Primary Stroke Prevention

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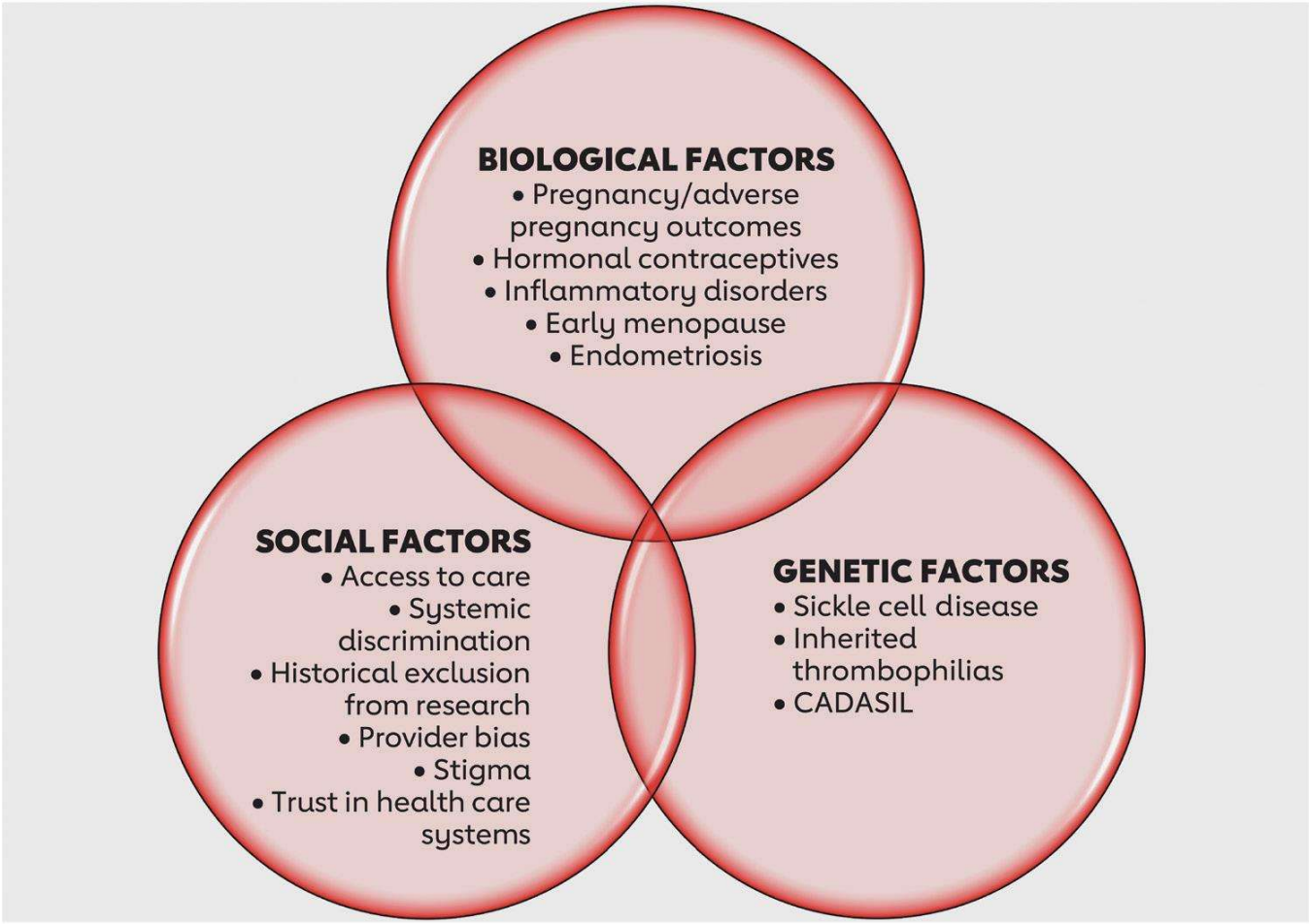
- No disclosures

Objectives

- Updates from 2024 AHA Guidelines
- Life’s Essential 8
- Hypertension management
- Lipoprotein (a)
- Pregnancy
- Hormonal therapy
- Menopause
- CREST-2 Results


BIOLOGICAL FACTORS
• Pregnancy/adverse pregnancy outcomes
• Hormonal contraceptives
• Inflammatory disorders
• Early menopause
• Endometriosis
SOCIAL FACTORS
• Access to care
• Systemic discrimination
• Historical exclusion from research
• Provider bias
• Stigma
• Trust in health care systems
GENETIC FACTORS
• Sickle cell disease
• Inherited thrombophilias
• CADASIL


Life's
Essential 8™
LIPIDS

Table 4. Key Conditions Affecting Stroke Risk and Screening Methods to Classify Them as Emphasized in This Guideline for Primary Prevention of Stroke

Risk condition	Screening method	Comment
BP	Office measurement	Elevated office measures should be confirmed with home or ambulatory monitoring per AHA guidance on BP classification.[67]
Cigarette smoking	Interview	Direct questioning helps classify individuals as never, past, or current cigarette smokers. It will identify whether a patient is ready to quit, which would be the clinician's cue to offer treatment options.
Diabetes	Blood test	Most convenient tests include fasting blood glucose and hemoglobin A1c.
Diet quality	Interview	Direct questioning of patients can help determine whether their current eating pattern emphasizes healthy foods and minimizes less healthy foods.[68] Instruments for clinical use include the Mediterranean Diet Adherence Screener and the Mediterranean Eating Pattern for Americans tool.[69,70]
Dyslipidemia	Blood test	Current guidelines offer nonfasting testing as convenient for patients with validity similar to that of fasting testing for key lipid fractions.
Overweight	Office measurement	BMI is the most common measure of weight health, but additional measures of central adiposity such as the WC may refine risk.
Physical inactivity	Interview	Direct inquiry can be used to determine whether a patient is meeting US Department of Health and Human Services guidelines for physical activity. Formal questionnaires are not accurate for clinical use.
SDOH	Interview/questionnaire	SDOH include employment status, household income, education, food insecurity, health care access, housing, access to transportation, neighborhood and built environment, and internet access. Screening instruments are available.[71]
Sleep disorder	Questionnaire	Clinicians can ask patients about sleep hours. Questionnaires include the Epworth Sleepiness Index, Berlin Questionnaire, and Pittsburgh Sleep Quality index.[72]
Substance use disorders	Interview/questionnaire	Direct questioning or use of validated instruments can identify individuals with substance use disorders related to stroke risk (ie, alcohol, cocaine, intravenous drug injection).

AHA indicates American Heart Association; BMI, body mass index; BP, blood pressure; SDOH, social determinants of health; and WC, waist circumference.

Lifestyle Factors

- Diet: Mediterranean diet still recommended for primary prevention (Level B-NR)
- Exercise: 150 min moderate intensity or 75 min vigorous intensity per week. Avoid sedentary lifestyle.
- Weight: Screen for overweight and obese status
- Sleep: Evidence lacking for role of OSA treatment in primary stroke prevention

Table 6. Anthropometric Measures of Obesity and Associated Stroke Risk

Obesity measure	Measurement technique	Obesity criteria and classification	Stroke risk
BMI	Weight (kg)/height (m^2)	Class I: 30–34.9 kg/m^2 Class II: 35–39.9 kg/m^2 Class III: ≥40 kg/m^2	Each 5-unit increase in BMI=10% increased stroke risk.[169]
WC*	Measured at midpoint between lower margin of the least palpable rib and top of the iliac crest	Women >80 cm: increased cardiometabolic risk >88 cm: substantially increased cardiometabolic risk Men >94 cm†: increased cardiometabolic risk >102 cm: substantially increased cardiometabolic risk[170]	For each 10-cm higher WC, RR is higher by 10% on average.[161]
WHR*	WC (cm)/hip circumference (cm) measured around the widest portion of the buttocks	Women >0.85 cm: substantially increased cardiometabolic risk Men >0.90 cm: substantially increased cardiometabolic risk[170]	0.1-unit increase in WHR=16% RR of stroke[161]
WHtR*	Waist circumference (cm)/height (m)	No available data	0.05-unit increase in WHtR=13% RR of stroke[161]
WWI*	Waist circumference (cm)/√weight (kg)	No available data	Stroke OR, 1.62 (95% CI, 1.06–2.48) in highest versus lowest WWI quartile[171]
VAI*	Calculated from WC, BMI, triglycerides, and HDL-C	No available data	Stroke HR, 1.45 (95% CI, 1.15–1.75) in highest versus lowest VAI quartile[172]

BMI indicates body mass index; HDL-C, high-density lipoprotein cholesterol; HR, hazard ratio; OR, odds ratio; RR, relative risk; VAI, visceral adiposity index; WC, waist circumference; WHR, waist-to-hip ratio; WHtR, waist-to-height ratio; and WWI, weight-adjusted waist index.

*Measures specific to abdominal obesity.

†South Asian/Chinese/Japanese cutoff for men: >90 cm.

Diabetes

- Diabetes: GLP-1 receptor agonist is effective to lower cardiovascular risk (including stroke) in patients with elevated CVD risk and A1c ≥ 7.0%
- Meta-analysis of 12 studies with >20,000 patients with diabetes showed reduction in stroke risk for those on GLP-1 receptor agonists over placebo (RR 0.73, CI 0.60-0.89)

Blood Pressure

- Adults with stage 2 HTN or stage 1 + higher CVD risk, goal BP< 130/80 mmHg is recommended
- Thiazides and Thiazide like diuretics, calcium channel blockers, angiotensin-converting enzyme inhibitors, and angiotensin receptor blockers are recommended as initial antihypertensive agents to prevent stroke
- In most adults with HTN, 2 or more agents are indicated to achieve adequate BP control

Lipid Lowering

- Adults age 20-75 with LDL>190, 10-year ASCVD risk≥ 20%, or 10-year ASCVD risk >7.5% plus 1 or more risk enhancers, statin in recommended.
- If unable to tolerate statin or statin in not effective, the benefit of PCSK9 inhibitors is uncertain
- Role of bempedoic acid is also not well established
- Elevated lipoprotein(a) level associated with higher stroke risk but data lacking on treatment

Table 8. Qualifications for Treatment With Lipid Therapy

Risk enhancer	Included conditions
Family history of premature ASCVD	…
Primary hypercholesterolemia	…
Metabolic syndrome	…
Chronic kidney disease	…
Chronic inflammatory conditions	Psoriasis, rheumatoid arthritis, lupus erythematosus, HIV/AIDS
High-risk race or ethnicity	South Asian ancestry
Lipids/biomarkers associated with increased ASCVD risk	Primary hypertriglyceridemia, elevated high-sensitivity C-reactive protein, elevated lipoprotein(a), elevated apolipoprotein B, ankle-brachial index <0.9
Conditions specific to women	For example, preeclampsia, premature menopause

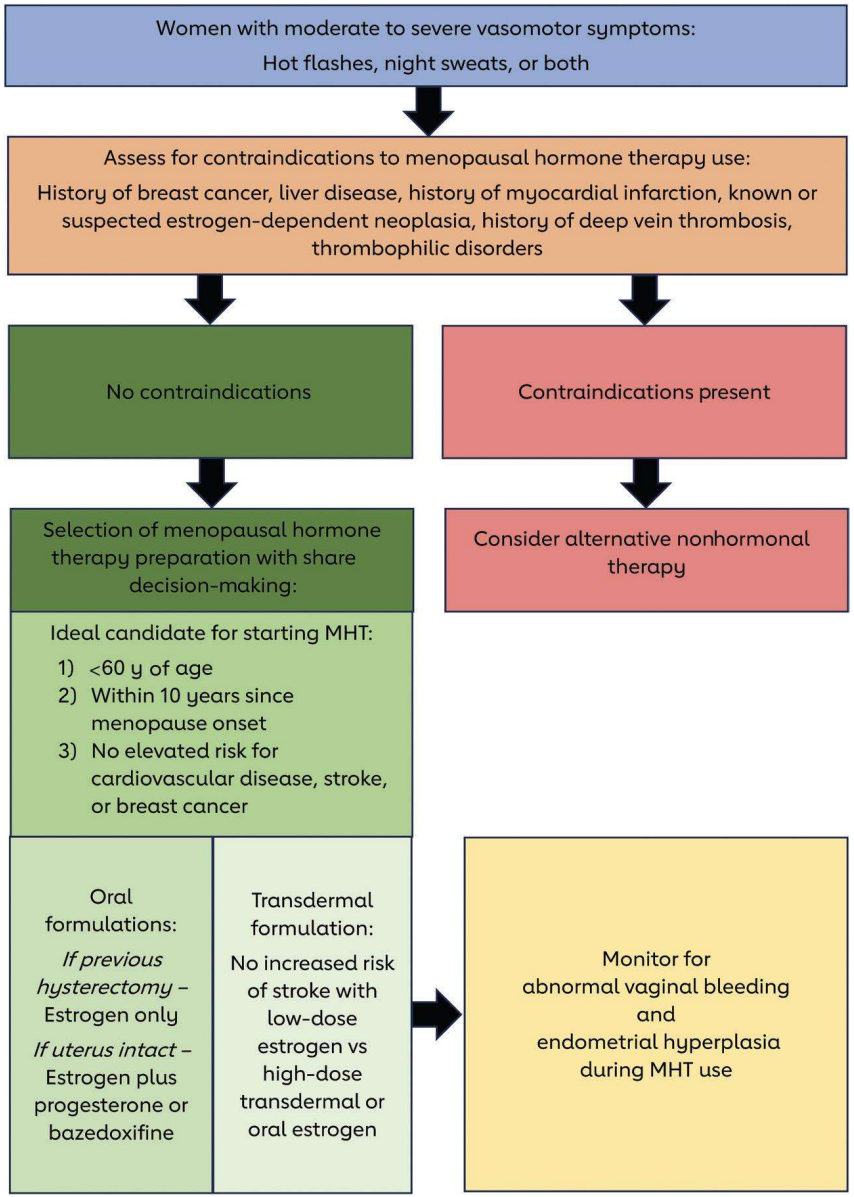
ASCVD indicates atherosclerotic cardiovascular disease.

Tobacco Use

- For active smokers counsel complete cessation. Behavioral therapy in combination with pharmacotherapy is recommended
- Limited data available on vaping and stroke risk but discouraged.

Special Populations

- Migraine patients should be screened for vascular risk factors. Avoid estrogen containing contraception to avoid increasing stroke risk.
- Patients with antiphospholipid syndrome should be started on aspirin 75-100mg daily for stroke prevention


Women with moderate to severe vasomotor symptoms:
Hot flashes, night sweats, or both
Assess for contraindications to menopausal hormone therapy use:
History of breast cancer, liver disease, history of myocardial infarction, known or suspected estrogen-dependent neoplasia, history of deep vein thrombosis, thrombophilic disorders
No contraindications
Contraindications present
Selection of menopausal hormone therapy preparation with share decision-making:
Consider alternative nonhormonal therapy
Ideal candidate for starting MHT:
1) <60 y of age
2) Within 10 years since menopause onset
3) No elevated risk for cardiovascular disease, stroke, or breast cancer
Oral formulations:
If previous hysterectomy – Estrogen only
If uterus intact – Estrogen plus progesterone or bazedoxifine
Transdermal formulation:
No increased risk of stroke with low-dose estrogen vs high-dose transdermal or oral estrogen
Monitor for abnormal vaginal bleeding and endometrial hyperplasia during MHT use

Asymptomatic Carotid Stenosis

- ACAS showed benefit of CEA for stroke reduction in asymptomatic carotid stenosis
- ACST-1 also showed benefit of CEA or CAS for 5-year risk reduction of stroke (majority of patients not on statin)
- SPACE-2 did not show clear superiority of revascularization over medical management (stopped early)
- Improvements in technique for CEA/CAS and intensive medical management

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Medical Management and Revascularization for Asymptomatic Carotid Stenosis

T.G. Brott,[1] G. Howard,[2] B.K. Lal,[3] J.H. Voeks,[4] T.N. Turan,[4] G.S. Roubin,[5] R.M. Lazar,[6] R.D. Brown, Jr.,[7] J. Huston III,[8] L.J. Edwards,[2] M. Jones,[9] W.M. Clark,[10] Á. Chamorro,[11] L. Llull,[11] C. Mena-Hurtado,[12] D. Heck,[13] R.S. Marshall,[14] V.J. Howard,[15] W.S. Moore,[16] K.M. Barrett,[1] B.M. Demaerschalk,[17] N. Sangha,[18] H. Aronow,[19] M. Foster,[20] W.C. Sternbergh III,[21] F. Shawl,[22] G. Lanzino,[23] J. Rapp,[24] H.S. Tran,[25] R. Ecker,[26] A. Mackey,[27] V. Ali,[28] C. Given II,[29] P. Teal,[30] V.S. Kashyap,[31] D. Mukherjee,[32] M. Harrigan,[33] S. Silverman,[34] M. Koopmann,[35] V.G. Wadley,[36] Y. Zhang,[2] J.D. Rhodes,[2] S. Chaturvedi,[37] and J.F. Meschia,[1] for the CREST-2 Investigators*

CREST-2

- 2 parallel randomized observer blinded trials
- >70% carotid stenosis without prior history of stroke, TIA, or amaurosis fugax within 180 days prior to randomization
- Carotid stenting + medical management vs medical management
- Carotid endarterectomy + medical management vs medical management
- Primary outcome: Any stroke or death within 44 days of randomization or ipsilateral stroke in 4 year follow-up

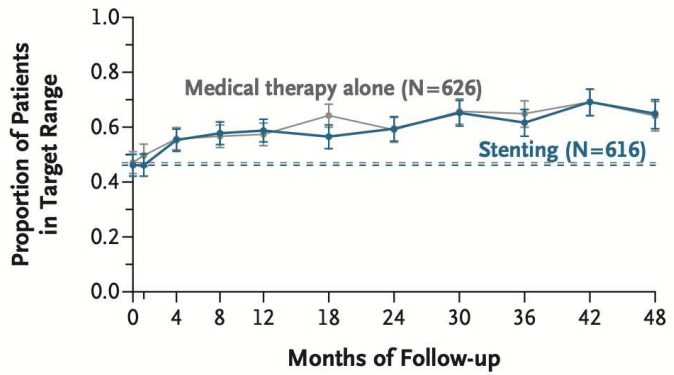
CREST-2

- >70% stenosis defined by carotid doppler (peak systolic velocity > 230 cm/s), CTA, MRA, or catheter angiogram
- Intensive Medical Management: Target systolic BP <130, LDL goal < 70, management of elevated glucose and lifestyle factors (smoking cessation, excess body weight, physical inactivity). Health coaching provided by phone. Medications provided at no cost if needed (including PCSK9 inhibitor).
- Carotid stenting group: Started aspirin 325mg + clopidogrel 75mg twice daily 48 hrs prior to stenting followed by DAPT (aspirin 75-325mg + clopidogrel 75mg daily) for 30 days

CREST-2

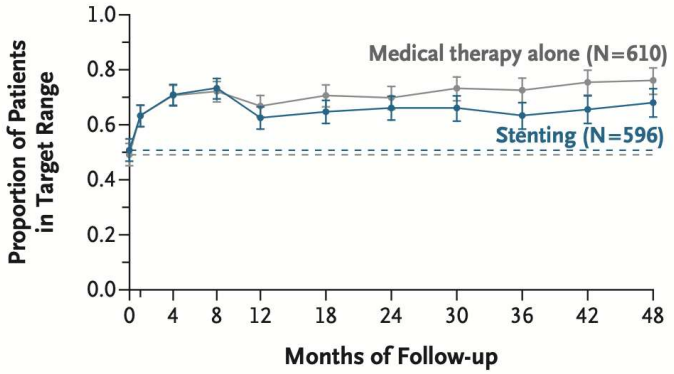
- Carotid endarterectomy: Started on aspirin 325mg daily 48 hrs prior to procedure. Continued on aspirin 70-325mg daily after procedure.
- In person follow-up at 12hrs, 36 hrs, 44 days, 4 mon, 8 mon, 12mon and every 6 months up to 48 months
- Questionnaire verifying stroke free status, modified Rankin scale, and NIHSS collected
- MRI Brain or CT Head completed if stroke suspected
- Doppler obtained annually

A Stenting Trial: Systolic Blood Pressure



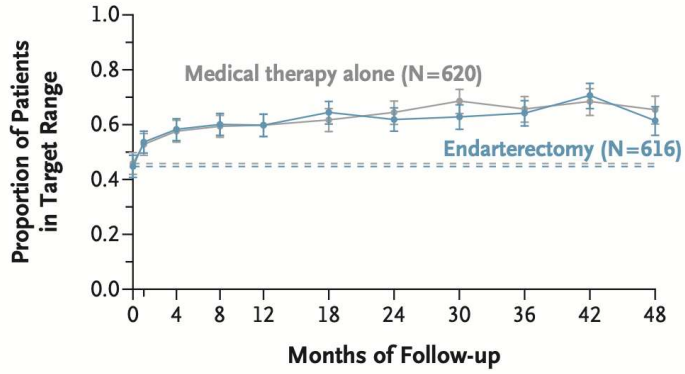
No. of Patients										
Medical therapy alone	615	597	587	575	528	474	421	399	360	323
Stenting	607	595	583	570	531	478	425	396	370	336

B Stenting Trial: LDL Cholesterol



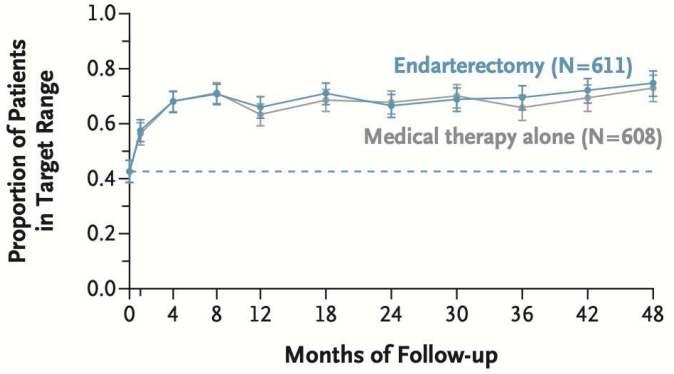
No. of Patients										
Medical therapy alone	607	595	585	573	526	472	419	399	360	323
Stenting	596	586	577	567	529	476	425	396	370	336

C Endarterectomy Trial: Systolic Blood Pressure



No. of Patients										
Medical therapy alone	613	607	590	580	542	498	459	420	377	353
Endarterectomy	611	609	605	586	549	515	466	437	399	358

D Endarterectomy Trial: LDL Cholesterol



No. of Patients										
Medical therapy alone	608	604	588	579	541	497	459	420	377	353
Endarterectomy	610	610	606	586	549	515	466	437	399	358

Outcomes

4-year incidence of primary outcome:

Stenting comparison

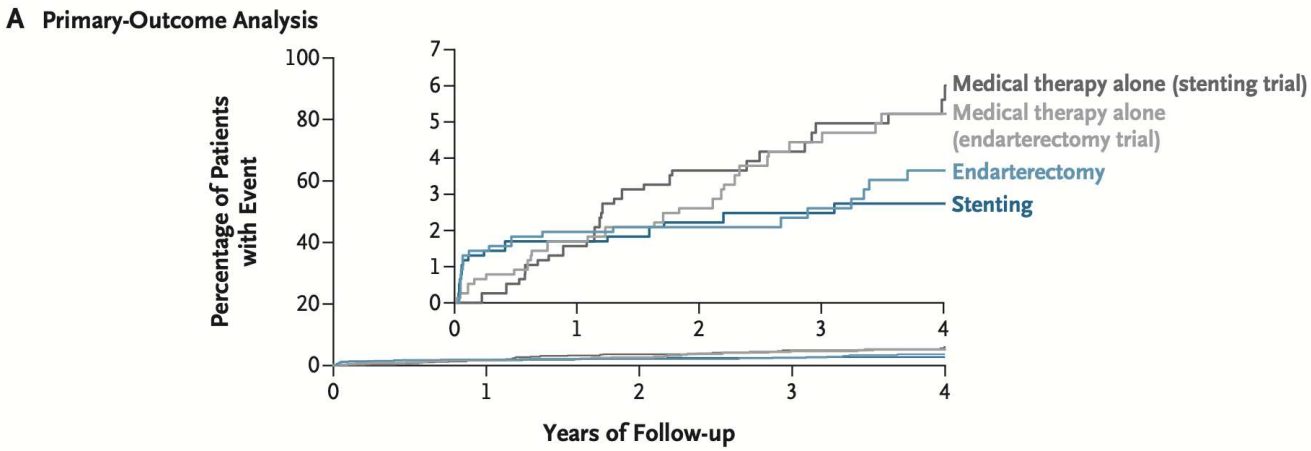
6.0% CI (3.8-8.3) in MM vs

2.8% CI (1.5-4.3) in CAS group (p=0.02)

Endarterectomy comparison

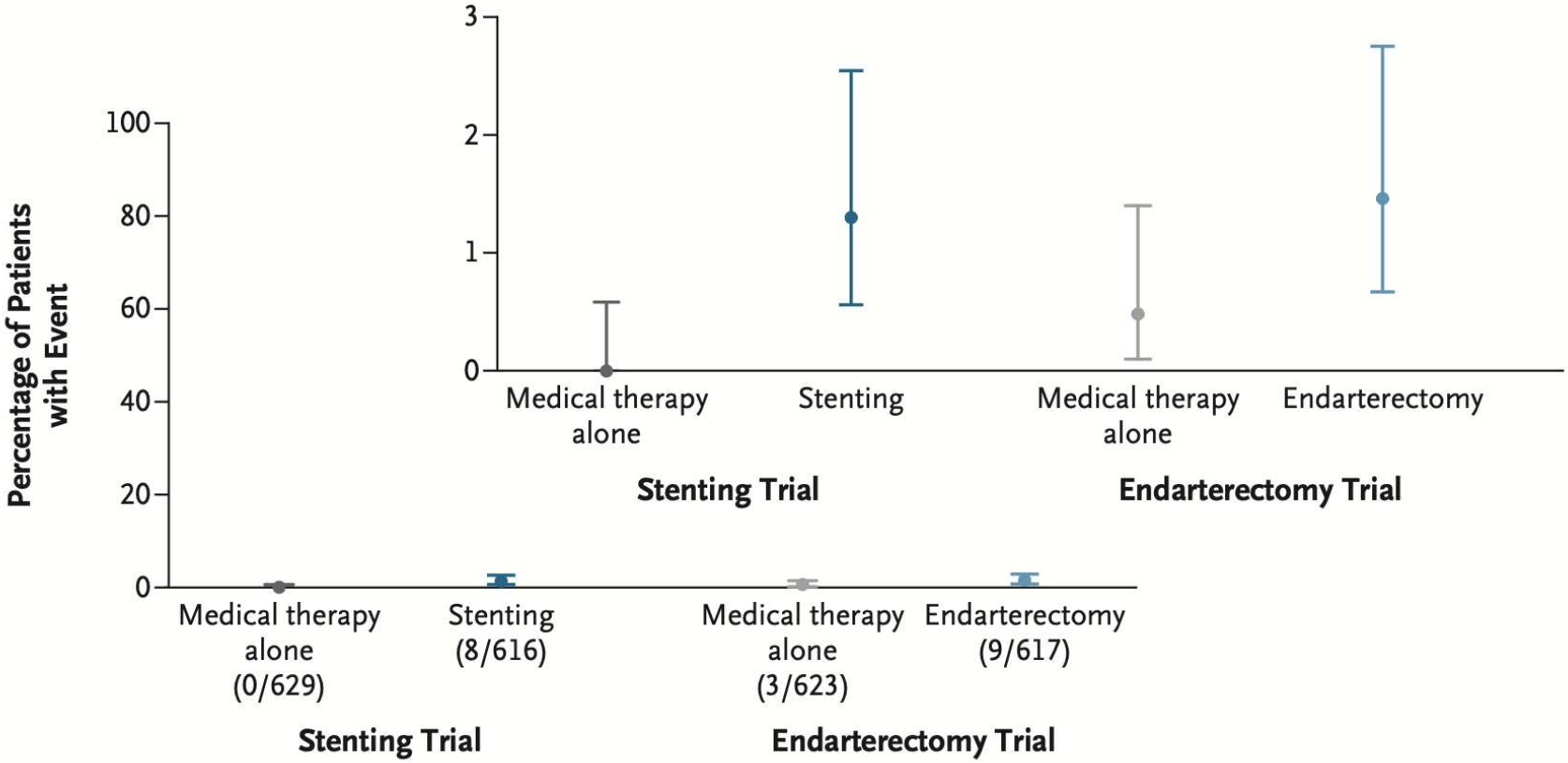
5.3% CI (3.3 -7.4) in MM vs

3.7% CI (2.1-5.5) in CEA group (p=0.24)



No. of Patients					
Stenting trial					
Medical therapy alone	629	537	428	360	276
Stenting	616	543	431	375	289
Endarterectomy trial					
Medical therapy alone	623	550	461	381	304
Endarterectomy	617	561	482	411	319

B **Periprocedural Component of Primary-Outcome Analysis (days 0 to 44)**



Conclusions

- Stenting led to lower risk of perioperative stroke/death or 4-year risk of ipsilateral stroke compared to medical management
- No significant benefit of carotid endarterectomy over medical management