INTEGRATIVE MEDICINE AS AN ECONOMIC STRATEGY FOR CHRONIC DISEASE

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Co-FOUNDER & MEDICAL DIRECTOR OF GUARNERI INTEGRATIVE HEALTH, INC.
Pacific Pearl, La Jolla, CA

Board-certified in Cardiovascular Disease, Internal Medicine, Nuclear Cardiology and Integrative Holistic Medicine, Mimi Guarneri, MD, FACC, ABOIM is President of the Academy of Integrative Health and Medicine (AIHM) and the Past President of the American Board of Integrative Holistic Medicine (ABIHM). She served as Senior Advisor to the Atlantic Health System for the Chambers Center for Well Being. Dr. Guarneri currently serves on the Founding Board of the American Board Physician Specialties in Integrative Medicine, and is a Clinical Associate Professor at University of California, San Diego (UCSD).

Dr. Guarneri is Co-founder and Medical Director of Guarneri Integrative Health, Inc. at Pacific Pearl La Jolla in La Jolla, California, U.S.A. since 2014. She was an English Literature major as an undergraduate at New York University. Her medical degree is from SUNY Medical Center in New York, where she graduated number one in her class. Dr. Guarneri served her internship and residency at Cornell Medical Center, where she later became Chief Medical Resident. She served cardiology fellowships at both New York University Medical Center and Scripps Clinic. She is a Fellow Member of the American College of Cardiology, Alpha Omega Alpha, and the American Medical Women’s Association.

Dr. Guarneri co-founded the Scripps Center for Integrative Medicine and served as Medical Director for 15 years. She began her career at Scripps Clinic as an attending in interventional cardiology, where she placed thousands of coronary stents. Recognizing the need for a more comprehensive and more holistic approach to cardiovascular disease, she pioneered the Scripps Center for Integrative Medicine where state-of-the-art cardiac imaging technology and lifestyle change programs are used to aggressively diagnose, prevent and treat cardiovascular disease. Dr. Guarneri then co-founded Guarneri Integrative Health, Inc. and Pacific Pearl La Jolla where she maintains her clinical practice and serves as Medical Director to a team of experts in Conventional, Integrative and Natural Medicine in La Jolla, California.

Dr. Guarneri is author of “108 Pearls to Awaken Your Healing Potential” (Hay House, 2017) and “The Heart Speaks” (Simon & Schuster, 2007). She is co-author of the book, “Total Engagement: The Healthcare Practitioner’s Guide to Heal Yourself, Your Patients & Your Practice,” (Changewell, 2014). She also is the professor of The Great Courses video/audio series, “The Science of Natural Healing.” Dr. Guarneri and her work have been featured on numerous television shows such as NBC Today and PBS, among others. She also was featured in a 2-part documentary, “The New Medicine,” from PBS.

Dr. Guarneri has been recognized for her national leadership in Integrative Medicine by the Bravewell Collaborative and has served as chair of the Bravewell Clinical Network for Integrative Medicine. In 2009, Dr. Guarneri was honored as the ARCS Scientist of the Year (Achievement
Rewards for College Scientists). In 2011, Dr. Guarneri was the winner of the Bravewell Leadership Award which honors a physician leader who has made significant contributions to the transformation of the U.S. health care system. She received the 2012 Linus Pauling Functional Medicine Lifetime Achievement Award from the Institute for Functional Medicine and the Grace A. Goldsmith Award from the American College of Nutrition. In 2015, Newsmax Media ranked her as number six out of the top 100 physicians who embrace Integrative Medicine. She was honored in 2016 with the Lights of LightBridge Award from the LightBridge Hospice Foundation and also as 2016 Health & Wellness Pioneer from San Diego Magazine’s Woman of the Year Awards.

**OBJECTIVES:**
Participants should be better able to:

1. Overview of chronic disease nationally and globally;
2. Overview of research on etiology of chronic disease;
3. Integrative health treatment strategies and care plans to decrease burden of chronic disease.
Integrative Cardiology: Health Creation as an Economic Strategy

NAMDCR’S 41st Annual Meeting
Omni La Costa Resort 2018
Mimi Guarneri MD FACC ABOIM
President Academy Integrative Health and Medicine
Cardiovascular diseases are the leading causes of death in the world

Around 3 in 10 deaths globally are caused by cardiovascular diseases – diseases of the heart and blood vessels that can cause heart attacks and stroke. At least 80% of premature deaths from cardiovascular diseases could be prevented through a healthy diet, regular physical activity and avoiding the use of tobacco.

WHO 2016
Adult Obesity Rate by State, 2013

Select years with the slider to see historical data. Hover over states for more information. Click a state to lock the selection. Click again to unlock.

Percent of obese adults (Body Mass Index of 30+)

- 0 - 9.9%
- 10 - 14.9%
- 15 - 19.9%
- 20 - 24.9%
- 25 - 29.9%
- 30 - 34.9%
- 35%+
NAFLD on the Rise

If the current rates of obesity and diabetes continue for another two decades, the prevalence of **NAFLD** in the US is expected to increase by 50% in 2030.

Almost 1 in 10 Adults has Diabetes

Almost 10% of the world’s adult population has diabetes, measured by elevated fasting blood glucose (≥126 mg/dl). People with diabetes have increased risk of heart disease and stroke. Deaths due to diabetes have been increasing since the year 2000, reaching 1.5 million deaths in 2012.

WHO 2016
The Cost of Care

The United States spends more on medical care per person than any country, yet life expectancy is shorter than in most other developed nations and many developing countries. The U.S. healthcare system costs the nation an estimated $8,800 per person a year. Why the high cost? The U.S. has a fee-for-service system—paying medical providers primarily for appointments, surgery, and the like. That can lead to unnecessary treatment that doesn’t reliably improve a patient’s health. Says Gerard Anderson, a professor at Johns Hopkins Bloomberg School of Public Health who studies health insurance worldwide, “More care does not necessarily mean better care.”

Michelle Andrews

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Health care spending per person, in U.S. dollars

<table>
<thead>
<tr>
<th>Country</th>
<th>Spending per Person</th>
</tr>
</thead>
<tbody>
<tr>
<td>Switzerland</td>
<td>$14,317</td>
</tr>
<tr>
<td>Luxembourg</td>
<td>$12,813</td>
</tr>
<tr>
<td>Canada</td>
<td>$10,655</td>
</tr>
<tr>
<td>Australia</td>
<td>$9,705</td>
</tr>
<tr>
<td>France</td>
<td>$9,911</td>
</tr>
<tr>
<td>Denmark</td>
<td>$8,912</td>
</tr>
<tr>
<td>Sweden</td>
<td>$3,333</td>
</tr>
<tr>
<td>AVERAGE</td>
<td></td>
</tr>
<tr>
<td>Australia</td>
<td>$2,167</td>
</tr>
<tr>
<td>UK</td>
<td>$2,235</td>
</tr>
<tr>
<td>Ireland</td>
<td>$2,450</td>
</tr>
<tr>
<td>Spain</td>
<td>$2,711</td>
</tr>
<tr>
<td>New Zealand</td>
<td>$2,793</td>
</tr>
<tr>
<td>Portugal</td>
<td>$3,150</td>
</tr>
<tr>
<td>South Korea</td>
<td>$2,840</td>
</tr>
<tr>
<td>Czech Republic</td>
<td>$2,850</td>
</tr>
<tr>
<td>Slovak Republic</td>
<td>$2,999</td>
</tr>
<tr>
<td>Hungary</td>
<td>$3,200</td>
</tr>
<tr>
<td>Poland</td>
<td>$3,290</td>
</tr>
<tr>
<td>Costa Rica</td>
<td>$3,333</td>
</tr>
<tr>
<td>Mexico</td>
<td>$3,417</td>
</tr>
</tbody>
</table>

Average number of visits a year

- Switzerland: 9
- Luxembourg: 8
- Canada: 7
- Australia: 6
- France: 5
- Denmark: 5
- Sweden: 4
- Average: 5
- Australia: 12
- UK: 11
- Ireland: 10
- Spain: 9
- New Zealand: 9
- Portugal: 9
- South Korea: 8
- Czech Republic: 8
- Slovak Republic: 8
- Hungary: 8
- Poland: 8
- Costa Rica: 8
- Mexico: 8

Average life expectancy at birth

- Switzerland: 84
- Luxembourg: 80
- Canada: 79
- Australia: 79
- France: 79
- Denmark: 79
- Sweden: 78
- Average: 78

Dollar figures reflect all public and private spending on care, from doctor visits to hospitals, to the nation’s health. June 2007


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AIHIM

Academy of Integrative Heath & Medicine
Each individual diagnosis becomes a distinct entity unto itself.
Pharmaceutical Industry and GDP

Poly-pills for poly-ills?
“The United States spends much more money on health care than any other country. Yet Americans die sooner and experience more illness than residents in many other countries. While the length of life has improved in the United States, other countries have gained life years even faster, and our relative standing in the world has fallen over the past half Century. The nation’s current health trajectory is lower in success and higher in cost than it should be. The cost of inaction is high”.

Harvey Fineburg
President IOM
“It ain’t what you don’t know that gets you into trouble. It’s what you know for sure that just ain’t so.”

Mark Twain
Health as an Economic Strategy

Your Genes Are Not Your Destiny

- Genetics
- Physiology / Biochemistry
- Environment
- Lifestyle

70 - 90% of chronic disease
Our Genes Haven’t changed, but our Environment Has...

“According to the thrifty genotype theory, few if any changes in genes or gene sequences have occurred over the past 10,000 years.”


What Epigenetics Means

The Gene-Environment Connection

"Turning Off" Cancer-Causing Genes by Intensive Lifestyle Changes
(red = turned on; green = turned off)

Pre-intervention

Post-intervention
Understanding The Origin Of Chronic Disease

Environment

Body

Decreased Energy Production

Oxidative Stress

Toxic Chemical Exposure

Radiation

Drugs, Alcohol

Smoking

Stress, Negative Emotions

Poor Diet

Trauma

Smoking

Lack of Exercise

Diet

Poor

Trauma

Drugs, Alcohol

Stress,

Negative

Emotions

Smoking

Lack of

Exercise

Inflammation and Preclinical Symptoms

Chronic Disease

Structural Stresses

WHO 2017

Delegates at the World Health Assembly adopted a resolution to address the health impacts of air pollution – the world’s largest single environmental health risk. Every year 4.3 million deaths occur from exposure to indoor air pollution and 3.7 million deaths are attributable to outdoor air pollution. This was the first time the Health Assembly had debated the topic.

2017 Air pollution is number one cause of stroke and an independent risk factor for CAD.

CAPITAL BREATHES UNEASY

Tops global cities with worst air pollution

1. NEW DELHI, INDIA
2. BEIJING, CHINA
3. CAIRO, EGYPT
4. SANTIAGO, CHILE
5. MEXICO CITY, MEXICO

INDIA SUPS IN RANK TOO

Is second most polluted among its neighbours

2014

2018

2019

Bangladesh

169

139

India

199

129

Pakistan

148

125

Nepal

139

59

China

138

121

Sri Lanka

69

50

- Ranking based on 9 parameters: Health impact, air quality, water & sanitation, vector borne disease, crop yield, agriculture productivity, forest biodiversity & habitat, dengue fever & chikungunya.
- On list of 226 countries, India ranks as 25th worst air pollution, 127th on health impact.
- CLEANEST COUNTRIES: Switzerland, Luxembourg, Australia, Singapore and Czech Republic.
Arsenic in Drinking Water

Elevated mortality rates were observed for both males and females for all diseases of the circulatory system [SMR ≈ 1.13], cerebrovascular diseases [SMR = 1.19], diabetes mellitus [SMR ≈ 1.28], and kidney diseases [SMR ≈ 1.33].


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Persistent organic pollutants, mitochondrial dysfunction, and metabolic syndrome


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Much evidence has emerged showing that environmental toxins, including POPs, affect mitochondrial function and subsequently induce insulin resistance.\(^5\)

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**Introduction**

What is metabolic syndrome? During the past few decades, cardiovascular disease has been ranked as the main cause of morbidity and mortality in developed countries. Multiple cardiovascular disease risk factors, such as obesity, type 2 diabetes mellitus (T2DM), dyslipidemia, and hyper tension are often present.\(^1\) This clustering of risk factors and its association with insulin resistance led investigators to propose a pathophysiological condition called “metabolic” or “insulin resistance syndrome.”\(^2\)

While the definition of metabolic syndrome emphasizes its clinical aspect, insulin resistance is regarded as its common pathophysiological abnormality. Insulin resistance is an important pathophysiological factor in the development of T2DM and cardiovascular disease. Insulin resistance is caused by a complex interplay between nutrient overload, systemic fatty acid excess, oxidative damage, inflammation, hyperglycemia, and endoplasmic reticulum (ER) stress. Reactive oxygen species and oxidative damage. During the process of reduction of oxygen to water by the electron transport chain, reactive oxygen species (ROS), such as superoxide, hydrogen peroxide, the hydroxyl radical, and nitric oxide, are generated and cause oxidative damage to target tissues.\(^3\) An imbalance between the production of ROS and antioxidants is a hallmark of insulin resistance.\(^2\)

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**Keywords:** persistent organic pollutants; mitochondrial dysfunction; metabolic syndrome; insulin resistance


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**Inflammation.** Obesity, insulin resistance, and T2DM are closely associated with chronic “inflammation,” characterized by abnormal cytokine production, increased levels of acute-phase reactants, and activation of a network of inflammatory signaling pathways. There is much experimental and clinical evidence that the presence of chronic inflammation may play a significant role in the pathophysiology of metabolic syndrome.\(^2\)
Acute or Chronic Lead Exposure

Whether acute exposure or chronic accumulation, blood lead and tibial lead levels were associated with the degree and occurrence of hypertension.


Evaluating the Endothelium which Maintains Vascular Health

Dilatation
Growth Inhibition
Antithrombotic
Anti-inflammatory
Antioxidant

Nitric Oxide

Constriction
Growth
promotion
Pro-thrombotic
Pro-inflammatory
Pro-oxidant

Angiotensin II
Risk Determinants of Health

hs-CRP
LPa
LDL-P Size & Number
LDL Pattern A vs. B
HDL 2B
VLDL3
Modified LDL (oxLDL)
Dysfunctional HDL
ApoBApoA1 ratio
Homocysteine
Vitamin D deficiency
TMAO

Oxidative stress (markers MPO, F2I)
Lp-PLA2
CIMT
CAC Scoring
Nutrition
Stress
Depression
Social isolation
Pollution
Toxins and heavy metals
Microbiome
So Where Do We Begin?

- Type 2 Diabetes
- Atherosclerosis
- Dyslipidemia
- Muscle loss
- Hypertension
- Sleep Apnea
- Erectile Dysfunction
- Gout
- Fatty Liver
- Osteoporosis
- Cognitive Decline / Alzheimer's Disease

52-year-old man
Lifestyle:
- Occasional alcohol use
- AHA diet and exercise program for 6 months

Comorbidities
- Type 2 diabetes
- Hypertension
- Sleep apnea
- CAD s/pCABG
- Medications
  - Lisinopril/HCTZ
  - Aspirin
  - Metformin

Fasting Lipid panel:
- TG: 585 mg/dL
- TC: 209 mg/dL
- HDL-C: 38 mg/dL
- LDL-C: incalculable
- Non-HDL-C: 171 mg/dL

Fasting blood sugar:
- 125 mg/dL

HbA$\text{1c}$:
- 6.9%
- hsCRP 3.5

Other results:
- WNL
Conventional Treatment Guidelines

Treat hypertension
Goal blood pressures < 130/80 mm Hg

Treat hyperlipidemia
LDL-C goal: <100 mg/dl (<130 mg/dl - primary prevention)
Statins
Optimize triglycerides and HDL goals
Goal trigs <100 mg/dl; HDL >50F, >40M
Fibrates, Niacin, and/or Omega 3 Fatty Acids

Treat diabetes
Goal FBG < 100 mg/dl
Metformin as first-line drug therapy
Aspirin therapy

“We will never be able to solve our problems at the same order of complexity we used to create our problems”

Albert Einstein
Prevention Is The Best Intervention
Lifestyle Is An Intervention

Let Food Be Your Medicine
Mediterranean Diet

Lyon Diet Heart Study, 27 month prospective RCT, n=300

- 70% RR reduction for overall mortality, 73% RR reduction for fatal and non-fatal MI
- Significant RR reductions for: angina, stroke, heart failure, pulmonary embolism and CVT
- Outcomes independent of TC, systolic BP, male sex, aspirin use
- Compliance >70%

Substantial evidence indicates that diets using non hydrogenated fats as the predominant dietary fat, whole grains as the main form of carbohydrates, an abundance of fruit and vegetables, and adequate omega-3 fatty acids can offer significant protection against CHD.

Compared with patients consuming the control diet, patients consuming the intervention diet had significantly reduced serum concentrations of hs-CRP, IL-6, IL-7, and IL-18, as well as decreased insulin resistance.”

“A Mediterranean-style diet might be effective in reducing the prevalence of the metabolic syndrome and its associated cardiovascular risk.”

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

Knoops KTB et al. 

**PREDIMED:** Mediterranean Diet vs. Low-Fat Diet

Three groups:
1. Med. Diet + EVOO (Extra Virgin Olive Oil)
2. Med. Diet + nuts
3. Low-fat diet
4. Educed the incidence of major cardiovascular events by 30% and 28% respectively

**Dietary Interventions: Summary**

**Cardiovascular-Related Outcomes of Selected Diets**

<table>
<thead>
<tr>
<th>DIET TYPE</th>
<th>LDL</th>
<th>HDL</th>
<th>TRIGLYCERIDES</th>
<th>CARDIOVASCULAR EVENTS</th>
<th>BMI</th>
<th>STRENGTH OF EVIDENCE FOR CARDIOVASCULAR OUTCOMES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very low-carbohydrate</td>
<td>No change</td>
<td>Increase</td>
<td>Decrease</td>
<td>No data</td>
<td>Decrease</td>
<td>C</td>
</tr>
<tr>
<td>Low-carbohydrate/low-glycemic index</td>
<td>No change</td>
<td>No change</td>
<td>No change</td>
<td>No data</td>
<td>Decrease</td>
<td>C</td>
</tr>
<tr>
<td>Very low-fat</td>
<td>Decrease</td>
<td>Decrease</td>
<td>Decrease</td>
<td>Decrease</td>
<td>Decrease</td>
<td>B</td>
</tr>
<tr>
<td>Mediterranean diet</td>
<td>Decrease/no change</td>
<td>Increase</td>
<td>Decrease</td>
<td>Decrease</td>
<td>No change</td>
<td>A</td>
</tr>
<tr>
<td>American Heart Association guidelines</td>
<td>Decrease</td>
<td>Increase</td>
<td>No change</td>
<td>No data</td>
<td>Decrease</td>
<td>C*</td>
</tr>
</tbody>
</table>


**Intensive Lifestyle Changes for Reversal of Coronary Heart Disease**

Lifestyle Heart Trial (Ornish, 1998), 5 yr intervention

- 10% fat whole foods vegetarian diet
- Aerobic exercise
- Stress management training
- Smoking cessation
- Group psychosocial support

**Outcomes**

- 8% relative stenosis diameter improvement (control 28% relative worsening)
- 2.47 RR for cardiac events in control vs treatment

Lifestyle Heart Trial
Stenosis Reduction

No diet is healthy without exercise!

You lose muscle mass

Leads to Yo-Yo dieting
increases cardio-vascular risk

Diabetes Prevention Program

3234 overweight subjects (Ages 25-85 years) with IGT

High-Risk for Diabetes

- 45% Non-white
- Women with history of gestational DM
- Subjects with first-degree-relative with DM

3 years

Lifestyle intervention to reduce weight by 7%
- Diet
- Exercise

Metformin 850 mg bid

Placebo
Anti-inflammatory effect of exercise training in subjects with type 2 diabetes and the metabolic syndrome is dependent on exercise modalities and independent of weight loss

Weight Loss & Hypertension

Each lost pound of weight loss $\rightarrow$ 1 mmHg drop in systolic and diastolic blood pressure

This is independent of blood pressure medication and sodium restriction

52-year-old man

Lifestyle:
- Occasional alcohol use
- AHA diet and exercise program for 6 months

Comorbidities
- Type 2 diabetes
- Hypertension
- Obesity
- CAD s/pCABG

Medications
- Lisinopril/HCTZ
- Aspirin
- Metformin

Fasting Lipid panel:
- TG: 585 mg/dL
- TC: 209 mg/dL
- HDL-C: 38 mg/dL
- LDL-C: incalculable
- Non–HDL-C: 171 mg/dL

Fasting blood sugar:
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Other results:
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Low Glycemic
- Apples
- Berries/Cherries
- Peach
- Pear
- Grapefruit
- Legumes
- Nuts and Seeds
- Oatmeal Slow Cooked
- Fiber one
- Green Leafy Veggies
- Tomatoes
- Cruciferous Vegetables
- Eggplant
- 100% Whole Grains

High Glycemic
- Candy
- Cookies
- Juices
- White Potatoes and Fries
- Chips
- Sugar
- Breakfast Cereals
- Soda/alcohol
- Sweet snacks
- White bread/bagels
- White Rice
- Soda
- Fruit Juice
- Alcohol
- Wheat
Pharmacologic Treatment Options for Hypertriglyceridemia

- Omega 3
- Statins
- Fibrates
- Niacin

LOVAZA 4 g/day Significantly Reduced Triglycerides

The LDL-C value for patients receiving LOVAZA increased from a median baseline of 89 mg/dL to a median of 109 mg/dL, a median increase of 45%.

- There was a 6.7% median increase in triglycerides with placebo.
**Curcumin Extract for Prevention of Type 2 Diabetes**

Chuengsamarn and Associates

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**Probiotics**

"Intake of L. acidophilus NCFM for 4 weeks preserved insulin sensitivity compared with placebo...."

Magnesium and Insulin Resistance

Dietary Magnesium Intake in Relation to Plasma Insulin Levels and Risk of Type 2 Diabetes in Women

Magnesium is a mineral that is essential for energy production and other metabolic processes. Low magnesium intake has been associated with an increased risk of type 2 diabetes. The study conducted by researchers in Japan aimed to investigate the relationship between dietary magnesium intake and plasma insulin levels in women.

**Objective:** To determine if there is a significant association between magnesium intake and plasma insulin levels in a group of Japanese women.

**Methods:** A cross-sectional study was conducted involving 1,656 women aged 65 years or older. Dietary intake was assessed using a 3-day food record, and plasma insulin levels were measured.

**Results:** The study found a positive correlation between magnesium intake and plasma insulin levels. Women in the highest quartile of magnesium intake had significantly higher plasma insulin levels compared to those in the lowest quartile.

**Conclusions:** The study suggests that a higher magnesium intake may be associated with increased plasma insulin levels in older Japanese women, although further research is needed to confirm these findings and understand the underlying mechanisms.

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**Magnesium Intake in Relation to Systemic Inflammation, Insulin Resistance and Incidence of Diabetes**

Magnesium Deficiency → ↑ insulin resistance, ↑ hs-CRP, ↑ fibrinogen, ↑ IL-6

Magnesium ↑ = ↓ hs CRP, ↓ IR

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**Diabetes Care 2010 Aug 31.**
Song, Y. Diabetes Care 2004; 27:134-140.
Bergamot

RCT shows reduction in TC, LDL, TG and glucose; increase in HDL
Has vasodilatory effect
Reduces LDL-P
Mechanism is inhibition of HMG-CoA reductase activity

420 patients with class III or IV HF who were randomized to CoQ10 three times daily or placebo.

Significant reduction in the incidence of major adverse cardiovascular events in the CoQ10 group: 14% (29 patients) in the CoQ10 group versus 25% (55 patients) in the placebo group (hazard ratio 2.0, CI 1.3-3.2, p=0.003). Significant reduction in overall mortality: 9% (18 patients) in the CoQ10 group versus 17% (18 patients) in the placebo group (HR 2.1, CI 1.2-3.8, p=0.01). There were also significant reductions in cardiovascular mortality (p=0.02) and HF hospitalizations (p=0.05).

<table>
<thead>
<tr>
<th>Agent</th>
<th>Dose</th>
<th>Reported Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trans Resveratrol</td>
<td>250 mg QD</td>
<td>Reduces TC, TG, and LDL; blocks uptake of modified LDL by CD36SR (1)</td>
</tr>
<tr>
<td>N-Acetyl-Cysteine</td>
<td>1000 mg BID</td>
<td>Blocks uptake of modified LDL by CD36SR (1)</td>
</tr>
<tr>
<td>Aged Garlic Extract</td>
<td>600-900 mg BID</td>
<td>Reduces CAC and plaque progression and lowers HS-CRP (2,3)</td>
</tr>
<tr>
<td>Niacin (B3) Nicotinic Ac.</td>
<td>500 to 4000 mg QD as tolerated</td>
<td>Reduces TC, LDL, APO-B, TG, and shifts LDL from small type B to large type A (4)</td>
</tr>
<tr>
<td>Red Yeast Rice</td>
<td>2400-4800 mg QD</td>
<td>Statin like effects (5)</td>
</tr>
<tr>
<td>Curcumin</td>
<td>500 mg BID</td>
<td>Inhibits atherosclerosis, increases HDL, anti-inflammatory (6, 7)</td>
</tr>
<tr>
<td>Green Tea/ EGCG</td>
<td>500-1000 mg QD or 60 oz tea</td>
<td>Inhibits HMG-CoA, reduces oxiLDL and APO-B, increases PON-1 and LDL receptor; decreases inflammation decreases body fat. (8, 9)</td>
</tr>
<tr>
<td>Plant Sterols</td>
<td>2-3 g QD</td>
<td>Reduces TC and LDL, anti-inflammatory (10, 11)</td>
</tr>
<tr>
<td>Pomegranate</td>
<td>8 oz. juice or 1-2 cups of seeds QD</td>
<td>Anti-inflammatory, improves function of HDL, inhibits platelets, reduces IMT (12, 13, 14)</td>
</tr>
<tr>
<td>Pantethine</td>
<td>300 mg TID or 450 mg BID</td>
<td>Reduces TC, LDL, APO-B, and TG; increases HDL and APO-A1 (15, 16)</td>
</tr>
<tr>
<td>Probiotics</td>
<td>60-100b organisms QD</td>
<td>Reduce TC, LDL, and TG (17)</td>
</tr>
<tr>
<td>Berberine HCL</td>
<td>500 mg QD</td>
<td>Reduces TC, LDL, and TG (19)</td>
</tr>
<tr>
<td>Omega-3 Fatty Acids</td>
<td>1-5g QD mixed EPA DHA</td>
<td>Reduces TG (18), COX-2 inhibition by DHA, (21), IL-1b inhibition by EPA (22), Increases HDL/HDL2 (23), EPA reduces pattern-B, sLDL &amp; CRP (24)</td>
</tr>
</tbody>
</table>
“Of the ten leading causes of illness and death in the U.S., seven could be greatly reduced if the following lifestyle habits were modified - alcohol abuse, lack of exercise, poor diet, smoking, and unhealthy maladaptive responses to stress and tension.”

Former U.S. Surgeon General
Julius B. Richmond, M.D.

So What Is Stress?

Stress can be defined as a state one experiences when there is a mismatch between perceived demands and our perceived ability to cope.

Stress can be acute or chronic.
The Stress Response

- Response
- Perception
- Initiating Event
- Effect
50 years ago, a method for the quantification of representative life-changing events was developed by Drs. Rahe and Holmes.
Dr. Rahe’s next study, of 67 fellow physicians, found ranges of Illness Risks from LCU values:

0 - 150 LCU = 0% of illness
151 - 300 LCU = 30% illnesses
301 - 500 LCU = 50% illness
The Los Angeles County Coroner reported a sharp increase (5x) in cardiovascular disease related sudden deaths on the day of the Northridge earthquake.

NEJM 1996;334:413-419

The Stress Response

Enhanced coagulation
High Renin Angiotensin

Increased sympathetic
Parasympathetic
tone

- Trophic effects
- High blood pressure
- Tachycardia arrhythmia
- Abnormal lipids
- Weight increase
- Insulin resistance
Warning Signs

• Loss of focus and mental clarity
• Lack of ability to relax and sleep
• Loss of self esteem
• Feeling tired and on edge/Anger

High Cortisol : Low DHEA

Brain cell death (Kerr et al., 1991; Sapolsky, 1992)
Impaired memory and learning (Kerr et al., 1991; Sapolsky, 1992)
Decreased bone density; increased osteoporosis (Manolagas, 1979)
Reduced muscle mass (Beme, 1993)
Reduced skin growth and regeneration (Beme, 1993)
Impaired immune function (Hiemke, 1994)
Increased blood sugar (DeFeo, 1989)
Increased fat accumulation around waist / hips (Marin, 1992)
Gut disturbance, dysbiosis and immune dysregulation
Elevation in IL1, IL6 TNF-alpha and thus hs CRP
Decrease in testosterone'
Poor conversion of T4 to T3

Chronic stress = excess cortisol = accelerated aging
STRESS AND CORONARY HEART DISEASE

• Stress can cause coronary vasoconstriction and increased platelet stickiness that promote clot formation.

• Type A behavior, depression, anxiety, hostility, stressful life change events have all been linked to CHD.

• Stress increases homocysteine, CRP and fibrinogen, all of which are associated with increased risk for CHD.

• Stress causes deep abdominal fat deposits which secrete inflammatory cytokines that promote insulin resistance and the cardiovascular complications of metabolic syndrome.

• Stress causes atrial fibrillation, the most common sustained arrhythmia as well as ventricular fibrillation, the leading cause of sudden death.

• Stress causes Takotsubo cardiomyopathy, also referred to as “Broken Heart Syndrome”. This “myocardial stunning” is due to severe left ventricular contractile dysfunction that frequently mimics a massive myocardial infarction.

• Stress reduces heart rate variability

• Stress can precipitate and/or worsen congestive heart failure.
Top Ten U.S. Addictions

1. Alcohol
2. Smoking
3. Drugs
4. Gambling
5. Overeating
6. Video games
7. Internet
8. Sex
9. Shopping
10. Work

STRESS MECHANISMS THAT PROMOTE ATHEROSCLEROSIS

HPA=Hypothalamic-Pituitary Adrenal Axis
SNS=Sympathetic Nervous System
Follow-up of 5.4 years, there was a 48% risk reduction in the primary end point in the TM group (hazard ratio, 0.52; 95% confidence interval, 0.29–0.92; P=0.025).

The TM group also showed a 24% risk reduction in the secondary end point (hazard ratio, 0.76; 95% confidence interval, 0.51–0.1.13; P=0.17).

There were reductions of 4.9 mmHg in systolic blood pressure (95% confidence interval –8.3 to –1.5 mmHg; P=0.01) and anger expression (P<0.05 for all scales). Adherence was associated with survival.