Supplements, Vitamins, Hormones, etc. in Heart Disease: Do any of them work? Do any of them hurt?

J. Brent Muhlestein, MD, FACC
Director of Cardiology, Intermountain Medical Center, Intermountain Healthcare; Chair, The Deseret Foundation Professor of Internal Medicine, University of Utah
Supplements, Vitamins, etc.
In Heart Disease:
Do Any of Them Work?

Brent Muhlestein, MD
Intermountain Heart Institute
Dietary supplement use in the United States has increased since the National Health and Nutrition Examination Survey (NHANES) III (1988–1994).

Figure 1. Trends in the percentage of persons using dietary supplements, by gender for adults aged 20 and over: United States, 1988–2006
what are you waiting for?

Get on the path to good health today with Isotonix® Vitamin B-12 Special Formula!

With an excellent source of vitamin B12 and folic acid, Isotonix® Vitamin B-12 Special Formula is a great addition to your daily regimen. Taking Isotonix® Vitamin B-12 Special Formula may assist with promoting overall general health and well-being.

the time is now
to make it happen

I don't know about you, but I am sick and tired of hearing about how poorly our economy is doing. Each day the news gets worse, and it's everywhere you turn — on the morning radio shows, major network stations, and every newspaper are filled with more and more depressing headlines. Maybe it's because I anticipated this whole collapse coming, but enough is enough. I'm fed up with it now, and I'm ready to move on!

The problem is that when you surround yourself with this bad news, eventually you'll start to believe it. Sometimes, you can get so caught up focusing on the problem that you can't see it and ignore the solution. Don't give in to the fact that things are tough and simply hope to weather the economic storm. Instead, you should be surrounding yourself with successful, forward-thinking individuals, positive uplifting messages and, most of all, you should be seizing the opportunity at hand as the economic cards are being redistributed across the board.

Although it's true that we cannot change the troubled state of the world overnight, what we can do collectively is learn from past mistakes so we don't fall into them again, and to fully comprehend the problems so that we can properly plan our way out. Change is the core of our global economy. Overseas, Australian sales are still relatively strong and production and printing of Isotonix® Vitamin B-12 Special Formula is going well, and we are working on what we can do to maintain our current positioning and future plans. The challenge is that we are looking for alternative channels of income as well as another way to buy. Market Australia offers both.

We have a plan, an economic stimulus plan, that has a 10-year track record of success. The Unfoimch® System provides an entrepreneurial environment where individuals or companies can engage in sales programs and service areas, without requiring $10,000 to start or the need to buy anything. The system also provides a source of income for our country's disabled workers, who can earn a living by selling and promoting Isotonix® Vitamin B-12 Special Formula.

It's a unique combination of Internet marketing and One-to-One Marketing. It creates a proprietary system for entrepreneurs to create an ongoing income, while providing consumers with a better way to shop. Simply, it's the economy of the future, and Market Australia is leading the charge.

Please believe me, you are growing!

J. F. Rodrigues
Manager - Retail Operations
New!
Miracle Cure!

Truly amazing!
Works in minutes!
Guaranteed!
Top Ten Proposed Nutritional Supplements For Cardiovascular Health

Do they work?
Are they safe?
#1. Fish Oil – Omega 3 Fatty Acids
Figure 1  Structure of n-3 PUFA

Alpha-linolenic acid (ALA, 18:3n-3) is an 18-carbon essential n-3 polyunsaturated fatty acid (PUFA) derived from plant sources. Long-chain n-3 PUFA include eicosapentaenoic acid (EPA, 20:5n-3), docosapentaenoic acid (DPA, 22:5n-3), and docosahexaenoic acid (DHA, 22:6n-3), predominantly derived from seafood consumption, as well as docosapentaenoic acid (DPA) that is contained in smaller amounts in seafood and also synthesized endogenously from EPA. The long hydrocarbon backbones, multiple double bonds, and location of the first double bond in the n-3 position result in complex and unique 3-dimensional configurations that contribute to the singular biological properties of these fatty acids.
Physiological Effects of n-3 PUFA That Might Influence CVD Risk

- **↓ Blood pressure**
- **↓ Systemic vascular resistance**
  - ↑ Vasodilatory response
  - ↑ Arterial wall compliance
  - ↓ Endothelial dysfunction
- **↓ Triglyceride production**
- **↑ Possible small effects on glucose release or gluconeogenesis**
- **↓ Heart rate**
  - ↓ Arrhythmia
- **↑ Myocardial efficiency (e.g., reduce oxygen consumption at given work output)**
- **↑ Left ventricular diastolic filling**
- **↑ Autonomic function/vagal tone**
- **↑ Production of arachidonic acid derived eicosanoids**
- **↑ Production of n-3 derived metabolites**

- Effect appears linear within ranges of typical dietary intake (<750mg/d), with smaller additional effects at higher levels.
- Effect appears linear across a wide range of intakes (at least up to 7g/d).
- Effect only appears potentially relevant at higher supplemental intakes (> 4g/d).
- Dose response relationship not established.
Figure 5 Molecular Pathways Affected by n-3 PUFA

- Displace Arachidonic acid
- Change membrane fluidity; modify lipid raft and caveolae formation; Altered protein localization and function (e.g., signal transduction and ion channel properties)
- Displace Arachidonic acid
- COX, LOX
- (e.g., cardiac Na^+ channels)
- Na^+ current
- Cytosolic Ca^{2+} fluctuation
- Myocyte excitability
- Signalling cascades (e.g., ERK1/2 kinases, NF-κB translocation)
- Nuclear receptors (e.g., PPAR-α, HNF-4α and RXR) and transcription factors (e.g., SREBP-1c)
- Altered gene expression (e.g., fatty acid synthase, cyclooxygenase-2)
- mRNA
- DNA
- n-3 FA bound to Fatty acid binding protein
- PMN
- Intermediate Metabolites
- Transcellular biosynthesis
- Platelet
- Resolvins
- Protectins
- Inflammation resolution
- n-3 FA
- (e.g., GPR 120 and Toll like receptor 4)
- cPLA_{2}
- DHA, AA
- cPLA_{2}
- Endoplasmic Reticulum
- CYP, COX, LOX
Early Protection Against Sudden Death by n-3 Polyunsaturated Fatty Acids After Myocardial Infarction: Time-Course Analysis of the Results of the Gruppo Italiano per lo Studio della Sopravvivenza nell’Infarto Miocardico (GISSI)-Prevenzione

Roberto Marchioli, MD; Federica Barzi, MS; Elena Bomba, MD; Carmine Chieffo, MD; Domenico Di Gregorio, MD; Rocco Di Mascio, MD; Maria Grazia Franzosi, MD; Enrico Geraci, MD; Giacomo Levantesi, MD; Aldo Pietro Maggioni, MD; Loredana Mantini, MD; Rosa Maria Marfisi, MS; G. Mastrogiuseppe, MD; Nicola Mininni, MD; Gian Luigi Nicolosi, MD; Massimo Santini, MD; Carlo Schweiger, MD; Luigi Tavazzi, MD; Gianni Tognoni, MD; Corrado Tucci, MD; Franco Valagussa, MD; on behalf of the GISSI-Prevenzione Investigators

Background—Our purpose was to assess the time course of the benefit of n-3 polyunsaturated fatty acids (PUFAs) on mortality documented by the GISSI-Prevenzione trial in patients surviving a recent (<3 months) myocardial infarction.

Methods and Results—In this study, 11,323 patients were randomly assigned to supplements of n-3 PUFAs, vitamin E (300 mg/d), both, or no treatment (control) on top of optimal pharmacological treatment and lifestyle advice. Intention-to-treat analysis adjusted for interaction between treatments was carried out. Early efficacy of n-3 PUFA treatment for total, cardiovascular, cardiac, coronary, and sudden death; nonfatal myocardial infarction; total coronary heart disease; and cerebrovascular events was assessed by right-censoring follow-up data 12 times from the first month after randomization up to 12 months. Survival curves for n-3 PUFA treatment diverged early after randomization, and total mortality was significantly lowered after 3 months of treatment (relative risk [RR] 0.59; 95% CI 0.36 to 0.97; P=0.037). The reduction in risk of sudden death was specifically relevant and statistically significant already at 4 months (RR 0.47; 95% CI 0.219 to 0.995; P=0.048). A similarly significant, although delayed, pattern after 6 to 8 months of treatment was observed for cardiovascular, cardiac, and coronary deaths.

Conclusions—The early effect of low-dose (1 g/d) n-3 PUFAs on total mortality and sudden death supports the hypothesis of an antiarrhythmic effect of this drug. Such a result is consistent with the wealth of evidence coming from laboratory experiments on isolated myocytes, animal models, and epidemiological and clinical studies. (Circulation. 2002;105:1897-1903.)

Key Words: fatty acids ■ death, sudden ■ trials ■ coronary disease ■ antiarrhythmia agents
Methods

• 11,323 patients with history of recent MI were randomly assigned to
  – Omega-3 fatty acids (1 g/d) or placebo and
  – Vitamin E (300 mg/d), both or placebo.
• Patients followed for 3.5 years
• Major endpoints:
  – Total, cardiovascular, cardiac, coronary, and sudden death
  – Nonfatal myocardial infarction
  – Total coronary heart disease
  – Cerebrovascular events
Figure 2. Effects of n-3 PUFA treatment on blood lipids.
Conclusions

• In post-MI patients, 1 g/d of omega-3 fatty acid supplementation results in a significant reduction in cardiovascular complications.
• Most of the benefit comes from a reduction in sudden death.
• Most of the benefit comes in the first year.
• This is the first dietary supplement to show outcomes benefit in large randomized studies.
Omega 3 Fatty Acids in Primary Prevention

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Number of studies</th>
<th>Number of subjects</th>
<th>Number of events</th>
<th>Unit</th>
<th>RR (95% CI)</th>
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</thead>
<tbody>
<tr>
<td>CHD death</td>
<td>5 PCs</td>
<td>155503</td>
<td>1573</td>
<td>High vs. low intake (mean difference of 1.2g/d)</td>
<td>0.79 0.60-1.04</td>
</tr>
<tr>
<td>Total CHD</td>
<td>5 PCs</td>
<td>145497</td>
<td>NR</td>
<td>High vs. low quantile of ALA intake</td>
<td>1.06 0.92-1.20</td>
</tr>
<tr>
<td>CVD events</td>
<td>1 RCT (Alpha Omega Trial)</td>
<td>4837</td>
<td>671</td>
<td>ALA vs. Placebo or EPA/DHA alone</td>
<td>0.91 0.78-1.05</td>
</tr>
</tbody>
</table>

**Figure 2**  
Meta-Analyses of Observational Studies and Results From a Large RCT of ALA Consumption and Risk of CVD Outcomes

Relatively few prospective cohort studies (PCs) have evaluated the relationship between consumption of ALA and risk of coronary heart disease (CHD). Meta-analyses of these studies suggest no significant association with total CHD and a trend toward lower risk of CHD death (16,18). A recent randomized controlled trial (RCT) found no significant effect of ALA supplementation (1.9 g/day) in patients with history of myocardial infarction, although only one-half of the patients in the comparison group received placebo, with the other one-half receiving long-chain n-3 PUFA (EPA+DHA) supplements (17). CI = confidence interval; CVD = cardiovascular disease; NR = not reported; RR = relative risk; other abbreviations as in Figure 1.
Omega 3 Fatty Acids: Summary

When combined with the robust global evidence from observational studies, the documented effects on risk factors in short-term trials, and the experimental and mechanistic evidence, it is clear that n-3 PUFA are bioactive nutrients that play an important role in cardiovascular health, in particular for reducing risk of cardiac mortality.

Eating lots of fish may be the best way to get this supplement, but taking fish oil capsules may also help.
#2. Coenzyme Q10 (Ubiquinone)

It is a vitamin-like, fat soluble quinone found in high concentrations in the mitochondria of the heart, liver, and kidney, where it is involved in electron and proton transfer during oxidative phosphorylation.

It is also an antioxidant and free radical scavenger with membrane stabilizing properties.

It has two proposed cardiac benefits

- Improves statin tolerance
- Reduces heart failure symptoms
Effect of CoQ10 on Statin Tolerance

Statins not only decrease the synthesis of cholesterol, they also decrease the synthesis of CoQ10, which plays an important role in muscle cell energy production.

It has been speculated that the reduction in CoQ10 may contribute to statin-induced muscle injury. Therefore supplementation may reduce the incidence of statin induced myopathy.

Three small randomized trials have tested the hypothesis:

- 32 patients with statin myopathy – received benefit from CoQ10 100 mg/day.
- 44 patients with statin myopathy – received no benefit from CoQ10 200 mg/day.
- <100 patient with statin myopathy – received no benefit from CoQ10 60 mg bid.
CoQ10 and Heart Failure

Myocardial biopsies from patients with HF have demonstrated depletion of coenzyme Q10, an observation that provided the rationale for randomized controlled trials.

30 patients with cardiomyopathy (mean LVEF 26%) who were treated with coenzyme Q10 or placebo, for three months received no benefit in regards to LVEF, cardiac volumes, hemodynamics, or quality-of-life indices.

55 patients with class III or IV HF who were randomized to coenzyme Q10 or placebo received no benefit in regards to LVEF, peak oxygen consumption, or exercise duration.

Based in part on these observations, coenzyme Q10 is not recommended as a therapy for HF by the ACC/AHA.
Coenzyme Q10 – Summary

May be helpful with preventing or treating statin-induce myopathy

Does not appear to work for heart failure.
#3. Garlic

The active component of garlic is an amino acid called alliin which is further converted to allicin and other active metabolites.

Garlic is proposed to be effective in lowering cholesterol in hyperlipidemic patients if taken on a regular basis.

Several small randomized trials proposed a small but potentially clinically significant reduction in LDL cholesterol by the use of garlic.

Then a large randomized trial was performed
192 hyperlipidemic adults (LDL-C = 130-190) randomized to four test groups:
  Raw garlic
  Powdered garlic
  Aged garlic
  Placebo
Patients were treated six days per week for six months
Garlic Summary

“We do not recommend garlic for the treatment of hypercholesterolemia.”
#4. Red Yeast Rice Extract
Characteristics of Red Yeast Rice

Red yeast rice is a fermented rice product that has been used in Chinese cuisine and medicinally to promote "blood circulation".

The product contains varying amounts of a family of naturally occurring substances called monacolins that have HMG CoA reductase inhibitor activity. Specifically, it contains varying levels of lovastatin.

Other active ingredients in red yeast rice that may affect cholesterol lowering include sterols (beta-sitosterol, campesterol, stigmasterol, sapogenin), isoflavones, and monounsaturated fatty acids.
Red Yeast Rice Randomized Trial

83 hyperlipidemic patients on other treatment were randomized to receive red yeast rice (2.4 g/day) or placebo for eight weeks.

Total cholesterol was significantly reduced by 17% (208 versus 251 mg/dL, P<0.01).

LDL-C was significantly reduced by 23% (135 versus 175 mg/dL, P<0.01).

HDL-C was unaffected.
Red Yeast Rice – Other Interesting Points

A dose of red yeast rice of 2.4 g/day translates into a daily lovastatin dose of 4.8 mg/day, which is much less than standard pharmaceutical doses of lovastatin, suggesting that other active ingredients in red yeast rice probably also contribute to its cholesterol lowering activity.

One study tested red yeast rice 1800 mg/day versus placebo in statin intolerant patients. It significantly reduced lipids and was as well tolerated as placebo.

There is substantial variability across commercial preparations of red yeast rice.

   In one study of 12 preparations, the amount of lovastatin per capsule ranged from 0.31 to 11.15 mg.

   Also, 4 of 12 preparations had elevated levels of citrinin, a potentially nephrotoxic mycotoxin.
Red Yeast Rice – Summary

Red yeast rice has cholesterol lowering ability due to the presence of lovastatin that has HMG CoA reductase inhibitor activity, and possibly other active substances.

However, these extracts suffer from the same problem as many other natural products, that is, a lack of standardization.

This results in marked variability across brands in the content of the active ingredient and thus in efficacy in reducing LDL-C.

Some statin intolerant people can tolerate red yeast rice
#5. Niacin

Is also known as vitamin B3 or nicotinic acid.

Is the best available agent to raise HDL cholesterol.

Also lowers LDL cholesterol.

Has the significant, but benign, side effect of flushing.

Has over-the-counter immediate release as well as branded sustained release forms.
CHD Risk According to HDL-C Levels

Framingham Study

Kannel WB. *Am J Cardiol* 1983;52:9B–12B.
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Coronary Drug Project

• Long-term efficacy and safety of five lipid-influencing drugs
  – Niacin, clofibrate, dextrothyroxine, and two estrogen regimens
• 8,341 men (aged 30–64 y) with previous MI
• Initial study conducted between 1966 and 1975 (mean follow-up: 6.2 y)
• At end of study, 6,008 survivors followed for additional mean 8.8 y

Canner PL et al. J Am Coll Cardiol 1986;8:1245–1255
Coronary Drug Project
Long-Term Mortality Benefit of Niacin in Post-MI Patients

Survival (%)

Years of follow-up

$P = 0.0012$
AIM-HIGH Trial

Atherothrombosis Intervention in Metabolic Syndrome with Low HDL/High Triglycerides and Impact on Global Health Outcomes
Entry Criteria

- Patients Age ≥ 45 Years with
  - Coronary Heart Disease (CHD), or
  - Cerebrovascular Disease (CVD), or
  - Peripheral Arterial Disease (PAD)
- And Dyslipidemia
  - Low Levels of Baseline HDL-C
    - <40 mg/dL for men; < 50 mg/dL for women;
  - Triglycerides 150-400 mg/dL;
  - LDL-C < 180 mg/dL
Study Design

Open-Label Run-In: Up-Titrare Niacin from 500mg to 2,000mg/day
4-8 weeks

ER Niacin + 40-80 mg/day simvastatin

Placebo + 40-80 mg/day simvastatin

Adjust simv to LDL 40 – 80 mg/dL

Follow to end of study

Months Relative to Randomization

-2  -1  0  1  2  3  6  12
HDL-C at Baseline & Follow-up

- **Combination Therapy**
- **Monotherapy**

P < 0.001

<table>
<thead>
<tr>
<th>Year</th>
<th>Combination Therapy</th>
<th>Monotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>25 mg/dL</td>
<td>25 mg/dL</td>
</tr>
<tr>
<td>Year 1</td>
<td>40 mg/dL</td>
<td>35 mg/dL</td>
</tr>
<tr>
<td>Year 2</td>
<td>40 mg/dL</td>
<td>35 mg/dL</td>
</tr>
<tr>
<td>Year 3</td>
<td>40 mg/dL</td>
<td>35 mg/dL</td>
</tr>
</tbody>
</table>
LDL-C at Baseline & Follow-up

- **Combination Therapy**
- **Monotherapy**

mg/dL

- Baseline
- Year 1
- Year 2
- Year 3

* P < 0.001
Primary Outcome

HR 1.02, 95% CI 0.87, 1.21
Log-rank P value = 0.79

N at risk:
- Monotherapy: 1696, 1581, 1381, 910, 436
- Combination Therapy: 1718, 1606, 1366, 903, 428
Niacin – Summary

Niacin can both lower LDL and HDL.

If taken for a long time by itself, it appears to be cardio-protective.

It does not appear to add benefit on top of a statin, at least in the setting of already well controlled LDL levels.

Some people like it because, after all, it is a vitamin.
#6. Vitamin D
Vitamin D Deficiency is an Epidemic Among the General Population, Regardless of the Season

Intermountain Medical Center, Murray, Utah; University of Utah, Salt Lake City, UT

METHODS: Between 2000-2009, a total of 41,497 patients within Intermountain Healthcare were tested for their serum concentration of 25[OH] vit D. Vit D was stratified into 3 categories: Normal: >30 ng/ml; Low: 15-30 ng/ml; and Very low: ≤15 ng/ml. Prevalence of patients in each category was analyzed based on age, gender and season in which the sample was taken.

Table: Proportions of patients with various levels of 25[OH] vitamin D

<table>
<thead>
<tr>
<th>Category</th>
<th>Normal vit D</th>
<th>Low vit D</th>
<th>Very low vit D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>36.4%</td>
<td>46.9%</td>
<td>16.6%</td>
</tr>
<tr>
<td>Males (n=10,387)</td>
<td>33.9%</td>
<td>48.5%</td>
<td>17.6%</td>
</tr>
<tr>
<td>Females (n=31,100)</td>
<td>37.3%</td>
<td>46.4%</td>
<td>16.3%</td>
</tr>
<tr>
<td>Age ≥ 50 (n=27,686)</td>
<td>36.5%</td>
<td>47.2%</td>
<td>16.3%</td>
</tr>
<tr>
<td>Age &lt; 50 (n=13,811)</td>
<td>36.2%</td>
<td>46.5%</td>
<td>17.3%</td>
</tr>
<tr>
<td>Tests in May-July</td>
<td>38.1%</td>
<td>47.7%</td>
<td>14.2%</td>
</tr>
<tr>
<td>Tests in December-February</td>
<td>35.2%</td>
<td>45.4%</td>
<td>19.4%</td>
</tr>
</tbody>
</table>
Vitamin D Therapy and Cardiovascular Risk: Intermountain Healthcare Study

- 7,515 patients (>18 yrs) with a low (<30) initial Vitamin D level
  - Follow-up vitamin D level obtained at least 1 year prior to the censor date (3/25/2010)
  - The last follow-up level used was either the first level where the vitamin D level was normalized (>30) or the last level obtained.
- Patients stratified by follow-up Vitamin D level
  - Vitamin D ≥ 30
  - Vitamin D <30
- Patients followed long-term (Ave f/u 2.5 years, max = 5.5 years.
- Cox Hazard adjusted for death, new diagnosis of coronary artery disease (CAD), myocardial infarction (MI), heart failure (HF), stroke, and renal failure.
Effect of Normalizing Vitamin D on Composite Endpoint

$P < 0.0001$
Effect of Normalizing Vitamin D: Adjusted Hazard Ratios

- Composite: 0.80
- Death: 0.77
- CAD: 0.85
- MI: 0.75
- Heart Failure: 0.83
- Stroke: 0.97
- Renal Failure: 0.76
Vitamin D Deficiency and Statin Myalgia

Some studies, but not all, have suggested that low vitamin D levels may be associated with statin myopathy.

Case reports, case series, and some small, inadequately controlled studies have reported improvement in symptoms of statin myopathy in patients supplemented with vitamin D.

If a patient with statin myopathy is known to be vitamin D deficient, it is reasonable to administer vitamin D replacement therapy and then re-challenge with statin therapy.
Vitamin D – Summary

Vitamin D deficiency is very common in Utah.

Vitamin D deficiency is associated with adverse cardiovascular events.

A large randomized clinical outcomes trial of vitamin D supplementation in patients with vitamin D deficiency has not yet been planned, let alone completed.

In the absence of evidence-based data, there are many differing opinions regarding whether to test for or treat vitamin D deficiency.

With the low cost and low risk associated with vitamin D testing and treatment, I still support doing it.
#7. Magnesium

Over half of Americans do not get the recommended daily dose of magnesium in their diets.

Approximately 20% of the elderly have been documented to be magnesium deficient.

Large studies have linked magnesium deficiency to high blood pressure, while some have shown an association between magnesium supplements and a decreased risk of death from heart disease.

A higher intake of magnesium may reduce the risk of developing type 2 diabetes.
<table>
<thead>
<tr>
<th></th>
<th>Disease associated with magnesium deficiency in man</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Cardiovascular diseases (congestive heart failure, paraxysmal ventricular fibrillation, digitalis intoxication etc)</td>
</tr>
<tr>
<td>2</td>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td>3</td>
<td>Diseases of gastrointestinal tract</td>
</tr>
<tr>
<td>4</td>
<td>Liver cirrhosis</td>
</tr>
<tr>
<td>5</td>
<td>Diseases of the thyroid and parathyroid glands</td>
</tr>
<tr>
<td>6</td>
<td>Renal diseases</td>
</tr>
</tbody>
</table>
SYSTEMATIC REVIEW

Effect of magnesium supplementation on blood pressure: a meta-analysis

L Kass¹, J Weekes¹ and L Carpenter²

To date, there has been inconclusive evidence regarding the effect of magnesium supplements on blood pressure (BP). This meta-analysis was conducted to assess the effect of magnesium supplementation on BP and to establish the characteristics of trials showing the largest effect size. Primary outcome measures were systolic blood pressure (SBP) and diastolic blood pressure (DBP) at the end of the follow-up period. One hundred and forty-one papers were identified, of which 22 trials with 23 sets of data (n = 1173), with 3 to 24 weeks of follow-up met the inclusion criteria, with a supplemented elemental magnesium range of 120–973 mg (mean dose 410 mg). 95% confidence intervals (CI) were calculated using DerSimonian and Laird’s random-effects model, with effect size calculated using Hedges G. Combining all data, an overall effect of 0.36 and 0.32 for DBP and SBP, respectively, was observed (95% CI 0.27–0.44 for DBP and 0.23–0.41 for SBP), with a greater effect being seen for the intervention in crossover trials (DBP 0.47, SBP 0.51). Effect size increased in line with increased dosage. Although not all individual trials showed significance in BP reduction, combining all trials did show a decrease in SBP of 3–4 mm Hg and DBP of 2–3 mm Hg, which further increased with crossover designed trials and intake >370 mg/day. To conclude, magnesium supplementation appears to achieve a small but clinically significant reduction in BP, an effect worthy of future prospective large randomised trials using solid methodology.
An average reduction of 3-4 mm SBP by >360 mg/day Mg supplementation
Magnesium – Summary

Magnesium deficiency is common among the elderly and should be checked for.

It is associated with a variety of cardiovascular diseases.

Supplementation of at least 360 mg/day of magnesium appears justified at least in the elderly.

Common one-a-day vitamins include about 140 mg of magnesium.
#8. Nattokinase

Natto is Japanese food made from boiled soybeans that have been fermented with a bacterium called Bacillus natto.

Nattokinase is an enzyme that is extracted from natto that was discovered by a University of Chicago researcher, Dr. Hiroyuki Sumi.

It binds to fibrin and breaks it down, enhancing the fibrinolytic properties of blood.

It is proposed for use for a variety of cardiovascular diseases HTN, stroke, atherosclerosis, DVT, hemorrhoids, varicose veins and PAD.

So far, only small trials have been conducted testing its clinical efficacy.

A case report described an incident of intra-cranial hemorrhage when nattokinase was used in combination with aspirin.
#9. Hawthorn Berry

Hawthorn has both vasodilating effects and positive inotropic properties.

It has therefore been proposed to be beneficial in patients with heart failure.

A meta-analysis of 14 randomized clinical trials of adjunctive hawthorn therapy for class I-II heart failure reported improved symptoms by its use.
#10. Guggul

Guggul is made from the sap of the mukul myrrh tree, which is native to India.

It has been used in traditional Indian medicine so extensively, the tree has become very scarce.

It has been proposed to lower cholesterol.

However, one randomized trial published in JAMA did not confirm any significant effect on lipids.
Nutritional Supplements – Summary

All kinds of nutritional supplements have been proposed and marketed for the treatment of cardiovascular disease. Some may actually have benefit.

However, in each case, evidence regarding their benefit remains limited.

Most of them are not dangerous, but some may have adverse interactions with other prescribed medications.

Many of our patients are using these nutritional supplements.

So it is good for us to know about them.