Cardiovascular Risk Reduction in Asians

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+ Hawaii & Pac. Rim
Disclosures

Research support through University from Amgen, Bristol Myers-Squibb, Gilead, and Regeneron

Advisory board: Genzyme

Consultant: Re-Engineering Healthcare
Global Burden of IHD and Cerebrovascular Disease (WHO 2011)
CVD will be the top cause for future total DALY lost in China
(Per 1000 Population)
Control Rate of CVD Risk Factors is Low

The control of hypertension in China %

The percentage of tobacco use in China over 15 years %

Chinese Cardiovascular disease report 2011
Heart disease is the leading cause of death.


Heart Disease as Percentage of All Deaths

- Vietnamese: 19.5%
- Chinese: 21.8%
- Samoan*: 27.1%
- Guamanian*: 30.4%
- Asian Indian*: 34.6%

*Heart disease is the leading cause of death
Incidence of Stroke in the Asian Pacific Region (2002)

- Philippines: 31
- Thailand: 39.9
- Singapore: 41
- Malaysia: 42.4
- Cambodia: 43.2
- USA: 56.3
- Indonesia: 57
- Laos: 65.5
- Myanmar: 68.4
- Vietnam: 72.6
- South Korea: 97.3
- Japan: 105.9
- China: 127.6

Incidence per 100,000

Prevalence of Heart Disease across California Ethnic Groups: California Health Interview Survey 2009

- Chinese: 4.1%
- Filipino: 3.6%
- South Asian: 2.4%
- Japanese: 8.8%
- Korean: 1.4%
- Vietnamese: 1.6%
- White: 7.4%
- Mexican: 4.1%
- Other Hispanic: 5.9%
- African American: 5.7%
- American Indian or Alaskan: 14.9%

*Doctor ever told have heart disease*
AAPI CV Health Status: Obesity

- Obesity generally less common in Asians (9.3%) compared to other ethnic groups (27-41%) in 2011.
- Prevalence of obesity ranged from 4% in Chinese, 5% in Vietnamese, 6% in Asian Indians, but 14% in Filipino adults.
- Native Hawaiians and Samoans are among the most obese people in the world
- Molokai Heart Study (Native Hawaiians): 64% were obese
BMI and CVD: Asia Pacific Cohort Studies Collaboration
(Ni Mhurchu et al Int J Epidemiol 2004)

- 33 cohort studies among 310,824 subjects with 2.1 million years of follow-up
- Each 2 kg/m$^2$ lower BMI associated with a 12% lower risk of ischemic stroke, 8% lower risk of hemorrhagic stroke, and 11% lower risk of IHD
- Similar associations between Asian and Australasian cohorts
Risk Factors Greater in Asians than in Caucasians (Williams, 1995)

- Sedentary lifestyle
- Truncal obesity
- Hyperinsulinemia and insulin resistance
- Diabetes mellitus
- Elevated triglycerides
- Low HDL-C
Metabolic Syndrome Risks in Asia-Pacific Region: Asia Pacific Cohort Studies Collaboration
(Diab Res Clin Prac 2006)

• 329,166 subjects in 26 cohorts; 5 cohorts involving 6,437 subjects had measures of all 5 risk factors to define modified NCEP metabolic syndrome
• Adjusted HR for CHD death was 2.05 (1.13-2.72)
Lifestyle Interventions Da Qing Study 20-Year Follow-Up

- Combined lifestyle intervention vs control
  - 51% lower incidence of diabetes during active intervention
  - 43% lower incidence over 20 years
  - 3.6 years fewer with diabetes

<table>
<thead>
<tr>
<th></th>
<th>Average Annual Incidence</th>
<th>20-Year Cumulative Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls</td>
<td>11%</td>
<td>93%</td>
</tr>
<tr>
<td>Combined lifestyle intervention</td>
<td>7%</td>
<td>80%</td>
</tr>
</tbody>
</table>

Diabetes in Asian Americans

- From 2007-2009 National Survey Data prevalence of diabetes:
  - 8.4% of Asian-Americans
  - 7.1% in non-Hispanic whites
  - 11.8% of Hispanics
  - 12.6% of non-Hispanic blacks.

- Prevalence of DM twice as high for Asian American adults (14%) compared to Chinese (6%) or Japanese (5%).

Source: AHA Heart and Stroke Facts 2013
Age-Adjusted Prevalence of Type 2 DM: California Adults Aged ≥18 Including Hispanic and Asian Subgroups 2009

- Cambodian/Other Asian: 8.38%
- Vietnamese: 2.85%
- Korean: 8.74%
- Japanese: 6.10%
- South Asian: 8.76%
- Filipino: 12.17%
- Chinese: 4.34%
- African American: 10.61%
- Other Hispanic: 10.83%
- Mexican: 12.58%
- White: 4.41%

N.D. Wong, California Health Interview Survey (unpublished)
Increasing prevalence of diabetes in urban China

Ministry of Health of the People’s Republic of China

2010: 92 Million with Diabetes in China
Control of DM Risk Factors in a Large Multipayer Outpatient Population in Northern California (n=15,826) (Holland and Palaniappan et al., J Diab Complic 2013)

<table>
<thead>
<tr>
<th>Goal</th>
<th>Non-hispanic whites</th>
<th>Asians (all)</th>
<th>Asian indians</th>
<th>Chinese</th>
<th>Filipinos</th>
<th>Japanese</th>
<th>Koreans</th>
<th>Vietnamese</th>
<th>Black/africans</th>
<th>Hispanic/latinos</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simultaneous</td>
<td>21.4%</td>
<td>24.2%*</td>
<td>24.2%</td>
<td>25.6%*</td>
<td>20.5%</td>
<td>24.3%</td>
<td>27.4%</td>
<td>24.3%</td>
<td>14.8%*</td>
<td>18.6%</td>
</tr>
<tr>
<td>20.5%-22.4%</td>
<td>22.9%-25.6%</td>
<td>21.1%-27.3%</td>
<td>23.4%-27.9%</td>
<td>17.5%-23.5%</td>
<td>19.8%-28.7%</td>
<td>19.0%-35.8%</td>
<td>16.8%-31.9%</td>
<td>10.3%-19.3%</td>
<td>16.5%-20.8%</td>
<td></td>
</tr>
<tr>
<td>HbA1c</td>
<td>71.9%</td>
<td>69.4%*</td>
<td>66.1%*</td>
<td>75.6%*</td>
<td>61.5%*</td>
<td>71.9%</td>
<td>64.6%</td>
<td>78.4%</td>
<td>62.3%*</td>
<td>61.3%*</td>
</tr>
<tr>
<td>70.9%-72.9%</td>
<td>68.0%-70.8%</td>
<td>62.7%-69.5%</td>
<td>73.4%-77.7%</td>
<td>58.2%-64.8%</td>
<td>67.3%-76.5%</td>
<td>54.4%-74.8%</td>
<td>71.9%-84.9%</td>
<td>56.9%-67.7%</td>
<td>58.8%-63.7%</td>
<td></td>
</tr>
<tr>
<td>BP</td>
<td>43.8%</td>
<td>49.5%*</td>
<td>48.6%*</td>
<td>53.0%*</td>
<td>41.7%</td>
<td>45.8%</td>
<td>51.6%</td>
<td>59.2%*</td>
<td>36.7%*</td>
<td>44.8%</td>
</tr>
<tr>
<td>42.7%-44.8%</td>
<td>48.0%-51.0%</td>
<td>45.2%-52.0%</td>
<td>50.5%-55.5%</td>
<td>38.4%-45.1%</td>
<td>40.9%-50.7%</td>
<td>41.4%-61.8%</td>
<td>50.9%-67.5%</td>
<td>31.3%-42.1%</td>
<td>42.3%-47.2%</td>
<td></td>
</tr>
<tr>
<td>LDL</td>
<td>60.3%</td>
<td>61.1%</td>
<td>60.7%</td>
<td>60.3%</td>
<td>62.7%</td>
<td>61.8%</td>
<td>53.4%</td>
<td>51.2%</td>
<td>56.6%</td>
<td>58.8%</td>
</tr>
<tr>
<td>59.2%-61.4%</td>
<td>59.6%-62.5%</td>
<td>57.3%-64.1%</td>
<td>57.8%-62.7%</td>
<td>59.4%-66.0%</td>
<td>56.9%-66.7%</td>
<td>44.1%-62.7%</td>
<td>40.4%-62.0%</td>
<td>51.2%-62.1%</td>
<td>56.4%-61.3%</td>
<td></td>
</tr>
</tbody>
</table>

*p= blood pressure; HbA1C= glycosylated hemoglobin; LDL = low-density lipoprotein cholesterol.

* Significant at P<0.05, compared to Non-Hispanic Whites.

Individual control of HbA1c, BP, and LDL ranged from 42-78% in Asians
Composite control of HbA1c, BP, and LDL ranged from 21 (Filipinos)-27% (Koreans)
Meta-Analysis of DPP4 Inhibitors in Asians vs. Non-Asians
(Kim et al Diabetologia 2013)

1) Systematic review of 809 studies; 55 trials included and comprised students of >=50% vs. <50% Asian participants

2) DPP4s lowered HbA1c to a greater extent in Asian vs. non-Asian Studies (-0.92% vs. -0.65%)

3) RR for achieving goal HbA1c<7% was 3.4 (2.6-4.7) in Asian vs. 1.9 (.8-2.0) in non-Asian studies.
Increasing epidemic of hypertension in China

Prevalence Rate

1979 1991 2002

(%)
High Blood Pressure

- In 2009, 18.7% of AAPI had high blood pressure, responsible for 1,871 deaths.
- Low levels of awareness and control
- Very little awareness among Cambodian, Laotian, and Vietnamese immigrants
- Significantly higher levels among Filipino Americans
- Significantly lower blood pressure screening rates among AAPIs
BP and CVD: Asia Pacific Cohort Studies Collaboration
(Lawes CM et al, J Hypertens 2003)

• 425,325 Asian participants with 3 million person-years of follow-up from Australia, China, Hong Kong, Japan, New Zealand, Singapore, South Korea, and Taiwan

• Continuous reduction in risk of stroke, IHD and CVD death down to SBP of 115 mmHg

• A 10mmHg lower SBP was associated with reductions in those aged <60, 60-69, and 70+:
  – 54%, 36%, and 25% lower stroke risk
  – 46%, 24%, and 16% lower ischemic heart disease risk

- Patients 60+ with SBP 160-219 and DBP <95 mmHg, 1253 active treatment (nitridipine, captopril, HCTZ) and 1142 control
- Active treatment reduced stroke 38% as well as reducing CVD endpoints
- Treatment reduced the excess risk associated with diabetes.
Effect of antihypertensive treatment on CVD events--a meta-analysis of four clinical trials in China (Li et al, Biomed Environ Med Sci 2001)

- Pooled results of four large-scale clinical trials, n=10,457, average time of treatment 3.4 years; average reduction in BP 9/4 mmHg

- Stroke was reduced by 36% (P < 0.001), CVD and total deaths were reduced by 22% and 20% respectively (P < 0.05) and total CVD events were reduced by 33% (P < 0.001).

- Reduction in CHD was much smaller and was not statistically significant (P > 0.05).
BP Treatment Considerations in Asians

1) Control of BP ranges from 7.5% in Koreans to 39% in Japanese
2) Some studies show greater sensitivity to beta-blockers in Chinese vs. White patients
3) Other studies show greater responses to other agents (Ca channel blockers and diuretics)
4) Asians experience more cough on ACE inhibitors (12-17% in Japanese, 42-48% in Hong Kong Chinese).
5) Large study shows drinking green and oolong tea lowered risk of developing HTN.

• 352,033 pts in 29 cohorts with 2 million person-years follow-up
• Each 1 mmol/L higher total cholesterol level associated with 35% increased risk of CHD death, 25% increase in stroke, and 20% decreased risk of fatal hemorrhagic stroke
• Similar associations of stroke in Asian and Australian/NZ cohorts.
Recommended Dose Ranges for Selected Statins Japan vs. US
(Liao et al, Am J Cardiol 2007)

<table>
<thead>
<tr>
<th>Statin</th>
<th>Japan</th>
<th>United States</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atorvastatin</td>
<td>10-40</td>
<td>10-80</td>
</tr>
<tr>
<td>Fluvastatin</td>
<td>20-60</td>
<td>20-80</td>
</tr>
<tr>
<td>Pravastatin</td>
<td>10-20</td>
<td>10-80</td>
</tr>
<tr>
<td>Rosuvastatin</td>
<td>2.5-20</td>
<td>5-40</td>
</tr>
<tr>
<td>Simvastatin</td>
<td>5-20</td>
<td>5-80</td>
</tr>
</tbody>
</table>

(80 no longer recommended)
## Randomized Clinical Trails of Lipid-Lowering Efficacy of Statin Therapy in Asians (Liao et al., Am J Cardiol 2007)

<table>
<thead>
<tr>
<th>TRIAL</th>
<th>N</th>
<th>Locale</th>
<th>Statin/Dose</th>
<th>Mean % LDL-C reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASIA</td>
<td>157</td>
<td>Multiple</td>
<td>Atorva 10-20, Simva 10-20</td>
<td>48%, 41%</td>
</tr>
<tr>
<td>Chan et al</td>
<td>76</td>
<td>China</td>
<td>Simva 10</td>
<td>33%</td>
</tr>
<tr>
<td>J-CLAS</td>
<td>121</td>
<td>Japan</td>
<td>Atorva 5-20</td>
<td>36-50%</td>
</tr>
<tr>
<td>Saito et al</td>
<td>112</td>
<td>Japan</td>
<td>Rosuvastatin 1-40</td>
<td>36-66%</td>
</tr>
<tr>
<td>Wang et al.</td>
<td>54</td>
<td>Taiwan</td>
<td>Atorvastatin 10</td>
<td>42%</td>
</tr>
<tr>
<td>Yamamoto et al</td>
<td>60</td>
<td>Japan</td>
<td>Rosuva 1-4</td>
<td>30-42%</td>
</tr>
</tbody>
</table>
## CVD Outcome Clinical Trials of Statin Therapy in Asian Patients (Japan) (Liao et al., Am J Cardiol 2007)

<table>
<thead>
<tr>
<th>TRIAL</th>
<th>N</th>
<th>Statin/Dose</th>
<th>Findings</th>
</tr>
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<tbody>
<tr>
<td>Randomized</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>KLIS</td>
<td>5640</td>
<td>Prava 10-20</td>
<td>14% lower CVD events</td>
</tr>
<tr>
<td>MEGA</td>
<td>7832</td>
<td>Prava 10-20 + diet</td>
<td>33% lower CHD incidence</td>
</tr>
<tr>
<td>PATE</td>
<td>665</td>
<td>Prava 5 vs 10-20</td>
<td>42 vs 29 CV events</td>
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<tr>
<td>Open Label</td>
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<td></td>
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<tr>
<td>CLIP</td>
<td>2529</td>
<td>Prava 10-20</td>
<td>2.33 vs. 5.16 CV events</td>
</tr>
<tr>
<td>Helicos-PAT</td>
<td>2243</td>
<td>Prava 10-20</td>
<td>26% lower CHD events</td>
</tr>
<tr>
<td>J-LIT</td>
<td>47234</td>
<td>Simva 10-20</td>
<td>0.91/1000 p-yrs CHD events</td>
</tr>
<tr>
<td>J-LIT #2</td>
<td>5127</td>
<td>Simva 5-10</td>
<td>4.45/1000 p-yrs CHD events</td>
</tr>
</tbody>
</table>
Effectiveness of Statin Prescribing on Reducing Mortality in South Asian, Chinese and White Patients with Diabetes
(Brunner NW, Can J Cardiol 2013)

• 143,630 white, 9529 South Asian, and 14,084 Chinese with newly diagnosed diabetes from administrative data
• Statin prescribing associated with lower mortality:
  • HR=0.69, p=0.001 in South Asians
  • HR=0.60, p<0.0001 in Chinese
  • HR=0.65, p<0.0001 in Whites
## Summary of Traditional Chinese Medical and Indian Ayurvedic Medical Therapies on Benefits in Cardiovascular Disease Risk Reduction (from Longhurst and Costello, 2011)

<table>
<thead>
<tr>
<th></th>
<th>Blood Pressure</th>
<th>Blood Lipids</th>
<th>Stress Reduction</th>
<th>Coronary Artery Disease or Angina Pectoris</th>
<th>Venous or Vascular Insufficiency</th>
<th>Obesity</th>
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</thead>
<tbody>
<tr>
<td><strong>Traditional Chinese medicine</strong></td>
<td></td>
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<td></td>
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<tr>
<td>Acupuncture, acupressure, moxibustion Energy therapies</td>
<td>Yes</td>
<td>Yes</td>
<td>Possibly</td>
<td>Yes</td>
<td></td>
<td>Yes</td>
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<tr>
<td>Tai Chi, Qigong</td>
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<td></td>
<td>Possibly</td>
<td>Yes</td>
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<tr>
<td><strong>Chinese herbs</strong></td>
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<td></td>
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<tr>
<td>Danshen</td>
<td>Yes*</td>
<td></td>
<td></td>
<td>Yes*</td>
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<tr>
<td>Compounded Sahvia</td>
<td>Yes*</td>
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<td>Yes*</td>
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<td>Suxiao jiuxin wan</td>
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<td>Tongxinluo</td>
<td>Yes</td>
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<td>Red yeast rice</td>
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<td><strong>Ayurvedic medicine</strong></td>
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<td>Yoga</td>
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<td>Herbs</td>
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<td>Garlic</td>
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</tr>
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<td>Terminalia arjuna</td>
<td>No</td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>
Effect of Xuezhikang, an Extract from Read Yeast Chinese Rice on CHD Events in 4870 Chinese Adults with Prior Myocardial Infarction (Lu Z et al., Am J Cardiol 2008)

Frequency of CHD events 10.4% in placebo vs. 5.7% in XZK groups, for a 4.7% absolute and 45% relative risk reduction. CV and total mortality also reduced 30% and 33%. LDL-C reduced 17.6%, HDL-C increased 4.2%.
AAPI CV Health Status: Cigarette Smoking

• 9.6% of Asian adults are smokers; Korean adults more likely to be current smokers (22%) than Japanese (12%), Asian Indian (7%) or Chinese (7%) adults.

• Highest rates among Southeast Asians

• Southeast Asian males start smoking early in life

• High tobacco use among Korean men in California
Prevalence estimates for poor and intermediate **Smoking Status** across California racial and ethnic groups  
(California Health interview Survey 2009)

<table>
<thead>
<tr>
<th></th>
<th>Intermediate: Quit Smoking</th>
<th>Poor: Current Smoker</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chinese</td>
<td>4.9%</td>
<td>9.4%</td>
</tr>
<tr>
<td>Filipino</td>
<td>11.6%</td>
<td></td>
</tr>
<tr>
<td>South Asian</td>
<td>5.0%</td>
<td></td>
</tr>
<tr>
<td>Japanese</td>
<td>11.9%</td>
<td>24.4%</td>
</tr>
<tr>
<td>Korean</td>
<td>15.5%</td>
<td>15.1%</td>
</tr>
<tr>
<td>Vietnamese</td>
<td>16.3%</td>
<td>20.8%</td>
</tr>
<tr>
<td>White</td>
<td>14.2%</td>
<td>16.4%</td>
</tr>
<tr>
<td>Mexican</td>
<td>12.8%</td>
<td>17.8%</td>
</tr>
<tr>
<td>Other Hispanic</td>
<td>11.9%</td>
<td>17.8%</td>
</tr>
<tr>
<td>African American</td>
<td>16.2%</td>
<td>19.8%</td>
</tr>
<tr>
<td>American Indian or Alaskan Native</td>
<td>26.6%</td>
<td>26.3%</td>
</tr>
</tbody>
</table>

*Note:*
Intermediate: Quit Smoking
Poor: Current Smoker
Smoking, Quitting, and CVD Risk: Asia Pacific Cohort Studies Collaboration
(Woodward M, Int J Epidemiol 2005)

• 40 cohort studies among more than 550,000 subjects.
• Clear dose response relation with number of cigarettes and CHD and stroke.
• Quitting smoking was related to a 29% lower risk of CHD and 16% lower risk of stroke.
Lack of Cardiac Rehabilitation / Secondary Prevention in China

- Medical insurance does not cover
- Reimbursement only for procedures and events
- No care/service after procedure
- The care/service of cardiac patients is not as good as for cars!
Big Gap in use of Evidence Based Drugs for Secondary Prevention in China

PURE study

Cardiac Rehabilitation/Secondary Prevention in China: 10 year Plan

• Strength the structure of academic institute (societies, publications, guidelines and consensus)
• Concentrate more attention to rehabilitation under the leadership of government, Social mobilization, multi–party cooperation, make a concerted effort
• Pooled investment from government, NGO, medical insurance and foreign capital
• Investigate the pattern and mechanism of rehabilitation through pilot project
Six of the top 10 causes of death globally are cardiometabolic / behavioral risk factors
The Global CVD Taskforce calls on the CVD community to endorse and support the following top 4 targets to address NCDs and help ensure achievement of the 2025 goal of reducing NCD mortality by 25%:

1) Physical inactivity: 10% relative reduction in prevalence of insufficient physical activity
2) Raised blood pressure: 25% relative reduction in prevalence of raised blood pressure
3) Salt/Sodium Intake: 30% relative reduction in mean population intake of salt, with aim of achieving recommended level of <5 g/d (2000 mg of sodium) (note various organizations such as the AHA call for a limit of 1500 mg/day)
4) Tobacco: 30% relative reduction in prevalence of current tobacco smoking

Smith SC et al., 2012
Nutrition, physical activity and NCD prevention

- Up to 80% of heart disease, stroke and type 2 diabetes and over a third of the most common cancers could be prevented by eliminating obesity, unhealthy diets and physical inactivity.

- Call for commitments at the global and national level to address these risk factors including:
  - Control food supply, food information and marketing and promotion of energy-dense, nutrient-poor foods that are high in saturated, trans-fat, salt or refined sugars.

The NCD Alliance is calling for solid commitment to action in the following areas:

- National regulations to achieve substantial reductions in consumption of saturated fat, trans-fat, salt and refined sugars. Aim to reduce worldwide salt intake to less than 5 g/day per capita (2,000 mg sodium/day) by 2025.
- Global and national trade and fiscal measures to provide incentives for production, distribution and marketing of vegetables, fruit and relatively unprocessed foods.
- National strategies to decrease childhood obesity by 2030 and the elimination of all forms of marketing, particularly those aimed at children, for foods high in saturated fat, trans-fat, salt and refined sugars by 2016.
- National policies to encourage walking, cycling, and active travel, play and leisure.

This is a summary of a full briefing paper (with references) which can be found at www.ncdalliance.org or www.wcrf.org.
Treatment and Prevention Strategies Specific for Asians

- Marketing of low-fat food products needed in Asian countries and culturally sensitive dietary tools developed
- Significant tobacco problem in Asia requires social and economic policies to discourage smoking (including smokeless tobacco)
- Physical activity should also be marketed to Asian populations, where urbanization has caused a decrease in such activity.
Treatment and Prevention Strategies Specific for Asians (cont)

• Dissemination of prevention guidelines and appropriate education of physicians in these guidelines

• Studies of nontraditional therapies:
  – Ayurvedic Medicine involving meditation and herbals/nutritionals
  – Acupuncture effects on hypertension, angina, other CVD effects
  – Herbal and nutritional supplement effects on lipids, blood pressure, CVD system? (e.g., soy protein, garlic)
Healthy Eating Habits

• The *Japanese* eat very little fat and suffer fewer heart attacks than the British or Americans.

• On the other hand, the *French* eat a lot of fat and suffer fewer heart attacks than the British or Americans.

• The *Japanese* drink very little red wine and suffer fewer heart attacks than the British or Americans.

• On the other hand, *Italians* drink excessive amounts of red wine and also suffer fewer heart attacks than the British or Americans.

• **Conclusion:** Eat and drink what you like. It appears that *speaking English* is what kills you.
Braunwald’s Preventive Cardiology Now Available

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