David Kritchevsky Memorial Lecture:
Diet and Lifestyle in Hypertension Prevention and Management:

Seeking Evidence and Elixirs

Lawrie Beilin
University of Western Australia
Declaration of Interests

Faculty: Lawrence Beilin AO. Honorary Senior Research Fellow
School of Medicine and Pharmacology. University of Western Australia

- Independent Research Support
- National Health and Medical Research Council Australia
- National Heart Foundation
- Australian Kidney Foundation
- Health Promotion Foundation Western Australia
- West Australian State Government Diabesity Research Program
- Medical Research Foundation Royal Perth Hospital
- CIHR. European Union
- Rotary Perth
- Past Industry Support for Research
- Meat and Livestock Australia Research Program
- Fisheries and Research Development Corporation Western Australia
- Dairy Innovation Australia

Past Consultancies- MSD, Pfizer, Astra-Zeneca- no conflict with work presented
Conceptual issues

Dietary patterns

The Elixir of life.
Epidemiologic Pitfalls

• People eat foods not nutrients

• Clustering of health behaviours

• Measurement errors: food intake, blood pressure, confounders
Randomised Double Blind Controlled Trials and Meta-analyses.

The Gold Standard?
Additional Pitfalls with Diet/Lifestyle Trials

• Changing one food alters others

• Iso-caloric diets difficult

• Blinding

• Adherence

• Short duration

• Blood pressure only a **Surrogate**

• Few Clinical Outcome trials

• Mega-dose micronutrients = **pharmacology** ‘kill or cure’
Established Dietary/Lifestyle effects on BP in Hypertensives

Systolic BP ↓ mmHg

Weight ↓ 5kg 5
Salt ↓ 5g/day 6
Veg/ DASH diet 5/11
Alcohol ↓ 80% 4
Physical Activity 4

viz- Guidelines JNC8, ISH, ESH/ESC, NICE, AHA
and Systematic review Dickinson et al J Ht 2006 24 215-233
Dietary Patterns

• Vegetarian
• DASH
• Mediterranean
Vegetarian Barbecue
The Relationship of Blood Pressure to Diet and Lifestyle in Two Religious Populations

7th DAY ADVENTISTS

v.s.

MORMONS

Avoid

{ALKOHOL, TOBACCO, CAFFEINE}

VEGETARIAN

OMNIVORE (Meat eaters)
Hypertension in Seventh Day Adventists and Mormons

Percentage of people aged 25-44 with high blood pressure

140/90+

(Taken from Rouse, Armstrong and Bellin 1983)
Controlled Trial of Vegetarian diet in Normotensives

Rouse et al Lancet 1983 ;1 5-10
Double blind RCT of Vegetarian Diet in Meat Eaters

Rouse et al Lancet 1983.1.5
Margetts et al BMJ 1986.293
Dietary Pattern Foods

Emphasizes:
- Fruits, Vegetables, Low-fat Dairy Foods
- Whole Grains, Nuts, Poultry, Fish

Reduced:
- Fats, Red Meat,
- Sweets, Sugar-containing Beverages
The Dietary Approaches to Stop Hypertension (DASH) trial

- In Hypertensives: Combination vs Control, -11/5 mmHg

Appel et al. NEJM 1997; 336:1117
Are BP effects of lifestyle factors additive?

2 factors: $5 + 5 = 10$

5 factors: $5 \times 5 = ?$
Two Lifestyle changes Additive Syst BP \downarrow \sim 10+mmHg

- **Weight loss** (Calories)
  - + Salt restriction Whelton 1997 (Tone).
  - + Alcohol reduction Puddey 1992
  - + Daily Fish meal Bao 1998
  - + Exercise Cox 2001

- **Soy Protein + Soluble Fibre** Hodgson 2001

- **Fruit and Vegetables + Low Fat Dairy (DASH)** Appel 1997

- **DASH + Salt restriction**; Sacks 2001
Multiple intervention BP effects not additive: 5x5=5-10

e.g. PREMIER 2003, ADAPT 2005 DEWIT, ENCORE 2010,

**Systolic Blood Pressure**

![Graph showing systolic blood pressure changes over time for different interventions.](Image)

- Advice only
- 4 Established
- DASH + 4 Established

*JAMA 2003*
Results of the Diet, Exercise and Weight Loss Intervention Trial (DEW-IT)

Miller et al Hypertension 2002 40 612

DEW-IT vs Control
-9.5/5.3 mmHg
Combination lifestyle interventions benefit multiple risk factors

- PREMIER  Appel 2003,
- ADAPT  Burke 2005
- DEWIT  Miller 2002
- ENCORE  Blumenthal 2010

Insulin sensitivity
Lipids
LV Mass
Arterial Stiffness
Inflammatory markers
Physical activity and fitness
Reduced medications
Diet and Lifestyle Risk Factors Associated With Incident Hypertension in Women

Factors:

3 Factors: Highest DASH quintile 0.42
BMI <25
Daily Vigorous Activity

4 Factors: + v low alcohol 0.38

5 Factors: + little analgesic use 0.23

6 Factors: + Folate supplements 0.10

Hazard ratio Incident HT vs No healthy Lifestyle Factors

JAMA 2009. 302.
The Search for the Elixir
DASH/Vegetarian diet patterns

What are the Active Components?
DASH Diet Pattern: The Active Elements?

More BP reducing foods?  
- **Low fat dairy**, casein, peptides, calcium,  
- **Nuts** - fibre or n3 fats  
- **Fish** - n3 fatty acids  
- **Fruit and vegetable**  
  - K, Mg,  
  - Fibre  
  - Protein-soy-legume  
  - Alpha linolenic acid (flaxseed)  

Less Blood pressure raising?  
- **Meat**  
- **Saturated Fat**  
- **Sugars**, sucrose/fructose

Micronutrients
- Anti-oxidant
- Anti-inflammatory
- NO generating
- Vitamins: C, B group, folate, D.
The Active Components?

**BP reducing foods?**

- **Low fat dairy**, casein, peptides, calcium,  
- **Nuts** - fibre or n3 fats  
- **Fish** - n3 fatty acids  
- **Fruit and vegetable**  
  - K, Mg,  
  - Fibre  
  - Protein-soy-legume  
  - Alpha linolenic acid (flaxseed)

**Micronutrients**  
- Anti-oxidant  
- Anti-inflammatory  
- NO generating  
- Vitamins: C, B group, folate, D.

**Less BP Raising Foods?**

- **Meat**  
- **Saturated Fat**  
- **Sugars**, sucrose/fructose
Effects of Dietary Fish and Weight Reduction on Ambulatory Blood Pressure in Treated Hypertensives- Factorial Trial

Bao et al Hypertension 1998; 32:710
Independent and additive effect of fish meals and weight loss on awake ambulatory blood pressure vs controls

<table>
<thead>
<tr>
<th></th>
<th>FISH</th>
<th>Wt LOSS</th>
<th>FISH + Wt LOSS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>-6.0 / -3.0</td>
<td>-5.5 / -2.2</td>
<td>-13.0 / -9.3</td>
</tr>
<tr>
<td></td>
<td>(2.2 / 1.4)</td>
<td>(2.9 / 1.3)</td>
<td>(2.4 / 1.4)</td>
</tr>
</tbody>
</table>

Bao et al Hypert 1998; 32:710
Fish Oil the Elixir?

- GISSI-Prevenzione 
  *Lancet* 1999; 354: 447
- JELIS
  *Lancet* 2007; 369: 1090

**CV Events**

- ORIGIN trial  The Risk and Prevention Study in Patients with Dysglycemia  *NEJM* 2013; 368: 1800  No effect

Meta-analysis and Systematic Review- no effect on composite CVD outcomes

*Kotwal et al* *Circ Cardiovasc Qual Outcomes*. 2012; 5 808

**Doses too low?** 0.8 -2 g/day **or too late??**
Alpha linolenic acid and BP?

Potent Antihypertensive Action of Dietary Flaxseed in Hypertensive Patients  Delphin et al Hypertension 2013.62 1081

- 110 peripheral vascular disease patients
- Double blind RCT 6 months
- 30g milled flaxseed or placebo
- BP 10/7mmHg on flaxseed (non sig)
- Significant only in the Hypertensive subgroup
Does the source of Protein matter?
BP ↓ with Protein vs Carbohydrate

Lean meat        Hodgson- Am J Clin Nutr 2006.83:780
Soy protein      Burke- Hypertension. 2001.38.821
Milk Protein     He- Circ 2011.124. 589
Lupin kernel rich bread Lee- Am J Clin Nutr. 2009.89
40g. Soy vs Milk Protein vs Carbohydrate

He et al Circ 2011. 124, 589

Figure 2. Net changes (95% confidence interval) in systolic and diastolic blood pressure (BP) associated with dietary protein supplemenations.
Searching for the Elixir
Some Bioactive Compounds in Fruit and Vegetables

- Alkaloids
  - Caffeine
- Carotenoids
  - Lycopene
- Phenolic acids
- Coumarins
  - Coumarin
- Flavonoids
  - Flavonols
  - Flavones
  - Flavanols
  - Flavanones
  - Anthocyanidins
  - Isoflavones
- Polyphenols
  - Sulphuraphan
- N and S containing compounds
  - Oleuropein
  - Stilbenes
  - Resveratrol
  - Lignans
  - Secoisolariciresinol
Flavonoids and CVD population studies

> 50 studies

High compared to low: tea / cocoa / soy / flavonoid intake

10-20% lower risk of CVD

Arab et al. Stroke. 2009
Hooper et al Am J Clin Nutr 2008
Tea the Source of \(~50\%\) of Flavonoid intake
Figure. Effects of black tea on 24-hour ambulatory blood pressure (intent-to-treat population, n=95). Data are the unadjusted mean ambulatory systolic blood pressure (SBP) and diastolic blood pressure (DBP) for each hour over 24 hours according to beverage (placebo or tea) at baseline, 3 months, and 6 months.
Primary Prevention of Cardiovascular Disease with a Mediterranean Diet

A Primary End Point (acute myocardial infarction, stroke, or death from cardiovascular causes)

- Med diet, EVOO: hazard ratio, 0.70 (95% CI, 0.53–0.91); P=0.009
- Med diet, nuts: hazard ratio, 0.70 (95% CI, 0.53–0.94); P=0.02

No. at Risk

<table>
<thead>
<tr>
<th>Diet Type</th>
<th>Years</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control diet</td>
<td>2450</td>
<td>2268</td>
<td>2020</td>
<td>1583</td>
<td>1268</td>
<td>946</td>
<td></td>
</tr>
<tr>
<td>Med diet, EVOO</td>
<td>2543</td>
<td>2486</td>
<td>2320</td>
<td>1987</td>
<td>1687</td>
<td>1310</td>
<td></td>
</tr>
<tr>
<td>Med diet, nuts</td>
<td>2454</td>
<td>2343</td>
<td>2093</td>
<td>1657</td>
<td>1389</td>
<td>1031</td>
<td></td>
</tr>
</tbody>
</table>

Estruch et al NEJM April 4 2013
Primary Prevention of Cardiovascular Disease with a Mediterranean Diet

Estruch et al NEJM April 4 2013

A Primary End Point (acute myocardial infarction, stroke, or death from cardiovascular causes)

- Med diet, EVOO: hazard ratio, 0.70 (95% CI, 0.53–0.91); P=0.009
- Med diet, nuts: hazard ratio, 0.70 (95% CI, 0.53–0.94); P=0.02

Control diet

Med diet, nuts 30g/d

Med diet, EVOO

1 Litre/wk

No. at Risk

<table>
<thead>
<tr>
<th></th>
<th>Control diet</th>
<th>Med diet, EVOO</th>
<th>Med diet, nuts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Years</td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>No. at Risk</td>
<td>2450</td>
<td>2543</td>
<td>2454</td>
</tr>
<tr>
<td></td>
<td>2268</td>
<td>2486</td>
<td>2343</td>
</tr>
<tr>
<td></td>
<td>2020</td>
<td>2320</td>
<td>2093</td>
</tr>
<tr>
<td></td>
<td>1583</td>
<td>1987</td>
<td>1657</td>
</tr>
<tr>
<td></td>
<td>1268</td>
<td>1687</td>
<td>1389</td>
</tr>
<tr>
<td></td>
<td>946</td>
<td>1310</td>
<td>1031</td>
</tr>
</tbody>
</table>
Mediterranean Diet, Lifestyle Factors, and 10-Year Mortality in Elderly European Men and Women

2400 healthy aged 70-90

• 11 European countries

Mortality Risk reduced by:

    Mediterranean diet,
    Moderate alcohol
    Physically active
    Not smoking

• All 4 behaviours lowered all cause mortality to 0.35

• Lack of all 4 gave popn attributable risk of 60%

    Knoops et al JAMA 2004 292: 1433
When does life (lifestyle) begin?
West Australian Birth Cohort at 14
29% in High Risk Metabolic Cluster

Huang. Diabetes Care 2009. 32. 695

<table>
<thead>
<tr>
<th></th>
<th>High risk</th>
<th>Low risk</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI</td>
<td>27.9</td>
<td>20.2</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Syst BP</td>
<td>120.1</td>
<td>112.1</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Triglyc</td>
<td>1.5</td>
<td>0.9</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Insulin</td>
<td>24.6</td>
<td>10.2</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Huang. J Clin Endocrinol Metab 2012. 97 E1022
New Years Eve
Cottesloe Beach
Editorial Review

The fifth Sir George Pickering memorial lecture

Epitaph to essential hypertension – a preventable disorder of known aetiology?

Lawrence J. Beilin

Journal of Hypertension 1988, 6:85–94
What are the Active Components of DASH/Veg patterns?

**BP Lowering foods?**

**Low fat dairy,**
casein, milk peptides, calcium

**Fruit and vegetable,**
K, Mg, Fibre
Protein-Soy
Alpha linolenic acid (flaxseed)

**Micronutrients**
Anti-oxidant
Anti-inflammatory
Nitric oxide generation
Vitamins: C, B, folate, D.

**Nuts**- fibre or N3 fats

**Fish**- N3 fatty acids
Conclusions

• Hypertension is preventable and sometimes reversible
• Drug requirements can be minimised
• Complex dietary patterns may operate through complex mechanisms
• Critically, risk factors other than Blood pressure should be targetted
• High doses of micronutrients can be harmful
• A single elixir remains elusive
• The “elixir of life” is to translate current evidence re smoking, physical activity, alcohol, diet patterns
• Achieving this is both a personal and societal issue
• Requiring education and personal and political will
The Dietary Approaches to Stop Hypertension (DASH) trial

Mediterranean Diet, Lifestyle Factors, and 10-Year Mortality in Elderly European Men and Women
The HALE Project

Kim T. B. Knöps, MSc
Lisette C. P. G. M. de Groot, PhD
Daan Kromhout, PhD
Anne-Elisabeth Perrin, MD, MSc
Olga Moreiras-Varela, PhD
Alessandro Menotti, MD, PhD
Wija A. van Staveren, PhD

The number of older people is growing rapidly worldwide. More than 580 million people are older than 60 years, and the number is projected to rise to 1000 million by 2020.1 With the increase in life expectancy, the leading causes of death have shifted dramatically from infectious diseases to noncommunicable diseases and from younger to older individuals. In industrialized countries, about 75% of deaths in persons older than the age of 65 are now from cardiovascular diseases and cancer.2

Regardless of predisposing factors, diet and lifestyle influence morbidity and mortality during the course of life.2 Because of the cumulative effect of adverse factors throughout life, it is particularly important for older persons to

Context Dietary patterns and lifestyle factors are associated with mortality from all causes, coronary heart disease, cardiovascular diseases, and cancer, but few studies have investigated these factors in combination.

Objective To investigate the single and combined effect of Mediterranean diet, being physically active, moderate alcohol use, and nonsmoking on all-cause and cause-specific mortality in European elderly individuals.

Design, Setting, and Participants The Healthy Ageing: a Longitudinal study in Europe (HALE) population, comprising individuals enrolled in the Survey in Europe on Nutrition and the Elderly: a Concerned Action (SENECA) and the Finland, Italy, the Netherlands, Elderly (FINE) studies, includes 1507 apparently healthy men and 832 women, aged 70 to 90 years in 11 European countries. This cohort study was conducted between 1988 and 2000.

Main Outcome Measures Ten-year mortality from all causes, coronary heart disease, cardiovascular diseases, and cancer.

Results During follow-up, 935 participants died: 371 from cardiovascular diseases, 233 from cancer, and 145 from other causes; for 186, the cause of death was unknown. Adhering to a Mediterranean diet (hazard ratio [HR], 0.77; 95% confidence interval [CI], 0.68-0.88), moderate alcohol use (HR, 0.78; 95% CI, 0.67-0.91), physical activity (HR, 0.63; 95% CI, 0.55-0.72), and nonsmoking (HR, 0.65; 95% CI, 0.57-0.75) were associated with a lower risk of all-cause mortality (HRs controlled for age, sex, years of education, body mass index, study, and other factors). Similar results were observed for mortality from coronary heart disease, cardiovascular diseases, and cancer. The combination of 4 low risk factors lowered the all-cause mortality rate to 0.35 (95% CI, 0.28-0.44). In total, lack of adherence to this low-risk pattern was associated with a population attributable risk of 60% of all deaths, 64% of deaths from coronary heart disease, 61% from cardiovascular diseases, and 60% from cancer.

Conclusion Among individuals aged 70 to 90 years, adherence to a Mediterranean diet and healthful lifestyle is associated with a more than 50% lower rate of all-causes and cause-specific mortality.

JAMA. 2004;292:1433-1439

www.jama.com
Mediterranean Diet, Lifestyle Factors, and 10-Year Mortality in Elderly European Men and Women

- 2400 healthy men and women aged 70-90
- 11 European countries
- 10 years follow up
- 935 deaths: CVD (40%) Cancer (25%)
Mortality Risk was reduced by:

- Mediterranean diet,
- Moderate alcohol
- Physically active
- Not smoking

All 4 behaviours lowered all cause mortality to 0.35

Lack of all 4 gave population attributable risk of 60%

Knoops et al JAMA 2004 292: 1433
BACKGROUND

ω3 FATTY ACIDS beneficial effects on:

- PLATELET FUNCTION
- INFLAMMATION
- TRIGLYCERIDES / VLDL ; HDL₂ - C
- ENDOTHELIAL FUNCTION
- VASCULAR REACTIVITY
- BLOOD PRESSURE & HEART RATE
- OXIDATIVE STRESS MARKERS
Common Lifestyle Factors for Chronic Diseases

- Smoking
- Overweight/Obesity
- Physical Inactivity
- Diet quality/quantity
- Alcohol

- Cardiovascular/Stroke
- Diabetes
- Cancers
- Sleep Apnoea
- Osteoarthritis
- Non-alcoholic fatty liver disease
- Chronic Airways disease
- Mental Health
- ? Cognitive Function

Psycho-social-cultural influences
25% of Children in ‘High Risk Metabolic Cluster

Huang et al Int J Obesity 2006
Huang et al Diabetes Care 2009
Huang et al JCEM In press 2012
Multiple interventions $5 \times 5 = 5-10$ mmHg
Cumulative Lifestyle Effects on Disease prevention:

**Coronary heart disease - women**  
Stampfer *NEJM* 2000;243

**Diabetes - older adults**  
Mozaffarian *Arch Int Med.* 2009;169

- women  
Chiuve *Circ.* 2008;118

**Stroke**  
Hu *NEJM.* 2001;345
Common Lifestyle = Common Risks

Smoking - Western Diet – Inactivity - Alcohol

CVD - Cancers – Diabetes - Alzheimers
n−3 Fatty Acids and Cardiovascular Outcomes in Patients with Dysglycemia

The ORIGIN Trial Investigators

n−3 FATTY ACIDS AND CARDIOVASCULAR OUTCOMES


Figure 2. Primary and Secondary Outcomes

A  Death from Cardiovascular Causes

Hazard ratio, 0.98 (95% CI, 0.87−1.10)
P=0.72

- n−3 Fatty acids
- Placebo

No. at Risk
- n−3 Fatty acids: 6281, 6161, 6034, 5882, 5706, 5503, 3896, 879
- Placebo: 6255, 6143, 6017, 5848, 5685, 5492, 3893, 837

B  Myocardial Infarction, Stroke, or Cardiovascular Death

Hazard ratio, 1.01 (95% CI, 0.93−1.10)
P=0.81

- n−3 Fatty acids
- Placebo

No. at Risk
- n−3 Fatty acids: 6281, 6044, 5843, 5630, 5403, 5154, 3601, 791
- Placebo: 6255, 6051, 5852, 5616, 5387, 5140, 3604, 766

C  Death from Any Cause

Hazard ratio, 0.98 (95% CI, 0.89−1.07)
P=0.63

- n−3 Fatty acids
- Placebo

No. at Risk
- n−3 Fatty acids: 6281, 6161, 6034, 5882, 5706, 5503, 3896, 879
- Placebo: 6255, 6143, 6017, 5848, 5685, 5492, 3893, 837

D  Death from Arrhythmia

Hazard ratio, 1.10 (95% CI, 0.93−1.30)
P=0.26

- n−3 Fatty acids
- Placebo

No. at Risk
- n−3 Fatty acids: 6281, 6161, 6034, 5882, 5706, 5503, 3896, 879
- Placebo: 6255, 6143, 6017, 5848, 5685, 5492, 3893, 837
Primary Prevention of Cardiovascular Disease with a Mediterranean Diet

Figure 1. Kaplan–Meier Estimates of the Incidence of Outcome Events in the Total Study Population.
Panel A shows the incidence of the primary end point (a composite of acute myocardial infarction, stroke, and death from cardiovascular causes), and Panel B shows total mortality. Hazard ratios were stratified according to center (Cox model with robust variance estimators). CI denotes confidence interval, EVOO extra-virgin olive oil, and Med Mediterranean.
n-3 polyunsaturated fatty acids

- The cardioprotective effect of n-3 PUFAs (mainly EPA and DHA) may be mediated by improvement in hypertriglyceridaemia (inhibition of TG synthesis and enhanced degradation of apoB-100/apoB-48)
- Antiarrhythmic, antioxidant, antiplatelet and antithrombic properties

- Clinical outcome trials with n-3 PUFAs (1-2g/day) show inconsistent results

- GISSI-Prevenzione trial/JELIS trial
  

- ORIGIN trial/The Risk and Prevention Study
  

Low Dose ??
Purified Docosahexaenoic acid but not Eicosapentaenoic acid lowers Ambulatory Blood Pressure & Heart Rate in humans – a double blind randomised trial controlled trial

DHA reduces 24hr BP and Heart rate

<table>
<thead>
<tr>
<th></th>
<th>EPA</th>
<th>DHA</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABP</td>
<td>-2.5 / -1.3</td>
<td>-5.8* / -3.3 *</td>
</tr>
<tr>
<td>vs</td>
<td>Control</td>
<td>Control</td>
</tr>
</tbody>
</table>

Mori et al Hypertension 1999;34:253
STUDY DESIGN

NORMAL ENERGY / FAT INTAKE

SCREEN - 3 0 6 Wks
BASELINE INTERVENTION

PLACEBO (4g/day) (n = 14)

EPA (4g/day) (n = 13)

DHA (4g/day) (n = 13)

Mori et al Hypert 1999;34:253
DHA reduces 24hr BP and Heart rate

EPA

ABP -2.5 / -1.3

vs

Control

DHA

-5.8* / -3.3 *

* P<0.05; adjusted for age, baseline wt, baseline value

Mori et al Hypert 1999;34:253
Forearm Blood Flow responses to ACETYLCHOLINE

Δ FBF between groups Relative to olive oil:

- DHA (P=0.040), EPA (P=0.244)

Mori et al Circ 2000:102;1264
The Effects of Comprehensive Lifestyle Modification on Blood Pressure:
Main Results of the PREMIER Clinical Trial

Randomization

ADVICE ONLY
EST
EST + DASH

↑ = Data Visit
Primary Outcomes (6 months)
End of Intervention (18 months)
The Effects of Comprehensive Lifestyle Modification on Blood Pressure: Main Results of the PREMIER Clinical Trial

**SUMMARY**

- Compared to Advice Only, the Established and the Established Plus DASH interventions:
  - reduced weight
  - reduced sodium
  - increased physical fitness
  - reduced saturated and total fat intake
  - lowered systolic and diastolic BP
  - reduced the prevalence of hypertension
  - increased the prevalence of optimal BP
DASH-SODIUM TRIAL: Study Design

Control Diet, N = 204
DASH Diet, N = 208

Run-in: (11-14 days)

Randomization

50 mmol/d
Lower Sodium
Intermediate Sodium
Higher Sodium

100 mmol/d

150 mmol/d

Intervention (Three 30-day periods, random order)

Sacks et al NEJM 2001;344:3
Potent Antihypertensive Action of Dietary Flaxseed in Hypertensive Patients

**Figure 3.** Mean systolic and diastolic blood pressure at baseline, 1 month, and 6 months for placebo (PL) and flaxseed (FX) groups. *P=0.04, flaxseed vs placebo for systolic blood pressure at 6 months; †P=0.004, flaxseed vs placebo for diastolic blood pressure at 6 months.

**Figure 4.** Mean systolic and diastolic blood pressure among hypertensive patients (BP ≥140/90 mm Hg) on flaxseed (FX) at baseline, 1 month, and 6 months. *P=0.04 baseline vs 1 month; †P=0.002 baseline vs 6 months; ‡P=0.01 baseline vs 1 month; §P=0.003 baseline vs 6 months. PL indicates placebo.
6 mo intervention trial study design

**Placebo / control (n=48)**
- 3 cups per day
- flavour & caffeine matched, containing no tea solids

**Tea (n=44)**
- 3 cups per day
- 1.5 g powdered black tea / 429 mg of polyphenols / 96 mg of caffeine

Baseline
- 3 cups per day
- regular leaf tea

Blood sample and 24 hour urine sample

24 hour ambulatory blood pressure assessment
Acute effects of dietary nitrate on BP in healthy men and women

Nitric oxide status

Salivary nitrite

Plasma nitrite

Study 1
Burke et al. Hypertension 2001

- Aim: to assess the effect of higher protein from soy with carbohydrate
- 36 treated hypertensive individuals
- Followed a low protein, high carbohydrate diet
- 66 g of soy protein (with and without increased fibre intake) was compared with 66 g of carbohydrate: provided as supplements
- Effects on 24-hour ambulatory BP were evaluated
Net effect of protein:  
- Systolic BP 5.9 mm Hg (P<0.05)  
- Diastolic BP 2.6 mm Hg (p<0.05)
**Study 2**

_Hodgson et al. Am J Clin Nutr 2006_

- **Aim:** to determine whether partial substitution of carbohydrate (bread/pasta) with animal protein from lean red meat changes blood pressure

- 60 treated and untreated hypertensive individuals (Mean BP: 138/78 mm Hg)

- Increased protein intake 36 g/d

- Effects on 24-hour ambulatory BP were evaluated
Energy and nutrient intakes

- Energy (mJ/d)
- Protein (%)
- Total carbohydrate (%)
- Sugar (%)
- Starch (%)
- Total Fat (%)
- Saturated Fat (%)
- Monounsaturated Fat (%)
- Polyunsaturated Fat (%)
- Alcohol (%)
- Dietary Fibre (g/d)

Between group difference

P < 0.001
Systolic BP (mm Hg) vs. Diastolic BP (mm Hg)

**Ambulatory** vs. **Clinic**

- **Systolic BP**
  - Ambulatory: P<0.05
  - Clinic: P<0.05

- **Diastolic BP**
  - Ambulatory: NS
  - Clinic: NS
Acknowledgements

- Bruce Armstrong
- Ian Rouse
- Barry Margetts
- Bob Vandongen
- Peter Arkwright
- Ian Puddey
- Trevor Mori
- Kevin Croft
- Anne Barden
- Jonathan Hodgson
- Kay Cox
- Valerie Burke
- Rae-Chi Huang
- Danny Bao
- Sally Burrows
- Richard Woodman
- Penny Rogers
- Diane Dunbar
- David Dunstan
Effects of the DASH Diet Alone and in Combination With Exercise and Weight Loss on Blood Pressure and Cardiovascular Biomarkers in Men and Women With High Blood Pressure

The ENCORE Study

James A. Blumenthal, PhD; Michael A. Babyak, PhD; Alan Hinderliter, MD; Lana L. Watkins, PhD; Linda Craighead, PhD; Pao-Hwa Lin, PhD; Carla Caccia, RD; Julie Johnson, PA-C; Robert Waugh, MD; Andrew Sherwood, PhD

Background: Although the DASH (Dietary Approaches to Stop Hypertension) diet has been shown to lower blood pressure (BP) in short-term feeding studies, it has not been shown to lower BP among free-living individuals, nor has it been shown to alter cardiovascular biomarkers of risk.

Objective: To compare the DASH diet alone or combined with a weight management program with usual diet controls among participants with prehypertension or stage 1 hypertension (systolic BP, 130-159 mm Hg; or diastolic BP, 85-99 mm Hg).


Participants: Overweight or obese, unmedicated outpatients with high BP (N = 144).

Interventions: Usual diet controls, DASH diet alone, and DASH diet plus weight management.

Outcome Measures: The main outcome measure is BP measured in the clinic and by ambulatory BP monitoring. Secondary outcomes included pulse wave velocity, flow-mediated dilation of the brachial artery, baroreflex sensitivity, and left ventricular mass.

Results: Clinic-measured BP was reduced by 16.1/9.9 mm Hg (DASH plus weight management); 11.2/7.5 mm (DASH alone); and 3.4/3.8 mm (usual diet controls) (P < .001). A similar pattern was observed for ambulatory BP (P < .05). Greater improvement was noted for DASH plus weight management compared with DASH alone for pulse wave velocity, baroreflex sensitivity, and left ventricular mass (all P < .05).

Conclusion: For overweight or obese persons with above-normal BP, the addition of exercise and weight loss to the DASH diet resulted in even larger BP reductions, greater improvements in vascular and autonomic function, and reduced left ventricular mass.

Clinical Trial Registration: clinicaltrials.gov Identifier: NCT00571844

Arch Intern Med. 2010;170(2):126-135
Effect of ω-3 fatty acids on composite cardiovascular outcomes. CI indicates confidence interval.
THIS IS NOT A BREAKFAST BUFFET
Regular alcohol use raises blood pressure in treated hypertensive subjects. A randomised controlled trial.

Lancet 1987 1. 647-651
Puddey et al
Independent & Combined effect of Calorie Restriction and Alcohol Moderation in Overweight Men

Puddey et al Hypertension 1992;20:533

Control

Weight loss 5Kg
OR Alcohol ↓ 80%

Wt and Alcohol ↓ BP-14/-9 mmHg vs control
The Relationship of Blood Pressure to Diet and Lifestyle in Two Religious Populations

Ian L. Rouse, Bruce K. Armstrong and Lawrence J. Beilin

The association between blood pressure and a vegetarian diet was studied in relation to obesity, sex, age and lifestyle in 98 Seventh-day Adventist (SDA) lacto-ovo vegetarians, 82 SDA omnivores and 113 Mormon omnivores aged 25 to 44 years. Mean blood pressures adjusted for age, height and weight were significantly lower in SDA vegetarians than in Mormon omnivores (115.6/68.7 and 121.2/72.2, respectively, in males and 109.1/66.7 and 114.9/72.6, respectively, in females) and were not related to past or current use of alcohol, tobacco, tea and coffee, physical activity, personality or religious observance. Mean blood pressures in SDA omnivore males (121.7/71.7) were similar to those in Mormon males, while those in SDA omnivore females (109.9/67.4) were similar to SDA vegetarian females. Quetelet’s Index in these subgroups demonstrated the same patterns.
Mozaffarian, Dariush; MD, DrPH; Appel, Lawrence; MD, MPH; Van Horn, Linda; PhD, RD

Circulation. 123(24):2870-2891, June 21, 2011. DOI: 10.1161/CIRCULATIONAHA.110.968735

<table>
<thead>
<tr>
<th>Component</th>
<th>No. of studies</th>
<th>No. of subjects</th>
<th>No. of events</th>
<th>Unit</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fruits</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total CHD</td>
<td>16 P/Cs</td>
<td>222,706</td>
<td>—</td>
<td>High vs. lowest quartile</td>
<td>0.80 (0.72-0.89)</td>
</tr>
<tr>
<td>Total CVD</td>
<td>6 P/Cs</td>
<td>189,412</td>
<td>2,306</td>
<td>Each year/yr</td>
<td>0.93 (0.89-0.96)</td>
</tr>
<tr>
<td>Total stroke</td>
<td>5 P/Cs</td>
<td>233,961</td>
<td>1,858</td>
<td>Each year/yr</td>
<td>0.88 (0.75-1.04)</td>
</tr>
<tr>
<td>Ischemic stroke</td>
<td>4 P/Cs</td>
<td>209,769</td>
<td>1,708</td>
<td>Each year/yr</td>
<td>0.86 (0.71-1.04)</td>
</tr>
<tr>
<td>Vegetables</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total CHD</td>
<td>9 P/Cs</td>
<td>221,964</td>
<td>—</td>
<td>High vs. lowest quartile</td>
<td>0.77 (0.70-0.86)</td>
</tr>
<tr>
<td>Total CVD</td>
<td>7 P/Cs</td>
<td>199,652</td>
<td>5,330</td>
<td>Each year/yr</td>
<td>0.80 (0.69-0.95)</td>
</tr>
<tr>
<td>Total stroke</td>
<td>4 P/Cs</td>
<td>172,144</td>
<td>993</td>
<td>Each year/yr</td>
<td>0.97 (0.80-1.15)</td>
</tr>
<tr>
<td>Ischemic stroke</td>
<td>3 P/Cs</td>
<td>171,320</td>
<td>896</td>
<td>Each year/yr</td>
<td>0.99 (0.62-1.61)</td>
</tr>
<tr>
<td>Whole Grains</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total CHD</td>
<td>11 P/Cs</td>
<td>286,485</td>
<td>1,980</td>
<td>High vs. lowest quartile</td>
<td>0.72 (0.64-0.82)</td>
</tr>
<tr>
<td>Total CVD</td>
<td>6 P/Cs</td>
<td>286,485</td>
<td>1,980</td>
<td>Each year/yr</td>
<td>0.79 (0.62-0.99)</td>
</tr>
<tr>
<td>Total stroke</td>
<td>4 P/Cs</td>
<td>238,143</td>
<td>933</td>
<td>Each year/yr</td>
<td>0.79 (0.66-0.96)</td>
</tr>
<tr>
<td>Total CVD</td>
<td>7 P/Cs</td>
<td>280,710</td>
<td>6,504</td>
<td>Each year/yr</td>
<td>0.79 (0.62-0.98)</td>
</tr>
<tr>
<td>Diabetics</td>
<td>6 P/Cs</td>
<td>280,125</td>
<td>10,244</td>
<td>Each 2-year period</td>
<td>0.76 (0.52-1.12)</td>
</tr>
<tr>
<td>Nuts</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total CHD</td>
<td>6 P/Cs</td>
<td>184,194</td>
<td>—</td>
<td>High vs. lowest quartile</td>
<td>0.75 (0.67-0.86)</td>
</tr>
<tr>
<td>CVD death</td>
<td>4 P/Cs</td>
<td>153,994</td>
<td>1,597</td>
<td>4 servings/wk vs. never</td>
<td>0.63 (0.51-0.80)</td>
</tr>
<tr>
<td>Fish</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total CHD</td>
<td>25 P/Cs</td>
<td>563,280</td>
<td>—</td>
<td>High vs. lowest quartile</td>
<td>0.81 (0.75-0.86)</td>
</tr>
<tr>
<td>CVD death</td>
<td>13 P/Cs</td>
<td>222,364</td>
<td>3,632</td>
<td>4 servings/wk vs. &lt; 1 serving/wk</td>
<td>0.73 (0.68-0.79)</td>
</tr>
<tr>
<td>Nor total H</td>
<td>5 P/Cs</td>
<td>181,151</td>
<td>2,119</td>
<td>3 servings/wk vs. &lt; 1 serving/wk</td>
<td>0.73 (0.69-0.99)</td>
</tr>
<tr>
<td>Total stroke</td>
<td>6 P/Cs</td>
<td>209,070</td>
<td>5,491</td>
<td>3 servings/wk vs. &lt; 1 serving/wk</td>
<td>0.64 (0.55-0.76)</td>
</tr>
<tr>
<td>Ischemic stroke</td>
<td>5 P/Cs</td>
<td>154,957</td>
<td>1,156</td>
<td>3 servings/wk vs. &lt; 1 serving/wk</td>
<td>0.65 (0.48-0.88)</td>
</tr>
<tr>
<td>Hemorrhagic stroke</td>
<td>5 P/Cs</td>
<td>154,957</td>
<td>548</td>
<td>3 servings/wk vs. &lt; 1 serving/wk</td>
<td>0.80 (0.64-1.04)</td>
</tr>
<tr>
<td>Meat</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total CHD</td>
<td>13 P/Cs</td>
<td>220,414</td>
<td>—</td>
<td>High vs. lowest quartile</td>
<td>1.23 (1.08-1.41)</td>
</tr>
<tr>
<td>Diabetics</td>
<td>4 P/Cs</td>
<td>163,265</td>
<td>5,579</td>
<td>Each 7-year period</td>
<td>1.28 (1.08-1.50)</td>
</tr>
<tr>
<td>Processed meats</td>
<td>5 P/Cs</td>
<td>220,065</td>
<td>7,583</td>
<td>Each 7-year period</td>
<td>1.20 (1.06-1.35)</td>
</tr>
<tr>
<td>Processed meats</td>
<td>5 P/Cs</td>
<td>220,065</td>
<td>7,583</td>
<td>Each 7-year period</td>
<td>1.20 (1.06-1.35)</td>
</tr>
<tr>
<td>Milk/dairy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total CHD</td>
<td>11 P/Cs</td>
<td>263,346</td>
<td>7,434</td>
<td>High vs. lowest quartile</td>
<td>0.81 (0.62-1.06)</td>
</tr>
<tr>
<td>Total CVD</td>
<td>6 P/Cs</td>
<td>210,800</td>
<td>—</td>
<td>High vs. lowest quartile</td>
<td>0.94 (0.79-1.11)</td>
</tr>
<tr>
<td>Total stroke</td>
<td>7 P/Cs</td>
<td>418,097</td>
<td>14,308</td>
<td>High vs. lowest quartile</td>
<td>0.79 (0.63-0.95)</td>
</tr>
<tr>
<td>Diabetics</td>
<td>6 P/Cs</td>
<td>121,263</td>
<td>4,851</td>
<td>High vs. lowest quartile</td>
<td>0.92 (0.68-1.26)</td>
</tr>
<tr>
<td>Eggs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total CHD</td>
<td>6 P/Cs</td>
<td>259,211</td>
<td>—</td>
<td>High vs. lowest quartile</td>
<td>1.05 (0.92-1.23)</td>
</tr>
</tbody>
</table>
Table 1. Food-Based Components of Dietary Patterns That Improve Cardiometabolic Health

<table>
<thead>
<tr>
<th>Food</th>
<th>Serving Size</th>
<th>Nutrient Benefits</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 medium-sized fruit</td>
<td>4 to 5 servings</td>
<td>Whole fruit is a rich source of vitamins, minerals, fiber, and phytochemicals.</td>
</tr>
<tr>
<td>1 cup of fresh, frozen, or canned fruit</td>
<td>daily</td>
<td>Fish, cooked, and minimally processed nonstarchy vegetables contribute protein, magnesium, fiber, antioxidant vitamins, and other microelements.</td>
</tr>
<tr>
<td>1 cup of raw leafy vegetable, 1 cup of cut up raw vegetables, or 1 cup of whole vegetables</td>
<td>daily</td>
<td>Fish servings of vegetables (including tomatoes) contribute 189 to 300 kcal.</td>
</tr>
<tr>
<td>1 slice of whole grain bread, 1 cup of high-fiber whole grain cereal, 3/4 cup of cooked whole grain rice, pasta, or cereal</td>
<td>daily</td>
<td>Whole grains contribute vitamins, minerals, fiber, and other microelements.</td>
</tr>
<tr>
<td>Fish and seafood</td>
<td>2 servings/month, preferably once a week</td>
<td>Provide omega-3 fatty acids, protein, selenium, magnesium, vitamin D, and other nutrients. One serving contains ~79 to 110 kcal.</td>
</tr>
<tr>
<td>Nuts</td>
<td>4 to 5 servings/wk</td>
<td>Nuts are preferred to minimize sodium intake.</td>
</tr>
<tr>
<td>Dairy products</td>
<td>2 to 3 servings/d</td>
<td>Limit dairy products to one serving of milk or yogurt per day.</td>
</tr>
<tr>
<td>Vegetable oils</td>
<td>2 to 6 servings/d</td>
<td>Limit total fats to 20% of total daily calories.</td>
</tr>
</tbody>
</table>

Table 1. Food-Based Components of Dietary Patterns That Improve Cardiometabolic Health
Figure 1. Relationships of consumption of different foods with incidence of coronary heart disease (CHD), stroke, and diabetes in meta-analyses of prospective cohort studies (PCs). Adapted with permission from Mozaffarian.29 Dashes indicate not reported; CVD, cardiovascular disease; and RR (95% CI), relative risk (95% confidence interval).
Table 2. Evidence From Human Studies Using Different Research Paradigms for Effects of Selected Foods, Nutrients, and Dietary Patterns on Cardiovascular Diseases

<table>
<thead>
<tr>
<th>Foods and beverages</th>
<th>Ecologic Studies of Clinical End Points*</th>
<th>Randomized Trials of Risk Factors</th>
<th>Prospective Cohort Studies of Clinical End Points*</th>
<th>Randomized Trials of Clinical End Points*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fruits</td>
<td>+++</td>
<td>+++</td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Vegetables</td>
<td>+++</td>
<td></td>
<td>+++</td>
<td></td>
</tr>
<tr>
<td>Whole grains</td>
<td>-</td>
<td></td>
<td>++</td>
<td></td>
</tr>
<tr>
<td>Fish</td>
<td>+++</td>
<td></td>
<td>+++</td>
<td></td>
</tr>
<tr>
<td>Nuts</td>
<td>+++</td>
<td></td>
<td>+++</td>
<td></td>
</tr>
<tr>
<td>Processed meats</td>
<td>++</td>
<td></td>
<td>+++</td>
<td></td>
</tr>
<tr>
<td>Unprocessed red meats</td>
<td>++</td>
<td></td>
<td>+++</td>
<td></td>
</tr>
<tr>
<td>Dairy</td>
<td>+</td>
<td></td>
<td>+++</td>
<td></td>
</tr>
<tr>
<td>Sugar-sweetened</td>
<td>+</td>
<td></td>
<td>+++</td>
<td></td>
</tr>
<tr>
<td>Beverages</td>
<td>+++</td>
<td></td>
<td>+++</td>
<td></td>
</tr>
<tr>
<td>Alcohol</td>
<td>+++</td>
<td></td>
<td>+++</td>
<td></td>
</tr>
<tr>
<td>Nutrients</td>
<td>+++</td>
<td></td>
<td>+++</td>
<td></td>
</tr>
<tr>
<td>Sodium</td>
<td>+++</td>
<td></td>
<td>+++</td>
<td></td>
</tr>
<tr>
<td>Dietary fiber</td>
<td>+++</td>
<td></td>
<td>+++</td>
<td></td>
</tr>
<tr>
<td>Refined carbohydrates</td>
<td>-</td>
<td></td>
<td>+++</td>
<td></td>
</tr>
<tr>
<td>and starches</td>
<td>++</td>
<td></td>
<td>+++</td>
<td></td>
</tr>
<tr>
<td>Total fat</td>
<td>+++</td>
<td></td>
<td>+++</td>
<td></td>
</tr>
<tr>
<td>Polyunsaturated fat in place of:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Saturated fat</td>
<td>++</td>
<td></td>
<td>+++</td>
<td></td>
</tr>
<tr>
<td>Carbohydrates</td>
<td>+</td>
<td></td>
<td>+++</td>
<td></td>
</tr>
<tr>
<td>Monounsaturated fat in place of:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Saturated fat</td>
<td>++</td>
<td></td>
<td>+++</td>
<td></td>
</tr>
<tr>
<td>Carbohydrates</td>
<td>+</td>
<td></td>
<td>+++</td>
<td></td>
</tr>
<tr>
<td>Saturated fat in place of:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carbohydrates</td>
<td>++</td>
<td></td>
<td>+++</td>
<td></td>
</tr>
<tr>
<td>Stearidol</td>
<td>+</td>
<td></td>
<td>+++</td>
<td></td>
</tr>
</tbody>
</table>

*Based on the strength of evidence for an effect on any major clinical end point, including coronary heart disease, stroke, or death.

** Based on the strength of evidence for effects on any major major clinical end point, including diabetes, lipid disorders, obesity, or cancer.

† Based on the strength of evidence for effects on any major major clinical end point, including diabetes, lipid disorders, obesity, or cancer.

§ Based on the strength of evidence for effects on any major major clinical end point, including diabetes, lipid disorders, obesity, or cancer.

|| Based on the strength of evidence for effects on any major major clinical end point, including diabetes, lipid disorders, obesity, or cancer.

* Based on the strength of evidence for effects on any major major clinical end point, including diabetes, lipid disorders, obesity, or cancer.

† Based on the strength of evidence for effects on any major major clinical end point, including diabetes, lipid disorders, obesity, or cancer.

§ Based on the strength of evidence for effects on any major major clinical end point, including diabetes, lipid disorders, obesity, or cancer.

** Based on the strength of evidence for effects on any major major clinical end point, including diabetes, lipid disorders, obesity, or cancer.

†† Based on the strength of evidence for effects on any major major clinical end point, including diabetes, lipid disorders, obesity, or cancer.

§§ Based on the strength of evidence for effects on any major major clinical end point, including diabetes, lipid disorders, obesity, or cancer.

© 2011 American Heart Association, Inc. Published by American Heart Association.
Figure 2

<table>
<thead>
<tr>
<th>Type</th>
<th>Processing and Structure</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intact whole grains</td>
<td>Whole grain with the bran, germ, and endosperm from the natural cereal intact</td>
<td>Brown rice, bulgur wheat, amaranth, wheat berries</td>
</tr>
<tr>
<td>Minimally processed whole grains</td>
<td>Some processing is performed to improve palatability or digestibility yet the bran and germ remain partially intact</td>
<td>Stone-ground whole wheat bread, cracked wheat, steel-cut oats</td>
</tr>
<tr>
<td>Milled whole grains</td>
<td>The whole grain, including bran, germ, and endosperm, is milled to fine flour</td>
<td>Most commercially available whole grain breads, whole grain breakfast cereals, whole grain pasta</td>
</tr>
<tr>
<td>Refined grains†</td>
<td>The bran and germ are removed during processing, leaving the endosperm comprised largely of refined starch</td>
<td>White bread, white rice, most ready-to-eat breakfast cereals, instant oatmeal, regular pasta</td>
</tr>
<tr>
<td>Starchy vegetables†</td>
<td>Plants that have been bred or engineered to contain high levels of starch with relatively low dietary fiber and micronutrients</td>
<td>Potatoes, corn</td>
</tr>
<tr>
<td>Refined sugars†</td>
<td>Natural and industrially-produced mono- and di-, and oligosaccharides, including sucrose, glucose, fructose, high fructose corn syrup, maltose, dextrose, and maltodextran</td>
<td>Candies, other sugars added to foods</td>
</tr>
<tr>
<td>Sweetened refined grains†</td>
<td>Refined grains with added refined sugars</td>
<td>Sweetened breakfast cereals, grain-based desserts (cakes, cookies, pies, doughnuts, sweet rolls, muffins)</td>
</tr>
<tr>
<td>Refined sugars in liquid form†</td>
<td>Natural and industrially-produced mono- and disaccharides in liquid form</td>
<td>Sugar-sweetened beverages, including sodas, iced teas, sports drinks, and fruit drinks</td>
</tr>
</tbody>
</table>

Figure 2. Types of processing and structure of grains, sugars, and starches. A major research and policy gap is the absence of one accepted taxonomy to define whole grains or carbohydrate quality that incorporates their various characteristics that can influence cardiometabolic health, including extent of processing, food structure, dietary fiber content, content of bran and germ, and glycemic response to ingestion. This Figure presents a proposed taxonomy to integrate these various characteristics. Types of foods with evidence for cardiometabolic benefits are shaded green, and those with evidence for adverse cardiometabolic effects are shaded red. Intact and minimally processed whole grains (darker green; ie, greater benefits) may plausibly have greater benefits than milled whole grains (lighter green; ie, lesser benefits) because of intact food structure and lower glycemic response; refined sugars in liquid form (darkest red, ie, greatest harms) may have greater adverse effects than refined grains, starches, and sugars (lighter red; ie, lesser harms) because of particularly unfavorable effects on satiety and weight gain. + Both simple and complex refined carbohydrates induce similarly high glycemic responses following ingestion and, in amounts typically consumed in Western diets, induce de novo lipogenesis in the liver, ie, the conversion of carbohydrates to fat. Compared to glucose, fructose produces smaller blood glycemic responses but more strongly stimulates de novo lipogenesis, Animal-experimental and limited human studies suggest that fructose, which represents about half of all sugars in Western diets, causes greater de novo lipogenesis than glucose. — Multiple carbohydrates, such as sucrose, may exhibit intermediate responses between glucose and fructose. ** Medicinal use such as the ingestion of fructose-containing products (eg, fructose in soda, fructose in sacraments) during the Middle Ages (300–1500 AD) may have played a role in the development of the Western cardiometabolic epidemic. Since the Middle Ages, the carbohydrate content of the diet has increased.
Table 3. Examples of Dietary Patterns With Evidence for Cardiovascular Health Benefits

<table>
<thead>
<tr>
<th>Dietary Pattern</th>
<th>Mediterranean (US)</th>
<th>Vegetarian</th>
<th>Traditional Japanese</th>
<th>Traditional Chinese</th>
</tr>
</thead>
<tbody>
<tr>
<td>Component</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fruits</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vegetables</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nuts and seeds</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fish</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Milk and eggs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nutrient density</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calories</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total fat</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Saturated fat</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cholesterol</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carbohydrates</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Protein</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sodium</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Values are based on the average (mean) consumption levels in the population, not on the optimal consumption levels for a traditional cardioprotective diet.

Adjustments made to lifelong diet.


1. Values are based on the average (mean) consumption levels in the population, not on the optimal consumption levels for a traditional cardioprotective diet.
2. Adjustments made to lifelong diet.
3. Vegetarian diets are defined by what is not consumed (i.e., meats, soy, dairy, eggs, and nuts). Thus, although many vegetarian diets contain milk products and may consume 100% of fruits, vegetables, nuts, and grains, what nutrients are consumed can vary considerably and no typical vegetarian diet can be reliably defined.
Figure 3. Effects of dietary patterns on cardiovascular risk factors in randomized controlled trials. Effects of the DASH (Dietary Approaches to Stop Hypertension) low-fat, high-protein, and high-monounsaturated-fat (MUFA) diets compared with baseline among 162 participants in a 6-week feeding trial; and of the Mediterranean diet compared with a low-fat diet among 180 participants in a 2-year dietary advice trial. All differences were statistically significant at P<0.05, except for changes in high-density lipoprotein cholesterol (HDL-C) with the DASH high-MUFA diet and in triglycerides with the DASH low-fat diet. Where no results are shown (eg, DASH diets and glucose-insulin measures), findings were not reported. Across diets, blood pressure and low-density lipoprotein cholesterol (LDL-C) were generally improved to a greater extent with DASH dietary patterns, whereas atherogenic dyslipidemia and glucose-insulin measures were generally improved to a greater extent with Mediterranean dietary patterns. Overall risk factor changes with any of these dietary patterns would predict substantial reductions in cardiovascular risk. SBP indicates systolic blood pressure; DBP, diastolic blood pressure; CRP, C-reactive protein.
Table 4. Summary of Evidence of the Effects of Vitamin Supplements on Cardiovascular Disease

<table>
<thead>
<tr>
<th>Component</th>
<th>Evidence of Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta-carotene</td>
<td>Some cohort studies have linked low serum levels or low dietary intake of beta-carotene with higher CVD risk. RCTs of beta-carotene supplements document no benefit in the general population and increased risk of lung cancer.</td>
</tr>
<tr>
<td>Calcium</td>
<td>Calcium supplementation with vitamin D is recommended as a means to prevent osteoporosis, especially in women. A recent meta-analysis of RCTs suggests that calcium supplementation may improve the risk of myocardial infarction.</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>Emerging evidence from observational studies suggests that low serum vitamin D levels are associated with higher risk of CVD events. RCTs of vitamin D supplementation have not shown consistent reductions in risk of CVD.</td>
</tr>
<tr>
<td>Vitamin E</td>
<td>Additional trials using higher doses of vitamin E supplementation are ongoing. Several prospective cohort studies have linked lower serum vitamin E levels or supplementation with lower risk of CVD. RCTs have failed to show reductions in CVD events with supplementation.</td>
</tr>
<tr>
<td>Folic acid, vitamin B6, and vitamin B12</td>
<td>Observational studies have associated low intake or low serum levels and high homocysteine levels with higher risk of CVD. However, RCTs have confirmed that folic acid supplementation lowers blood homocysteine levels. Long-term RCTs have not documented benefits of folic acid with or without vitamin B6 and vitamin B12. In some trials, folic acid alone was associated with increased risk of CVD.</td>
</tr>
<tr>
<td>Fish oils</td>
<td>Multiple cohort studies have documented an inverse relationship between fish intake and subsequent CVD, in particular CHD death. A meta-analysis of 12 RCTs demonstrated a reduction in total mortality with fish oil supplements. However, patients with existing CVD demonstrated reductions in CHD events; several of these trials had methodologic limitations.</td>
</tr>
<tr>
<td>Multivitamins</td>
<td>Although some cohort studies have observed lower CVD risk with multivitamin supplements, RCTs, limited by poor quality, have not documented any clear CVD benefit of multivitamins in treated populations.</td>
</tr>
</tbody>
</table>

CVD indicates cardiovascular disease; RCT, randomized, controlled trial; and CHD, coronary heart disease.
Table 5. Evidence-Based Strategies for Promoting Individual-Level Dietary Change to Reduce Cardiovascular Disease Risk

<table>
<thead>
<tr>
<th>Cognitive/behavioral strategies</th>
<th>Goal Setting: Target dietary behaviors with specific, proximal goals.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Feedback: Provide feedback on progress toward goals.</td>
</tr>
<tr>
<td></td>
<td>Follow-Up: Establish a plan for frequency and duration of follow-up contacts (e.g., in-person, oral, written, electronic) in accordance with individual needs to assess and reinforce progress toward goal achievement.</td>
</tr>
<tr>
<td>Motivational interviewing: Use motivational interviewing strategies, particularly when an individual is resistant or ambivalent about behavior change.</td>
<td></td>
</tr>
<tr>
<td>Combination strategies: Use a combination of 2 or more of the above strategies in an intervention.</td>
<td></td>
</tr>
<tr>
<td>Long-term support: Provide direct or peer-based long-term support and follow-up, such as referral to ongoing community-based programs to offset the common occurrence of declining adherence over time.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Intervention process and/or delivery strategies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class 1A: Individual sessions: Use individual-oriented sessions to assess where the individual is in relation to behavior change, to jointly identify the goals for risk reduction or improved cardiovascular health, and to develop a personalized plan to achieve it.</td>
</tr>
<tr>
<td>Class 1B: Group sessions: Use group sessions with cognitive-behavioral strategies to teach skills to modify behavior to provide risk modeling and positive observational learning, while maximizing the benefits of peer support and group problem solving.</td>
</tr>
</tbody>
</table>

| E-Promise: For some cases of multiple, complex, and computer-based programs to target behavior change, evidence including E-counseling and feedback. |
| Individualized feedback: For web- and media-based strategies, use individualized (rather than generalized) approaches. |

<table>
<thead>
<tr>
<th>Strategies to address cultural and social context</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class 1A: Multicomponent: Use a multiple-component delivery strategy that includes both individual and group components.</td>
</tr>
<tr>
<td>Cultural adaptations: Use culturally adapted strategies, including use of peer or lay health advisors to increase motivation as well as establish health liaisons and counseling strategies sensitive to cultural beliefs, values, language, setting, and settings of the individual.</td>
</tr>
<tr>
<td>Class 1B: Settings: Use work, community, church, or clinic settings for delivery of interventions.</td>
</tr>
</tbody>
</table>

| Problem solving: Use problem-solving strategies to address barriers such as lack of access to healthy foods, lack of knowledge related to cooking or food preparation, or transportation barriers. |

Adapted from Atienza et al. [20]
Table 6. Evidence-Based Strategies for Promoting Population-Level Dietary Change to Reduce Cardiovascular Disease Risk

<table>
<thead>
<tr>
<th>Strategies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Policies directed at targeting selected nutrients to increase or reduce levels in foods&lt;sup&gt;1,2&lt;/sup&gt;</td>
</tr>
<tr>
<td>Direct subsidies on prices</td>
</tr>
<tr>
<td>Coordinated, multi-component media, education, and labeling</td>
</tr>
<tr>
<td>Changes in the food environment&lt;sup&gt;3&lt;/sup&gt;</td>
</tr>
<tr>
<td>Increasing availability of healthier foods, eg. in cafeterias, grocery stores, or neighborhoods</td>
</tr>
<tr>
<td>Changes in food pricing by means of subsidies or taxation</td>
</tr>
<tr>
<td>Promote foods with pre-package nutrition and education</td>
</tr>
<tr>
<td>Media and other educational strategies&lt;sup&gt;4,7&lt;/sup&gt;</td>
</tr>
<tr>
<td>Integrate mass media campaigns promoting one simple message</td>
</tr>
<tr>
<td>National logo or simple branding to identify healthy foods</td>
</tr>
<tr>
<td>Provide of focused, targeted messages as part of a larger multi-component strategy</td>
</tr>
<tr>
<td>Regulation of advertising to particular at-risk groups</td>
</tr>
<tr>
<td>Posting of information on food labels or menus/cards</td>
</tr>
<tr>
<td>Social and community supports&lt;sup&gt;5&lt;/sup&gt;</td>
</tr>
<tr>
<td>Coordinated educational and environmental efforts in schools, workplaces, community centers, and religious centers</td>
</tr>
<tr>
<td>Group sessions and self-monitoring strategies</td>
</tr>
<tr>
<td>Multi-strategic approaches&lt;sup&gt;6,8&lt;/sup&gt;</td>
</tr>
<tr>
<td>Group efforts, people, policies, and media campaigns, and downstream community approaches</td>
</tr>
</tbody>
</table>

<sup>1</sup>Swisher and others experience greatest success when multiple stakeholders (community leaders, local organizations, policy makers) are involved throughout planning, implementation, and sustainability<sup>6</sup><sup>,7,9</sup><sup>2</sup>

<sup>1</sup>Evidence that this strategy alters consumer behavior is still relatively limited, but this strategy appears to at least contribute to food industry changes in terms of what is offered.

Table 6. Evidence-Based Strategies for Promoting Population-Level Dietary Change to Reduce Cardiovascular Disease Risk

Mozaffarian, Dariush; MD, DrPH; Appel, Lawrence; MD, MPH; Van Horn, Linda; PhD, RD

DOI: 10.1161/CIRCULATIONAHA.110.968735
Figure 1. Line graph shows mean±SEM alcohol consumption for four study groups. •—•, normal alcohol intake/normal caloric intake (n=20); •—○, normal alcohol intake/low caloric intake (n=22); ○—○, low alcohol intake/normal caloric intake (n=21); ○—○, low alcohol intake/low caloric intake (n=23).

Figure 2. Line graph shows mean±SEM change in weight for four study groups. •—•, normal alcohol intake/normal caloric intake (n=20); •—○, normal alcohol intake/low caloric intake (n=22); ○—○, low alcohol intake/normal caloric intake (n=21); ○—○, low alcohol intake/low caloric intake (n=23).

Bf during the intervention (r=0.41, p<0.001 and R=0.33, p=0.002, respectively). Baseline alcohol con-
EFFECTS ON BLOOD PRESSURE OF REDUCED DIETARY SODIUM AND THE DIETARY APPROACHES TO STOP HYPERTENSION (DASH) DIET

FRANK M. SACKS, M.D., LAURA P. SVETKEY, M.D., WILLIAM M. VOLLMER, PH.D., LAWRENCE J. APPEL, M.D., GEORGE A. BRAY, M.D., DAVID HARSHA, PH.D., EVA OBARZANEK, PH.D., PAUL R. CONLIN, M.D., EDGAR R. MILLER III, M.D., PH.D., DENISE G. SIMONS-MORTON, M.D., PH.D., NJERI KARANJA, PH.D., AND PAO-HWA LIN, PH.D.,
Diet and Lifestyle Risk Factors Associated With Incident Hypertension in Women

John P. Forman, MD, MSc
Meir J. Stampfer, MD, DrPH
Gary C. Curhan, MD, ScD

**Context** Hypertension is an important preventable risk factor for death among women. While several modifiable risk factors have been identified, their combined risk and distribution in the population have not been assessed.

<table>
<thead>
<tr>
<th>No Family History of Hypertension</th>
<th>No. (%) of Participants</th>
<th>No. of Hypertension Cases</th>
<th>Multivariable HR (95% CI)</th>
<th>Cases per 1000 Person-Years</th>
<th>NNT for 10 y</th>
<th>PAR, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of low-risk factors</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3: highest DASH quintile, daily vigorous exercise, BMI &lt;25&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1386 (3.2)</td>
<td>54</td>
<td>0.42 (0.32-0.56)</td>
<td>4.60</td>
<td>21.7</td>
<td>57 (43-67)</td>
</tr>
<tr>
<td>4: the 3 factors above plus alcohol intake 0.1-10.0 g/d&lt;sup&gt;f&lt;/sup&gt;</td>
<td>736 (1.7)</td>
<td>21</td>
<td>0.34 (0.23-0.53)</td>
<td>5.04</td>
<td>19.8</td>
<td>66 (47-77)</td>
</tr>
<tr>
<td>5: the 4 factors above plus nonnarcotic analgesic use &lt;1 d/wk&lt;sup&gt;g&lt;/sup&gt;</td>
<td>300 (0.9)</td>
<td>7</td>
<td>0.23 (0.11-0.48)</td>
<td>5.86</td>
<td>17.1</td>
<td>77 (52-89)</td>
</tr>
<tr>
<td>6: the 5 factors above plus folic acid supplementation ≥400 µg/d&lt;sup&gt;h&lt;/sup&gt;</td>
<td>123 (0.3)</td>
<td>1</td>
<td>0.10 (0.01-0.68)</td>
<td>6.82</td>
<td>14.7</td>
<td>90 (32-99)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Family History of Hypertension</th>
<th>No. (%) of Participants</th>
<th>No. of Hypertension Cases</th>
<th>Multivariable HR (95% CI)</th>
<th>Cases per 1000 Person-Years</th>
<th>NNT for 10 y</th>
<th>PAR, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of low-risk factors</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3: highest DASH quintile, daily vigorous exercise, BMI &lt;25&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1217 (3.0)</td>
<td>91</td>
<td>0.48 (0.39-0.59)</td>
<td>7.66</td>
<td>13.1</td>
<td>51 (40-60)</td>
</tr>
<tr>
<td>4: the 3 factors above plus alcohol intake 0.1-10.0 g/d&lt;sup&gt;f&lt;/sup&gt;</td>
<td>649 (1.6)</td>
<td>43</td>
<td>0.46 (0.34-0.63)</td>
<td>7.75</td>
<td>12.9</td>
<td>53 (37-66)</td>
</tr>
<tr>
<td>5: the 4 factors above plus nonnarcotic analgesic use &lt;1 d/wk&lt;sup&gt;g&lt;/sup&gt;</td>
<td>325 (0.8)</td>
<td>14</td>
<td>0.31 (0.19-0.53)</td>
<td>9.86</td>
<td>10.1</td>
<td>69 (47-81)</td>
</tr>
<tr>
<td>6: the 5 factors above plus folic acid supplementation ≥400 µg/d&lt;sup&gt;h&lt;/sup&gt;</td>
<td>122 (0.3)</td>
<td>5</td>
<td>0.31 (0.13-0.75)</td>
<td>9.87</td>
<td>10.1</td>
<td>69 (25-87)</td>
</tr>
</tbody>
</table>

Abbreviations: ARD, absolute risk difference; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); DASH, Dietary Approaches to Stop Hypertension; HR, hazard ratio; NNT, number needed to treat.

<sup>a</sup> The percentage represents those within the given strata (ie, among those with or without a family history of hypertension).

<sup>b</sup> Indicates the adjusted difference in hypertension incidence rate among the higher risk group minus the incidence rate among the lower risk group.

<sup>c</sup> Indicates the number of higher risk women that would have to adopt the low-risk factors for a period of 10 years to prevent the occurrence of 1 hypertension case.

<sup>d</sup> Indicates the percentage of new hypertension cases in the population that would hypothetically not have occurred if all women had been in the low-risk group.

<sup>e</sup> Adjusted for age, race, use of oral contraceptive pills, smoking status, alcohol use, nonnarcotic analgesic use, and supplemental folic acid intake.

<sup>f</sup> Adjusted for everything in footnote "e" except nonnarcotic analgesic use.

<sup>g</sup> Adjusted for everything in footnote "e" except nonnarcotic analgesic and alcohol use.

<sup>h</sup> Adjusted for everything in footnote "e" except folic acid intake.

©2009 American Medical Association. All rights reserved.
Healthy Lifestyle Through Young Adulthood and the Presence of Low Cardiovascular Disease Risk Profile in Middle Age

The Coronary Artery Risk Development in (Young) Adults (CARDIA) Study

Kiang Liu, PhD; Martha L. Daviglus, MD, PhD; Catherine M. Loria, PhD; Laura A. Colangelo, MS; Bonnie Spring, PhD; Arlen C. Moller, PhD; Donald M. Lloyd-Jones, MD, ScM

Background—A low cardiovascular disease risk profile (untreated cholesterol <200 mg/dL, untreated blood pressure <120/80 mm Hg, never smoking, and no history of diabetes mellitus or myocardial infarction) in middle age is associated with markedly better health outcomes in older age, but few middle-aged adults have this low risk profile. We examined whether adopting a healthy lifestyle throughout young adulthood is associated with the presence of the low cardiovascular disease risk profile in middle age.

Methods and Results—The Coronary Artery Risk Development in (Young) Adults (CARDIA) study sample consisted of 3154 black and white participants 18 to 30 years of age at year 0 (1985–1986) who attended the year 0, 7, and 20 examinations. Healthy lifestyle factors defined at years 0, 7, and 20 included average body mass index <25 kg/m², no or moderate alcohol intake, higher healthy diet score, higher physical activity score, and never smoking. Mean age (25 years) and percentage of women (56%) were comparable across groups defined by number of healthy lifestyle factors. The age-, sex-, and race-adjusted prevalences of low cardiovascular disease risk profile at year 20 were 3.0%, 14.6%, 29.5%, 39.2%, and 60.7% for people with 0 or 1, 2, 3, 4, and 5 healthy lifestyle factors, respectively (P for trend <0.0001). Similar graded relationships were observed for each sex-race group (all P for trend <0.0001).

Conclusions—Maintaining a healthy lifestyle throughout young adulthood is strongly associated with a low cardiovascular disease risk profile in middle age. Public health and individual efforts are needed to improve the adoption and maintenance of healthy lifestyles in young adults. (Circulation. 2012;125:996-1004.)
Does the source of Protein matter?

Effect of Dietary Protein Supplementation on Blood Pressure
A Randomized, Controlled Trial

Jiang He, MD, PhD; Marion R. Wofford, MD; Kristi Reynolds, PhD, MPH; Jing Chen, MD, MSc;
BLOOD-PRESSURE-LOWERING EFFECT OF A VEGETARIAN DIET: CONTROLLED TRIAL IN NORMOTENSIVE SUBJECTS

IAN L. ROUSE
BRUCE K. ARMSTRONG
LAWRENCE J. BEILIN
ROBERT VANDONGEN

TRIAL DESIGN

<table>
<thead>
<tr>
<th>Period 1</th>
<th>Period 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 weeks</td>
<td>6 weeks</td>
</tr>
</tbody>
</table>

1. Omnivore Diet (19)
2. Vegetarian Diet (19)
3. Omnivore Diet (20)

All Subjects — 50mg Vitamin C

Lancet 1983;1:5-10
Additive effects of Lifestyle changes can be large but not all cumulative

- Weight loss (Calories)
  - + Salt restriction  Tone TOHP 1 and 2
  - + Alcohol moderation Puddey 1992
  - + Daily Fish meal Bao 1998
  - + Exercise Cox 2001

- Soy Protein + Soluble Fibre Hodgson 2001

- Fruit and Vegetables + Low Fat Dairy (DASH) Appel 1997

- DASH + Salt restriction; Sacks 2001

- Multiple interventions eg. PREMIER 2003, ADAPT 2005 DEWIT, ENCORE 2010,
Effect of Sodium Level on Systolic Blood Pressure

Sacks et al. NEJM 2001;344:3
Acute effects of dietary nitrate on BP in healthy men and women

study design

Randomized controlled cross-over trial

Spinach meal (250 g spinach / 220 mg nitrate)

Control meal (rice milk 100ml as energy control)

THE DASH-SODIUM TRIAL

The Effects on Blood Pressure of Reduced Dietary Sodium and the DASH Dietary Pattern

Sacks et al NEJM 2001;344:3
Vegetarian diet in mild hypertension: a randomised controlled trial

BARRIE M MARGETTS, LAWRENCE J BEILIN, ROBERT VANDONGEN, BRUCE K ARMSTRONG

BRITISH MEDICAL JOURNAL, 6th December 1986, 293, 1468-1471

**FIG 2**—Changes in systolic blood pressure and weight in the three groups during trial. Broken lines represent period of ovolacto-vegetarian diet.
Conclusions

Despite the strong preclinical evidence of positive cardiometabolic effects, studies to date have not confirmed resveratrol’s benefit in humans.
1. Flavonoids (fruit/tea)
2. Nitrate (green leafy vegetables)

Linked via the proposed mechanism of benefit on BP: nitric oxide
Flavonoids and CVD
population studies

> 50 studies

High compared to low: tea / cocoa / soy / flavonoid intake

10-20% lower risk of CVD

Arab et al. Stroke. 2009
Hooper et al Am J Clin Nutr 2008
Tea and endothelial function

* Acute

* Chronic

Green tea

Black tea

Tea and FMD: RCTs

<table>
<thead>
<tr>
<th>Study</th>
<th>Net response (%)</th>
<th>95% CI</th>
<th>Weight (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ardalan et al. 2007</td>
<td>6.7</td>
<td>(4.4; 9.1)</td>
<td>4.3</td>
</tr>
<tr>
<td>Park et al. 2009</td>
<td>4.2</td>
<td>(2.1; 6.2)</td>
<td>4.7</td>
</tr>
<tr>
<td>Jochmann et al. 2008 (green tea)</td>
<td>3.8</td>
<td>(2.5; 5.1)</td>
<td>7.0</td>
</tr>
<tr>
<td>Duffy et al. 2001 (short-term)</td>
<td>3.7</td>
<td>(2.6; 4.8)</td>
<td>7.6</td>
</tr>
<tr>
<td>Alexopoulos et al. 2008</td>
<td>3.7</td>
<td>(0.7; 6.7)</td>
<td>3.2</td>
</tr>
<tr>
<td>Duffy et al. 2001 (long-term)</td>
<td>3.4</td>
<td>(2.3; 4.5)</td>
<td>7.5</td>
</tr>
<tr>
<td>Jochmann et al. 2008 (black tea)</td>
<td>2.7</td>
<td>(1.2; 4.2)</td>
<td>6.5</td>
</tr>
<tr>
<td>Grassi et al. 2009 (high dose)</td>
<td>2.5</td>
<td>(2.0; 3.0)</td>
<td>9.5</td>
</tr>
<tr>
<td>Hodgson et al. 2002</td>
<td>2.3</td>
<td>(0.7; 3.9)</td>
<td>6.3</td>
</tr>
<tr>
<td>Lorenz et al. 2007</td>
<td>2.2</td>
<td>(0.4; 4.0)</td>
<td>5.7</td>
</tr>
<tr>
<td>Grassi et al. 2009 (medium dose)</td>
<td>1.8</td>
<td>(1.2; 2.4)</td>
<td>9.4</td>
</tr>
<tr>
<td>Grassi et al. 2009 (low dose)</td>
<td>1.3</td>
<td>(0.5; 2.1)</td>
<td>8.7</td>
</tr>
<tr>
<td>Grassi et al. 2009 (very low dose)</td>
<td>1.2</td>
<td>(0.4; 2.0)</td>
<td>8.7</td>
</tr>
<tr>
<td>Hodgson et al. 2005 (without meal)</td>
<td>0.9</td>
<td>(-0.7; 2.5)</td>
<td>6.3</td>
</tr>
<tr>
<td>Hodgson et al. 2005 (with meal)</td>
<td>0.5</td>
<td>(-1.5; 2.5)</td>
<td>5.0</td>
</tr>
<tr>
<td>Overall effect</td>
<td>2.6</td>
<td>(1.8; 3.3)</td>
<td>100</td>
</tr>
</tbody>
</table>

Ras TE et al. Plos ONE 2011
6 mo intervention trial
study design

Baseline
3 cups per day
regular leaf tea

Placebo / control (n=48)
3 cups per day
flavour & caffeine matched, containing no tea solids

Tea (n=44)
3 cups per day
1.5 g powdered black tea / 429 mg of polyphenols / 96 mg of caffeine

Blood sample and 24 hour urine sample
24 hour ambulatory blood pressure assessment
Effect of the Mediterranean diet on blood pressure in the PREDIMED trial: results from a randomized controlled trial

Toledo et al.

Figure 2 Adjusted mean systolic and diastolic blood pressure at baseline and yearly visits according to intervention group. Values are adjusted for center, sex, age, type 2 diabetes and baseline blood pressure.
Framingham guidelines for the prevention and treatment of hypertension recommend sodium reduction, weight loss, Dietary Approaches to Stop Hypertension (DASH) diet, and regular aerobic exercise. However, no trial has assessed the efficacy of simultaneously implementing all of these recommendations. The objective of this study was to determine the effects of a lifestyle intervention on blood pressure and other cardiovascular disease risk factors of a comprehensive lifestyle intervention study. A randomized controlled trial of 44 hypertensive, overweight adults on a single blood pressure medication was randomized to a lifestyle or control group. For 9 weeks, the lifestyle group was fed a hypocaloric version of the DASH diet that provided 100 mmol/d of sodium. This group also participated in a supervised, high-intensity exercise program 3 times per week. The control group received no intervention. Outcomes included systolic blood pressure, serum lipids, weight, and fitness. At the end of the intervention, mean weight loss in the lifestyle group, net of control, was 4.9 kilograms. In the lifestyle group mean net reductions in 24-hour ambulatory systolic and diastolic blood pressures were 9.5 mm Hg ($P<0.001$) and 5.3 mm Hg ($P<0.002$), respectively. Corresponding changes in daytime systolic and diastolic blood pressures were 12.1 mm Hg ($P<0.001$) and 6.6 mm Hg ($P<0.001$). The lifestyle group experienced mean reductions in total cholesterol ($-25$ mg/dL, $P<0.001$), low-density lipoprotein cholesterol ($-18$ mg/dL, $P=0.005$), high-density lipoprotein cholesterol ($-5$ mg/dL, $P<0.001$). In conclusion, among hypertensive overweight adults already on antihypertensive medication, a comprehensive lifestyle intervention can substantially lower blood pressure and improve blood pressure control. *(Hypertension. 2018)*

**Key Words:** hypertension, essential □ clinical trials □ nutrition □ lifestyle
Cumulative Effects of Healthy Weight, Healthy Diet, not Smoking, and Exercise on Disease prevention:

**Coronary heart disease** - women
  Stampfer *NEJM* 2000;243

*Diabetes* - older adults
  Mozaffarian *Arch Int Med.* 2009;169

- women
  Chiuve *Circ.* 2008;118

**Stroke**
  Hu *NEJM.* 2001;345
What are the Active Components of DASH/Veg patterns? BP Lowering foods?

**Low fat dairy,**
- casein
- milk peptides
- calcium

**Fruit and vegetable,**
- K, Mg
- Fibre
- Protein-Soy, Legumes
- Alpha linolenic acid (flaxseed)

**Micronutrients**
- Anti-oxidant
- Anti-inflammatory
- Nitric oxide generating
- Vitamins: C, B, folate, D.

**Nuts**- fibre or N3 fats

**Fish**- N3 fats DHA
What are the Active Components of DASH diet patterns?

**BP Lowering foods?**

Low fat dairy,

Fruit and vegetable,

Nuts

Fish

Micronutrients
Some Foods and Nutrients that lower BP in RCT’s

- Fish and N3 fatty acids
- Flaxseed oil
- Soluble fibre-Psyllium
- Legumes
- Protein- Lean Meat vs Carbohydrate
  - Soy
  - Casein (low fat dairy)
- Beetroot juice and other fruit / vegetable extracts
- Tea
Diet and Lifestyle in Hypertension
Prevention and Management:
Seeking Evidence and Elixirs

Why bother?
Are BP effects of lifestyle factors additive?

2 factors: $5 + 5 = 10$

5 factors: $5 \times 5 = 25$
Randomised Double Blind Controlled Trials and Meta-analyses.

The Gold Standard ?
More Trial Issues

Population - selection bias

Blood pressure a surrogate

Diet/ Lifestyle changes multiple effects

Few “Clinical Outcome” trials
The Dietary Approaches to Stop Hypertension (DASH) trial

Appel LJ et al. NEJM 1997; 336:1117
THE DASH DIETARY PATTERN: *Foods*

**Emphasizes:**
- Fruits, Vegetables, Low-fat Dairy Foods
- Whole Grains, Nuts, Poultry, Fish

**Reduced:**
- Fats, Red Meat,
- Sweets, Sugar-containing Beverages.

Tea and endothelial function

Tea and FMD: RCTs

* Acute

* Chronic

Green tea

Black tea

Ras TE et al. Plos ONE 2011
combinations of 3 (normal BMI, daily vigorous exercise, and DASH-style diet), 4 (3 low-risk factors plus modest alcohol intake), 5 (4 low-risk factors plus avoidance of nonnarcotic analgesics), and 6 (folic acid supplementation 400 μg/d) low-risk factors and the risk of developing hypertension was analyzed.

**Main Outcome Measures** Adjusted hazard ratios for incident self-reported hypertension and population attributable risks (PARs).

**Results** A total of 12,319 incident cases of hypertension were reported. All 6 modifiable risk factors were independently associated with the risk of developing hypertension during follow-up after also adjusting for age, race, family history of hypertension, smoking status, and use of oral contraceptives. For women who had all 6 low-risk factors (0.3% of the population), the hazard ratio for incident hypertension was 0.22 (95% confidence interval [CI], 0.10-0.51); the hypothetical PAR was 78% (95% CI, 49%-90%) for women who lacked these low-risk factors.