Annals of Internal Medicine | ARTICLE

Effect of a Multivitamin and Mineral Supplement on Infection and Quality of Life

A Randomized, Double-Blind, Placebo-Controlled Trial

Thomas A. Barringer, MD; Julienne K. Kirk, PharmD; Amy C. Santaniello, PharmD; Kristie Long Foley, PhD; and Robert Michielutte, PhD

Background: **Use of multivitamin and mineral supplements is common among U.S. adults, yet few well-designed trials have assessed the reputed benefits.**

Objective: **To determine the effect of a daily multivitamin and mineral supplement on infection and well-being.**

Design: **Randomized, double-blind, placebo-controlled trial.**

Setting: **Primary care clinics at two medical centers in North Carolina.**

Participants: **130 community-dwelling adults stratified by age (45 to 64 years or ≥65 years) and presence of type 2 diabetes mellitus.**

Intervention: **Multivitamin and mineral supplement or placebo taken daily for 1 year.**

Measurements: **Incidence of participant-reported symptoms of infection, incidence of infection-associated absenteeism, and scores on the physical and mental health subscales of the Medical Outcomes Study 12-Item Short Form.**

Results: **More participants receiving placebo reported an infectious illness over the study year than did participants receiving multivitamin and mineral supplements (73% vs. 43%; $P < 0.001$). Infection-related absenteeism was also higher in the placebo group than in the treatment group (57% vs. 21%; $P < 0.001$). Participants with type 2 diabetes mellitus ($n = 51$) accounted for this finding. Among diabetic participants receiving placebo, 93% reported an infection compared with 17% of those receiving supplements ($P < 0.001$). Medical Outcomes Study 12-Item Short Form scores did not differ between the treatment and placebo groups.**

Conclusions: **A multivitamin and mineral supplement reduced the incidence of participant-reported infection and related absenteeism in a sample of participants with type 2 diabetes mellitus and a high prevalence of subclinical micronutrient deficiency. A larger clinical trial is needed to determine whether these findings can be replicated not only in diabetic persons but also in any population with a high rate of suboptimal nutrition or potential underlying disease impairment.**

Ann Intern Med. 2003;138:365-371. www.annals.org

For author affiliations, see end of text.

See editorial comment on pp 430-431.

The U.S. Centers for Disease Control and Prevention estimates that 40% of U.S. adults use supplements regularly and spend $1.3 to $1.7 billion on them annually. About half of these persons take a combination vitamin and mineral product (1). Despite this extensive use, however, little evidence supports the purported health benefits (2).

Most of the research on vitamin and mineral supplementation has been related to its effects on immunity and infectious disease. Various degrees of malnutrition, even of individual micronutrients, are known to markedly impair immune function (3). The extent to which subtle deficiencies of various micronutrients contribute to clinically significant infections is unclear. Several studies indicate that vitamin supplementation may improve various immunologic factors (4–6). However, other trials demonstrated impaired immunologic response in participants who consumed larger than recommended quantities of certain nutrient supplements (7–10).

Healthy, community-dwelling elderly persons, who have been shown to have impaired markers of immune function and a high prevalence of subclinical micronutrient deficiency (5, 11–13), have made up the study samples in the only known randomized, controlled trials of the effect of a multivitamin and mineral supplement on clinically apparent infection in persons not obviously malnourished or seriously immunocompromised (11, 14). Of interest, these two trials reached opposite conclusions about a protective benefit. Our study was designed to assess the effect of a standard multivitamin and mineral supplement on participant-reported infection. We also used a validated quality-of-life instrument to assess the subjective effect of supplementation on physical and emotional well-being.

METHODS

Study Design

We conducted a randomized, double-blind, placebo-controlled trial in two academic primary care clinics. Study participants were recruited by announcements made in the primary care clinics, at senior group meetings in the community, and to employees in the medical facilities where the study was conducted. Participants had to be 45 years of age or older and willing to be randomly assigned to the treatment or placebo group. Persons were excluded if they were currently using immunosuppressive drugs or anticoagulants; had used vitamin or mineral supplements (except calcium) in the past month; had a history of kidney stones; had malignant disease, renal insufficiency, hepatic impairment, dementia, or uncontrolled hypertension; abused alcohol or drugs; or were pregnant or lactating.

Study Sample

A total of 158 persons were enrolled and provided written informed consent. The institutional review boards of Carolinas Medical Center, Charlotte, and Wake Forest

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Context

Forty percent of U.S. adults use vitamin and mineral supplements, yet evidence of the health benefits of these supplements is lacking. The purported benefits of supplements relate to the immune system.

Contribution

In this randomized, controlled trial, participants taking multivitamin and mineral supplements reported fewer infections and days absent from work than participants taking placebo. The results were largely due to striking benefits in participants with type 2 diabetes mellitus.

Implications

Multivitamin and mineral supplements appear to reduce infections in people with type 2 diabetes mellitus, a group at risk for micronutrient deficiency.

–The Editors

Medical Center, Winston-Salem, North Carolina, approved the study. After stratification by age (45 to 64 years or ≥65 years) and diabetes status (type 2 diabetes mellitus only), a computer-generated list was used to randomly assigned participants to the treatment group ($n = 78$) or the placebo group ($n = 80$). Participants were stratified by age and diabetes because increasing age and presence of diabetes may decrease immune function and increase the likelihood of subclinical micronutrient deficiencies and susceptibility to infection. The **Figure** illustrates the flow of participants through the study.

Intervention

Participants in the treatment group received a daily oral tablet that contained amounts of vitamins and minerals very similar to those found in most commercially available multivitamin and mineral supplements. **Table 1** lists the exact ingredients of each tablet. Participants in the placebo group received a daily oral tablet containing calcium, 120 mg; magnesium, 100 mg; and vitamin B_2 (riboflavin), 3.4 mg. These ingredients were chosen so that the tablet would look and smell as similar as possible to the complete multivitamin and mineral supplement and would cause similar changes in the color of participants' urine. Tishcon Corp. (Westbury, New York) prepared the supplement and placebo pills specifically for this study. All participants were required to take the tablets daily for 1 year.

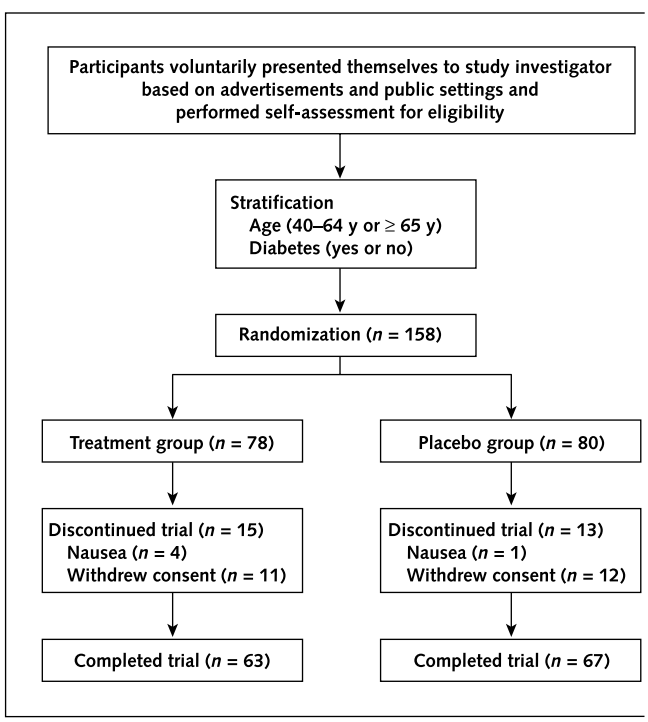
Data Collection

Baseline measurements included sociodemographic characteristics, clinical data, nutritional status, level of stress, health behaviors, and quality of life. All sociodemographic data were dichotomized and included age (45 to 64 years or ≥65 years), sex, ethnicity (black or white), and years of education (less than high school or high school graduate and beyond). Clinical data included body mass index (normal, <25 kg/m^2; overweight, 25 to 29.9 kg/m^2; obese, ≥30 kg/m^2). Hemoglobin A_{1c} level was measured among participants with diabetes. We also assessed history of vitamin use in the year before the study, previous influenza immunization, and whether the participant had had at least one infection in the previous year.

Nutritional status was assessed with a 3-day food diary that participants kept at baseline and at 6 months. At randomization, participants were given detailed written and verbal instructions on how to fill out the food diary, and the study nutritionist reviewed each completed diary with the participant. Analysis was performed by using Nutritionist V, version 2.0 (First DataBank, Inc., San Bruno, California). Nutrient deficiency, for the purpose of this study, was defined as intake below the 33rd percentile of the recommended daily allowance (RDA) for zinc; selenium; iron; folic acid; or vitamins A, C, E, or B_6. Selection was based on research indicating that even moderate deficiencies of these individual nutrients can impair markers of immune function (3–6, 15–17). Our choice of the 33rd percentile was somewhat arbitrary. There is no standard cut-point for micronutrient deficiency as it relates to impairment of immune function because the role of each micronutrient depends on many other factors, such as age, chronic disease, other nutrient deficiencies, and bioavailability. Because many variables are unique to each individual and sample, previous studies demonstrating an immune function benefit from supplementation have defined deficiency post hoc (11, 16).

Stress, which has been shown to influence susceptibil-

Figure. **Flow of participants through the study.**



ity to minor infection (18, 19), was measured by using a 10-item scale that assessed perceived stress during the previous month (20). Each question was measured on a scale of 0 to 4 points, yielding a possible range of 0 to 40 points. For health behaviors, we included smoking status (current, past, or never) and measures of routine physical and recreational exercise (very or moderately active vs. inactive), using items from the National Health and Nutrition Examination Survey II.

The primary end point of our study was incidence of participant-reported infection. Infection data were obtained from symptom checklist diaries recorded daily by the study participants. Detailed instructions on keeping the diaries were given to each participant at the start of the study, and participants were encouraged to call with any questions if they became uncertain. Each participant brought his or her diary to every quarterly study visit, and all aspects of the recorded data were reviewed with participants for clarity, accuracy, and completeness. Using this record of illness, the study physician then assigned a specific diagnosis and duration. Standard criteria were used to diagnose common adult infectious illnesses (upper respiratory tract infection, lower respiratory tract infection, influenza-like syndrome, gastrointestinal infection, and urinary tract infection). Symptom checklist records that fit into the above categories prompted further detailed interview by the physician to confirm or exclude other infectious and noninfectious entities (for example, allergic rhinitis and medication-induced diarrhea).

Infection incidence was determined by using both continuous and categorical variables. First, we calculated the mean number of total "symptomatic days" due to infection per year. Because many study participants ($n = 54$) reported no infection and the data were therefore considerably skewed, the dichotomous variable of infection versus no infection proved more meaningful. We also assessed the significance of infections by ascertaining "absentee" days, that is, days of infection-related illness that resulted in missed work or inability to perform planned activities.

The secondary end point, quality of life, was assessed at baseline and at 12 months. Proxy measures of physical and mental health were obtained by using the Medical Outcomes Study 12-Item Short Form (SF-12) (21). We computed total scores using weighted-item response categories similar to those used to score the 36-Item Short-Form Health Survey (22). Adverse effects, adherence, and any substantial change in medical status were assessed at the quarterly visits.

Statistical Analysis

Descriptive statistics for baseline covariates were assessed by using frequencies for dichotomous variables and medians and interquartile ranges for continuous variables. Chi-square tests and *t*-tests were used to evaluate the differences between the treatment and placebo groups across all categorical and continuous baseline covariates, respectively. These analyses were conducted for all 158 participants recruited to the study and for the 130 participants who followed the protocol for the entire study year.

Table 1. **Supplement Formulation**

Ingredient	Amount
Vitamins	
A	4000 IU
β-Carotene	1000 IU
B_1 (thiamine)	4.5 mg
B_2 (riboflavin)	3.4 mg*
B_3 (niacin)	20 mg
B_6 (pyridoxine)	6 mg
B_{12} (cyanocobalamin)	30 μg
C (ascorbic acid)	120 mg
D	400 IU
E	60 IU
K	20 μg
Biotin	0.03 mg
Pantothenic acid	15 mg
Folic acid	400 μg
Minerals	
Calcium	120 mg*
Magnesium	100 mg*
Manganese	4 mg
Copper	2 mg
Iron	16 mg
Zinc	22.5 mg
Iodine	150 μg
Selenium	105 μg
Chromium	180 μg

* These ingredients and doses were used in the placebo tablet so that it would look and smell as similar as possible to the complete multivitamin and mineral supplement and would cause similar changes in the color of participants' urine.

Twenty-eight participants withdrew from the study between collection of the baseline data and initial evaluation of the study end points. Because no data were available on the study end points for these participants, we evaluated the effect of attrition using "worst-case" and "best-case" scenarios. First, we assumed all participants who withdrew had an infection and analyzed the data using an intention-to-treat analysis. We then repeated the analysis assuming that all participants who withdrew did not have an infection. Neither of these assumptions affected the directionality or statistical significance of our results. Thus, we proceeded with our analysis using the total number of participants who completed the trial ($n = 130$). All analyses were conducted by using Stata 7.0 (Stata Corp., College Station, Texas).

For our primary outcomes, we calculated the absolute and relative risk for infection and infection-associated absenteeism for all persons who completed the 12-month trial ($n = 130$), according to study group, age, and diabetes status. A Mantel–Haenszel test of homogeneity was performed to test for differences between the age and diabetes subgroups. We also conducted univariate and multivariate analyses using ordinary least-squares regression to evaluate the effect of the supplement on physical and mental quality of life while controlling for age, diabetes status, nutritional deficiency, and physical activity.

Role of the Funding Source

The funding source had no role in the design, conduct, or reporting of the study.

RESULTS

Participant Characteristics

Table 2 summarizes the characteristics of the study participants. The treatment group was more physically active and better nourished than the placebo group but was similar with respect to baseline covariates. The overall sample was predominately female, white, and between the ages of 45 and 64 years. Approximately 10% of participants had not finished high school. Two thirds of the sample were overweight or obese, and approximately 30% had type 2 diabetes mellitus. Approximately 18% of the total sample were classified as nutritionally deficient. Slightly more than half of the participants in both the placebo and treatment groups remembered having had at least one infection in the previous year.

Twenty-eight persons did not complete the trial (15 in the treatment group vs. 13 in the placebo group). Participants who withdrew were more likely to be 45 to 64 years of age and nondiabetic at baseline, but no other differences were noted (**Figure**). The most commonly reported reason for withdrawal was the inconvenience of keeping a daily diary or attending quarterly physician visits. One serious adverse event, a cardiac arrest, occurred during the trial; the affected participant was successfully resuscitated and continued in the study.

Infection Outcomes

No infections requiring hospitalization occurred during the study period. Forty-two percent of participants had upper respiratory tract infections, 19% had influenza-like syndromes, 12% had gastrointestinal infections, 7% had lower respiratory tract infections, and fewer than 2% had urinary tract infections or miscellaneous infections. Twenty percent of persons experienced more than one type of infection over the study year.

Seventy-three percent of the placebo group experienced one or more infection-related illnesses versus 43% of the treatment group ($P < 0.001$). Similarly, 57% of the placebo group reported illness-related absenteeism versus 21% of the treatment group (**Table 3**). Analysis within the age and diabetes subgroups showed that the differential effect of vitamin supplementation on infection was found primarily among participants with diabetes. Ninety-three percent of diabetic participants in the placebo group experienced an infectious illness versus only 17% of diabetic

Table 2. **Baseline Demographic Characteristics and Clinical, Stress, Health Behavior, and Quality-of-Life Data according to Study Group***

Variable	Placebo Group ($n = 80$)	Treatment Group ($n = 78$)	*P* Value†
Demographic, %			
Age ≥65 y	21.25	23.08	>0.2
Women	66.25	76.92	0.14
Black ethnicity	27.50	25.64	>0.2
<12 y of education	11.25	5.13	0.16
Clinical, %			>0.2
Overweight (BMI, 25.0–29.9 kg/m^2)	41.25	30.77	
Obese (BMI ≥ 30.0 kg/m^2)	31.25	38.46	
Cardiovascular disease	12.66	11.69	>0.2
Type 2 diabetes mellitus‡	33.75	30.77	>0.2
Median hemoglobin A_{1c} level	8.6 (8–8.9)	9.2 (8–9.4)	0.20
Vitamin intake in the previous year	26.85	24.32	>0.2
Previous influenza shot	54.43	60.53	>0.2
≥1 illness in the previous year	55.13	52.70	>0.2
Deficient in ≥1 nutrient§	26.25	15.38	0.09
Median stress level‖	13 (8–18)	11 (8–16)	>0.2
Health behavior, %			
Smoking status			>0.2
Current	13.92	12.99	
Past	36.71	33.77	
Never	49.37	53.25	
Physical activity			
Moderately or very active, nonrecreational	69.23	83.12	0.04
Moderately or very active, leisure	61.54	66.23	>0.2
Quality of life¶			
Median SF-12 physical score	48.77 (43.01–56.69)	51.81 (43.25–55.61)	>0.2
Median SF-12 mental score	51.13 (40.48–54.68)	50.88 (44.08–54.69)	>0.2

* BMI = body mass index; SF-12 = Medical Outcomes Study 12-Item Short Form. Values in parentheses are interquartile ranges.
† Significant differences in baseline characteristics across treatment group as measured by *t*-tests and chi-square tests for continuous and categorical variables, respectively.
‡ 51 participants.
§ Deficiency was defined as intake below the 33rd percentile of the recommended daily allowance for zinc; selenium; iron; folic acid; or vitamins A, C, E, or B_6.
‖ Measured by using a 10-item scale that assessed perceived stress during the previous month (20). Each question was measured on a scale of 0 to 4 points, yielding a possible range of 0 to 40 points.
¶ 128 participants.

Table 3. **Effect of a Multivitamin and Mineral Supplement on Infection Incidence and Infection-Related Absenteeism according to Diabetes Status and Age**

Variable	Participants	Infection Incidence				Infection-Related Absenteeism*			
		Placebo Group	Treatment Group	Relative Risk (95% CI)	*P* Value	Placebo Group	Treatment Group	Relative Risk (95% CI)	*P* Value
	n	%				%			
Main effect									
Overall study group	130	73	43	0.59 (0.43–0.81)	<0.001	57	21	0.36 (0.21–0.62)	<0.001
Stratified analysis†									
Age					>0.2				>0.2
<65 y	97	78	43	0.55 (0.38–0.78)		58	21	0.37 (0.20–0.67)	
≥65 y	33	59	44	0.74 (0.38–1.47)		53	19	0.35 (0.12–1.08)	
Diabetes status					<0.001				0.002
No diabetes	79	60	59	0.98 (0.68–1.41)		35	33	0.95 (0.52–1.76)	
Type 2 diabetes mellitus	51	93	17	0.18 (0.07–0.44)		89	0	0	

* Absenteeism was used as the marker for severity of infection and was calculated as the percentage of participants who experienced any days during which planned activities could not be performed because of infection-related illness.
† Chi-square test for relative risk calculated within groups. A Mantel–Haenszel test of homogeneity was computed to test for differences according to age groups and diabetes status. Statistically significant differences were seen only between participants with and those without diabetes. Age group comparisons were not statistically significant.

participants in the treatment group (relative risk, 0.18 [95% CI, 0.07 to 0.44]). Similarly, 89% of diabetic participants in the placebo group reported one or more absentee days compared with 0% of diabetic participants in the treatment group. Participants without diabetes did not differ by study group.

We did not find an effect of age on infection. However, the lack of a statistically significant effect among participants older than 65 years of age does not allow us to draw any meaningful conclusions because only 33 participants were in this age group. Participants younger than 65 years of age experienced an apparent reduction in infection because of vitamin supplementation (78% in the placebo group vs. 43% in the treatment group); however, the difference in outcome between the two age groups was not statistically significant ($P > 0.2$) (**Table 3**). At baseline, diabetic participants were more likely than nondiabetic participants to be deficient in one or more micronutrients (33% vs. 19%; $P = 0.06$) (**Table 4**).

Treatment Effects on Quality of Life

The quality-of-life scores in our study were similar to those in persons who reported minor medical problems in a validation study of the SF-12 (21). In multivariate analyses, vitamin supplementation had no effect on physical or mental health scores (difference, 1.02 [CI, −2.22 to 4.2] and 0.98 [CI, −1.97 to 3.94], respectively). No additional analyses of quality of life were conducted within the age and diabetes subgroups because treatment had no main effect on outcome.

Discussion

The purpose of this study was to assess the effect of a typical "one-a-day" multivitamin and mineral supplement on infection rate and perceived quality of life in a fairly broad sample of relatively healthy adults. We found no difference between the treatment and placebo groups in physical and mental health measures of quality of life. Furthermore, within the SF-12 instrument, the specific items of "general health" and "energy" were analyzed separately and showed no difference in treatment effects between the study groups. Thus, it seems that multivitamin and mineral supplements do not enhance health or energy level any more than does placebo.

Our trial, which was performed in a sample of middle-aged persons, demonstrated a benefit in incidence of infection. However, this benefit was almost entirely observed in participants with diabetes, for whom the magnitude was dramatic. Correction of micronutrient deficiencies would be the most biologically plausible explanation for our results. When we defined nutritional deficiency as intake below the 33rd percentile of the RDA, participants who were diabetic at baseline were more likely than nondiabetic participants to be deficient in one or more micronutrients. It remains uncertain, however, whether these small differ-

Table 4. **Nutritional Deficiency among Subgroups of Diabetes Status and Age**

Nutritional Deficiency*	Diabetes Status			Age		
	Type 2 Diabetes Mellitus	No Diabetes	*P* Value	<65 y	≥65 y	*P* Value
	%			%		
≥1 nutrient	33	19	0.06	28	15	0.14
Vitamin A	8	3	0.16	4	6	>0.2
Vitamin C	8	1	0.06	5	0	0.18
Vitamin E	20	8	0.04	15	3	0.06
Vitamin B_6	2	1	>0.2	2	0	>0.2
Zinc	2	6	>0.2	6	0	0.14
Selenium	6	10	>0.2	9	6	>0.2
Iron	0	0		0	0	
Folic acid	0	0		0	0	

* Defined as intake below the 33rd percentile of the recommended daily allowance.

ences in nutritional status were enough to account for the dramatic difference in outcome. This uncertainty is due not only to the limitations of our study but also to inherent difficulties in defining micronutrient deficiency.

Most of the previous research on vitamin and mineral supplementation has evaluated its effect on various markers of immune function (3–10, 15, 16). A few studies have evaluated clinical outcomes, although mostly in severely compromised or malnourished persons. Research in samples of relatively healthy elderly persons, however, has shown that even mild nutrient deficiencies can impair immune response (3–6, 12, 13, 16). Such subclinical deficiencies are common in community-dwelling elderly persons and probably account for some of the impaired immunity in this population (11–13, 15–17). Whether these data can be extrapolated to other minimally compromised groups, such as middle-aged participants with stable chronic disease processes, is unknown.

Only two published trials have evaluated the effect of a multivitamin and mineral supplement on clinical infection in apparently healthy samples of community-dwelling elderly persons. Chavance and colleagues (14) found no difference in incidence of infection, but their trial was methodologically flawed. Infection data were gathered by using personal recall at 2-month intervals, and the study was too short (4 months) to exclude a treatment effect or to examine seasonal variation. In addition, persons with chronic illness or possible micronutrient deficiency were excluded.

Chandra's 12-month study (11) of 96 healthy elderly persons showed a statistically significant difference in the mean number of days with an infection-related illness (23 days vs. 48 days) in favor of the group that received the vitamin and mineral supplement. No reported results showed an effect on severity of illness (other than number of days antibiotics were taken). In addition, participants in the treatment group had statistically significant improvement in several reliable indices of immune function. Nutritional status was determined by using biochemical measurements, and deficiency in a given nutrient was defined as a blood concentration value below the fifth percentile in a previously established reference range developed by the same researcher from a similar sample. Although the study groups had equal prevalence of deficiency at baseline, the treatment group had less severe deficiencies of vitamin A, β-carotene, vitamin B_6, vitamin C, iron, and zinc. However, the author noted some statistically significant improvements in markers of immune function even among persons who were not deficient by the same criterion (12). This illustrates the important unresolved issue of how to define micronutrient deficiency. In our trial, we used the criterion of intake below the 33rd percentile of the RDA for zinc; selenium; iron; or vitamins A, C, E, or B_6. These micronutrients were specifically chosen because studies have demonstrated that even minor deficiencies lead to impairment in indices of immune function (3–6, 15–17).

One of the limitations of our study was that we determined micronutrient status with a 3-day food diary, which has only a moderate correlation with more accurate and expensive methods. Nevertheless, even if the quantitation of intake were highly accurate, there remains the challenging problem of defining deficiency. The relationship between intake of a nutrient and levels of the same nutrient in serum or tissue depends on numerous bioavailability variables. Defining deficiency on the basis of response to supplementation depends on the specified response end point, numerous physiologic characteristics of the study sample, and biological interconnections and interactions among various micronutrients. All of these factors disallow a simple association between a specific nutrient deficit (however defined) and a given physiologic or clinical outcome. We believe, however, that the diabetic persons we studied had substantial preexisting micronutrient deficiencies. They were also less likely than nondiabetic participants to be white, to have a high school degree, and to have previously used vitamins and were more likely to have experienced illnesses before the trial, to be obese, and to have perceived stress. Lower socioeconomic status and poor health are strongly associated with poorer nutritional status.

Although substantial research shows that certain infections are associated with diabetes (for example, foot ulcer infections, urinary tract infections, and unusual fungal infections), little published work addresses common upper respiratory tract infections, which accounted for the largest proportion of sick days in our trial. The type and severity of impaired immunity in diabetic persons have been studied to some extent, but scant literature exists on ways in which to improve such impairment, other than possibly by improving glycemic control (23–25). Some research has suggested that antioxidant systems are impaired in diabetes, thus providing a theoretical basis for benefit from a supplement with antioxidant potential (26).

Age was the other prespecified subgroup in this trial. No effect of supplementation was noted among those 65 years of age and older. Because few elderly participants were included, however, even a large effect may have been missed, as shown by the large CI (**Table 3**).

Unlike most researchers performing studies of nutritional supplements, we tested the blinding of our drug intervention. Although we went to great effort to have the pills look and smell as identical as possible, most participants correctly guessed what they were taking. Nevertheless, we doubt that this partial unblinding substantially influenced the results. First, at least some differential effect of supplementation would be expected in all of the subgroups. However, in the largest subgroup (nondiabetic persons), no difference was seen between those who received vitamins and those who received placebo. Second, in the group in which treatment had the largest effect on infection rate, unblinding had no effect on the secondary outcome of interest, quality of life.

Infection type and severity could have varied by season of the year, but randomization did not differ by season,

and the 12-month study duration provided equal exposure to seasonal variability for all participants. It should be reiterated that the infections prevented in this study were minor, primarily respiratory tract infections and influenza-like illnesses. Nonetheless, because such infections are very common, they account for a large share of the productive days lost in industrialized societies (27, 28).

Our findings suggest that in certain diabetic samples, perhaps those with a high prevalence of micronutrient deficiency, daily use of a multivitamin and mineral supplement can decrease infection frequency. These dramatic results warrant testing in a larger clinical trial, both for confirmation and to disentangle the effects of chronic disease status from those of other important factors, such as ethnicity and obesity, that serve as proxies for socioeconomic status and poorer nutrition. Multivitamin and mineral supplements are convenient and relatively inexpensive. If our results are confirmed in a larger trial, the widespread implementation of this preventive measure could have a substantial economic impact and could ease the burden of suffering in our society.

From University of North Carolina School of Medicine at Carolinas Medical Center, Charlotte, and Wake Forest University School of Medicine, Winston-Salem, North Carolina.

Acknowledgments: The authors thank Dave Reboussin, PhD, for his assistance in the statistical analysis. Dr. Barringer thanks Geraldine D. Anastasio, PharmD, his original co-investigator who initiated the research project, for her enthusiasm and encouragement to continue the study in her absence.

Grant Support: By the Charlotte-Mecklenburg Health Services Foundation, an independent, charitable foundation that supports medical education and research within the Carolinas HealthCare System.

Potential Financial Conflicts of Interest: None disclosed.

Requests for Single Reprints: Thomas A. Barringer, MD, Department of Family Practice, Carolinas Medical Center, CMC-MP Building, 1350 South Kings Drive, Charlotte, NC 28207; e-mail, tbarringer@carolinas.org.

Current author addresses and author contributions are available at www.annals.org.

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Current Author Addresses: Dr. Barringer: Department of Family Practice, Carolinas Medical Center, CMC-MP Building, 1350 South Kings Drive, Charlotte, NC 28207.
Drs. Kirk and Michielutte: Department of Family Medicine, Wake Forest University School of Medicine, Medical Center Boulevard, Winston-Salem, NC 27157.
Dr. Santaniello: 8918 Waltham Forest Court, Waxhaw, NC 28173.
Dr. Foley: Department of Public Health Sciences, Wake Forest University School of Medicine, Medical Center Boulevard, Winston-Salem, NC 27157.

Author Contributions: Conception and design: T.A. Barringer, J.K. Kirk.
Analysis and interpretation of the data: T.A. Barringer, J.K. Kirk, K.L. Foley, R. Michielutte.
Drafting of the article: T.A. Barringer, J.K. Kirk, A.C. Santaniello, K.L. Foley.
Critical revision of the article for important intellectual content: T.A. Barringer, J.K. Kirk, K.L. Foley, R. Michielutte.
Final approval of the article: T.A. Barringer, J.K. Kirk, A.C. Santaniello, R. Michielutte.
Provision of study materials or patients: T.A. Barringer, J.K. Kirk, A.C. Santaniello.
Statistical expertise: T.A. Barringer, K.L. Foley, R. Michielutte.
Obtaining of funding: T.A. Barringer.
Administrative, technical, or logistic support: T.A. Barringer, J.K. Kirk.
Collection and assembly of data: T.A. Barringer, J.K. Kirk, A.C. Santaniello.