Prevention of Ischemic Stroke

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Conflicts of Interest

- I have received grant support from Merck, Schering-Plough, and NMT Medical.

- I also receive grant support from NINDS.

- I will be discussing new medications that have not been approved by the FDA.
Importance of Prevention of Ischemic Stroke

- Successful prevention is a cost-effective strategy
  - Acute hospitalization and rehabilitation
  - Long-term care
  - Lost productivity and disability
- Prevention reduces the human suffering from stroke
- Primary prevention – treatment of patients who have not had neurological symptoms
- Secondary prevention – treatment of patients who have had a stroke, TIA, or amaurosis fugax
Risk for Ischemic Stroke

- Asymptomatic but presence of risk factors
- Symptomatic atherosclerotic disease
  - Coronary artery or peripheral arterial disease
- Asymptomatic cerebrovascular disease
  - Carotid bruit or stenosis
- Atrial fibrillation
- Amaurosis fugax
- Transient ischemic attack
- Ischemic stroke
Transient Ischemic Attacks

- TIA should not be considered as different from ischemic stroke
  - It is the mild end of the spectrum
  - It is a stroke with signs that cleared
  - A lesion is often found on brain imaging
- Identifies a high risk for ischemic stroke
  - Instability of the underlying vascular lesion
- Warrants emergency evaluation and treatment
Diagnosis of TIA

- Not all episodes of transient neurological dysfunction are TIA
  - Focal neurological symptoms – loss of function
  - Fit one vascular territory of the brain
  - Sudden onset, usually maximal at beginning
  - May have some gradual resolution
  - Rarely cause confusion or loss of consciousness
  - May have headache

- Definition of 24 hours is out-of-date
  - Most symptoms are 5 - 20 minutes
Differential Diagnosis of TIA

- Seizures (with focal neurological signs)
- Migraine
- Metabolic disorder (hypoglycemia)
- Mass
  - Subdural hematoma
  - Tumor
- Syncope or pre-syncope
- Somatization disorder
- Primary ocular disease
- Labyrinthine causes of vertigo
A TIA is a Symptom

- The cause of TIA is particularly important in stroke prevention because it affects treatment decisions
- General categories of underlying causes
  - Large artery atherosclerosis
  - Small artery disease (lacunes)
  - Cardioembolism
  - Non-atherosclerotic arterial diseases
  - Prothrombotic disorders
  - Cryptogenic
Evaluation of the Patient with Suspected TIA

- Brain imaging: CT or MRI
- Vascular imaging: carotid duplex, TCD, CTA, MRA, or arteriography
- Cardiac studies: ECG, Holter monitor, TEE, TTE
- Blood work: CBC, platelet count, INR, aPTT, renal studies, hemoglobin A1C, glucose, fasting lipid profile
- Specialized testing, such as studies inherited or acquired disorders of coagulation or inflammatory disorders are occasionally done
Components of Management Prevention of Ischemic Stroke

- Selected on a case-by-case basis
- General components
  - Address controllable risk factors
  - Antithrombotic medications
    - Anticoagulants
    - Antiplatelet agents
  - Local (surgical) interventions
    - Carotid endarterectomy
    - EC/IC bypass
    - Angioplasty and stenting
Factors that Affect Decisions for Management

- Presence or absence of modifiable risk factors
- Presence or absence of symptomatic disease
  - Coronary artery or peripheral artery disease
- Presumed cause of ischemic symptoms
- Prior therapies aimed at preventing stroke
- Presence of specific contraindications for treatments
  - Allergy to aspirin
- Preferences of the patient
Major Modifiable Risk Factors
Advanced Atherosclerosis

- Arterial hypertension
  - Isolated systolic hypertension
- Hyperlipidemia
  - Increased LDL cholesterol
  - Decreased HDL cholesterol
- Diabetes mellitus
- Smoking
- Ischemic heart disease
Recommended Management Risk Factors for Atherosclerosis

- **Lower blood pressure**
  - Major impact with even a 5 or 10 mm Hg decline
  - Goals: 120 – 140/80 – 90 mm Hg
  - Involves lifestyle changes and medications

- **Lower lipid levels**
  - Goals: LDL cholesterol < 70 – 100 mg/dL
  - Involves lifestyle changes and medications

Sacco et al, Stroke, 2006; 37: 577
Recommended Management
Risk Factors for Atherosclerosis

- Treat diabetes mellitus
  - Achieve normoglycemia: Hemoglobin A1C < 7%
  - Treat blood pressure
  - Lower lipid levels: LDL cholesterol < 70 mg/dL

- Quit smoking
  - Lifestyle changes, nicotine replacement, medications

- Limit alcohol consumption
- Reduce weight
- Increase exercise

Sacco et al, Stroke, 2006; 37: 577
Antithrombotic Medications

- Mainstay of measures to prevent ischemic stroke
- Controls for trials testing surgical interventions
- Should be prescribed to almost all persons at high risk for ischemic stroke
- Measure of quality of care by the Joint Commission
- May be given singly or in various combinations
- Complements measures to treat risk factors and surgical interventions
Use of Antithrombotic Medications among Stroke Survivors, 2000 - 2006

- Medical Expenditure Panel Surveys of 4168 persons with cerebrovascular disease
- Use of antithrombotic medications
  - Any antithrombotic agent – 3074 (75.3%)
  - Any antiplatelet agent – 2729 (65.9%)
- Use associated with the following:
  - Men
  - Age older than 65
  - Presence of usual source of care
  - Poor-to-fair health

Oral Anticoagulants

- Widely used to prevent stroke among persons with cardiac lesions associated with high risk of embolism
  - Atrial fibrillation complicating structural heart disease
  - Recent myocardial infarction
  - Mechanical prosthetic valves (mitral)
  - Rheumatic heart disease (mitral stenosis/atrial fibrillation)
  - Dilated cardiomyopathy
  - Intraventricular or intra-atrial thrombus
- Possible role in some prothrombotic disorders
Oral Anticoagulants
Non-Valvular Atrial Fibrillation

- Tested in multiple clinical trials
  - Asymptomatic (primary) or symptomatic (secondary) prevention
- Comparisons with placebo, fixed low dose warfarin, aspirin, or combinations of antiplatelet agents
- Adjusted dose anticoagulation with desired INR 2 – 3
  - Absolute risk reduction: 1.4% - 4.5%
  - Relative risk reduction: 68% (50% - 79%)
- Increase risk of symptomatic bleeding
  
  Sacco et al, Stroke, 2006; 37: 577
Impact of Level of Anticoagulation
Thromboembolism or Intracranial Hemorrhage
Non-Valvular Atrial Fibrillation

- Analysis of 9217 patients with AF in ATRIA Study
- Risks of thromboembolism or intracranial hemorrhage at other levels of INR compared to INR 2.0 – 2.5
- Risk of thromboembolism low and stable when INR is > 1.8
  - INR 1.4 – 1.7: Odds Ratio 3.72 (95% CI 2.67 – 5.19)
- Risk of intracranial hemorrhage low and stable when INR is < 3.6
  - INR 3.6 – 4.5: Odds Ratio 3.56 (95% CI 1.70 – 7.46)
  - No lower risk with INR < 2

## Warfarin VS Aspirin/Clopidogrel
Atrial Fibrillation (ACTIVE – W)

<table>
<thead>
<tr>
<th>Event</th>
<th>Clopidogrel and Aspirin N = 3335</th>
<th>Warfarin N = 3371</th>
<th>RR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary outcome</td>
<td>235</td>
<td>165</td>
<td>1.44 (1.18 – 1.76)</td>
</tr>
<tr>
<td>Stroke</td>
<td>100</td>
<td>59</td>
<td>1.72 (1.27 – 2.37)</td>
</tr>
<tr>
<td>Ischemic Stroke</td>
<td>90</td>
<td>42</td>
<td>2.17 (1.51 – 3.13)</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>10</td>
<td>93</td>
<td>1.10 (0.83 – 1.45)</td>
</tr>
</tbody>
</table>

Active, Lnacet, 2006; 367: 1903
### Adjusted Dose Warfarin or Dabigatran in Atrial Fibrillation

<table>
<thead>
<tr>
<th></th>
<th>Dabigatran 110 mg/day N = 6015</th>
<th>Dabigatran 150 mg/day N = 6076</th>
<th>Warfarin N = 6022</th>
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<tbody>
<tr>
<td>CHADS2</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>0-1</td>
<td>1958</td>
<td>1958</td>
<td>1859</td>
</tr>
<tr>
<td>2</td>
<td>2088</td>
<td>2137</td>
<td>2230</td>
</tr>
<tr>
<td>3-6</td>
<td>1968</td>
<td>1981</td>
<td>1933</td>
</tr>
<tr>
<td>Prior warfarin use</td>
<td>3011</td>
<td>3049</td>
<td>2929</td>
</tr>
<tr>
<td>Events</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Embolus/stroke</td>
<td>182</td>
<td>134</td>
<td>199</td>
</tr>
<tr>
<td>Stroke</td>
<td>171</td>
<td>122</td>
<td>185</td>
</tr>
<tr>
<td>ICH</td>
<td>14</td>
<td>12</td>
<td>45</td>
</tr>
<tr>
<td>Serious bleeding</td>
<td>322</td>
<td>375</td>
<td>397</td>
</tr>
</tbody>
</table>

Connolly et al, NEJM, 2009; 361: 1139
Oral Anticoagulants
Persons with Arterial Disease

WARFARIN – ASPIRIN RECURRENT STROKE STUDY
Death/ischemic stroke:
Warfarin: 17.8%  Aspirin: 16.0%

WARFARIN – ASPIRIN SYMPTOMATIC INTRACRANIAL DISEASE STUDY
Death/ischemic stroke/ICH:
Warfarin: 21.8%  Aspirin: 22.1%

Mohr et al NEJM, 2001; 345: 1444
Chimowitz et al, NEJM, 2005: 352: 1305
Antiplatelet Agents

- Most extensively studied therapies to prevent stroke
  - Broad spectrum of arterial diseases
  - Standard against which surgical therapies and anticoagulants are compared
- Overall, reduce the risk of stroke by 16% - 25%
- Used in both primary and secondary prevention
- Effective in men and women of all ages
- Effective in presence or absence of hypertension
- Effective in presence or absence of diabetes mellitus
Current Choices for Antiplatelet Agents

- Aspirin 30 – 1500 mg/day
  - Usual doses 81 – 325 mg/day
- Dipyridamole 400 mg/day
- Ticlopidine 500 mg/day
- Clopidogrel 75 mg/day
Aspirin

- Extensively studied in prevention of ischemia and first effective therapy to prevent stroke
- Used as monotherapy or in combination with other antiplatelet agents or anticoagulants
- Inexpensive over-the-counter medication that is available in enteric formulations
- Most bleeding complications are not dose-related
- Gastric side effects are associated with larger doses of aspirin
Dipyridamole

- Blocks update of adenosine by the platelet
- Reversible inhibition of platelet aggregation
- Prolongs platelet survival
- Potent vasodilator
- In regular and sustained release formulations
- Most commonly tested as an adjunct to aspirin
- Most common side effect is headache
  - Particular problem in persons who have migraines
- Some increase in risk of bleeding
Aspirin/Dipyridamole vs Aspirin Prevention of Recurrent Stroke

<table>
<thead>
<tr>
<th>European Stroke Preventions Study - 2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Aspirin</strong></td>
</tr>
<tr>
<td>N = 1649</td>
</tr>
<tr>
<td>Stroke</td>
</tr>
<tr>
<td>Stroke/Death</td>
</tr>
<tr>
<td><strong>ESPRIT</strong></td>
</tr>
<tr>
<td><strong>Aspirin</strong></td>
</tr>
<tr>
<td>N = 1376</td>
</tr>
<tr>
<td>Stroke</td>
</tr>
<tr>
<td>Primary event</td>
</tr>
</tbody>
</table>

Diener et al J Neurol Sci, 1996; 143: 1
ESPRIT, Lancet, 2006; 367: 1665
## Aspirin/Dipyridamole Vs Clopidogrel Prevention of Recurrent Stroke (PRoFESS)

<table>
<thead>
<tr>
<th></th>
<th>Clopidogrel</th>
<th>Aspirin/Dipyridamole</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N = 10151</td>
<td>N = 10818</td>
</tr>
<tr>
<td>Stroke</td>
<td>898</td>
<td>916</td>
</tr>
<tr>
<td></td>
<td>8.8%</td>
<td>9%</td>
</tr>
<tr>
<td>Stroke/MI</td>
<td>1333</td>
<td>1333</td>
</tr>
<tr>
<td>Vascular death</td>
<td>1333</td>
<td>1333</td>
</tr>
<tr>
<td></td>
<td>13.1%</td>
<td>13.1%</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>365</td>
<td>419</td>
</tr>
<tr>
<td></td>
<td>3.6%</td>
<td>4.1%</td>
</tr>
</tbody>
</table>

Sacco et al, NEJM, 2008; 359: 1238
Clopidogrel

- A prodrug whose metabolite that irreversibly blocks the platelet ADP receptor
- Secondarily inactivates the GP IIb/IIIa receptor
- Daily dose is 75 mg - takes 3 – 7 days for effects on platelet function
- For immediate effects - loading dose of 300 – 600 mg
- Rare hematologic reactions
  - Thrombotic thrombocytopenia purpura
  - Less common than with ticlopidine
- Used alone or in combination with aspirin
Trial of Clopidogrel or Aspirin Patients at Risk for Ischemic Events (CAPRIE)

- Large randomized trial enrolling symptomatic patients with heart disease, TIA, stroke, or peripheral artery disease
- Goal of preventing stroke, myocardial infarction or vascular death
- Aspirin 325 mg/day or clopidogrel 75 mg/day
  - Aspirin: 5.83% annual risk
  - Clopidogrel: 5.32% annual risk
- Benefit primarily among persons with peripheral artery disease

CAPRIE, Lancet, 1996; 348: 1329
### Trial of Clopidogrel and Aspirin or Clopidogrel (MATCH)

**Diener et al, Lancet, 2004; 364: 331**

<table>
<thead>
<tr>
<th>Event</th>
<th>Clopidogrel N = 3802</th>
<th>Clopidogrel and Aspirin N = 3797</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stroke, MI</strong></td>
<td>636 16.7%</td>
<td>596 15.7%</td>
</tr>
<tr>
<td><strong>Vascular death</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Serious bleeding</strong></td>
<td>49 1.3%</td>
<td>96 2.6%</td>
</tr>
</tbody>
</table>
## Trial of Clopidogrel and Aspirin or Aspirin (CHARISMA)

<table>
<thead>
<tr>
<th></th>
<th>Aspirin</th>
<th>Aspirin and Clopidogrel</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All subjects</strong></td>
<td>N = 7721</td>
<td>N = 7802</td>
</tr>
<tr>
<td><strong>Stroke, MI, Vascular death</strong></td>
<td>573 (7.3%)</td>
<td>534 (6.4%)</td>
</tr>
<tr>
<td><strong>Serious bleeding</strong></td>
<td>104 (1.3%)</td>
<td>130 (1.7%)</td>
</tr>
<tr>
<td><strong>Symptomatic</strong></td>
<td>N = 4743</td>
<td>N = 4735</td>
</tr>
<tr>
<td><strong>Stroke, MI, Vascular death</strong></td>
<td>416 (8.8%)</td>
<td>347 (7.3%)</td>
</tr>
<tr>
<td><strong>Serious bleeding</strong></td>
<td>79 (1.7%)</td>
<td>71 (1.5%)</td>
</tr>
</tbody>
</table>

Bhatt et al, NEJM, 2006; 354: 1706
Bhatt et al, JACC, 2007; 49: 1982
Trial of Aspirin and Clopidogrel or Aspirin – Atrial Fibrillation

<table>
<thead>
<tr>
<th>Event</th>
<th>Aspirin N = 3782</th>
<th>Aspirin and Clopidogrel N = 3772</th>
<th>Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischemic Stroke</td>
<td>343</td>
<td>236</td>
<td>0.68 (0.57 - 0.80)</td>
</tr>
<tr>
<td>Hemorrhagic stroke</td>
<td>22</td>
<td>30</td>
<td>1.37 (0.79 - 2.37)</td>
</tr>
<tr>
<td>Fatal stroke</td>
<td>93</td>
<td>70</td>
<td>0.75 (0.55 - 1.03)</td>
</tr>
<tr>
<td>Myocardial infarct</td>
<td>115</td>
<td>90</td>
<td>0.78 (0.59 - 1.03)</td>
</tr>
<tr>
<td>Vascular death</td>
<td>599</td>
<td>600</td>
<td>1.00 (0.89 - 1.03)</td>
</tr>
</tbody>
</table>

ACTIVE Investigators
NEJM, 2009; 360: 2006
Short-term Combination Therapy
Patients with Recent TIA
(FASTER Study)

- Pilot study that enrolled patients within 24 hours of TIA or minor stroke and followed for 90 days
- Clopidogrel 300 mg loading dose followed by 75 mg/day and aspirin or aspirin monotherapy
- Aspirin: 194 subjects
  - Ischemic or hemorrhagic stroke: 21 (10.8%)
- Aspirin and clopidogrel: 199 subjects
  - Ischemic or hemorrhagic stroke: 14 (7.1%)

Prasugrel

- Recently approved thienopyridine antiplatelet agent for treatment of patients with percutaneous coronary artery interventions
- Prodrug with metabolite that inhibits platelet ADP receptor
- More potent and faster onset of action than clopidogrel
- Less inter-patient variations in response than clopidogrel

Argiolillo et al, Expert Opin Pharmacotherapy, 2008; 9: 2893
Bhatt et al, NEJM, 2009; 361: 940
Trial of Prasugrel or Clopidogrel
TRITON – TIMI 38 Trial

- Randomized trial of 13,608 subjects with high-risk coronary artery disease
  - Most received either bare or drug-eluting stents
  - Prasugrel: 60 mg loading dose and then 10 mg/day
  - Clopidogrel: 300 mg loading dose and then 75 mg/day
- Efficacy outcome of vascular death, MI or stroke
  - Clopidogrel: 12.1%  Prasugrel: 9.9% (p < 0.01)
- Safety outcome of major bleeding
  - Clopidogrel: 1.8%  Prasugrel: 2.4% (p = 0.03)

Prasugrel
Implications for Stroke

- Limitations in use of medication
  - Not recommended
    - Persons older than 75
    - Active pathological bleeding
    - Persons with a history of TIA or ischemic stroke

- Risk factors for bleeding complications
  - Low weight, bleeding history
  - Concomitant use of other antithrombotic medications

- Try to avoid stopping suddenly in case of bleeding
Ticagrelor vs. Clopidogrel
Acute Coronary Syndromes (PLATO)

- Randomized trial of 16,624 subjects with acute coronary artery syndromes
  - Clopidogrel: 300 – 600 mg and then 150 mg/day
  - Ticagrelor: 180 mg and then 180 mg/day
- Vascular death, stroke or myocardial infarction
  - Clopidogrel: 11.7%  Ticagrelor: 9.8% (p <0.001)
- Strokes
  - Clopidogrel: 1.3%  Ticagrelor: 1.5% (p = 0.22)
- Major bleeding complications
  - Clopidogrel: 11.2%  Ticagrelor: 11.6% (p = 0.43)

Wallentin et al, NEJM, 2009; 361: 1045
Carotid Endarterectomy

- Remains an important option for treatment of patients with moderate-to-severe stenosis of origin of internal carotid artery
- Benefits for surgery are greater among symptomatic persons than those with an asymptomatic stenosis
- Decisions influenced by presence of ulceration of plaque or presence of intraluminal thrombus
- The patient’s overall health, the complexity of the arterial pathology, neurological status, and the track record of the surgeon affect recommendations
Carotid Endarterectomy

- Recommended for symptomatic persons < 6 months
  - Stenosis of 70% - 99%, some cases 50% - 69%
  - Good operative risk and skilled surgeon
  - Surgery preferred within 2 weeks of TIA or minor stroke

Sacco et al, Stroke, 2006; 37: 577
Extracranial – Intracranial Arterial Bypass Operations

- Most commonly is STA/MCA anastomosis
- Tested in a large clinical trial in 1980’s
  - Stenosis of MCA/ICA
  - Occlusion of ICA
  - No net benefit from the operation
- Used to treat some patients with moyamoya
- Being tested again in a subset of patients with occlusion of the ICA
  - Poor collateral flow as demonstrated on PET scans
  - Very high risk group of patients for stroke
Endovascular Interventions

- Rapidly evolving intervention for prevention of stroke

**Procedure**
- Angioplasty and often placement of a stent
- Use of a distal protection device

**Indications**
- Treatment of a stenosis secondary to atherosclerosis or an arterial dissection
- Extracranial or intracranial artery in either the carotid or vertebrobasilar circulation

- Most available data is for treatment of stenosis of the origin of the internal carotid artery
Stent Protected Angioplasty Vs. Carotid Endarterectomy (SPACE)

<table>
<thead>
<tr>
<th>Symptomatic patients &lt; 120 days &amp; stenosis &gt;70%</th>
<th>CEA</th>
<th>CAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 607</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>N = 589</td>
<td>31</td>
<td>39</td>
</tr>
</tbody>
</table>

30 Days

| Death | 32 | 28 |
| Ipsilateral stroke | 43 | 49 |

2 Years

Eckstein et al, Lancet Neurology, 2008; 7: 893
## Endarterectomy VS Angioplasty
### Symptomatic Severe Carotid Stenosis (EVA – 3S)

<table>
<thead>
<tr>
<th>Symptomatic patients &lt; 120 days &amp; stenosis &gt;70%</th>
<th>CEA (N = 262)</th>
<th>CAS (N = 265)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>30 Days</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Stroke</td>
<td>9</td>
<td>24</td>
</tr>
<tr>
<td><strong>4 Years</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>34</td>
<td>36</td>
</tr>
<tr>
<td>Non-ipsi stroke</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Ipsilateral stroke</td>
<td>15</td>
<td>30</td>
</tr>
</tbody>
</table>

Mas et al, Lancet Neurology, 2008; 7: 885
High-risk patients with carotid stenosis
- Symptomatic > 50%, asymptomatic > 80%

Angioplasty and stenting – 167 subjects
- 159 treated, 30-day morbidity: 4.8%
- 1 year: 12 deaths, 7 ipsilateral strokes
- 3 years: 31 deaths, 11 ipsilateral strokes

Carotid endarterectomy – 167 subjects
- 152 treated, 30-day morbidity: 9.8%
- 1 year: 21 deaths, 7 ipsilateral strokes
- 3 years: 35 deaths, 9 ipsilateral strokes

Gurm et al, NEJM, 2008; 358: 1572
Endovascular Treatment
Extracranial Internal Carotid Artery

- Recommendations likely to change soon
- Current recommendations
  - Symptomatic severe stenosis
  - Location difficult to reach with carotid endarterectomy
  - Prior radiation therapy to neck
  - Prior carotid endarterectomy with recurrent stenosis
  - High-risk medical condition

Sacco et al, Stroke, 2006; 37: 577
Endovascular Treatment of Posterior Circulation Stenosis or Intracranial Arterial Stenosis

- Limited data about safety and efficacy
- Origin of the vertebral artery from subclavian artery
- Extracranial vertebral artery
  - Symptomatic patients
  - Recurrent symptoms despite medical therapy
- Intracranial stenosis
  - Symptomatic severe stenosis
  - Recurrent symptoms despite medical therapy

Sacco et al, Stroke, 2006; 37: 577
Conclusions

- Management is multifaceted and selected on a case-by-case basis
- Should include aggressive management of risk factors for accelerated atherosclerosis
  - Arterial hypertension
  - Hyperlipidemia
  - Smoking
  - Diabetes mellitus
- Involve both lifestyle changes and medications
- Prescribed to both symptomatic and asymptomatic medications
Conclusions
Antithrombotic Medications

- Antithrombotic medications should be prescribed to almost all patients at high risk for stroke
- Includes both anticoagulants and antiplatelet agents
- Prescribed as a monotherapy or in combinations
- Prevention of cardioembolic stroke
  - Oral anticoagulants remain the preferred intervention
  - Adjusted doses of warfarin with an INR of 2 – 3
  - Aspirin or aspirin/clopidogrel are alternatives for persons who cannot take oral anticoagulants
  - Combination of oral anticoagulant and aspirin
Antithrombotic Agents to Prevent Ischemic Stroke

- Antiplatelet agents are preferred antithrombotic therapy for most non-cardiac causes of TIA or stroke
- Selected on a case-by-case basis
- May be combined with local interventions
  - Endovascular interventions – initial dual therapy
- May be prescribed as monotherapy or in combinations
  - Aspirin
  - Aspirin and dipyridamole
  - Clopidogrel
  - Aspirin and clopidogrel
Conclusions
Local Interventions

- Carotid endarterectomy is the preferred therapy for treatment of stenosis of origin of internal carotid artery
- Role of bypass operations is being tested again
- Role of endovascular therapies is expanding
  - Extracranial stenosis of internal carotid artery
  - Extracranial stenosis of vertebral artery
  - Intracranial stenosis - internal carotid artery, vertebral artery, basilar artery, or middle cerebral artery
Future Advances
Prevention of Ischemic Stroke

- New antithrombotic medications
  - Prasugrel
  - Ticagrelor
  - Dabigatran

- Aggressive management of arterial endothelium
  - Statins
  - Antihypertensive medications

- Expansion of endovascular interventions