Table 1. Biomedical and other databases searched

Database	Years
Allied & Complementary Medicine	1984–2001 Feb
Biosis Previews	1969–2002 Jan
CAB Health	1983–2001 Dec
Cancerlit	1975–2001 Oct
Cochrane Library	1922–2001
Database of Systematic Reviews	
Controlled Trials Register	
Elsevier Biobase	1994–2002 Jan
Embase	1974–2002 Jan
MANTIS	1880–2001 Oct
Medline	1966–2002 Jan
SciSearch Cited Ref Sci	1974–1989 Dec
Social SciSearch(R)	1972–2002 Jan
SciSearch Cited Ref Sci	1990–2002 Jan
TGG Health&Wellness DB	1976–2002 Dec

Table 2. Additional search terms for antioxidants studied

Vitamin C	Vitamin E	Coenzyme Q10
ascorbic acid	alpha tocopherol	ubiquinone
dehydroascorbic acid	d alpha tocopherol	ubidecarenone
ascorbate	rrr alpha tocopherol	ubidecarenon
antiscorbutic vitamin	all rac alpha tocopherol	isoprostane
cevitamic acid		

Table 3. Summary of search strategy

Name	Description	Number of References
Search 1	Focused search on intervention (Coenzyme Q10), disease state (cardiovascular disease), and human in on-line databases.	582
Search 2a	Focused search on intervention (Vitamin C), disease state, and human in on-line databases.	2228
Search 2b	Search of Cochrane databases for intervention (Vitamin C) and disease state.	169
Search 3a	Focused search on intervention (Vitamin E), disease state, type of therapy, and human for on-line databases.	3578
Search 3b	Search of Cochrane databases for intervention (Vitamin E) and disease state.	192
Search 4	Search of on-line databases for Coenzyme Q10 synonyms	503
Search 5	Search on Cochrane databases for intervention (Coenzyme Q10).	111
Total references found (duplicate articles included in total):		**8173**

Table 4. Outcomes reported for vitamin C studies (37 studies)

Outcome	Frequency	Percent
Blood levels of antioxidants	25	19.5
Oxidative status	20	15.6
Lipid level	17	13.3
Hypertension	8	6.2
Death	7	5.5
Electrocardiogram	6	4.7
Myocardial infarction, fatal	6	4.7
Myocardial infarction, nonfatal	6	4.7
Markers of myocardial injury	4	3.1
Arrhythmias	3	2.3
Blood vessel reactivity	3	2.3
Cerebrovascular Accident	3	2.3
Degree of stenosis	3	2.3
Endothelial dysfunction	2	1.6
Hemodynamics at rest	2	1.6
Angina	1	0.8
Heart failure severity	1	0.8
C reactive protein	1	0.8
Cancer diagnosis	1	0.8
Carotid artery thickness	1	0.8
Cell adhesion molecules	1	0.8
Ejection fraction	1	0.8
Echocardiogram	1	0.8
Homocysteine levels	1	0.8
Platelet aggregation	1	0.8
Restenosis rate	1	0.8
Thallium scan	1	0.8
Urine nitrite excretion	1	0.8

Table 5. Outcomes reported for coenzyme Q10 studies (54 studies)

Outcome	Frequency	Percent
Hemodynamics at rest	26	11.9
Ejection fraction	20	9.2
Blood levels of antioxidants	19	8.7
Heart failure severity	14	6.4
Hemodynamics at exercise	12	5.5
Electrocardiogram	11	5.0
Exercise tolerance	11	5.0
Hypertension	11	5.0
Angina	9	4.1
Death	9	4.1
Lipid level	9	4.1
Markers of myocardial injury	8	3.7
Oxidative status	8	3.7
Cardiac output / cardiac index	7	3.2
Arrhythmias	6	2.8
Stroke Volume	5	2.3
Left Ventricular End Diastolic Volume	4	1.8
Heart rate	3	1.4
Handgrip	2	0.9
Hospitalizations	2	0.9
Myocardial infarction, fatal	2	0.9
Myocardial infarction, nonfatal	2	0.9
Nitroglycerin use	2	0.9
Quality of life measure	2	0.9
Systolic time intervals	2	0.9
VO2	2	0.9
Blood vessel reactivity	1	0.5
CV complications	1	0.5
Fractional shortening	1	0.5
General side effects	1	0.5
Mitochondrial score	1	0.5
Pulmonary capillary wedge pressure	1	0.5
Right atrial pressure	1	0.5
Syncope	1	0.5
Tilt table testing	1	0.5
Weaning from Intraaortic balloon pump	1	0.5

Table 6. Primary, secondary, and treatment trials considered for analysis

Named Trial	First Author Year	Outcomes	Follow-ups (in months)	Arm #	Intervention		
Primary Prevention Trials:							
ASAP	Salonen 2000	Carotid artery thickness, Blood levels of antioxidants	36	1	Placebo		
				2	VE		
				3	VC		
				4	VC, VE		
ATBC	Leppala 2000 Jan	CVA, Death	72	1	Placebo		
				2	VE		
				3	BC		
				4	VE, BC		
	Leppala 2000 Oct	CVA, Death	72	1	Placebo		
				2	BC		
				3	VE		
				4	VE, BC		
	Tornwall 2001	AAA development, Death	69.6	1	Placebo		
				2	VE		
				3	BC		
				4	VE, BC		
	Virtamo 1998	MI (fatal), MI (non-fatal), Death	73.2	1	Placebo		
				2	VE		
				3	BC		
				4	VE, BC		
Linxian	Mark 1998	CVA, Death, Cancer diagnosis, HTN	63	1	Placebo	5	VE, MV
				2	Niacin, MV	6	VC, VE, MV
				3	VC, MV	7	VC, VE, MV
				4	VC, MV	8	VE, MV
PPP	de Gaetano 2001	MI (fatal), MI (non-fatal), CVA, Death, TIA, Angina, PVOD	43.2	1	Placebo		
				2	VE		
Other	Takamatsu 1995	Blood levels of antioxidants, MI (non-fatal), ECG, Lipid level, Oxidative status, HTN, Angina	12, 24, 36, 48, 60, 72	1	VE		
				2	VE		

VE = vitamin E
VC = vitamin C
CVA = cerebral vascular accident
BC = beta-carotene
VA = vitamin A

AAA = abdominal aortic aneurysm
MI = myocardial infarction
MI = myocardial infarction
HTN = hypertension
LDL = low density lipoprotein

MV = multi-vitamin
TIA = transient ischemic attack
PVD = peripheral vascular disease
ECG = electrocardiogram

CAD = coronary artery disease
n3 = omega 3
PUFA = polyunsaturated fatty acids
CHF = chronic heart failure
Control = control or usual care group

CO/CI = cardiac output/index
SV = stroke volume
LVEDV = left ventricular end diastolic volume
EF = ejection fraction

Table 6. Primary, secondary, and treatment trials considered for analysis (continued)

Secondary Prevention Trials:		Population				
ATBC	Rapola 1998	Angina	Angina, MI (fatal), MI (non-fatal), Death	12, 24, 36, 48, 60, 72	1 2 3 4	Placebo VE BC VE, BC
	Rapola 1997 Jun	CAD	MI (fatal), MI (non-fatal), Death, Blood levels of antioxidants	63.6	1 2 3 4	Placebo BC VE VE, BC
	Rapola 1997 Aug	CAD	Death, MI (fatal), MI (non-fatal)	63.6	1 2 3 4	Placebo VE BC VE, BC
CHAOS	Ness 1999	CAD	MI (fatal), Death	N/A	1 2	Placebo VE
	Stephens 1996	CAD	MI (fatal), MI (non-fatal), Death, Lipid level	N/A	1 2 3	Placebo VE VE
	Stephens 1996 Mar	CAD	Blood levels of antioxidants, MI (fatal), MI (non-fatal), Death, CVA, Arrhythmias	16.75	1 2 3	Placebo VE VE
GISSI/GIZZI	GISSI Prevenzione Investigators 1999	CAD, CVA/TIA	MI (non-fatal), CVA, Death, Lipid level, Cancer diagnosis	6, 42	1 2 3 4	Placebo n3 PUFA VE VE, n3 PUFA
HATS	Brown 2001	CAD, CVA/TIA, angina	MI (fatal), MI (non-fatal), CVA, Death, Degree of stenosis, Lipid level	12, 24, 36, 38	1 2 3 4	Placebo Niacin, Statin drug VE, VC, BC, Selenium Selenium, BC, VE, VC, Niacin, Statin drug

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Table 6. Primary, secondary, and treatment trials considered for analysis (continued)

Named Trial	ID	First Author Year	Population	Outcomes	Follow-ups (in months)	Arm #	Intervention
HOPE		Yusuf 2000	CAD, CVA/TIA	MI (fatal), MI (non-fatal), CVA, Death, Angina, CHF severity	54	1 2	Placebo VE
MVP		Tardif 1997	CAD	Degree of stenosis, Restenosis rate, Death, MI (fatal), MI (non-fatal)	7	1 2 3 4	Placebo Statin drug VC, VE, BC, VE Statin drug, VC, VE, BC, VE
SPACE		Boaz 2000	CAD, CVA/TIA, PVD, angina	Angina, MI (fatal), MI (non-fatal), CVA, Death, PVD	17	1 2	Placebo VE
Others		Di Somma 1991	CAD, CHF	CHF severity, Angina, Lipid level, HTN, Death	2, 4, 6	1 2	Control Co-Q10
		Gillilan 1977	CAD	Systolic time intervals, ECG, Exercise tolerance, Angina, Death, Blood levels of antioxidants	6	1 2	Placebo VE
		Haeger 1968	PVD	Claudication symptoms, Death, Amputation rate, Exercise tolerance	12, 24, 36, 48, 60, 0	1 2 3 4	Vasodilators Coumadin MV VE
		Judy 1991	CHF	Death, Blood levels of antioxidants, EF, Hemodynamics at rest, CHF severity	12, 24, 36, 48, 60, 72	1 2	Control Co-Q10
		Judy 1986	CHF	Hemodynamics at rest, EF, Blood levels of antioxidants, Death	1, 2, 3, 4, 5, 6	1 2	Placebo Co-Q10
		Judy 1986	CHF	CO/CI, SV, EF, LVEDV, Death, Blood levels of antioxidants, Hospitalizations, Tilt table testing, CHF	0.99, 1.97, 2.96, 3.94, 6, 12	1 2	Control Co-Q10
		Khatta 2000	CHF	Exercise tolerance, EF, Hemodynamics at exercise	6	1 2	Placebo Co-Q10
		Kuklinski 1994	CAD	Markers of myocardial injury, ECG, Death, Arrhythmias, MI (fatal), MI (non-fatal)	0.8, 6, 12	1 2	Placebo Co-Q10, VE, Selenium, VC

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SV = stroke volume
LVEDV = left ventricular end diastolic volume
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Table 6. Primary, secondary, and treatment trials considered for analysis (continued)

Named Trial	ID	First Author Year	Population	Outcomes	Follow-ups (in months)	Arm #	Intervention
		MRC/BHF Heart Protection Study Collaborative group 2002	CAD	MI (non-fatal), Lipid level, MI (fatal), Death, CVA	12, 24, 36, 48, 60	1 2	Placebo VE, VC, BC
		Morisco 1993	CHF	Death, CHF severity, Hospitalizations, CV complications, Arrhythmias	3, 6, 12	1 2	Placebo Co-Q10
		Singh 1996	CAD	ECG, Markers of myocardial injury, Blood levels of antioxidants, Oxidative status, Arrhythmias, Angina, HTN, MI (fatal), MI (nonfatal), Death, CHF Severity	0.92	1 2	Placebo VA, VC, VE, BC
		Singh 1998	CAD, angina	Oxidative status, Blood levels of antioxidants, MI (fatal), MI (non-fatal), Angina, CHF severity, Arrhythmias Death HTN	0.92	1 2	Placebo Co-Q10
		Sisto 1995	CAD	MI (fatal), MI (non-fatal), ECG, Arrhythmias, Markers of myocardial injury, Oxidative status, Blood level of antioxidants	0.92	1 2 3 4	Control VE, VC, Allopurinol Control VE, VC, Allopurinol
		Steiner 1995	CVA/TIA	Blood levels of antioxidants, CVA, TIA, Platelet aggregation, Death	24	1 2	Aspirin VE, Aspirin
		Watson 1999	CHF	CHF severity, EF, Hemodynamics at rest, Quality of life measure, Blood levels of antioxidants	3, 6	1 2	Placebo Co-Q10
Treatment Trials:							
MASI		Porkkala-Sarataho 1998	CAD	Oxidative status, Lipid level, Blood levels of antioxidants	2	1 2 3	Placebo VE VC, VE
Others		Brown 1994	CAD, LDL oxidation	Blood levels of antioxidants, Oxidative status, Lipid level	2.5	1 2	Placebo VE
		De Waart 1997	CAD	Oxidative status, Lipid level, Blood levels of antioxidants	3	1 2	Placebo VE

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Table 6. Primary, secondary, and treatment trials considered for analysis (continued)

Named Trial	ID	First Author Year	Population	Outcomes	Follow-ups (in months)	Arm #	Intervention
		DeMaio 1992	CAD, repefusion injury	Blood levels of antioxidants, Lipid level, Degree of stenosis, Restenosis rate	4	1 2	Placebo VE
		Fuller 1996	CAD, LDL oxidation	Oxidative status, Lipid level, Blood levels of antioxidants	2	1 2	Placebo VE
		Hoffman 1999	CAD, LDL oxidation	Blood levels of antioxidants, Oxidative status, Lipid level	6	1 2	Placebo VE
		Jain 1996	CAD	Lipid level, Oxidative status, Blood levels of antioxidants	3	1 2	Placebo VE
		Jialal 1995	CAD, LDL oxidation	Lipid level, Oxidative status, Blood levels of antioxidants	2	1 2 3 4 5 6	Placebo VE VE VE VE VE
		Jialal 1992	CAD	Lipid level, Oxidative status, Blood levels of antioxidants	1.5, 3	1 2	Placebo VE
		Jialal 1993	CAD	Lipid level, Oxidative status, Blood levels of antioxidants	3	1 2	Placebo VE, VC, BC
		Kaikkonen 2000	CAD	Lipid level, Oxidative status, Blood levels of antioxidants	3	1 2 3 4	Placebo VE, Co-Q10 Co-Q10 VE
		McDowell 1994	CAD, LDL oxidation	Lipid level, Oxidative status, Blood levels of antioxidants, ECG	1, 2	1 2 3	Placebo, Statin drug Probucol, Statin drug VE, Statin drug
		McGavin 2001	CAD	Lipid level, Blood levels of antioxidants	0.5, 1, 1.5, 2	1 2 3	Placebo VE VE
		Mosca 1997	CAD	Lipid level, Oxidative status, Blood levels of antioxidants	1.5, 3	1 2 3	Placebo VE, VC, BC VE, VC, BC

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Table 6. Primary, secondary, and treatment trials considered for analysis (continued)

Named Trial	ID	First Author Year	Population	Outcomes	Follow-ups (in months)	Arm #	Intervention
		Mottram 1999	CAD	Arterial compliance, Lipid level, Blood levels of antioxidants, HTN	1, 2	1 2	Placebo VE
		Nyyssonen 1997	CAD	Oxidative status, Blood levels of antioxidants, Lipid level	3	1 2	Placebo VC, VE, Selenium, BC
		Paolisso 1995	CAD	Lipid level, HTN, Oxidative status, Blood levels of antioxidants	4	1 2	Placebo VE
		Schafer 1990	CAD, LDL oxidation	Oxidative status, Lipid level, Blood levels of antioxidants	3	1 2	Placebo VE, Selenium
		Stampfer 1983	CAD	Lipid level	2, 4	1 2	Placebo VE
		Tomeo 1995	Carotid atherosclerosis	Lipid level, Blood levels of antioxidants, Oxidative status, Degree of stenosis	3, 6, 9, 12, 18	1 2	Palm olein VE, Palm olein, Alpha tocotrienol, Gamma tocotrienol
		de Lorgeril 1994	CAD	Lipid level, Platelet aggregation	2	1 2	Control VE

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PUFA = polyunsaturated fatty acids
CHF = chronic heart failure
Control = control or usual care group

CO/CI = cardiac output/index
SV = stroke volume
LVEDV = left ventricular end diastolic volume
EF = ejection fraction

Table 7. Risk ratios for vitamin E alone vs. Placebo: all-cause mortality

Named Trial	Author, Yr.	Intervention	Sample Size	Followup Time	# of Deaths	RR (95% CI)
SPACE	Boaz, 2000[119]	Vitamin E	97	519 days[a]	31	1.09 (0.72, 1.66)
		Placebo	99	519 days[a]	29	
HOPE	Yusuf, 2000[112]	Vitamin E	4761	4.5 yrs.	535	1.00 (0.89, 1.12)
		Placebo	4780	4.5 yrs.	537	
GISSI	GISSI, 1999[115]	Vitamin E	2830	3.5 yrs.	252	0.86 (0.73, 1.01)
		Placebo	2828	3.5 yrs.	293	
CHAOS	Stephens, 1996[116]	Vitamin E	1035	510 days[a]	36	1.29 (0.79, 2.13)
		Placebo	967	510 days[a]	26	
—	Haeger, 1968[131]	Vitamin E	104	7 yrs.	9	0.52 (0.21, 1.30)
		Placebo	42	7 yrs.	7	
Random Effects		Vitamin E	8827		863	**0.96 (0.84, 1.10)[b]**
Pooled Estimate		Placebo	8716		892	
Not Pooled:						
—	Gillian, 1977[120]	Vitamin E	26	6 mos.	2	0.85 (0.13, 5.52)
		Placebo	22	6 mos.	2	
ASAP	Salonen, 2000[114]	Vitamin E	130	3 yrs.	3	3.00 (0.32, 28.47)
		Placebo	130	3 yrs.	1	
PPP	de Gaetano, 2001[111]	Vitamin E	2231	3.6 yrs.[c]	72	1.07 (0.78, 1.49)
		Placebo	2264	3.6 yrs.[c]	68	

[a]median
[b]chi-squared test of heterogeneity p=0.22
[c]mean

Table 8. Publication bias test results

Study/Analysis	Number of Studies	Adjusted Rank Correlation Test	Regression Asymmetry Test
Vitamin E alone vs. placebo: all-cause mortality	5	p=1.00	p=0.91
Vitamin E alone vs. placebo: cardiovascular death	5	p=0.81	p=0.88
Vitamin E in combination vs. placebo: cardiovascular death	4	p=1.00	p=0.95
Vitamin E alone vs. placebo: fatal myocardial infarction	5	p=0.81	p=0.77
Vitamin E in combination vs. placebo: fatal myocardial infarction	4	p=1.00	p=0.89
Vitamin E alone vs. placebo: nonfatal myocardial infarction	5	p=0.09	p=0.07
Vitamin E in combination vs. placebo: nonfatal myocardial infarction	4	p=0.31	p=0.26
Vitamin E alone vs. placebo: total cholesterol	15	p=0.37	p=0.81
Vitamin E alone vs. placebo: low-density lipoprotein	14	p=0.91	p=0.64
Vitamin E alone vs. placebo: high-density lipoprotein	15	p=0.32	p=0.02
Vitamin E in combination vs. placebo: total cholesterol	7	p=0.37	p=0.61
Vitamin E in combination vs. placebo: low-density lipoprotein	5	p=0.22	p=0.80
Vitamin E in combination vs. placebo: high-density lipoprotein	5	p=0.81	p=0.24

Table 9. Risk ratios for vitamin E in combination vs. Placebo: all-cause mortality

Named Trial	Author, Year	Intervention	Sample Size	Followup Time	# of Deaths	RR (95% CI)
ASAP	Salonen, 2000[114]	Vitamin E in Combination	130	3 yrs.	1	1.00 (0.06, 15.82)
		Placebo	130	3 yrs.	1	
Linxian	Mark, 1998[110]	Vitamin E in Combination	14819	5.25 yrs.	101	0.91 (0.84, 0.99)
		Placebo	14765	5.25 yrs.	110	
MVP	Tardif, 1997[118]	Vitamin E in Combination	78	6 mos.	0	0.34 (0.01, 8.16)
		Vitamin E in Combination with Probucol	80	6 mos.	1	0.99 (0.06, 15.51)
		Placebo	79	6 mos.	1	
GISSI	GISSI, 1999[115]	Vitamin E in Combination	2830	3.5 yrs.	236	0.80 (0.68, 0.95)
		Placebo	2828	3.5 yrs.	293	
MRC/BHF	HPSCG, 2002[94]	Vitamin E in Combination	10269	5 yrs.	144	1.04 (0.97, 1.11)
		Placebo	10267	5 yrs.	138	

Table 10. Risk ratios for vitamin E alone vs. Placebo: cardiovascular deaths

Named Trial	Author, Year	Intervention	Sample Size	Followup Time	# of Deaths	RR (95% CI)
SPACE	Boaz, 2000[119]	Vitamin E	97	519 days[a]	9	0.61 (0.28, 1.33)
		Placebo	99	519 days[a]	15	
HOPE	Yusuf, 2000[112]	Vitamin E	4761	4.5 yrs.	342	1.05 (0.90, 1.21)
		Placebo	4780	4.5 yrs.	328	
ATBC	Rapola, 1997[108]	Vitamin E	466	5.3 yrs.[a]	54	1.30 (0.88, 1.92)
		Placebo	438	5.3 yrs.[a]	39	
GISSI	GISSI, 1999[115]	Vitamin E	2830	3.5 yrs.	155	0.80 (0.65, 0.99)
		Control	2828	3.5 yrs.	193	
CHAOS	Stephens, 1996	Vitamin E	1035	510 days[a]	27	1.10 (0.63, 1.90)
		Placebo	967	510 days[a]	23	
Random Effects		Vitamin E	9189		587	**0.97 (0.80, 1.19)**[b]
Pooled Estimate		Placebo	17257		598	

[a]median
[b]chi-squared test of heterogeneity p=0.09

Table 11. Risk ratios for vitamin E in combination vs. Placebo: cardiovascular deaths

Named Trial	Author, Year	Intervention	Sample Size	Followup Time	# of Deaths	RR (95% CI)
HATS	Brown, 2001[117]	Vitamin E in combination	84	38 mos.	1	0.90 (0.06, 13.97)
		Placebo	38	38 mos.	1	
ATBC	Rapola, 1997[108]	Vitamin E in combination	497	5.3 yrs.[a]	67	1.51 (1.04, 2.20)
		Placebo	438	5.3 yrs.[a]	39	
GISSI	GISSI, 1999[115]	Vitamin E in combination	2830	3.5 yrs.	155	0.80 (0.65, 0.99)
		Placebo	2828	3.5 yrs.	193	
MRC/BHF	HPSCG, 2002[94]	Vitamin E in combination	10269	5 yrs.	878	1.05 (0.95, 1.14)
		Placebo	10267	5 yrs.	840	
Random Effects		Vitamin E in combination	13680		1101	**1.03 (0.81,1.32)[b]**
Pooled Estimate		Placebo	13571		1073	
Not Pooled:						
—	Singh, 1996[122]	Vitamin E in combination	63	28 days	6	0.66 (0.25, 1.73)
		Placebo	62	28 days	9	
ATBC	Rapola, 1998[109]	Vitamin E in combination	456	4 yrs.	43	1.14 (0.75, 1.73)
		Placebo	456	4 yrs.	38	
ATBC	Virtamo, 1998[107]	Vitamin E in combination	6781	6.1 yrs.	222	0.94 (0.79, 1.13)
		Placebo	6849	6.1 yrs.	238	

[a]median
[b]chi-squared test of heterogeneity p=0.02

Table 12. Risk ratios for vitamin E alone vs. Placebo: fatal myocardial infarction

Named Trial	Author, Year	Intervention	Sample Size	Followup Time	# of Fatal MI	RR (95% CI)
SPACE	Boaz, 2000[119]	Vitamin E	97	519 days[a]	2	0.26 (0.06, 1.17)
		Placebo	99	519 days[a]	8	
HOPE	Yusuf, 2000[112]	Vitamin E	4761	4.5 yrs.	287	1.04 (0.89, 1.22)
		Placebo	4780	4.5 yrs.	277	
ATBC	Rapola, 1997[108]	Vitamin E	466	5.3 yrs.[a]	54	1.30 (0.88, 1.92)
		Placebo	438	5.3 yrs.[a]	39	
GISSI	GISSI, 1999[115]	Vitamin E	2830	3.5 yrs.	114	0.75 (0.59, 0.96)
		Control	2828	3.5 yrs.	151	
CHAOS	Stephens, 1996[116]	Vitamin E	1035	510 days[a]	18	1.29 (0.64, 2.63)
		Placebo	967	510 days[a]	13	
Random Effects		Vitamin E	9189		475	**0.97 (0.74,1.27)[b]**
Pooled Estimate		Placebo	9112		488	
Not Pooled:						
PPP	de Gaetano, 2001[111]	Vitamin E	2231	3.6 yrs.	3	0.43 (0.11, 1.60)
		Placebo	2264	3.6 yrs.	7	
ATBC	Rapola, 1998[109]	Vitamin E	460	4 yrs.	45	1.18 (0.78, 1.78)
		Placebo	459	4 yrs.	38	
ATBC	Virtamo, 1998[107]	Vitamin E	6820	6.1 yrs.	212	0.89 (0.75, 1.07)
		Placebo	6849	6.1 yrs.	238	

[a]median
[b]chi-squared test of heterogeneity p=0.03

Table 13. Risk ratios for vitamin E in combination vs. Placebo: fatal myocardial infarction

Named Trial	Author, Year	Intervention	Sample Size	Followup Time	No. of Fatal MI	RR (95% CI)
HATS	Brown, 2001[117]	Vitamin E in combination	84	38 mos.	1	0.45 (0.03, 7.04)
		Placebo	38	38 mos.	1	
ATBC	Rapola, 1997[108]	Vitamin E in combination	497	5.3 yrs.[a]	67	1.51 (1.04, 2.20)
		Placebo	438	5.3 yrs.[a]	39	
GISSI	GISSI, 1999[115]	Vitamin E in combination	2830	3.5 yrs.	114	0.75 (0.59, 0.96)
		Placebo	2828	3.5 yrs.	151	
MRC/BHF	HPSCG, 2002[94]	Vitamin E in combination	10269	5 yrs.	684	1.05 (0.95, 1.17)
		Placebo	10267	5 yrs.	630	
Random Effects Pooled Estimate		Vitamin E in combination	13639		822	**1.02 (0.77, 1.37)**[b]
		Placebo	13592		820	
Not Pooled:						
—	Singh, 1996[122]	Vitamin E in combination	63	28 days	6	0.66 (0.25, 1.73)
		Placebo	62	28 days	9	
ATBC	Virtamo, 1998[107]	Vitamin E in combination	6781	6.1 yrs.	222	0.94 (0.83, 1.19)
		Placebo	6849	6.1 yrs.	235	

[a]median
[b]chi-squared test of heterogeneity p=0.01

Table 14. Risk ratios of vitamin E alone vs. Placebo: nonfatal myocardial infarction

Named Trial	Author, Year	Intervention	Sample Size	Followup Time	# of Nonfatal MIs	RR (95% CI)
SPACE	Boaz, 2000[119]	Vitamin E	97	519 days[a]	3	0.34 (0.09, 1.22)
		Placebo	99	519 days[a]	9	
HOPE	Yusuf, 2000[112]	Vitamin E	4761	4.5 yrs.	245	1.00 (0.84, 1.18)
		Placebo	4780	4.5 yrs.	247	
ATBC	Rapola, 1997[108]	Vitamin E	466	5.3 yrs.[a]	40	0.68 (0.46, 1.01)
		Placebo	438	5.3 yrs.[a]	55	
GISSI	GISSI, 1999[115]	Vitamin E	2830	3.5 yrs.	112	1.04 (0.80, 1.34)
		Placebo	2828	3.5 yrs.	108	
CHAOS	Stephens, 1996[116]	Vitamin E	1035	510 days[a]	14	0.32 (0.18, 0.58)
		Placebo	967	510 days[a]	41	
Random Effects		Vitamin E	9189		414	**0.72 (0.51,1.02)[b]**
Pooled Estimate		Placebo	9112		460	
Not Pooled:						
PPP	de Gaetano, 2001[111]	Vitamin E	2231	3.6 yrs.[c]	19	1.07 (0.56, 2.04)
		Placebo	2264	3.6 yrs.[c]	18	
ATBC	Virtamo, 1998[107]	Vitamin E	6820	6.1 yrs.	307	1.04 (0.89, 1.22)
		Placebo	6849	6.1 yrs.	296	

[a]median
[b]chi-squared test of heterogeneity p=0.01
[c]mean

Table 15. Risk ratios of vitamin E in combination vs. Placebo: nonfatal myocardial infarction

Named Trial	Author, Year	Intervention	Sample Size	Followup Time	# of Nonfatal MIs	RR (95% CI)
HATS	Brown, 2001[117]	Vitamin E in combination	84	38 mos.	4	0.45 (0.12,1.71)
		Placebo	38	38 mos.	4	
ATBC	Rapola, 1997[108]	Vitamin E in combination	497	5.3 yrs.[a]	56	0.74 (0.48, 1.16)
		Placebo	438	5.3 yrs.[a]	55	
GISSI	GISSI, 1999[115]	Vitamin E in combination	2830	3.5 yrs.	114	1.05 (0.81, 1.37)
		Placebo	2828	3.5 yrs.	108	
MRC/BHF	HPSCG, 2002[94]	Vitamin E in combination	10269	5 yrs.	464	0.99 (0.88, 1.13)
		Placebo	10267	5 yrs.	467	
Random Effects		Vitamin E in combination	13639		613	**0.99 (0.89, 1.10)[b]**
Pooled Estimate		Placebo	13592		621	
Not Pooled:						
—	Singh, 1996[122]	Vitamin E in combination	63	28 days	7	0.69 (0.28, 1.69)
		Placebo	62	28 days	10	
—	Sisto, 1995[136]	Vitamin E in combination[c]	20	4 wks.	1	0.63 (0.06, 6.41)
		Control #1	25	4 wks.	2	
		Vitamin E in combination[d]	17	4 wks.	1	0.19 (0.02, 1.39)
		Control #2	19	4 wks.	6	
ATBC	Virtamo, 1998[107]	Vitamin E	6781	6.1 yrs.	289	0.99 (0.84, 1.16)
		Placebo	6849	6.1 yrs.	296	

[a]median
[b]chi-squared test of heterogeneity p=0.60
[c]stable disease
[d]unstable disease

Table 16. Risk ratios for vitamin E alone vs. Placebo: total cholesterol

Named Trial	Author, Year	Intervention	n	Followup Time	Effect Size (95% CI)
—	Brown, 1994[167]	Vitamin E	50	2.5 mos.	–0.18 (–0.57, 0.22)
		Placebo	50	2.5 mos.	
—	De Waart, 1997[168]	Vitamin E	41	3 mos.	–0.08 (–0.51, 0.35)
		Placebo	41	3 mos.	
—	DeMaio, 1992[169]	Vitamin E	52	4 mos.	0.10 (–0.29, 0.49)
		Placebo	48	4 mos.	
—	Fuller, 1996[170]	Vitamin E	15	2 mos.	0.09 (–0.65, 0.83)
		Placebo	13	2 mos.	
—	Hoffman, 1999[171]	Vitamin E	22	6 mos.	0.03 (–0.69, 0.75)
		Placebo	11	6 mos.	
—	Jain, 1996[172]	Vitamin E	13	3 mos.	–0.38 (–1.12, 0.36)
		Placebo	16	3 mos.	
—	Jialal, 1995[173]	Vitamin E	8	2 mos.	0.50 (–0.50, 1.49)
		Placebo	8	2 mos.	
—	Jialal, 1992[174]	Vitamin E	12	3 mos.	0.10 (–0.70, 0.90)
		Placebo	12	3 mos.	
—	Kaikkonen, 2000[151]	Vitamin E	10	3 mos.	3.18 (0.29, –0.59)
		Placebo	10	3 mos.	
—	McGavin, 2001[177]	Vitamin E	10	2 mos.	0.19 (–0.51, 0.90)
		Placebo	35	2 mos.	
—	Mottram, 1999[178]	Vitamin E	14	2 mos.	–0.10 (–0.84, 0.64)
		Placebo	14	2 mos.	
—	Paolisso, 1995[180]	Vitamin E	15	4 mos.	–2.31 (–3.23, –1.38)
		Placebo	15	4 mos.	
MASI	Porkkala–Sarataho, 1998[113]	Vitamin E	20	2 mos.	–0.08 (–0.70, 0.54)
		Placebo	20	2 mos.	
—	de Lorgeril, 1994[184]	Vitamin E	10	2 mos.	0.52 (–0.37, 1.41)
		Placebo	10	2 mos.	
—	Stampfer, 1983[182]	Vitamin E	15	4 mos.	0.09 (–0.63, 0.80)
		Placebo	15	4 mos.	
Random Effects		Vitamin E	307		**–0.07 (–0.31, 0.18)[a]**
Pooled Estimate		Placebo	318		
Not Pooled:					
GISSI	GISSI, 1999[115]	Vitamin E	2830	6 mos.	–0.01 (–0.07, 0.04)
		Placebo	2828	6 mos.	

[a]chi–squared test of heterogeneity p=0.01

Table 17. Risk ratios for vitamin E alone vs. Placebo: low-density lipoprotein

Named Trial	Author, Year	Intervention	n	Followup Time	Effect Size (95% CI)
—	Brown, 1994[167]	Vitamin E	50	2.5 mos.	–0.25 (–0.64, 0.15)
		Placebo	50	2.5 mos.	
—	De Waart, 1997[168]	Vitamin E	41	3 mos.	0.01 (–0.42, 0.44)
		Placebo	41	3 mos.	
—	DeMaio, 1992[169]	Vitamin E	52	4 mos.	0.27 (–0.12 0.66)
		Placebo	48	4 mos.	
—	Fuller, 1996[170]	Vitamin E	15	2 mos.	0.28 (–0.47, 1.02)
		Placebo	13	2 mos.	
—	Hoffman, 1999[171]	Vitamin E	22	6 mos.	–0.25 (–0.97, 0.48)
		Placebo	11	6 mos.	
—	Jain, 1996[172]	Vitamin E	13	3 mos.	–0.31 (–1.05, 0.43)
		Placebo	16	3 mos.	
—	Jialal, 1995[173]	Vitamin E	8	2 mos.	0.45 (–0.54, 1.44)
		Placebo	8	2 mos.	
—	Jialal, 1992[174]	Vitamin E	12	3 mos.	0.11 (–0.69, 0.91)
		Placebo	12	3 mos.	
—	Kaikkonen, 2000[151]	Vitamin E	10	3 mos.	0.08 (–0.80, 0.95)
		Placebo	10	3 mos.	
—	McGavin, 2001[177]	Vitamin E	10	2 mos.	0.11 (–0.59, 0.81)
		Placebo	35	2 mos.	
—	Mottram, 1999[178]	Vitamin E	14	2 mos.	–0.53 (–1.28, 0.23)
		Placebo	14	2 mos.	
—	Paolisso, 1995[180]	Vitamin E	15	4 mos.	–0.90 (–1.65, –0.15)
		Placebo	15	4 mos.	
MASI	Porkkala–Sarataho, 1998[113]	Vitamin E	20	2 mos.	–0.29 (–0.92, 0.33)
		Placebo	20	2 mos.	
—	Stampfer, 1983[182]	Vitamin E	15	4 mos.	–0.02 (–0.69, 0.74)
		Placebo	15	4 mos.	
Random Effects		Vitamin E	307		**–0.07 (–0.24, 0.10)[a]**
Pooled Estimate		Placebo	318		
Not Pooled:					
GISSI	GISSI, 1999[115]	Vitamin E	2830	6 mos.	–0.02 (–0.08, 0.03)
		Placebo	2828	6 mos.	

[a]chi–squared test of heterogeneity p=0.41

Table 18. Risk ratios for vitamin E alone vs. Placebo: high-density lipoprotein

Named Trial	Author, Year	Intervention	n	Followup Time	Effect Size (95% CI)
—	Brown, 1994[167]	Vitamin E	50	2.5 mos.	–0.18 (–0.57, 0.22)
		Placebo	50	2.5 mos.	
—	De Waart, 1997[168]	Vitamin E	41	3 mos.	–0.20 (–0.63, 0.24)
		Placebo	41	3 mos.	
—	DeMaio, 1992[169]	Vitamin E	52	4 mos.	–0.59 (–0.99, –0.19)
		Placebo	48	4 mos.	
—	Fuller, 1996[170]	Vitamin E	15	2 mos.	–0.63 (–1.39, 0.13)
		Placebo	13	2 mos.	
—	Hoffman, 1999[171]	Vitamin E	22	6 mos.	0.26 (–0.46, 0.99)
		Placebo	11	6 mos.	
—	Jain, 1996[172]	Vitamin E	13	3 mos.	0.00 (–0.73, 0.73)
		Placebo	16	3 mos.	
—	Jialal, 1995[173]	Vitamin E	8	2 mos.	–0.43 (–1.42, 0.56)
		Placebo	8	2 mos.	
—	Jialal, 1992[174]	Vitamin E	12	3 mos.	0.63 (–0.19, 1.45)
		Placebo	12	3 mos.	
—	Kaikkonen, 2000[151]	Vitamin E	10	3 mos.	0.63 (–0.27, 1.53)
		Placebo	10	3 mos.	
—	McGavin, 2001[177]	Vitamin E	10	2 mos.	0.27 (–0.44, 0.97)
		Placebo	35	2 mos.	
—	Mottram, 1999[178]	Vitamin E	14	2 mos.	0.62 (–0.14, 1.38)
		Placebo	14	2 mos.	
—	Paolisso, 1995[180]	Vitamin E	15	4 mos.	0.37 (–0.35, 1.09)
		Placebo	15	4 mos.	
MASI	Porkkala–Sarataho, 1998[113]	Vitamin E	20	2 mos.	0.06 (–0.56, 0.68)
		Placebo	20	2 mos.	
—	de Lorgeril, 1994[184]	Vitamin E	10	2 mos.	–0.15 (–1.03, 0.72)
		Placebo	10	2 mos.	
—	Stampfer, 1983[182]	Vitamin E	15	4 mos.	0.35 (–0.37, 1.08)
		Placebo	15	4 mos.	
Random Effects Pooled Estimate		Vitamin E	307		**0.01 (–0.21, 0.22)[a]**
		Placebo	318		
Not Pooled:					
GISSI	GISSI, 1999[115]	Vitamin E	2830	6 mos.	–0.03 (–0.09, 0.02)
		Placebo	2828	6 mos.	

[a]chi–squared test of heterogeneity p=0.07

Table 19. Risk ratios for vitamin E in combination vs. Placebo: total cholesterol

Named Trial	Author, Year	Intervention	n	Followup Time	Effect Size (95% CI)
—	Jialal, 1993[175]	Vitamin E in combination	12	3 mos.	0.36 (–0.45,1.17)
		Placebo	12	3 mos.	
—	Kaikkonen, 2000[151]	Vitamin E in combination	10	3 mos.	–0.09 (–0.97, 0.79)
		Placebo	10	3 mos.	
—	McDowell, 1994[176]	Vitamin E in combination	8	2 mos.	–0.71 (–1.72, 0.30)
		Placebo	8	2 mos.	
—	Mosca, 1997[55]	Vitamin E in combination	14	3 mos.	1.11 (0.31, 1.90)
		Placebo	14	3 mos.	
—	Nyyssonen, 1994[179]	Vitamin E in combination	20	3 mos.	0.35 (–0.28, 0.97)
		Placebo	20	3 mos.	
—	Schafer, 1990[181]	Vitamin E in combination	15	3 mos.	0.26 (–0.46, 0.98)
		Placebo	15	3 mos.	
—	Tomeo, 1995[183]	Vitamin E in combination	25	3 mos.	0.12 (–0.44, 0.67)
		Placebo	25	3 mos.	
Random Effects		Vitamin E in combination	104		**0.24 (–0.10, 0.59)[a]**
Pooled Estimate		Placebo	104		
Not Pooled:					
GISSI	GISSI, 1999[115]	Vitamin E in combination	2830	6 mos.	0.07 (0.02,0.13)
		Placebo	2828	6 mos.	
MRC/BHF	HPSCG, 2002[94]	Vitamin E in combination	10241	60 mos.	0.09 (0.06, 0.11)
		Placebo	10228	60 mos.	

[a]chi–squared test of heterogeneity p=0.18

Table 19. Risk ratios for vitamin E in combination vs. Placebo: total cholesterol

Named Trial	Author, Year	Intervention	n	Followup Time	Effect Size (95% CI)
—	Jialal, 1993[175]	Vitamin E in combination	12	3 mos.	0.36 (–0.45,1.17)
		Placebo	12	3 mos.	
—	Kaikkonen, 2000[151]	Vitamin E in combination	10	3 mos.	–0.09 (–0.97, 0.79)
		Placebo	10	3 mos.	
—	McDowell, 1994[176]	Vitamin E in combination	8	2 mos.	–0.71 (–1.72, 0.30)
		Placebo	8	2 mos.	
—	Mosca, 1997[55]	Vitamin E in combination	14	3 mos.	1.11 (0.31, 1.90)
		Placebo	14	3 mos.	
—	Nyyssonen, 1994[179]	Vitamin E in combination	20	3 mos.	0.35 (–0.28, 0.97)
		Placebo	20	3 mos.	
—	Schafer, 1990[181]	Vitamin E in combination	15	3 mos.	0.26 (–0.46, 0.98)
		Placebo	15	3 mos.	
—	Tomeo, 1995[183]	Vitamin E in combination	25	3 mos.	0.12 (–0.44, 0.67)
		Placebo	25	3 mos.	
Random Effects		Vitamin E in combination	104		**0.24 (–0.10, 0.59)[a]**
Pooled Estimate		Placebo	104		
Not Pooled:					
GISSI	GISSI, 1999[115]	Vitamin E in combination	2830	6 mos.	0.07 (0.02,0.13)
		Placebo	2828	6 mos.	
MRC/BHF	HPSCG, 2002[94]	Vitamin E in combination	10241	60 mos.	0.09 (0.06, 0.11)
		Placebo	10228	60 mos.	

[a]chi–squared test of heterogeneity p=0.18

Table 20. Risk ratios for vitamin E in combination vs. Placebo: low-density lipoprotein

Named Trial	Author, Year	Intervention	n	Followup Time	Effect Size (95% CI)
—	Jialal, 1993[175]	Vitamin E in Combination	12	3 mos.	0.48 (–0.33, 1.29)
		Placebo	12	3 mos.	
—	Kaikkonen, 2000[151]	Vitamin E in Combination	10	3 mos.	–0.12 (–1.00, 0.76)
		Placebo	10	3 mos.	
—	McDowell, 1994[176]	Vitamin E in Combination	8	2 mos.	–0.73 (–1.74, 0.28)
		Placebo	8	2 mos.	
—	Mosca, 1997[55]	Vitamin E in Combination	14	3 mos.	1.17 (0.37, 1.97)
		Placebo	14	3 mos.	
—	Tomeo, 1995[183]	Vitamin E in Combination	25	3 mos.	0.09 (–0.46, 0.65)
		Placebo	25	3 mos.	
Random Effects		Vitamin E in Combination	104		**0.21 (–0.35, 0.77)**[a]
Pooled Estimate		Placebo	104		
Not Pooled:					
GISSI	GISSI, 1999[115]	Vitamin E in Combination	2830	6 mos.	0.13 (0.07, 0.18)
		Placebo	2828	6 mos.	
MRC/BHF	HPSCG, 2002[94]	Vitamin E in Combination	10241	60 mos.	0.06 (0.03, 0.08)
		Placebo	10228	60 mos.	

[a]chi–squared test of heterogeneity p=0.04

Table 21. Risk ratios for vitamin E in combination vs. Placebo: high-density lipoprotein

Named Trial	Author, Year	Intervention	n	Followup Time	Effect Size (95% CI)
—	Jialal, 1993[175]	Vitamin E in Combination	12	3 mos.	–0.05 (–0.85, 0.75)
		Placebo	12	3 mos.	
—	Kaikkonen, 2000[151]	Vitamin E in Combination	10	3 mos.	0.06 (–0.81, 0.94)
		Placebo	10	3 mos.	
—	McDowell, 1994[176]	Vitamin E in Combination	8	2 mos.	0.00 (–0.98, 0.98)
		Placebo	8	2 mos.	
—	Mosca, 1997[55]	Vitamin E in Combination	14	3 mos.	0.29 (–0.46, 1.03)
		Placebo	14	3 mos.	
—	Tomeo, 1995[183]	Vitamin E in Combination	25	3 mos.	–0.33 (–0.89, 0.23)
		Placebo	25	3 mos.	
Random Effect		Vitamin E in Combination	104		**–0.06 (–0.40, 0.27)**[a]
Pooled Estimate		Placebo	104		
Not Pooled:					
GISSI	GISSI, 1999[115]	Vitamin E in Combination	2830	6 mos.	–0.02 (–0.07, 0.03)
		Placebo	2828	6 mos.	
MRC/BHF	HPSCG, 2002[94]	Vitamin E in Combination	10241	60 mos.	0.06 (0.03, 0.09)
		Placebo	10228	60 mos.	

[a]chi–squared test of heterogeneity p=0.76