Epidemiology and Prevention of Stroke

- Epidemiology
- Medical Therapy for Secondary Prevention
  - Lifestyle
  - Anticoagulation
  - Platelet anti-aggregants
  - Blood pressure
  - Statins

Disclosures

- No unlabeled treatments
- No relevant disclosures
  - Pfizer

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- References to the deleted material are provided for each slide.
**Stroke**

Primary vs. Secondary Prevention

- **First Stroke**: 77%
- **Recurrent Stroke**: 23%

*795,000 Strokes Annually*

Data from Benjamin et al. *Circulation* 2017;135: e146-e603

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**World-Wide Burden of Stroke**

- Second leading cause of death
- Third leading cause of lost disability-adjusted life years
  - US 5th leading cause of death
  - A leading cause of disability

Benjamin et al. *Circulation* 2017;135: e146-e603
Murray CJ et al. *Lancet* 2012;380:2197-2223

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**Stroke Mortality – United States**

Stroke Death Rates, 2011-2013
Adults, Ages 25+, by County

**Stroke Mortality – Kentucky**

2012-2014 per 100,000; Age >35 years

[Map Link](https://www.cdc.gov/dhdsp/maps/atlas/index.htm)
Stroke Hospitalizations – United States

Medicare Beneficiaries, Ages 65+, by County

Age-Adjusted Average Annual Rates per 1,000

- 2.1 - 8.5
- 8.6 - 10.6
- 10.7 - 12.1
- 12.2 - 13.4
- 13.5 - 24.1
- Insufficient Data

Rates are spatially smoothed to enhance the stability of rates in counties with small populations.

Data Source: Centers for Medicare & Medicaid Services Medicare Provider Analysis and Review (MEDPAR) file, Part A

Stroke Hospitalizations – Kentucky

2011-2013 per 100,000; Age ≥65 years

https://www.cdc.gov/dhdsp/maps/atlas/index.htm

Stroke-Related Disability – United States

Graph showing stroke is the 7th leading cause of DALY loss in the United States

www.healthmetricsandevaluation.org

Stroke Mortality Trends

United States 2004-2013

Stroke 41% reduction thru 2013

Data from Benjamin et al. Circulation 2017;136: e146-e603
Stroke Mortality Trends
United States 2004-2015

Data from Benjamin et al. *Circulation* 2017;135: e146-e603; CDC, VSS

Stroke Lifestyle Risk Factors
INTERSTROKE Study

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current smoking</td>
<td>2.09 (1.75-2.51)</td>
</tr>
<tr>
<td>&quot;Poor&quot; diet</td>
<td>1.35 (1.11-1.64)</td>
</tr>
<tr>
<td>Regular physical activity</td>
<td>0.69 (0.53-0.90)</td>
</tr>
<tr>
<td>Waist:hip ratio (T3 vs T1)*</td>
<td>1.65 (1.36-1.99)</td>
</tr>
<tr>
<td>&gt;30 Alcoholic drinks/month or binging</td>
<td>1.51 (1.18-1.92)</td>
</tr>
<tr>
<td>Psychosocial factors</td>
<td></td>
</tr>
<tr>
<td>Psychosocial stress</td>
<td>1.30 (1.06-1.60)</td>
</tr>
<tr>
<td>Depression</td>
<td>1.35 (1.10-1.66)</td>
</tr>
</tbody>
</table>

23 Worldwide case-control studies 2007-2010
N=6000

O'Donnell et al. *Lancet* 2010;376:112-123

Impact of Healthy Lifestyle
Risk of First Stroke

Fig. Panel A showing increasing reduction of stroke risk with greater number of healthy lifestyle factors followed

- 43,685 men, Health Professionals Follow-up Study
- 71,243 women, Nurses Health Study
- 5 Lifestyle factors
  - Not smoking
  - Healthy diet
  - At least 30 min per day of moderate or vigorous physical activity
  - Optimal weight (BMI < 25kg/m²)
  - 1- alcoholic drink/day for women, 1-2 for men

Chiuve et al. *Circulation* 2008;118:947-954

O'Donnell et al. *Lancet* 2010;376:112-123
### Atrial Fibrillation
#### Epidemiology
- Increases stroke risk ~ 5-fold
  - Responsible for at least 15% to 20% of all ischemic strokes
- Estimated prevalence 2.7 to 6.1 million in 2010
  - Increase to 5.6 to 12 million by 2050
- Mean age
  - Men: 66.8 years
  - Women: 74.6 years

#### Established Antithrombotic Treatments
- Aspirin vs placebo
  - RRR 22% (2-38%), ARR 1.7%/year, NNT=59
- Warfarin vs aspirin
  - RRR= 36% (95% CI 14-52%), ARR 0.8%/yr; NNT= 125

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### Pooled Outcomes
Forest plot from meta-analysis showing reductions in hemorrhagic stroke and intracranial hemorrhage with NOACs vs warfarin in patients with non-valvular atrial fibrillation

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### Platelet Anti-Aggregants
Secondary Prevention in Patients with Stroke or TIA

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**Event Rates**

<table>
<thead>
<tr>
<th>Event Type</th>
<th>Mean 3-yr Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>MI</td>
<td>1.0%</td>
</tr>
<tr>
<td>Stroke</td>
<td>2.6%</td>
</tr>
<tr>
<td>Vascular Death</td>
<td>9.1%</td>
</tr>
<tr>
<td>Any Death</td>
<td>12.3%</td>
</tr>
</tbody>
</table>

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Mozaffarian et al. *Circulation* 2014;131:e29-e322


Antiplatelet Trialists Collaboration *BMJ* 1994;308:81-106
Aspirin for Secondary Stroke Prevention

Dose Response

Mega-regression analysis showing no dose response for aspirin from 50 mg/day to 1500 mg/day. The lowest efficacious dose is 50 mg/day.

Data from ACP Guidelines Chest 2012;141:e601S-e636S

Secondary Stroke Prevention

Aspirin vs. Placebo

Data from ACP Guidelines Chest 2012;141:e601S-e636S

Secondary Stroke Prevention

Clopidogrel vs. Aspirin

Data from ACP Guidelines Chest 2012;141:e601S-e636S

Secondary Stroke Prevention

Aspirin plus Dipyridamole vs. Aspirin

Data from ACP Guidelines Chest 2012;141:e601S-e636S
Antihypertensive Treatment and Stroke Risk
Single Drug Trials

10 mmHg reduction associated with 31% Risk reduction

Forest plot of meta-analysis showing reductions in stroke across classes of antihypertensives

Law et al. BMJ 2009;338:b1665

Antihypertensive Treatment and Stroke Risk
Single Drug vs All Other Drugs

Forest plot of meta-analysis showing increased risk of stroke with beta-blockers vs other classes of antihypertensives

Law et al. BMJ 2009;338:b1665

Antihypertensives & BP Variability
Effect on Stroke Risk

Class vs. Other Classes

Decreasing Variability

Hazard Ratio (95% CI)

Data from Webb et al. Lancet 2010;375:906-915

Statins and Recurrent Stroke
Meta-analysis

Forest plot of meta-analysis showing 12% reduction in the risk of recurrent non-cardioembolic stroke with statins

Statin Withdrawal

- Prospective RCT
- Hemispheric ischemic stroke
- Admitted < 24 Hrs
- Statin withdrawal X 3-days vs. atorvastatin 20 mg/day
- Adjusted for admission NIH-SS and age

3-month death or dependency (mRS>2)
Early neurological deterioration

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Withdrawal N=46</th>
<th>Continue d N=45</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death or Dependency</td>
<td>60%</td>
<td>39%</td>
<td>4.68 (1.46, 14.91)</td>
</tr>
<tr>
<td>END Early Neurological deterioration</td>
<td>65%</td>
<td>21%</td>
<td>8.67 (3.05, 24.63)</td>
</tr>
</tbody>
</table>


Epidemiology and Prevention of Stroke

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  - Platelet anti-aggregants
  - Blood pressure
  - Statins