Appendix 1 Characteristics of Trials Included in the Final Meta-Analysis (n = 50) [posted as supplied by author]

Source (Project Name)		Country Location	Design (Type of Prevention)	Participants (Average Age, y; Women, %)	Duration of Supplementation, y (Follow-up Period, y)	Intervention vs. Control	Main Outcome Measures Used in the Present Meta-analysis	No. of participants for major CV events /No. of participants	
								Supplement group	Conrol group
1	Korpela et al, 1989	n.a.	RDBPCT (Secondary)	81 patients with AMI	6 (6)	Selenium-rich yeast (122 µg/d) vs. placebo	Cardiac death and non-fatal reinfarct	1/40	6/41
2	Kuklinski et al, 1994	Germany	RDBPCT (Secondary)	61 patients with AMI	1(1)	Sodium selenite (100 µg/d) + coenzyme Q10 (100 mg/d) vs. placebo	Cardiac death	0/32	6/29
3	Steiner et al, 1995	U.S.	RDBPCT (Secondary)	100 patients with TIA (71; 58)	2 (2)	Vitamin E (400 IU/d) + aspirin (325 mg/d) vs. aspirin (325 mg/d)	Stroke, recurrent TIA, hemorrhagic events, and other CV events	9/52	13/48
4	Omenn et al, 1996 (CARET)	U.S.	RDBPCT (Primary)	18314 smokers (current and former) and workers exposed to asbestos (57;44)	4 (4)	Beta-carotene (30 mg/d) + vitamin A (25,000 IU/d) vs. placebo	CV death	226/9420	151/8894
5	Stephens et al, 1996 (CHAOS)	U.K.	RDBPCT (Secondary)	2002 patients with angiographically proven coronary atherosclerosis (62; 16)	1.5 (1.5)	Vitamin E (400 or 800 IU/d) vs. placebo	Major CV events	41/1035	62/967
6	Mark et al, 1996 (LNIT)	China	RDBPCT (Primary)	3318 patients with esophageal dysplasia (54; 56)	6 (6)	Multiple vitamin/mineral supplements* daily vs. placebo	Cerebrovascular death	22/1657	35/1661
7	Hennekens et al, 1996 (PHS)	U.S.	RDBPCT (Primary)	22071 U.S. male physicians (40-84; 0)	12 (12)	Beta-carotene (50 mg/alternate day) vs. placebo	All important CV events	967/11036	972/11035
8	Greenberg et al, 1996 (SCP)	U.S.	RDBPCT (Primary)	1720 patients with nonmelanoma skin cancer (basal cell or squamous cell skin cancer) (63; 31)	4.3 (8.2)	Beta-carotene (50 mg/d) vs. placebo	CV death	68/861	59/859
9	Rapola et al, 1997 (ATBC)	Finland	RDBPCT (Secondary)	1862 men with a history of myocardial infarction (60; 0)	5.3 (5.3)	Beta-carotene (20 mg/d) or vitamin E (50 mg/d) vs. placebo	All coronary events	330/1424	94/438

10	Virtamo et al, 1998 (ATBC)	Finland	RDBPCT (Primary)	27171 male smokers with no history of myocardial infarction (57; 0)	6.1 (6.1)	Beta-carotene (20 mg/d) or vitamin E (50 mg/d) vs. placebo	Primary major coronary events	1577/20422	534/6849
11	Marchioli et al, 1999 (GISSI)	Italy	OLRCT (Secondary)	11324 patients surviving recent (<3 months) myocardial infarction (59; 15)	3.5 (3.5)	Vitamin E (300 mg/d) vs. none	CV death, non-fatal MI, and non-fatal stroke	571/5666	584/5668
12	Komulainen et al, 1999 (KOS)	Finland	RDBPCT (Primary)	323 postmenopausal women (53; 100)	5 (5)	Vitamin D3 (300 and 100 IU/d during the fifth year) + calcium (93 mg/d) with or without HRT vs. calcium (93 mg/d)	MI	4/228	0/115
13	Green et al, 1999 (NSCP)	Australia	RDBPCT (Primary)	1621 residents (49; 56)	4.5 (4.5)	Beta-carotene (30 mg/d) with or without daily application of a sun protection factor 15-plus sunscreen vs. placebo	CVD	6/801	12/820
14	Yusuf et al, 2000 (HOPE)	Canada	RDBPCT (Secondary)	9541 patients with a history CVD or DM at high risk for CV events (66; 27)	4.5 (4.5)	Vitamin E (400 IU/d) with or without ramipril vs. placebo	MI, stroke, and death from CV causes	772/4761	739/4780
15	Boaz et al, 2000 (SPACE)	Israel	RDBPCT (Secondary)	196 hemodialysis patients with pre-existing cardiovascular disease (65; 31)	1.4 (1.4)	Vitamin E (800 IU/d) vs. placebo	Total CVD endpoints including sudden death	18/97	34/99
16	Brown et al, 2001 (HATS)	Canada and U.S.	RDBPCT (Secondary)	160 patients with coronary disease and low HDL cholesterol levels (53; 13)	3 (3)	Vitamin C (1000 mg/d) + vitamin E (800 IU/d) + natural beta-carotene (25 mg/d) + selenium (100 µg/d) vs. placebo	CV death or nonfatal infarct	3/42	7/38

17	Roncaglioni et al, 2001 (PPP)	Italy	OLRCT (Secondary)	4495 patients with hypertension, hypercholesterolemia, DM, obesity, family history of premature myocardial infarction, or elderly individuals (64; 58)	3.6 (3.6)	Vitamin E (300 mg/d) with or without aspirin (100 mg/d) vs. control	Total CV events or CVD	158/2231	170/2264
18	You et al, 2001	China	RDBPCT (Primary)	3411 residents (35-69; n.a.)	3.3 (3.3)	Vitamin C (500 mg/d) + vitamin E (200 IU/d) + beta-carotene (15 mg/d) + selenium (75 µg/d) vs. placebo	CV death	9/1706	12/1705
19	Baker et al, 2002	n.a.	RDBPCT (Secondary)	1882 patients with CHD (n.a.)	1.7 (n.a.)	Folic acid (5 mg/d) vs. placebo	CHD	23/942	12/940
20	Collins et al, 2002 (HPS)	U.K.	RDBPCT (Secondary)	20536 patients with coronary disease, other occlusive disease, or DM (40-80; 25)	5 (5)	Vitamin C (250 mg/d) + vitamin E (600 mg/d) + beta-carotene (20 mg/d) vs. placebo	Any major vascular event	2306/10269	2312/10267
21	Schnyder et al, 2002 (SHS)	Switzerland	RDBPCT (Secondary)	553 patients with established coronary atherosclerosis after percutaneous coronary intervention (63; 20)	0.5 (0.9)	Folic acid (1 mg/d) + vitamin B6 (10 mg/d) + vitamin B12 (400 µg/d) vs. placebo	Nonfatal MI and cardiac death	10/272	18/281
22	Waters et al, 2002 (WAVE)	U.S. and Canada	RDBPCT (Secondary)	423 postmenopausal women with coronary stenosis (65; 100)	2.8 (2.8)	Vitamin C (500 mg twice/d) + vitamin E (400 IU twice/d) vs. placebo	CV death or nonfatal MI	14/212	8/211
23	Liem et al, 2003 (Goes)	The Netherlands	OLRCT (Secondary)	593 patients with stable CAD (65; 22)	2 (2)	Folic acid (0.5 mg/d) vs. control	CV death and or any CV events	32/300	28/293
24	Righetti et al, 2003	Italy	OLRCT (Primary)	81 chronic hemodialysis patients (64; 44)	1 (1)	Folic acid (5 mg or 15 mg/d) vs. control	New CV events	13/51	11/30
25	Trivedi et al, 2003	U.K.	RDBPCT (Primary)	2686 men and women living in the general community (75; 24)	5 (5)	Vitamin D3 (100,000 IU/4 m) vs. placebo	CVD	477/1345	503/1341

26	Lange et al, 2004	Germany and the Netherlands	RDBPCT (Secondary)	636 patients who had undergone successful coronary stenting (61; 73)	0.5 (0.5)	Folic acid (1.2 mg/d) + vitamin B6 (48 mg/d) + vitamin B12 (60 µg/d) vs. placebo	Major adverse coronary events	53/316	35/320
27	Hercberg et al, 2004 (SU.VI.MAX)	France	RDBPCT (Primary)	12,741 adults (35-60; 61)	7.5 (7.5)	Vitamin C (120 mg/d) + vitamin E (30 mg/d) + beta-carotene (6 mg/d) + selenium (100 µg/d) + zinc (20 mg/d) vs. placebo	Ischemic CVD	134/6364	137/6377
28	Toole et al, 2004 (VISP)	U.S., Canada, and Scotland	RDBPCT (Secondary)	3,680 patients with nondisabling ischemic stroke (66; 38)	2 (2)	High dose: folic acid (2.5 mg/d) + vitamin B6 (25 mg/d) + vitamin B12 (0.4 mg/d) vs. low dose: folic acid (20 µg/d) + vitamin B6 (200 µg/d) + vitamin B12 (6 µg/d)	Ischemic stroke or CHD	249/1827	257/1853
29	Wrone et al, 2004	U.S.	RDBPCT (Primary)	510 patients with ESRD (60; 50)	2 (2)	Folic acid (5 mg/d) or folic acid (15 mg/d) vs. folic acid (1 mg/d) with multivitamins† in all arms	MI, cerebrovascular accident, and TIA	34/342	13/168
30	Brazier et al, 2005	France	RDBPCT (Primary)	192 ambulatory elderly women with vitamin D insufficiency (75; 100)	1 (1)	Vitamin D3 (400 IU twice/d) + calcium carbonate (500 mg twice/d) vs. placebo	CV events	6/95	5/96
31	Lee et al, 2005 (WHS)	U.S.	RDBPCT (Primary)	39876 healthy women (55; 100)	10.1 (10.1)	Vitamin E (600 IU/alternate day) vs. placebo	Major CV events	482/19937	517/19939
32	Zoungas et al, 2006 (ASFAST)	Australia and New Zealand	RDBPCT (Primary)	315 patients with CRF (57; 32)	3.6 (3.6)	Folic acid (15 mg/d) vs. placebo	All CV events or death from CV cause	77/156	86/159

33	Lonn et al, 2006 (HOPE-2)	13 countries including Canada, U.S., Brazil, western Europe, Slovakia, etc.	RDBPCT (Secondary)	5,522 patients who had vascular disease or diabetes (69; 28)	5 (5)	Folic acid (2.5 mg/d) + vitamin B6 (50 mg/d) + vitamin B12 (1 mg/d) vs. placebo	Composite of death from CV causes, myocardial infarction, or stroke	519/2758	547/2764
34	Bonaa et al, 2006 (NORVIT)	Norway	RDBPCT (Secondary)	3,749 patients who had had an acute MI (63; 26)	3 (3)	Folic acid (0.8 mg/d) + vitamin B6 (40 mg/d) + vitamin B12 (0.4 mg/d) / folic acid (0.8 mg/d) + vitamin B12 (0.4 mg/d)/ vitamin B6 (40 mg/d) vs. placebo	Nonfatal or fatal MI (including sudden death attributed to coronary heart disease) and nonfatal or fatal stroke	544/2806	172/943
35	Stranges et al, 2006 (NPC)	U.S.	RDBPCT (Primary)	1,004 nonmelanoma skin cancer patients without CVD	7.6 (7.6)	Selenium (200 µg/d) vs. placebo	All CVD	103/504	96/500
36	Jamison et al, 2007 (HOST)	U.S.	RDBPCT (Primary)	2,056 patients with advanced chronic kidney disease or ESRD (66; 2)	3.2 (3.2)	Folic acid (40 mg/d) + vitamin B6 (100 mg/d) + vitamin B12 (2 mg/d) + vs. placebo	MI and stroke	166/1032	191/1024
37	Hsia et al, 2007 (WHI)	U.S.	RDBPCT (Primary)	36,282 postmenopausal women (62; 100)	7 (7)	Vitamin D3 (200 IU twice/d) + calcium carbonate (500 mg twice/d) vs. placebo	CV events	2281/18176	2172/18106
38	Berggren et al, 2008	Sweden	OLRCT (Primary)	199 older people with femoral neck fractures (82; 74)	1 (1)	Vitamin D (800 IU/d) + calcium (1000 mg/d) vs. control	CVD	47/102	40/97
39	Millman et al, 2008 (ICARE)	Israel	RDBPCT (Primary)	1,434 patients with DM (69; 52)	1.5 (1.5)	Vitamin E (400 IU/d) vs. placebo	MI, stroke, and CV death	16/102	40/97
40	Prince et al, 2008	Australia	RDBPCT (Primary)	302 elderly women with a low serum 25-hydroxy vitamin D concentration (77; 100)	1 (1)	Vitamin D2 (1,000 IU/d) + calcium citrate (1,000 mg/d) vs. placebo + calcium citrate (1,000 mg/d)	Ischemic heart disease and stroke	5/151	6/151

41	Albert et al, 2008 (WAFACS)	U.S.	RDBPCT (Secondary)	5,442 women who were US health professionals with either a history of CVD or 3 or more coronary risk factors (63; 100)	7.3 (7.3)	Folic acid (2.5 mg/d) + vitamin B6 (50 mg/d) + vitamin B12 (1 mg/d) vs. placebo	Combined major CVD	406/2721	390/2721
42	Ebbing et al, 2008 (WENBIT)	Norway	RDBPCT (Secondary)	3,096 patients with coronary artery disease or aortic valve stenosis (62; 79)	3.2 (3.2)	Folic acid (0.8 mg/d) + vitamin B6 (40 mg/d) + vitamin B12 (0.4 mg/d)/ folic acid (0.8 mg/d) + vitamin B12 (0.4 mg/d)/ vitamin B6 (40 mg/d) vs. placebo	AMI, unstable angina, and stroke	313/2311	104/779
43	Hodis et al, 2009 (BVAIT)	U.S.	RDBPCT (Primary)	506 people with a high fasting plasma total homocysteine level (61; 39)	3.1 (3.1)	Folic acid (5 mg/d) + vitamin B6 (50 mg/d) + vitamin B12 (0.4 mg/d) vs. placebo	CV events	9/254	11/252
44	House et al, 2010 (DIVINe)	Canada	RDBPCT (Primary)	238 patients with type 1 or 2 diabetes and a clinical diagnosis of diabetic nephropathy (60; 11)	2.7 (2.7)	Folic acid (2.5 mg/d) + vitamin B6 (25 mg/d) + vitamin B12 (1 mg/d) vs. placebo	MI and stroke	14/119	5/119
45	Heinz et al, 2010	Germany	RDBPCT (Primary)	650 patients with ESRD (61; 42)	2 (2)	Folic acid (5 mg three times/w) + vitamin B6 (20 mg three times/w) + vitamin B12 (50 µg three times/w) vs. folic acid (0.2 mg three times/w) + vitamin B6 (1 mg three times/w) + vitamin B12 (4 µg three times/w)	CV events	83/327	98/323
46	Armitage et al, 2010 (SEARCH)	U.K.	RDBPCT (Secondary)	12,064 survivors of myocardial infarction (64; 17)	6.7 (6.7)	Folic acid (2 mg/d) + vitamin B12 (1 mg/d) vs. placebo	Major coronary events and stroke	1537/6033	1493/6031

47	Galan et al, 2010 (SU.FOL.OM3)	France	RDBPCT (Secondary)	2,501 patients with a history of MI, unstable angina, or ischaemic stroke (61; 20)	4.7 (4.7)	Folic acid (560 µg/d) + vitamin B6 (3 mg/d) + vitamin B12 (20 µg/d) ± omega-3 fatty acids (EPA and DHA at a ratio of 2:1) vs. placebo	Major CV events (non-fatal MI, stroke, or CV death)	75/1242	82/1259
48	Graeme et al, 2010 (VITATOPS)	20 countries from four continents including Australia, U.K., New Zealand, etc.)	RDBPCT (Secondary)	8,164 patients with recent TIA or stroke (63; 36)	3.4 (3.4)	Folic acid (2 mg/d) + vitamin B6 (25 mg/d) + vitamin B12 (0.5 mg/d) vs. placebo	Stroke, MI, or vascular death	616/4089	678/4075
49	Bostom et al, 2011 (FAVORIT)	U.S.	RDBPCT (Primary)	4,110 stable kidney transplant recipients (52; 37)	4 (4)	Folic acid (5.0 mg/d) + vitamin B6 (50 mg/d) + vitamin B12 (1 mg/d) vs. vitamin B6 (1.4 mg/d) + vitamin B12 (2.0 µg/d) with multivitamins in both arms	Any primary CVD outcome	269/2056	278/2054
50	Sesso et al, 2012 (PHS2)	U.S.	RDBPCT (Primary)	14,641 U.S. male physicians (64; 0)	11.2 (11.2)	Multivitamin vs. placebo	Major CV events	876/7317	856/7324

* Vitamins A/B_1/B_2/ B_6/ B_{12} /C/D/E, folic acid, beta-carotene, biotin, pantothenic acid, calcium, phosphorus, iodine, iron, magnesium, copper, manganese, potassium, chloride, molybdenum, selenium, and zinc.

†Vitamins B_1/B_3/B_6/ B_{12} /C, pantothenic acid, and biotin.

n.a., not available; RDBPCT, randomised, double-blind, placebo-controlled trial; OLRCT, open-label, randomised, controlled trial; AMI, acute myocardial infarction; TIA, transient ischemic attack; CV, cardiovascular; MI, myocardial infarction; HRT, hormone replacement therapy; DM, diabetes mellitus; HDL, high-density lipoprotein; CHD, coronary heart disease; CAD, coronary artery disease; CRF, chronic renal failure; EPA, eicosapentanoic acid; DHA, docosahexaenoic acid

CARET, the Beta-Carotene and Retinol Efficacy Trial; CHAOS, the Cambridge Heart Antioxidant Study; LNIT, the Linxian Nutrition Intervention Trial; PHS, the Physicians' Health Study; SCP, the Skin Cancer Prevention Study; ATBC, the Alpha-tocopherol Beta-carotene Cancer Prevention Study; GISSI, the Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto miocardico-Prevenzione trial; KOS, the Kuopio Osteoporosis Study; NSCP, the Nambour Skin Cancer Prevention trial; HOPE, the Heart Outcomes Prevention Evaluation Study; SPACE, Secondary Prevention with Antioxidants of Cardiovascular disease in Endstage renal disease; HATS, the HDL-Atherosclerosis Treatment Study; PPP, the Primary Prevention Project; HPS, the Heart Protection Study; SU.VI.MAX, the Supplemenatation en Vitamines et Mineraux Antioxydants; WHS, the Women's Health Study; ASFAST, the Atherosclerosis and Folic Acid Supplementation Trial; HOPE-2, The Heart Outcomes Prevention Evaluation 2 study; NORVIT, the Norwegian Vitamin Trial; NPC, the Nutritional Prevention of Cancer trial; WHI, the Women's Health Initiative; ICARE, the Israel Cardiovascular Events Reduction with Vitamin E trial; WAFACS, the Women's Antioxidant and Folic Acid Cardiovascular Study; WENBIT, the Western Norway B Vitamin Intervention Trial; BVAIT, the B-Vitamin Atherosclerosis Intervention Trial; DIVINe, the Diabetic Intervention with Vitamins to Improve Nephropathy; SEARCH, the Study of the Effectiveness of Additional Reductions in Cholesterol and Homocysteine study; SU.FOL.OM3, the

Supplémentation en Folates et Omega-3; VITATOPS, the Vitamins to Prevent Stroke trial; VISP, the Vitamin Intervention for Stroke Prevention randomised controlled trial; FAVORIT, the Folic Acid for Vascular Outcome Reduction in Transplantation trial.