Supplemental Evidence on Supplements

Supplement def'n
"something added to complete a thing, make up for a deficiency"
BUT
?Supplements for otherwise healthy people?

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Examples of benefits in deficiencies

RESEARCH

BMJ 2011;343:d5094 doi: 10.1136/bmj.d5094

Vitamin A supplements for preventing mortality, illness, and blindness in children aged under 5: systematic review and meta-analysis

OPEN ACCESS

IN DEVELOPING COUNTRIES
"43 trials with about 215,633 children were included. Seventeen trials including 194 483 participants reported a 24% reduction in all cause mortality (rate ratio=0.76, 95% confidence interval 0.69 to 0.83). Seven trials reported a 28% reduction in mortality associated with diarrhoea (0.72, 0.57 to 0.91). Vitamin A supplementation was associated with a reduced incidence of diarrhoea (0.85, 0.82 to 0.87) and measles (0.50, 0.37 to 0.67) and a reduced prevalence of vision problems, including night blindness (0.32, 0.21 to 0.50) and xerophthalmia (0.31, 0.22 to 0.45)"

Am J Clin Nutr 2006;84:1261-76 **Review Articles**

Iron supplementation in early childhood: health benefits and risks[1–3]

Lora L Iannotti, James M Tielsch, Maureen M Black, and Robert E Black

benefits in iron deficient or anemic children - developing countries

no benefit - maybe? harm if not iron deficient

Age-related Macular Degeneration AREDS study

3,640 - different categories of ARMD
Mean age 70 - followed for 6.3 years

- vitamin C 500 mg, vitamin E 400 IU, beta-carotene 15mg
- zinc
- vitamins plus zinc
- placebo

15 letter decrease in visual acuity from baseline in at least 1 eye

Placebo	Vitamins	Zinc	Both
29%	26%	25%	*23 %

* = stat sig from placebo

Arch Ophthalmol 2001;119:1439-52

Effects and safety of preventive oral iron or iron+folic acid supplementation for women during pregnancy

"Universal prenatal supplementation with iron or iron + folic acid provided either daily or weekly is effective to prevent anaemia and iron deficiency at term. We found no evidence, however, of a significant reduction in substantive maternal and neonatal adverse clinical outcomes (low birthweight, delayed development, preterm birth, infection, postpartum haemorrhage)"

CD004736

Effects and safety of periconceptional folate supplementation for preventing birth defects

Reduced incidence of neural tube defects (relative risk 0.28, 95% confidence interval 0.15 to 0.52)

1.5% versus 0.4%

“There is no statistically significant evidence of any effects on prevention of cleft palate, cleft lip, congenital cardiovascular defects, miscarriages or any other birth defects”

CD007950

Low dose iron supplementation

Patients

90 patients with iron deficiency anemia - 60% female, avg age 85 - mean hemoglobin 105 g/L

Treatment

30 patients in each dose group, were randomized to receive 15 mg, 50 mg, or 150 mg of elemental iron daily for a 2-month period

another 30 hospitalized patients without anemia were given 15 mg of iron daily for 60 days

Duration

2 months

Am J Med 2005;118:1142-7

Low dose iron supplementation

Hemoglobin changed approx 13 g/L in all 3 groups at 60 days - 2 in non-anemic control
Ferritin increased approx 40 g/L

DOSE	Abd discomfort (%)	N and V (%)	Constipation (%)	Diarrhea (%)	Darkened stools (%)
15 mg	20	13	0	13	44
50 mg	60	36	10	53	67
150 mg	70	67	23	70	91

Pyridoxine (vitamin B6) supplementation in pregnancy

“There is not enough evidence to detect clinical benefits of vitamin B6 supplementation in pregnancy and/or labour other than one trial suggesting protection against dental decay”

CD000179

Folic acid with or without vitamin B12 for the prevention and treatment of healthy elderly and demented people.

“The small number of studies which have been done provide no consistent evidence either way that folic acid, with or without vitamin B12, has a beneficial effect on cognitive function of unselected healthy or cognitively impaired older people”

CD004514

Effects of Lowering Homocysteine Levels With B Vitamins on Cardiovascular Disease, Cancer, and Cause-Specific Mortality

Meta-analysis - 8 RCTs - 35,485 subjects

Median follow-up - 5 years

	Cancer	Vascular events	Mortality
Folic acid	8.7	24.9	13.8
Control	8.2	24.8	13.6
	NSS	NSS	NSS

Arch Intern Med 2010;170:1622-31

Multivitamins Slowing Cataract Progression

"There is no evidence from RCTs that supplementation with antioxidant vitamins (beta-carotene, vitamin C or vitamin E) prevents or slows the progression of age-related cataract. We do not recommend any further studies to examine the role of antioxidant vitamins beta-carotene, vitamin C and vitamin E in preventing or slowing the progression of age-related cataract."

CD004567

Antioxidant supplements for prevention of mortality in healthy participants and patients with various diseases

"We found no evidence to support antioxidant supplements for primary or secondary prevention. Beta-carotene and vitamin E seem to increase mortality, and so may higher doses of vitamin A"

CD007176

PAPER

Role of multivitamins and mineral supplements in preventing infections in elderly people: systematic review and meta-analysis of randomised controlled trials

BMJ 2005; 330 doi: http://dx.doi.org/10.1136/bmj.38399.495648.8F (Published 14 April 2005)
Cite this as: *BMJ* 2005;330:871

"The evidence for routine use of multivitamin and mineral supplements to reduce infections in elderly people is weak and conflicting"

Latest Multivitamin Study

2 reports from a large well designed study – 11 years – Physicians Health Study - 14,641 - male physicians – average age 64

Centrum Silver or placebo daily - vitamin E 400-IU on alternate days, vitamin C 500-mg daily, beta-carotene 50-mg on alternate days - precursor to Vitamin A

	Cancer	CVD	Mortality
Centrum	17.6	12	18.4
Placebo	18.8	11.7	19.3
	SS	NSS	NSS

JAMA 2012;308(17):1751-1760. doi:10.1001/jama.2012.14805
JAMA 2012;308(18):1871-1880. doi:10.1001/jama.2012.14641

Efficacy of Omega-3 Fatty Acid Supplements (Eicosapentaenoic Acid and Docosahexaenoic Acid) in the Secondary Prevention of Cardiovascular Disease

A Meta-analysis of Ran

Sang Mi Kwak, MD; Seung-Kwon for the Korean Meta-analysis Stu

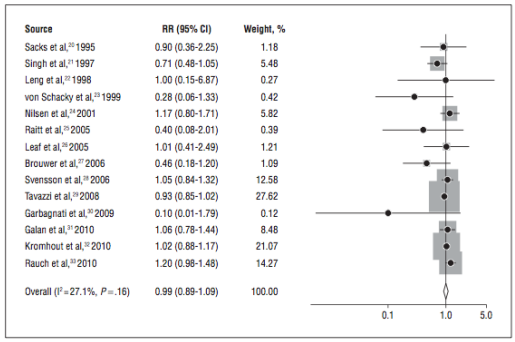


Figure 3. Efficacy of omega-3 fatty acid supplements in the secondary prevention of overall cardiovascular events in a random-effects meta-analysis of 14 randomized, double-blind, placebo-controlled trials. RR indicates relative risk. Horizontal lines indicate 95% CIs; gray boxes, the weight of each study. The box area is proportional to the weight of each study.

Arch Int Med 2012;172;686-94 (May 14)

n–3 Fatty Acids and Cardiovascular Outcomes in Patients with Dysglycemia

The ORIGIN Trial Investigators*

12,536 patients with or at risk for type-2 diabetes

6.2 years

n-3 fatty acids versus placebo

Did not reduce rate of cardiovascular events

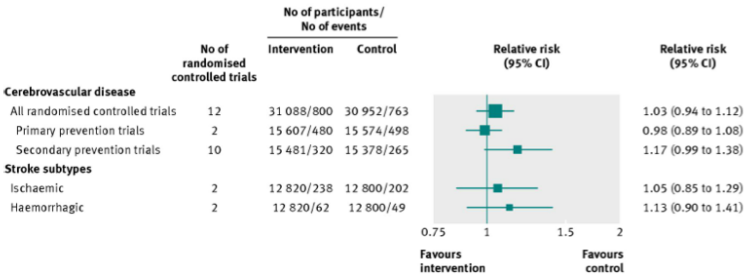
3 other trials still ongoing

NEJM June 12, 2012

Association between fish consumption, long chain omega 3 fatty acids, and risk of cerebrovascular disease: systematic review and meta-analysis

BMJ 2012;345:e6698 doi: 10.1136/bmj.e6698 (Published 30 October 2012)

"26 prospective cohort studies and 12 randomised controlled trials with aggregate data on 794,000 non-overlapping people and 34,817 cerebrovascular outcomes were included"



Cerebrovascular disease	Omega 3's (%)	Control (%)
All RCT	2.6	2.5
Primary	3.1	3.2
Secondary	2.1	1.7

Primary - 5-6 years
Secondary - 2-4 years
EPA+DHA 1-3g/day

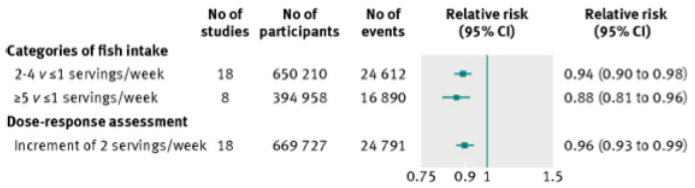


Fig 2 Association between fish consumption and risk of cerebrovascular disease in prospective cohort studies with information on intake categories and weekly increment of servings

Fish intake 2-4 versus </= 1 serving/week

Association Between Omega-3 Fatty Acid Supplementation and Risk of Major Cardiovascular Disease Events

A Systematic Review and Meta-analysis

20 studies (2 diet, 18 supplements) - 68,680 patients, avg 2 years, 13 secondary, 4 mixed, 2 ICD

Supplement data
Relative risks, 95% CI, absolute difference (if real)

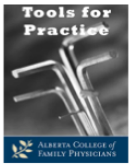
All-cause mortality - 0.96 (0.91 to 1.02) - 0.4%
Cardiac death - 0.91 (0.85 to 0.98) - 1.0%
Sudden death - 0.87 (0.75 to 1.01) - 0.3%
Myocardial infarction - 0.89 (0.76 to 1.04) - 0.2%
Stroke - 1.05 (0.93 to 1.18) - 0.1%

JAMA 2012;308:1024-33

Omega 3 fatty acid for the prevention of cognitive decline and dementia

"The results of the available studies show no benefit for cognitive function with omega-3 PUFA supplementation among cognitively healthy older people."

CD005379



Omega-3 Fatty Acids (Fish Oil) for Patients with Cardiovascular Disease (CVD)

Clinical Question: Do omega-3 fatty acid supplements reduce the risk of recurrent cardiovascular events in patients with existing cardiovascular disease (CVD)?

Evidence:
Three recent high-quality randomized controlled trials (RCTs)[1-3] and a subsequent meta-analysis (20,485 patients)[4] did not show a CVD or mortality benefit with omega-3 supplementation:

- 4837 Dutch patients with previous myocardial infarction (MI)[1]
  - Major cardiovascular events and cardiac interventions at 3.3 years: omega-3s 14.0% vs placebo 13.8% (p= 0.93)
- 2501 French patients with recent MI, unstable angina, or ischemic stroke[2]
  - Non-fatal MI, stroke, or cardiovascular death at 4.7 years: omega-3s 6.5% vs placebo 6.1% (p=0.64)
- 3851 German patients post-MI[3]
  - Sudden cardiac death at 1 year: omega-3s and placebo = 1.5% (p=0.84)

Another RCT published after the meta-analysis also found no cardiovascular benefit from 6 years of omega-3 supplementation in 12,536 diabetic or 'near diabetic' patients, 59% of whom had previous CVD.[5]

Tools For Practice

Effect of Coenzyme Q10 Supplementation on Statin-Induced Myalgias

76 statin patients reporting myalgia (age 62, 42% male - 57% recurrent pain)
randomized to CoQ10 60 mg twice daily or placebo

Table 2
Results of visual analog scale

Measurement Period	CoQ10		Placebo		p Value
	Patients (n)	Mean Score (cm)	Patients (n)	Mean Score (cm)	
Baseline	40	6.0 ± 2.2	36	5.9 ± 2.0	0.94
1 month	34	3.9 ± 2.2	32	4.0 ± 2.2	0.97
2 month	31	3.8 ± 2.2	30	3.8 ± 2.7	0.96
3 month	27	3.2 ± 2.3	26	3.1 ± 2.2	0.94

Data are presented as mean ± SD.
CoQ10 = coenzyme Q10.

Am J Cardiol 2012;110:526–9

Key Messages

Vitamin and mineral needs can usually be met by eating a balanced diet

Vitamin and mineral deficiencies should be treated

Folic acid

Vitamin D with calcium?

The rest - the evidence suggests no benefit and in some cases harm