

Web Table 1. Prospective Cohort Studies of Vitamin Intake and All-cause Mortality						
Author Date	Cohort Age of Subjects	# deaths/ # subjects	Study dates FU years	Vitamins	Risk estimate (95% CI)	Statistically adjusted for
Enstrom 1992 [1]	NHEFS 25-74 (mean = 53)	1809/ 10,550	1971-1984 10 (median)	Total C index	0.70 (0.56-0.84)  0.85 (0.69-1.01)	Age and sex  Age, sex, race, education, smoking, alcohol, exercise, cholesterol, history of serious disease, calories, fat, dietary vitamin A
Stampfer 1993 [2]	NHS 34-59 (mean = 50) women	974/ 87,245	1980-1988 8	Supplement E MV	0.87 (0.69-1.10) 1.10 (0.94-1.27)	Age, time period, smoking, alcohol, exercise, Quetelet index, cholesterol, aspirin use, hypertension, diabetes, total energy intake, menopausal status, HRT, vitamin E supplements, MV supplements
Kim 1993 [3]	NHEFS 25-74 (mean = 50)	2793/ 10,758	1971-1987 13 (mean)	MVM	1.02 (0.90-1.17) women 0.94 (0.82-1.06) men	Age, race, education, marital status, smoking, alcohol, BMI, serious medical conditions, special diet
Pandey 1993 [4]	Western Electric Study 40-55 men	552/ 1556	1958-1983 24	Dietary C  Dietary $\beta$ - carotene	0.93 medium vs. low 0.73 high vs. low P=0.007 for trend 0.82 medium vs. low 0.80 high vs. low P=0.01	Age, smoking, alcohol, BMI, blood pressure, cholesterol, family history of CVD, dietary intake of energy, cholesterol, iron, saturated fats, and polyunsaturated fats

Sahyoun 1996 [5]	Nutrition Status Survey 60-101 (mean = 73)	262/ 725	1981-1993 12	Total C  Total E  Dietary $\beta$ - carotene Supplement C Supplement E MV  Total C  Total E  Dietary $\beta$ - carotene	0.87 (0.62-1.23) medium vs. low 0.53 (0.38-0.84) high vs. low 0.79 (0.59-1.07) medium vs. low 0.77 (0.51-1.18) high vs. low 0.78 (0.56-1.08) medium vs. low 0.68 (0.44-1.07) high vs. low 0.88 (0.49-1.59) vs. no C/E/MV 1.44 (0.67-3.09) vs. no C/E/MV 0.89 (0.64-1.23) vs. no C/E/MV  0.85 (0.60-1.20) medium vs. low 0.55 (0.34-0.88) high vs. low 0.77 (0.56-1.04) medium vs. low 0.83 (0.54-1.27) high vs. low 0.77 (0.55-1.07) medium vs. low 0.72 (0.46-1.13) high vs. low	Age and sex       Age, sex, cholesterol, disease status, disabilities affecting shopping
Losonczy 1996 [6]	EPESE 65-105 (mean = 76)	3490/ 11,178	1984-1993	Supplements: E alone C alone E/C MVM  E alone C alone E/C MVM	Vs. no supplement use 0.80 (0.57-1.11) 1.04 (0.89-1.23) 0.58 (0.42-0.79) 1.04 (0.93-1.18)  0.87 (0.63-1.22) 1.09 (0.93-1.28) 0.63 (0.46-0.86) 1.03 (0.91-1.16)	Age, sex and other vitamins    Age, sex, race, education, smoking, alcohol, BMI, aspirin use, disease history (hypertension, coronary heart disease, stroke, diabetes, cancer) and other vitamins

Todd 1999 [7]	Scottish Heart Health Study 40-59 (mean=49)	350/ 7869	1984-1993	Dietary: C  E  $\beta$ -carotene  C  E  $\beta$ -carotene	Q4 vs. Q1 0.58 (0.32-1.03) women 0.57 (0.40-0.82) men 0.92 (0.53-1.60) women 0.73 (0.52-1.02) men 0.84 (0.50-1.41) women 0.76 (0.54-1.06) men  0.88 (0.47-1.63) women 0.68 (0.46-1.01) men 1.28 (0.72-2.28) women 0.91 (0.63-1.31) men 1.07 (0.63-1.82) women 0.87 (0.61-1.23) men	Age    Age, alcohol, activity, BMI, blood pressure, cholesterol, triglycerides, HDL-cholesterol, diabetes, energy, personality score, fibrinogen, carbon monoxide
Watkins 2000 [8]	CPS II $\geq 30$	14,753/ 1,063,023	1982-1989 7	Supplements: MVM  A, C or E  MVM  A, C or E	Vs. no supplement use 0.99 women 1.02 men 0.87 women 0.89 men  1.02 (1.00-1.05) women 1.05 (1.02-1.08) men 0.95 (0.92-0.98) women 0.98 (0.96-1.01) men	Age    Age, race, education, marital status, employment, smoking, alcohol, coffee, exercise, BMI, aspirin use, diuretic use, estrogen use (women), disease history (hypertension, heart disease, stroke, diabetes, cancer, cirrhosis, kidney disease), vegetable index
Genkinger 2004 [9]	Odyssey Cohort 30-93 (mean=56)	910/ 6151	1989-2002	Dietary: C E $\beta$ -carotene  C E $\beta$ -carotene	Q5 vs. Q1 0.88 (0.72-1.07) 0.94 (0.77-1.14) 0.81 (0.66-1.00)  0.95 (0.77-1.17) 0.98 (0.80-1.19) 0.81 (0.66-1.00)	Age and energy   Age, smoking, BMI, cholesterol, energy

Iso 2007 [10]	JACC 40-79	16,678/ 105,629	?-2003	MVM  Supplement C  Supplement E	0.98 (0.90-1.08) women 1.02 (0.95-1.10) men 0.93 (0.82-1.04) women 1.06 (0.95-1.18) men 0.92 (0.83-1.03) women 0.92 (0.81-1.04) men	Age and region
Hayden 2007 [11]	Cache County Study 65+ (mean=75)	1129/ 4416	1995-2002 7	Supplement E	0.93 (0.74-1.15)  1.00 (0.80-1.25)  Note increased risk in those with preexisting cardiac disease	Age and sex  Age, sex, disease history (myocardial infraction, stroke, diabetes, coronary artery bypass graft surgery), nitrates, warfarin, diuretics
Agudo 2007 [12]	EPIC-Spain 30-69 (mean=49)	562/ 41,358	1992-2002 6.5 (mean)	Dietary: C E Provitamin A β-carotene	Q4 vs. Q1 0.74 (0.58-0.94) 0.83 (0.64-1.08) 0.68 (0.53-0.87) 0.74 (0.58-0.95)	Age, sex, education, smoking, alcohol, physical activity, BMI, total energy
Messerer 2008 [13]	Swedish cohort 45-79 (mean=59) men	3403/ 38,944	1997-2005 8	Regular supplement use	1.00 (0.91-1.09)  1.04 (0.95-1.13)	Age  Age, education, marital status, smoking, physical activity, BMI, cholesterol, hypertension, diabetes, self-perceived health, and food score
Brzozowska 2008 [14]	SENECA Study 70-75 (mean = 73)	697/ 1900	1988-1999 10	Supplements: C  A  E	Vs. no supplement use 1.55 (0.97-2.46) smoker 0.71 (0.45-1.13) non-smoker 1.22 (0.73-2.03) smoker 0.82 (0.50-1.34) non-smoker 1.31 (0.78-2.21) smoker 0.97 (0.62-1.51) non-smoker	Age, sex, education, latitude, alcohol, physical activity, BMI, chronic diseases, Mediterranean diet score
Neuhauser 2009 [15]	WHI 50-79 women	9865/ 161,806	1993-2005 8 (median)	MVM	1.02 (0.97-1.07)	Age, ethnicity, education, geographic region, smoking, alcohol, physical activity, BMI, menopausal status, HRT, general health, fruit and vegetable intake, energy from fat, single supplements of C/E/calcium/other

Pocobelli 2009 [16]	VITAL Study 50-76	3577/ 77,673	2000-2006 5 (mean)	Supplements: MV C E  MV C E	10-yr average frequency (MV) or 10-yr average dose, T3 vs. 0 0.87 (0.81-0.91) 0.73 (0.66-0.80) 0.72 (0.69-0.79)  1.00 (0.92-1.09) 0.89 (0.81-0.98) 0.89 (0.81-0.98)	Age and sex  Age, sex, ethnicity, education, marital status, smoking, alcohol, physical activity, BMI, aspirin use, NSAID use, cholesterol meds, HRT, PSA screening, mammogram, sigmoidoscopy, self-rated health, morbidity score, parents' ages at death, fruit and vegetable intake, calories from saturated fats& trans-fats
Dietrich 2009 [17]	Framingham Heart Study & Framingham Offspring Study Mean=59	611/ 4270	1986-2005 10	Supplement E	1.01 (0.78-1.30)	Age, sex, smoking, BMI, blood pressure, blood pressure treatment, cholesterol, diabetes, cardiovascular disease
Mursu 2011 [18]	IWHS 55-69 (mean=62) women	15,594/ 38,722	1986-2008 19 (mean)	Supplements: MVM A $\beta$ -carotene C E  MVM A $\beta$ -carotene C E	Vs. no supplement use 1.02 (0.99-1.05) 0.99 (0.93-1.05) 1.00 (0.85-1.17) 0.96 (0.96-0.99) 0.94 (0.90-0.99)  1.06 (1.02-1.10) 1.06 (0.99-1.13) 1.10 (0.93-1.30) 1.01 (0.97-1.05) 1.01 (0.96-1.05)	Age and energy  Age, education, residence, smoking, alcohol, physical activity, BMI, waist-to-hip ratio, HRT, hypertension, diabetes, and intakes of total energy, saturated fat, whole grains, fruits, and vegetables

Park 2011 [19]	MEC Study 45-75 (mean = 60)	28,851/ 182,099	1993-2005 11 (mean)	MVM	0.96 (0.85-1.09) women 1.07 (0.96-1.19) men	Age, ethnicity, education, smoking, alcohol, physical activity, BMI, HRT, preexisting illness, menopausal status, fruit intake, vegetable intake, energy from fat, single supplement use
Li 2012 [20]	EPIC-Heidelberg 35-64 (mean=50)	1101/ 23,943	1994-2006 11 (mean)	Supplements: MVM Anti-oxidant Other	Vs. no supplement use 0.85 (0.63-1.14) 0.58 (0.38-0.88) 0.97 (0.84-1.11)	Age, sex, education, smoking, physical activity, BMI, waist-to- hip ratio, NSAID use, intakes of total energy and meat
Roswall 2012 [21]	Diet, Cancer and Health Study 50-64 (median=56)	6767/ 55,453	1993-2010 13.8 (mean)	Dietary: C E $\beta$ -carotene Supplements: C E $\beta$ -carotene	per 100 mg/day for C, 10 mg/day for E, 5000 $\mu$ g/day for $\beta$ - carotene 1.05 (0.99-1.11) 0.90 (0.80-1.02) 0.98 (0.95-1.01) 1.00 (0.99-1.01) 1.00 (1.00-1.01) 1.02 (0.91-1.15)	Education, smoking, alcohol, physical activity, BMI, waist circumference, and dietary intake for supplements and supplemental intake for dietary intake

Abbreviations: BMI, body mass index; CPS, Cancer Prevention Study; CVD, cardiovascular disease; EPES, Established Populations for Epidemiologic Studies of the Elderly; EPIC, European Prospective Investigation into Cancer and Nutrition; HRT, hormone replacement therapy; IWHS, Iowa Women's Health Study; JACC, Japan Collaborative Cohort study; MEC, Multiethnic Cohort; MV, multivitamin; MVM, multivitamin-multimineral; NHEFS, National Health and Nutrition Examination Survey I Epidemiologic Follow-up Study; NHS, Nurses' Health Study; NSAID, non-steroidal anti-inflammatory drug; SENECA, Survey in Europe on Nutrition and the Elderly, a Concerted Action; VITAL, Vitamins and Lifestyle; WHI, Women's Health Initiative

1. Enstrom JE, Kanim LE, Klein MA. Vitamin C intake and mortality among a sample of the United States population. *Epidemiology* 1992; 3(3):194-202.
2. Stampfer MJ, Hennekens CH, Manson JE, et al. Vitamin E consumption and the risk of coronary disease in women. *N Engl J Med* 1993;328(20):1444-1449.
3. Kim I, Williamson DF, Byers T, Koplan JP. Vitamin and mineral supplement use and mortality in a US cohort. *Am J Public Health* 1993;83(4):546-550.
4. Pandey DK, Shekelle R, Selwyn BJ, Tangney C, Stamler J. Dietary vitamin C and  $\beta$ -carotene and risk of death in middle-aged men. The Western Electric Study. *Am J Epidemiol* 1995;142(12):1269-1278.
5. Sahyoun NR, Jacques PF, Russell RM. Carotenoids, vitamins C and E, and mortality in an elderly population. *Am J Epidemiol* 1996;144(5):501-511.
6. Losonczy KG, Harris TB, Havlik RJ. Vitamin E and vitamin C supplement use and risk of all-cause and coronary heart disease mortality in older persons: the Established Populations for Epidemiologic Studies of the Elderly. *Am J Clin Nutr* 1996;64(2):190-196.
7. Todd S, Woodward M, Turnstall-Pedoe H, Bolton-Smith C. Dietary antioxidant vitamins and fiber in the etiology of cardiovascular and all-causes mortality: results from the Scottish Heart Health Study. *Am J Epidemiol* 1999;150(10):1073-1080.
8. Watkins ML, Erickson JD, Thun MJ, Mulinaire J, Heath CW Jr. Multivitamin use and mortality in a large prospective study. *Am J Epidemiol* 2000;152(2):149-162.
9. Genkinger JM, Platz EA, Hoffman SC, Comstock GW, Helzlsouer KJ. Fruit, vegetable, and antioxidant intake and all-cause, cancer, and cardiovascular disease mortality in a community-dwelling population in Washington County, Maryland. *Am J Epidemiol* 2004; 160(2) 1223-1233.
10. Iso H, Kubota Y. Nutrition and disease in the Japan Collaborative Cohort Study for

- Evaluation of Cancer (JACC). *Asian Pacific J Cancer Prev* 2007; 8 Suppl: 35-40.
11. Hayden KM, Welsh-Bohmer KA, Wengreen HJ, et al. Risk of mortality with vitamin E supplements: The Cache County Study. *Am J Med* 2007;120(2):180-184.
  12. Agudo A, Cabrera L, Amiano P, et al. Fruit and vegetable intakes, dietary antioxidant nutrients, and total mortality in Spanish adults: findings from the Spanish cohort of the European Prospective Investigation into Cancer and Nutrition (EPIC-Spain). *Am J Clin Nutr* 2007;85(6):1634-1642.
  13. Messerer M, Håkansson, Wolk A, Åkesson A. Dietary supplement use and mortality in a Swedish cohort. *Brit J Nutr* 2008;99(3):626-631.
  14. Brzozowska A, Kaluza J, Knoop KTB, de Groot LCPGM. Supplement use and mortality: the SENECA study. *Eur J Nutr* 2008;47(3):131-137.
  15. Neuhauser ML, Wasserheil-Smoller S, Thomson C, et al. Multivitamin use and risk of cancer and cardiovascular disease in the Women's Health Initiative Cohorts. *Arch Intern Med* 2009;169(3):294-304.
  16. Pocobelli G, Peters U, Kristal AR, White E. Use of supplements of multivitamins, vitamin C, and vitamin E in relation to mortality. *Am J Epidemiol* 2009; 170(4):472-483.
  17. Dietrich M, Jacques PF, Pencina MJ, et al. Vitamin E supplement use and incidence of cardiovascular disease and all-cause mortality in the Framingham Heart Study: does the underlying health status play a role? *Atherosclerosis* 2009;205(2):549-543.
  18. Mursu J, Robien K, Harnack LJ, Park K, Jacobs DR Jr. Dietary supplements and mortality rate in older women. *Arch Intern Med* 2011;171(18):1625-1633.
  19. Park S-Y, Murphy SP, Wilkens LR, Henderson BE, Kolonel LN. Multivitamin use and the risk of mortality and cancer incidence. The Multiethnic Cohort Study. *Am J*



Epidemiol 2011;173(8):906-914.

20. Li K, Kaaks R, Linselsen J, Rohrmann S. Vitamin/mineral supplementation and cancer, cardiovascular, and all-cause mortality in a German prospective cohort (EPIC-Heidelberg). *Eur J Nutr* 2012;51(4):407-413.
21. Roswall N, Olsen A, Christensen J, Hansen L, et al. Micronutrient intake in relation to all-cause mortality in a prospective Danish cohort. *Food & Nutrition Research* 2012;56:5466.