Multivitamin-multimineral supplements' effect on total nutrient intake[1–4]

Suzanne P Murphy, Kami K White, Song-Yi Park, and Sangita Sharma

ABSTRACT

Use of multivitamin-multimineral supplements is widespread and can contribute substantially to total nutrient intakes. In the Hawaii-Los Angeles Multiethnic Cohort (MEC), 48% of men and 56% of women without chronic diseases reported use of multivitamin supplements at least weekly over the past year. We calculated the prevalence of nutrient adequacy for 17 nutrients based on responses to a self-administered quantitative food-frequency questionnaire administered to MEC participants at baseline in 1993–1996. Although the prevalence of nutrient adequacy from food only was higher for multivitamin supplement users (n = 21 056) than for nonusers (n = 69 715), differences averaged only 2 percentage points. For multivitamin users, the prevalence of adequacy improved by an average of 8 percentage points for both men and women when intake from supplements was included. Users were also more likely to have potentially excessive intakes, particularly for iron, zinc, vitamin A, and niacin. The 26 735 MEC participants in Hawaii who answered an open-ended question about multivitamin use in 1999–2001 reported using 1246 different products. The nutrient profile of these products varied widely, and the composition of products at the 90th percentile was 10-fold greater than the composition at the median for some nutrients. We conclude that analyses of nutrient adequacy and excess for supplement users should be extended to national samples and that composition data on actual supplements used are preferable to assuming a default nutrient profile for multivitamin supplements. Multivitamin products could be better formulated to reduce the prevalence of inadequacy and also to reduce the risk of excessive intakes. *Am J Clin Nutr* 2007;85(suppl):280S–4S.

KEY WORDS Multivitamins, dietary supplements, nutrient adequacy, excessive intakes

INTRODUCTION

The most common type of dietary supplement reported in the United States is a multivitamin supplement (1). Many of these products contain nutrient amounts that approximate recommended intakes [Recommended Dietary Allowance (RDA) or Adequate Intake (AI)], but many contain higher amounts and many also contain nutrients or other compounds that do not have recommended intakes (1–3). Even the name is misleading, because most formulations also contain one or more minerals. Although these products are usually specified as a daily supplement on the product label, some users take them more or less often than once a day and some take more than one type of multivitamin (3). In this article, we use the term *multivitamin supplement* to refer to any product containing ≥2 vitamins with or without minerals and with or without herbal or botanical components.

For individuals who take multivitamins, data are limited on usual intakes from these supplements or on usual intakes from foods plus supplements. The few reports that are available usually did not evaluate the intakes by estimating the prevalence of adequacy or the prevalence of potentially excessive intakes.

We have conducted several analyses with the use of data from the Hawaii-Los Angeles Multiethnic Cohort (MEC) (4), which includes 215 823 adults who were aged ≥45 y at baseline in 1993–1996. Participants are primarily from 5 ethnic groups: Native Hawaiian, Japanese American, Caucasian, African American, and Latino. A questionnaire mailed to each participant included a self-administered quantitative food-frequency questionnaire (QFFQ) as well as a 1-page questionnaire on regular supplement use. One question asked about the frequency and duration of use of multivitamins or multivitamins with minerals over the past year.

CHARACTERISTICS OF SUPPLEMENT USERS

Of the 100 196 MEC participants without chronic diseases, 48% of men and 56% of women reported using a multivitamin supplement at least once weekly for the past year (5). In models adjusted for several demographic covariates, persons who used any of 7 supplements regularly reported a lower percentage of energy from fat and higher fiber intakes. Better dietary intakes by supplement users than by nonusers was also recently reported by other investigators (6–8).

NUTRIENT ADEQUACY OF SUPPLEMENT USERS COMPARED WITH NONUSERS

Nutrient intakes were calculated on the basis of responses to the 180 questions included in the QFFQ. For each food item, the frequency of consumption and usual portion size were indicated, assisted by food photographs printed on the QFFQ. The QFFQ

[1] From the Cancer Research Center of Hawaii, University of Hawaii, Honolulu, HI.

[2] Presented at the conference "Multivitamin/Mineral Supplements and Chronic Disease Prevention," held at the National Institutes of Health, Bethesda, MD, May 15–17, 2006.

[3] Supported by USDA-NRI 2002-00793, NCI R01 CA54821.

[4] Reprints not available. Address correspondence to SP Murphy, Cancer Research Center of Hawaii, 1236 Lauhala Street, #407, Honolulu, HI 96813. E-mail: suzanne@crch.hawaii.edu.

TABLE 1
Prevalence of dietary nutrient adequacy among multivitamin users and nonusers (excludes users of single supplements)[1]

Nutrient	Men: Nonusers ($n = 38\,374$)	Men: Users: food only ($n = 11\,125$)	Men: Users: foods + supplements ($n = 11\,125$)[2]	Women: Nonusers ($n = 31\,341$)	Women: Users: food only ($n = 9931$)	Women: Users: foods + supplements ($n = 9931$)[2]
	%			%		
Protein	86 ± 31	86 ± 30	86 ± 30[3]	85 ± 31	87 ± 30	87 ± 30[3]
Vitamin C	72 ± 42	76 ± 40	89 ± 29	82 ± 37	86 ± 33	93 ± 25
Vitamin A	59 ± 42	61 ± 41	87 ± 30	69 ± 39	73 ± 37	89 ± 28
Vitamin E[4]	27 ± 41	28 ± 41	68 ± 43	22 ± 38	23 ± 39	60 ± 45
Thiamine	82 ± 35	84 ± 33	94 ± 23	79 ± 37	82 ± 35	92 ± 25
Riboflavin	87 ± 30	89 ± 28	95 ± 19	77 ± 20	79 ± 19	90 ± 16
Niacin	89 ± 27	90 ± 25	96 ± 18	84 ± 32	86 ± 30	94 ± 22
Folate	93 ± 23	94 ± 21	97 ± 15	88 ± 30	90 ± 27	95 ± 20
Vitamin B-6	79 ± 37	81 ± 36	93 ± 24	73 ± 41	77 ± 39	90 ± 28
Vitamin B-12	90 ± 28	90 ± 27	96 ± 18	83 ± 35	85 ± 34	94 ± 23
Calcium[5]	54 ± 32	57 ± 31	66 ± 29	51 ± 32	53 ± 31	62 ± 30
Phosphorus	93 ± 23	94 ± 21	94 ± 21[3]	88 ± 30	90 ± 27	90 ± 27[3]
Magnesium	42 ± 44	43 ± 44	43 ± 44[3]	52 ± 45	56 ± 45	56 ± 45[3]
Iron	94 ± 19	95 ± 17	98 ± 13	90 ± 23	92 ± 20	96 ± 16
Zinc	66 ± 43	68 ± 42	89 ± 30	74 ± 40	77 ± 38	91 ± 27
Copper	90 ± 27	92 ± 25	92 ± 25[3]	84 ± 33	86 ± 31	86 ± 31[3]
Potassium[5]	53 ± 28	53 ± 27	53 ± 27[3]	48 ± 29	50 ± 28	50 ± 28[3]
Average of all 17 nutrients	74 ± 25	76 ± 23[6]	84 ± 19[7]	72 ± 27	75 ± 25[6]	83 ± 20[7]

[1] All values are $\bar{x}$ ± SD.
[2] Default nutrient profile of the multivitamin supplement is the average of the 2 most commonly reported supplements.
[3] Nutrient is not contained in the default nutrient profile of the multivitamin supplement.
[4] Vitamin E intake was expressed as α-tocopherol equivalents; therefore, the prevalence of adequacy is overestimated because only α-tocopherol intake should be considered when evaluating vitamin E adequacy.
[5] For nutrients with an Adequate Intake (AI), the probability of adequacy for each person was estimated; intakes <25% of the AI were assigned 0% probability of adequacy, 25–50% of the AI = 25% probability of adequacy, 50–75% of the AI = 50% probability of adequacy, 75–100% of the AI = 75% probability of adequacy, >100% of the AI = 100% probability of adequacy.
[6] Significantly different from nonusers, $P < 0.0001$ (paired analyses).
[7] Significantly different from users: food only, $P < 0.0001$ (paired analysis).

was validated as part of a calibration study (9). Mean calculated energy intakes were 2159 kcal/d for men and 1762 kcal/d for women (4), which is comparable with values reported during a 1994–1996 national nutrition survey using dietary recalls (10). We calculated the probability of nutrient adequacy for each MEC participant for each of 17 nutrients by using the appropriate method for the Dietary Reference Intakes (DRIs) (11). For most nutrients, the probability was determined from the distribution of requirements as specified by the Estimated Average Requirement (EAR) and the SD of the requirement (12–17). For iron, the probability of adequacy was based on tables provided (15). For 2 nutrients of interest—calcium and potassium—an AI rather than an EAR was available. For these nutrients, we estimated the probability of adequacy for each person by using quartiles of the AI, as described previously (18): intakes <25% of the AI were assigned 0% probability of adequacy, 25–50% of the AI = 25% probability of adequacy, 50–75% of the AI = 50% probability of adequacy, 75–100% of the AI = 75% probability of adequacy, and >100% of the AI = 100% probability of adequacy.

The prevalence of adequacy for a group was estimated as the mean probability of adequacy (11). Two groups were compared: those who did not use any of the specified 7 dietary supplements (a multivitamin supplement and 6 single supplements; 38 347 men and 31 341 women) and those who had used a multivitamin supplement for ≥2 y but who did not take any of the specified single supplements (11 125 men and 9931 women). Users of single supplements were excluded from these analyses to allow a direct evaluation of the effect of multivitamin use. No adjustments were made for day-to-day variation in intakes because the QFFQ was designed to reflect usual intake over the past year.

As shown in **Table 1**, the prevalence of dietary nutrient adequacy based on food intake alone was similar for multivitamin supplement users and nonusers. The average prevalence of adequacy calculated across all 17 nutrients was 74 ± 25% for men who did not use multivitamin supplements and 76 ± 23% for those who did. For women, the corresponding figures were 72 ± 27% and 75 ± 25%. Thus, the mean difference was only 2–3 percentage points, although this difference was significant ($P < 0.0001$).

Intake from multivitamins was calculated by using a default nutrient profile based on the 2 most commonly reported supplements in a calibration study: Centrum Silver and Centrum Hi Potency (Wyeth Consumer Healthcare, Madison, NJ). The default nutrient profile for the supplements used composition data from the product labels because analytic values were not available. The default profile assumed that protein, phosphorus, magnesium, copper, and potassium were not present. When intake from the multivitamin was added to intake from food, the prevalence of adequacy increased significantly for both men and women who used these supplements: to 84 ± 19% for men and

TABLE 2
Prevalence of intakes above the Tolerable Upper Intake Level (UL) for food only compared with food plus multivitamin supplements and multivitamin supplements only

Nutrient	UL	Men: Food only (*n* = 96 961)	Men: Foods + supplements (*n* = 11 125)[1]	Men: Supplements only (*n* = 10 993)[2]	Women: Food only (*n* = 118 862)	Women: Foods + supplements (*n* = 9931)[1]	Women: Supplements only (*n* = 15 742)[2]
		%			%		
Vitamin C	2000 mg	0.04	0.0	0.6	0.03	0.02	0.3
Vitamin A	3000 μg	1.8[3]	15.6[3]	4.0	2.2[3]	15.7[3]	3.8
Vitamin E	1000 mg	0	0	0	0	0	0
Niacin	35 mg	23.9[3]	61.1[3]	17.5	15.6[3]	47.7[3]	15.7
Folate	1000 μg	35.6[3]	52.2[3]	0	28.7[3]	42.5[3]	0
Vitamin B-6	100 mg	0	0	0	0	0	0
Calcium	2500 mg	2.9	2.6	0	2.6	2.2	0.01
Phosphorus	3500 mg	3.1	NA[4]	0	2.4	NA[4]	0
Iron	45 mg	4.7	13.9	0.4	3.6	10.8	0.5
Zinc	40 mg	2.8	12.9	2.0	2.0	9.7	1.0
Copper	10 mg	0.2	NA[4]	0.01	0.3	NA[4]	0.02

[1] Default nutrient profile of the multivitamin supplement is the average of the 2 most commonly reported supplements.
[2] Based on specific multivitamins reported.
[3] These estimates are likely to be high because the units of intake do not match the units for the UL. The vitamin A UL is for preformed vitamin A only, but intakes from foods are expressed as retinol activity equivalents and thus include the activity of provitamin A carotenoids; the niacin UL refers only to niacin in fortification and supplements but intakes from foods include all preformed niacin; the folate UL also refers only to fortification and supplemental forms and is not expressed in dietary folate equivalents (DFE), but intakes from foods are expressed in DFE and include naturally occurring forms of folate.
[4] Nutrient is not contained in the default nutrient profile of the multivitamin supplement.

to 83 ± 20% for women (Table 1). Improvements were particularly great for vitamin E, vitamin A, and zinc adequacy.

PREVALENCE OF INTAKES AT RISK OF BEING EXCESSIVE

We also calculated the prevalence of intakes above the Tolerable Upper Intake Level (UL) as an indication of the percentage of the group at risk of excessive intakes (12–15). We looked at intakes from foods for all MEC participants and at intakes from foods plus supplements for the subset of participants who took multivitamin supplements but not single supplements. As shown in **Table 2**, intakes of some nutrients may be undesirably high. For iron and zinc, <5% of the MEC participants reported intakes from food only that exceeded the UL. However, when nutrients from multivitamins were included, >10% of participants' intakes would be considered undesirably high. Intakes of 3 vitamins appeared to be high, but differences in the units of the intake variables and those of the UL led to an overestimate of the prevalences for vitamin A, niacin, and folate. The vitamin A UL refers only to preformed retinol (15), yet the food intakes include the contribution of provitamin A carotenoids. Even so, intakes from foods only were seldom above the UL (≈2% of the participants), whereas intakes from foods plus multivitamins were at risk of being excessive for >15% of the participants. Because retinol is the primary form of vitamin A in supplements, it is likely that the risk of excessive intakes is undesirably high for multivitamin users. The large estimates of intakes above the UL for niacin and folate also reflect a discordance in the units: both of these ULs refer only to intakes from fortification and supplementation (13), whereas the intake variables also include naturally occurring forms of the nutrients. In addition, the folate variable is expressed in micrograms of dietary folate equivalents (DFE), whereas the UL is expressed in micrograms of folate without adjustment for an increased activity of synthetic forms of folate (13).

To better understand the contribution of multivitamins to potentially excessive intakes, we also examined intakes only from multivitamins based on a second questionnaire that was mailed to MEC participants in 1999–2001. This short questionnaire did not ask about food intakes but contained an open-ended question about use of supplements that contained ≥2 vitamins (and were considered multivitamins by participants). Participants could specify the name and brand of up to 3 multivitamin products along with an indication of the frequency of use for each. Complete information on use of such products was reported by 26 735 participants living in Hawaii (3). The 1246 product brands and names were matched to an extensive supplement composition table based on product labels and maintained by the staff of the Nutrition Support Shared Resource at the Cancer Research Center of Hawaii. Daily intakes from multivitamin supplements were then calculated for each participant. The prevalences of intakes exceeding the UL from the multivitamin products are shown in Table 2. Niacin stands out as the nutrient whose intake from multivitamins was most likely to exceed the UL (18% of men and 16% of women). These data are expressed in the same way as the UL and thus support concerns about potentially excessive intakes by both men and women. In contrast, no MEC participant reported folate intakes from multivitamins that exceeded the UL, which suggests that the apparently high prevalence of potentially excessive intakes from the earlier data may have been the result of expressing the intake data in micrograms of DFE rather than in micrograms of folate. Potentially excessive intakes of preformed vitamin A from multivitamins alone were seen for about 4% of the participants.

TABLE 3
Median and default nutrient profiles for multivitamin supplements[1]

	Median[2]	Default 1	Default 2
Vitamin C (mg)	120 (0, 600)	60.0	75.6
Vitamin A (μg retinol)	1375 (0, 3000)	1833	1086
Vitamin E (mg α-tocopherol)	20.3 (0, 180)	16.9	16.6
Thiamine (mg)	5.0 (0, 50.0)	1.5	2.4
Riboflavin (mg)	5.1 (0, 50.0)	1.7	2.6
Niacin (mg)	20 (0, 100)	20.0	18.6
Folate (μg DFE)	680 (0, 680)	300	527
Vitamin B-6 (mg)	5.0 (0, 50.0)	2.5	3.2
Vitamin B-12 (μg)	12 (0, 100)	15.5	14.8
Calcium (mg)	54.3 (0, 498)	180	198
Magnesium (mg)	38.8 (0, 200)	100	82.1
Iron (mg)	1.7 (0, 18.0)	13.5	6.6
Zinc (mg)	15.0 (0, 22.6)	15.0	12.8

[1] Default 1 is the average of Centrum Silver and Centrum Hi Potency (Wyeth Consumer Healthcare, Madison, NJ) at the time of the study and is based on the product labels; default 2 is calculated to minimize the squared deviation of estimated intake from actual intake (3).

[3] Median (10th and 90th percentiles in parentheses) of 1246 reported products on the basis of product labels (3).

COMPOSITION OF MULTIVITAMIN SUPPLEMENTS

We examined the composition of the 1246 products reported on the second questionnaire. The median, 10th, and 90th percentiles of nutrient composition are shown in **Table 3**. We also compared the default nutrient composition that was assumed for multivitamin supplements when evaluating the nutrient adequacy from the first questionnaire (default 1) with a new default value calculated from the second questionnaire [default 2, as shown in Park et al (3)]. The original default values were based on an average of the 2 most commonly reported supplements in the MEC calibration study. The composition shown as default 2 was more recently calculated to minimize the sum of the squared deviations between estimated intake (using default values) and actual intake (using the composition of the reported supplements). For several of the 13 nutrients in Table 3, the newer default values are higher than the earlier defaults (especially for vitamin C, folate, and several other B vitamins), but for others, the newer defaults are lower. For iron, the newer default value is reduced by 50% (from 13.5 to 6.6 mg per dose). Likewise, the newer default value for vitamin A is substantially reduced, and those for niacin and zinc are also somewhat lower. All of these changes would tend to reduce the prevalence of intakes above the ULs that are shown in Table 2, although it would not be appropriate to use the values for default 2 (based on multivitamin products and use in 1999–2001) with dietary data collected in 1993–1996. The median values for the 1246 multivitamin products shown in Table 3 should not be used as a default composition for most nutrients because the median does not consider the frequency of use of the products.

We also examined the variability in the nutrient content stated on the label of the 1246 multivitamin supplements reported on the second questionnaire. As shown in Table 3, the range between the 10th and 90th percentiles of the nutrient content of the products was large. For all 13 nutrients examined, ≥10% of the products contained none of the nutrient. For 3 nutrients (thiamine, vitamin B-6, and iron), the level in products at the 90th percentile was 10 times higher than the level in products at the median. As would be expected, the large variability in the composition of multivitamin supplements led to large variations in nutrient intakes from these supplements (3). Thus, use of a single default composition value for all multivitamin products (either default 1 or default 2) could substantially reduce the variation in nutrient intakes and lead to incorrect estimates of intake distributions.

CONCLUSIONS AND RECOMMENDATIONS

The prevalence of nutrient adequacy from food was similar for users and nonusers of multivitamin supplements, but the contribution of nutrients from the multivitamin supplements significantly increased the mean prevalence of adequacy across 17 nutrients for older adults (aged 45–75 y) who participated in the MEC. The adequacy of vitamin A, vitamin E, and zinc intakes was particularly improved. However, the prevalence of potentially excessive intakes was 10–15% for vitamin A, iron, and zinc among multivitamin users and may also be relatively high for niacin and folate. Accurate comparisons to the UL for some nutrients are hampered by the expression of intakes in forms and units that do not match those specified by the ULs.

The nutrient profiles of multivitamin products vary widely as do intakes from these dietary supplements. Care must be taken when assuming default values for the composition of multivitamin products, because the resulting estimates of the distribution of total intakes may be altered. As a result, estimates of intakes above or below a cutoff (such as the EAR or the UL) may be incorrect.

More information about the distribution of intakes from multivitamin products is needed for a national sample that includes age groups other than those presented here and is representative of other regions of the United States. In particular, information is lacking on the prevalence of intakes that may be excessive based on total intakes from foods and supplements.

An ideal multivitamin would be formulated to fill the gaps in nutrient adequacy (eg, for vitamin E, potassium, and calcium for the older adults in this study) while omitting or reducing the amounts of those nutrients that may be excessive (eg, vitamin A, iron, and niacin for older adults). Multivitamin products that are better formulated to target public health concerns could contribute more effectively to improving the nutrient intakes of Americans.

SPM was responsible for the design of the analyses, reviewing the analyses, and writing the manuscript. KKW was responsible for the data analyses and review of the manuscript. S-YP and SS were responsible for reviewing the analyses and revising the manuscript. None of the authors had a financial or personal affiliation with the agencies sponsoring the research.

REFERENCES

1. Radimer K, Bindewald B, Hughes J, Ervin B, Swanson C, Picciano MF. Dietary supplement use by US adults: data from the National Health and Nutrition Examination Survey, 1999–2000. Am J Epidemiol 2004;160:339–49.
2. Radimer KL, Subar AF, Thompson FE. Nonvitamin, nonmineral dietary supplements: issues and findings from NHANES III. J Am Diet Assoc 2000;100:447–54.
3. Park SY, Murphy SP, Wilkens LR, Yamamoto JF, Kolonel LN. Allowing for variations in multivitamin supplement composition improves nutrient intake estimates for epidemiologic studies. J Nutr 2006;136:1359–64.
4. Kolonel LN, Henderson BE, Hankin JH, et al. A multiethnic cohort in Hawaii and Los Angeles: baseline characteristics. Am J Epidemiol 2000;151:346–57.

5. Foote JA, Murphy SP, Wilkens LR, Hankin JH, Henderson BE, Kolonel LN. Factors associated with dietary supplement use among healthy adults of five ethnicities. The Multiethnic Cohort Study. Am J Epidemiol 2003;157:888–97.
6. Dwyer JT, Garceau AO, Evans M, et al. Do adolescent vitamin-mineral supplement users have better nutrient intakes than nonusers? Observations from the CATCH tracking study. J Am Diet Assoc 2001;101: 1340–6.
7. Sheldon J, Pelletier DL. Nutrient intakes among dietary supplement users and nonusers in the Food Stamp Population. Fam Econ Nutr Rev 2003;15(2):3–10.
8. Ervin RB, Kennedy-Stephenson J. Mineral intakes of elderly adult supplement and non-supplement users in the Third National Health and Nutrition Examination Survey. J Nutr 2002;132:3422–7.
9. Stram DO, Hankin JH, Wilkens LR, et al. Calibration of the dietary questionnaire for a multiethnic cohort in Hawaii and Los Angeles. Am J Epidemiol 2000;151:358–70.
10. US Department of Agriculture. Continuing Survey of Food Intakes by Individuals 1994–96, 1998 Data Set. CD-ROM. Accession Number PB2000-500027. Springfield, VA: National Technical Information Service, 2000.
11. Institute of Medicine. Dietary reference intakes. Applications in dietary assessment. Washington, DC: National Academy Press, 2000.
12. Institute of Medicine. Dietary reference intakes for calcium, phosphorus, magnesium, vitamin D, and fluoride. Washington, DC: National Academy Press, 1997.
13. Institute of Medicine. Dietary reference intakes for thiamin, riboflavin, niacin, vitamin B_6, folate, vitamin B_{12}, pantothenic acid, biotin, and choline. Washington, DC: National Academy Press, 1998.
14. Institute of Medicine. Dietary reference intakes for vitamin C, vitamin E, selenium, and carotenoids. Washington, DC: National Academy Press, 2000.
15. Institute of Medicine. Dietary reference intakes for vitamin A, vitamin K, arsenic, boron, chromium, copper, iodine, iron, manganese, molybdenum, nickel, silicon, vanadium, and zinc. Washington, DC: National Academy Press, 2001.
16. Institute of Medicine. Dietary reference intakes for energy, carbohydrate, fiber, fat, fatty acids, cholesterol, protein, and amino acids. Washington, DC: National Academy Press, 2002.
17. Institute of Medicine. Dietary reference intakes for water, potassium, sodium, chloride, and sulfate. Washington, DC: National Academies Press, 2005.
18. Foote JA, Murphy SP, Wilkens LR, Basiotis PP, Carlson A. Dietary variety increases the probability of nutrient adequacy among adults. J Nutr 2004;134:1779–85.