- Evaluating Non-Inferiority: Dual Antiplatelet Therapy vs. Alteplase in Minor Non-Disabling Acute Stroke

Objectives

- Review management strategies for acute ischemic stroke.
- Examine previous guidelines for acute ischemic stroke treatment.
- Analyze the role of alteplase thrombolysis versus DAPT in managing acute minor

Etiology of Acute Ischemic Stroke

- **Definition:** Caused by the blockage of a cerebral artery leading to reduced blood flow to the brain.
- **Common Causes:**
  - Embolism (cardioembolic or artery-to-artery).
  - Thrombosis (atherosclerosis).
  - Small vessel occlusion (lacunar infarction).
- **Risk Factors:** Hypertension, diabetes, atrial fibrillation, smoking, hyperlipidemia, and sedentary lifestyle.

Management of Acute Ischemic Stroke

- **Primary Goals:**
  - Restore cerebral perfusion.
  - Prevent progression and recurrence.
  - Minimize long-term neurological deficits.
- **Initial Steps:**
  - Rapid assessment and imaging (CT/MRI).
  - Exclusion of hemorrhagic stroke.
- **Key Interventions:**
  - Thrombolysis with intravenous alteplase (if eligible).
  - Antiplatelet therapy (aspirin, clopidogrel).
  - Mechanical thrombectomy for large vessel occlusions.

Previous Guidelines for Acute Ischemic Stroke

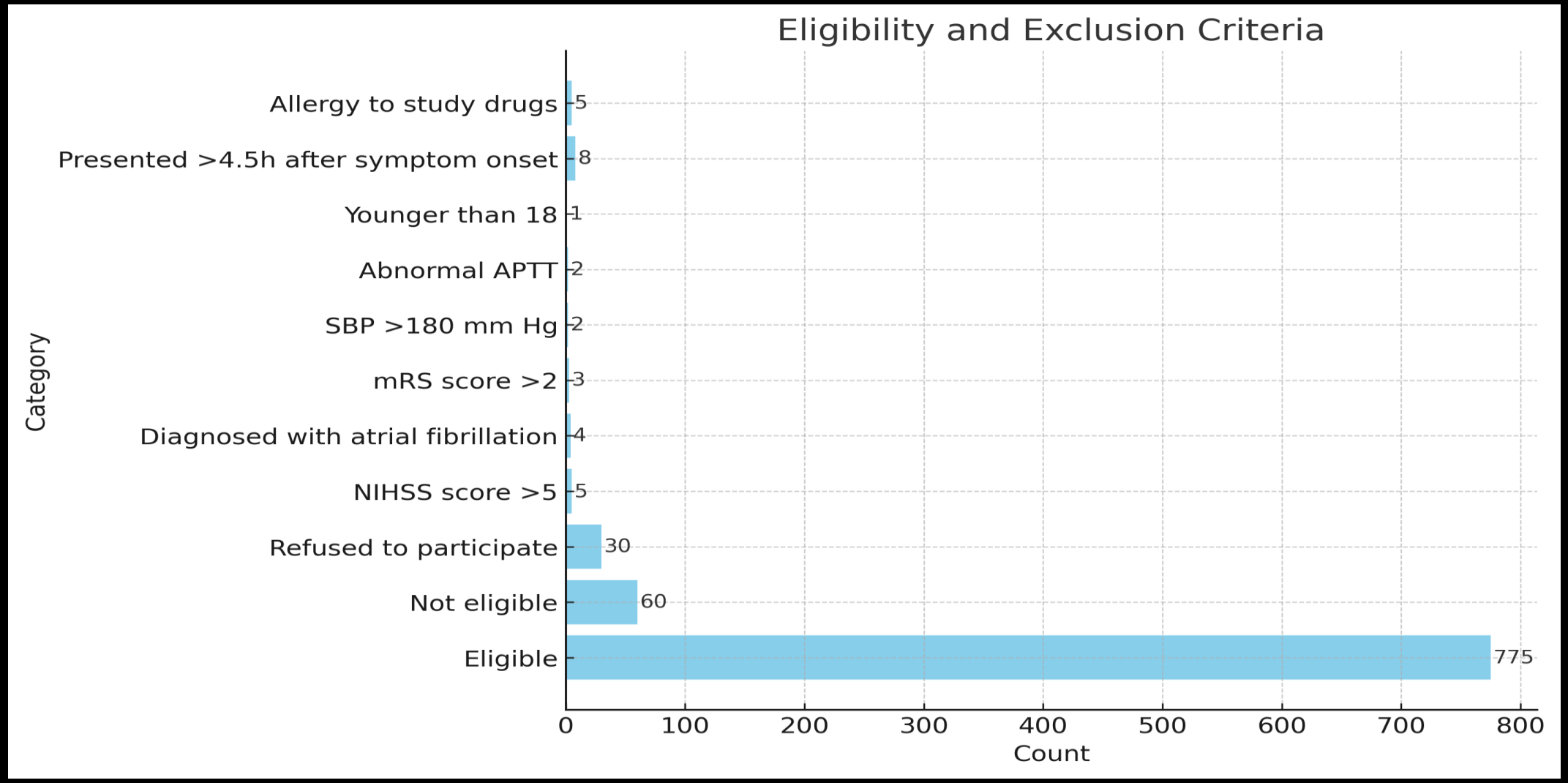
- **2018 AHA/ASA Guidelines:**
  - Alteplase indicated for patients presenting within 4.5 hours of symptom onset.
  - Antiplatelet therapy initiated within 24-48 hours of onset if thrombolysis is not performed.
- **Limitations of Prior Guidelines:**
  - Uncertainty regarding management of minor strokes.
  - Risks of bleeding with alteplase in mild presentations.

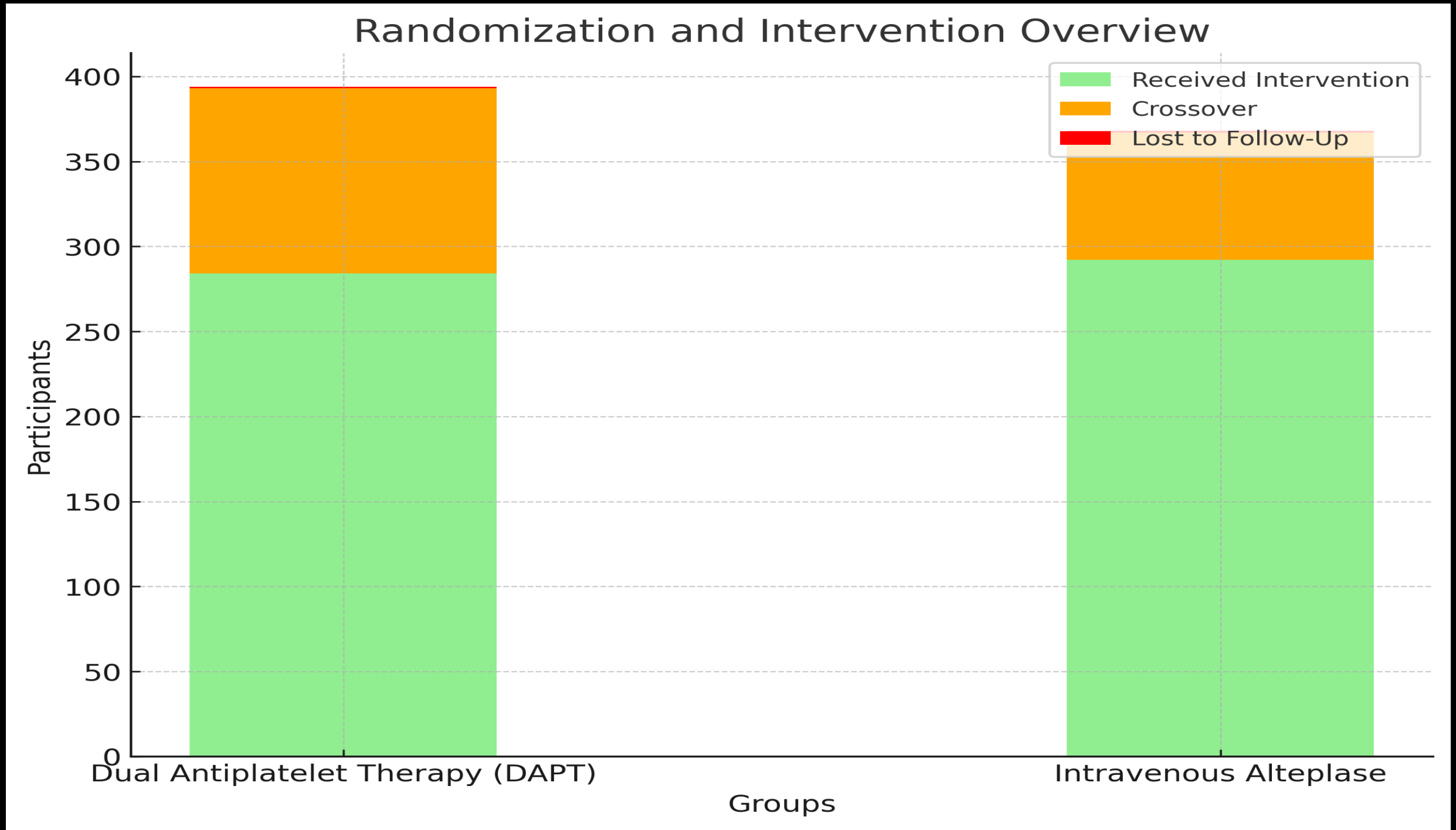
ARAMIS Trial: Overview

- **Objective:**
  - Compare alteplase thrombolysis and DAPT in acute minor ischemic stroke.
- **Key Inclusion Criteria:**
  - Minor ischemic stroke (NIHSS ≤ 5).
  - Onset of symptoms within a manageable timeframe.
- **Study Interventions:**
  - Alteplase: Standard IV dose for eligible patients.
  - DAPT: Combination of aspirin and clopidogrel.

The study aimed to evaluate whether dual antiplatelet therapy (DAPT) is noninferior to intravenous thrombolysis with alteplase in patients with minor nondisabling acute ischemic stroke.
The trial included 760 patients randomized within 4.5 hours of symptom onset. Participants in the DAPT group received a combination of clopidogrel and aspirin, while the alteplase group received intravenous alteplase.

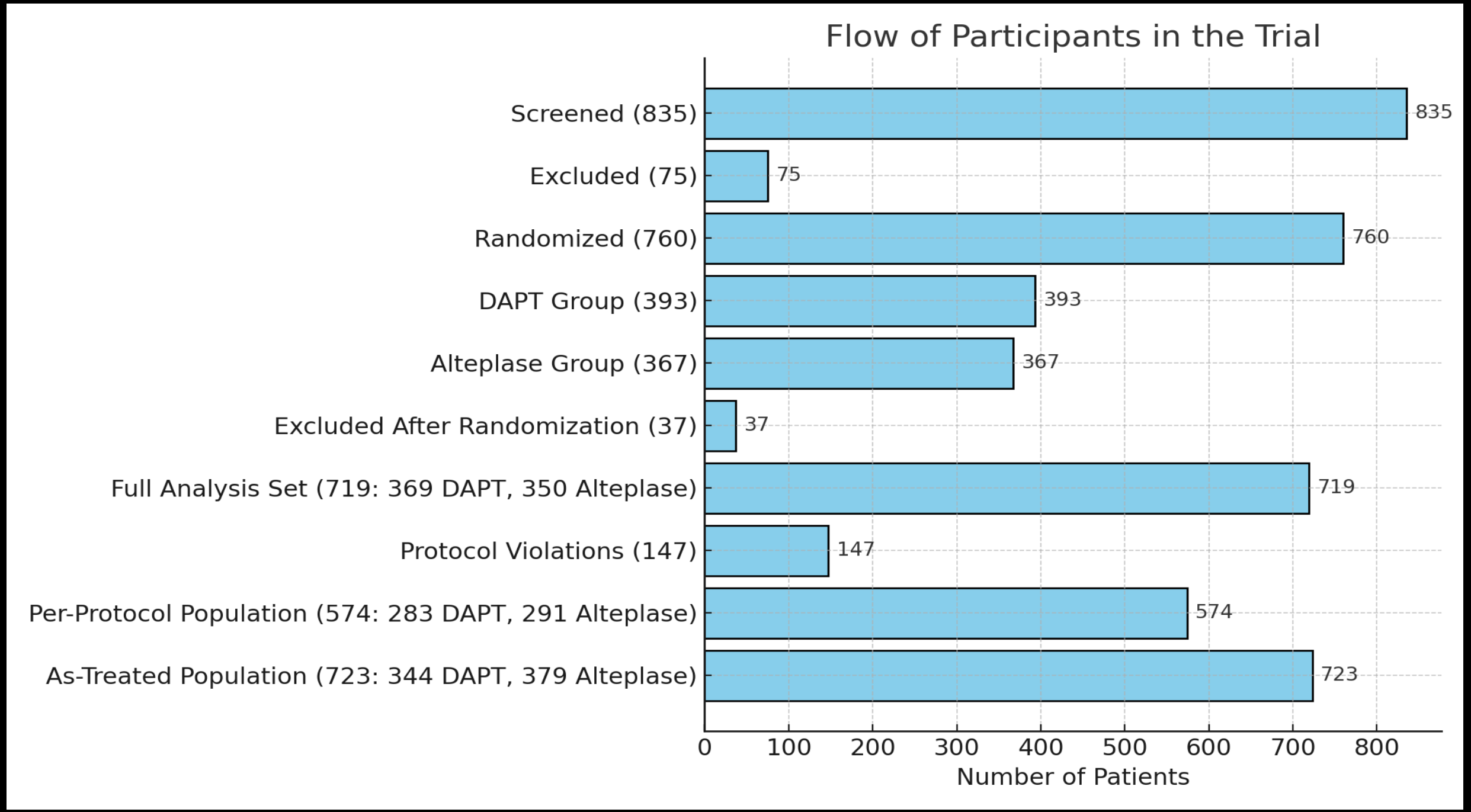
ARAMIS TRIAL




Randomization and Intervention Overview
Received Intervention
Crossover
Lost to Follow-Up
Participants
400
350
300
250
200
150
100
50
0
Dual Antiplatelet Therapy (DAPT)
Intravenous Alteplase
Groups

- Recap:
- The ARAMIS trial explored whether dual antiplatelet therapy (DAPT) (clopidogrel and aspirin) is noninferior to intravenous alteplase (tPA) in patients with acute minor ischemic stroke and nondisabling deficits, presenting within 4.5 hours of symptom onset. The study was conducted across 38 hospitals in China, with 760 participants randomized equally into two treatment groups.
- Current context: Guidelines recommend alteplase for acute ischemic stroke, but its benefit in minor strokes remains uncertain, with prior studies (e.g., PRISMS) showing no significant functional improvement and higher bleeding risks.
- DAPT, validated by CHANCE and POINT trials, has shown efficacy in reducing recurrent strokes in similar populations within 12-24 hours of symptom onset.
- Key Methods:
- Eligible patients had an NIHSS score ≤5, nondisabling symptoms, and no major contraindications (e.g., pre-stroke disability or need for anticoagulation).
- Patients were randomized to:
  - DAPT group: Clopidogrel (loading dose, then daily) + aspirin (daily).
  - Alteplase group: Standard IV alteplase (0.9 mg/kg).
- Primary outcome: 90-day functional status (mRS score 0-1).
- Safety outcome: Symptomatic intracerebral hemorrhage (sICH).
- Conclusion:
- The study supports DAPT as a noninferior treatment option for patients with minor nondisabling ischemic strokes. This conclusion aligns with prior evidence favoring DAPT's safety and efficacy while highlighting a reduced risk of bleeding compared to alteplase. These findings could influence future guidelines, providing clinicians with a safer,

- Conclusion:
- This study compared the effectiveness and safety of dual antiplatelet therapy (DAPT) versus intravenous alteplase in patients with minor nondisabling acute ischemic stroke presenting within 4.5 hours of symptom onset.
- Primary Findings:
  - DAPT was noninferior to alteplase in achieving an excellent functional outcome (mRS 0-1) at 90 days.
  - The risk difference of 2.3% (95% CI: -1.5% to 6.2%) supported the noninferiority margin of -4.5%.
- Safety Results:
  - The DAPT group had a lower rate of symptomatic intracerebral hemorrhage (0.3% vs. 0.9%), indicating better safety.
- Secondary Outcomes:
  - Favorable functional outcomes, early neurological improvement, and deterioration rates were similar between the two groups.
  - Bleeding events were more common in the alteplase group.
  - Implications: DAPT offers a safe and effective alternative to intravenous alteplase for minor ischemic stroke, with fewer bleeding complications and comparable long-term functional outcomes. These findings may influence future guidelines and


Flow of Participants in the Trial
Screened (835)
Excluded (75)
Randomized (760)
DAPT Group (393)
Alteplase Group (367)
Excluded After Randomization (37)
Full Analysis Set (719: 369 DAPT, 350 Alteplase)
Protocol Violations (147)
Per-Protocol Population (574: 283 DAPT, 291 Alteplase)
As-Treated Population (723: 344 DAPT, 379 Alteplase)
835
75
760
393
367
37
719
147
574
723
0
100
200
300
400
500
600
700
800
Number of Patients

- Conclusion
- The trial demonstrated that **DAPT was noninferior to alteplase** for achieving excellent functional outcomes mRS (Modified Rankin Scale) scores of 0 or 1 at 90 days).
- **Outcomes at 90 Days:**
  - DAPT group: 93.8% (346/369).
  - Alteplase group: 91.4% (320/350).
- **Risk Difference:** 2.3% (95% CI: −1.5% to 6.2%; adjusted CI: −1.6% to 6.1%; P < .001 for noninferiority).
- Sensitivity analyses and subgroup evaluations consistently supported the noninferiority of DAPT, unaffected by protocol crossovers or alternative scenarios. These findings suggest that DAPT is a viable alternative to alteplase in achieving favorable outcomes for stroke management.

- Final conclusion
- Conclusion
- This trial concluded that dual antiplatelet therapy (DAPT) is noninferior to intravenous alteplase in achieving excellent functional outcomes at 90 days for patients with minor nondisabling acute ischemic stroke treated within 4.5 hours of symptom onset.
- Key Results:
  - Primary Outcome: DAPT demonstrated similar efficacy to alteplase with lower rates of early neurological deterioration and bleeding events.
  - Secondary Outcomes: No significant differences were observed between groups except for a lower rate of early neurological deterioration in the DAPT group.
  - Safety: DAPT had fewer adverse events, including symptomatic intracranial hemorrhage and other bleeding events.

- Clinical Implications:
  - DAPT offers a safer and effective alternative to alteplase for this patient population, especially given the challenges of administering alteplase and its associated risks.
  - Subgroup analyses highlighted no significant heterogeneity across demographics or clinical factors.
- Limitations:
  - High crossover rates, lack of vessel imaging in some cases, and the study's focus on a Chinese population may limit generalizability. Confirmation in diverse populations is warranted.
  - Final Takeaway
  - DAPT provides a viable, guideline-supported option for treating minor nondisabling strokes with comparable efficacy to alteplase and improved safety outcomes, guiding clinicians toward more tailored stroke management strategies.