Emerging Global Dietary Habits and the Burden of Cardiovascular Diseases

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April 13, 2009

IOM – Preventing the Global Epidemic of CVD
Meeting the Challenges in Developing Countries

Division of Cardiovascular Medicine, Brigham & Women’s Hospital and Harvard Medical School
Depts of Epidemiology and Nutrition, Harvard School of Public Health
Cardiovascular Risk Factors

- Dyslipidemia
- Hypertension
- Diabetes
- Smoking

→

Coronary Heart Disease
Cardiovascular Risk Factors

Mozaffarian et al., Circulation 2008
The Traditional Diet-Heart Paradigm

Ecologic Studies (across countries or populations)

Biochemical & Metabolic Pathways

Hypothesis Generation
Advances in Nutritional Science

Strength of Evidence

Randomized Trials of Disease Outcomes ↔ Prospective Cohorts of Disease Outcomes

Randomized Trials of Physiologic Measures / Risk Factors

Retrospective Case-Control Studies of Disease Outcomes

Animal Studies ↔ Ecologic Studies ↔ Prevalence Studies
A More Complete Diet-Heart Paradigm

Arrhythmia
Hemodynamics
Inflammation
Endothelial Function
Satiety & Weight Gain
Insulin Sensitivity
Thrombosis
Cholesterol

Methods

Modifying Factors

Diabetes Mellitus

Modifying Factors

Mozaffarian D. Curr Atheroscler Rep 2005
Essential Dietary Habits for CVD Health

1. Seafood / n-3 fatty acids
2. No Trans Fat
3. Whole Grains (carbohydrate quality)
4. Fruits, Vegetables
5. Polyunsaturated Fat for Saturated Fat
6. Nuts, Seeds, Beans
7. Lower Salt (blood pressure)
8. Smaller Portion Sizes
9. Rare Sweetened Drinks
“Behavior Can’t Be Changed”
Behavior Can't Be Changed
(or, the Poly-pill plan)

Is this your child?
Then you need these

Don't make your children suffer
Buy additive-rich foods today!

As recommended by the Trice Food Research Laboratory
Obesity Trends* Among U.S. Adults
BRFSS, 1990

(*BMI ≥30, or ~ 30 lbs overweight for 5’ 4” person)
Obesity Trends* Among U.S. Adults
BRFSS, 1995

(*BMI ≥30, or ~ 30 lbs overweight for 5’ 4” person)
Obesity Trends* Among U.S. Adults
BRFSS, 2000

(*BMI ≥30, or ~ 30 lbs overweight for 5’ 4” person)
Obesity* Trends Among U.S. Adults
BRFSS, 2004

(*BMI ≥30, or ~ 30 lbs overweight for 5’ 4” person)
U.S. Macronutrient Intakes, 1970 to 2000

Behavior Can Be Changed
What is the global burden of cardiovascular diseases due to poor dietary habits?
Diseases and Risk Factors

• Mortality and morbidity can be attributed to:
  – disease or injury outcomes
  – risk factors

• For example, 1.2 million annual lung cancer deaths:

- Cigarette Smoking 71%
- Air Pollution 7%
- Occupational Exposures 10%
- Poverty / Low Education 50%
Comparative Risk Assessment (CRA)

- Quantify, using comparable methods, the role of selected major risk factors in global and regional burdens of disease.
Comparative Risk Assessment (CRA)

• **Current Distributions of Exposure**
  – Corrected for missing data and bias
  – By relevant subgroups (e.g., age, gender)

• **Optimal Distributions of Exposure**
  – Theoretical Minimum Risk Exposure Distribution (TMRED)

• **Causal Effects (RR) of Exposure on Disease**
  – By relevant subgroups (e.g., age, gender)

• **Estimation of Burdens of Disease**
  – Absolute rates of disease, corrected for bias
  – Mortality vs. morbidity (DALYs)
  – Attributable risk, Population attributable risk
## Risk Factors in Prior CRA

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Child &amp; maternal under-nutrition</strong></td>
<td>Childhood and maternal underweight, Iron deficiency anaemia, Vitamin A deficiency, Zinc deficiency, Suboptimal breastfeeding, Term IUGR</td>
</tr>
<tr>
<td><strong>Other nutrition-related risks &amp; inactivity</strong></td>
<td>High blood pressure, High cholesterol, High blood glucose, Overweight and obesity, Low fruit and vegetable intake, Physical inactivity</td>
</tr>
<tr>
<td><strong>Addictive substances</strong></td>
<td>Smoking and oral tobacco use, Alcohol use, Illicit drug use</td>
</tr>
<tr>
<td><strong>Sexual and reproductive health risks</strong></td>
<td>Unsafe sex, Non-use / ineffective use of contraception (unwanted pregnancy)</td>
</tr>
<tr>
<td><strong>Environmental risks</strong></td>
<td>Unsafe water, sanitation, and hygiene, Urban air pollution, Indoor smoke from household solid fuel use, Lead exposure, Global climate change</td>
</tr>
<tr>
<td><strong>Occupational risks</strong></td>
<td>Risk factors for injury, Carcinogens, Airborne particulates, Ergonomic stressors, Noise</td>
</tr>
<tr>
<td><strong>Other selected risks to health</strong></td>
<td>Contaminated health care injections, Child sexual abuse</td>
</tr>
</tbody>
</table>

* Subsequent analysis
Deaths Attributable to Major Risk Factors in 2000

- High blood pressure
- Tobacco
- High cholesterol
- Underweight
- Unsafe sex
- Low fruit and vegetable intake
- Overweight and obesity
- Physical inactivity
- Alcohol
- Unsafe water, sanitation, and hygiene
- Indoor smoke from solid fuels
- Iron deficiency
- Urban air pollution
- Zinc deficiency
- Vitamin A deficiency
- Contaminated health care injections
- Occupational airborne particulates
- Occupational risk factors for injury
- Lead exposure
- Illicit drugs

Mortality in thousands (Total 55.86 million)

Ezzati et al. Lancet 2002
Metabolic Risks by National Income

Women


- Mean BMI (kg/m²)
- Mean cholesterol (mmol/L)
- SBP: 125 mmHg
- SBP: 135 mmHg

GDP (Int $)
Distribution of Burden Attributable to Risk Factors by Exposure Levels

Attributable DALYs (000s)

Hypertension

Hypercholesterolaemia

Obesity

Systolic blood pressure (mmHg)

Cholesterol (mmol/l)

Body mass index (kg/m²)

Exposure levels

Distribution of CVD burden attributable to high blood pressure by exposure and region
Global Burden of Disease Study – 2010 Report

- Estimate the global burden of diseases, injuries, and risk factors for 1990 and 2005 using consistent and comparable methods, assumptions, and data sources.

- Launched Sep 2007 with announcement in *The Lancet*.

- Global consortium of 40 Expert Groups for different diseases, injuries, and risks factors.

- Final results to be published in 2010 and subsequently.
Specific Aims:

1. Identify the effects of nutritional factors on CVD and Cancers.
   - Identify relevant diet-disease relationships.
   - Quantify causal diet-disease relative risks.

2. Estimate exposure distribution of major nutritional risk factors for chronic disease in 21 world regions, by age and sex.
   - Define exposure metrics and units of measurement.
   - Collect exposure distributions, using comparable methods.
Nutrition and Chronic Disease Expert Group

**Nutritional Exposures:**
- **Barbara Bowman**, Acting Director, Division of Cancer Prevention and Control, Associate Director for Science, National Center for Chronic Disease Prevention & Health Promotion, CDC.
- **Ibrahim Elmadfa**, Professor, Institute of Nutritional Sciences, University of Vienna, Austria.
- **Patricia Constante Jamie**, Nutrition Department, University of Sao Paulo, Brazil.
- **Shadi Kalantarian**, Visiting Scientist, Harvard School of Public Health (HSPH).
- **Karen Lock**, Lecturer in Public Health, London School of Hygiene and Tropical Medicine, UK.
- **Renata Micha**, Postdoctoral fellow in Epidemiology, HSPH.
- **Joceline Pomerleau**, Lecturer, European Centre on Health of Societies in Transition, London School of Hygiene and Tropical Medicine, UK.
- **Pattra Wirojratana**, Masters of Science candidate, HSPH.

**Nutrition and CVD:**
- **Goodarz Danaei**, Doctoral candidate, Epidemiology, Population & International Health, HSPH.
- **Eric Ding**, Postdoctoral fellow in Epidemiology, HSPH.
- **Majid Ezzati**, Associate Professor of International Health and Environmental Health, HSPH.
- **John Powles**, Professor of Public Health & Primary Care, Institute of Public Health, Cambridge UK.

**Nutrition and Cancer:**
- **Tim Byers**, Professor and Vice Chair, Preventive Medicine and Biometrics, Univ. of Colorado.
- **Edward Giovannucci**, Professor of Nutrition and Epidemiology, HSPH.
- **Stephanie Smith-Warner**, Assistant Professor of Nutrition and Epidemiology, HSPH.

**Administrative Staff:**
Advisory Role / Corresponding Members

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- **Mohannad Al-Nsour**, Disease Control Directorate, Ministry of Health, Amman, Jordan.
- **Suad Al-Hooti**, Kuwait Institute for Scientific Research, Kuwait.
- **Katica Antonic-Degac**, Croatian Institute of Public Health, Department for Nutrition, Croatia.
- **Larissa Aviles-Santa**, National Heart, Lung, and Blood Institute, Bethesda, MD.
- **Noel Barengo**, University of Helsinki, Helsinki, Finland.
- **Roma Bartkeviciute**, Institute for Biomedical Research, Univ. of Medicine, Kaunas, Lithuania.
- **Lajos Biro**, National Institute of Food Hygiene and Nutrition, Budapest, Hungary.
- **Mario Capanzana**, Director of Food and Nutrition Research Institute, Philippines.
- **Li Dan**, Medical Officer Non-communicable Diseases, WHO Office for the South Pacific, Fiji.
- **Habiba Hassan-Wassef**, University of Cairo, Egypt.
- **Nahla C Houwalla**, American University of Beirut, Lebanon.
- **Yasuhiro Matsumura**, Kiryu University, Japan.
- **Hanyu Ni**, National Institutes of Health, Bethesda, MD.
- **John Potter**, Professor, Fred Hutchinson Cancer Research Center, Seattle, WA.
- **L Szponar**, National Food and Nutrition Institute, Warsaw, Poland.
- **Antonia Trichopoulou**, University of Athens School of Medicine, Greece.
- **Ricardo Uauy**, President, International Union of Nutrition Sciences, Institute of Nutrition and Food Technology, University of Chile, Santiago, Chile.
- **Sirje Vaask**, Eesti Haigekassa, Estonian Health Insurance Fund, Estonia.
- **Anna Waskiewicz**, The Cardinal Stefan Wyszyński Institute of Cardiology, Warsaw, Poland.
- **Gabor Zajkás**, National Institute of Food Hygiene and Nutrition, Budapest, Hungary.
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  – Attributable risk, Population attributable risk
Current Distributions of Exposure

- New Systematic Reviews
- Identification and Selection of Appropriate Studies
- Obtaining Data
- Adjustment for Variability and Bias in Methods
- Missing Data and Imputation
Optimal Distributions of Exposure (TMRED)

Vander Hoorn et al., WHO http://www.who.int/publications/cra/chapters/volume2/2129-2140.pdf
Casual Effects on Disease (RR’s)

- Selection of Risk Factors
- New Systematic Reviews
- New Meta-Analyses
- Effect Modification (e.g., by age, gender)
  - Relative risk scale
  - Absolute risk scale
Estimation of Burdens of Disease

\[
P_{AF} = \frac{\int_{x=0}^{m} RR(x)P(x) \, dx - \int_{x=0}^{m} RR(x)P'(x) \, dx}{\int_{x=0}^{m} RR(x)P(x) \, dx},
\]

\(RR(x)\): relative risk at exposure level \(x\)

\(P(x)\): population distribution of exposure

\(P'(x)\): counterfactual distribution of exposure, and

\(m\): maximum exposure level
Nutrition and Chronic Diseases Expert Group

Global Burden of Diseases, Injuries, and Risk Factors Regions
## Causal Diet-Disease Relative Risks

<table>
<thead>
<tr>
<th>Nutritional Risk Factors</th>
<th>Disease outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Fruits</td>
<td>CHD, stroke</td>
</tr>
<tr>
<td>2. Vegetables</td>
<td>CHD, stroke</td>
</tr>
<tr>
<td>3. Whole grains</td>
<td>CHD, stroke, diabetes</td>
</tr>
<tr>
<td>4. Dietary fiber</td>
<td>CHD, diabetes</td>
</tr>
<tr>
<td>5. Sodium/ salt</td>
<td>CHD, stroke</td>
</tr>
<tr>
<td>6. Seafood omega-3 fats</td>
<td>CHD, stroke</td>
</tr>
<tr>
<td>7. Polyunsaturated fat for saturated fat</td>
<td>CHD</td>
</tr>
<tr>
<td>8. Trans fatty acids</td>
<td>CHD</td>
</tr>
<tr>
<td>9. Dietary cholesterol</td>
<td>?</td>
</tr>
<tr>
<td>10. Red meats</td>
<td>? CHD, stroke, diabetes</td>
</tr>
<tr>
<td>11. Processed meats</td>
<td>? CHD, stroke, diabetes</td>
</tr>
</tbody>
</table>
Seafood Omega-3 Fats: Effects on Risk Factors

Clinical Effect

- Antiarrhythmia: Weeks
- Triglyceride-Lowering: Months to Years
- Heart Rate-Lowering: Months
- BP-Lowering: Months to Years
- Antithrombosis: Weeks

Mozaffarian & Rimm, JAMA 2006
Dietary EPA+DHA and Sudden Death

Case-control study of out-of-hospital primary cardiac arrest (295 cases, 398 controls), adjusted for other cardiovascular risk factors, lifestyle risk factors, and dietary habits.

Siscovick et al. JAMA 1995
Membrane EPA+DHA and Sudden Death

Case-control study of out-of-hospital primary cardiac arrest, adjusted for other cardiovascular risk factors, lifestyle risk factors, and dietary habits.

Siscovick et al. JAMA 1995
Prospective case-control study of sudden cardiac death (98 cases, 184 controls), adjusted for other cardiovascular risk factors, lifestyle risk factors, and dietary habits.

Albert et al. NEJM 2002

Blood EPA+DHA and Sudden Death

Quartiles of Blood EPA+DHA Levels

Prospective case-control study of sudden cardiac death (98 cases, 184 controls), adjusted for other cardiovascular risk factors, lifestyle risk factors, and dietary habits.

Albert et al. NEJM 2002
Membrane EPA+DHA and Sudden Death

Quartiles of RBC EPA+DHA

Case-control study of out-of-hospital primary cardiac arrest, adjusted for other cardiovascular risk factors, lifestyle risk factors, and dietary habits.

Siscovick et al. JAMA 1995
# Fish Intake & CHD Death: Prospective Cohort Studies

**Total of 326,572 individuals (4,473 cardiac deaths) in U.S., Europe, and Asia.**

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of Participants</th>
<th>Number of CHD Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Kromhout 1985 – Zutphen Elderly Study</td>
<td>852</td>
<td>78</td>
</tr>
<tr>
<td>2. Dolecek 1991 – Multiple Risk Factor Intervention Trial</td>
<td>16,258</td>
<td>175</td>
</tr>
<tr>
<td>3. Fraser 1992 – Adventist Health Study</td>
<td>26,473</td>
<td>260</td>
</tr>
<tr>
<td>4. Kromhout 1995 – Rotterdam Cohort Study</td>
<td>272</td>
<td>58</td>
</tr>
<tr>
<td>5. Daviglus 1997 – Chicago Western Electric Study</td>
<td>1,822</td>
<td>430</td>
</tr>
<tr>
<td>6. Albert 1998 – Physicians Health Study</td>
<td>20,551</td>
<td>133</td>
</tr>
<tr>
<td>7. Oomen 2000 – Seven Countries Study</td>
<td>2,738</td>
<td>463</td>
</tr>
<tr>
<td>8. Yuan 2001 – Shanghai Cohort Study</td>
<td>18,244</td>
<td>74</td>
</tr>
<tr>
<td>9. Hu 2002 – Nurses Health Study</td>
<td>84,688</td>
<td>484</td>
</tr>
<tr>
<td>10. Mozaffarian 2003 – Cardiovascular Health Study</td>
<td>3,910</td>
<td>247</td>
</tr>
<tr>
<td>11. Osler 2003 – Danish Monica Cohort</td>
<td>7,529</td>
<td>247</td>
</tr>
<tr>
<td>12. Folsom 2004 – Iowa Women’s Health Study</td>
<td>41,836</td>
<td>922</td>
</tr>
<tr>
<td>13. Mozaffarian 2005 – Health Professionals Follow-up Study</td>
<td>45,722</td>
<td>218</td>
</tr>
<tr>
<td>15. Iso 2006 – Japanese Public Health Center Cohort</td>
<td>41,578</td>
<td>62</td>
</tr>
<tr>
<td><strong>Totals</strong></td>
<td><strong>326,572</strong></td>
<td><strong>4,473</strong></td>
</tr>
</tbody>
</table>
## Fish Intake & CHD Death: Randomized Controlled Trials

<table>
<thead>
<tr>
<th>Randomized Controlled Trials</th>
<th>Number of Participants</th>
<th>Number of CHD Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>DART – 1989</td>
<td>2,033</td>
<td>194</td>
</tr>
<tr>
<td>DART 2 – 2003</td>
<td>3,114</td>
<td>319</td>
</tr>
<tr>
<td>GISSI-Prevenzione – 1999</td>
<td>5,664</td>
<td>273</td>
</tr>
<tr>
<td>JELIS Primary &amp; Secondary Prevention – 2007</td>
<td>18,645</td>
<td>60</td>
</tr>
<tr>
<td>GISSI-Heart Failure – 2008</td>
<td>6,975</td>
<td>632</td>
</tr>
<tr>
<td><strong>Totals</strong></td>
<td><strong>36,431</strong></td>
<td><strong>1,478</strong></td>
</tr>
</tbody>
</table>

*Total of 36,431 individuals (1,478 cardiac deaths)*

*in U.S., Europe, and Asia*
Pooled Analysis of Studies of Cardiac Death

Meta-analysis of 16 prospective cohort studies (n=326,572) and 4 randomized controlled trials (n=29,456) from the U.S., Europe, and Asia.

Total risk reduction = 36%  
(95% CI= 20 to 50%; p<0.001)

250 mg/day  
(~ 2 g/week)

Mozaffarian & Rimm. JAMA 2006
CVD – Seafood and omega-3 fats

**Figure 1:** Relationship between intake of fish or fish oil and rates of CHD death in 16 prospective cohort studies and 4 RCTs¹.

**Figure 2:** Relative risk of stroke, comparing high (2-4 times/wk) vs. low (<1 time/month) fish intake².

<table>
<thead>
<tr>
<th>Disease</th>
<th>RR</th>
<th>95% lower CI</th>
<th>95% higher CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHD fatal¹</td>
<td>0.86</td>
<td>0.79</td>
<td>0.92</td>
</tr>
<tr>
<td>Stroke²</td>
<td>0.82</td>
<td>0.72</td>
<td>0.94</td>
</tr>
</tbody>
</table>

1. Including 4 RCTs and 16 cohort studies, 356,028 participants, 5,319 fatal CHD events
2. Including 9 cohort studies, 200,575 participants, 3,491 stroke events

CVD – Fruits

**Figure 1:** Relative risks of CHD for 1 portion/d increment in fruit intake\(^1\).

**Figure 2:** Relative risks of stroke for 1 portion/d increment in fruit intake\(^2\).

<table>
<thead>
<tr>
<th>Disease</th>
<th>RR</th>
<th>95% lower CI</th>
<th>95% higher CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHD event(^1)</td>
<td>0.93</td>
<td>0.89</td>
<td>0.96</td>
</tr>
<tr>
<td>Stroke(^2)</td>
<td>0.89</td>
<td>0.85</td>
<td>0.93</td>
</tr>
</tbody>
</table>

1. Including 6 cohort studies, **184,412** participants, and **3,346** CHD events
2. Including 5 cohort studies, **210,601** participants, and **1,853** stroke events

---

CVD – Vegetables

**Figure 1:** Relative risks of CHD for 1 portion/d increment in vegetable intake\(^1\).

<table>
<thead>
<tr>
<th>Disease</th>
<th>RR</th>
<th>95% lower CI</th>
<th>95% higher CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHD event(^1)</td>
<td>0.89</td>
<td>0.83</td>
<td>0.95</td>
</tr>
<tr>
<td>Stroke(^1)</td>
<td>0.97</td>
<td>0.92</td>
<td>1.04</td>
</tr>
</tbody>
</table>

1. Including 7 cohort studies, **199,632** participants, and **3,833** CHD events
2. Including 4 cohort studies, **172,164** participants, and **933** stroke events

CVD – Whole Grains

Figure 1: Odds ratios of CVD, comparing high (2.5 servings/d) vs. low (0.2 servings/d) whole grain intake.

<table>
<thead>
<tr>
<th>Disease</th>
<th>RR</th>
<th>95% lower CI</th>
<th>95% higher CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>CVD</td>
<td>0.79</td>
<td>0.73</td>
<td>0.86</td>
</tr>
<tr>
<td>CHD event</td>
<td>0.76</td>
<td>0.69</td>
<td>0.83</td>
</tr>
<tr>
<td>Stroke</td>
<td>0.83</td>
<td>0.68</td>
<td>1.02</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0.79</td>
<td>0.72</td>
<td>0.87</td>
</tr>
</tbody>
</table>

1. Including 7 cohort studies, 285,376 participants, and N/A CVD events
2. Including 6 cohort studies, 286,125 participants, and 10,944 diabetes events

# CVD – Dietary Fiber

<table>
<thead>
<tr>
<th>Disease</th>
<th>RR</th>
<th>95% lower CI</th>
<th>95% higher CI</th>
<th>N of cohort studies</th>
<th>No of participants</th>
<th>No of events</th>
<th>Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHD&lt;sup&gt;1&lt;/sup&gt;</td>
<td>0.86</td>
<td>0.78</td>
<td>0.96</td>
<td>10</td>
<td>336,244</td>
<td>7,260</td>
<td>10 g/ d increment</td>
</tr>
<tr>
<td>Diabetes&lt;sup&gt;2&lt;/sup&gt; (cereal fiber)</td>
<td>0.67</td>
<td>0.62</td>
<td>0.72</td>
<td>9</td>
<td>328,212</td>
<td>8,517</td>
<td>14 g/ d vs. 5 g/ d (high vs. low intake)</td>
</tr>
<tr>
<td>Diabetes&lt;sup&gt;2&lt;/sup&gt; (fruit fiber)</td>
<td>0.96</td>
<td>0.88</td>
<td>1.04</td>
<td>9</td>
<td>308,444</td>
<td>6,132</td>
<td>9 g/ d vs. 2 g/ d (high vs. low intake)</td>
</tr>
<tr>
<td>Diabetes&lt;sup&gt;2&lt;/sup&gt; (vegetable fiber)</td>
<td>1.04</td>
<td>0.94</td>
<td>1.15</td>
<td>7</td>
<td>296,193</td>
<td>4,685</td>
<td>9 g/ d vs. 3 g/ d (high vs. low intake)</td>
</tr>
</tbody>
</table>

1. Including 7 cohort studies, 336,244 participants, and 7,260 CVD events
2. Including 9 cohort studies, 328,212 participants, and 8,517 diabetes events

Relative risk of CHD for polyunsaturated fat intake (11-21%E) substituting SFA\(^1\).

<table>
<thead>
<tr>
<th>Clinical Trial</th>
<th>No. subjects</th>
<th>No. events</th>
<th>N-6 PUFA (% energy)</th>
<th>RR (95% CI)</th>
<th>% Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>LA Veterans</td>
<td>846</td>
<td>125</td>
<td>15%</td>
<td>0.76 (0.54, 1.05)</td>
<td>16.0</td>
</tr>
<tr>
<td>MRC Soy Oil</td>
<td>393</td>
<td>92</td>
<td>18%</td>
<td>0.90 (0.63, 1.28)</td>
<td>14.5</td>
</tr>
<tr>
<td>Oslo-Diet Heart</td>
<td>412</td>
<td>142</td>
<td>21% *</td>
<td>0.76 (0.58, 0.99)</td>
<td>19.1</td>
</tr>
<tr>
<td>Minn. CS - men</td>
<td>4393</td>
<td>143</td>
<td>15% *</td>
<td>0.93 (0.67, 1.29)</td>
<td>16.2</td>
</tr>
<tr>
<td>Minn. CS - women</td>
<td>4664</td>
<td>109</td>
<td>15% *</td>
<td>1.31 (0.90, 1.90)</td>
<td>13.9</td>
</tr>
<tr>
<td>Finnish MH - men</td>
<td>~462</td>
<td>72</td>
<td>11%</td>
<td>0.55 (0.34, 0.90)</td>
<td>9.9</td>
</tr>
<tr>
<td>Finnish MH - women</td>
<td>~357</td>
<td>73</td>
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<tr>
<td>Overall Pooled Effect</td>
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<td></td>
<td></td>
<td>0.83 (0.69, 0.99)</td>
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Including 7 randomized trials, 11,527 participants, and 756 CHD events

Relative risk of CHD for trans-fatty acid intake (each 2%E)\(^1\).

Including 4 cohort studies, 139,836 participants, and 4,965 CHD events

## CVD – Red & Processed Meats

### New Meta-Analysis: Summary Table

<table>
<thead>
<tr>
<th>First author</th>
<th>Year</th>
<th>Country</th>
<th>Total un-processed</th>
<th>Total processed</th>
<th>Disease</th>
<th>Study design</th>
<th>Cohort</th>
<th>Age range</th>
<th>Sample size</th>
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<td>35,988</td>
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</table>

Including **24** cohort studies, **918,094** participants, and **20,084** events

Relative Risks – Challenges Identified

- Unbiased estimates not available for all dietary risk factors of interest (e.g., dietary cholesterol, red meats).
  - New systematic meta-analyses.

- Differing metrics for relative risks vs. exposure distributions.

- No correction for measurement error.
  - Errors in assessment.
  - Changes over time (regression dilution bias).
  - Potentially very large underestimation.
Selection of Nutritional Risk Factors

Definition (metric, unit of measurement)

Exposure distribution

Nutritional Risk factors:

1. Fruits
2. Vegetables
3. Whole grains
4. Dietary fiber
5. Sodium/Salt
6. Seafood omega-3 fatty acids
7. Plant omega-3 fatty acids
8. Omega-6 fatty acids
9. Trans fatty acids
10. Saturated fatty acids
11. Dietary cholesterol
12. Milk
13. Dietary calcium
14. Red meats
15. Processed meats
# Definitions of Nutritional Risk Factors

<table>
<thead>
<tr>
<th>OPTIMAL METRIC/ DEFINITION</th>
<th>ACCEPTABLE ALTERNATIVE METRICS</th>
<th>OPTIMAL MEASUREMENT UNITS</th>
<th>ALTERNATIVE MEASUREMENT UNITS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1. FRUITS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Total fruit intake (including fresh, frozen, cooked, canned, dried), excluding fruit juices and salted or pickled fruits. | 1. Total fruit intake, including juices  
2. Total fruit & vegetable, excluding juices  
3. Total fruit & vegetable, including juices | g/day | servings/day |
| *(Secondary data collection to help in estimating the optimal metrics: Total fruit juices intake, if available)* |                                  |                           |                               |
| **2. VEGETABLES**           |                                 |                           |                               |
| Total vegetable intake (including fresh, frozen, cooked, canned, dried), excluding salted or pickled vegetables, vegetable juices, starchy vegetables (e.g., potatoes, corn), legumes, nuts and seeds. | 1. Total vegetable intake, including juices  
2. Total f&v intake, excluding juices  
3. Total f&v intake, including juices | g/day | servings/day |
| **3. WHOLE GRAINS/ WHOLE GRAIN FOODS** | Other food-survey-specific definition of whole grains (e.g., based on other fiber content, based on food or product names, etc) | servings/day  
(i.e. ounce equivalents) | N/A |
| Total whole grain intake from breakfast cereals, bread, rice and pasta (and other foods such as crackers, waffles, granola bars, biscuits, muffins, tortilla, pita, pancake etc). A whole grain is defined as a food with ≥51% whole-grain content (by weight) per reference amount customarily consumed (RACC). Compliance with the definition is determined by ≥1.1 g of fiber per 10 g of CHO (reference to the fiber content of whole wheat). | | | |
| **4. DIETARY FIBER**        | N/A                             | g/day  
(ideally energy adjusted) | N/A |
| Total dietary fiber intake from all dietary sources (fruits, vegetables, grains, legumes, pulses), excluding supplements. | | | |
| **5. SATURATED FATTY ACIDS** | N/A                             | % kcal  
(energy contribution) | g/day  
(ideally energy adjusted) |
Data Retrieval

For each of the 21 regions:

I. Systematic literature search
II. Survey identification
III. Survey quality assessment
IV. Contact / expert identification
V. Data retrieval
I. Systematic Literature Search

Search Strategy: “Baseline Search” within each country (Medline search)

"Baseline Search":
("nutrition" OR "diet" OR "food habits" OR "nutrition surveys" OR "diet surveys" OR "food habits"[mesh] OR "diet"[mesh] OR "nutrition surveys"[mesh] OR "diet surveys"[mesh]) AND ("country")

Refine by adding:
AND ( (national OR population-based OR urban OR rural) OR ("recall" OR "questionnaire" OR "record") )

Expand search by replacing “Baseline Search” with:
("recall" OR "questionnaire" OR "record" OR "nutrition" OR "diet" OR "food habits" OR "nutrition surveys" OR "diet surveys" OR "food habits"[mesh] OR "diet"[mesh] OR "nutrition surveys"[mesh] OR "diet surveys"[mesh]) AND ("country")

if “Baseline Search” > 100 hits

if “Baseline Search” <50 hits

if “Baseline Search” still >100 hits
II. Survey Identification

Initial screening eligibility criteria

Inclusion:

- Relevant dietary intake estimates were observed
- Survey is as population-based and representative as available
- Sample size >100
- Adult population (≥20 y)

Further issues to be considered:

- Wide age-range for adult population
- Gender-specific estimates are provided
- Survey performed during desired time-frame
- Sample as representative as available of reference population
- Valid dietary assessment as available
III. Survey Quality Assessment

I. Suspect Strong Selection Bias (use for exclusion):
   1. No
   2. Unsure
   3. Yes (survey will not be included)

II. Representativeness (i.e. survey coverage):
   1. National, representative sampling
   2. National, without representative sampling
   3. Regional
   4. Urban or rural
   5. Local selected cohort (e.g., NHS)

III. Sample size:
   1. >1,000
   2. 501-999
   3. 251-500
   4. 100-250
   5. <100 (survey will not be included)

IV. Validation of dietary assessment method:
   1. Multiple (≥2) short-term diet recalls/records with correction for within-person variation
   2. Multiple (≥2) short term diet recalls/records without correction for within-person variation
   3. Food frequency questionnaires, food surveys, or household surveys
   4. Single short-term diet recalls/ records
IV. Contact / Expert Identification

A1 Invitation letter
   - after 1 wk
      - No response
         - No
         - Yes
            - Resend letter, addressing it to all survey authors
               - after 1 wk
                  - No
                  - Yes
A2 Yes, participation
   - Request data
      - after 1 wk
A3 Requested format
A4 Raw data
   - after 1 wk
      - No-1st reminder
         - No
         - Yes
      - No-2nd reminder
         - No
         - Yes
      - No-3rd reminder
         - No
A5 No-1st reminder
   - after 1 wk
A6 No-2nd reminder
   - after 1 wk
A7 No-3rd reminder
   - after 1 wk
A8 Request survey info
A9 Reanalyze raw data
   - after 1 wk
      - No
      - Yes
A10 Data extraction
C Enquire about other experts in that country
   - after 1 wk
      - New contacts
         - No
B1 Resend letter, addressing it to all survey authors
   - after 1 wk
      - No
      - Yes
B2 Resend letter
   - after 1 wk
B3 Call authors & contact nutrition authorities
   - after 1 wk
B4 GBD group: potential contacts
   - after 2 wks
B5 Group meeting
## V. Data Retrieval

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<th>Females</th>
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<td>Sample size</td>
<td>Mean intake</td>
<td>SD</td>
<td>Sample size</td>
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<td>55 – 64 years</td>
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<tr>
<td>Country</td>
<td>Population (July 2008)</td>
<td>Population %</td>
<td>STATUS</td>
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### EUROPE, CENTRAL

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### SUB-SAHARAN AFRICA, CENTRAL

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<td>Survey, cross-sectional</td>
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<th>Dietary Assessment Method</th>
<th>Response Rate</th>
<th>Units of Measurement for Each Dietary Factor (all units assessed)</th>
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<td>Fruits</td>
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<td>grams/person/day</td>
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<tr>
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<td>1994 National</td>
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<td>Fruits, Vegetables, Meat, Meat products, Fish and fish products, Animal fat, Vegetable oil, Milk, Kitchen salt, Cereal, bread, flour</td>
<td>Household Budget survey (HBS)</td>
<td>1994 National</td>
<td>420 Diaries/Households</td>
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Exposures – Challenges Identified

Published primary nutritional data – very limited.
- Need data in GBD gender and age categories.
- Relying on identified contacts – time-consuming & laborious.

Certain important exposures unlikely to be widely available.
- Trans fats (challenging quantification from foods, consumption in developing countries could be much higher).
- Whole grains – no established operational definition.
- Processed meats vs. red meats – often not separated.

Assessing quality of identified surveys – quality scores?
- Selection bias, representativeness, sample size, validity of dietary assessment method.

Comparability of collected data (within- and between-regions).

Individualized dietary data vs. household budget survey data.
Analytical Challenges

§ Year of analysis vs. year of available data.

§ Missing data within and across regions – variation and appropriateness of imputing exposure.

§ Defining “theoretical minimum exposure distribution.”
  § Optimal intake levels.
  § Simple consumption vs. “replacement” modeling (macronutrients).

§ Correcting population distribution (SD) for within-person variation.

§ Standardizing energy adjustment.
Patterns of Global Dietary Habits
Preliminary Results
Global Burden of Diseases, Injuries, and Risk Factors Regions

Surveys: # identified / # with corresponding member/ # with data retrieved.
Burden of Dietary Habits on CVD
Preliminary Results - USA
Men and Women (age 30+ yrs)

Deaths attributable to individual risks (thousands) a

-50 50 150 250 350 450

Smoking
High blood pressure
Overweight-obesity (high BMI)
Physical inactivity
High blood glucose
High LDL cholesterol
High dietary sodium (salt)
Low dietary omega-3 fatty acids (seafood)
High dietary trans fatty acids
Alcohol use
Low intake of fruits and vegetables
Low dietary polyunsaturated fatty acids

GBD Preliminary Results: USA

Danaei G et al Plos Medicine in press
GBD Preliminary Results: USA

Deaths attributable to individual risks (thousands) $^a$

- Men and Women (age 30-70 yrs)

- Smoking
- Overweight-obesity (high BMI)
- High blood pressure
- High blood glucose
- Physical inactivity
- High LDL cholesterol
- Alcohol use
- High dietary trans fatty acids
- Low dietary omega-3 fatty acids (seafood)
- High dietary sodium (salt)
- Low intake of fruits and vegetables
- Low dietary polyunsaturated fatty acids

- Cardiovascular
- Cancer
- Diabetes
- Respiratory
- Other NCD
- Injury

Danaei G et al Plos Medicine in press
Current Work

- What is the global burden of CVD due to poor dietary habits?

- Which dietary habits cause the largest burdens?

- How does this vary by world region?

- How does this vary by country income?

- How does this vary for mortality vs. morbidity?

- What are the implications for interventions and cost-effectiveness?
## Next Steps / Timetable

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- **Data Retrieval**
- **Estimation of Exposure Distribution**
- **Estimation of Burden of Disease**
- **Writing**
- **WHO Report**