

W H I T E   P A P E R

# Stroke and CVA

## Circulatory Disorders Causing Dependency

*Ischemic · Hemorrhagic · TIA · Atrial Fibrillation · Carotid Disease*

*A Complete Guide for Patients, Families, and Caregivers*

Acute Treatment · Secondary Prevention · Rehabilitation · Caregiver Support

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*Sources: American Heart Association, American Stroke Association, CDC, FDA, NIH ClinicalTrials.gov*

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# 1. EXECUTIVE SUMMARY

Stroke — also called Cerebrovascular Accident (CVA) — is a sudden interruption of blood supply to the brain. It is the leading cause of long-term adult disability in the United States and one of the most common reasons a previously independent adult suddenly becomes dependent on others for daily care.

Unlike many chronic diseases, a stroke can transform a healthy 65-year-old into someone needing 24-hour care overnight. About 795,000 Americans suffer a stroke each year — one every 40 seconds. Some recover fully. Two out of three are left with permanent disability. A large portion can no longer perform basic Activities of Daily Living without help.

Stroke does not occur in isolation. It is the most visible outcome of broader circulatory disease — atrial fibrillation, carotid artery stenosis, high blood pressure, atherosclerosis, and heart disease. Each of these conditions independently raises the risk of stroke, and several cause dependency in their own right through chronic fatigue, cognitive impairment, and reduced mobility.

This white paper gives patients, family members, and caregivers an honest, current picture of stroke and related circulatory disorders — from acute emergency through recovery and caregiving. It covers:

- What stroke is and how each type causes damage
- The related circulatory disorders that cause or follow stroke
- How stroke severity and disability are measured
- How stroke is diagnosed and treated acutely — including the 2025 FDA approval of tenecteplase
- Current secondary prevention medications and the new factor XI inhibitors in trials
- Rehabilitation pathways and long-term recovery
- How caregivers can navigate the acute-to-chronic transition and protect their own wellbeing
- The critical importance of prevention, prompt recognition, and advance directives — before the stroke happens

## 2. UNDERSTANDING STROKE AND CVA

### What Is a Stroke?

A stroke (CVA) occurs when blood flow to part of the brain is suddenly interrupted. Brain cells deprived of oxygen begin dying within minutes. The longer the interruption, the larger the area of permanent damage. Time, in stroke care, is brain — every minute of delay destroys approximately 1.9 million additional neurons.

Stroke is fundamentally a vascular event — the consequence of a diseased circulatory system breaking down at its weakest point. That is why preventing stroke is largely a matter of managing blood pressure, cholesterol, atrial fibrillation, diabetes, and lifestyle.

### The Major Types of Stroke

#### Ischemic Stroke — 87% of all strokes

Caused by a blockage in an artery supplying the brain. A clot either forms in the artery itself or travels there from somewhere else in the body (most often the heart, in patients with atrial fibrillation).

- **Thrombotic:** A clot forms in a diseased brain artery — usually at the site of atherosclerotic plaque.
- **Embolic:** A clot travels to the brain from elsewhere — most commonly the left atrium of the heart in atrial fibrillation, or from the carotid arteries.
- **Lacunar:** Small-vessel disease deep in the brain, strongly associated with chronic hypertension and diabetes.
- **Cryptogenic:** Ischemic stroke of undetermined cause after standard workup — approximately 25–30% of all ischemic strokes. Often linked to undetected atrial fibrillation or patent foramen ovale.

#### Hemorrhagic Stroke — 13% of all strokes

Caused by bleeding into or around the brain. Less common than ischemic stroke but more often fatal, and harder to treat. Treatment focuses on controlling blood pressure, reversing any anticoagulants, and surgical intervention when appropriate.

- **Intracerebral hemorrhage (ICH):** Bleeding into the brain tissue itself. Most often caused by uncontrolled chronic hypertension; less often by amyloid angiopathy or vascular malformations.
- **Subarachnoid hemorrhage (SAH):** Bleeding into the space around the brain, usually from a ruptured aneurysm. Sudden, severe 'thunderclap' headache is the classic presentation.

#### Transient Ischemic Attack (TIA) — The Warning Stroke

A TIA produces stroke symptoms that resolve completely within 24 hours, usually within an hour. The mechanism is the same as ischemic stroke — but the clot dissolves before permanent damage occurs.

- TIA is a medical emergency. 10–15% of patients have a full stroke within 90 days if untreated.

- Up to half of post-TIA strokes occur within 48 hours.
- A TIA is the single best opportunity to prevent a major disabling stroke — if acted on immediately.

## **Related Circulatory Disorders Causing Dependency**

Stroke is the most visible cerebrovascular event, but several other circulatory conditions independently cause long-term dependency or dramatically increase stroke risk.

### **Atrial Fibrillation (AFib)**

An irregular heart rhythm in which the upper chambers quiver instead of contracting normally. Blood pools and can form clots that travel to the brain. AFib increases stroke risk approximately five-fold and is responsible for 15–20% of all ischemic strokes.

- More than 6 million Americans have diagnosed AFib; many more cases are undetected
- Prevalence rises sharply with age — over 9% of adults age 65 and older
- Often paroxysmal (comes and goes), making detection challenging without extended cardiac monitoring
- Anticoagulation reduces stroke risk by 60–70% in eligible patients

### **Carotid Artery Stenosis**

Atherosclerotic narrowing of the carotid arteries that supply the brain. Plaque can rupture, causing a clot that embolizes to the brain. Significant stenosis (greater than 70%) usually warrants intervention — carotid endarterectomy or stenting — to prevent stroke.

### **Hypertensive Heart Disease and Chronic Hypertension**

Long-term high blood pressure is the single most important modifiable risk factor for both ischemic and hemorrhagic stroke. It damages small vessels throughout the brain, contributes to atrial fibrillation, and stiffens the heart muscle. Untreated, chronic hypertension causes both stroke and the cumulative small-vessel damage that produces vascular dementia.

### **Peripheral Artery Disease (PAD)**

Atherosclerotic narrowing of arteries to the legs. PAD is rarely a direct cause of dependency on its own, but it is a marker of widespread vascular disease — patients with PAD have markedly elevated stroke and heart attack risk and reduced mobility that compounds dependency from other causes.

### **Congestive Heart Failure (CHF)**

The heart's inability to pump effectively. Causes chronic fatigue, exercise intolerance, fluid overload, and reduced brain perfusion that can mimic or accelerate cognitive decline. Severe CHF is a major contributor to dependency and frequent hospitalization in older adults.

### **Coronary Artery Disease and Post-MI Complications**

Heart attacks (myocardial infarctions) damage the heart muscle and can leave behind weakened areas where clots form. They also strongly correlate with widespread atherosclerosis affecting the brain's blood supply.

## **Vascular Cognitive Impairment**

Repeated strokes, undetected mini-strokes, and chronic small-vessel disease accumulate over years and produce vascular dementia — covered separately in our white paper on dementias. About half of patients diagnosed with vascular dementia have a history of clinical stroke; the other half developed it through silent vascular damage.

## How Common Is Stroke?

**795,000** Americans suffer a stroke each year — one every 40 seconds

**7.8 million** U.S. adults living with a history of stroke

**162,639** Americans died from stroke in 2023 — one death every 3 minutes 14 seconds

**#4** Stroke's rank among causes of death in the United States

**1 in 4** strokes occur in someone who has had a previous stroke

**Two-thirds** of stroke survivors are left with some form of permanent disability

**#1** Stroke is the leading cause of long-term adult disability in the U.S.

## What Causes Stroke?

Stroke results from a combination of cumulative damage to the blood vessels and acute triggering events. Multiple risk factors usually act together.

### Major Modifiable Risk Factors

- High blood pressure — the single most important modifiable factor
- Atrial fibrillation — increases stroke risk fivefold
- Diabetes — accelerates atherosclerosis and damages small vessels
- High cholesterol — drives atherosclerotic plaque
- Smoking — doubles ischemic stroke risk
- Obesity and physical inactivity
- Heavy alcohol use
- Sleep apnea — independently raises stroke risk
- Carotid artery disease

### Non-Modifiable Risk Factors

- Age — stroke risk doubles every decade after age 55
- Family history of stroke
- Race — Black Americans have nearly twice the stroke risk of White Americans
- Sex — more women than men have strokes (women live longer; risk rises with age)
- Prior stroke or TIA

*Up to 80% of strokes are preventable. Aggressive control of blood pressure, treatment of atrial fibrillation, statin therapy when indicated, smoking cessation, and diabetes management — taken together — could eliminate four out of five strokes. Source: CDC and American Stroke Association.*

## Symptoms of Stroke — Know the Warning Signs

Stroke symptoms appear suddenly. Recognition and immediate 911 calls determine whether a survivor walks out of the hospital or never walks again. The BE-FAST mnemonic captures the most common warning signs.

| Letter      | Warning Sign                                                                   |
|-------------|--------------------------------------------------------------------------------|
| B — Balance | Sudden loss of balance or coordination                                         |
| E — Eyes    | Sudden vision changes — blurred, double, or loss of vision in one or both eyes |
| F — Face    | One side of the face droops or feels numb                                      |
| A — Arm     | One arm is weak or numb; drifts down when raised                               |
| S — Speech  | Slurred speech, inability to speak, or hard to understand                      |
| T — Time    | Call 911 immediately — do not drive, do not wait, do not 'lie down and see'    |

*Only about 38% of Americans are aware of all stroke symptoms AND know to call 911. The single largest reason patients arrive too late for tPA or thrombectomy is that they or a family member tried to 'wait it out.' The first call must be to 911 — not to a doctor's office, not to a family member, not to wait until morning. Source: CDC Stroke Facts.*



## How Stroke Causes Long-Term Dependency — The Modified Rankin Scale

The Modified Rankin Scale (mRS) is the universal stroke disability scale. It is used in every major stroke trial and in routine clinical care planning. The scale runs from 0 (no symptoms) to 6 (death). The threshold between independence and dependency falls between scores of 2 and 3 — and the threshold between home care and institutional placement typically falls between 4 and 5.

| mRS | Description                                | Independence Level                                                         | Care Setting                                         |
|-----|--------------------------------------------|----------------------------------------------------------------------------|------------------------------------------------------|
| 0   | No symptoms                                | Fully independent                                                          | Home, no care                                        |
| 1   | No significant disability despite symptoms | Carries out all usual activities                                           | Home, no care                                        |
| 2   | Slight disability                          | Can manage own affairs without help; some restrictions on prior activities | Home, possibly minor help                            |
| 3   | Moderate disability —<br>DEPENDENCY BEGINS | Requires some help; walks unassisted                                       | Home with part-time help or assisted living          |
| 4   | Moderately severe disability               | Cannot walk without help; needs help with bodily care                      | Full-time home care or assisted living / memory care |
| 5   | Severe disability                          | Bedridden, incontinent, requires constant nursing                          | Skilled nursing facility                             |
| 6   | Dead                                       | —                                                                          | —                                                    |

Clinical thresholds used in stroke research and care planning:

- **mRS 0-1:** Excellent outcome — the goal of all acute therapy (clot-busting drugs and thrombectomy).
- **mRS 0-2:** Functional independence — the primary endpoint of most stroke trials.
- **mRS 3-5:** Dependent — long-term care required at varying levels.
- **mRS 4-5:** Heavy care burden — typically requires either round-the-clock paid help at home or institutional placement.

Other widely used scales include the Barthel Index (0–100 measure of Activities of Daily Living), the Functional Independence Measure (FIM, used in rehabilitation facilities), and the NIH Stroke Scale (NIHSS, 0–42 measure of acute neurologic deficit). For understanding day-to-day care needs, the

Modified Rankin Scale and Barthel Index are most directly relevant — they describe what the survivor can and cannot do.

*Most strokes that cause permanent dependency leave the survivor at mRS 3 or 4 — moderate to moderately severe disability. These patients are not bedridden, but they cannot walk unassisted, dress themselves, or safely live alone. They need help every day for the rest of their lives.*

### 3. DIAGNOSIS

Stroke diagnosis is built around three priorities — confirm a stroke is happening, determine whether it is ischemic or hemorrhagic, and identify the cause so prevention can be tailored. The first hour after arrival at the emergency department is the most consequential in a stroke patient's life.

#### Pre-Hospital Recognition

Family members, caregivers, and bystanders make the first diagnostic call. Use BE-FAST. If any one sign appears suddenly, call 911. Note the exact time symptoms began — eligibility for clot-busting drugs and thrombectomy depends on the time of onset.

#### Emergency Department Workup

| Study                                                                 | Purpose                                                            | Notes                                                      |
|-----------------------------------------------------------------------|--------------------------------------------------------------------|------------------------------------------------------------|
| Non-contrast CT (NCCT)                                                | Rule out hemorrhage first; standard initial scan                   | Available at virtually every hospital; takes minutes       |
| CT Angiography (CTA)                                                  | Detect large vessel occlusion (LVO) — eligibility for thrombectomy | Imaging head and neck simultaneously with CT               |
| CT Perfusion (CTP)                                                    | Identify ischemic penumbra — salvageable brain tissue              | Critical for extended-window thrombectomy (6–24 hours)     |
| MRI / DWI                                                             | Most sensitive for acute ischemia; detects within minutes          | Used when patient is stable and MRI available              |
| Carotid Ultrasound / CTA neck                                         | Detect carotid artery stenosis as a source                         | Standard workup after ischemic stroke or TIA               |
| Echocardiography (TTE / TEE)                                          | Identify cardiac sources of embolism — clot, valve disease, PFO    | Especially important in cryptogenic stroke                 |
| Cardiac monitoring (Holter, event monitor, implantable loop recorder) | Detect paroxysmal atrial fibrillation                              | Extended monitoring significantly increases AFib detection |
| Laboratory studies                                                    | CBC, basic metabolic panel, coagulation, glucose, lipids, HbA1c    | Rules out mimics; identifies cardiovascular risk factors   |

## AI-Assisted Stroke Detection

As of 2025–2026, FDA-cleared artificial intelligence platforms are reshaping how stroke is detected and treated:

- **Viz.ai:** AI software that automatically detects large vessel occlusions on CTA, calculates ASPECTS scores, and alerts the stroke team — significantly reducing time to thrombectomy.
- **RapidAI:** AI analysis of CT perfusion to quantify infarct core and penumbra; used to determine eligibility for extended-window thrombectomy. A 2025 head-to-head study showed RapidAI significantly outperforms Viz.ai for detecting medium-vessel occlusions.

*AI stroke triage has cut door-to-needle and door-to-thrombectomy times by 30–60 minutes at many comprehensive stroke centers. For a stroke patient, that translates directly into preserved brain tissue and a higher probability of returning home.*

## 4. ACUTE TREATMENT — THE FIRST FEW HOURS

Acute stroke treatment splits sharply by stroke type. Ischemic strokes (caused by clots) are treated by dissolving or removing the clot. Hemorrhagic strokes (caused by bleeding) are treated by controlling blood pressure, reversing any anticoagulants, and sometimes by surgery. CT scanning is the first step because it tells the emergency team which treatment is possible.

*Time is brain. Every minute that passes during an acute ischemic stroke destroys an estimated 1.9 million additional neurons. Treatments that work within 3 hours often fail by hour 6. Treatments that work within 6 hours rarely work by hour 24. The single most important determinant of recovery is how quickly the patient reaches a stroke-capable hospital.*

### Ischemic Stroke — Clot-Busting Drugs (IV Thrombolysis)

IV thrombolysis — clot-dissolving medications given through a vein — has been the foundation of acute ischemic stroke treatment for nearly 30 years. In March 2025, the FDA approved the first new acute stroke drug in nearly three decades.

#### Tenecteplase (TNKase) — FDA Approved March 3, 2025

- Manufacturer: Genentech (Roche Group)
- First new acute stroke medicine FDA-approved in nearly 30 years
- Single 5-second IV bolus — replaces the previous 60-minute infusion of alteplase
- Dose: 0.25 mg/kg; new 25 mg vial introduced in early 2025
- Window: FDA label up to 3 hours; AHA/ASA guidelines extend to 4.5 hours
- Based on the AcT trial — non-inferior to alteplase with comparable safety
- Now preferred at many stroke centers for ease of administration and lower cost

#### Alteplase (Activase, tPA) — The 29-Year Standard

- FDA-approved in 1996 — the original IV clot-buster
- 0.9 mg/kg IV (10% bolus, remainder over 60 minutes); maximum 90 mg
- Time window: Within 4.5 hours of symptom onset (AHA/ASA guidelines)
- Still appropriate where tenecteplase is not yet available

### Mechanical Thrombectomy

Mechanical thrombectomy is a procedure in which an interventional neuroradiologist threads a catheter from a leg artery up to the blocked brain artery and physically removes the clot using a stent retriever or aspiration device. It is the most powerful stroke treatment available.

- **Indication:** Large vessel occlusion (LVO) — internal carotid, M1 or M2 middle cerebral, or basilar artery.
- **Standard window:** Up to 6 hours from last known well.

- **Extended window — up to 24 hours:** For selected patients based on imaging mismatch (DAWN trial, DEFUSE 3 trial criteria). This is one of the most important advances in stroke care of the last decade.
- **Bridging therapy:** Often performed in addition to IV thrombolysis when the clot is large.
- **Outcomes:** Selected patients have a 35–50% chance of returning to functional independence (mRS 0–2) at 90 days versus 10–20% with medical therapy alone.

*Mechanical thrombectomy must be performed at a Comprehensive Stroke Center or Thrombectomy-Capable Stroke Center. Not every hospital can do it. When 911 is called for a suspected stroke, paramedics route the patient to the appropriate level of stroke center based on the suspected severity. This is why arriving by ambulance — not by personal car — saves lives.*

## Hemorrhagic Stroke — Stopping the Bleed

For brain bleeding, the priorities are stopping further bleeding and reducing pressure inside the skull. Clot-busters are absolutely contraindicated — they make hemorrhagic stroke far worse.

### Intracerebral Hemorrhage (ICH)

- Aggressive blood pressure control — target systolic <140 mmHg
- Reversal of any anticoagulant: vitamin K and prothrombin complex concentrate for warfarin; idarucizumab (Praxbind) for dabigatran; andexanet alfa (Andexxa) for apixaban/rivaroxaban
- Neurosurgical consultation — large or expanding hemorrhages may need evacuation
- Minimally invasive surgical approaches (ENRICH trial) are emerging as an option

### Subarachnoid Hemorrhage (SAH)

- Aneurysm repair — neurosurgical clipping or endovascular coiling, typically within 24–72 hours
- Nimodipine to prevent vasospasm
- Intensive care unit monitoring for at least 2 weeks

## 5. SECONDARY PREVENTION MEDICATIONS (2026)

After a first stroke or TIA, the risk of a second stroke is highest in the first 90 days. Secondary prevention is built on three pillars: an antiplatelet or anticoagulant medication, aggressive blood pressure control, and a high-intensity statin. Diabetes and lifestyle factors are addressed in parallel.

### Class 1: Antiplatelet Therapy

For non-cardioembolic ischemic stroke or TIA — meaning strokes not caused by atrial fibrillation or a cardiac clot — antiplatelet drugs prevent new clots from forming on diseased arteries.

| Brand Name            | Generic Name              | Approval                   | Notes                                                                                                                                                                        |
|-----------------------|---------------------------|----------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Generic               | Aspirin                   | —                          | 81–325 mg/day. The foundational antiplatelet for over 50 years. Inexpensive.                                                                                                 |
| Plavix                | Clopidogrel               | 1997                       | 75 mg/day. First-line alternative to aspirin. Used in dual therapy in selected cases.                                                                                        |
| Aspirin + Clopidogrel | DAPT                      | —                          | Short-term combination (21–90 days) for high-risk TIA / minor stroke. POINT and CHANCE trials showed ~25% reduction in recurrence. Long-term combination increases bleeding. |
| Aggrenox              | Aspirin + dipyridamole ER | 1999                       | 25/200 mg twice daily. Modestly superior to aspirin alone; headache side effect limits use.                                                                                  |
| Brilinta              | Ticagrelor                | 2011 (ACS); used in stroke | Studied in THALES trial: combined with aspirin for minor stroke / high-risk TIA — reduces recurrence but increases bleeding.                                                 |

## Class 2: Anticoagulation for Cardioembolic Stroke (Atrial Fibrillation)

For stroke caused by atrial fibrillation or another cardiac source, the standard is full anticoagulation. Direct oral anticoagulants (DOACs) are now preferred over warfarin in non-valvular atrial fibrillation.

| Brand Name | Generic Name | Approval | Notes                                                                                                                                                                 |
|------------|--------------|----------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Coumadin   | Warfarin     | 1954     | INR target 2–3. Long history; multiple drug and food interactions; requires regular blood monitoring. Still used in valvular AFib and when DOACs are contraindicated. |
| Eliquis    | Apixaban     | 2012     | Factor Xa inhibitor. ARISTOTLE trial showed superiority to warfarin with less major bleeding. Most widely preferred first-line DOAC.                                  |
| Xarelto    | Rivaroxaban  | 2011     | Factor Xa inhibitor. Once-daily dosing. ROCKET-AF trial data.                                                                                                         |
| Pradaxa    | Dabigatran   | 2010     | Direct thrombin inhibitor. RE-LY trial. Reversible with idarucizumab (Praxbind).                                                                                      |
| Savaysa    | Edoxaban     | 2015     | Factor Xa inhibitor. Once-daily. ENGAGE-AF trial data.                                                                                                                |

*Important — when to start anticoagulation after a stroke: Anticoagulation is typically started 2–14 days after an ischemic stroke depending on infarct size. Starting too early in a large infarct can convert it to a hemorrhagic stroke. Starting too late leaves the patient unprotected against a second clot. This is a critical clinical judgment made by the stroke team and the prescribing physician.*



### Class 3: Blood Pressure Management

Blood pressure lowering is the single most effective intervention to prevent recurrent stroke. The post-stroke target is generally less than 130/80 mmHg, individualized to the patient.

- **ACE inhibitors:** Lisinopril, ramipril, enalapril.
- **Angiotensin receptor blockers (ARBs):** Losartan, valsartan, telmisartan.
- **Calcium channel blockers:** Amlodipine, nifedipine.
- **Thiazide diuretics:** Chlorthalidone, hydrochlorothiazide.

### Class 4: Lipid Lowering

| Brand Name | Generic Name | Approval | Notes                                                                                                                           |
|------------|--------------|----------|---------------------------------------------------------------------------------------------------------------------------------|
| Lipitor    | Atorvastatin | 1996     | High-intensity statin. SPARCL trial: atorvastatin 80 mg reduced recurrent stroke by 16%.                                        |
| Crestor    | Rosuvastatin | 2003     | High-intensity statin. Used at 20–40 mg for post-stroke patients.                                                               |
| Repatha    | Evolocumab   | 2015     | PCSK9 inhibitor injection every 2 weeks. Reduces LDL 50–60% on top of statin. For very high-risk or statin-intolerant patients. |
| Praluent   | Alirocumab   | 2015     | PCSK9 inhibitor — similar mechanism and benefit to evolocumab.                                                                  |
| Leqvio     | Inclisiran   | 2021     | Small interfering RNA (siRNA) injection. Twice-yearly dosing dramatically improves adherence. Reduces LDL ~50%.                 |

### Class 5: Cardiometabolic Agents (Emerging Stroke Prevention)

Two major drug classes originally developed for diabetes and obesity have shown important stroke-prevention benefits — and are being incorporated into secondary prevention regimens for selected patients.

### SGLT2 Inhibitors

- Empagliflozin (Jardiance), dapagliflozin (Farxiga), canagliflozin (Invokana)
- AHA Scientific Sessions 2024: an analysis of more than 7,000 stroke survivors showed SGLT2 use was associated with a 67% lower risk of recurrent stroke
- Also reduce heart failure events and slow kidney disease progression

### GLP-1 Receptor Agonists

- Semaglutide (Ozempic, Wegovy), liraglutide, dulaglutide, tirzepatide
- Meta-analysis of 82,140 patients across 11 trials: GLP-1 agonists reduced stroke risk by 16%
- Combined with SGLT2 inhibitors, stroke survivors saw approximately 74% lower mortality risk in AHA 2024 data

*The integration of GLP-1 agonists and SGLT2 inhibitors into post-stroke care represents one of the most important shifts in secondary prevention in recent years. For stroke patients with diabetes, obesity, or heart failure, these drugs do more than control blood sugar — they actively reduce future stroke risk.*

## 6. PROMISING CLINICAL TRIALS — 2026 UPDATE

Stroke care has entered a period of unusually rapid change. The 2025 approval of tenecteplase, the maturation of mechanical thrombectomy data, the new factor XI inhibitor anticoagulants in late-stage trials, and the integration of AI into emergency stroke triage have all reshaped what is possible. The most important developments fall into five areas.

### Category A: Factor XI Inhibitors — A New Class of Anticoagulant

Current anticoagulants (warfarin and DOACs) prevent strokes but cause bleeding. The factor XI pathway is essential for forming pathological clots but plays only a minor role in normal blood clotting. In theory, blocking factor XI should prevent stroke with much less bleeding. Three programs are racing to prove this.

#### Abelacimab (Anthos Therapeutics) — LILAC-TIMI 76

- Type: Monoclonal antibody binding factor XI
- AZALEA-TIMI 71 (Phase 2): stopped early because of dramatic bleeding reduction — 81% reduction in major bleeding vs. rivaroxaban
- LILAC-TIMI 76 (Phase 3): abelacimab vs. placebo in approximately 1,900 atrial fibrillation patients unsuitable for standard anticoagulation; FDA Fast Track designation
- Why it matters: would establish an entirely new anticoagulant class for patients who currently cannot tolerate any therapy

#### Milvexian (BMS / Janssen) — LIBREXIA Program

- Type: Oral small-molecule factor XI inhibitor
- AXIOMATIC-SSP (Phase 2): post-stroke / TIA — fewer recurrences with most doses; no significant bleeding increase
- LIBREXIA-AF (Phase 3): milvexian vs. apixaban in approximately 15,500 atrial fibrillation patients; completion expected approximately 2027
- Also enrolling in LIBREXIA-STROKE and LIBREXIA-ACS (more than 50,000 patients across the program)
- Why it matters: if non-inferior to apixaban with less bleeding, would be a major advance

#### Asundexian (Bayer) — OCEANIC Program

- OCEANIC-AF (Phase 3): TERMINATED EARLY in November 2023. Asundexian showed approximately 4x higher stroke / systemic embolism rate compared with apixaban — a clear failure on efficacy
- OCEANIC-STROKE (ongoing): asundexian vs. placebo in post-stroke patients; different patient population from OCEANIC-AF
- Why it still matters: the failure narrowed the field — the remaining factor XI candidates must now prove they do not share the same efficacy gap

*The factor XI story is the most important anticoagulation story of 2025–2026. If abelacimab and milvexian succeed where asundexian failed, an entirely new generation of stroke-prevention drugs becomes available with substantially lower bleeding risk — particularly important for elderly patients who currently cannot tolerate warfarin or DOACs.*

## **Category B: Left Atrial Appendage Closure — Watchman FLX**

For atrial fibrillation patients who cannot tolerate anticoagulants, mechanical closure of the left atrial appendage — where most AFib-related clots form — offers an alternative. The Watchman device is the most established option.

- CHAMPION-AF (results presented March 2026): Watchman FLX was non-inferior to DOACs for the composite endpoint of cardiovascular death, stroke, and systemic embolism at 3 years
- Substantially lower non-procedural bleeding (10.9% vs. 19.0% with DOACs)
- More than 600,000 patients implanted worldwide
- New Watchman FLX Pro device with improved safety profile available
- Why it matters: For the first time, a one-time procedure may match the stroke-prevention efficacy of lifelong anticoagulation, while dramatically reducing bleeding risk

## **Category C: Post-Stroke Recovery and Rehabilitation**

### **Vivistim — Vagus Nerve Stimulation for Arm Recovery**

- FDA-approved 2021 for chronic upper-limb weakness after ischemic stroke
- Implanted device delivers vagus nerve stimulation paired with rehabilitation exercises
- 1-year durability data published in Stroke 2025 showed sustained improvement in arm function — months and years after the original stroke
- Why it matters: until Vivistim, no FDA-approved therapy existed for chronic post-stroke motor impairment

### **Stem Cell Therapy for Stroke Recovery**

- Multiple programs in development; the MASTERS-2 Phase 3 trial of MultiStem (invivestrocet) was suspended in May 2024 due to insufficient power
- Other stem cell programs continue — none yet FDA-approved
- Why it matters: even modest functional gains in chronic stroke survivors would dramatically change day-to-day independence and quality of life

### **Brain-Computer Interfaces**

- Synchron, Neuralink, and Blackrock Neurotech are developing implantable BCIs for paralyzed patients — many of whom became paralyzed from severe strokes
- Early human trials are demonstrating cursor control, typing, and limb-control prosthetics
- Years from broad availability, but represent a long-term reshaping of stroke disability

## Category D: AI-Driven Stroke Triage

Viz.ai and RapidAI are now in widespread clinical use. Their impact on door-to-treatment times is one of the most measurable advances in stroke care this decade. A 2025 head-to-head study showed RapidAI significantly outperforms Viz.ai for detecting medium-vessel occlusions.

## Category E: Acute Treatment Window Extension

Multiple ongoing trials are testing thrombectomy in patients beyond the current 24-hour window, and in patients with larger established infarcts than current criteria allow. The boundary of who can benefit from thrombectomy continues to expand.

### Trial Summary Table

| Drug / Therapy            | Target                    | Phase                     | Status                                                       | Expected Data |
|---------------------------|---------------------------|---------------------------|--------------------------------------------------------------|---------------|
| Tenecteplase (TNKase)     | Acute ischemic stroke     | FDA Approved              | Approved March 2025; first new acute stroke drug in 30 years | In market     |
| Abelacimab                | Factor XI (anticoagulant) | Phase 3                   | LILAC-TIMI 76; 81% bleeding reduction in Phase 2             | 2025–2026     |
| Milvexian                 | Factor XI (anticoagulant) | Phase 3                   | LIBREXIA-AF (15,500 patients); ongoing                       | 2027          |
| Asundexian                | Factor XI (anticoagulant) | Phase 3                   | OCEANIC-AF FAILED Nov 2023; OCEANIC-STROKE continues         | Mixed         |
| Watchman FLX (LAAC)       | AFib stroke prevention    | Approved + new trial data | CHAMPION-AF March 2026: non-inferior to DOACs                | Available     |
| Vivistim (VNS)            | Post-stroke arm recovery  | FDA Approved 2021         | 1-year durability data in Stroke 2025                        | Available     |
| MultiStem / Invivestrocet | Stem cell recovery        | Phase 3 suspended         | MASTERS-2 suspended May 2024 (insufficient power)            | Future        |
| BCI (Synchron,            | Severe stroke             | Phase 1                   | Early human trials                                           | Long term     |

| Drug / Therapy                 | Target                   | Phase       | Status                            | Expected Data |
|--------------------------------|--------------------------|-------------|-----------------------------------|---------------|
| Neuralink,<br>Blackrock)       | disability               |             | ongoing                           |               |
| AI triage (Viz.ai,<br>RapidAI) | Acute detection /<br>LVO | FDA-cleared | Widespread clinical<br>deployment | Available     |

## 7. REHABILITATION — RECOVERING FUNCTION

Most stroke recovery happens in the first 3–6 months, but functional gains can continue for years with appropriate therapy. Rehabilitation is delivered across multiple settings, each appropriate to a different level of disability.

### Levels of Post-Acute Care

| Setting                                     | Who It Serves                                                       | Intensity                       | Notes                                                                        |
|---------------------------------------------|---------------------------------------------------------------------|---------------------------------|------------------------------------------------------------------------------|
| Acute inpatient rehabilitation (IRF)        | Patients who can tolerate $\geq 3$ hours of therapy per day         | Highest                         | Average stay 2–4 weeks. Best outcomes for moderate strokes.                  |
| Skilled nursing facility (SNF) — rehab unit | Patients who cannot tolerate 3 hours/day                            | Moderate                        | Average stay 1–4 weeks. Medicare covers up to 100 days post-hospitalization. |
| Long-term acute care hospital (LTACH)       | Medically complex patients needing ventilator weaning or wound care | High medical / moderate therapy | For very ill stroke patients; average stay 25+ days.                         |
| Home health rehab                           | Patients well enough to go home but still needing therapy           | Variable                        | Physical, occupational, and speech therapy delivered at home.                |
| Outpatient rehab                            | Independent or near-independent patients                            | Variable                        | Continues for months — often the longest phase.                              |

### The Major Rehabilitation Therapies

- **Physical Therapy (PT):** Walking, balance, transferring, fall prevention, strength.
- **Occupational Therapy (OT):** Activities of Daily Living — dressing, bathing, eating, toileting. Adaptive equipment training.
- **Speech-Language Pathology (SLP):** Aphasia therapy (language recovery), dysarthria (slurred speech), swallowing assessment and treatment.
- **Cognitive Rehabilitation:** For post-stroke cognitive impairment — attention, memory, executive function.
- **Constraint-Induced Movement Therapy:** Forced use of the affected arm to drive recovery.
- **Robotic-Assisted Rehabilitation:** Exoskeletons and robotic devices for gait and upper-limb retraining.
- **Functional Electrical Stimulation (FES):** Helps re-activate weak muscles.

- **Telerehabilitation:** Remote therapy by video, expanded dramatically since 2020 — particularly useful for rural patients and for ongoing maintenance.
- **Spasticity Management:** Botulinum toxin injections (Botox), oral baclofen, intrathecal baclofen pumps for severe cases.

*The first 90 days after a stroke are the highest-yield rehabilitation window. Aggressive, well-coordinated rehabilitation during this period produces the largest functional gains — and is the difference between returning home independently and long-term dependency. Every therapy session in the first 12 weeks matters more than any session that comes later.*



## 8. THE CAREGIVER BURDEN

Stroke caregiving is among the most physically demanding forms of family caregiving — a stroke survivor with mRS 4 or 5 often cannot walk, transfer, or perform self-care safely. Unlike dementia, where the burden is largely cognitive supervision, stroke caregiving involves daily physical work — lifting, transferring, toileting, bathing, and managing equipment.

**27–49 hours/week** typical stroke caregiver time commitment

**40%** of stroke caregivers experience clinical depression

**66%** of stroke caregivers have at least one chronic health condition of their own

**60%+** of stroke caregivers are spouses or partners

### What Stroke Caregivers Need to Know

- Stroke caregiving begins suddenly — usually before the family has had time to adapt their home, finances, or work arrangements
- The first 6 months after a stroke are the most intense — most functional recovery happens then, requiring constant therapy attendance
- Respite care — temporary relief for caregivers — is available through Medicaid waiver programs in most states, Area Agencies on Aging, and community-based nonprofits including many faith communities and veteran service organizations
- Home modifications (grab bars, ramps, walk-in showers, stair lifts) are essential; occupational therapists can perform a home safety assessment and many Area Agencies on Aging offer modification grants or low-cost programs
- Adult day programs provide structured daytime care for stroke survivors while caregivers continue to work or recover — contact your local Area Agency on Aging ([eldercare.acl.gov](http://eldercare.acl.gov)) to locate programs near you
- Home health aides dramatically reduce caregiver strain and delay nursing home placement; ask your rehab hospital case manager or Area Agency on Aging for agency referrals
- Support groups for stroke survivors and caregivers are available through the American Stroke Association ([stroke.org](http://stroke.org)) and most rehabilitation hospitals

*The most dangerous caregiver is the spouse who tries to lift, transfer, and care for a moderately-disabled stroke survivor alone, without training or help. Caregiver injury rates are highest in the first year after stroke. Hiring help is not extravagance — it is the difference between sustainable care and a second medical crisis.*

## 9. KEY RESOURCES

| Organization                                    | What They Offer                                                                          | Website            |
|-------------------------------------------------|------------------------------------------------------------------------------------------|--------------------|
| American Stroke Association                     | Patient and family education; Stroke Warmline (1-888-4-STROKE); support groups           | stroke.org         |
| American Heart Association                      | Cardiovascular education; annual Heart Disease & Stroke Statistics; prevention resources | heart.org          |
| CDC Stroke                                      | Government health agency; statistics; prevention guidance; signs and symptoms            | cdc.gov/stroke     |
| National Stroke Association (now ASA)           | Patient education; survivor stories; rehab resources                                     | stroke.org         |
| NIH NINDS                                       | National Institute of Neurological Disorders and Stroke; research; clinical trials       | ninds.nih.gov      |
| NIH ClinicalTrials.gov                          | Database of active U.S. clinical trials; searchable by condition and location            | clinicaltrials.gov |
| National Academy of Elder Law Attorneys (NAELA) | Locate an elder law attorney for advance directives and legal planning                   | naela.org          |
| Family Caregiver Alliance                       | Caregiver education, support groups, respite guidance, condition-specific fact sheets    | caregiver.org      |
| AARP                                            | Caregiver resources and Medicare guidance                                                | aarp.org           |
| Eldercare Locator                               | Federal service connecting older adults and families to local services (1-800-677-1116)  | eldercare.acl.gov  |
| Area Agencies on Aging (AAA)                    | Local case management, respite, adult day, home-modification help, transportation        | eldercare.acl.gov  |

## 10. NEXT STEPS — GET THE HELP YOU NEED

*Stroke is the most unpredictable cause of long-term care dependency. It can strike in an instant. The families who navigate stroke best are those who prepare medically and legally BEFORE the stroke happens — and who reach out to the right medical and community support the moment it does. You do not have to figure this out alone.*

Whether you are recovering from a stroke, caring for a stroke survivor, or planning ahead to protect your family from cardiovascular risk, the following steps protect what matters:

### Step 1 — Know Your Cardiovascular Risk

Schedule a comprehensive cardiovascular evaluation with your primary care physician or a cardiologist. The key tests include blood pressure (multiple readings over weeks), cholesterol panel, hemoglobin A1c (diabetes), an EKG (atrial fibrillation screen), and — for higher-risk patients — carotid ultrasound and extended cardiac monitoring. Many strokes are preventable when their underlying risk factors are identified and treated.

### Step 2 — Treat Atrial Fibrillation Aggressively

If you have atrial fibrillation, your stroke risk is five times higher than your peers without AFib. Anticoagulation reduces that risk by 60–70%. The newest factor XI inhibitor anticoagulants in clinical trials may further reduce that risk with less bleeding. Work with a cardiologist to choose the right agent.

### Step 3 — Recognize Stroke Symptoms and Call 911

Every member of your household should know BE-FAST. The single biggest cause of disability after stroke is delay. Time spent calling family or 'lying down to see if it passes' costs irreplaceable brain tissue. Call 911 first — every time.

### Step 4 — Execute Legal Documents While You Have Capacity

Before a stroke happens, finalize:

- Durable Power of Attorney (financial) — allows a trusted person to manage finances
- Health Care Proxy / Durable POA for Healthcare — allows a trusted person to make medical decisions
- Living Will / Advance Directive — specifies wishes for end-of-life care
- Will and trusts as appropriate — updated to reflect current circumstances

After a severe stroke with cognitive impairment, signing these documents may no longer be possible — and the family must seek guardianship through the courts.

## **Step 5 — Engage Your Medical Advocacy Team**

If a stroke has already occurred, your most important allies are the rehabilitation hospital case manager, social worker, and neurologist. Ask directly for a written care plan that includes: rehab goals, medication reconciliation, follow-up appointments, home safety recommendations, and referrals to community-based support. If you feel dismissed or under-informed, request a formal care conference — you are entitled to one.

## **Step 6 — Connect to Community and Caregiver Support**

Connection with others who have navigated stroke is consistently cited as one of the most valuable resources. Contact the American Stroke Association for local survivor and caregiver support groups, rehab center referrals, and the Stroke Warmline (1-888-4-STROKE). Contact your Area Agency on Aging ([eldercare.acl.gov](http://eldercare.acl.gov), 1-800-677-1116) for respite care, adult day programs, and home-modification help. Most rehabilitation hospitals also run support groups.

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