

Supplemental Online Content

Loftfield E, O'Connell CP, Abnet CC, et al. Multivitamin use and mortality risk in 3 prospective US cohorts. *JAMA Netw Open*. 2024;7(6):e2418729. doi:10.1001/jamanetworkopen.2024.18729

eFigure 1. Flowchart for Final Analytic Sample

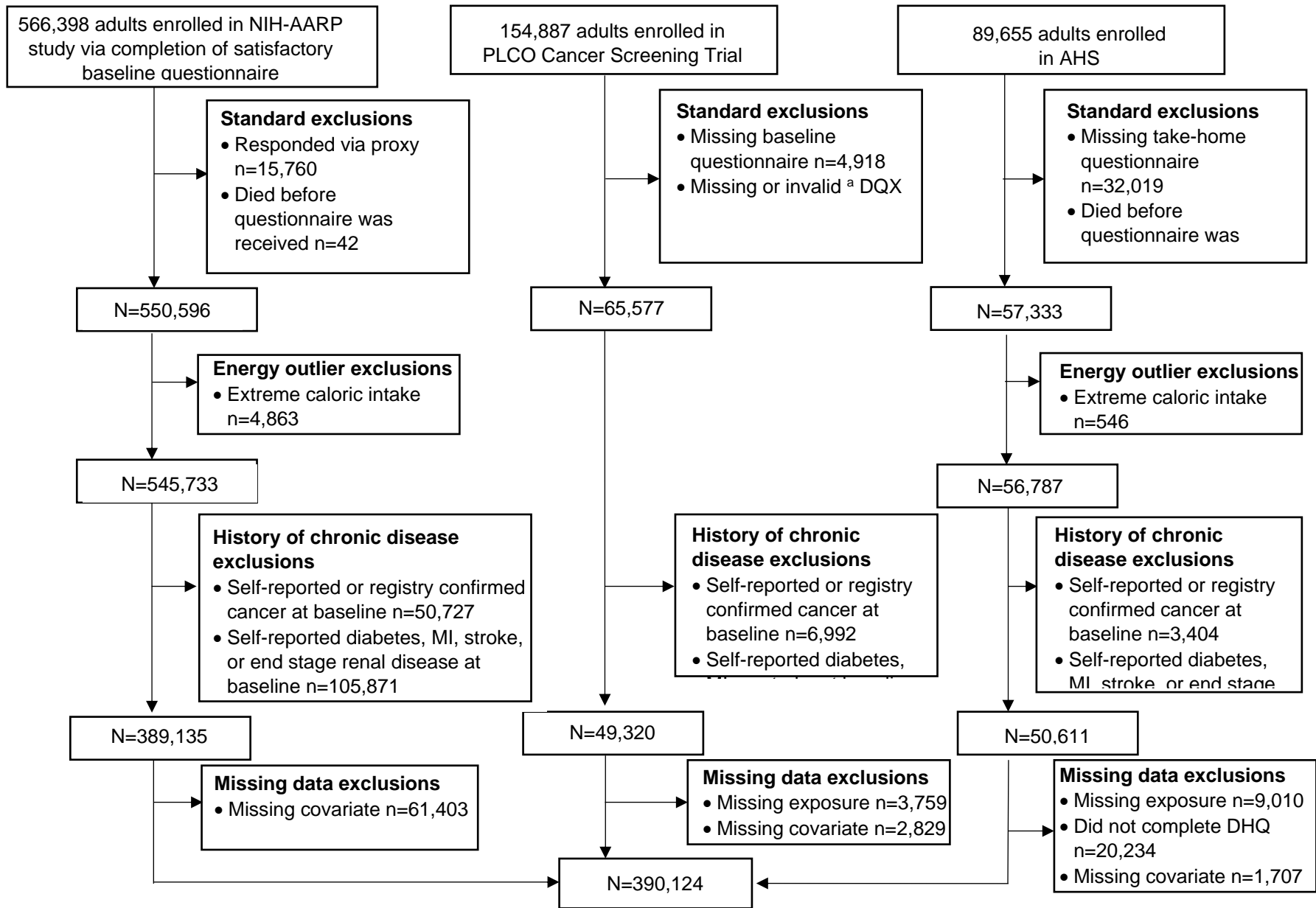
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This supplemental material has been provided by the authors to give readers additional information about their work.



eFigure 1. Flowchart for final analytic sample

^a A Dietary Questionnaire (DQX) was considered invalid if the participant died before completion, had more than 8 missing or multiple-frequency responses, had a missing completion date or had extreme calorie consumption.

eTable 1. Baseline characteristics of study participants by cohort, according to multivitamin use

Characteristic, No. (%) ^a	Nonuse N=144947	Nondaily use N=41829	Daily use N=140956	Overall N=327732
AARP participants				
Age, median (IQR), y	62.0 (57.2 - 66.2)	60.7 (56.2 - 65.2)	62.2 (57.4 - 66.3)	61.9 (57.2 - 66.1)
Sex				
Female	55143 (38.0%)	19723 (47.2%)	66615 (47.3%)	141481 (43.2%)
Male	89804 (62.0%)	22106 (52.8%)	74341 (52.7%)	186251 (56.8%)
Race/Ethnicity				
American Indian/Alaskan Native	362 (0.2%)	114 (0.3%)	324 (0.2%)	800 (0.2%)
Asian/Pacific Islander	1897 (1.3%)	729 (1.7%)	1832 (1.3%)	4458 (1.4%)
Hispanic	2601 (1.8%)	855 (2.0%)	2371 (1.7%)	5827 (1.8%)
Non-Hispanic Black	5101 (3.5%)	1843 (4.4%)	3931 (2.8%)	10875 (3.3%)
Non-Hispanic White	134986 (93.1%)	38288 (91.5%)	132498 (94.0%)	305772 (93.3%)
Education				
less than 8 years, 8-11 years	8612 (5.9%)	1731 (4.1%)	5999 (4.3%)	16342 (5.0%)
12 years, completed high school, GED	30566 (21.1%)	6987 (16.7%)	26094 (18.5%)	63647 (19.4%)
post-high school training	14910 (10.3%)	4171 (10.0%)	13964 (9.9%)	33045 (10.1%)
some college	33294 (23.0%)	10475 (25.0%)	34327 (24.4%)	78096 (23.8%)
college and postgraduate	57565 (39.7%)	18465 (44.1%)	60572 (43.0%)	136602 (41.7%)
Smoking status				
Never smoker	54867 (37.9%)	16847 (40.3%)	54369 (38.6%)	126083 (38.5%)
Former smoker	70391 (48.6%)	19271 (46.1%)	70506 (50.0%)	160168 (48.9%)
Current smoker	19689 (13.6%)	5711 (13.7%)	16081 (11.4%)	41481 (12.7%)
Physical activity level				
Never/Rarely	27309 (18.8%)	6437 (15.4%)	20777 (14.7%)	54523 (16.6%)
Low (few times a month)	21516 (14.8%)	6973 (16.7%)	17804 (12.6%)	46293 (14.1%)
Moderate (few times a week)	32581 (22.5%)	10848 (25.9%)	30416 (21.6%)	73845 (22.5%)
High (many times a week)	63541 (43.8%)	17571 (42.0%)	71959 (51.1%)	153071 (46.7%)
Individual supplement use	50977 (35.2%)	34005 (81.3%)	119735 (84.9%)	204717 (62.5%)
BMI category				
< 18.5 kg/m ²	1421 (1.0%)	454 (1.1%)	1685 (1.2%)	3560 (1.1%)
18.5 to < 25 kg/m ²	49798 (34.4%)	15558 (37.2%)	56361 (40.0%)	121717 (37.1%)
25 to < 30 kg/m ²	63020 (43.5%)	17639 (42.2%)	58095 (41.2%)	138754 (42.3%)
≥ 30 kg/m ²	30708 (21.2%)	8178 (19.6%)	24815 (17.6%)	63701 (19.4%)
Alcohol category				
0 drinks per day	32001 (22.1%)	7829 (18.7%)	30147 (21.4%)	69977 (21.4%)
Less than 1 drink per day	76670 (52.9%)	24509 (58.6%)	77338 (54.9%)	178517 (54.5%)
1-2 drinks per day	18147 (12.5%)	4988 (11.9%)	17730 (12.6%)	40865 (12.5%)
2-3 drinks per day	5755 (4.0%)	1510 (3.6%)	5535 (3.9%)	12800 (3.9%)
3 or more drinks per day	12374 (8.5%)	2993 (7.2%)	10206 (7.2%)	25573 (7.8%)
Coffee intake				
None	15380 (10.6%)	3920 (9.4%)	15509 (11.0%)	34809 (10.6%)
Less than 1 cup per day	21837 (15.1%)	7065 (16.9%)	23029 (16.3%)	51931 (15.8%)
1 cup per day	22996 (15.9%)	6190 (14.8%)	23186 (16.4%)	52372 (16.0%)
2-3 cups per day	60156 (41.5%)	17598 (42.1%)	57639 (40.9%)	135393 (41.3%)
4-5 cups per day	18685 (12.9%)	5444 (13.0%)	16650 (11.8%)	40779 (12.4%)
6 or more cups per day	5893 (4.1%)	1612 (3.9%)	4943 (3.5%)	12448 (3.8%)

eTable 1. Baseline characteristics of study participants by cohort, according to multivitamin use (continued)

Characteristic, No. (%) ^a	Nonuse	Nondaily use	Daily use	Overall
HEI-2015 quartile				
Quartile 1	43563 (30.1%)	10502 (25.1%)	29369 (20.8%)	83434 (25.5%)
Quartile 2	37355 (25.8%)	10834 (25.9%)	33620 (23.9%)	81809 (25.0%)
Quartile 3	33827 (23.3%)	10601 (25.3%)	36995 (26.2%)	81423 (24.8%)
Quartile 4	30202 (20.8%)	9892 (23.6%)	40972 (29.1%)	81066 (24.7%)
Marital status				
Married or living as married	104174 (71.9%)	27806 (66.5%)	92912 (65.9%)	224892 (68.6%)
Divorced or separated	19786 (13.7%)	7658 (18.3%)	24134 (17.1%)	51578 (15.7%)
Widowed	14059 (9.7%)	4353 (10.4%)	16555 (11.7%)	34967 (10.7%)
Never married	6928 (4.8%)	2012 (4.8%)	7355 (5.2%)	16295 (5.0%)
Family history of cancer	74673 (51.5%)	21758 (52.0%)	73402 (52.1%)	169833 (51.8%)
Type of multivitamin				
Stress- tab/B-complex/Other type	0 (0%)	2822 (6.7%)	6239 (4.4%)	9061 (2.8%)
Therapeutic or Theragran type	0 (0%)	5824 (13.9%)	21726 (15.4%)	27550 (8.4%)
One-a-day type	0 (0%)	30287 (72.4%)	95962 (68.1%)	126249 (38.5%)
More than 1 type	0 (0%)	2896 (6.9%)	17029 (12.1%)	19925 (6.1%)
PLCO participants	N=19353	N=4471	N=18908	N=42732
Age, median (IQR), y	62.0 (58.0 - 66.0)	61.0 (57.0 - 65.0)	62.0 (58.0 - 66.0)	62.0 (58.0 - 66.0)
Sex				
Female	8187 (42.3%)	2503 (56.0%)	11414 (60.4%)	22104 (51.7%)
Male	11166 (57.7%)	1968 (44.0%)	7494 (39.6%)	20628 (48.3%)
Race/Ethnicity ^b				
American Indian/Alaskan Native	33 (0.2%)	13 (0.3%)	36 (0.2%)	82 (0.2%)
Asian/Pacific Islander	599 (3.1%)	175 (3.9%)	674 (3.6%)	1448 (3.4%)
Hispanic	241 (1.2%)	59 (1.3%)	267 (1.4%)	567 (1.3%)
Non-Hispanic Black	676 (3.5%)	135 (3.0%)	500 (2.6%)	1311 (3.1%)
Non-Hispanic White	17804 (92.0%)	4089 (91.5%)	17431 (92.2%)	39324 (92.0%)
Education				
less than 8 years, 8-11 years	1322 (6.8%)	173 (3.9%)	949 (5.0%)	2444 (5.7%)
12 years, completed high school, GED	4735 (24.5%)	821 (18.4%)	4236 (22.4%)	9792 (22.9%)
post-high school training	2411 (12.5%)	529 (11.8%)	2372 (12.5%)	5312 (12.4%)
some college	3948 (20.4%)	991 (22.2%)	4176 (22.1%)	9115 (21.3%)
college and postgraduate	6937 (35.8%)	1957 (43.8%)	7175 (37.9%)	16069 (37.6%)
Smoking status				
Never smoker	9114 (47.1%)	2284 (51.1%)	9321 (49.3%)	20719 (48.5%)
Former smoker	8177 (42.3%)	1754 (39.2%)	7963 (42.1%)	17894 (41.9%)
Current smoker	2062 (10.7%)	433 (9.7%)	1624 (8.6%)	4119 (9.6%)
Physical activity level				
Never/Rarely	3245 (16.8%)	466 (10.4%)	2420 (12.8%)	6131 (14.3%)
Low (few times a month)	3660 (18.9%)	874 (19.5%)	3108 (16.4%)	7642 (17.9%)
Moderate (few times a week)	5366 (27.7%)	1358 (30.4%)	5387 (28.5%)	12111 (28.3%)
High (many times a week)	7082 (36.6%)	1773 (39.7%)	7993 (42.3%)	16848 (39.4%)
Individual supplement use	6554 (33.9%)	3638 (81.4%)	15398 (81.4%)	25590 (59.9%)

eTable 1. Baseline characteristics of study participants by cohort, according to multivitamin use (continued)

Characteristic, No. (%) ^a	Nonuse	Nondaily use	Daily use	Overall
BMI category				
< 18.5 kg/m ²	105 (0.5%)	31 (0.7%)	159 (0.8%)	295 (0.7%)
18.5 to < 25 kg/m ²	6111 (31.6%)	1751 (39.2%)	7255 (38.4%)	15117 (35.4%)
25 to < 30 kg/m ²	8682 (44.9%)	1817 (40.6%)	7713 (40.8%)	18212 (42.6%)
≥ 30 kg/m ²	4455 (23.0%)	872 (19.5%)	3781 (20.0%)	9108 (21.3%)
Alcohol category				
0 drinks per day	3810 (19.7%)	878 (19.6%)	4188 (22.1%)	8876 (20.8%)
Less than 1 drink per day	10369 (53.6%)	2553 (57.1%)	10511 (55.6%)	23433 (54.8%)
1-2 drinks per day	2322 (12.0%)	479 (10.7%)	2052 (10.9%)	4853 (11.4%)
2-3 drinks per day	889 (4.6%)	207 (4.6%)	791 (4.2%)	1887 (4.4%)
3 or more drinks per day	1963 (10.1%)	354 (7.9%)	1366 (7.2%)	3683 (8.6%)
Coffee intake				
None	2106 (10.9%)	572 (12.8%)	2398 (12.7%)	5076 (11.9%)
Less than 1 cup per day	3724 (19.2%)	967 (21.6%)	3867 (20.5%)	8558 (20.0%)
1 cup per day	4225 (21.8%)	856 (19.1%)	4195 (22.2%)	9276 (21.7%)
2-3 cups per day	5934 (30.7%)	1330 (29.7%)	5622 (29.7%)	12886 (30.2%)
4-5 cups per day	2172 (11.2%)	528 (11.8%)	1947 (10.3%)	4647 (10.9%)
6 or more cups per day	1192 (6.2%)	218 (4.9%)	879 (4.6%)	2289 (5.4%)
HEI-2015 quartile				
Quartile 1	5880 (30.4%)	969 (21.7%)	3713 (19.6%)	10562 (24.7%)
Quartile 2	5193 (26.8%)	1101 (24.6%)	4489 (23.7%)	10783 (25.2%)
Quartile 3	4539 (23.5%)	1156 (25.9%)	5090 (26.9%)	10785 (25.2%)
Quartile 4	3741 (19.3%)	1245 (27.8%)	5616 (29.7%)	10602 (24.8%)
Marital status				
Married or living as married	15757 (81.4%)	3378 (75.6%)	14455 (76.4%)	33590 (78.6%)
Divorced or separated	1720 (8.9%)	598 (13.4%)	2133 (11.3%)	4451 (10.4%)
Widowed	1297 (6.7%)	338 (7.6%)	1702 (9.0%)	3337 (7.8%)
Never married	579 (3.0%)	157 (3.5%)	618 (3.3%)	1354 (3.2%)
Family history of cancer	10798 (55.8%)	2541 (56.8%)	10760 (56.9%)	24099 (56.4%)
Type of multivitamin				
Stress- tab/B-complex/Other type	0 (0%)	926 (20.7%)	3171 (16.8%)	4097 (9.6%)
Therapeutic or Theragran type	0 (0%)	276 (6.2%)	1611 (8.5%)	1887 (4.4%)
One-a-day type	0 (0%)	1861 (41.6%)	9739 (51.5%)	11600 (27.1%)
More than 1 type	0 (0%)	1408 (31.5%)	4387 (23.2%)	5795 (13.6%)
AHS participants	N=15366	N=851	N=3443	N=19660
Age, median (IQR), y	47.0 (39.0 - 56.0)	45.0 (37.0 - 55.0)	48.0 (38.0 - 57.0)	47.0 (38.0 - 56.0)
Sex				
Female	7298 (47.5%)	549 (64.5%)	2490 (72.3%)	10337 (52.6%)
Male	8068 (52.5%)	302 (35.5%)	953 (27.7%)	9323 (47.4%)
Race/Ethnicity^b				
American Indian/Alaskan Native	22 (0.1%)	1 (0.1%)	3 (0.1%)	26 (0.1%)
Asian/Pacific Islander	4 (0.0%)	0 (0.0%)	1 (0.0%)	5 (0.0%)
Hispanic	115 (0.7%)	5 (0.7%)	19 (0.6%)	139 (0.7%)
Non-Hispanic Black	66 (0.4%)	2 (0.3%)	9 (0.3%)	77 (0.4%)
Non-Hispanic White	15159 (98.7%)	843 (99.1%)	3411 (99.1%)	19413 (98.7%)

eTable 1. Baseline characteristics of study participants by cohort, according to multivitamin use (continued)

Characteristic, No. (%) ^a	Nonuse	Nondaily use	Daily use	Overall
Education				
less than 8 years, 8-11 years	677 (4.4%)	21 (2.5%)	116 (3.4%)	814 (4.1%)
12 years, completed high school, GED	6515 (42.4%)	261 (30.7%)	1211 (35.2%)	7987 (40.6%)
post-high school training	1735 (11.3%)	124 (14.6%)	409 (11.9%)	2268 (11.5%)
some college	2377 (15.5%)	156 (18.3%)	587 (17.0%)	3120 (15.9%)
college and postgraduate	3530 (23.0%)	237 (27.8%)	881 (25.6%)	4648 (23.6%)
other	532 (3.5%)	52 (6.1%)	239 (6.9%)	823 (4.2%)
Smoking status				
Never smoker	9862 (64.2%)	600 (70.5%)	2428 (70.5%)	12890 (65.6%)
Former smoker	3855 (25.1%)	182 (21.4%)	794 (23.1%)	4831 (24.6%)
Current smoker	1649 (10.7%)	69 (8.1%)	221 (6.4%)	1939 (9.9%)
Physical activity level				
Never/Rarely	3265 (21.2%)	119 (14.0%)	569 (16.5%)	3953 (20.1%)
Low (few times a month)	2797 (18.2%)	166 (19.5%)	616 (17.9%)	3579 (18.2%)
Moderate (few times a week)	2816 (18.3%)	181 (21.3%)	687 (20.0%)	3684 (18.7%)
High (many times a week)	6488 (42.2%)	385 (45.2%)	1571 (45.6%)	8444 (43.0%)
Individual supplement use	5044 (32.8%)	505 (59.3%)	2037 (59.2%)	7586 (38.6%)
BMI category				
< 18.5 kg/m ²	101 (0.7%)	12 (1.4%)	50 (1.5%)	163 (0.8%)
18.5 to < 25 kg/m ²	5462 (35.5%)	389 (45.7%)	1541 (44.8%)	7392 (37.6%)
25 to < 30 kg/m ²	6514 (42.4%)	312 (36.7%)	1320 (38.3%)	8146 (41.4%)
≥ 30 kg/m ²	3289 (21.4%)	138 (16.2%)	532 (15.5%)	3959 (20.1%)
Alcohol category				
0 drinks per day	5504 (35.8%)	278 (32.7%)	1310 (38.0%)	7092 (36.1%)
Less than 1 drink per day	8677 (56.5%)	519 (61.0%)	1962 (57.0%)	11158 (56.8%)
1-2 drinks per day	851 (5.5%)	40 (4.7%)	134 (3.9%)	1025 (5.2%)
2-3 drinks per day	244 (1.6%)	10 (1.2%)	23 (0.7%)	277 (1.4%)
3 or more drinks per day	90 (0.6%)	4 (0.5%)	14 (0.4%)	108 (0.5%)
Coffee intake				
None	4543 (29.6%)	253 (29.7%)	1086 (31.5%)	5882 (29.9%)
Less than 1 cup per day	3140 (20.4%)	195 (22.9%)	720 (20.9%)	4055 (20.6%)
1 cup per day	2016 (13.1%)	100 (11.8%)	443 (12.9%)	2559 (13.0%)
2-3 cups per day	3990 (26.0%)	214 (25.1%)	846 (24.6%)	5050 (25.7%)
4-5 cups per day	1226 (8.0%)	68 (8.0%)	258 (7.5%)	1552 (7.9%)
6 or more cups per day	451 (2.9%)	21 (2.5%)	90 (2.6%)	562 (2.9%)
HEI-2015 quartile				
Quartile 1	7713 (50.2%)	353 (41.5%)	1239 (36.0%)	9305 (47.3%)
Quartile 2	4189 (27.3%)	251 (29.5%)	1047 (30.4%)	5487 (27.9%)
Quartile 3	2282 (14.9%)	151 (17.7%)	692 (20.1%)	3125 (15.9%)
Quartile 4	1182 (7.7%)	96 (11.3%)	465 (13.5%)	1743 (8.9%)
Marital status				
Married or living as married	14262 (92.8%)	792 (93.1%)	3296 (95.7%)	18350 (93.3%)
Divorced or separated	245 (1.6%)	20 (2.4%)	32 (0.9%)	297 (1.5%)
Widowed	77 (0.5%)	6 (0.7%)	12 (0.3%)	95 (0.5%)
Never married	782 (5.1%)	33 (3.9%)	103 (3.0%)	918 (4.7%)
Family history of cancer	7431 (48.4%)	410 (48.2%)	1720 (50.0%)	9561 (48.6%)

eTable 1. Baseline characteristics of study participants by cohort, according to multivitamin use (continued)

Characteristic, No. (%) ^a	Nonuse	Nondaily use	Daily use	Overall
Type of multivitamin				
Stress- tab/B-complex/Other	0 (0%)	84 (9.9%)	219 (6.4%)	303 (1.5%)
Therapeutic or Theragran	0 (0%)	63 (7.4%)	266 (7.7%)	329 (1.7%)
One-a-day	0 (0%)	684 (80.4%)	2826 (82.1%)	3510 (17.9%)
More than 1 type	0 (0%)	20 (2.4%)	132 (3.8%)	152 (0.8%)

Abbreviations: HEI-2015 – Healthy Eating Index 2015; BMI – Body Mass Index

^a Percentages are column percentages.

^b Race or ethnic group was self-reported.

eTable 2. Study-specific hazard ratios between multivitamin use and mortality (all-cause and cause-specific)

Cause of Death	NIH-AARP				P value for trend
	Follow-up period 1 ^a		Follow-up period 2 ^a		
	Nondaily use	Daily use	Nondaily	Daily	
All-cause mortality					
N deaths	4063	15980	12678	47269	
Age and sex-adjusted HR (95%CI)	1.06 (1.02-1.10)	1.00 (0.98-1.02)	0.92 (0.85-0.99)	0.99 (0.94-1.04)	0.58
Multivariable-adjusted HR (95%CI) ^b	1.09 (1.05-1.13)	1.05 (1.02-1.07)	0.94 (0.88-1.02)	1.03 (0.98-1.08)	<.001
Heart disease mortality					
N deaths	706	3073	2701	10458	
Age and sex-adjusted HR (95%CI)	0.98 (0.90-1.06)	1.00 (0.96-1.06)	0.90 (0.76-1.07)	0.99 (0.89-1.10)	0.80
Multivariable-adjusted HR (95%CI) ^b	1.02 (0.94-1.11)	1.06 (1.01-1.12)	0.92 (0.78-1.10)	1.03 (0.93-1.15)	0.01
Cancer mortality					
N deaths	1761	6625	3454	11923	
Age and sex-adjusted HR (95%CI)	1.03 (0.98-1.09)	0.96 (0.93-0.99)	0.90 (0.80-1.01)	0.94 (0.87-1.01)	0.01
Multivariable-adjusted HR (95%CI) ^b	1.06 (1.01-1.12)	1.02 (0.98-1.05)	0.93 (0.83-1.05)	0.98 (0.91-1.06)	0.38
Cerebrovascular diseases mortality					
N deaths	162	723	761	3000	
Age and sex-adjusted HR (95%CI)	1.04 (0.87-1.23)	1.07 (0.96-1.19)	0.97 (0.68-1.39)	1.07 (0.85-1.33)	0.21
Multivariable-adjusted HR (95%CI) ^b	1.02 (0.86-1.21)	1.06 (0.95-1.18)	0.96 (0.67-1.37)	1.05 (0.84-1.32)	0.28

Cause of Death	PLCO				P value for trend
	Follow-up period 1 ^a		Follow-up period 2 ^a		
	Nondaily use	Daily use	Nondaily	Daily	
All-cause mortality					
N deaths	548	2379	927	4495	
Age and sex-adjusted HR (95%CI)	0.96 (0.88-1.06)	0.91 (0.86-0.96)	0.92 (0.75-1.14)	1.07 (0.95-1.21)	0.14
Multivariable-adjusted HR (95%CI) ^b	1.00 (0.91-1.10)	0.95 (0.90-1.01)	0.95 (0.77-1.18)	1.10 (0.97-1.25)	0.99
Heart disease mortality					
N deaths	104	428	188	958	
Age and sex-adjusted HR (95%CI)	1.04 (0.84-1.29)	0.93 (0.82-1.06)	0.91 (0.57-1.47)	1.10 (0.83-1.47)	0.69
Multivariable-adjusted HR (95%CI) ^b	1.13 (0.91-1.40)	0.99 (0.86-1.14)	0.96 (0.59-1.55)	1.15 (0.86-1.54)	0.65

eTable 2. Study-specific hazard ratios between multivitamin use and mortality (all-cause and cause-specific) (continued)

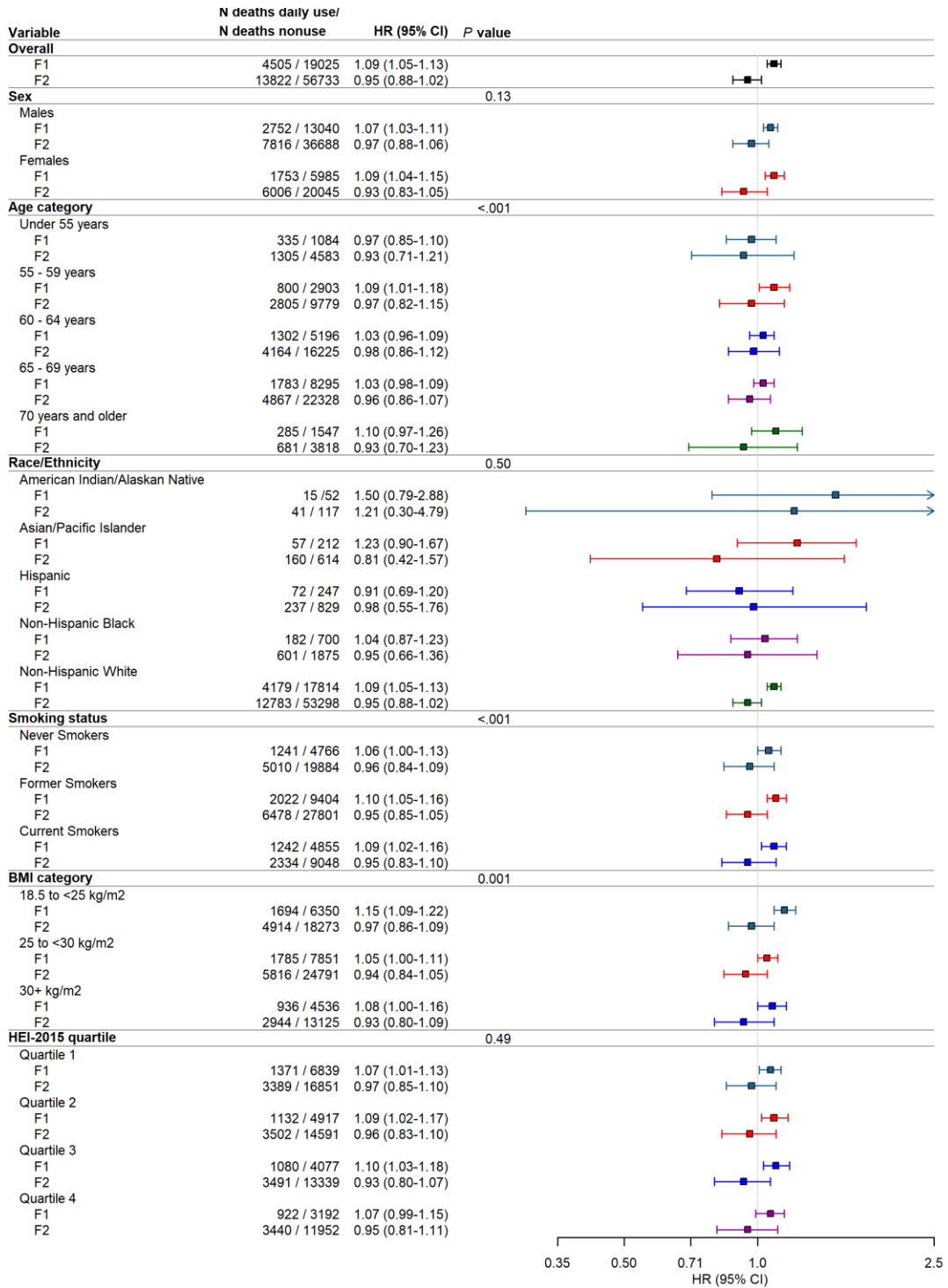
PLCO (continued)	Follow-up period 1 ^a		Follow-up period 2 ^a		P value for trend
Cancer mortality					
N deaths	211	955	217	966	
Age and sex-adjusted HR (95%CI)	0.87 (0.75-1.01)	0.89 (0.82-0.97)	0.87 (0.61-1.24)	0.96 (0.78-1.19)	0.11
Multivariable-adjusted HR (95%CI) ^b	0.90 (0.77-1.04)	0.93 (0.84-1.02)	0.90 (0.63-1.29)	0.99 (0.80-1.23)	0.61
Cerebrovascular diseases mortality					
N deaths	27	117	69	304	
Age and sex-adjusted HR (95%CI)	0.97 (0.64-1.47)	0.87 (0.68-1.13)	1.11 (0.45-2.75)	1.13 (0.65-1.96)	0.26
Multivariable-adjusted HR (95%CI) ^b	0.99 (0.65-1.52)	0.91 (0.70-1.18)	1.14 (0.45-2.84)	1.14 (0.65-2.00)	0.34

Cause of Death	AHS				P value for trend
	Follow-up period 1 ^a		Follow-up period 2 ^a		
	Nondaily use	Daily use	Nondaily	Daily	
All-cause mortality					
N deaths	25	102	86	452	
Age and sex-adjusted HR (95%CI)	1.08 (0.72-1.63)	0.97 (0.78-1.21)	0.85 (0.36-2.02)	1.00 (0.63-1.58)	0.83
Multivariable-adjusted HR (95%CI) ^b	1.04 (0.69-1.56)	1.18 (0.95-1.48)	0.92 (0.38-2.21)	1.08 (0.67-1.72)	0.12
Heart disease mortality					
N deaths	3	27	17	87	
Age and sex-adjusted HR (95%CI)	Did not converge	1.12 (0.73-1.72)	Did not converge	0.92 (0.37-2.30)	0.53
Multivariable-adjusted HR (95%CI) ^b	Did not converge	1.54 (0.98-2.40)	Did not converge	0.98 (0.38-2.51)	<.001
Cancer mortality					
N deaths	13	41	29	137	
Age and sex-adjusted HR (95%CI)	1.35 (0.77-2.38)	0.99 (0.70-1.39)	0.92 (0.27-3.20)	1.03 (0.49-2.13)	0.99
Multivariable-adjusted HR (95%CI) ^b	1.46 (0.82-2.60)	1.17 (0.83-1.67)	1.00 (0.28-3.55)	1.10 (0.52-2.31)	0.32
Cerebrovascular diseases mortality					
N deaths	1	10	5	24	
Age and sex-adjusted HR (95%CI)	Did not converge	1.69 (0.78-3.68)	Did not converge	0.86 (0.16-4.51)	0.002
Multivariable-adjusted HR (95%CI) ^b	Did not converge	2.16 (0.96-4.87)	Did not converge	0.92 (0.16-5.14)	<.001

eTable 2. Study-specific hazard ratios between multivitamin use and mortality (all-cause and cause-specific) (continued)

^a The proportional hazards assumption was violated ($P < .001$). Therefore, follow-up time was stratified by the midpoint, and hazard ratios were calculated using an interaction term between follow-up period and the exposure variable. **NIH-AARP**: Maximum follow-up time was 24 years; follow-up period 1 was the first 12 years of follow-up and follow-up period 2 was the last 12 years of follow-up. **PLCO**: Maximum follow-up was 27 years; follow-up period 1 was the first 12 years of follow-up and follow-up period 2 was the last 15 years of follow-up. **AHS**: Maximum follow-up was 26 years; follow-up period 1 was the first 12 years of follow-up and follow-up period 2 was the last 14 years of follow-up.

^b Models were adjusted for sex (male or female), age at enrollment (years), race/ethnicity (American Indian/Alaskan Native, Asian/Pacific Islander, Hispanic, Non-Hispanic Black, or Non-Hispanic White), education (11 years or less; 12 years, completed high school or GED; post high school training; some college; college and postgraduate; or other), body mass index category ($< 18.5 \text{ kg/m}^2$, 18.5 to $<25 \text{ kg/m}^2$, 25 to $<30 \text{ kg/m}^2$, $30+$ kg/m^2), marital status (married or living as married, divorced or separated, widowed, or never married), smoking status (never smoker, former smoker, current smoker ≤ 20 cigarettes/day, current smoker 21-40 cigarettes/day, or current smoker > 40 cigarettes/day), alcohol consumption (0 drinks per day, < 1 drink/day, 1 to <2 drinks/day, 2 to <3 drinks/day, 3 or more drinks/day), physical activity level (never, low: few times a month, moderate: few times per week, high: many times a week), coffee intake (0 cups/day, <1 cup/day, 2-3 cups/day, 4-5 cups/day, or 6+ cups/day), family history of cancer (yes or no), Healthy Eating Index 2015 (HEI-2015) quartile (**NIH-AARP**: Quartile 1: 21.5 to <61.5 , Quartile 2: 61.5 to <68.6 , Quartile 3: 68.6 to <74.7 , Quartile 4: 74.7 to 98; **PLCO**: Quartile 1: 28.5 to <60.8 , Quartile 2: 60.8 to <67.3 , Quartile 3: 67.3 to <73.1 , Quartile 4: 73.1 to 95; **AHS**: Quartile 1: 21.9 to <55.3 , Quartile 2: 55.3 to <61.8 , Quartile 3: 61.8 to <68.2 , Quartile 4: 68.2 to 95), and use of individual supplements (yes or no). CI denotes confidence intervals and numbers represent hazard ratios and 95% confidence intervals for daily multivitamin users and nondaily users in adjusted models.



eFigure 2. Forest plot of stratified baseline estimates for the association of nondaily multivitamin use and all-cause mortality, N=390,124

Abbreviations: Follow-up period 1 (F1); Follow-up period 2 (F2); Body Mass Index (BMI); Healthy Eating Index-2015 (HEI-2015)

The proportional hazards assumption was violated ($P<.001$). Therefore, follow-up time was stratified by the midpoint, and hazard ratios were calculated using an interaction term between follow-up period and the exposure variable. Maximum follow-up time was

24 years for the AARP cohort, 27 years for the PLCO cohort, and 26 years for the AHS cohort; follow-up period 1 (F1) was the first 12 years of follow-up and follow-up period 2 (F2) was the last 15 years of follow-up.

P value represents significance of likelihood ratio test for each effect modifier.

Models were stratified by study and adjusted for sex (male or female), age at enrollment (years), race/ethnicity (American Indian/Alaskan Native, Asian/Pacific Islander, Hispanic, Non-Hispanic Black, or Non-Hispanic White), education (11 years or less; 12 years, completed high school or GED; post high school training; some college; college and postgraduate; or other), body mass index category (< 18.5 kg/m², 18.5 to <25 kg/m², 25 to <30 kg/m², 30+ kg/m²), marital status (married or living as married, divorced or separated, widowed, or never married), smoking status (never smoker, former smoker, current smoker ≤20 cigarettes/day, current smoker 21-40 cigarettes/day, or current smoker > 40 cigarettes/day), alcohol consumption (0 drinks per day, < 1 drink/day, 1 to <2 drinks/day, 2 to <3 drinks/day, 3 or more drinks/day), physical activity level (never, low: few times a month, moderate: few times per week, high: many times a week), coffee intake (0 cups/day, <1 cup/day, 2-3 cups/day, 4-5 cups/day, or 6+ cups/day), family history of cancer (yes or no), Healthy Eating Index 2015 (HEI-2015) quartile (Quartile 1: 21.55 to <60.90, Quartile 2: 60.90 to <68.00, Quartile 3: 68.00 to <74.20, Quartile 4: 74.20 to <96.10), and use of individual supplements (yes or no).

eTable 3. Baseline characteristics of time-varying analysis participants by cohort, according to multivitamin use

Characteristic, No. (%)	Nonuse N=76010	Nondaily use N=21922	Daily use N=74564	P	Overall N=172496
AARP participants					
Age, median (IQR), y	62.3 (57.9-66.7)	60.9 (52.0-69.8)	62.4 (53.6-71.2)	<.001	62.1 (57.7-66.5)
Sex				<.001	
Female	28410 (37.4%)	10294 (47.0%)	35013 (47.0%)		73717 (42.7%)
Male	47600 (62.6%)	11628 (53.0%)	39551 (53.0%)		98779 (57.3%)
Race/Ethnicity ^a				<.001	
American Indian/Alaskan Native	144 (0.2%)	48 (0.2%)	146 (0.2%)		338 (0.2%)
Asian/Pacific Islander	935 (1.2%)	329 (1.5%)	825 (1.1%)		2089 (1.2%)
Hispanic	1152 (1.5%)	400 (1.8%)	1089 (1.5%)		2641 (1.5%)
Non-Hispanic Black	2307 (3.0%)	802 (3.7%)	1780 (2.4%)		4889 (2.8%)
Non-Hispanic White	71472 (94.0%)	20343 (92.8%)	70724 (94.9%)		162539 (94.2%)
Education				<.001	
less than 8 years, 8-11 years	3569 (4.7%)	728 (3.3%)	2491 (3.3%)		6788 (3.9%)
12 years, completed high school, GED	14898 (19.6%)	3417 (15.6%)	12776 (17.1%)		31091 (18.0%)
post-high school training	7625 (10.0%)	2116 (9.7%)	7220 (9.7%)		16961 (9.8%)
some college	17175 (22.6%)	5371 (24.5%)	17850 (23.9%)		40396 (23.4%)
college and postgraduate	32743 (43.1%)	10290 (46.9%)	34227 (45.9%)		77260 (44.8%)
Smoking status				<.001	
Never smoker	29146 (38.3%)	8931 (40.7%)	28962 (38.8%)		67039 (38.9%)
Former smoker	36995 (48.7%)	10066 (45.9%)	37214 (49.9%)		84275 (48.9%)
Current smoker	9869 (13.0%)	2925 (13.3%)	8388 (11.2%)		21182 (12.3%)
Physical activity level				<.001	
Never/Rarely	13905 (18.3%)	3326 (15.2%)	10858 (14.6%)		28089 (16.3%)
Low (few times a month)	11311 (14.9%)	3607 (16.5%)	9436 (12.7%)		24354 (14.1%)
Moderate (few times per week)	17211 (22.6%)	5725 (26.1%)	16164 (21.7%)		39100 (22.7%)
High (many times a week)	33583 (44.2%)	9264 (42.3%)	38106 (51.1%)		80953 (46.9%)
Individual supplement use	26754 (35.2%)	17755 (81.0%)	63151 (84.7%)	<.001	107660 (62.4%)
BMI category				<.001	
< 18.5 kg/m ²	761 (1.0%)	254 (1.2%)	911 (1.2%)		1926 (1.1%)
18.5 to < 25 kg/m ²	26734 (35.2%)	8306 (37.9%)	30352 (40.7%)		65392 (37.9%)
25 to < 30 kg/m ²	32773 (43.1%)	9183 (41.9%)	30375 (40.7%)		72331 (41.9%)
≥ 30 kg/m ²	15742 (20.7%)	4179 (19.1%)	12926 (17.3%)		32847 (19.0%)
Alcohol category				<.001	
0 drinks per day	15708 (20.7%)	3827 (17.5%)	14958 (20.1%)		34493 (20.0%)
Less than 1 drink per day	40429 (53.2%)	12999 (59.3%)	41428 (55.6%)		94856 (55.0%)
1-2 drinks per day	10025 (13.2%)	2685 (12.2%)	9658 (13.0%)		22368 (13.0%)
2-3 drinks per day	3128 (4.1%)	804 (3.7%)	3038 (4.1%)		6970 (4.0%)
3 or more drinks per day	6720 (8.8%)	1607 (7.3%)	5482 (7.4%)		13809 (8.0%)
Coffee intake, n (%)				<.001	
None	8111 (10.7%)	2056 (9.4%)	8156 (10.9%)		18323 (10.6%)
Less than 1 cup per day	11469 (15.1%)	3592 (16.4%)	12294 (16.5%)		27355 (15.9%)
1 cup per day	11907 (15.7%)	3225 (14.7%)	11990 (16.1%)		27122 (15.7%)
2-3 cups per day	31848 (41.9%)	9330 (42.6%)	30653 (41.1%)		71831 (41.6%)
4-5 cups per day	9730 (12.8%)	2894 (13.2%)	8882 (11.9%)		21506 (12.5%)
6 or more cups per day	2945 (3.9%)	825 (3.8%)	2589 (3.5%)		6359 (3.7%)

eTable 3. Baseline characteristics of time-varying analysis participants by cohort, according to multivitamin use (continued)

Characteristic (AARP continued)	Nonuse	Nondaily use	Daily use	P	Overall
HEI-2015 quartile				<.001	
Quartile 1	22229 (29.2%)	5374 (24.5%)	15159 (20.3%)		42762 (24.8%)
Quartile 2	19581 (25.8%)	5624 (25.7%)	17746 (23.8%)		42951 (24.9%)
Quartile 3	18042 (23.7%)	5593 (25.5%)	19755 (26.5%)		43390 (25.2%)
Quartile 4	16158 (21.3%)	5331 (24.3%)	21904 (29.4%)		43393 (25.2%)
Marital status				<.001	
Married or living as married	55052 (72.4%)	14630 (66.7%)	49106 (65.9%)		118788 (68.9%)
Divorced or separated	9820 (12.9%)	3897 (17.8%)	12500 (16.8%)		26217 (15.2%)
Widowed	7217 (9.5%)	2268 (10.3%)	8703 (11.7%)		18188 (10.5%)
Never married	3921 (5.2%)	1127 (5.1%)	4255 (5.7%)		9303 (5.4%)
Family history of cancer	39878 (52.5%)	11554 (52.7%)	39173 (52.5%)	<.001	90605 (52.5%)
PLCO participants	N=19353	N=4471	N=18908		N=42732
Age, median (IQR), y	62.0 (58.0 - 66.0)	61.0 (57.0 - 65.0)	62.0 (58.0 - 66.0)	<.001	62.0 (58.0 - 66.0)
Sex				<.001	
Female	8187 (42.3%)	2503 (56.0%)	11414 (60.4%)		22104 (51.7%)
Male	11166 (57.7%)	1968 (44.0%)	7494 (39.6%)		20628 (48.3%)
Race/Ethnicity ^a				<.001	
American Indian/Alaskan Native	33 (0.2%)	13 (0.3%)	36 (0.2%)		82 (0.2%)
Asian/Pacific Islander	599 (3.1%)	175 (3.9%)	674 (3.6%)		1448 (3.4%)
Hispanic	241 (1.2%)	59 (1.3%)	267 (1.4%)		567 (1.3%)
Non-Hispanic Black	676 (3.5%)	135 (3.0%)	500 (2.6%)		1311 (3.1%)
Non-Hispanic White	17804 (92.0%)	4089 (91.5%)	17431 (92.2%)		39324 (92.0%)
Education				<.001	
less than 8 years, 8-11 years	1322 (6.8%)	173 (3.9%)	949 (5.0%)		2444 (5.7%)
12 years, completed high school, GED	4735 (24.5%)	821 (18.4%)	4236 (22.4%)		9792 (22.9%)
post-high school training	2411 (12.5%)	529 (11.8%)	2372 (12.5%)		5312 (12.4%)
some college	3948 (20.4%)	991 (22.2%)	4176 (22.1%)		9115 (21.3%)
college and postgraduate	6937 (35.8%)	1957 (43.8%)	7175 (37.9%)		16069 (37.6%)
Smoking status				<.001	
Never smoker	9114 (47.1%)	2284 (51.1%)	9321 (49.3%)		20719 (48.5%)
Former smoker	8177 (42.3%)	1754 (39.2%)	7963 (42.1%)		17894 (41.9%)
Current smoker	2062 (10.7%)	433 (9.7%)	1624 (8.6%)		4119 (9.6%)
Physical activity level				<.001	
Never/Rarely	3245 (16.8%)	466 (10.4%)	2420 (12.8%)		6131 (14.3%)
Low (few times a month)	3660 (18.9%)	874 (19.5%)	3108 (16.4%)		7642 (17.9%)
Moderate (few times per week)	5366 (27.7%)	1358 (30.4%)	5387 (28.5%)		12111 (28.3%)
High (many times a week)	7082 (36.6%)	1773 (39.7%)	7993 (42.3%)		16848 (39.4%)
Individual supplement use	6554 (33.9%)	3638 (81.4%)	15398 (81.4%)	<.001	25590 (59.9%)
BMI category				<.001	
< 18.5 kg/m ²	105 (0.5%)	31 (0.7%)	159 (0.8%)		295 (0.7%)
18.5 to < 25 kg/m ²	6111 (31.6%)	1751 (39.2%)	7255 (38.4%)		15117 (35.4%)
25 to < 30 kg/m ²	8682 (44.9%)	1817 (40.6%)	7713 (40.8%)		18212 (42.6%)
≥ 30 kg/m ²	4455 (23.0%)	872 (19.5%)	3781 (20.0%)		9108 (21.3%)

eTable 3. Baseline characteristics of time-varying analysis participants by cohort, according to multivitamin use (continued)

Characteristic (PLCO continued)	Nonuse	Nondaily use	Daily use	P	Overall
Alcohol category				<.001	
0 drinks per day	3810 (19.7%)	878 (19.6%)	4188 (22.1%)		8876 (20.8%)
Less than 1 drink per day	10369 (53.6%)	2553 (57.1%)	10511 (55.6%)		23433 (54.8%)
1-2 drinks per day	2322 (12.0%)	479 (10.7%)	2052 (10.9%)		4853 (11.4%)
2-3 drinks per day	889 (4.6%)	207 (4.6%)	791 (4.2%)		1887 (4.4%)
3 or more drinks per day	1963 (10.1%)	354 (7.9%)	1366 (7.2%)		3683 (8.6%)
Coffee intake				<.001	
None	2106 (10.9%)	572 (12.8%)	2398 (12.7%)		5076 (11.9%)
Less than 1 cup per day	3724 (19.2%)	967 (21.6%)	3867 (20.5%)		8558 (20.0%)
1 cup per day	4225 (21.8%)	856 (19.1%)	4195 (22.2%)		9276 (21.7%)
2-3 cups per day	5934 (30.7%)	1330 (29.7%)	5622 (29.7%)		12886 (30.2%)
4-5 cups per day	2172 (11.2%)	528 (11.8%)	1947 (10.3%)		4647 (10.9%)
6 or more cups per day	1192 (6.2%)	218 (4.9%)	879 (4.6%)		2289 (5.4%)
HEI-2015 quartile				<.001	
Quartile 1	5880 (30.4%)	969 (21.7%)	3713 (19.6%)		10562 (24.7%)
Quartile 2	5193 (26.8%)	1101 (24.6%)	4489 (23.7%)		10783 (25.2%)
Quartile 3	4539 (23.5%)	1156 (25.9%)	5090 (26.9%)		10785 (25.2%)
Quartile 4	3741 (19.3%)	1245 (27.8%)	5616 (29.7%)		10602 (24.8%)
Marital status				<.001	
Married or living as married	15757 (81.4%)	3378 (75.6%)	14455 (76.4%)		33590 (78.6%)
Divorced or separated	1720 (8.9%)	598 (13.4%)	2133 (11.3%)		4451 (10.4%)
Widowed	1297 (6.7%)	338 (7.6%)	1702 (9.0%)		3337 (7.8%)
Never married	579 (3.0%)	157 (3.5%)	618 (3.3%)		1354 (3.2%)
Family history of cancer	10798 (55.8%)	2541 (56.8%)	10760 (56.9%)	0.074	24099 (56.4%)
AHS participants	N=15132	N=839	N=3394		N=19365
Age, median (IQR), y	46.0 (38.0-56.0)	45.0 (37.0-55.0)	48.0 (38.0-57.0)	<.001	47.0 (38.0-56.0)
Sex				<.001	
Female	7207 (47.6%)	545 (65.0%)	2458 (72.4%)		10210 (52.7%)
Male	7925 (52.4%)	294 (35.0%)	936 (27.6%)		9155 (47.3%)
Race/Ethnicity ^a				0.46	
American Indian/Alaskan Native	4 (0.0%)	0 (0%)	3 (0.1%)		26 (0.1%)
Asian/Pacific Islander	22 (0.1%)	1 (0.1%)	1 (0.0%)		5 (0.0%)
Hispanic	112 (0.7%)	5 (0.6%)	19 (0.6%)		136 (0.7%)
Non-Hispanic Black	64 (0.4%)	2 (0.2%)	9 (0.3%)		75 (0.4%)
Non-Hispanic White	14930 (98.7%)	831 (99.0%)	3362 (99.1%)		19123 (98.8%)
Education				<.001	
less than 8 years, 8-11 years	656 (4.3%)	20 (2.4%)	112 (3.3%)		788 (4.1%)
12 years, completed high school, or GED	6401 (42.3%)	256 (30.5%)	1194 (35.2%)		7851 (40.5%)
post-high school training	1711 (11.3%)	123 (14.7%)	404 (11.9%)		2238 (11.6%)
Some college	2352 (15.5%)	154 (18.4%)	577 (17.0%)		3083 (15.9%)
College and postgraduate	3487 (23.0%)	234 (27.9%)	872 (25.7%)		4593 (23.7%)
Other	525 (3.5%)	52 (6.2%)	235 (6.9%)		812 (4.2%)
Smoking status				<.001	
Never smoker	9721 (64.2%)	595 (70.9%)	2398 (70.7%)		12714 (65.7%)
Former smoker	3791 (25.1%)	178 (21.2%)	779 (23.0%)		4748 (24.5%)
Current smoker	1620 (10.7%)	66 (7.9%)	217 (6.4%)		1903 (9.8%)

eTable 3. Baseline characteristics of time-varying analysis participants by cohort, according to multivitamin use (continued)

Characteristic (AHS continued)	Nonuse	Nondaily use	Daily use	P	Overall
Physical activity level				<.001	
Never	3209 (21.2%)	118 (14.1%)	556 (16.4%)		3883 (20.1%)
Low (few times a month)	2758 (18.2%)	164 (19.5%)	604 (17.8%)		3526 (18.2%)
Moderate (few times per week)	2775 (18.3%)	180 (21.5%)	680 (20.0%)		3635 (18.8%)
High (many times a week)	6390 (42.2%)	377 (44.9%)	1554 (45.8%)		8321 (43.0%)
Individual supplement use	4970 (32.8%)	499 (59.5%)	2003 (59.0%)	<.001	7472 (38.6%)
BMI category				<.001	
< 18.5 kg/m ²	100 (0.7%)	12 (1.4%)	50 (1.5%)		162 (0.8%)
18.5 to < 25 kg/m ²	5384 (35.6%)	387 (46.1%)	1522 (44.8%)		7293 (37.7%)
25 to < 30 kg/m ²	6415 (42.4%)	302 (36.0%)	1299 (38.3%)		8016 (41.4%)
≥ 30 kg/m ²	3233 (21.4%)	138 (16.4%)	523 (15.4%)		3894 (20.1%)
Alcohol category				<.001	
0 drinks per day	5410 (35.8%)	276 (32.9%)	1287 (37.9%)		6973 (36.0%)
Less than 1 drink per day	8554 (56.5%)	511 (60.9%)	1940 (57.2%)		11005 (56.8%)
1-2 drinks per day	836 (5.5%)	38 (4.5%)	133 (3.9%)		1007 (5.2%)
2-3 drinks per day	242 (1.6%)	10 (1.2%)	22 (0.6%)		274 (1.4%)
3 or more drinks per day	90 (0.6%)	4 (0.5%)	12 (0.4%)		106 (0.5%)
Coffee intake				0.002	
None	4485 (29.6%)	252 (30.0%)	1076 (31.7%)		5813 (30.0%)
Less than 1 cup per day	3099 (20.5%)	194 (23.1%)	713 (21.0%)		4006 (20.7%)
1 cup per day	1982 (13.1%)	100 (11.9%)	435 (12.8%)		2517 (13.0%)
2-3 cups per day	3912 (25.9%)	206 (24.6%)	828 (24.4%)		4946 (25.5%)
4-5 cups per day	1205 (8.0%)	68 (8.1%)	252 (7.4%)		1525 (7.9%)
6 or more cups per day	449 (3.0%)	19 (2.3%)	90 (2.7%)		558 (2.9%)
HEI-2015 quartile				<.001	
Quartile 1	4217 (27.9%)	159 (19.0%)	605 (17.8%)		4981 (25.7%)
Quartile 2	3942 (26.1%)	222 (26.5%)	742 (21.9%)		4906 (25.3%)
Quartile 3	3692 (24.4%)	219 (26.1%)	937 (27.6%)		4848 (25.0%)
Quartile 4	3281 (21.7%)	239 (28.5%)	1110 (32.7%)		4630 (23.9%)
Marital status				<.001	
Married or living as married	14041 (92.8%)	783 (93.3%)	3248 (95.7%)		18072 (93.3%)
Divorced or separated	239 (1.6%)	19 (2.3%)	32 (0.9%)		290 (1.5%)
Widowed	75 (0.5%)	6 (0.7%)	12 (0.4%)		93 (0.5%)
Never married	777 (5.1%)	31 (3.7%)	102 (3.0%)		910 (4.7%)
Family history of cancer	7310 (48.3%)	403 (48.0%)	1694 (49.9%)	0.071	9407 (48.6%)

Abbreviations: HEI-2015 – Healthy Eating Index 2015; BMI – Body Mass Index

^a Race or ethnic group was self-reported.