 95% CI 0.60-4.15, p=0.36) associated with dysphagia screening. The overall incidence of post-stroke pneumonia was 23.6%. 30-day mortality was 8.7%. Factors associated with pneumonia were age, female sex, a reduced level of consciousness on admission, aphasia, hemiplegia and diabetes.
Masrur et al. 2013 **USA & Canada** **Retrospective study**	NA	Records of 314,007 patients with ischemic stroke admitted to GWTG–Stroke hospitals between April 2003 and March 2009 were reviewed. Median age was 73 years, 48% male. Median NIHSS score was 4.	The outcomes of patients who had received a standardized swallowing screen by any method that was accepted by individual institutions (including bedside or instrumental methods) were compared with those of patients who had not been screened.	**Primary outcome:** The incidence of pneumonia occurring after 48 hours of admission.	216,372 (68.9%) patients were screened for dysphagia, 97,656 (31.1%) were not screened. 17,906 patients (5.7%) developed post-stroke pneumonia. Patients who were screened for dysphagia were more likely to develop pneumonia compared with those who did not develop pneumonia (7.5% vs. 68.5%, p<0.001). Significant predictors of whether a dysphagia

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					screen was completed were: increasing age, increasing NIHSS score, admission to an academic hospital, atrial fibrillation and dyslipidemia.
Sorensen et al. 2013 **Denmark** **Controlled trial**	NA	146 patients admitted to a hospital following acute stroke (ischemic, ICH or SAH), diagnosed with moderate or severe dysphagia were included. Median age was 84 years, 64% female.	Three groups of patients were studied: intervention group (n=58), internal historic control group, including patients from the same institution (n=58) and external control group, including patients admitted to another hospital (n=30). Patients in the intervention group were screened using the Gugging Swallowing Screen prior to initiating oral intake and also received heightened oral hygiene (mechanical tooth brushing and chlorhexidine rinses following meals). Dysphagia screening was performed in 72% of patients in the internal historical control group and was not performed in the external control group.	**Primary outcome:** Incidence of hospital-acquired pneumonia. **Secondary outcomes:** 30 and 180-day mortality	The incidence of x-ray confirmed pneumonia was significantly lower in the intervention group (7% vs. 28% & 27%, p<0.01). The incidence or confirmed or probable pneumonia was also significantly lower in the intervention group (34% vs. 43% & 43%, p<0.05). 30-day mortality was significantly lower in the intervention group (12% vs. 22% & 30%), as was 180-day mortality (33% vs. 43% & 57%).
Titsworth et al. 2013 **USA** **Controlled study**	NA	Patients admitted to a single institution with acute stroke (ischemic, ICH, SAH)	The outcomes of 1686 patients collected prior to the initiation of a dysphagia protocol were compared with those following its establishment in 2010 (n=648). The dysphagia protocol, including a screen (Modified Nursing Dysphagia Screen, which does not include an oral challenge) and prompt referral to an SLP when the patients failed the screen.	**Primary outcome:** Incidence of pneumonia during hospitalization **Secondary outcome:** Discharge destination	The percentage of patients screened following initiation of the new protocol increased significantly (39% to 74%, p<0.001). The incidence of hospital-acquired pneumonia fell significantly following the dysphagia initiative (6.5% to 2.85, p<0.001, adjusted OR=0.43, 95% CI 0.26-0.71, p=0.001). The dysphagia initiative was a significant independent predictor of pneumonia. Use of the MNDS tool did not result in lower pneumonia incidence (2.4% vs. 3.1%, p=0.57), although the patients with more severe stroke were screened more frequently (NIHSS 10.7 vs. 5.3, p<0.001).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					There were significantly more SLP referrals following the dysphagia initiative (153 to 179/month, p<0.01).
Miles et al. 2013 **New Zealand** **RCT**	CA: ☑ Blinding: Patient ☒ Assessor ☒ ITT: ☑	311 patients, recruited from 4 hospitals who were referred to SLP following stroke for swallowing assessment. Mean age was 78 years, 47% were men.	Patients were randomized to an experimental (n=149) or control group (n=163). Patients in the control group were assessed using local protocols. Patients in the experimental group used a cough reflex test (CFT), using nebulized citric acid, delivered by face mask, prior to the standard assessment	**Primary outcome:** Pneumonia at 3 months following recruitment **Secondary outcome:** 3-month mortality	Within the experimental group, 61% of patients passed the CRT with a strong cough, 21% passed with a weak cough (21%) and 18% failed the test. There were no significant differences between groups in the number of patients who developed pneumonia (experimental 26% vs. control 21%, p=0.38), or who were dead at 3 months (experimental 20% vs. control 14%, p=0.23).
Middleton et al. 2011 **Australia** **Cluster RCT** ***Quality in Acute Stroke Care (QASC)***	CA: ☑ Blinding: Patient ☑ Assessor ☑ ITT: ☑	19 large tertiary care facilities with acute stroke units. Patients were eligible if they had been admitted to one of these facilities with a diagnosis of stroke (ischemic or hemorrhagic) within 48 hours. Age was evenly distributed among 3 groups, age 65 to 85. 60% male. 41% mild stroke.	4,198 patients were randomized to receive care at institutions that had adopted nursing protocols to identify and manage 3 complications-hyperglycemia, fever and swallowing dysfunction or to a control facility. Clinicians at the participating control institutions received abridged guidelines only. The dysphagia component included education and training in the use of the ASSIST screening tool. Nurses were required to pass a clinical competency tests prior to conducting swallowing screening. Patients who failed the screen were referred to an SLP for assessment.	**Primary outcome:** Death or dependency at 90 days (mRS score of ≥2), BI, SF-36 (mental component summary score), physical component summary score **Secondary outcomes:** Mean temperature for first 72 hours, proportion of swallowing screenings completed within the first 24 hours of admission, pneumonia diagnosis, LOS	Intervention was associated with a decreased frequency of death or dependency at 90 days (42% vs. 58%, p=0.002). The % of patients with BI scores ≥95 was non-significantly higher in the intervention group (69% vs. 60%, p=0.07). **Dysphagia outcomes:** Swallowing screening was performed more frequently in the intervention group (46% vs. 7%, p<0.0001). There was no difference between groups in the incidence of pneumonia (2% vs. 3%, p=0.82).
Lakshminarayan et al. 2010 **USA**	NA	Records of 18,017 patients admitted and discharged for stroke from 222 hospitals in 6	Patients were classified according to their dysphagia screening status: unscreened vs. screen/pass vs.	**Primary outcome:** Pneumonia	Number (%) of patients: Unscreened: 4509 (25%) Screened/pass: 8406 (46.6%) Screened/fail: 5099 (28.3%)

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Audit of National Stroke Registry		states from March 1 to Dec 31, 2009, were reviewed.	screen/fail and associations between screening status and incidence of pneumonia was explored.		Adjusting for age, gender, race, weakness, aphasia and altered level of consciousness, unscreened patients were at higher risk of developing pneumonia compared to patients who passed screening (OR=2.2, 95% CI 1.7 to 2.7).
Hinchey et al. 2005 **USA** **Observational**	NA	15 institutions in the US (73% with dedicated stroke units) collected data prospectively on patients discharged with a diagnosis of ischemic stroke.	Adherence rates between sites with formal dysphagia screening protocols and those without formal protocols were examined for differences in pneumonia rates.	**Primary outcomes:** Pneumonia, mortality	6 of the 15 sites had formal dysphagia screening protocols. Screens were conducted more frequently at sites with a formal screening protocol (78% vs. 56%, p<0.0001. Pneumonia occurred less frequently at sites with formal screening protocols (2.4% vs. 5.4%). Mortality was higher among patients who developed pneumonia (21% vs. 4.8%, p<0.0001).
ii) Dysphagia Management					
Du et al. 2016 **China** **RCT**	CA: ☑ Blinding: Patient ☑ Assessor ☑ ITT: ☒	40 patients with dysphagia secondary to first-ever hemispheric ischemic stroke, recruited from a single institution from 2013-2014, with onset of symptoms within 2 months. Mean age was 58 years, mean time from stroke to recruitment was 7 days.	Patients were randomized to receive high-frequency (3-Hz), low-frequency (1-Hz), or sham (control) rTMS for 5 consecutive days.	**Primary outcome:** Standardized Swallowing Assessment (SSA) at 3 months **Secondary outcomes:** mRS score, Barthel Index Assessments were conducted at baseline, day 5, 1, 2 and 3 months	There was significant improvement in the SSA scores at 3 months for patients in both rTMS groups, which was maintained over time, but not for patients in the control group. There was significantly greater improvement in mean mRS and median BI scores over at 3 months for patients in both rTMS groups, but not for patients in the control group.
Geeganage et al. 2012 **UK** **Cochrane Review**	NA	33 RCTs (6,779 subjects) examining a variety of interventions associated with dysphagia and nutrition provided within the first 6 months of stroke onset.	Treatment interventions examined included: **Dysphagia** Acupuncture (5 RCTs), behavioral interventions (5 RCTs), drug therapy (2 RCTs), neuromuscular electrical stimulation (NMES) (1 RCT), pharyngeal electrical stimulation (PES) (1 RCT),	**Primary outcomes:** Death or dependency, death of disability (BI score of 0 to 55 or Rankin Scale score of 3 to 5) **Secondary outcomes:** Case fatality at the end of the trial, neurological deterioration, late disability or dependency	**Dysphagia outcomes** Case fatality at end of trial: No overall OR reported No significant treatment effect was associated with subgroup analysis by therapy type. Death or dependency at end of trial: OR=1.05, 95% CI 0.63 to 1.75, p=0.86. Results from 2 trials included. LOS: MD=-2.70, -5.68 to 0.28. p=0.076. Results

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			physical stimulation (thermal, tactile) (2 RCTs), transcranial direct current stimulation (TDCS) (1 RCT), transcranial magnetic stimulation (1 RCT). Nutrition Interventions and results reported in nutrition section (below)	at the end of the trial, proportion with dysphagia at the end of the trial, improvement in dysphagia (assessed by videofluoroscopy, pharyngeal transit time, swallowing time, normal water swallow test, improvement in swallow function scales, functional oral intake scale (FOIS), Watian swallow scale, return to normal diet and fluids), aspiration: clinical, videofluoroscopy, pneumonia, gastrointestinal bleeding, LOS, pressure sores.	from 4 trials included. Chest infections or pneumonia: No overall OR reported. No significant treatment effect was associated with subgroup analysis by therapy type (behavioral interventions, drug therapy, and electrical stimulation). Dysphagia at end of trail: No overall OR reported. Significant treatment effect was associated with acupuncture and behavioral interventions.
Xia et al. 2011 **China** **RCT**	CA: ☒ Blinding: Patient ☒ Assessor ☑ ITT: ☒	120 patients with post-stroke dysphagia (mean duration of 9 days) admitted to either the rehabilitation or neurology departments of a hospital.	Patients were randomly assigned to one of 3 groups: 1) conventional swallowing therapy group, 2) electrical stimulation (ES) with the VitalStim therapy group, and 3) VitalStim therapy plus conventional swallowing therapy group. Treatments with ES were given twice a day for 230 min each, 5 days a week for 4 weeks.	**Primary outcome:** Standardized Swallowing Assessment (SSA). **Secondary outcomes:** Dysphagia Severity Scale assessed using VMBS, Swallowing-related Quality of Life (SWAL-QoL) (44 items, higher scores indicate improvement). Assessments were conducted before and after treatment.	Significant improvement was associated with the 2 active treatment groups compared with the control group on all 3 swallowing outcomes. Mean±sd scores of groups 1, 2, 3 before and after treatment. SSA: 40.9±6.4 to 30.1±3.8 vs. 38.7±6.9 to 29.6±4.2 vs. 39.5±7.1 to 24.1±3.5. Significant differences in scores between: groups 1 vs. 3 and 2 vs. 3. Dysphagia Severity Scale: 2.74±1.63 to 5.32±1.43 vs. 2.65±1.56 to 5.63±1.57 vs. 2.53±1.58 to 6.88±1.58. Significant differences in scores between: groups 1 vs. 3 and 2 vs. 3. SWAL-QoL: 863±83 to 624±45 vs. 850±75 to 645±58 vs. 885±60 to 458±35. Significant differences in scores between: groups 1 vs. 3 and 2 vs. 3.
Carnaby et al. 2006	CA: ☑ Blinding:	306 patients with clinical-identified dysphagia admitted to hospital	Patients were randomly assigned to receive usual care (supervision for feeding	**Primary outcome:** Proportion of patients who had returned to their	Combining high-intensity and low-intensity groups into a single treatment group and comparing with the usual care group:

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
USA **RCT** **(Behavioral intervention)**	Patient ☒ Assessor ☑ ITT: ☑	within 7 days of acute stroke, with no previous history of dysphagia	and precautions for safe swallowing; n=102), standard low-intensity intervention (composed of environmental modifications, safe swallowing advice and appropriate dietary modifications; n=102), or standard high-intensity intervention and dietary prescription (daily direct swallowing exercises, dietary modification; n=102). Treatment continued for up to a month.	pre-stroke diet by 6 months. **Secondary outcomes:** Time to return to a normal diet, recovery of functional swallowing, number of dysphagia-related medical complications, death, need for institutionalization, dependency in ADL by 6 months after stroke.	Normal diet at 6 months: RR=1.19, 95% CI 0.98 to 1.45, p>0.05 Return to functional swallow: RR=1.41, 95% CI 1.03 to 1.94, p<0.05. Chest infection: RR=0.56, 95% CI 0.41 to 0.76, p<0.05 Death: RR=0.80, 95% CI 0.49 to 1.3, p>0.05 Institutionalization: RR=0.69, 95% CI 0.43 to 1.1, p>0.05 Dependency (Rankin ≥3) RR=1.05, 95% CI 0.82 to 1.3, p>0.05 Death or institutionalization: RR=0.73 95% CI 0.55 to 0.97, p<0.05 Drop outs and losses to follow-up: usual care n=23, low-intensity group n=21, high-intensity group n=19 Adverse events: No reporting

CA Concealed allocation; ITT intention-to-treat

Nutritional Supplementation & Enteral Feeding

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Geeganage et al. 2012 **UK** **Cochrane Review**	NA	33 RCTs (6,779 subjects) examining a variety of interventions associated with dysphagia and nutrition provided within the first 6 months of stroke onset.	Treatment interventions examined included: **Nutrition** Routes of feeding (5 RCTs), Timing of feeding (1 RCT), fluid supplementation (1 RCT), nutritional supplementation (8	**Primary outcomes:** Death or dependency, death of disability (BI score of 0 to 55 or Rankin Scale score of 3 to 5). **Secondary outcomes:** Case fatality at the end of the trial, neurological deterioration, late disability or	**Nutritional outcomes** Case fatality at end of trial (PEG vs. nasogastric tube): OR=0.81, 0.42 to 1.56, p=0.53. Results from 5 trials included. Death or dependency at end of trial (PEG vs. nasogastric tube): OR=0.80, 95% CI 0.12 to 5.55, p=0.82. Results from 3 trials included.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			RCTs). Dysphagia interventions and outcomes reported above in dysphagia section	dependency at the end of the trial, proportion with dysphagia at the end of the trial, improvement in dysphagia (assessed by videofluoroscopy, pharyngeal transit time, swallowing time, normal water swallow test, improvement in swallow function scales, functional oral intake scale (FOIS), Watian swallow scale, return to normal diet and fluids), aspiration: clinical, videofluoroscopy, pneumonia, gastrointestinal bleeding, feeding tube failures, nutritional measures (weight, albumin, mid-arm circumference (MAC)), LOS, pressure sores.	Pressure sores (PEG vs. NG): OR=3.10, 95% CI 0.98 to 9.83, p=0.055. Results from a single trial included. Chest infection or pneumonia (PEG vs. NG): OR=0.65, 95% CI 0.23 to 1.86, p=0.42. Results from 2 trials included. Case fatality at end of trial (initiation of feeding <7 days vs. ≥7 days): OR=0.79, 95% CI 0.61 to 1.01, p=0.093. Results from 1 trial included. Death or dependency at end of trial (initiation of feeding <7 days vs. ≥7 days): OR=0.94, 95% CI 0.68 to 1.31, p=0.72 Results from 1 trial included. Case fatality at end of trial (nutritional supplementation vs. no supplementation): OR=0.58, 95% CI 0.28 to 1.21, p=0.14. Results from 7 trials included. Death or dependency at end of trial (nutritional supplementation vs. no supplementation): OR=1.06, 95% CI 0.94 to 1.20, p=0.33. Results from 1 trial included. LOS (nutritional supplementation vs. no supplementation): MD=1.40, 95% CI -0.81 to 3.6, p=0.21. Results from 2 trials included.
Ha et al. 2010 **Norway** **RCT**	CA: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☒	124 acute stroke patients who were malnourished or at nutritional risk, identified by screening within 7 days of admission to hospital were included.	Patients were randomized to receive either individualized, nutritional care to prevent weight loss (n=58) or routine care (n=66) while in hospital Patients in the intervention group were prescribed oral	**Primary outcome:** Percentage of patients with weight loss ≥5% at 3 months. **Secondary outcomes:** QoL (EQ-5D), handgrip strength, length of hospital stay, energy and protein intake.	Patients in the intervention group received significantly more calories: Mean ±sd 80±29 vs. 64±20 Kj/kg/day, p=0.005, but not protein: 0.8±0.3 vs. 0.7±0.3 g/kg/day, p=0.34. % of patients in the intervention and control groups with weight loss ≥5% at 3 months: 20.7% vs. 36.4%, p=0.055.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			supplements and tube feeding when appropriate. Education to prevent was also provided prior to hospital discharge. In the control group, patients received oral sip feedings or tube feeding at the discretion of the attending physician. There were no standardized procedures for the treatment of malnutrition. Patients remained in hospital an average of 11 days.	Assessments were conducted at baseline and at 3 months.	EQ-5D: There were no significant differences between groups on any of the domains. Patients in the intervention group experienced significant improvement in means scores of mobility, self-care and usual activities. There was no significant improvement in scores on any of the dimensions for patient in the control group. Mean improvement in hand grip strength: 2.6 kg, 9% CI 1.0 to 4.2, p=0.002. Favors intervention. Median (range) LOS (days) for patients in the intervention and control groups: 12 (2-54) vs. 13 (3-55) days, p>0.05. Losses to follow-up: n=23 intervention group, n=18 control group.
Milne et al. 2009 **UK** **Cochrane Review**	N/A	62 RCTs (10,187 elderly subjects). Most participants (71%) were hospitalised in-patients admitted for acute conditions. 40 studies included older people with no specified disease or condition; other studies included patients with hip fracture, stroke patients (n=2), congestive heart failure, chronic obstructive pulmonary disease, older surgical patients and patients at home with diabetic foot ulcer.	Interventions included commercial oral supplements or fortification of normal food with the intention of improving protein and energy intake using only the normal oral route. The control condition was usually routine feed (no supplement). The trials aimed to provide between 175 and 1350 additional kcal/day and an additional 10-50 grams of protein/day. Therapy lasted from 10 days to 18 months (< 35 days in 17 trials, ≥ 35 days in 37 trials, from admission to discharge in 5 trials).	**Primary outcomes:** All-cause mortality, morbidity, number of people with complications, functional status.	Supplementation was not associated with a reduction in the risk of mortality: RR=0.92, 95% CI 0.81 to 1.04, p=0.20. Results from 40 trials included). Supplementation was associated with a reduction in mortality when patients were malnourished at study entrance (subgroup): RR=0.79, 95% CI 0.64 to 0.97, p=0.025. Results from 25 trials included. Supplementation was associated with a reduction in complications: RR=0.86, 95% CI 0.75 to 0.99, p=0.029. Results from 24 trials included. Supplementation was associated with an increase in weight: % wt change: MD=2.15, 95% CI 1.80 to 2.49, p<0.0001. Results from 45 trials included. Supplementation was associated with an increase in arm muscle circumference: MD=1.20 cm, 95% CI 0.45 to 1.96, p= 0.0019. Results from 16 trials included. Supplementation was not associated with a

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					decreased LOS: MD= -0.75, 95% CI -2.84 to 1.34, p=0.48. Results from 14 trials included.
Dennis et al. 2005 **The FOOD Trial** **(part 2- oral supplementation** **UK** **RCT)**	CA: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑	4,023 non-dysphagic patients admitted within 7 days of first or recurrent stroke. Clinician unsure whether to provide supplements (8% of patients malnourished at baseline).	Patients were randomized to receive an oral nutritional supplement (540 Kcals) in addition to a regular hospital diet (n=2016), provided for the duration of their entire hospital stay (median duration of hospital stay was 34 days- 28% of patients stopped taking supplements before discharge), or to a normal hospital diet only (n=2007).	**Primary outcome:** Death or disability (mRS score of 3-5) at 6 months. **Secondary outcomes:** mRS, EURO QoL, place of residence at 6 months.	Routine supplementation was not associated with benefit on any of the outcomes assessed. Death: OR=0.94, 95% CI 0.78 to 1.17, p, p>0.05 Absolute difference in risk of death: 0.7%, 95% CI -1.4 to 2.7. Death or poor outcome: OR=1.03, 95% CI 0.91 to 1.17, p>0.05. Absolute risk of death or poor outcome; 0.7%, 95% CI -2.3 to 3.8. Mean difference in EURO QoL scores between groups: 0.001, 95% CI -0.23 to 0.025, p>0.05. Losses to follow-up and drop-outs: n=260 (regular diet), n=245 (supplement). Adverse events: no significant differences in complications (pneumonia, urinary tract infections etc) between groups.
Gariballa et al. 1998 **UK** **RCT**	CA: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☒	42 patients who were conscious during the first week of stroke onset with intact swallowing and showed anthropometric evidence of malnutrition.	Patients were randomized to receive a standard hospital diet or a standard diet plus an oral supplement supplying an additional 1200Kcals, 40g protein daily for 4 weeks.	**Primary outcome:** Change in indicators of nutritional status **Secondary outcomes:** Barthel Index, infective complications, death within 3 months and discharge location. Outcomes were assessed at baseline, and weeks 2, 4 and 12.	Patients in the supplemented group consumed more calories and protein compared with those in the control group: 1,807 vs. 1,084 Kcals, p<0.001; protein 65.4 vs. 44.1 grams, p<0.001. Mean change (95% CI) from baseline for patients in supplement and control groups at week 12: Weight (kg): 0.2 (-1.1 to 1.4) vs. -0.7 (-2.7 to 1.4), p>0.05. Tricep skinfold; (mm) -0.9 (-1.9 to 0.1) vs. -0.6 (-1.5 to 0.4), p>0.05. Mid-arm muscle circumference (cm): -0.3 (-0.9 to 0.3) vs. -0.3 (-1.2 to 0.7), p>0.05. Serum albumin (g/L):-1.5 (-3.1 to 0.1) vs. -4.4 (-6.6 to -2.3), p=0.025. Serum transferrin (g/L): 0.1 (-0.4 to 0.5) vs. -0.3 (-0.6 to 0.10, p>0.05.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					Iron (µmol/L): 2.6 (-1.5 to 6.7) vs. -2.7 (-5.6 to 0.2), p=0.03. Median (IQR) BI scores at baseline and week 12 for patients in the supplement and control groups:45 (20-49) to 90 (60-94) vs. 35 (16-49) to 75 (47-88), p>0.05. Number of infective complications: supplement group n=9, control group n=11, p>0.05. Death within 3 months: supplement group n=2, control group n=7, p=0.127. Losses to follow-up, n=11.
ii) Enteral Feeding					
Dennis et al. 2005 **UK** **RCT** **The FOOD trial (part I- timing and method of feeding)**	CA: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑	1,210 patients admitted within 7 days of first or recurrent stroke, from 47 hospitals in 11 countries.	i) Patients were randomized to receive either a PEG (n=162) or NG feeding tube (n=159) within 3 days of enrolment into the study. ii) Patients were randomized to receive feeds as early as possible (n=429) or to avoid feeding for 7 days (n=460) using either a PEG or NG feeding tube.	**Primary outcome:** Death and poor outcome (defined as a Modified Rankin Score of 4-5) was assessed at 6 months.	Early vs. avoid groups: Early tube feeding was associated with a 1.2% (-4.2 to 6.6, p=0.7) absolute reduction in the risk of death or poor outcome at 6 months. Early tube feeding was associated with a 15.8% (-0.8 to 12.5, p=0.09) absolute reduction in the risk of death at 6 months. PEG vs. NG group: PEG feeding was associated with an absolute increase in risk of death of 1.0% (–10.0 to 11.9, p=0.9). PEG feeding was associated with and an increased risk of death or poor outcome of 7.8% (0.0 to 15.5, p=0.05). Drop-outs and losses to follow-up: n=545. Adverse events: Gastro-intestinal bleeds occurred more frequently in the early feeding group compared with the late group (22 vs. 11, p=0.04)

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					and with NG tubes compared with PEG (18 vs. 5, p=0.005). There were more pressure sores in the PEG group compared with NG (12 vs. 4, p=0·04).
Hamidon et al. 2006 **Malaysia** **RCT**	CA: ☑ Blinding: Patient ☒ Assessor ☒ ITT: ☒	23 consecutive patients admitted with acute ischemic stroke with persistent dysphagia for ≥7 days.	Patients were randomized to receive either an NG (n=13) or PEG feeding tube (n=10).	**Primary outcomes:** Changes in nutritional indices at 4 weeks follow-up including: tricep skinfold (TSF), bicep skinfold (BSF), mid-arm circumference (MAC), serum albumin, and treatment failure, defined as persistent blocked or dislodged tubes	22 patients completed the study. At the end of four weeks, subjects in the PEG group had significant increase in the median serum albumin values compared with baseline, whereas subjects in the NG group experienced a decrease (+2.5 vs. -5.0 g/L, p=0.045). There were more treatment failures in the NG group (5/10 vs. 0/8, p=0.036). There were no other significant differences between groups.
Norton et al. 1996 **UK** **RCT**	CA: ☑ Blinding: Patient ☒ Assessor ☒ ITT: ☑	30 patients admitted to 2 hospitals with severe stroke, who were unconscious at the time of admission and with dysphagia which persisted for ≥ 8 days. Mean age was 77 years, 63% female. Mean Barthel Index score at randomization was 3.	At a mean of 14 days post stroke, patients were randomized to receive either a gastrostomy (G, n=16) feeding tube or nasogastric (NG, n=14) feeding tube for enteral feeding.	**Primary outcomes:** Mortality at 6 weeks after initiation of feed and changes in nutritional state during this period. **Secondary outcomes:** Treatment failure, LOS	At 6 weeks, a significantly greater proportion of patients had died in the NG group compared to patients in the G group (2 vs 8). Patients in the G group had significantly better nutritional indices including weight, serum albumin, mid-arm circumference. There were no omitted feeds among patients in the G group compared to at least one missed feed in 10 patients in the NG group.

CA Concealed allocation; ITT intention-to-treat

Oral Hygiene

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Kim et al. 2014 **Korea** **RCT**	CA: ☒ Blinding: Patient ☒ Assessor ☒	90 patients consecutively admitted to a neurosurgical ICU following first-ever stroke, who had ≥6 teeth, and with no sign of infection	Patients were randomized to an intervention (n=45) or control group (n=45). Patients in the intervention group	**Primary outcomes:** Plaque Index (PI), Silness & Loe, 1964; Scores range from 0-3 with lower scores indicating better oral hygiene status; Gingival Index (GI)	34 patients dropped out during the first week. Data from 56 patients were used for analysis. Mean duration of treatment in the intervention group was 2.2 weeks.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
	ITT: ☒	with any contagious pathogen	received daily oral hygiene including tooth brushing, tongue cleaning and chlorhexidine application, performed by a dentist. Unclear what treatment patients in the control group received.	(Loe 1967). Scores range from 0-3 with lower scores indicating less gingival inflammation; Clinical Attachment Loss (CAL) **Secondary outcomes:** Candida colony counts of tongue and saliva	There was a significant decrease in mean PI scores from baseline to follow-up (mean 2.2 weeks) in both groups, although the decline was significantly greater in the intervention group (-1.24 vs. -0.25, p=0.001). There was a significant decrease in mean GI scores from baseline to follow-up (mean 2.2 weeks) in the intervention group (1.54 to 0.47, p=0.018, and a significant increase in the control group (1.3 to 1.60, p=0.023). There was no significant difference between groups in mean CAL change scores from baseline to follow-up. A significantly greater proportion of patients with no Candida colonization in the saliva increased from baseline to follow-up among patients in the intervention group
Lam et al. 2013 **China** **RCT**	CA: ☑ Blinding: Patient ☒ Assessor ☒ ITT: ☒	102 dentate patients admitted to a rehabilitation unit following ischemic stroke or ICH within the previous 7 days, with a Barthel index score of <70. Mean age was 70 years.	Patients were randomized to receive oral hygiene instruction (OHI, n=33), OHI + chlorhexidine (CHI) mouth rinse, (n=34), or OHI + CHI + assisted tooth brushing (n=35) twice daily for 3 weeks	**Primary outcomes:** Plaque Index (PI) (Silness & Loe, 1964). Scores range from 0-3 with lower scores indicating better oral hygiene status. Gingival Bleeding Index (GBI, Carter & Barnes, 1974). The presence or absence of gingival inflammation is noted after passing unwaxed dental floss at 6 sites into the proximal sulci. Bleeding is recorded as present or absent (0,1). **Secondary outcomes:** Pneumonia, treatment satisfaction. Outcomes were assessed before and after treatment	At baseline, only 33% of patients reported brushing their teeth daily. The mean PI scores of patients in the OHI+CHX and OHI+CHX+assisted brushing groups were improved significantly more than patients in the OHI group (p<0.001) Mean before/after treatment scores OHI: 2.0 to 1.2, OHI+CHX: 1.9 to 0.6, OHI+CHX+ assisted brushing: 1.9 to 0.5. The mean GBI score of patients in the OHI+CHX group was improved significantly more than patients in the OHI group (p<0.032) Mean before/after treatment scores OHI: 16.7 to 17.7, OHI+CHX: 18.8 to 10.0, OHI+CHX+ assisted brushing: 16.7 to 7.6. No patient in either group developed pneumonia during the treatment period. Only 1 patient dropped out of the study due to non-

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					compliance with CHX treatment.
Lam et al. 2011 **China** **Systematic review**	NA	8 studies that aimed to assess the effectiveness of oral health promotion activities in patients with cardiovascular disease. Patients included in these studies were diagnosed with hypertension (n=2), coronary artery disease and/or a previous coronary event (n=3) or were recovering from heart transplants (n=1). In one study, 67 patients residing in 20 nursing homes following stroke, were included.	Most interventions evaluated included cleaning, scaling, root planing and/or extractions. In the single RCT that included patients following stroke, an oral health care education program (OHCE) was provided to nursing home care assistants vs. delayed intervention.	**Primary outcome:** Periodontal health	Results from stroke-specific study There were no differences between groups in dental plaque, gingivitis, or denture-induced stomatitis at 1 and 6 months. The experimental group exhibited significantly less denture plaque than the control group at 1 and 6 months ($p<0.0001$) Nursing staff receiving OHCE program exhibited higher knowledge scores ($p<0.005$) at 1 month, and 6 months ($p<0.001$) and significantly better attitudes to oral care ($p= 0.001$)
Brady et al. 2006 **UK** **Cochrane review**	NA	3 RCTs (n=470) that included patients with a diagnosis of stroke receiving some form of assisted oral health care (OHC) within a healthcare facility. Patients included in these trials had been admitted to a neurological ICU (n=1), an acute stroke unit (n=1) and nursing homes (n=1).	Treatment contrasts included: OHC + timed tooth brushing in care bundle vs. standard care (n=1), OHC health care education session vs. delayed session (n=1) and selective decontamination of digestive tract using Orabase 500 mg gel applied to the mucous membranes of the mouth four times daily for 2-3 weeks (n=1).	**Primary outcomes:** Dental plaque (Plaque scale), Denture plaque (Denture Cleanliness Scale) **Secondary outcomes:** Patient satisfaction with care received, oral comfort and appearance, presence of oral disease: gingivitis; denture-induced stomatitis; periodontal disease and staff oral health knowledge and attitude**s**	Pooled analyses were not possible. Use of decontamination gel was associated with a reduction in the incidence of pneumonia: (OR=0.20, CI 95% 0.05 to 0.84, p = 0.03). Education session was not associated with a reduction in dental plaque tooth coverage, the presence of gingivitis, or denture-induced stomatitis at one or 6 months following training, but was associated with a significant reduction in denture plaque at both assessment points. One month after the educational session, care assistants that received the training had higher knowledge scores than the delayed group.

CA Concealed allocation; ITT intention-to-treat

Seizure Management

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Sykes et al. 2014 **UK** **Cochrane Review**	NA	Studies including patients of any age recovering from ischemic stroke or ICH, suffering from any seizure type.	Treatment contrasts evaluated included antiepileptic drugs compared vs. placebo or no drug for the primary and secondary prevention of post stroke seizures	**Primary Outcome:** Occurrence and timing of seizures during the follow up period. **Secondary Outcomes:** Seizure remission, death or dependency at end of scheduled follow up period.	A single study was included (Gilad et al. 2011). See full description and results of this trial below.
Gilad et al. 2011 **Israel** **RCT**	CA: ☑ Blinding: Patient ☑ Assessor ☑ ITT: ☒	84 patients with spontaneous non-traumatic and non-aneurysmatic ICH. Mean age was 70 years. Patients with a history of epilepsy, primary Intraventricular hemorrhage, SAH, infratentorial hemorrhage or SICH due to brain tumor, vascular malformation, brain surgery or infection, were excluded	For seizure prophylaxis, patients were randomized to receive 800 mg/day valproic acid (VA)(n=36) or placebo (n=36) daily for one month and followed for one year. The time to the start of the dosing after randomization was 14 ± 4 h in the treatment group and 16 ± 5 h in the placebo group.	**Primary outcome:** Witnessed seizure within the one-year study period **Secondary outcomes:** Neurological recover, assessed using NIHSS at one year.	At 1 year, there were 15 (21%) cases of new seizure. There were no differences in seizure occurrence between treatment group: All seizures: 7 vs. 8, p=0.8 Early seizure, within 14 days of randomization: 1 vs. 4, p=0.4 Late seizure, occurring >14 days: 6 vs. 4, p=0.5) Mortality: 6 vs. 5, p=0.7. Mean NIHSS scores were lower among patients in the VA group (4.4 vs. 8.6, p=0.002)
Van Tuijl et al. 2011 **UK** **RCT**	CA: ☑ Blinding: Patient ☑ Assessor ☑ ITT: ☒	Patients with lobar ICH or ischemic stroke, with a cortical syndrome and mRS≥3 or NIHSS ≥6 recruited from a single neurology department. Participants with previous history of epilepsy or history of antiepileptic medication were excluded.	Patients were randomized to receive either levetiracetam 1500mg daily divided in two doses or placebo, within 2 to 7 days following acute stroke. Treatment was scheduled to continue for 12 weeks.	**Primary Endpoint:** First late epileptic seizure (>1-week post stroke). **Secondary Endpoint:** Time to event (time between stroke and seizure), occurrence of early seizure (<7 days post stroke), seizure severity, neurological and neurocognitive function, handicap score, quality of life, and medication side effects.	The trial was stopped prematurely due to a failure to recruit sufficient numbers of patients. Planned sample size was 200 patients/group. At the point the trial was stopped, only 16 patients, recruited over a period of 16 months had been recruited. The authors concluded that a trial assessing the efficacy of prophylactic antiepileptics is not feasible.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
				Follow-up assessments were conducted by telephone at 1, 6, 16, and 52 weeks after enrollment	
Gilad et al. 2007 **Israel** **RCT**	CA: ☒ Blinding: Patient ☒ Assessor ☒ ITT: ☑	64 elderly patients admitted to a neurological department after stroke who had experienced a first seizure. Mean age was 72 years. 78% were male.	Participants were randomized to receive either lamotrigine (100mg BID) or carbamazepine (300mg BID) in a 1:1 ratio (both open labeled).	**Primary Outcome:** Appearance of a second seizure under treatment, or completion of the study period without a seizure. **Secondary Outcome:** Tolerability of study medications and withdrawal rate as a result of adverse side effects. Assessments were conducted at baseline and every three months for a period of 12 months	The number of patients who were seizure free at the end of the study period was non-significantly higher in the lamotrigine group (23 vs. 14, p=0.06). The total number of adverse events was significantly higher in the carbamazepine group (n=2, lamotrigine and n=12, carbamazepine; p=0.05), as was the number of withdrawals for adverse events (n=1, lamotrigine and n=10, carbamazepine; p=0.02).
Rowan et al. 2005 **USA** **RCT**	CA: ☑ Blinding: Patient ☑ Assessor ☑ ITT: ☑	593 adults over the age of 60 with a first diagnosed seizure of any type within the last 3 months. Cerebral infarction was the most common seizure etiology (29.9% of sample).	Participants were randomized to receive one of three medications: gabapentin (1500mg/day, n=195), lamotrigine (150mg/day, n=200), and carbamazepine (600mg/day, n=198). Medication doses were titrated over a 6-week period.	**Primary Outcome:** Determination of efficacy and tolerability through retention in the trial for 12 months. **Secondary Outcome:** Seizure freedom at 12 months, time to first seizure, and drug toxicity. Evaluations were conducted at baseline, biweekly to week 8, monthly to week 28, and bimonthly to week 52. Patients were given the option to remain in the study for an additional 12 months, and were evaluated every three months.	276 participants completed the trial. At 3, 6 and 12 months, 63.2%, 58.6% and 53.3% patients remained seizure free. Among those remaining in the study, there were no significant differences between treatment groups in the proportions of patients who remained seizure free (3 months, p=0.93; 6 months, p=0.39; and 12 months, p=0.09). Significantly more early terminating participants received carbamazepine than either lamotrigine (p<0.0001) or gabapentin (p=0.008). Lamotrigine patients terminated due to adverse events significantly less frequently than either carbamazepine (<0.0001) or gabapentin (p=0.015). Time to first, second, fifth, and tenth seizure during a 12-month period was not significantly different between the 3 treatment groups (p=0.12, 0.13, 0.74, and 0.96 respectively).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					Side effects included weight gain (significantly more in carbamazepine group) and water retention (significantly more in gabapentin). Skin irritations were more common in the carbamazepine group compared with lamotrigine (p=0.007). There were no significant between group differences for drug toxicities of any type.

CA Concealed allocation; ITT intention-to-treat

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