

APPROACH TO RECURRENT STROKE

Etiology · Evaluation · Prevention · Management

References: Harrison's Principles of Internal Medicine 22nd Ed | Kumar & Clarke Clinical Medicine 10th Ed | Davidson's Principles 24th Ed | Adams & Victor's Neurology | Goodman & Gilman's Pharmacology 14th Ed | Cecil Medicine 26th Ed | Snell's Clinical Neuroanatomy | Robbins & Cotran Pathology 10th Ed | Adams & Victor's Neurology | JNC/AHA/ASA Guidelines 2019–2024



DEFINITION & EPIDEMIOLOGY OF RECURRENT STROKE

10-15%

Early Recurrence Risk

*within 90 days of TIA/stroke
(Rothwell et al., Lancet 2007)*

~10-12%

1-Year Recurrence

*without secondary prevention
(Stroke 2022; AHA/ASA)*

25-40%

5-Year Recurrence

*ischaemic stroke patients
(Harrison's 22nd Ed, Ch. 380)*

KEY DEFINITIONS

Recurrent Stroke: A new stroke occurring after an index stroke, confirmed by clinical or neuroimaging criteria (Adams & Victor, 9th Ed)

Early Recurrence: Stroke within 90 days of initial event; highest risk period (ABCD² score; Johnston et al., NEJM 2016)

TIA → Stroke: 15-20% of strokes are preceded by TIA; ABCD² ≥4 predicts high risk (Rothwell, Lancet Neurology 2005)

Secondary Prevention: Interventions post-stroke to prevent recurrence (ASA/AHA Guidelines 2021)

PATHOPHYSIOLOGY & NEUROANATOMY OF RECURRENT STROKE

VASCULAR PATHOLOGY (Robbins & Cotran 10th Ed)

Atherosclerosis

Lipid plaque, fibrous cap rupture → thrombus → artery-to-artery embolism (Large vessel disease ~25%)

Cardioembolism

AF, LV thrombus, valvular disease → cerebral emboli (20-25% of ischaemic strokes)

Small Vessel Disease

Lipohyalinosis, lacunar infarcts → white matter changes (25-30%)

Cerebrovascular Inflammation

Vasculitis, antiphospholipid syndrome → recurrent thrombosis

Haemodynamic

Hypoperfusion from cardiac failure, carotid stenosis → watershed infarcts

NEUROANATOMY (Snell's Clinical Neuroanatomy 8th Ed)

Internal Carotid System

Supplies anterior 2/3 brain; MCA/ACA territory infarcts → contralateral weakness, aphasia

Vertebrobasilar System

Posterior fossa, brainstem, cerebellum; wallenberg, locked-in syndromes

Circle of Willis

Anastomoses; compensates 70% ICA stenosis; berry aneurysms at bifurcations → SAH

Deep Perforators

Lenticulostriate arteries → basal ganglia, internal capsule; lacunar infarcts

Watershed Zones

MCA-ACA, MCA-PCA junctions; vulnerable to hypoperfusion → cortical blindness, shoulder weakness

ETIOLOGY & RISK FACTORS FOR RECURRENT STROKE

TOAST CLASSIFICATION OF ISCHAEMIC STROKE (Adams et al., Stroke 1993 — Still Gold Standard)

Large Artery Atherosclerosis

25%

Hypertension, DM, dyslipidaemia,
smoking, age

Cardioembolism

20%

AF, MI, valvular disease, LV
dysfunction

Small Vessel (Lacunar)

25%

HTN, DM, smoking; lipohyalinosis

Other Determined

5%

Dissection, vasculitis,
hypercoagulable states

Cryptogenic (ESUS)

25%

PFO, occult AF, paradoxical embolism

MODIFIABLE RISK FACTORS

- Hypertension (most important — Harrison's 22nd)
- Atrial fibrillation (CHA₂DS₂-VASc ≥2 → OAC)
- Diabetes mellitus (HbA1c target <7%)
- Dyslipidaemia (LDL-C <1.8 mmol/L)
- Smoking cessation
- Obesity/physical inactivity
- Heavy alcohol use
- Obstructive sleep apnoea (OSA)
- Hyperhomocysteinaemia

NON-MODIFIABLE / SPECIAL RISK FACTORS

- Age (risk doubles per decade >55 yrs)
- Male sex (females: oral contraceptives, pregnancy)
- Race (Black > Asian > White — Davidson's 24th)
- Prior TIA or stroke (highest predictor)
- Family history / genetic thrombophilia
- Patent Foramen Ovale (ESUS patients)
- Antiphospholipid Syndrome
- Sickle cell disease
- Migraine with aura (females <55)

CLINICAL APPROACH: HISTORY & NEUROLOGICAL EXAMINATION

HISTORY TAKING

Onset & Progression

Sudden onset (embolic) vs stuttering (thrombotic) vs progressive (haemodynamic)

Symptom Pattern

FAST: Face-Arm-Speech-Time; also vision (TMVL), vertigo, diplopia, dysphagia

Vascular Territory

Anterior (carotid): contralateral hemiplegia, dysphasia. Posterior (vertebrobasilar): ataxia, diplopia, Horner's

Prior Stroke/TIA

Recurrence pattern, time interval, same vs different territory

Cardiac History

Palpitations, AF, MI, valvular disease, heart failure

Drug History

Antiplatelets, anticoagulants, OCP, illicit drugs (cocaine → vasospasm)

Compliance

Non-adherence to medications — MOST COMMON cause of recurrence (Davidson's 24th Ed)

Risk Factor Control

BP monitoring records, HbA1c, lipid profile trends

NEUROLOGICAL EXAMINATION

GCS / Consciousness

Level of consciousness, orientation, eye opening

NIHSS Score

0–42 scale: quantifies deficits; guides thrombolysis eligibility (AHA 2019)

Cranial Nerves

CN II (visual fields, fundus), CN III–VI (eye movements), CN VII (UMN vs LMN facial palsy), CN IX–X (dysphagia)

Motor System

Power (MRC scale), tone (spasticity), reflexes (hyperreflexia, upgoing plantar)

Sensory

Cortical loss, pain/temp (spinothalamic), proprioception

Cerebellar

Finger-nose, heel-shin, gait ataxia, nystagmus (HINTS exam in acute vertigo)

Cardiovascular

BP both arms, pulse (irregular → AF), carotid bruits, cardiac murmurs, fundoscopy

Cortical Functions

Aphasia (Broca/Wernicke), neglect, agnosia, apraxia; assess cognition (MMSE/MoCA)

INVESTIGATIONS — PART 1: NEUROIMAGING

Non-Contrast CT Brain

STAT — First Line

Within 25 min of arrival

- Excludes haemorrhage (hyperdense), mass lesion, before thrombolysis
- Detects early ischaemic changes: hyperdense MCA sign, loss of insular ribbon, obscured basal ganglia
- ASPECTS score (0-10) guides thrombolysis — score ≥ 6 favourable (ECASS Trial)
- Sensitivity for acute infarct <50% in first 6 hrs — CT negative does not rule out stroke

Ref: Harrison's 22nd | ECASS III Trial | AHA 2019 Stroke Guidelines

MRI Brain (DWI/FLAIR/GRE)

Gold Standard

As soon as available

- DWI: detects acute infarct within minutes (restricted diffusion) — 95% sensitivity
- FLAIR: shows older lesions (>6-8 hrs), periventricular white matter changes (SVD)
- GRE/SWI: detects haemosiderin, microbleeds, old haemorrhage → guides anticoagulation
- MRA: intracranial & neck vessel stenosis without contrast

Ref: Kidwell Radiology 2018 | DAWN (Nogueira NEJM 2018) | DEFUSE 3 (Albers NEJM 2018)

- PWI-DWI mismatch: penumbra estimation in late window (DAWN/DEFUSE 3 trials)

CT/MR Angiography

Urgent

With initial imaging

- CTA: rapid assessment of LVO (large vessel occlusion) — guides mechanical thrombectomy
- Circle of Willis, basilar artery, carotid bifurcation stenosis
- Carotid Doppler USS: stenosis >50% → NASCET criteria; >70% → CEA indicated
- DSA (gold standard for vasculitis, AVM, aneurysm evaluation)

Ref: NASCET Trial NEJM 1991 | Snell's Clinical Neuroanatomy | Harrison's 22nd

INVESTIGATIONS — PART 2: CARDIAC, HAEMATOLOGICAL & METABOLIC

CARDIAC INVESTIGATIONS

12-Lead ECG

AF (most common cause of cardioembolic stroke), LVH, ST changes, prolonged QTc

24-72hr Holter Monitor

Paroxysmal AF detection — increases yield to 12–16% (EMBRACE trial, NEJM 2014)

Transthoracic Echo (TTE)

LV thrombus, EF, valvular disease, wall motion abnormalities, pericardial effusion

TOE (TEE)

PFO, ASD, LA appendage thrombus, aortic arch atheroma (>4mm plaques → stroke risk)

Implantable Loop Recorder

AF detection up to 38% over 3 yrs (CRYSTAL-AF trial) — indicated in ESUS

Cardiac MRI

Myocarditis, cardiomyopathy, rare causes of cardioembolic stroke

HAEMATOLOGICAL & METABOLIC

FBC + ESR

Polycythaemia vera, thrombocytosis, anaemia (sickle cell), vasculitis (↑ ESR)

Coagulation Screen

PT, APTT, INR; factor deficiencies; on anticoagulants (warfarin, DOAC levels)

Thrombophilia Screen

APS (lupus anticoagulant, anti-cardiolipin Ab), Protein C/S, AT-III, Factor V Leiden

Lipid Profile

Total cholesterol, LDL, HDL, TG; LDL target <1.8 mmol/L post-stroke

HbA1c + Fasting Glucose

Diabetes/pre-diabetes; target HbA1c <7% for secondary prevention

Renal Function + Electrolytes

eGFR for DOAC dosing; hyponatraemia mimics stroke

Homocysteine

Elevated → independent RF; treat with B6, B12, folate

CRP / Inflammatory Markers

Vasculitis screen; high-sensitivity CRP (hsCRP) predicts recurrence

Drug levels

Antiplatelet/anticoagulant adherence; toxicology if young stroke

RISK STRATIFICATION SCORES

ABCD² SCORE — TIA Stroke Risk (Johnston, Lancet 2007)

A — Age	≥60 years = 1 point
B — Blood Pressure	≥140/90 mmHg = 1 point
C — Clinical features	Unilateral weakness = 2; speech only = 1
D — Duration	≥60 min = 2; 10–59 min = 1
D — Diabetes	Present = 1 point

Score 0–3 Low risk: 2-day stroke risk ~1%

Score 4–5 Moderate risk: 2-day stroke risk ~4%

Score 6–7 HIGH RISK: 2-day stroke risk ~8% → Admit!

CHA₂DS₂-VASc — AF Stroke Risk (Lip, Chest 2010)

C — Congestive HF	1 point
H — Hypertension	1 point
A ₂ — Age ≥75 yrs	2 points
D — Diabetes Mellitus	1 point
S ₂ — Stroke/TIA history	2 points (HIGHEST RISK FACTOR)
V — Vascular disease	1 point (MI, PAD, aortic plaque)
A — Age 65–74 yrs	1 point
Sc — Sex category (Female)	1 point

Score ≥2 (M), ≥3 (F)

→ OAC indicated (NOAC)

Other Scores: HAS-BLED (bleeding risk in AF, score ≥3 = high risk) | ESRS (European Stroke Risk Score for ischaemic stroke) | SRS (Stroke Recurrence Score)

SECONDARY PREVENTION: ANTITHROMBOTIC THERAPY

1. ANTIPLATELET THERAPY — Non-cardioembolic ischaemic stroke/TIA

Aspirin 75–325 mg/day

Class I, Level A

First-line; 25% RRR of stroke; cheap; GI side effects. Use 75–100 mg long-term (CAST, IST trials)

Clopidogrel 75 mg/day

Class I, Level B

CAPRIE trial: 8.7% RRR vs aspirin alone. Preferred if aspirin intolerant or PVD co-existing. CYP2C19 polymorphism reduces efficacy

Aspirin + Extended-release Dipyridamole (ERDP)

Class I, Level B

ESPRIT/ESPS-2: superior to aspirin alone. 200 mg BD dipyridamole. Headache limits tolerance. Second-line option

Dual Antiplatelet (DAPT): Aspirin + Clopidogrel

Class I, Level A (21 days)

POINT & CHANCE trials: for HIGH-RISK TIA/minor stroke (NIHSS ≤ 3 , ABCD² ≥ 4) — 21 days only, then monotherapy. Reduces early recurrence without excess bleeding (Johnston NEJM 2018)

Ticagrelor

Class IIb, Level B

SOCRATES trial: NOT superior to aspirin. THALES: Aspirin + Ticagrelor ↓ recurrence (NNT=92) vs aspirin; approved for 30-day DAPT in high-risk minor stroke (Wang NEJM 2020)

SECONDARY PREVENTION: ANTICOAGULATION IN RECURRENT STROKE

DIRECT ORAL ANTICOAGULANTS (DOACs) — Preferred over Warfarin in AF-related stroke (ESC 2020 / AHA/ASA 2021)

Drug	Mechanism	Dose	Key Trial	Advantage vs Warfarin
Dabigatran	Direct thrombin inhibitor	110 or 150 mg BD	RE-LY (NEJM 2009)	↓ ICH; 150 mg superior for stroke prevention; avoid if CrCl <30
Rivaroxaban	Factor Xa inhibitor	20 mg OD with food	ROCKET-AF (NEJM 2011)	OD dosing; similar efficacy; avoid if CrCl <15
Apixaban	Factor Xa inhibitor	5 mg BD (2.5 if ≥2 criteria)	ARISTOTLE (NEJM 2011)	↓ stroke, ↓ ICH, ↓ mortality vs warfarin; preferred in elderly/renal impairment
Edoxaban	Factor Xa inhibitor	60 mg OD (30 if low BW)	ENGAGE AF-TIMI 48 (NEJM 2013)	OD dosing; ↓ ICH vs warfarin; avoid if CrCl >95 (paradoxical)

WARFARIN — Still indicated: Mechanical heart valves (target INR 2.5–3.5) | Antiphospholipid syndrome | Severe renal failure (CrCl <15) | Rheumatic mitral stenosis

TIMING OF ANTICOAGULATION AFTER STROKE (1-3-6-12 Rule — Consensus Guidelines)

TIA	Small infarct (NIHSS <8)	Moderate infarct (NIHSS 8–16)	Large infarct / Severe stroke
Anticoagulate IMMEDIATELY	After 1–3 days	After 6 days	After 12–14 days (haemorrhagic transformation risk)

VASCULAR RISK FACTOR MANAGEMENT IN SECONDARY PREVENTION

BLOOD PRESSURE CONTROL

- Target: <130/80 mmHg (AHA/ASA 2021); avoid over-treatment in bilateral carotid stenosis
- Start antihypertensives 24–72 hours after acute stroke (avoid acute hypotension)
- ACE inhibitor + thiazide diuretic combination: PROGRESS trial showed 28% ↓ stroke recurrence
- SPS3 trial: intensive BP control (<130 mmHg) reduced ICH recurrence by 63%
- All classes effective; ACEi/ARB preferred with DM/proteinuria; CCB in isolated systolic HTN

Ref: PROGRESS Lancet 2001 | SPS3 NEJM 2019

LIPID-LOWERING THERAPY

- High-intensity statin: Atorvastatin 40–80 mg/day — SPARCL trial showed 16% RRR stroke recurrence
- LDL-C target: <1.8 mmol/L (<70 mg/dL) for ischaemic stroke/TIA
- If LDL-C ≥ 2.6 mmol/L despite max statin → add Ezetimibe (IMPROVE-IT trial)
- PCSK9 inhibitors (Evolocumab/Alirocumab) if still above target; FOURIER/ODYSSEY OUTCOMES trials
- Statin contraindicated in haemorrhagic stroke — may increase ICH risk (SPARCL subgroup)

Ref: SPARCL NEJM 2006 | FOURIER Lancet 2017 | ODYSSEY OUTCOMES Lancet 2017

GLYCAEMIC CONTROL

- Target: HbA1c <7% (individualize — avoid hypoglycaemia in elderly/long DM duration)
- Hyperglycaemia in acute stroke worsens outcome → treat if BG >10 mmol/L
- GLP-1 agonists (Semaglutide) — SUSTAIN-6: ↓ stroke risk in T2DM patients
- Hypoglycaemia mimics stroke → always check glucose in acute presentations
- Pioglitazone: IRIS trial — ↓ stroke/MI recurrence in insulin-resistant non-diabetic patients post-stroke

Ref: UKPDS 11 Lancet 1998 | Davidson's 24th Ed

Ref: PROGRESS Lancet 2001 | SPARCL NEJM 2006 | IRIS NEJM 2016 | SUSTAIN-6 NEJM 2016 | Harrison's 22nd | Kumar & Clarke 10th | Davidson's 24th | Cecil Medicine 26th

SURGICAL & INTERVENTIONAL MANAGEMENT

Carotid Endarterectomy (CEA)

- Symptomatic stenosis $\geq 70\%$ (NASCET criteria) — NNT = 6; benefit greatest within 2 weeks of TIA/minor stroke
- Symptomatic 50–69%: CEA reduces absolute risk by 4.6% (NASCET trial, NEJM 1991)
- Asymptomatic $\geq 60\%$: ACAS trial; CEA preferred over medical therapy in good surgical candidates
- Contraindications: recent large infarct, contralateral occlusion, poor surgical fitness

Ref: NASCET NEJM 1991 | ACAS JAMA 1995 | ESC Guidelines 2017
Perioperative stroke risk: ~3% (experienced centres); 30-day mortality <1%

Carotid Artery Stenting (CAS)

- Alternative to CEA in high surgical risk patients (SPACE, EVA-3S, ICSS trials)
- Higher periprocedural stroke risk in elderly (>70 yrs) compared to CEA (CREST trial)
- CREST-2 (2024): medical therapy alone vs CEA/CAS for asymptomatic carotid stenosis — ongoing
- Use distal embolic protection devices; dual antiplatelet pre/post-procedure

Ref: CREST NEJM 2010 | SPACE Lancet 2006 | ESC Carotid Guidelines 2017
Preferred: radiation-induced stenosis, restenosis after previous CEA, tandem lesions

Mechanical Thrombectomy (MT) / Endovascular Therapy

- LVO (MCA M1/M2, ICA, basilar): thrombectomy up to 24 hours if penumbra present (DAWN/DEFUSE 3)
- mTICI $\geq 2b$ reperfusion goal; use stent retrievers \pm aspiration (ASTER, COMPASS trials)
- 90-day functional independence (mRS 0–2): 44% MT vs 17% control (pooled analysis)
- Basilar artery occlusion: BASICS trial — MT + BMT vs BMT alone; MT superior in severe strokes

Ref: MR CLEAN NEJM 2015 | DAWN NEJM 2018 | DEFUSE 3 NEJM 2018 | BASICS NEJM 2021
Combined with IV alteplase (bridging thrombolysis) or direct MT (MR CLEAN-NO IV trial)

PFO Closure / AF Ablation / LAAC

- PFO closure: CLOSE/REDUCE/DEFENSE-PFO — superior to antiplatelet in cryptogenic stroke <60 yrs
- AF catheter ablation reduces AF burden and stroke recurrence (CASTLE-AF, CABANA trials)
- Left Atrial Appendage Closure (LAAC — Watchman device): non-inferior to warfarin in AF patients unsuitable for OAC (PROTECT-AF, PREVAIL trials)

Ref: CLOSE NEJM 2017 | CASTLE-AF NEJM 2018 | PROTECT-AF NEJM 2014 | Snell Neuroanatomy

Ref: Harrison's 22nd Ed | Kumar & Clarke 10th | Adams & Victor's Neurology | NASCET 1991 | DAWN/DEFUSE 3 2018 | CLOSE 2017 | ESC/AHA Guidelines

SPECIAL SITUATIONS IN RECURRENT STROKE

RECURRENT HAEMORRHAGIC STROKE (ICH)

- Cease ALL antithrombotics; reverse anticoagulation (PCC for warfarin; Idarucizumab for dabigatran; Andexanet alfa for Xa inhibitors)
- Control BP aggressively: target systolic <140 mmHg within 1 hr (INTERACT-2, ATACH-2 trials)
- Restart OAC after 4–8 weeks if AF present; weigh ICH recurrence risk (APACHE-AF, RETRACE registry)
- CAA (Cerebral Amyloid Angiopathy): lobar microbleeds on SWI; avoid anticoagulation; aspirin risk vs benefit

CRYPTOGENIC STROKE / ESUS

- ESUS (Embolic Stroke of Undetermined Source): Hart et al., NEJM 2017 — 20–30% of ischaemic strokes
- Extended cardiac monitoring (ILR) → paroxysmal AF detected in ~38% over 3 years (CRYSTAL-AF)
- NAVIGATE ESUS/RESPECT ESUS: Rivaroxaban/Dabigatran NOT superior to aspirin → aspirin standard
- Recent ATTICUS (Apixaban) trial ongoing; PFO closure if confirmed RLS in young patients

SICKLE CELL DISEASE / RARE CAUSES

- TCD monitoring + chronic transfusion programme → reduces stroke risk 90% (STOP trial, NEJM 1998)
- Exchange transfusion acutely; hydroxyurea for long-term prevention; bone marrow transplant curative
- Vasculitis: immunosuppression (steroids ± cyclophosphamide); regular vessel imaging
- CADASIL/MELAS: no proven disease-modifying therapy; genetic counselling; avoid vasoconstrictors

STROKE IN YOUNG ADULTS (<50 YEARS)

- Extended workup: thrombophilia screen, APS, connective tissue disorders, CADASIL (NOTCH3 gene)
- Cervical artery dissection: MRI/MRA neck; anticoagulation or antiplatelet for 3–6 months (CADISS trial)
- PFO with RLS: CLOSE/REDUCE criteria for closure; bubble contrast echocardiography
- Oral contraceptives + migraine with aura: AVOID OCP (relative risk 8× increase)

STROKE IN AF WITH PRIOR ICH

- Highest risk scenario: thromboembolic and haemorrhagic risk both elevated
- PFO/LAAC (Watchman): consider if ICH makes long-term OAC unacceptable (LAAOS III trial)
- Resume anticoagulation after 4–8 weeks if: small ICH, controlled BP, non-lobar location
- Shared decision-making essential; multidisciplinary team (neurology + cardiology + haematology)

LIFESTYLE MODIFICATIONS & STROKE REHABILITATION



Smoking Cessation

Stroke risk ↓ to baseline within 5 years. NRT, Varenicline (Champix), Bupropion. Relative risk of stroke smoking vs non-smoking: 1.9×. Passive smoking also doubles risk (Kumar & Clarke 10th)



Alcohol Reduction

Heavy use (>60 g/day) → 2× ischaemic, 3× haemorrhagic stroke risk. Moderate (<14 units/week) may be protective — NIHSS-adjusted analysis. Advise abstinence or heavy reduction



Physical Activity

≥150 min/week moderate aerobic exercise (brisk walk); swimming, cycling. Reduces BP, obesity, DM, dyslipidaemia. Yoga/Tai Chi in elderly — balance, falls prevention post-stroke



Diet (DASH/Mediterranean)

↑ Fruit/vegetables, whole grains, fish (omega-3). ↓ Saturated fats, sodium (<6 g/day salt). PREDIMED trial: Mediterranean diet + olive oil → 30% ↓ cardiovascular events



Weight Management

Target BMI 18.5–24.9 kg/m². Waist circumference <94 cm (M), <80 cm (F). 5–10% weight loss → significant BP and glucose improvement. Bariatric surgery in morbid obesity



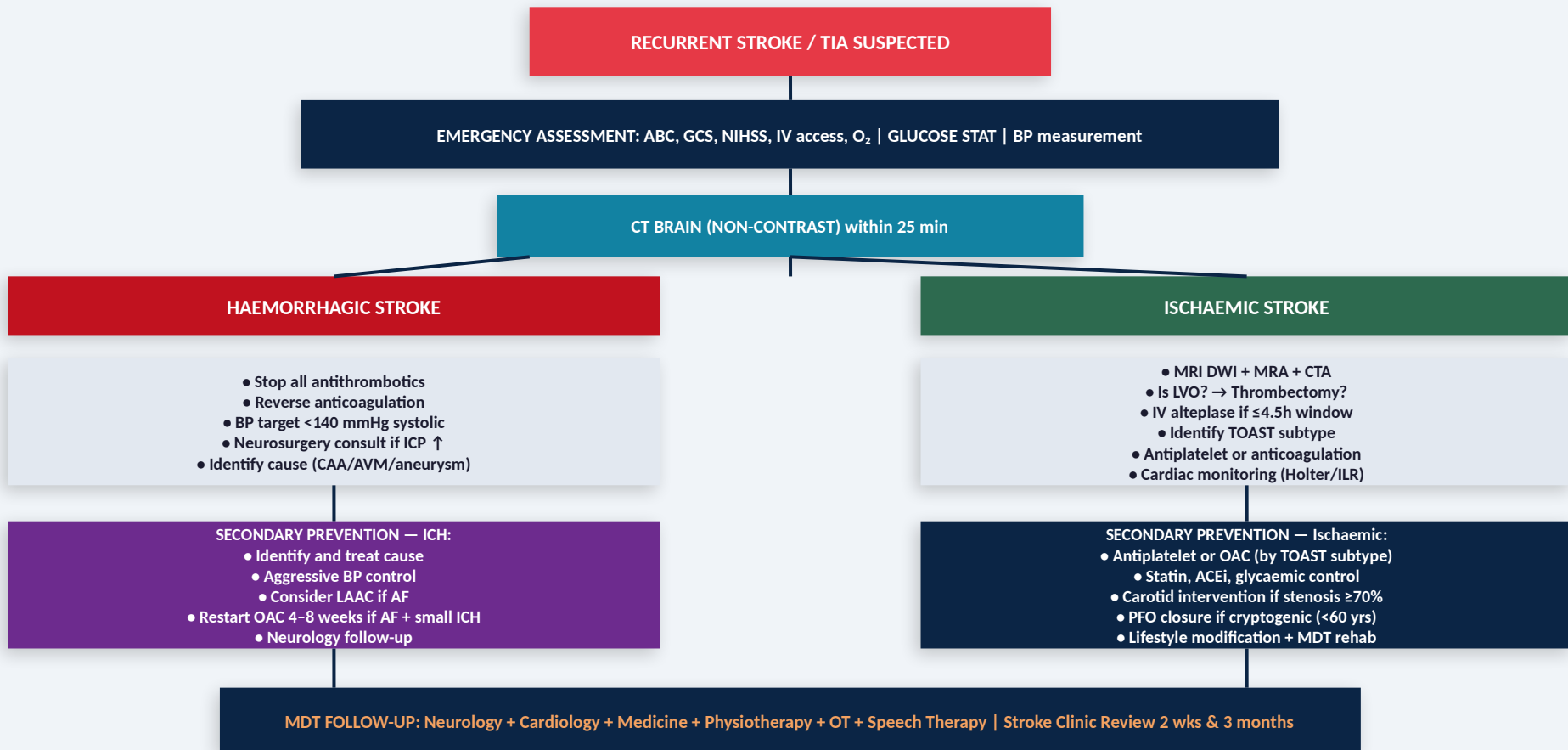
OSA Management

CPAP in OSA + stroke patients → ↓ BP, ↓ recurrent cardiovascular events; SAVE trial. PSG/limited sleep study for screening — AHI >15 events/hr significant

KEY LANDMARK CLINICAL TRIALS — RECURRENT STROKE PREVENTION

Trial	Year	Design	Key Finding	Recommendation
NASCET	1991	RCT	CEA vs medical in symptomatic carotid stenosis $\geq 70\%$ \rightarrow 17% ARR stroke at 2 yrs	CEA for symptomatic stenosis $\geq 70\%$
CAPRIE	1996	RCT	Clopidogrel vs aspirin \rightarrow 8.7% RRR in composite vascular events	Clopidogrel as alternative to aspirin
IST/CAST	1997	RCT	Aspirin 160/300 mg within 48h acute stroke \rightarrow \downarrow death and recurrence at 14d	Aspirin STAT in acute ischaemic stroke
PROGRESS	2001	RCT	Perindopril \pm indapamide: 28% \downarrow stroke recurrence; 43% \downarrow in combination arm	ACEi + diuretic for BP lowering
SPARCL	2006	RCT	Atorvastatin 80 mg vs placebo \rightarrow 16% RRR recurrent stroke; \uparrow small ICH risk	High-intensity statin post-ischaemic stroke
CHANCE	2013	RCT	DAPT (ASA+Clopi) vs ASA alone in high-risk TIA/minor stroke \rightarrow 32% \downarrow recurrence at 90d	DAPT for 21 days in high-risk TIA
DAWN/DEFUSE 3	2018	RCT	Thrombectomy 6–24h in selected patients (DWI-FLAIR mismatch) \rightarrow mRS 0–2: 49% vs 13%	MT up to 24h with imaging selection
POINT	2018	RCT	DAPT (ASA+Clopi) vs ASA in TIA/minor stroke: \downarrow recurrence 22% vs 11% at 90d \rightarrow stopped early	DAPT 21 days (POINT/CHANCE consistent)
THALES	2020	RCT	ASA+Ticagrelor vs ASA: \downarrow composite stroke/death (5.5% vs 6.6%); \uparrow bleeding	Ticagrelor+ASA for 30 days in high risk
CLOSE	2017	RCT	PFO closure vs antiplatelet in cryptogenic stroke < 60 yrs \rightarrow 0% vs 6% recurrence at 5 yrs	PFO closure in young cryptogenic stroke

CLINICAL ALGORITHM: APPROACH TO RECURRENT STROKE



COMPREHENSIVE REFERENCES

MEDICAL TEXTBOOKS

- Harrison's Principles of Internal Medicine, 22nd Edition (2025) — Fauci et al. Ch.380: Cerebrovascular Diseases
- Kumar & Clarke's Clinical Medicine, 10th Edition (2021) — Siddiqui & Clarke. Ch.21: Neurology
- Davidson's Principles & Practice of Medicine, 24th Edition (2022) — Penman et al. Ch.28: Neurological Disease
- Cecil Medicine / Goldman-Cecil Medicine, 26th Edition (2020) — Goldman & Schafer. Ch.380: Stroke

NEUROLOGY TEXTBOOKS

- Adams & Victor's Principles of Neurology, 11th Edition (2019) — Ropper, Samuels & Klein
- Bradley's Neurology in Clinical Practice, 8th Edition (2022) — Daroff et al.
- Merritt's Neurology, 13th Edition (2020) — Bhanu Bhanu. Ch.: Cerebrovascular Disease

PHARMACOLOGY & PATHOLOGY

- Goodman & Gilman's Pharmacological Basis of Therapeutics, 14th Edition (2023) — Brunton et al.
- Robbins & Cotran Pathologic Basis of Disease, 10th Edition (2020) — Kumar, Abbas & Aster
- Anderson's Pathology, 10th Edition — Damjanov & Linder

ANATOMY

- Snell's Clinical Neuroanatomy, 8th Edition (2019) — Lawrence Ryan. Ch.7: Blood Supply of Brain & Spinal Cord
- Gray's Anatomy, 42nd Edition (2020) — Standring

KEY JOURNALS & TRIALS (2019-2024)

- THALES Trial — Wang et al. NEJM 2020 | DAWN Trial — Nogueira NEJM 2018 | DEFUSE 3 — Albers NEJM 2018
- CLOSE Trial — Mas NEJM 2017 | CRYSTAL-AF — Sanna NEJM 2014 | EMBRACE — Gladstone NEJM 2014
- ASA/AHA Stroke Guidelines 2021 — Stroke 2021;52:e364 | ESC AF Guidelines 2020 | ACC/AHA 2019
- CREST-2 — ongoing | BASICS NEJM 2021 | MR CLEAN NEJM 2015 | ESCAPE NEJM 2015
- Peer-reviewed: Stroke, Lancet Neurology, NEJM, Lancet, Circulation, European Heart Journal (2019–2024)