Table 1: Stroke Chain of Survival[1]

Detection	Patient or bystander recognition of stroke signs and symptoms
Dispatch	Priority EMS dispatch
Delivery	Prompt triage and transport to most appropriate stroke hospital and pre-hospital notification
Door	Immediate ED triage* to high-acuity area
Data	Prompt ED evaluation, stroke team activation, laboratory studies, and brain imaging
Decision	Diagnosis and determination of most appropriate therapy; discussion with patient and family
Drug	Administration of appropriate drugs or other interventions
Disposition	Timely admission to stroke unit, intensive care unit, or Transfer

ED: emergency department; EMS: emergency medical services

* ED triage categories of patients admitted from an ED presentation into a large multispecialty hospital with a Stroke Care Unit.

Table 2: Definition of Stroke[2]

Ischemic stroke	An episode of neurological dysfunction caused by focal cerebral, spinal, or retinal infarction.
Stroke caused by intracerebral hemorrhage	Rapidly developing clinical signs of neurological dysfunction attributable to a focal collection of blood within the brain parenchyma or ventricular system that is not caused by trauma
Stroke caused by subarachnoid hemorrhage	Rapidly developing clinical signs of neurological dysfunction and/or headache because of bleeding into the subarachnoid space which is not caused by trauma
Stroke caused by cerebral venous thrombosis	Infarction or hemorrhagein the brain, spinal cord, or retina because of thrombosis of a cerebral venous structure. Symptoms or signs caused by reversible edema without infarction or hemorrhage do not qualify as stroke.

Table 3: Symptoms of Stroke

- Numbness or weakness, especially on one side of the body
- Loss of consciousness or altered consciousness
- Decreased vision in one or both eyes
- Language difficulties, either in speaking or understanding
- Difficulty walking; loss of balance or coordination
- Confusion or loss of memory
- Swallowing difficulties
- Paralysis of anybody area, including face
- Sudden, severe headache with no known cause
- Neck pain
- Nausea and vomiting

Table 4: Recommended stroke services and clinical profile (based on Acute Stroke Services Framework 2011)[3]

Component of care	**Comprehensive stroke centre**	**Primary stroke centre**	**Basic hospital service**
Stroke unit	✓	✓	✓/ ✗ if no stroke unit then protocols in place or transfer
Onsite CT brain (24/7)	✓	✓	✓/ ✗
Carotid artery imaging	✓	✓	✓/ ✗
Advanced imaging capability (e.g. MRI, advanced CT, catheter angiography).	✓	✓/ ✗	✗
Neuro-interventional services (e.g. for use in intra-arterial or mechanical thrombolysis)	✓/ ✗	✗	✗
Neurosurgical services (e.g. for hemicraniectomy due to large middle cerebral artery infarcts)	✓*	✗	✗
Delivery of intravenous tissue plasminogen activator (tPA)	✓ 24/7	✓#	✗
Ability to provide acute monitoring (telemetry and other physiological monitoring) for up to 72 hours	✓	✓	✓/ ✗
Dedicated stroke coordinator position	✓	✓	✗
Dedicated medical lead	✓^	✓	✗
Access to High Dependency Unit (HDU) / Intensive Care Unit (ICU) (for complex patients)	✓	✓	✗
Rapid (within 48 hours) Transient Ischaemic Attack (TIA) assessment clinics/services	✓	✓	✗
Vascular Surgery Service for Carotid Artery Intervention	✓	✓/ ✗	✗

Component of care	**Comprehensive stroke centre**	**Primary stroke centre**	**Basic hospital service**
Focus on early rehabilitation (including strong integration and access to specialist rehabilitation services e.g. inpatient rehabilitation or early supported discharge services)	✓	✓	✓/✗
Routine involvement of carers in the rehabilitation process	✓	✓	✓/✗
Routine use of guidelines, care plans and Protocols	✓	✓	✓/✗
Regular audit and stroke specific quality improvement activities	✓	✓	✓/✗
Access and collaboration with other specialist services (cardiology, palliative care, vascular)	✓	✓/✗	✗
Regional responsibility	Commonly	Occasionally	✗
# If tPA not currently provided, services should have plan to develop or systems in place to transfer appropriate patients to service that offers tPA * Or clear transfer arrangements to centres with this service ^ Dedicated medical lead who has primary focus on stroke (stroke centre director)			

Table 5 Recommendations regarding the door-to-needle-time2

Action	Time
Door to physician	≤ 10 minutes
Door to stroke team	≤ 15 minutes
Door to CT initiation	≤ 25 minutes
Door to CT interpretation	≤ 45 minutes
Door to drug (≥80% compliance)	≤ 60 minutes
Door to stroke unit admission	≤ 3 hours
CT indicates computed tomography; and ED, emergency department.	

Table 6 Neurological Score Scales

National Institutes of Health Stroke Scale (NIHSS)	**Tested Item Title** **Responses and scores** 1A Level of consciousness 0—Alert 1—Drowsy 2—Obtunded 3—Coma/unresponsive 1B Orientation questions (2) 0—Answers both correctly 1—Answers 1 correctly 2—Answers neither correctly 1C Response to commands (2) 0—Performs both tasks correctly 1—Performs 1 task correctly 2—Performs neither 2 Gaze 0—Normal horizontal movements 1—Partial gaze palsy 2—Complete gaze palsy 3 Visual fields 0—No visual field defect 1—Partial hemianopia 2—Complete hemianopia 3—Bilateral hemianopia 4 Facial movement 0—Normal 1—Minor facial weakness 2—Partial facial weakness 3—Complete unilateral palsy 5 Motor function (arm) a. Left b. Right 0—No drift 1—Drift before 5 seconds 2—Falls before 10 seconds 3—No effort against gravity 4—No movement 6 Motor function (leg) a. Left b. Right 0—No drift 1—Drift before 5 seconds 2—Falls before 5 seconds 3—No effort against gravity 4—No movement 7 Limb ataxia 0—No ataxia 1—Ataxia in 1 limb 2—Ataxia in 2 limbs 8 Sensory 0—No sensory loss 1—Mild sensory loss 2—Severe sensory loss 9 Language 0—Normal 1—Mild aphasia 2—Severe aphasia 3—Mute or global aphasia 10 Articulation 0—Normal 1—Mild dysarthria 2—Severe dysarthria 11 Extinction or inattention 0—Absent 1—Mild (loss 1 sensory modality lost) 2—Severe (loss 2 modalities lost)

Face arm speech test (FAST)	The FAST test can act as a mnemonic to help detect and enhance responsiveness to stroke patient needs. • Facial drooping: A section of the face, usually only on one side, that is drooping and hard to move • Arm weakness: The inability to raise one's arm fully • Speech difficulties: An inability or difficulty to understand or produce speech • Time: If any of the symptoms above are showing, time is of the essence and it's time to call the emergency services or go to the hospital.
Cincinnati Pre-hospital Evaluation scale	This scale was derived from a simplification of the 15-item NIHSS and evaluates the presence or absence of facial palsy, asymmetric arm weakness, and speech abnormalities in potential stroke patients. Items are scored as either normal or abnormal- • Facial droop The patient shows teeth or smiles **Normal:** Both sides of face move equally **Abnormal**: One side of face does not move as well as the other. • Arm Drift The patient closes their eyes and extends both arms straight out for 10 seconds. **Normal**: Both arms move the same, or both arms do not move at all. **Abnormal**: One arm either does not move, or one arm drifts down compared to the other. • Speech The patient repeats some statement or simple, familiar saying. **Normal**: The patient says correct words with no slurring of words. **Abnormal:** The patient slurs words, says the wrong words, or is unable to speak.

Los Angeles prehospital stroke screen (LAPSS)4	The LAPSS is a longer instrument consisting of 4 history items, a blood glucose measurement, and 3 examination items designed to detect unilateral motor weakness (facial droop, hand grip, and arm strength). Yes No Age over 45 No prior history of seizure disorder New onset of neurologic symptoms in the last 24 hours Patient was ambulatory at baseline (prior to the event)? Blood glucose between 60 and 400 Obvious asymmetry Normal Right Left Facial Droop Grip Arm weakness Yes No Based on exam, patient has only unilateral (and not bilateral) weakness If yes (or unknown) to all items above LAPSS screening criteria met
Rule out stroke in the emergency room (ROSIER) Scale	Yes (-1) No (0) Has there been loss of consciousness or syncope? Has there been seizure activity? Is there a new onset (or waking from sleep)? Asymmetric facial weakness Asymmetric arm weakness Asymmetric leg weakness Speech disturbance Visual field defect Stroke is likely if total score is >0 Scores of ≤ 0 have low probability of stroke but not excluded.

Table 7: Pre-hospital Evaluation and Management of Potential Stroke Patients2

Recommended	Not Recommended
• Assess and manage ABCs • Initiate cardiac monitoring • Provide supplemental oxygen to maintain O_2 saturation > 94% • Establish IV access per local protocol • Determine blood glucose and treat accordingly • Determine time of symptom onset or last known normal, and obtain family contact information, preferably a cell phone • Triage and rapidly transport patient to nearest most appropriate stroke hospital • Notify hospital of pending stroke patient arrival	• Do not initiate interventions for hypertension unless directed by medical command • Do not administer excessive IV fluids • Do not administer dextrose-containing fluids in non-hypoglycemic patients • Do not administer medications by mouth (maintain NPO) • Do not delay transport for pre-hospital interventions
ABCs: airway, breathing, and circulation; IV: intravenous; NPO: nothing by mouth	

Table 8: Features of Clinical Situations Mimicking Stroke2

Psychogenic	Lack of objective cranial nerve findings, neurological findings in a nonvascular distribution, inconsistent examination
Seizures	History of seizures, witnessed seizure activity, postictal period
Hypoglycemia	History of diabetes, low serum glucose, decreased level of consciousness
Migraine with aura (complicated migraine)	History of similar events, preceding aura, headache
Hypertensive encephalopathy	Headache, delirium, significant hypertension, cortical blindness, cerebral edema, seizure
Wernicke's encephalopathy	History of alcohol abuse, ataxia, ophthalmoplegia, confusion
CNS abscess	History of drug abuse, endocarditis, medical device implant with fever

CNS tumor	Gradual progression of symptoms, other primary malignancy, seizure at onset
Drug toxicity	Lithium, phenytoin, carbamazepine
CNS: central nervous system	

Table 9: Physical Examination for Patients Having Stroke[4]

- ABC (airway, breathing, circulation)
- Temperature
- Oxygen saturation
- Signs of head trauma (contusions)
- Seizure (tongue laceration)
- Carotid bruits- Presence of a neck bruit favours partial common carotid or vertebral artery occlusion. Facial pulses may be lost if there is an ipsilateral common carotid artery occlusion or even increased if there is an internal carotid artery occlusion.
- Peripheral pulses- Absent pulses (lower extremity, radial or carotid) favours a diagnosis of atherosclerosis with thrombosis, though a sudden-onset cold, cyanosed limb suggests embolism. An occlusion of the common carotid may be picked up by the absence of a carotid pulse.
- Cardiac auscultation- Cardiac findings such as atrial fibrillation, murmurs and cardiomegaly may indicate a cardioembolic source.
- Evidence of petechiae, purpura or jaundice
- Fundoscopic examination may reveal cholesterol crystals, white intravascular occlusions (fibrin-platelet embolus), or red clot emboli.

Table 10: Immediate Diagnostic Studies: Evaluation of a Patient With Suspected Acute Ischemic Stroke[2]

All Patients

- Noncontrast brain CT or brain MRI
- Blood glucose
- Oxygen saturation
- Serum electrolytes/renal function tests
- Complete blood count, including platelet count
- Markers of cardiac ischemia
- BT, CT, Prothrombin time/INR
- Activated partial thromboplastin time
- ECG

Selected Patients

- TT and/or ECT if it is suspected the patient is taking direct thrombin inhibitors or direct factor Xa inhibitors
- Hepatic function tests
- Toxicology screen
- Blood alcohol level
- Pregnancy test
- Arterial blood gas test (if hypoxia is suspected)
- Chest radiography (if lung disease is suspected)
- Lumbar puncture (if subarachnoid hemorrhage is suspected and CT scan is negative for blood
- Electroencephalogram (if seizures are suspected)

CT: Computed tomography; ECG- electrocardiogram; ECT- ecarin clotting time; INR- International normalized ratio; MRI- Magnetic resonance imaging and TT, thrombin time

Table 11 Comparison of Various Brain Imaging Techniques[5]

Imaging Technique	Advantages	Disadvantages
CT		
Non-contrast CT	• Widely available, cheap, quick, easy to perform and well tolerated • Information on early signs of ischaemia • Exclusion of other stroke mimics • Identifies ICH and SAH	• Provides solely structural not physiological information and cannot reliably differentiate between irreversibly damaged brain tissue from penumbral tissue. • Cannot detect petechial haemorrhages • Insensitive for detection of small cortical or subcortical infarct especially in the posterior fossa
Multimodal CT	• Less time consuming than multimodal MRI	• CT angiography and CT perfusion may expose patients to additional radiation and intravenous contrast agent.
CT perfusion	• Provides information about the penumbra and infarct core	
CT angiogram	• Location and extent of arterial occlusion or stenosis and dissection	
CT venogram	• Detection of cerebral venous thrombosis	
MRI	• More accurate in demonstrating posterior circulation stroke	• Takes longer to perform than CT • Not widely available and expensive
Multimodal MRI		• Contraindicated in patients with pacemakers, defibrillator and metal implants.
DWI	• Location, age and extent of acute ischaemia • DWI can detect cortical and subcortical lesions	

PWI	• Location and extent of the hypoperfused area	
T_2-/FLAIR images	• Exclusion of other stroke mimics • Information on brain parenchyma	
T_2*-weighted images	• Exclusion of intracranial haemorrhages • can detect small haemosiderin deposits not apparent on CT	
MRA	• Location and extent of arterial occlusion/stenosis and dissection	
MRV	• Detection of cerebral venous thrombosis	
DWI = diffusion-weighted imaging; ICH = intracerebral haemorrhage; PWI = perfusion-weighted imaging; MRA = magnetic resonance angiography; MRV = magnetic resonance venogram; SAH = subarachnoid haemorrhage.		

Table 12 ABCD2 Scoring System for the Evaluation of Transient Ischemic Attack[6]

		HR (95%CI)	Score
Age	≥ 60 years	2.6 (0.7 to 8.8)	1
Blood pressure	SBP > 140 systolic and/or DBP>90	9.6 (2.2 to 42)	1
Clinical features	Unilateral weakness Speech disturbance	6.6 (1.5 to 28) 2.6 (0.5 to 14)	2 1
Duration of Symptoms	> 60 mins > 10-59 mins	6.2 (1.4 to 27) 3.1 (0.6 to 15)	2 1
Diabetes	Present		1
CI: confidence interval; DBP: diastolic blood pressure; HR: hazard ratio; SBP: systolic blood pressure			

Table 13: Use of Anti-hypertensives in Patients Having Stroke[7]

- Patient otherwise eligible for acute reperfusion therapy except that BP is >185/110 mm Hg:
  - Labetalol 10–20 mg IV over 1–2 minutes, may repeat 1 time; or
  - Nicardipine 5 mg/h IV, titrate up by 2.5 mg/h every 5–15 minutes, maximum 15 mg/h; when desired BP reached, adjust to maintain proper BP limits; or
  - Other agents (hydralazine, enalaprilat, etc) may be considered when appropriate
- If BP is not maintained at or below 185/110 mm Hg, do not administer rtPA
- Management of BP during and after rtPA or other acute reperfusion therapy to maintain BP at or below 180/105 mm Hg:
  - Monitor BP every 15 minutes for 2 hours from the start of rtPA therapy, then every 30 minutes for 6 hours, and then every hour for 16 hours
- If systolic BP >180–230 mm Hg or diastolic BP >105–120 mm Hg:
  - Labetalol 10 mg IV followed by continuous IV infusion 2–8 mg/min; or
  - Nicardipine 5 mg/h IV, titrate up to desired effect by 2.5 mg/h every 5–15 minutes, maximum 15 mg/h
- If BP is not controlled or diastolic BP >140 mm Hg, consider IV sodium Nitroprusside

BP: blood pressure, IV: intravenous, rtPA: recombinant tissue type plasminogen activator

Table 14 Summary of Major Clinical Trials with Intravenous Tissue Plasminogen Activator

Trial (Year)	tPA Dose	Time Window, hours	Outcome Measures	Number of Patients	Results	Notes
ECASS I (1995)	1.1 mg/kg	≤6	Barthel index and mRS at 90 days	620	No significant difference in ITT analysis. Significant increase in large ICH in tPA group.	High rate of protocol violations (17.4% of patients)
NINDS tPA Trial (1995)	0.9 mg/kg	≤3	Part 1—improvement in NIHSS by ≥4 points or resolution of symptoms within 24 hours of onset Part 2—Barthel index, mRS, GCS, and NIHSS at 3 months	624	Part 1—no significant difference between placebo and tPA Part 2—significant improvement in BI, mRS, GCS, and NIHSS for tPA group 6.4% vs 0.6% rate of symptomatic ICH in tPA vs placebo. No difference in mortality	First trial demonstrating the efficacy of IV tPA in improving neurologic outcome
ECASS II (1998)	0.9 mg/kg	≤6	Favorable outcome (mRS 0 or 1) at 90 days	800	Stratified analyses of primary and secondary outcomes: no significant difference between IV tPA vs placebo in the 3-6-hour time window	Treatment effect attenuated since the median NIHSS was 11 compared to 14 in NINDS trial
ATLANTIS-part B (1999)	0.9 mg/kg	3-5	Excellent neurologic recovery (NIHSS 0-1) at 90 days	613	No significant difference between tPA and placebo	Study stopped early due to slow recruitment. Almost 80% of patients were enrolled in the 4 to 5 hours interval
ECASS III (2008)	0.9 mg/kg	3-4.5	Favorable outcome (mRS 0-1) at 90 days	821	tPA group had significant likelihood of favorable outcome (OR 1.42 [1.02-1.98]). Significantly higher rate of sICH in tPA group but no difference in mortality	Strength: enrollment was spread evenly over time window, large sample size
IST-3 (2012)	0.9 mg/kg	≤6	Alive and independent (OHS 0-2) at 6 months	3035	No significant difference in primary outcome	Demonstrated possible benefit and safety of tPA in patients age >80 years

ITT, intention to treat; mRS, modified Rankin scale; NIHSS, National Institute of Health Stroke Scale; GCS, Glasgow Coma Scale; OHS, Oxford Handicap Score; IST-3, third International Stroke Trial; BI, Barthel index; tPA, tissue-type plasminogen activator; ECASS-III, European Cooperative Acute Stroke Study III; NINDS, National Institute of Neurological Disorders and Stroke; ATLANTIS, Alteplase ThromboLysis for Acute Noninterventional Therapy in Ischemic Stroke; OR, odds ratio; sICH, symptomatic intracerebral hemorrhage

Table 15: Patient Eligibility Criteria for Being Treated with Intravenous Recombinant Tissue Plasminogen Activator[2]

Inclusion criteria	Exclusion criteria	Relative exclusion criteria
Diagnosis of ischemic stroke causing measurable neurological deficit Onset of symptoms <3 hours before beginning treatment Aged ≥18 years	Significant head trauma or prior stroke in previous 3 months Symptoms suggest subarachnoid hemorrhage Arterial puncture at noncompressible site in previous 7 days History of previous intracranial hemorrhage Intracranial neoplasm, arteriovenous malformation, or aneurysm Recent intracranial or intraspinal surgery Elevated blood pressure (systolic >185 mm Hg or diastolic >110 mm Hg) Active internal bleeding Acute bleeding diathesis, including but not limited to Platelet count <100 000/mm^3 Heparin received within 48 hours, resulting in abnormally elevated aPTT greater than the upper limit of normal Current use of anticoagulant with INR >1.7 or PT >15 seconds Current use of direct thrombin inhibitors or direct factor Xa inhibitors with elevated sensitive laboratory tests (such as aPTT, INR, platelet count, and ECT; TT; or appropriate factor Xa activity assays) Blood glucose concentration <50 mg/dL (2.7 mmol/L) CT demonstrates multilobar infarction (hypodensity >1/3 cerebral hemisphere)	Recent experience suggests that under some circumstances—with careful consideration and weighting of risk to benefit—patients may receive fibrinolytic therapy despite 1 or more relative contraindications. Consider risk to benefit of IV rtPA administration carefully if any of these relative contraindications are present: Only minor or rapidly improving stroke symptoms (clearing spontaneously) Pregnancy Seizure at onset with postictal residual neurological impairments Major surgery or serious trauma within previous 14 days Recent gastrointestinal or urinary tract hemorrhage (within previous 21 days) Recent acute myocardial infarction (within previous 3 months)
Onset of symptoms within 3 to 4.5 hours before beginning treatment	Same as above-	Same as above with additional exclusion criteria as follow: Aged >80 years Severe stroke (NIHSS>25) Taking an oral anticoagulant regardless of INR History of both diabetes and prior ischemic stroke
aPTT: activated partial thromboplastin time; CT: computed tomography; ECT: ecarin clotting time; FDA: Food and Drug Administration; INR: international normalized ratio; IV: intravenous; NIHSS: National Institutes of Health Stroke Scale; PT: partial thromboplastin time; rtPA: recombinant tissue plasminogen activator; TT: thrombin time		

Table 16: Recent Randomized Clinical Trial of Endovascular Treatments for Acute Ischemic Stroke[8]

Study	Treatment Arm Active vs. Control	Devices	Treatment time window	Baseline NIHSS score	Imaging tools	ASPECTS	Recanalization success	Clinical outcome	Symptomatic hemorrhage
SYNTHESIS Expansion	IA drug/ any device/ both vs. IVrtPA	Mixed	6 hrs to IAT	≤ 25	Not defined	No	Not disclosed	90 day mRS 0-1, 30.4% (vs. 34.8% with IV tPA, adjusted OR 0.71, P=0.16	10%
IMS III	2/3 standard dose IV rtPA + IA drug/ any device/ both vs. IV rtPA	Mixed (Microcatether infusion of IA tPA 49.1%, MERCI 28.4%, Penumbra 16.2%, Solitaire 1.5%)	5 hrs to IAT	≥ 10 or 8-9 with occlusion	Not defined	< 4	TICI 2-3, 81% for ICA occlusion, 86% for M1, 88% M2	90 day mRS 0-2, 40.8% (vs. 38.7% with IV tPA, age adjusted absolute difference 1.5%, 95% CI 6.1-9.1 %	6.2%

Study	Treatment Arm Active vs. Control	Devices	Treatment time window	Baseline NIHSS score	Imaging tools	ASPECTS	Recanalization success	Clinical outcome	Symptomatic hemorrhage
MR RESCUE	Standard (± IV rtPA) + MERCI or Penumbra vs. Standard (± IV rtPA)	Mixed (MERCI alone 60.7%, Pneumbra alone 23%, both devices 16.4%)	8 hrs to IAT stop by 9 hrs	6-29	CTA, MRA	No	TICI 2a-3, 67%	90 day mRS mean, 3.9 (vs 3.9 with standard care, P=0.99)	4.7%
MR CLEAN	Standard (± IV rtPA) + IA UK, rtPA, device vs. Standard (± IV rtPA)	Mixed (Microcatheter infusion of IA tPA, MERCI, Pneumbra, Solitaire)	6 hrs to IAT	> 2	CTA, MRA, DSA	No	TICI 2b-3, 58.7%	90 day mRS 0-2, 32.6% (vs. 19.1% with standard care, adjusted OR 2.16, 95% CI 1.39-3.38)	7.7%
ESCAPE	Standard (± IV rtPA) + stent retriever vs. standard (± IV rtPA)	Mixed (Solitaire in 77%)	12 hrs to randomization	• >5	• CTA	• ≥ 6	• TICI 2b-3, 72.4%	90 day mRS 0-2, 53% (vs. 29.3% with standard care, adjusted OR 1.7, 95% CI 1.3-2.2)	• 3.6%

Study	Treatment Arm Active vs. Control	Devices	Treatment time window	Baseline NIHSS score	Imaging tools	ASPECTS	Recanalization success	Clinical outcome	Symptomatic hemorrhage
SWIFT PRIME	Standard (± IV rtPA) + stent retriever vs. standard (± IV rtPA)	Solitaire	6 hrs to groin	• 8-29	• CTA, MRA	• ≥ 6	• TICI 2b-3, 88%	90 day mRS 0-2, 60% (vs. 35% with IV tPA, OR 1.7, 95% CI 1.23-2.33	• 3%
EXTEND-IA	Standard (± IV rtPA) + stent retriever vs. standard (± IV rtPA)	Solitaire	6 hrs to groin complete in 8 hrs	• none	• CTA, MRA	• No	• TIMI 2-3, 89%	90 day mRS 0-2, 71% (vs. 40% with IV tPA, adjusted OR 4.2, 95% CI 1.4-12)	• 0%
REVASCAT	Standard (± IV rtPA) + stent retriever vs. standard (± IV rtPA)	Solitaire	8 hrs to groin	• ≥ 6	• CTA, MRA, DSA	• ≥ 7 (NECT) • ≥ 6 (MRI-DWI) • ≥ 8, age > 81-85	• TICI 2b-3, 65.7%	90 day mRS 0-2, 43.7% (vs. 28.2% with standard care, adjusted OR 1.2, 95% CI 1.1-4)	• 1.9%

Study	Treatment Arm Active vs. Control	Devices	Treatment time window	Baseline NIHSS score	Imaging tools	ASPECTS	Recanalization success	Clinical outcome	Symptomatic hemorrhage
ASPECTS Alberta Stroke Program Early CT score; CT computed tomography; CTA computed tomography angiography; d days; EC extra-cranial; ESCAPE Endovascular Treatment for Small Core and Anterior Circulation Proximal Occlusion with Emphasis on Minimizing CT to Recanalization Times; EXTEND-IA Extending the Time for Thrombolysis in Emergency Neurological Deficits- Intra-Arterial; hrs hours; IA intra-arterial; IAT intra-arterial therapy; ICA internal carotid artery; IMS III Interventional Management of Stroke Trial III; IQR interquartile range; IV intravenous; MCA middle cerebral artery; min minutes; mos months; MR magnetic resonance; MR CLEAN The Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke; MR RESCUE MR and Recanalization of Stroke Clots Using Embolectomy; ICH intracerebral hemorrhage; mRS modified Rankin scale; N number; NIHSS National Institutes of Health Stroke Scale; OR odds ratio; rtPA recombinant tissue plasminogen activator; SD standard deviation; SWIFT PRME Solitaire FR with the Intention for Thrombectomy as Primary Endovascular Treatment of Acute Ischemic Stroke; T terminus (of the internal carotid artery); TICI thrombolysis in cerebral infarction; yrs years									

Table 17 Studies Assessing Effects of Combined Intra-Venous and Intra-Arterial Thrombolysis

Study	Year	Treatment Arms	Result
Emergency Management of Stroke (EMS) Bridging trial (IA-rtPA to be given if the vessel remained occluded)	1999	• IV-rtPA followed by IA-rtPA • placebo followed by IA-rtPA	- no difference in clinical outcomes
Keris et al	2001	• IAT followed by IV-rtPA • no thrombolysis	- no symptomatic intracerebral hemorrhages in IAT plus IV-rtPA arm - very high proportion of patients receiving IAT plus IV-rtPA became functionally independent at 12 months (83% vs. 33%) - less mortality rates in the IAT plus IV-rtPA arm (17% vs. 64%)
Interventional Management of Stroke (IMS) Primary comparison with similar subset in NINDS rtPA trial	2004	• IV-rtPA followed by IA-rtPA • Placebo plus IV-rtPA	- patients in the IMS trial had significantly better outcomes at 3 months (56%) than the NINDS placebo group for all outcome measures
IMS II,	2007	• IV-rtPA followed by IA-rtPA	- very low mortality in 3 months (16%) - 46% had mRS of 0 to 2
IMS III	2006	• IV rt-PA • IVT/IAT combination	- results pending
Shaltoni et al.		• rtPA followed by intra-arterial fibrinolysis (with reteplase, alteplase, or urokinase)	- low mortality (17%) - high proportion of patients having total or partial reperfusion (72.5%) - discharge for 55% of cases

Table 18: Studies Demonstrating Safety and Efficacy of Carotid Endarterectomy

Study/ Systemic Review	Results
Sbarigia et al	- overall 30-day morbidity/mortality of 7.3% - significant improvement in most patients - no cases of hemorrhagic transformation or new cerebral infarction
Ballotta et al	- none of the patients experienced new strokes, hemorrhagic conversions, or cerebral edema
Huber et al Welsh et al	- combined stroke and death rates were 16% and 21%, respectively
Paty et al	- for every 1 cm increase in the diameter of infarct size, risk of permanent neurological impairment increased by a factor of 1.7, post CEA.
Rerkasem and Rothwell	- relatively high combined stroke and death rates for urgent CEA in settings of stroke-in-evolution (20.2%) and crescendo TIA (11.4%) - no improvement in outcomes over time - incidence of stroke and death was significantly higher in patients who required emergent surgery for stroke-in-evolution or crescendo TIA than in patients with nonemergency CEA
CEA: carotid endarterectomy; TIA: transient ischemic attack	

Table 19: Risk Factors of Stroke[9, 10]

Unchangeable risk factors	Changeable, treatable, or controllable risk factors	Less well-documented risk factors
Age: elderly more prone **Heredity (family history)**: related to genetic disorders like Cerebral Autosomal Dominant Arteriopathy with Sub-cortical Infarcts and Leukoencephalopathy **Race**: African-Americans at higher risk of death due to stroke **Gender**: females more prone possibly due to use of birth control pills, pregnancy (due to hypercoagulability), history of pre-eclampsia/ eclampsia or gestational diabetes, and post-menopausal hormone therapy **Prior stroke, transient ischemic attack or heart attack**: more common in patients with prior episodes	**Hypertension:** leading cause of stroke **Cigarette smoking**: nicotine and carbon monoxide in cigarette smoke **Diabetes mellitus**: occurrences of high blood pressure, high blood cholesterol, and obesity is high **Carotid or other artery disease**: blood clot due to atherosclerosis **Peripheral artery disease**: higher risk of carotid artery disease **Atrial fibrillation**: can lead to blood clot formation **Other heart disease**: Chronic heart disease or heart failure, dilated cardiomyopathy, heart valve disease etc **Sickle cell anemia**: blood cells tend to stick to blood vessel walls, which can block arteries to the brain **High blood cholesterol:** Causes damage to blood vessels walls eventually leading to stroke. Contributes to blood vessel disease often leading to stroke **Poor diet**: diets high in saturated fats, trans fat, cholesterol, sodium, and having excess calories can lead to development of other risk factors **Physical inactivity or obesity**: increases the risk of developing other risk factors	**Socioeconomic factors**: more common among low-income people **Alcohol abuse**: can lead to multiple medical complications **Drug abuse**: Drug abusers (addiction of drugs like cocaine, amphetamines, and heroin) have an increased risk of both hemorrhagic and ischemic stroke

Table 20: Summary of the Effectiveness of Drug Therapies for the Primary Prevention of First-Ever Stroke in a Population of One Million People[11]

Strategy/ intervention	Target population (% of general population)	Relative risk (95% CI)	Stroke risk per year		Relative risk reduction (RRR) (95% CI)	Absolute risk reduction (ARR)	Number of strokes avoided per year among target population	% of 1,400 first-ever ischemic strokes avoided each year in a population of one million
			Control	Intervention				
Nil	988,000	1.0	0.14%	N/A	0	0	0	0
Blood pressure lowering (by 10 mm Hg systolic)	115,600 (11.7%)	3.6 (2.2-5.8)	0.51%	0.28%	46% (35-55%)	0.23%	266	19%
LDL-cholesterol lowering (by 1.0 mmol/l)	197,600 (20%)	1.4	0.19%	0.14%	36% (22-48%)	0.05%	99	7%
Anticoagulation for atrial fibrillation (AF)	4,887 (50% of individuals aged > 40 years with AF	5.0	0.70%	0.25%	64% (49-74%)	0.35%	22	2%
Cigarette smoking cessation	181,792 (18.4%)	1.9 (1.6-2.2)	0.27%	0.14%	47%	0.13%	236	17%
Nicotine replacement therapy	5,454 (3% of 181,792)	1.9 (1.6-2.2	0.27%	0.14%	47%	0.13%	7	0.5%
HbA_{1c} lowering	42,484 (4.3%)	3.8 (1.8-8.2)	0.53%	0.49%	7% (-6-19%)	0.04%	17	1%

CI: confidence interval; HbA_{1c}: glycosylated hemoglobin; LDL: low density lipoprotein

Table 21: Summary of the Effectiveness of Interventions for the (Secondary) Prevention of Recurrent Stroke Among 10,000 Prevalent and 2,000 Incident Stroke and Transient Ischemic Attack Survivors in a Population of One Million People[12]

Strategy/ intervention	Target population (% of general population)	Stroke risk per year		Relative risk reduction (RRR) (95% CI)	Absolute risk reduction (ARR)	Number of strokes avoided per year among target population	% of 600 recurrent ischemic strokes avoided each year in a population of one million
		Control	Intervention				
Nil	12,000	5.0%				0	0%
Carotid revascularization	300 (15% of 2,000)	6.5%	3.5%	48% (38-60%)	3.0%	9	2%
Aspirin	9,240 (77%)	5.0%	4.4%	13% (6-19%)	0.7%	60	10%
Aspirin and ER dipyridamole	7,800 (65%)	4.4%	3.6%	18% (8-28%)	0.8%	51	8%
Anticoagulants	960 (8%)	12.0%	4.0%	61% (37-75%)	7.3%	70	12%
Blood pressure lowering (by 10 mm Hg systolic)	10,800 (90%)	5.0%	3.3%	34% (21-44%)	1.7%	184	31%
LDL-cholesterol lowering (by 1mmol/l LDL)	9,600 (80%)	5.0%	4.4.%	12% (1-22%)	0.6%	58	10%
HbA_{1c} lowering (by 0.9%)	2,400 (20%)	5.0%	4.65%	7% (-6-19%)	0.35%	8	1%
Cessation of cigarette smoking	2,400 (20%)	5.0%	2.6%	47%	2.4%	58	10%
ER: emergency room; HbA_{1c}: glycosylated hemoglobin; LDL: low density lipoprotein							

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