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Self-reported health without clinically measurable benefits among adult users of multivitamin and multimineral supplements: a cross-sectional study

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ABSTRACT

Objectives: Multiple clinical trials fail to identify clinically measurable health benefits of daily multivitamin and multi-mineral (MVM) consumption in the general adult population. Understanding the determinants of widespread use of MVMs may guide efforts to better educate the public about effective nutritional practices. To compare self-reported and clinically measurable health outcomes among MVM users and non-users in a large, nationally representative sample of adult civilian non-institutionalized population of the US surveyed on the use of complementary health practices.

Design: Cross-sectional analysis of the effect of MVM consumption on self-reported overall health and clinically measurable health outcomes.

Participants: Adult MVM users and non-users from the 2012 National Health Interview Survey (n=21,603).

Primary and secondary outcome measures: Five psychological, physical, and functional health outcomes 1) self-rated health status, 2) needing help with routine needs, 3) history of 10 chronic diseases, 4) presence of 19 health conditions in the past 12 months, and 5) Kessler 6-Item (K6) Psychological Distress Scale to measure nonspecific psychological distress in the past month.

Results: Among 4,933 adult MVM users and 16,670 adult non-users, MVM users self-reported 30% better overall health than non-users (Adjusted OR: 1.31; 95% CI: 1.17-1.46 FDR-adjusted P<.001). There were no differences between MVM users and non-users in history of 10 chronic diseases, number of present health conditions, severity of current psychological distress on the

K6 scale and rates of needing help with daily activities. No effect modification was observed after stratification by sex, education, and race.

***Conclusions*:** MVM users self-reported better overall health despite no apparent differences in clinically measurable health outcomes. These results suggest that widespread use of non-prescription multivitamins in adults may be a result of individuals' positive expectation that multivitamin use leads to better health outcomes or a self-selection bias in which MVM users intrinsically harbor more positive views regarding their health.

STRENGTHS AND LIMITATIONS OF THE STUDY

- This is the first study to link increased self-reported health, absence of clinically measurable benefits, and multivitamin and multimineral supplement use in the same population
- Data are derived from a large, national survey across the US
- Results have broad implications for public health and the multibillion-dollar supplement industry
- Cross-sectional study design precludes the demonstration of a causal relationship between self-reported health and multivitamin and multimineral supplements
- Self-reported health can be inherently biased and confounding

INTRODUCTION

Consumption of multivitamins (MVs) and multi-minerals (MMs) (together: MVMs) as dietary supplements is widespread in the general US adult population, with some reports estimating 33% of Americans regularly take MVMs[1–4]. While MVM supplementation is warranted for some individuals at high-risk because of disease-related defiency[5], the consumption of non-prescription, over-the-counter MVMs has not produced robust evidence for the wide-ranging health benefits expected by the general adult population. Likewise, large randomized clinical trials that evaluate MVM at different doses, across both men and women at varied ages, have failed to demonstrate benefit in prevention of chronic diseases. The Physicians' Health Study II (PHS II), a randomized placebo-controlled clinical trial of low-dose daily MV use in older male physicians, found no reduction in major CVD events, myocardial infarction, stroke, and CVD mortality[6], and these results were independent of baseline nutritional status[7]. A prospective cohort study of middle-aged and elderly women also indicated no effect of MV use for the same CVD outcomes in PHS II[8]. The SU.VI.MAX Study, a clinical trial of antioxidative MVMs in adults, found no effect on incidence of ischemic CVD[9], and high-dose MVMs did not reduce CVD events[10]. Meta-analysis of these and other studies (N=18) found no improvement in CVD outcomes in the general population[11]. Based on these studies, the US Preventative Services Task Force does not recommend MVM use for the prevention of CVD[12,13].

Data on the effect of MVM consumption on cognitive function in adults are also inconclusive. While results from PHS II found that long-term use of daily MVs did not provide cognitive benefits in men[14], a meta-analysis on 10 studies concluded that MVs selectively enhanced free recall memory but no other cognitive functions[15]. Intriguingly, nine weeks of MVM use appears to improve multi-tasking and cognitive function during fatigue in women[16].

With regard to cancer, PHS II demonstrated moderately reduced all-cancer risk in men consuming MVs[17] while data from the Women's Health Initiative Clinical Trials revealed no association[18]. Some studies even link MVM use with increased cancer risk – a prospective cohort study of Swedish women found increased breast cancer risk associated with MV use[19].

The association of MVM use with all-cause mortality, like CVD, is null. While data from the Multiethnic Cohort Study cohort study indicated no association between MV use and all-cause mortality,[20] the Cancer Prevention Study (II) reported a five percent higher rate of all-cause death among men using MVs[21] and The Iowa Women's Health Study identified an association between MVM use and increased total mortality risk[22]. A meta-analysis of these and other randomized trials (N=21) demonstrated no effect of MVM use on mortality risk[23].

While numerous reports on MVM consumption establish the lack of broad-spectrum, clinically measurable health benefits, the determinants of widespread MVM use by the general population are not well understood. Because nutritional supplements constitute a multibillion-dollar industry, understanding the determinants of widespread MVM use has significant medical and financial consequences. Moreover, it is unclear whether MVM users, despite not being physiologically different from non-users, simply believe they are healthier. To address this question, we utilized data from the 2012 National Health Interview Survey[24] (NHIS), which included a complementary and alternative (CAM) questionnaire comprising of 21,603 participants across the US.

METHODS

Data source

All data was obtained from the 2012 The National Health Interview Survey (NHIS), a nationally representative health survey conducted annually among civilian and noninstitutionalized US participants by the Centers for Disease Control (CDC). All data was publicly available and did not require institutional review board approval. The 2012 NHIS was comprised of a core questionnaire on health information administered to each selected household member. A randomly selected adult in each household was administered a more detailed health survey which included questions on access to care, specific health conditions and use of CAM(2012 only). In 2012, 77.6% of households completed the survey and 79.7% of adults selected completed the detailed survey[24].

Health Status and Health Outcome Measures

We obtained data on adults (age ≥ 18 years) derived from the Sample Adult Component who also participated in the Adult CAM File. This file surveys use of alternative medicines and therapies including daily MVM consumption, yoga, and meditation. Consistent with previous NHIS studies[25], we considered five psychological, physical, and functional health outcomes from questions in the Sample Adult Component: 1) self-rated health status (poor/fair vs. excellent/very good/good), 2) needing help with routine needs such as eating (yes or no), 3) history of ten chronic diseases (cancer, hypertension, coronary heart disease, stroke, chronic obstructive pulmonary disease, asthma, diabetes, arthritis, hepatitis, and weak/failing kidneys), 4) presence of 19 health conditions in the past 12 months (digestive, skin, and other allergy, acid reflux, hay fever, chest cold, nausea and vomiting, sore threat, infectious disease, recurring headache, memory loss, neurological problems, sprains, and abdominal, dental, muscle/bone, chronic, and skin pain), and 5) Kessler 6-Item (K6) Psychological Distress Scale[26] score to measure nonspecific psychological distress in the past month. Participants who refused to answer or did not know the answers to at least one of these questions were excluded from the study. Participants were classified as MVM users or non-users from their response to the question "During the past 12 months, did take multi-vitamins or multi-minerals?" in the Adult CAM File. Participants who refused to answer or did not know their MVM use in the past 12 months were excluded from analyses.

Statistical Analysis

For each outcome, the relationship between MVM use in the past year and health outcome was estimated using a logistic regression model adjusting for age, sex, race, region, education, income, employment status, health insurance status, presence of child in household, marital status, unmet medical care due to cost in the past year, and not seeing a health professional in office in the past two weeks. Multinomial logistic regression was used for outcomes with more than two levels (e.g., number of chronic diseases, number of diseases in the past 12 months, Kessler-6 Item score). Binary logistic regression was used for outcomes with two levels (self-reported health and needing help with daily routines such as eating). Standard errors were estimated using weights provided by NHIS to account for the complex survey design and produce nationally representative estimates. A multiple imputation strategy was used to estimate income in cases of missing responses to income as recommended by National Center for Health Statistics[27]. All analyses were conducted using R (v3.5.1). *P* values were adjusted for multiple comparisons using a Benjamini-Hochberg procedure with FDR<0.01 deemed significant.

Stratified analyses were conducted in age- (18-44 years, 45-64 years and 65+ years), race- (white and non-white), sex- (female and male), family income- (<100%, 100%-199%, 200%-299%, 300-399%, and 400% relative to the federal poverty level), education level- (did not graduate high school, high school graduate, college graduate or higher) to assess the effect of MVM use on self-reported health in sociodemographic subgroups. In addition to stratified analyses, statistical interaction effects between MVM use and demographic variable (age, race, sex, family income, and education) on self-reported health was assessed using a multivariate regression model.

Patients and Public Involvement

Patients and the public were not involved in this study, including data collection, analysis and interpretation.

RESULTS

Study Cohort Characteristics

Sociodemographic differences between MVM users and non-users are presented in Table 1. Our study included 4,933 MVM users and 16,670 non-users (Table 1). As previously reported in data from the 2007-2010 and 2010-2014 National Health and Nutrition Examination Surveys (NHANES)[28,29], compared to non-users, MVM users were significantly older, earned more income, more likely to be female, more likely to be a college graduate, more likely to be married, more likely to have health insurance. Unlike in previous studies, compared to MVM non-users, MVM users were less likely to be unemployed, have a minor child in their household, and not have an office visit for healthcare in the past two weeks (Table 1). We observed no significant differences in percent of non-English speaking interviews and percent having foregone medical care due to cost in the past year between MVM users and non-users (Table 1).

Effect of MVM usage on Health Status and Health Outcomes

Differences in health status and health outcomes between MVM users and non-users are displayed in Table 2. Multivariate regression revealed that MVM users self-reported 30% better overall health than non-users (OR: 1.31; 95% CI: 1.17-1.46 FDR-adjusted P<.001 ; Table 2). Strikingly, MVM users and non-users did not differ in history of 10 chronic disease (MVM users mean 1.09 conditions; 95% CI: 1.06-1.11 vs non-users mean: 1.07; 95% CI: 1.03-1.11) number of present health conditions (MVM users mean: 2.7 conditions; 95% CI: 2.7-2.8 vs non-users mean: 2.8; 95% CI: 2.7-2.9), severity of psychological distress on the K6 scale (MVM users mean K6 score = 2.3; 95% CI: 2.3-2.4 vs non-users mean = 2.5; 95% CI: 2.4-2.6), and needing help with daily activities (OR: 0.86; 95% CI: 0.71-1.04).

Stratified Analyses: Effect of MVM Usage on Self-Reported Overall Health in Sociodemographic Subgroups

Table 3 reports the effect of MVM usage on self-reported overall health in age, race, sex, income, and education-stratified subgroups (Table 3). MVM use was associated with better self-reported health in the 18-44-year (OR: 1.26; 95% CI: 1.00-1.61) and 45-64-year groups (OR: 1.30; 95% CI: 1.08-1.57) and near significant among respondents ≥ 65 years (OR: 1.20; 95% CI: 0.95-1.52; FDR *P* value = 0.06) (Table 3). MVM use was associated with better self-reported health amongst both white (OR: 1.34; 95% CI: 1.07-1.67) and non-white (OR: 1.26; 95% CI:

1.09-1.45) respondents (Table 3). MVM use was associated with better self-reported health in both male (OR: 1.33; 95% CI: 1.10-1.63) and female (OR: 1.22; 95% CI: 1.05-1.41) respondents (Table 3). Interestingly, MVM use was associated with better self-reported health in families with income < 100% of the federal poverty level (FPL) (OR: 1.42; 95% CI: 1.12-1.80), 100%-199% FPL (OR: 1.37; 95% CI: 1.10-1.69) and 200%-299% FPL (OR: 1.32; 95% CI: 1.01-1.72) but not in families whose income was 300%-399% FPL (OR: 1.32; 95% CI: 0.88-1.98) or ≥400% FPL (OR: 1.15; 95% CI: 0.85-1.56) (Table 3). MVM use was associated with better self-reported health in all education subgroups analyzed, including respondents that did not complete high school (OR: 1.38; 95% CI: 1.06-1.81), high school graduates (OR: 1.21; 95% CI: 1.04-1.41), and college graduates (OR: 1.37; 95% CI: 1.00-1.88) (Table 3). All stratified analyses were conducted after adjusting for the potential confounding effects of age, sex, race, region, education, income, employment status, health insurance status, presence of child in household, marital status, unmet medical care due to cost in the past year, and not seeing a health professional in office in the past two weeks. The variable of stratification was not included as a covariate.

Statistical interaction effects between MVM use and demographic variables (age, race, family income, and education) on self-reported overall health was assessed through a multivariate regression model in Table S1. We observed no significant effect between MVM use and age, MVM use and race, MVM use and family income, and MVM use and education on self-reported overall income (Table S1).

DISCUSSION

This present study is the first to simultaneously analyze the association between MVM use and both self-reported health and clinical health outcomes. In this work, we found that MVM users self-report 30% better overall health than non-users despite any clinically assessed differences in health. Our finding that MVM users and non-users do not differ in various psychological, physical, and functional outcomes corroborates previous reports that MVMs do not improve overall health in the general adult population [5-22] . Our stratified analysis revealed that MVM use is associated with better self-reported overall health across all race, sex, and education groups, and in individuals under 65 and with family incomes below 300% FPL. The lack of association between MVM usage and self-reported health in individuals with family income greater than 300% FPL may be related to sample size and should be replicated in a larger cohort. Taken together, these findings help elucidate explanations underlying widespread MVM usage despite no generalized clinical benefits.

The results here suggest two potential explanations underlying widespread MVM consumption in the absence of clinically measurable benefits: 1) MVM users believe in the efficacy of MVMs by harboring a positive expectation regarding the health benefits of MVMs and/or 2) MVM users intrinsically harbor a more positive outlook on their personal health regardless of MVM usage. A growing body of evidence suggests that positive expectation influence treatment outcomes for diseases including heart disease[30–33], cancer[34,35], musculoskeletal disorders[36,37], injuries[38,39], and obesity[40–42]. Under a positive expectation model, MVM users are more likely to harbor a positive expectation regarding the clinical efficacy of MVMs and thus more likely to self-report as having excellent or good overall health. In the case of MVM usage, it is interesting the presence of positive expectation did not influence clinically measurable health outcomes, unlike in other treatments. The effect of positive expectations in the MVM user community is made even more stronger when one considers that the majority of MVM and supplements are sold to the so-called "worried-well" population[43] who may assign greater weight to the purported health benefits of dietary supplements and alternative therapies. It is possible that members of this population are more susceptible to positive expectations and may thereby continue to use MVMs in the absence of clinical benefits.

The second mechanism, in which MVM users intrinsically harbor greater positive views about their health, may be explained in part by certain combinations of sociodemographic determinants that influence self-reported health. While age, sex, income, education, and location of residence have been previously shown to affect self-reported health in diverse populations[44–46], combinations of other characteristics may also cause MVM users to harbor intrinsically more positive views regarding their health in the absence of clinical differences. Further research is necessary to elucidate these characteristics.

Our results are consistent with existing work from two studies: the first being a 2013 study involving 11,956 adults from the 2007-2010 NHANES that demonstrated MVM users exhibit greater self-reported health than non-users[29], and second, a 2014 study involving 5536 Coast Guard and military study which found that MVM users were significantly more likely to self-report their general health as excellent or good[47]. While informative, these previous studies only focused on self-reported health as an outcome. In the present study, we considered self-reported health in addition to clinically measurable health outcomes. This is an important distinction in order to establish that MVM users experience greater self-reported health in the absence of clinically measurable health improvement. Nevertheless, it is encouraging that our

results are consistent across the NHANES, military and Coast Guard and NHIS study cohorts, and robust to different statistical analysis methodologies.

Limitations of this study include the cross-sectional design, reliability of self-reported health, and income estimation using multiple imputation. First, the cross-sectional study design prevents a demonstration of causal relationship between MVM use and self-reported health. The lack of longitudinal data available to assess changes in self-reported health before and after MVM supplementation prevents us from differentiating the two aforementioned explanations that may contribute to widespread MVM use. Second, self-reported health may inherently harbor reporting bias and residual confounding. Third, despite being recommended by the NHIS[27], the multiple imputation technique used to calculate income in cases in which data was missing may generate estimation errors. Another limitation to the income-stratified results for self-reported overall health may stem from the inability to factor income mobility. Interestingly, it has been previously demonstrated that while high incomes are associated with longer life expectancies, accounting for income mobility reduces the gap by approximately 50%[48].

Conclusions

Using nationally representative survey data on health outcomes, our study reveals that MVM users self-report better overall health than non-users despite not exhibiting improved health by clinically measurable standards. Furthermore, we identify specific sociodemographic subgroups of MVM users that are more prone to this behavior. The multibillion-dollar nature of the nutritional supplement industry makes understanding the determinants of widespread MVM have significant medical and financial consequences. Our findings may assist public health efforts to better educate the general public about effective MVM use practices.

CONTRIBUTORS

MDP and ACC conceived and designed the study. MDP extracted data from NHANES. MDP, ACC, IP, PQD, JKW, RO, NJR, AA, AH, CCL, VO, IU, ALN, BSG, KTH, DHM, and GNN analyzed the data. MDP, ACC, KTH, and DHM wrote the manuscript. MDP, ACC, KTH, DHM, GNN, and RSC critically revised the manuscript for important intellectual content. All authors commented and approved the manuscript.

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COMPETING INTERESTS

None declared.

PATIENT CONSENT

None required.

ETHICS APPROVAL

None required.

DATA SHARING

All data used in the study is publicly available from the National Health Interview Survey.

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Table 1: Characteristics of American Adults by Multivitamin and Multimineral Supplement (MVM) Usage

Characteristic	MVM non-users (n = 4933[a])	MVM users (n = 16670[a])	FDR-adjusted *P* value[b]
Weighted sample %	22.4 (21.8-23.0)	77.6 (76.9-78.0)	
Age, % (95% CI[c])			
Mean age in years (95% CI)	48.1 (47.4-48.7)	49.7 (49.3-50.2)	
18-27 years	14.9 (13.8-16.2)	13.1 (12.2-14.1)	
28-37 years	16.6 (15.4-18.0)	16.9 (16.2-17.7)	
38-47 years	17.4 (16.3-18.6)	15.3 (14.6-15.9)	<0.001
48-57 years	17.7 (16.4-19.0)	17.6 (16.9-18.3)	
58-67 years	14.3 (13.2-15.5)	15.4 (14.8-16.1)	
68-80 years	10.1 (9.2-11.1)	12.8 (12.1-13.5)	
≥ 80 years	5.9 (5.1-6.8)	6.2 (5.7-6.7)	
Race, % (95% CI[c])			
White only	82.2 (81.0-83.3)	82.9 (82.1-83.6)	
Black/African American only	11.4 (10.4-12.5)	10.4 (9.9-11.0)	
American Indian/ Alaskan Native only	1.1 (0.8-1.4)	0.6 (0.5-0.8)	<0.001
Asian only	3.5 (3.1-4.0)	4.3 (3.9-4.6)	
Multiple race	1.8 (1.5-2.2)	1.9 (1.6-2.1)	
% Female (95% CI[c])	54.1 (52.6-55.6)	59.1 (58.2-60.1)	<0.001
Family Income, relative to federal poverty level (95% CI[c])			
<100%	16.9 (15.3-18.4)	12.4 (11.5-13.3)	
100%-199%	19.7 (18.2-21.2)	17.9 (17.1-18.8)	
200%- 299%	17.3 (15.8-18.7)	17.0 (16.2-17.8)	<0.001
300%-399%	12.8 (11.4-14.2)	13.4 (12.6-14.1)	
400% +	33.4 (31.1-35.6)	39.4 (37.9-40.9)	
Education status, % (95% CI[c])			
Did not graduate high school	11.7 (10.7-12.8)	9.6 (9.0-10.1)	
Grade 12 or GED	26.6 (24.8-28.5)	22.4 (21.4-23.4)	
Some college, no degree	22.1 (20.5-23.8)	21.2 (20.1-22.4)	<0.001
Associates degree	10.8 (9.7-11.9)	12.0 (11.4-12.6)	
College graduate or higher	28.7 (26.7-30.7)	34.7 (33.3-36.2)	
Relationship status, % (95% CI[c])			

Married or living with partner	49.0 (46.4-51.7)	51.0 (49.4-52.7)	
Separated, divorced, or widowed	26.6 (25.0-28.3)	26.7 (25.6-27.8)	<0.001
Never married	24.3 (22.5-26.1)	22.3 (21.0-23.5)	
Employment status, % (95% CI[c])			
Employed	58.1 (55.2-60.9)	58.6 (56.7-60.5)	
Unemployed, looking for work	6.1 (5.2-7.0)	5.2 (4.8-5.6)	0.05
Not in labor force	35.8 (33.7-37.9)	36.2 (34.8-37.6)	
Minor child in household, % (95% CI[c])	30.4 (28.8-32.0)	26.5 (25.5-27.3)	<0.001
Non-English-speaking interview, % (95% CI[c])	3.6 (3.1-4.1)	3.5 (3.1-3.8)	0.66
Has health insurance, % (95% CI[c])	84.3 (83.1-85.4)	87.4 (86.9-88.0)	<0.001
No office visit for health care in the past two weeks, % (95% CI[c])	79.8 (78.6-81.0)	76.4 (75.7-77.1)	<0.001
Unmet medical care due to cost in the past year, % (95% CI[c])	9.4 (8.5-10.3)	8.7 (8.3-9.2)	0.19

a. Unweighted sample size

b. FDR-adjusted P value was computed using the Benjamini-Hochberg procedure. P values were computed using a two-sample t-test or chi-square test for independence.

c. All confidence intervals were computed based on a Rao-Scott-scaled chi-squared distribution for the loglikelihood from a binomial distribution using the Survey package in R.

Table 2. Effect of MVM Usage on Health Status

Characteristic	MVM non-users	MVM users	Adjusted Effect of MVM usage, β or OR (95% CI)[a]	FDR-adjusted *P* value[e]
Self-rated overall health as excellent, very good or good, % (95% CI[f])	84.9 (83.8-86.0)	88.3 (87.7-88.9)	OR=1.3 (1.2-1.5)	<0.001
Needs help with ADLs, % (95% CI[f])	5.6 (4.8-6.3)	4.8 (4.4-5.2)	OR = 0.86 (0.7-1.04)	0.07
History of chronic conditions, % (95% CI[f])				
Mean number of chronic conditions	1.07 (1.03-1.11)	1.09 (1.06-1.11)	β = 0.03 (-0.07-0.007)	0.07
No chronic conditions	44.4 (42.0-46.8)	43.0 (41.4-44.5)		
1 chronic condition	26.3 (24.5-28.2)	26.4 (25.4-27.5)		
Multiple chronic conditions	28.4 (26.7-30.0)	29.7 (28.6-30.7)		
Health conditions in past year[d] (95% CI[f])				
Mean number of present conditions	2.8 (2.7-2.9)	2.7 (2.7-2.8)	β=-0.06 (-0.2-0.02)	0.08
0-5 present conditions	84.7 (81.3-88.1)	85.2 (83.0-87.6)		
6-10 present conditions	12.7 (11.6-13.8)	12.4 (11.7-13.0)		
≥10 present conditions	1.5 (1.1-1.9)	1.4 (1.2-1.6)		
Kessler 6-item score, % (95% CI[f])				
Mean Kessler score	2.5 (2.4 -2.6)	2.3 (2.3-2.4)	β=-0.08 (-0.2–0.04)	0.13
No impairment	80.9 (77.4-84.4)	82.3 (80.0-84.6)		
Moderate Impairment	15.4 (14.2-16.6)	14.8 (14.1-15.5)		
Severe Impairment	3.7 (3.1-4.2)	2.9 (2.6-3.2)		

a) Estimates were produced after adjusting for age, sex, race, region, education level, income, employment status, health insurance status, presence of child in household,

marital status, unmet medical care due to cost in the past year, and not seeing a health professional in office in the past two weeks

b) *P* value was defined using a multivariate regression model controlling for age, sex, race, region, education level, income, employment status, health insurance status, presence of child in household, marital status, unmet medical care due to cost in the past year, and not seeing a health professional in office in the past two weeks

c) Ten chronic diseases included: cancer, hypertension, coronary heart disease, stroke, chronic obstructive pulmonary disease, asthma, diabetes, arthritis, hepatitis, and weak/failing kidneys

d) 19 health conditions in the past 12 months included: respiratory, digestive, skin, and other allergy, acid reflux, hay fever, chest cold, nausea and vomiting, sore threat, infectious disease, recurring headache, memory loss, neurological problems, sprains, and abdominal, dental, muscle/bone, chronic, and skin pain

e) FDR-adjusted P values were computed using the Benjamini-Hochberg procedure

f) All confidence intervals were computed based on a Rao-Scott-scaled chi-squared distribution for the loglikelihood from a binomial distribution using the Survey package in R.

Table 3: Association Between MVM Usage and Self-Reported Overall Health in Sociodemographic Subgroups

Group	Self-rated overall health as excellent, very good or good, % (95% CI[a]), MVM Non-Users	Self-rated overall health as excellent, very good or good, % (95% CI[a]), MVM Users	Adjusted Effect of MVM usage on self-reported health, OR (95% CI[a])[b]	FDR Adjusted *P* value[c]
Age				
18-44 years	92.3 (91.1-93.5)	94.2 (93.6-94.8)	1.3 (1.0-1.6)	0.03
45-64 years	79.9 (77.8-82.1)	85.3 (84.2-86.4)	1.3 (1.1-1.6)	0.009
65+ years	77.2 (73.8-80.5)	82.0 (80.6-83.4)	1.2 (1.0-1.5)	0.06
Race				
White	85.9 (84.7-87.2)	89.1 (88.5-89.7)	1.3 (1.1-1.7)	0.009
Non-white	80.0 (77.2-82.7)	84.2 (82.8-85.6)	1.3 (1.1-1.5)	0.007
Sex				
Female	84.0 (82.5-85.4)	88.1 (87.4-88.9)	1.2 (1.1-1.4)	0.009
Male	85.9 (84.2-87.7)	88.4 (87.5-89.3)	1.3 (1.1-1.6)	0.009
Family Income, relative to federal poverty level (95% CI)				
<100%	71.7 (68.0-75.4)	75.6 (73.1-78.1)	1.4 (1.1-1.8)	0.007
100%-199%	76.4 (73.6-79.2)	80.7 (79.0-82.4)	1.4 (1.1-1.7)	0.007
200%- 299%	84.8 (82.1-87.5)	87.3 (85.9-88.6)	1.3 (1.0-1.7)	0.04
300%-399%	89.6 (86.4-92.7)	91.0 (89.6-92.4)	1.3 (0.9-2.0)	0.15
400% +	94.8 (93.5-96.1)	95.2 (94.6-95.8)	1.1 (0.8-1.6)	0.23
Education				
Did not graduate high school	67.2 (63.1-71.3)	71.9 (69.7-74.2)	1.4 (1.1-1.9)	0.01

High school graduate	84.1 (82.6-85.5)	86.7 (85.9-87.4)	1.2 (1.0-1.4)	0.01
College graduate or higher	93.8 (92.4-95.1)	95.3 (94.7-95.9)	1.4 (1.0-1.9)	0.03

a) All confidence intervals were computed based on a Rao-Scott-scaled chi-squared distribution for the loglikelihood from a binomial distribution using the Survey package in R.

b) Estimates were produced after adjusting for age, sex, race, region, education level, income, employment status, health insurance status, presence of child in household, marital status, unmet medical care due to cost in the past year, and not seeing a health professional in office in the past two weeks.

c) FDR-adjusted P values were computed using the Benjamini-Hochberg procedure. *P* value was defined using a multivariate regression model controlling for age, sex, race, region, education level, income, employment status, health insurance status, presence of child in household, marital status, unmet medical care due to cost in the past year, and not seeing a health professional in office in the past two weeks.

Supplement for:

Self-reported health without clinically measurable benefits among adult users of multivitamin and multimineral supplements: a cross-sectional study

Paranjpe, Chin et. al.

Tables:

Table S1: Interaction between demographic variable and MVM use on self-reported health

Table S1: Interaction between demographic variable and MVM use on self-reported health

Demographic Variable	MVM use:demographic variable interaction on self-reported overall health, $\beta_{\text{Interaction}}$ (95% CI)[a]	FDR Adjusted *P* value[b]
Age (18-44 years, 45-64 years, 65+ years)	1.1 (0.9-1.2)	0.50
Race (White or non-white)	1.0 (0.9-1.1)	0.50
Sex	1.0 (0.8-1.3)	0.50
Family Income, relative to federal poverty level (<100%, 100-199%, 200-299%, 300-399%, 400%+)	1.0 (0.9-1.1)	0.50
Education (Did not graduate high school, high school graduate, , college graduate)	1.0 (1.0-1.1)	0.50

a) Estimates were produced after adjusting for age, sex, race, region, education level, income, employment status, health insurance status, presence of child in household, marital status, unmet medical care due to cost in the past year, and not seeing a health professional in office in the past two weeks.

b) FDR-adjusted P values were computed using the Benjamini-Hochberg procedure. *P* value was defined using a multivariate regression model controlling for age, sex, race, region, education level, income, employment status, health insurance status, presence of child in household, marital status, unmet medical care due to cost in the past year, and not seeing a health professional in office in the past two weeks.

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	2
Methods			
Study design	4	Present key elements of study design early in the paper	6-7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6-7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-7
6Bias	9	Describe any efforts to address potential sources of bias	6-7
Study size	10	Explain how the study size was arrived at	6-7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7
		(*b*) Describe any methods used to examine subgroups and interactions	7
		(*c*) Explain how missing data were addressed	7
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	7
		(*e*) Describe any sensitivity analyses	7
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8
		(b) Give reasons for non-participation at each stage	8
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8
		(b) Indicate number of participants with missing data for each variable of interest	8
Outcome data	15*	Report numbers of outcome events or summary measures	8-10
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	8-10

		(*b*) Report category boundaries when continuous variables were categorized	8-10
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9-10
Discussion			
Key results	18	Summarise key results with reference to study objectives	10-11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	12-13
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11-13
Generalisability	21	Discuss the generalisability (external validity) of the study results	12
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	14

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Self-reported health without clinically measurable benefits among adult users of multivitamin and multimineral supplements: a cross-sectional study

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Self-reported health without clinically measurable benefits among adult users of multivitamin and multimineral supplements: a cross-sectional study

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ABSTRACT

Objectives: Multiple clinical trials fail to identify clinically measurable health benefits of daily multivitamin and multi-mineral (MVM) consumption in the general adult population. Understanding the determinants of widespread use of MVMs may guide efforts to better educate the public about effective nutritional practices. The objective of this study was to compare self-reported and clinically measurable health outcomes among MVM users and non-users in a large, nationally representative sample of adult civilian non-institutionalized population of the US surveyed on the use of complementary health practices.

Design: Cross-sectional analysis of the effect of MVM consumption on self-reported overall health and clinically measurable health outcomes.

Participants: Adult MVM users and non-users from the 2012 National Health Interview Survey (n=21,603).

Primary and secondary outcome measures: Five psychological, physical, and functional health outcomes 1) self-rated health status, 2) needing help with routine needs, 3) history of 10 chronic diseases, 4) presence of 19 health conditions in the past 12 months, and 5) Kessler 6-Item (K6) Psychological Distress Scale to measure nonspecific psychological distress in the past month.

Results: Among 4,933 adult MVM users and 16,670 adult non-users, MVM users self-reported 30% better overall health than non-users (Adjusted OR: 1.31; 95% CI: 1.17-1.46 FDR-adjusted P<.001). There were no differences between MVM users and non-users in history of 10 chronic diseases, number of present health conditions, severity of current psychological distress on the K6 scale and rates of needing help with daily activities. No effect modification was observed after stratification by sex, education, and race.

***Conclusions*:** MVM users self-reported better overall health despite no apparent differences in clinically measurable health outcomes. These results suggest that widespread use multivitamins in adults may be a result of individuals' positive expectation that multivitamin use leads to better health outcomes or a self-selection bias in which MVM users intrinsically harbor more positive views regarding their health.

STRENGTHS AND LIMITATIONS OF THE STUDY

- This is the first study to link increased self-reported health, absence of clinically measurable benefits, and multivitamin and multimineral supplement use in the same population
- Data are derived from a large, national survey across the US
- Results have broad implications for public health and the multibillion-dollar supplement industry
- Cross-sectional study design precludes the demonstration of a causal relationship between self-reported health and multivitamin and multimineral supplements
- Self-reported health can be inherently biased and confounding

INTRODUCTION

Consumption of multivitamins (MVs) and multi-minerals (MMs) (together: MVMs) as dietary supplements is widespread in the general US adult population, with some reports estimating 33% of Americans regularly take MVMs[1–4]. While MVM supplementation is warranted for some individuals at high-risk because of disease-related defiency[5], the consumption of non-prescription, over-the-counter MVMs has not produced robust evidence for the wide-ranging health benefits expected by the general adult population. Likewise, large randomized clinical trials that evaluate MVM at different doses, across both men and women at varied ages, have failed to demonstrate benefit in prevention of chronic diseases. The Physicians' Health Study II (PHS II), a randomized placebo-controlled clinical trial of low-dose daily MVM use in older male physicians, found no reduction in major CVD events, myocardial infarction, stroke, and CVD mortality[6], and these results were independent of baseline nutritional status[7]. A prospective cohort study of middle-aged and elderly women also indicated no effect of MVM use for the same CVD outcomes in PHS II[8]. The SU.VI.MAX Study, a clinical trial of antioxidative MVMs in adults, found no effect on incidence of ischemic CVD[9], and high-dose MVMs did not reduce CVD events[10]. Meta-analysis of these and other studies (N=18) found no improvement in CVD outcomes in the general population[11]. Based on these studies, the US Preventative Services Task Force does not recommend MVM use for the prevention of CVD[12,13].

Data on the effect of MVM consumption on cognitive function in adults are also inconclusive. While results from PHS II found that long-term use of daily MVs did not provide cognitive benefits in men[14], a meta-analysis on 10 studies concluded that MVs selectively enhanced free recall memory but no other cognitive functions[15]. Intriguingly, nine weeks of MVM use appears to improve multi-tasking and cognitive function during fatigue in women[16].

With regard to cancer, PHS II demonstrated moderately reduced all-cancer risk in men consuming MVs[17] while data from the Women's Health Initiative Clinical Trials revealed no association[18]. Some studies even link MVM use with increased cancer risk – a prospective cohort study of Swedish women found increased breast cancer risk associated with MVM use[19].

The association of MVM use with all-cause mortality, like CVD, is null. While data from the Multiethnic Cohort Study cohort study indicated no association between MVM use and all-cause mortality,[20] the Cancer Prevention Study (II) reported a five percent higher rate of all-cause death among men using MVs[21] and The Iowa Women's Health Study identified an association between MVM use and increased total mortality risk[22]. A meta-analysis of these and other randomized trials (N=21) demonstrated no effect of MVM use on mortality risk[23].

While numerous reports on MVM consumption establish the lack of broad-spectrum, clinically measurable health benefits, the determinants of widespread MVM use by the general population are not well understood. That the majority (52%) of MVM users report using MVMs in an effort to prevent disease is even more puzzling in light of the paucity of randomized and observation data showing a positive health benefit of MVMs[24]. Because nutritional supplements constitute a multibillion-dollar industry and can even be harmful when taken in excess[25], understanding the determinants of widespread MVM use has significant medical and financial consequences. Moreover, it is unclear whether MVM users, despite not being physiologically different from non-users, simply believe they are healthier. To address this question, we utilized data from the 2012 National Health Interview Survey[26] (NHIS), which included a complementary and alternative (CAM) questionnaire comprising of 21,603 participants across the US.

METHODS

Data source

All data was obtained from the 2012 The National Health Interview Survey (NHIS), a nationally representative health survey conducted annually among civilian and noninstitutionalized US participants by the Centers for Disease Control (CDC). All data was publicly available and did not require institutional review board approval. The 2012 NHIS was comprised of a core questionnaire on health information administered to each selected household member. A randomly selected adult in each household was administered a more detailed health survey which included questions on access to care, specific health conditions and use of CAM(2012 only). In 2012, 77.6% of households completed the survey and 79.7% of adults selected completed the detailed survey[26].

Health Status and Health Outcome Measures

We obtained data on adults (age $\geq$ 18 years) derived from the Sample Adult Component who also participated in the Adult CAM File. This file surveys use of alternative medicines and therapies including daily MVM consumption, yoga, and meditation. Consistent with previous NHIS studies[27], we considered five psychological, physical, and functional health outcomes from questions in the Sample Adult Component: 1) self-rated health status (poor/fair vs. excellent/very good/good), 2) needing help with routine needs such as eating (yes or no), 3) history of ten chronic diseases (cancer, hypertension, coronary heart disease, stroke, chronic obstructive pulmonary disease, asthma, diabetes, arthritis, hepatitis, and weak/failing kidneys), 4) presence of 19 health conditions in the past 12 months (digestive, skin, and other allergy, acid reflux, hay fever, chest cold, nausea and vomiting, sore threat, infectious disease, recurring headache, memory loss, neurological problems, sprains, and abdominal, dental, muscle/bone, chronic, and skin pain), and 5) Kessler 6-Item (K6) Psychological Distress Scale[28] score to measure nonspecific psychological distress in the past month. Participants who refused to answer or did not know the answers to at least one of these questions were excluded from the study. Participants were classified as MVM users or non-users from their response to the question "During the past 12 months, did take multi-vitamins or multi-minerals?" in the Adult CAM File. Participants who refused to answer or did not know their MVM use in the past 12 months were excluded from analyses.

Statistical Analysis

For each outcome, the relationship between MVM use in the past year and health outcome was estimated using a logistic regression model adjusting for age, sex, race, region, education, income, employment status, health insurance status, presence of child in household, marital status, unmet medical care due to cost in the past year, and not seeing a health professional in office in the past two weeks. Multinomial logistic regression was used for outcomes with more than two levels (e.g., number of chronic diseases, number of diseases in the past 12 months, Kessler-6 Item score). Binary logistic regression was used for outcomes with two levels (self-reported health and needing help with daily routines such as eating). Standard errors were estimated using weights provided by NHIS to account for the complex survey design and produce nationally representative estimates. A multiple imputation strategy was used to estimate income in cases of missing responses to income as recommended by the National Center for Health Statistics[29]. All analyses were conducted using R (v3.5.1). *P* values were adjusted for multiple comparisons using a Benjamini-Hochberg procedure with FDR<0.01 deemed significant.

Stratified analyses were conducted in age- (18-44 years, 45-64 years and 65+ years), race- (white and non-white), sex- (female and male), family income- (<100%, 100%-199%, 200%-299%, 300-399%, and 400% relative to the federal poverty level), education level- (did not graduate high school, high school graduate, college graduate or higher) stratified groups to assess the association between MVM use and self-reported health in sociodemographic subgroups. In addition to stratified analyses, statistical interaction effects between MVM use and demographic variable (age, race, sex, family income, and education) on self-reported health was assessed using a multivariate regression model.

Patients and Public Involvement

Patients and the public were not involved in this study, including data collection, analysis and interpretation.

RESULTS

Study Cohort Characteristics

Sociodemographic differences between MVM users and non-users are presented in Table 1. Our study included 4,933 MVM users and 16,670 non-users (Table 1). As previously reported in data from the 2007-2010 and 2010-2014 National Health and Nutrition Examination Surveys (NHANES)[30,31], compared to non-users, MVM users were significantly older, earned more income, more likely to be female, more likely to be a college graduate, more likely to be married, and more likely to have health insurance. Unlike in previous studies, compared to MVM non-users, MVM users were less likely to be unemployed, have a minor child in their household, and not have an office visit for healthcare in the past two weeks (Table 1). We observed no significant differences in percent of non-English speaking interviews and percent having foregone medical care due to cost in the past year between MVM users and non-users (Table 1).

Association between MVM usage and Health Status and Health Outcomes

Differences in health status and health outcomes between MVM users and non-users are displayed in Table 2. Multivariate regression revealed that MVM users self-reported 30% better overall health than non-users (OR: 1.31, 95% CI: 1.17-1.46, FDR-adjusted P<.001 ; Table 2). Strikingly, MVM users and non-users did not differ in history of 10 chronic disease (MVM users mean 1.09 conditions, 95% CI: 1.06-1.11 vs non-users mean: 1.07, 95% CI: 1.03-1.11) number of present health conditions (MVM users mean: 2.7 conditions, 95% CI: 2.7-2.8 vs non-users mean: 2.8, 95% CI: 2.7-2.9), severity of psychological distress on the K6 scale (MVM users mean K6 score = 2.3, 95% CI: 2.3-2.4 vs non-users mean = 2.5, 95% CI: 2.4-2.6), and needing help with daily activities (OR: 0.86, 95% CI: 0.71-1.04).

Stratified Analyses: Association between MVM Usage and Self-Reported Overall Health in Sociodemographic Subgroups

Table 3 reports the association between MVM usage and self-reported overall health in age, race, sex, income, and education-stratified subgroups (Table 3). MVM use was associated with better self-reported health in the 18-44-year (OR: 1.26, 95% CI: 1.00-1.61) and 45-64-year groups (OR: 1.30, 95% CI: 1.08-1.57) and near significant among respondents ≥ 65 years (OR: 1.20, 95% CI: 0.95-1.52, FDR *P* value = 0.06) (Table 3). MVM use was associated with better self-reported health amongst both white (OR: 1.34, 95% CI: 1.07-1.67) and non-white (OR: 1.26;

95% CI: 1.09-1.45) respondents (Table 3). MVM use was associated with better self-reported health in both male (OR: 1.33, 95% CI: 1.10-1.63) and female (OR: 1.22, 95% CI: 1.05-1.41) respondents (Table 3). Interestingly, MVM use was associated with better self-reported health in families with income < 100% of the federal poverty level (FPL) (OR: 1.42, 95% CI: 1.12-1.80), 100%-199% FPL (OR: 1.37, 95% CI: 1.10-1.69) and 200%-299% FPL (OR: 1.32, 95% CI: 1.01-1.72) but not in families whose income was 300%-399% FPL (OR: 1.32, 95% CI: 0.88-1.98) or ≥400% FPL (OR: 1.15, 95% CI: 0.85-1.56) (Table 3). MVM use was associated with better self-reported health in all education subgroups analyzed, including respondents that did not complete high school (OR: 1.38, 95% CI: 1.06-1.81), high school graduates (OR: 1.21, 95% CI: 1.04-1.41), and college graduates (OR: 1.37, 95% CI: 1.00-1.88) (Table 3). All stratified analyses were conducted after adjusting for the potential confounding effects of age, sex, race, region, education, income, employment status, health insurance status, presence of child in household, marital status, unmet medical care due to cost in the past year, and not seeing a health professional in office in the past two weeks. The variable of stratification was not included as a covariate.

Statistical interaction effects between MVM use and demographic variables (age, race, family income, and education) on self-reported overall health was assessed through a multivariate regression model in Table S1. We observed no significant association between MVM use and age, MVM use and race, MVM use and family income, and MVM use and education on self-reported overall income (Table S1).

DISCUSSION

This present study is the first to simultaneously analyze the association between MVM use and both self-reported health and clinical health outcomes. In this work, we found that MVM users self-report 30% better overall health than non-users despite no clinically assessed differences in health. Our finding that MVM users and non-users do not differ in various psychological, physical, and functional outcomes corroborates previous reports that MVMs do not improve overall health in the general adult population [5-22]. Our stratified analysis revealed that MVM use is associated with better self-reported overall health across all race, sex, and education groups, and in individuals under 65 and with family incomes below 300% FPL. The lack of association between MVM usage and self-reported health in individuals with family income greater than 300% FPL may be related to sample size and should be replicated in a follow up study. Taken together, these findings help elucidate explanations underlying widespread MVM usage despite no generalized clinical benefits.

The results here suggest two potential explanations underlying widespread MVM consumption in the absence of clinically measurable benefits: 1) MVM users believe in the efficacy of MVMs by harboring a positive expectation regarding the health benefits of MVMs and/or 2) MVM users intrinsically harbor a more positive outlook on their personal health regardless of MVM usage. A growing body of evidence suggests that positive expectation influence treatment outcomes for diseases including heart disease[32–35], cancer[36,37], musculoskeletal disorders[38,39], injuries[40,41], and obesity[42–44]. Under a positive expectation model, MVM users are more likely to harbor a positive expectation regarding the clinical efficacy of MVMs and thus more likely to self-report as having excellent or good overall health. In the case of MVM usage, it is interesting that the presence of positive expectation did not influence clinically measurable health outcomes, unlike in other treatments. The effect of positive expectations in the MVM user community is made even more stronger when one considers that the majority of MVM and supplements are sold to the so-called "worried-well" population[45] who may assign greater weight to the purported health benefits of dietary supplements and alternative therapies. It is possible that members of this population are more susceptible to positive expectations and may thereby continue to use MVMs in the absence of clinical benefits.

The second mechanism, in which MVM users intrinsically harbor greater positive views about their health, may be explained in part by certain combinations of sociodemographic determinants that influence self-reported health. While age, sex, income, education, and location of residence have been previously shown to affect self-reported health in diverse populations[46–48], combinations of other characteristics may also cause MVM users to harbor intrinsically more positive views regarding their health in the absence of clinical differences. Further research is necessary to elucidate these characteristics.

Our results are consistent with existing work from two studies: the first being a 2013 study involving 11,956 adults from the 2007-2010 NHANES that demonstrated MVM users exhibit greater self-reported health than non-users[31], and second, a 2014 study involving 5536 Coast Guard and military study which found that MVM users were significantly more likely to self-report their general health as excellent or good[49]. While informative, these previous studies only focused on self-reported health as an outcome. In the present study, we considered self-reported health in addition to clinically measurable health outcomes. This is an important distinction in order to establish that MVM users experience greater self-reported health in the absence of clinically measurable health improvement. Nevertheless, it is encouraging that our

results are consistent across the NHANES, military and Coast Guard and NHIS study cohorts, and robust to different statistical analysis methodologies.

Limitations of this study include the cross-sectional design, reliability of self-reported health within NHIS, income estimation using multiple imputation, indication bias and nonresponse bias. First, the cross-sectional study design prevents a demonstration of causal relationship between MVM use and self-reported health. The lack of longitudinal data available to assess changes in self-reported health before and after MVM supplementation prevents us from differentiating the two aforementioned explanations that may contribute to widespread MVM use. Second, self-reported health within the NHIS may inherently harbor reporting bias and residual confounding. In addition to reporting bias and residual confounding, a self-reported binary response to the question of whether one has taken MVMs in the past 12 months precludes any analysis of dose-dependent effects of MVMs in our cohort. This is especially important considering some vitamins and minerals have known U-shaped associations with disease in which disease risk is elevated at both high and low vitamin and mineral levels [50–53]. Further, use of both multivitamins and multiminerals were asked together as part of the same question in the NHIS questionnaire. This prevented us from analyzing multivitamin and multimineral effects in isolation. Moreover, different MVM preparations can differ in their nutritional composition, quality, and bioavailability. Some individuals may take multiple MVMs whose constituents could interact with each other. Because the brand of multivitamin being taken was not asked of MVM users in NHIS, we could not identify differences in nutritional composition, quality, bioavailability, and chemical interaction that may be driving the results in this study.

Third, despite being recommended by the NHIS[29], the multiple imputation technique used to calculate income in cases in which data was missing may generate estimation errors.

Another limitation to the income-stratified results for self-reported overall health may stem from the inability to factor income mobility. Interestingly, it has been previously demonstrated that while high incomes are associated with longer life expectancies, accounting for income mobility reduces the gap by approximately 50%[54].

A portion of our cohort may have been prescribed MVMs, specific vitamins or specific minerals for indications including micronutrient deficiency, pregnancy, iron deficiency anemia, osteoporosis, Crohn's disease and others, thereby contributing to indication bias[55–60]. Previous estimates have suggested approximately 1% of physician office visits in the United States include a prescription or recommendation for MVMs[61] . One can imagine a scenario in which MVM users and non-users are imbalanced in the proportion of medical cases that require MVM supplementation (ie. micronutrient deficiency or pregnancy). In such a scenario, it may falsely appear that MVM use is not associated with clinical benefits. In the present study, owing to a lack of information regarding the reason for taking MVMs, we were unable to fully account for indication bias present in our cohort.

In addition to indication bias, the NHIS, like other surveys, is known to suffer from nonresponse bias[62]. For example, a previous study found that the 1990-2009 NHIS population had an approximately 14% lower mortality than the general population[62]. Post-hoc methods to address nonresponse bias include creating sample weights based on demographic variables and selection probabilities, as was used in the present study. However, survey weighting, while a standard practice, may not fully account for nonresponse bias, especially if the survey weights do not take into account common differences between survey responders and non-responders such as smoking and alcohol use[63]. As a result, non-response bias may limit the generalizability of our results to the broader population.

Conclusions

Using nationally representative survey data on health outcomes, our study reveals that MVM users self-report better overall health than non-users despite not exhibiting improved health by clinically measurable standards. Furthermore, we identify specific sociodemographic subgroups of MVM users that are more prone to this behavior. The multibillion-dollar nature of the nutritional supplement industry makes understanding the determinants of widespread MVM have significant medical and financial consequences. Our findings suggest that widespread use multivitamins in adults may be a result of individuals' positive expectation that multivitamin use leads to better health outcomes or a self-selection bias in which MVM users intrinsically harbor more positive views regarding their health.

CONTRIBUTORS

MDP and ACC conceived and designed the study. MDP extracted data from NHANES. MDP, ACC, IP, PQD, JKW, RO, NJR, AA, AH, CCL, VO, IU, ALN, BSG, KTH, DHM, and GNN analyzed the data. MDP, ACC, KTH, and DHM wrote the manuscript. MDP, ACC, KTH, DHM, GNN, and RSC critically revised the manuscript for important intellectual content. All authors commented and approved the manuscript.

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COMPETING INTERESTS

None declared.

PATIENT CONSENT

None required.

ETHICS APPROVAL

None required.

DATA SHARING

All data used in the study is publicly available from the National Health Interview Survey.

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Table 1: Characteristics of American Adults by Multivitamin and Multimineral Supplement (MVM) Usage

Characteristic	MVM non-users (n = 4933[a])	MVM users (n = 16670[a])	FDR-adjusted *P* value[b]
Weighted sample %	22.4 (21.8-23.0)	77.6 (76.9-78.0)	
Age, % (95% CI[c])			

Mean age in years (95% CI)	48.1 (47.4-48.7)	49.7 (49.3-50.2)	
18-27 years	14.9 (13.8-16.2)	13.1 (12.2-14.1)	
28-37 years	16.6 (15.4-18.0)	16.9 (16.2-17.7)	
38-47 years	17.4 (16.3-18.6)	15.3 (14.6-15.9)	<0.001
48-57 years	17.7 (16.4-19.0)	17.6 (16.9-18.3)	
58-67 years	14.3 (13.2-15.5)	15.4 (14.8-16.1)	
68-80 years	10.1 (9.2-11.1)	12.8 (12.1-13.5)	
≥ 80 years	5.9 (5.1-6.8)	6.2 (5.7-6.7)	
Race, % (95% CI[c])			
White only	82.2 (81.0-83.3)	82.9 (82.1-83.6)	
Black/African American only	11.4 (10.4-12.5)	10.4 (9.9-11.0)	
American Indian/ Alaskan Native only	1.1 (0.8-1.4)	0.6 (0.5-0.8)	<0.001
Asian only	3.5 (3.1-4.0)	4.3 (3.9-4.6)	
Multiple race	1.8 (1.5-2.2)	1.9 (1.6-2.1)	
% Female (95% CI[c])	54.1 (52.6-55.6)	59.1 (58.2-60.1)	<0.001
Family Income, relative to federal poverty level (95% CI[c])			
<100%	16.9 (15.3-18.4)	12.4 (11.5-13.3)	
100%-199%	19.7 (18.2-21.2)	17.9 (17.1-18.8)	
200%- 299%	17.3 (15.8-18.7)	17.0 (16.2-17.8)	<0.001
300%-399%	12.8 (11.4-14.2)	13.4 (12.6-14.1)	
400% +	33.4 (31.1-35.6)	39.4 (37.9-40.9)	
Education status, % (95% CI[c])			
Did not graduate high school	11.7 (10.7-12.8)	9.6 (9.0-10.1)	
Grade 12 or GED	26.6 (24.8-28.5)	22.4 (21.4-23.4)	
Some college, no degree	22.1 (20.5-23.8)	21.2 (20.1-22.4)	<0.001
Associates degree	10.8 (9.7-11.9)	12.0 (11.4-12.6)	
College graduate or higher	28.7 (26.7-30.7)	34.7 (33.3-36.2)	
Relationship status, % (95% CI[c])			
Married or living with partner	49.0 (46.4-51.7)	51.0 (49.4-52.7)	
Separated, divorced, or widowed	26.6 (25.0-28.3)	26.7 (25.6-27.8)	<0.001
Never married	24.3 (22.5-26.1)	22.3 (21.0-23.5)	
Employment status, % (95% CI[c])			
Employed	58.1 (55.2-60.9)	58.6 (56.7-60.5)	
Unemployed, looking for work	6.1 (5.2-7.0)	5.2 (4.8-5.6)	0.05
Not in labor force	35.8 (33.7-37.9)	36.2 (34.8-37.6)	
Minor child in household, % (95% CI[c])	30.4 (28.8-32.0)	26.5 (25.5-27.3)	<0.001

Non-English-speaking interview, % (95% CI[c])	3.6 (3.1-4.1)	3.5 (3.1-3.8)	0.66
Has health insurance, % (95% CI[c])	84.3 (83.1-85.4)	87.4 (86.9-88.0)	<0.001
No office visit for health care in the past two weeks, % (95% CI[c])	79.8 (78.6-81.0)	76.4 (75.7-77.1)	<0.001
Unmet medical care due to cost in the past year, % (95% CI[c])	9.4 (8.5-10.3)	8.7 (8.3-9.2)	0.19

a. Unweighted sample size

b. FDR-adjusted P value was computed using the Benjamini-Hochberg procedure. P values were computed using a two-sample t-test or chi-square test for independence.

c. All confidence intervals were computed based on a Rao-Scott-scaled chi-squared distribution for the loglikelihood from a binomial distribution using the Survey package in R.

Table 2. Association between MVM Usage and Health Status

Characteristic	MVM non-users	MVM users	Adjusted Effect of MVM usage, β or OR (95% CI)[a]	FDR-adjusted *P* value[e]
Self-rated overall health as excellent, very good or good, % (95% CI[f])	84.9 (83.8-86.0)	88.3 (87.7-88.9)	OR=1.3 (1.2-1.5)	<0.001
Needs help with ADLs, % (95% CI[f])	5.6 (4.8-6.3)	4.8 (4.4-5.2)	OR = 0.86 (0.7-1.04)	0.07
History of chronic conditions, % (95% CI[f])				
Mean number of chronic conditions	1.07 (1.03-1.11)	1.09 (1.06-1.11)	β = 0.03 (-0.07-0.007)	0.07
No chronic conditions	44.4 (42.0-46.8)	43.0 (41.4-44.5)		
1 chronic condition	26.3 (24.5-28.2)	26.4 (25.4-27.5)		
Multiple chronic conditions	28.4 (26.7-30.0)	29.7 (28.6-30.7)		
Health conditions in past year[d] (95% CI[f])				
Mean number of present conditions	2.8 (2.7-2.9)	2.7 (2.7-2.8)	β=-0.06 (-0.2-0.02)	0.08
0-5 present conditions	84.7 (81.3-88.1)	85.2 (83.0-87.6)		
6-10 present conditions	12.7 (11.6-13.8)	12.4 (11.7-13.0)		
≥10 present conditions	1.5 (1.1-1.9)	1.4 (1.2-1.6)		
Kessler 6-item score, % (95% CI[f])				
Mean Kessler score	2.5 (2.4 -2.6)	2.3 (2.3-2.4)	β=-0.08 (-0.2–0.04)	0.13
No impairment	80.9 (77.4-84.4)	82.3 (80.0-84.6)		
Moderate Impairment	15.4 (14.2-16.6)	14.8 (14.1-15.5)		
Severe Impairment	3.7 (3.1-4.2)	2.9 (2.6-3.2)		

a) Estimates were produced after adjusting for age, sex, race, region, education level, income, employment status, health insurance status, presence of child in household,

marital status, unmet medical care due to cost in the past year, and not seeing a health professional in office in the past two weeks

b) *P* value was defined using a multivariate regression model controlling for age, sex, race, region, education level, income, employment status, health insurance status, presence of child in household, marital status, unmet medical care due to cost in the past year, and not seeing a health professional in office in the past two weeks

c) Ten chronic diseases included: cancer, hypertension, coronary heart disease, stroke, chronic obstructive pulmonary disease, asthma, diabetes, arthritis, hepatitis, and weak/failing kidneys

d) 19 health conditions in the past 12 months included: respiratory, digestive, skin, and other allergy, acid reflux, hay fever, chest cold, nausea and vomiting, sore threat, infectious disease, recurring headache, memory loss, neurological problems, sprains, and abdominal, dental, muscle/bone, chronic, and skin pain

e) FDR-adjusted P values were computed using the Benjamini-Hochberg procedure

f) All confidence intervals were computed based on a Rao-Scott-scaled chi-squared distribution for the loglikelihood from a binomial distribution using the Survey package in R.

Table 3: Association Between MVM Usage and Self-Reported Overall Health in Sociodemographic Subgroups

Group	Self-rated overall health as excellent, very good or good, % (95% CI[a]), MVM Non-Users	Self-rated overall health as excellent, very good or good, % (95% CI[a]), MVM Users	Adjusted Effect of MVM usage on self-reported health, OR (95% CI[a])[b]	FDR Adjusted *P* value[c]
Age				
18-44 years	92.3 (91.1-93.5)	94.2 (93.6-94.8)	1.3 (1.0-1.6)	0.03
45-64 years	79.9 (77.8-82.1)	85.3 (84.2-86.4)	1.3 (1.1-1.6)	0.009
65+ years	77.2 (73.8-80.5)	82.0 (80.6-83.4)	1.2 (1.0-1.5)	0.06
Race				
White	85.9 (84.7-87.2)	89.1 (88.5-89.7)	1.3 (1.1-1.7)	0.009
Non-white	80.0 (77.2-82.7)	84.2 (82.8-85.6)	1.3 (1.1-1.5)	0.007
Sex				
Female	84.0 (82.5-85.4)	88.1 (87.4-88.9)	1.2 (1.1-1.4)	0.009
Male	85.9 (84.2-87.7)	88.4 (87.5-89.3)	1.3 (1.1-1.6)	0.009
Family Income, relative to federal poverty level (95% CI)				
<100%	71.7 (68.0-75.4)	75.6 (73.1-78.1)	1.4 (1.1-1.8)	0.007
100%-199%	76.4 (73.6-79.2)	80.7 (79.0-82.4)	1.4 (1.1-1.7)	0.007
200%- 299%	84.8 (82.1-87.5)	87.3 (85.9-88.6)	1.3 (1.0-1.7)	0.04
300%-399%	89.6 (86.4-92.7)	91.0 (89.6-92.4)	1.3 (0.9-2.0)	0.15
400% +	94.8 (93.5-96.1)	95.2 (94.6-95.8)	1.1 (0.8-1.6)	0.23
Education				
Did not graduate high school	67.2 (63.1-71.3)	71.9 (69.7-74.2)	1.4 (1.1-1.9)	0.01

High school graduate	84.1 (82.6-85.5)	86.7 (85.9-87.4)	1.2 (1.0-1.4)	0.01
College graduate or higher	93.8 (92.4-95.1)	95.3 (94.7-95.9)	1.4 (1.0-1.9)	0.03

a) All confidence intervals were computed based on a Rao-Scott-scaled chi-squared distribution for the loglikelihood from a binomial distribution using the Survey package in R.

b) Estimates were produced after adjusting for age, sex, race, region, education level, income, employment status, health insurance status, presence of child in household, marital status, unmet medical care due to cost in the past year, and not seeing a health professional in office in the past two weeks.

c) FDR-adjusted P values were computed using the Benjamini-Hochberg procedure. *P* value was defined using a multivariate regression model controlling for age, sex, race, region, education level, income, employment status, health insurance status, presence of child in household, marital status, unmet medical care due to cost in the past year, and not seeing a health professional in office in the past two weeks.

Supplement for:

Self-reported health without clinically measurable benefits among adult users of multivitamin and multimineral supplements: a cross-sectional study

Paranjpe, Chin et. al.

Tables:

Table S1: Interaction between demographic variable and MVM use on self-reported health

Table S1: Interaction between demographic variable and MVM use on self-reported health

Demographic Variable	MVM use:demographic variable interaction on self-reported overall health, $\beta_{Interaction}$ (95% CI)[a]	FDR Adjusted *P* value[b]
Age (18-44 years, 45-64 years, 65+ years)	1.1 (0.9-1.2)	0.50
Race (White or non-white)	1.0 (0.9-1.1)	0.50
Sex	1.0 (0.8-1.3)	0.50
Family Income, relative to federal poverty level (<100%, 100-199%, 200-299%, 300-399%, 400%+)	1.0 (0.9-1.1)	0.50
Education (Did not graduate high school, high school graduate, , college graduate)	1.0 (1.0-1.1)	0.50

a) Estimates were produced after adjusting for age, sex, race, region, education level, income, employment status, health insurance status, presence of child in household, marital status, unmet medical care due to cost in the past year, and not seeing a health professional in office in the past two weeks.

b) FDR-adjusted P values were computed using the Benjamini-Hochberg procedure. *P* value was defined using a multivariate regression model controlling for age, sex, race, region, education level, income, employment status, health insurance status, presence of child in household, marital status, unmet medical care due to cost in the past year, and not seeing a health professional in office in the past two weeks.

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	2
Methods			
Study design	4	Present key elements of study design early in the paper	6-7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6-7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-7
6Bias	9	Describe any efforts to address potential sources of bias	6-7
Study size	10	Explain how the study size was arrived at	6-7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7
		(*b*) Describe any methods used to examine subgroups and interactions	7
		(*c*) Explain how missing data were addressed	7
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	7
		(*e*) Describe any sensitivity analyses	7
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8
		(b) Give reasons for non-participation at each stage	8
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8
		(b) Indicate number of participants with missing data for each variable of interest	8
Outcome data	15*	Report numbers of outcome events or summary measures	8-10
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	8-10

		(*b*) Report category boundaries when continuous variables were categorized	8-10
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9-10
Discussion			
Key results	18	Summarise key results with reference to study objectives	10-11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	12-13
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11-13
Generalisability	21	Discuss the generalisability (external validity) of the study results	12
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	14

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Self-reported health without clinically measurable benefits among adult users of multivitamin and multimineral supplements: a cross-sectional study

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Self-reported health without clinically measurable benefits among adult users of multivitamin and multimineral supplements: a cross-sectional study

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ABSTRACT

Objectives: Multiple clinical trials fail to identify clinically measurable health benefits of daily multivitamin and multi-mineral (MVM) consumption in the general adult population. Understanding the determinants of widespread use of MVMs may guide efforts to better educate the public about effective nutritional practices. The objective of this study was to compare self-reported and clinically measurable health outcomes among MVM users and non-users in a large, nationally representative sample of adult civilian non-institutionalized population of the US surveyed on the use of complementary health practices.

Design: Cross-sectional analysis of the effect of MVM consumption on self-reported overall health and clinically measurable health outcomes.

Participants: Adult MVM users and non-users from the 2012 National Health Interview Survey (n=21,603).

Primary and secondary outcome measures: Five psychological, physical, and functional health outcomes 1) self-rated health status, 2) needing help with routine needs, 3) history of 10 chronic diseases, 4) presence of 19 health conditions in the past 12 months, and 5) Kessler 6-Item (K6) Psychological Distress Scale to measure nonspecific psychological distress in the past month.

Results: Among 4,933 adult MVM users and 16,670 adult non-users, MVM users self-reported 30% better overall health than non-users (Adjusted OR: 1.31; 95% CI: 1.17-1.46 FDR-adjusted P<.001). There were no differences between MVM users and non-users in history of 10 chronic diseases, number of present health conditions, severity of current psychological distress on the K6 scale and rates of needing help with daily activities. No effect modification was observed after stratification by sex, education, and race.

***Conclusions*:** MVM users self-reported better overall health despite no apparent differences in clinically measurable health outcomes. These results suggest that widespread use multivitamins in adults may be a result of individuals' positive expectation that multivitamin use leads to better health outcomes or a self-selection bias in which MVM users intrinsically harbor more positive views regarding their health.

STRENGTHS AND LIMITATIONS OF THE STUDY

- This is the first study to link better self-reported health, absence of clinically measurable benefits, and multivitamin and multimineral supplement use in the same population
- Data are derived from a large, national survey across the US
- Results have broad implications for public health and the multibillion-dollar supplement industry
- Cross-sectional study design precludes the demonstration of a causal relationship between self-reported health and multivitamin and multimineral supplements
- Self-reported health can be inherently biased and confounding

INTRODUCTION

Consumption of multivitamins (MVs) and multi-minerals (MMs) (together: MVMs) as dietary supplements is widespread in the general US adult population, with some reports estimating 33% of Americans regularly take MVMs[1–4]. While MVM supplementation is warranted for some individuals at high-risk because of disease-related defiency[5], the consumption of non-prescription, over-the-counter MVMs has not produced robust evidence for the wide-ranging health benefits expected by the general adult population. Likewise, large randomized clinical trials that evaluate MVM at different doses, across both men and women at varied ages, have failed to demonstrate benefit in prevention of chronic diseases. The Physicians' Health Study II (PHS II), a randomized placebo-controlled clinical trial of low-dose daily MVM use in older male physicians, found no reduction in major CVD events, myocardial infarction, stroke, and CVD mortality[6], and these results were independent of baseline nutritional status[7]. A prospective cohort study of middle-aged and elderly women also indicated no effect of MVM use for the same CVD outcomes in PHS II[8]. The SU.VI.MAX Study, a clinical trial of antioxidative MVMs in adults, found no effect on incidence of ischemic CVD[9], and high-dose MVMs did not reduce CVD events[10]. Meta-analysis of these and other studies (N=18) found no improvement in CVD outcomes in the general population[11]. Based on these studies, the US Preventative Services Task Force does not recommend MVM use for the prevention of CVD[12,13].

Data on the effect of MVM consumption on cognitive function in adults are also inconclusive. While results from PHS II found that long-term use of daily MVs did not provide cognitive benefits in men[14], a meta-analysis on 10 studies concluded that MVs selectively enhanced free recall memory but no other cognitive functions[15]. Intriguingly, nine weeks of MVM use appears to improve multi-tasking and cognitive function during fatigue in women[16].

With regard to cancer, PHS II demonstrated moderately reduced all-cancer risk in men consuming MVs[17] while data from the Women's Health Initiative Clinical Trials revealed no association[18]. Some studies even link MVM use with increased cancer risk – a prospective cohort study of Swedish women found increased breast cancer risk associated with MVM use[19].

The association of MVM use with all-cause mortality, like CVD, is null. While data from the Multiethnic Cohort Study cohort study indicated no association between MVM use and all-cause mortality,[20] the Cancer Prevention Study (II) reported a five percent higher rate of all-cause death among men using MVs[21] and The Iowa Women's Health Study identified an association between MVM use and increased total mortality risk[22]. A meta-analysis of these and other randomized trials (N=21) demonstrated no effect of MVM use on mortality risk[23].

While numerous reports on MVM consumption establish the lack of broad-spectrum, clinically measurable health benefits, the determinants of widespread MVM use by the general population are not well understood. That the majority (52%) of MVM users report using MVMs in an effort to prevent disease is even more puzzling in light of the paucity of randomized and observation data showing a positive health benefit of MVMs[24]. Because nutritional supplements constitute a multibillion-dollar industry and can even be harmful when taken in excess[25], understanding the determinants of widespread MVM use has significant medical and financial consequences. Moreover, it is unclear whether MVM users, despite not being physiologically different from non-users, simply believe they are healthier. To address this question, we utilized data from the 2012 National Health Interview Survey[26] (NHIS), which included a complementary and alternative (CAM) questionnaire comprising of 21,603 participants across the US.

METHODS

Data source

All data was obtained from the 2012 The National Health Interview Survey (NHIS), a nationally representative health survey conducted annually among civilian and noninstitutionalized US participants by the Centers for Disease Control (CDC). All data was publicly available and did not require institutional review board approval. The 2012 NHIS was comprised of a core questionnaire on health information administered to each selected household member. A randomly selected adult in each household was administered a more detailed health survey which included questions on access to care, specific health conditions and use of CAM(2012 only). In 2012, 77.6% of households completed the survey and 79.7% of adults selected completed the detailed survey[26].

Health Status and Health Outcome Measures

We obtained data on adults (age ≥ 18 years) derived from the Sample Adult Component who also participated in the Adult CAM File. This file surveys use of alternative medicines and therapies including daily MVM consumption, yoga, and meditation. Consistent with previous NHIS studies[27], we considered five psychological, physical, and functional health outcomes from questions in the Sample Adult Component: 1) self-rated health status (poor/fair vs. excellent/very good/good), 2) needing help with routine needs such as eating (yes or no), 3) history of ten chronic diseases (cancer, hypertension, coronary heart disease, stroke, chronic obstructive pulmonary disease, asthma, diabetes, arthritis, hepatitis, and weak/failing kidneys), 4) presence of 19 health conditions in the past 12 months (digestive, skin, and other allergy, acid reflux, hay fever, chest cold, nausea and vomiting, sore threat, infectious disease, recurring headache, memory loss, neurological problems, sprains, and abdominal, dental, muscle/bone, chronic, and skin pain), and 5) Kessler 6-Item (K6) Psychological Distress Scale[28] score to measure nonspecific psychological distress in the past month. Participants who refused to answer or did not know the answers to at least one of these questions were excluded from the study. Participants were classified as MVM users or non-users from their response to the question "During the past 12 months, did take multi-vitamins or multi-minerals?" in the Adult CAM File. Participants who refused to answer or did not know their MVM use in the past 12 months were excluded from analyses.

Statistical Analysis

For each outcome, the relationship between MVM use in the past year and health outcome was estimated using a logistic regression model adjusting for age, sex, race, region, education, income, employment status, health insurance status, presence of child in household, marital status, unmet medical care due to cost in the past year, and not seeing a health professional in office in the past two weeks. Multinomial logistic regression was used for outcomes with more than two levels (e.g., number of chronic diseases, number of diseases in the past 12 months, Kessler-6 Item score). Binary logistic regression was used for outcomes with two levels (self-reported health and needing help with daily routines such as eating). Standard errors were estimated using weights provided by NHIS to account for the complex survey design and produce nationally representative estimates. A multiple imputation strategy was used to estimate income in cases of missing responses to income as recommended by the National Center for Health Statistics[29]. All analyses were conducted using R (v3.5.1). *P* values were adjusted for multiple comparisons using a Benjamini-Hochberg procedure with False Discovery Rate (FDR) <0.01 deemed significant.

Stratified analyses were conducted in age- (18-44 years, 45-64 years and 65+ years), race- (white and non-white), sex- (female and male), family income- (<100%, 100%-199%, 200%-299%, 300-399%, and 400% relative to the federal poverty level), education level- (did not graduate high school, high school graduate, college graduate or higher) stratified groups to assess the association between MVM use and self-reported health in sociodemographic subgroups. In addition to stratified analyses, statistical interaction effects between MVM use and demographic variable (age, race, sex, family income, and education) on self-reported health was assessed using a multivariate regression model.

Patients and Public Involvement

Patients and the public were not involved in this study, including data collection, analysis and interpretation.

RESULTS

Study Cohort Characteristics

Sociodemographic differences between MVM users and non-users are presented in Table 1. Our study included 4,933 MVM users and 16,670 non-users (Table 1). As previously reported in data from the 2007-2010 and 2010-2014 National Health and Nutrition Examination Surveys (NHANES)[30,31], compared to non-users, MVM users were significantly older, earned more income, more likely to be female, more likely to be a college graduate, more likely to be married, and more likely to have health insurance. Unlike in previous studies, compared to MVM non-users, MVM users were less likely to be unemployed, have a minor child in their household, and not have an office visit for healthcare in the past two weeks (Table 1). We observed no significant differences in percent of non-English speaking interviews and percent having foregone medical care due to cost in the past year between MVM users and non-users (Table 1).

Association between MVM usage and Health Status and Health Outcomes

Differences in health status and health outcomes between MVM users and non-users are displayed in Table 2. Multivariate regression revealed that MVM users self-reported 30% better overall health than non-users (OR: 1.31, 95% CI: 1.17-1.46, FDR-adjusted P<.001 ; Table 2). Strikingly, MVM users and non-users did not differ in history of 10 chronic disease (MVM users mean 1.09 conditions, 95% CI: 1.06-1.11 vs non-users mean: 1.07, 95% CI: 1.03-1.11) number of present health conditions (MVM users mean: 2.7 conditions, 95% CI: 2.7-2.8 vs non-users mean: 2.8, 95% CI: 2.7-2.9), severity of psychological distress on the K6 scale (MVM users mean K6 score = 2.3, 95% CI: 2.3-2.4 vs non-users mean = 2.5, 95% CI: 2.4-2.6), and needing help with daily activities (OR: 0.86, 95% CI: 0.71-1.04).

Stratified Analyses: Association between MVM Usage and Self-Reported Overall Health in Sociodemographic Subgroups

Table 3 reports the association between MVM usage and self-reported overall health in age, race, sex, income, and education-stratified subgroups (Table 3). MVM use was associated with better self-reported health in the 18-44-year (OR: 1.26, 95% CI: 1.00-1.61) and 45-64-year groups (OR: 1.30, 95% CI: 1.08-1.57) and near significant among respondents ≥ 65 years (OR: 1.20, 95% CI: 0.95-1.52, FDR *P* value = 0.06) (Table 3). MVM use was associated with better self-reported health amongst both white (OR: 1.34, 95% CI: 1.07-1.67) and non-white (OR: 1.26;

95% CI: 1.09-1.45) respondents (Table 3). MVM use was associated with better self-reported health in both male (OR: 1.33, 95% CI: 1.10-1.63) and female (OR: 1.22, 95% CI: 1.05-1.41) respondents (Table 3). Interestingly, MVM use was associated with better self-reported health in families with income < 100% of the federal poverty level (FPL) (OR: 1.42, 95% CI: 1.12-1.80), 100%-199% FPL (OR: 1.37, 95% CI: 1.10-1.69) and 200%-299% FPL (OR: 1.32, 95% CI: 1.01-1.72) but not in families whose income was 300%-399% FPL (OR: 1.32, 95% CI: 0.88-1.98) or ≥400% FPL (OR: 1.15, 95% CI: 0.85-1.56) (Table 3). MVM use was associated with better self-reported health in all education subgroups analyzed, including respondents that did not complete high school (OR: 1.38, 95% CI: 1.06-1.81), high school graduates (OR: 1.21, 95% CI: 1.04-1.41), and college graduates (OR: 1.37, 95% CI: 1.00-1.88) (Table 3). All stratified analyses were conducted after adjusting for the potential confounding effects of age, sex, race, region, education, income, employment status, health insurance status, presence of child in household, marital status, unmet medical care due to cost in the past year, and not seeing a health professional in office in the past two weeks. The variable of stratification was not included as a covariate.

Statistical interaction effects between MVM use and demographic variables (age, race, family income, and education) on self-reported overall health was assessed through a multivariate regression model in Table S1. We observed no significant association between MVM use and age, MVM use and race, MVM use and family income, and MVM use and education on self-reported overall income (Table S1).

DISCUSSION

This present study is the first to simultaneously analyze the association between MVM use and both self-reported health and clinical health outcomes. In this work, we found that MVM users self-report 30% better overall health than non-users despite no clinically assessed differences in health. Our finding that MVM users and non-users do not differ in various psychological, physical, and functional outcomes corroborates previous reports that MVMs do not improve overall health in the general adult population [5-22] . Our stratified analysis revealed that MVM use is associated with better self-reported overall health across all race, sex, and education groups, and in individuals under 65 and with family incomes below 300% FPL. The lack of association between MVM usage and self-reported health in individuals with family income greater than 300% FPL may be related to sample size and should be replicated in a follow up study. Taken together, these findings help elucidate explanations underlying widespread MVM usage despite no generalized clinical benefits.

The results here suggest two potential explanations underlying widespread MVM consumption in the absence of clinically measurable benefits: 1) MVM users believe in the efficacy of MVMs by harboring a positive expectation regarding the health benefits of MVMs and/or 2) MVM users intrinsically harbor a more positive outlook on their personal health regardless of MVM usage. A growing body of evidence suggests that positive expectation influence treatment outcomes for diseases including heart disease[32–35], cancer[36,37], musculoskeletal disorders[38,39], injuries[40,41], and obesity[42–44]. Under a positive expectation model, MVM users are more likely to harbor a positive expectation regarding the clinical efficacy of MVMs and thus more likely to self-report as having excellent or good overall health. In the case of MVM usage, it is interesting that the presence of positive expectation did not influence clinically measurable health outcomes, unlike in other treatments. The effect of positive expectations in the MVM user community is made even more stronger when one considers that the majority of MVM and supplements are sold to the so-called "worried-well" population[45] who may assign greater weight to the purported health benefits of dietary supplements and alternative therapies. It is possible that members of this population are more susceptible to positive expectations and may thereby continue to use MVMs in the absence of clinical benefits.

The second mechanism, in which MVM users intrinsically harbor greater positive views about their health, may be explained in part by certain combinations of sociodemographic determinants that influence self-reported health. While age, sex, income, education, and location of residence have been previously shown to affect self-reported health in diverse populations[46–48], combinations of other characteristics may also cause MVM users to harbor intrinsically more positive views regarding their health in the absence of clinical differences. Further research is necessary to elucidate these characteristics.

Our results are consistent with existing work from two studies: the first being a 2013 study involving 11,956 adults from the 2007-2010 NHANES that demonstrated MVM users exhibit better self-reported health than non-users[31], and second, a 2014 study involving 5536 Coast Guard and military study which found that MVM users were significantly more likely to self-report their general health as excellent or good[49]. While informative, these previous studies only focused on self-reported health as an outcome. In the present study, we considered self-reported health in addition to clinically measurable health outcomes. This is an important distinction in order to establish that MVM users experience better self-reported health in the absence of clinically measurable health improvement. Nevertheless, it is encouraging that our

results are consistent across the NHANES, military and Coast Guard and NHIS study cohorts, and robust to different statistical analysis methodologies.

Limitations of this study include the cross-sectional design, reliability of self-reported health within NHIS, income estimation using multiple imputation, indication bias and nonresponse bias. First, the cross-sectional study design prevents a demonstration of causal relationship between MVM use and self-reported health. The lack of longitudinal data available to assess changes in self-reported health before and after MVM supplementation prevents us from differentiating the two aforementioned explanations that may contribute to widespread MVM use. Second, self-reported health within the NHIS may inherently harbor reporting bias and residual confounding. In addition to reporting bias and residual confounding, a self-reported binary response to the question of whether one has taken MVMs in the past 12 months precludes any analysis of dose-dependent effects of MVMs in our cohort. This is especially important considering some vitamins and minerals have known U-shaped associations with disease in which disease risk is elevated at both high and low vitamin and mineral levels [50–53]. Further, use of both multivitamins and multiminerals were asked together as part of the same question in the NHIS questionnaire. This prevented us from analyzing multivitamin and multimineral effects in isolation. Moreover, different MVM preparations can differ in their nutritional composition, quality, and bioavailability. Some individuals may take multiple MVMs whose constituents could interact with each other. Because the brand of multivitamin being taken was not asked of MVM users in NHIS, we could not identify differences in nutritional composition, quality, bioavailability, and chemical interaction that may be driving the results in this study.

Third, despite being recommended by the NHIS[29], the multiple imputation technique used to calculate income in cases in which data was missing may generate estimation errors.

Another limitation to the income-stratified results for self-reported overall health may stem from the inability to factor income mobility. Interestingly, it has been previously demonstrated that while high incomes are associated with longer life expectancies, accounting for income mobility reduces the gap by approximately 50%[54].

A portion of our cohort may have been prescribed MVMs, specific vitamins or specific minerals for indications including micronutrient deficiency, pregnancy, iron deficiency anemia, osteoporosis, Crohn's disease and others, thereby contributing to indication bias[55–60]. Previous estimates have suggested approximately 1% of physician office visits in the United States include a prescription or recommendation for MVMs[61] . One can imagine a scenario in which MVM users and non-users are imbalanced in the proportion of medical cases that require MVM supplementation (ie. micronutrient deficiency or pregnancy). In such a scenario, it may falsely appear that MVM use is not associated with clinical benefits. In the present study, owing to a lack of information regarding the reason for taking MVMs, we were unable to fully account for indication bias present in our cohort.

In addition to indication bias, the NHIS, like other surveys, is known to suffer from nonresponse bias[62]. For example, a previous study found that the 1990-2009 NHIS population had an approximately 14% lower mortality than the general population[62]. Post-hoc methods to address nonresponse bias include creating sample weights based on demographic variables and selection probabilities, as was used in the present study. However, survey weighting, while a standard practice, may not fully account for nonresponse bias, especially if the survey weights do not take into account common differences between survey responders and non-responders such as smoking and alcohol use[63]. As a result, non-response bias may limit the generalizability of our results to the broader population.

Conclusions

Using nationally representative survey data on health outcomes, our study reveals that MVM users self-report better overall health than non-users despite not exhibiting improved health by clinically measurable standards. Furthermore, we identify specific sociodemographic subgroups of MVM users that are more prone to this behavior. The multibillion-dollar nature of the nutritional supplement industry makes understanding the determinants of widespread MVM use have significant medical and financial consequences. Our findings suggest that widespread use multivitamins in adults may be a result of individuals' positive expectation that multivitamin use leads to better health outcomes or a self-selection bias in which MVM users intrinsically harbor more positive views regarding their health.

CONTRIBUTORS

MDP and ACC conceived and designed the study. MDP extracted data from NHANES. MDP, ACC, IP, PQD, JKW, RO, NJR, AA, AH, CCL, VO, IU, ALN, BSG, KTH, DHM, and GNN analyzed the data. MDP, ACC, KTH, and DHM wrote the manuscript. MDP, ACC, KTH, DHM, GNN, and RSC critically revised the manuscript for important intellectual content. All authors commented and approved the manuscript.

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COMPETING INTERESTS

None declared.

PATIENT CONSENT

None required.

ETHICS APPROVAL

None required.

DATA SHARING

All data used in the study is publicly available from the National Health Interview Survey.

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Table 1: Characteristics of American Adults by Multivitamin and Multimineral Supplement (MVM) Usage

Characteristic	MVM non-users (n = 4933[a])	MVM users (n = 16670[a])	FDR-adjusted *P* value[b]
Weighted sample %	22.4 (21.8-23.0)	77.6 (76.9-78.0)	
Age, % (95% CI[c])			

Mean age in years (95% CI)	48.1 (47.4-48.7)	49.7 (49.3-50.2)	
18-27 years	14.9 (13.8-16.2)	13.1 (12.2-14.1)	
28-37 years	16.6 (15.4-18.0)	16.9 (16.2-17.7)	
38-47 years	17.4 (16.3-18.6)	15.3 (14.6-15.9)	<0.001
48-57 years	17.7 (16.4-19.0)	17.6 (16.9-18.3)	
58-67 years	14.3 (13.2-15.5)	15.4 (14.8-16.1)	
68-80 years	10.1 (9.2-11.1)	12.8 (12.1-13.5)	
≥ 80 years	5.9 (5.1-6.8)	6.2 (5.7-6.7)	
Race, % (95% CI[c])			
White only	82.2 (81.0-83.3)	82.9 (82.1-83.6)	
Black/African American only	11.4 (10.4-12.5)	10.4 (9.9-11.0)	
American Indian/ Alaskan Native only	1.1 (0.8-1.4)	0.6 (0.5-0.8)	<0.001
Asian only	3.5 (3.1-4.0)	4.3 (3.9-4.6)	
Multiple race	1.8 (1.5-2.2)	1.9 (1.6-2.1)	
% Female (95% CI[c])	54.1 (52.6-55.6)	59.1 (58.2-60.1)	<0.001
Family Income, relative to federal poverty level (95% CI[c])			
<100%	16.9 (15.3-18.4)	12.4 (11.5-13.3)	
100%-199%	19.7 (18.2-21.2)	17.9 (17.1-18.8)	
200%- 299%	17.3 (15.8-18.7)	17.0 (16.2-17.8)	<0.001
300%-399%	12.8 (11.4-14.2)	13.4 (12.6-14.1)	
400% +	33.4 (31.1-35.6)	39.4 (37.9-40.9)	
Education status, % (95% CI[c])			
Did not graduate high school	11.7 (10.7-12.8)	9.6 (9.0-10.1)	
Grade 12 or GED	26.6 (24.8-28.5)	22.4 (21.4-23.4)	
Some college, no degree	22.1 (20.5-23.8)	21.2 (20.1-22.4)	<0.001
Associates degree	10.8 (9.7-11.9)	12.0 (11.4-12.6)	
College graduate or higher	28.7 (26.7-30.7)	34.7 (33.3-36.2)	
Relationship status, % (95% CI[c])			
Married or living with partner	49.0 (46.4-51.7)	51.0 (49.4-52.7)	
Separated, divorced, or widowed	26.6 (25.0-28.3)	26.7 (25.6-27.8)	<0.001
Never married	24.3 (22.5-26.1)	22.3 (21.0-23.5)	
Employment status, % (95% CI[c])			
Employed	58.1 (55.2-60.9)	58.6 (56.7-60.5)	
Unemployed, looking for work	6.1 (5.2-7.0)	5.2 (4.8-5.6)	0.05
Not in labor force	35.8 (33.7-37.9)	36.2 (34.8-37.6)	
Minor child in household, % (95% CI[c])	30.4 (28.8-32.0)	26.5 (25.5-27.3)	<0.001

Non-English-speaking interview, % (95% CI[c])	3.6 (3.1-4.1)	3.5 (3.1-3.8)	0.66
Has health insurance, % (95% CI[c])	84.3 (83.1-85.4)	87.4 (86.9-88.0)	<0.001
No office visit for health care in the past two weeks, % (95% CI[c])	79.8 (78.6-81.0)	76.4 (75.7-77.1)	<0.001
Unmet medical care due to cost in the past year, % (95% CI[c])	9.4 (8.5-10.3)	8.7 (8.3-9.2)	0.19

a. Unweighted sample size

b. FDR-adjusted P value was computed using the Benjamini-Hochberg procedure. P values were computed using a two-sample t-test or chi-square test for independence.

c. All confidence intervals were computed based on a Rao-Scott-scaled chi-squared distribution for the loglikelihood from a binomial distribution using the Survey package in R.

Table 2. Association between MVM Usage and Health Status

Characteristic	MVM non-users	MVM users	Adjusted Effect of MVM usage, β or OR (95% CI)[a]	FDR-adjusted *P* value[e]
Self-rated overall health as excellent, very good or good, % (95% CI[f])	84.9 (83.8-86.0)	88.3 (87.7-88.9)	OR=1.3 (1.2-1.5)	<0.001
Needs help with ADLs, % (95% CI[f])	5.6 (4.8-6.3)	4.8 (4.4-5.2)	OR = 0.86 (0.7-1.04)	0.07
History of chronic conditions, % (95% CI[f])				
Mean number of chronic conditions	1.07 (1.03-1.11)	1.09 (1.06-1.11)	β = 0.03 (-0.07-0.007)	0.07
No chronic conditions	44.4 (42.0-46.8)	43.0 (41.4-44.5)		
1 chronic condition	26.3 (24.5-28.2)	26.4 (25.4-27.5)		
Multiple chronic conditions	28.4 (26.7-30.0)	29.7 (28.6-30.7)		
Health conditions in past year[d] (95% CI[f])				
Mean number of present conditions	2.8 (2.7-2.9)	2.7 (2.7-2.8)	β=-0.06 (-0.2-0.02)	0.08
0-5 present conditions	84.7 (81.3-88.1)	85.2 (83.0-87.6)		
6-10 present conditions	12.7 (11.6-13.8)	12.4 (11.7-13.0)		
≥10 present conditions	1.5 (1.1-1.9)	1.4 (1.2-1.6)		
Kessler 6-item score, % (95% CI[f])				
Mean Kessler score	2.5 (2.4 -2.6)	2.3 (2.3-2.4)	β=-0.08 (-0.2–0.04)	0.13
No impairment	80.9 (77.4-84.4)	82.3 (80.0-84.6)		
Moderate Impairment	15.4 (14.2-16.6)	14.8 (14.1-15.5)		
Severe Impairment	3.7 (3.1-4.2)	2.9 (2.6-3.2)		

a) Estimates were produced after adjusting for age, sex, race, region, education level, income, employment status, health insurance status, presence of child in household,

marital status, unmet medical care due to cost in the past year, and not seeing a health professional in office in the past two weeks

b) *P* value was defined using a multivariate regression model controlling for age, sex, race, region, education level, income, employment status, health insurance status, presence of child in household, marital status, unmet medical care due to cost in the past year, and not seeing a health professional in office in the past two weeks

c) Ten chronic diseases included: cancer, hypertension, coronary heart disease, stroke, chronic obstructive pulmonary disease, asthma, diabetes, arthritis, hepatitis, and weak/failing kidneys

d) 19 health conditions in the past 12 months included: respiratory, digestive, skin, and other allergy, acid reflux, hay fever, chest cold, nausea and vomiting, sore threat, infectious disease, recurring headache, memory loss, neurological problems, sprains, and abdominal, dental, muscle/bone, chronic, and skin pain

e) FDR-adjusted P values were computed using the Benjamini-Hochberg procedure

f) All confidence intervals were computed based on a Rao-Scott-scaled chi-squared distribution for the loglikelihood from a binomial distribution using the Survey package in R.

Table 3: Association Between MVM Usage and Self-Reported Overall Health in Sociodemographic Subgroups

Group	Self-rated overall health as excellent, very good or good, % (95% CI[a]), MVM Non-Users	Self-rated overall health as excellent, very good or good, % (95% CI[a]), MVM Users	Adjusted Effect of MVM usage on self-reported health, OR (95% CI[a])[b]	FDR Adjusted *P* value[c]
Age				
18-44 years	92.3 (91.1-93.5)	94.2 (93.6-94.8)	1.3 (1.0-1.6)	0.03
45-64 years	79.9 (77.8-82.1)	85.3 (84.2-86.4)	1.3 (1.1-1.6)	0.009
65+ years	77.2 (73.8-80.5)	82.0 (80.6-83.4)	1.2 (1.0-1.5)	0.06
Race				
White	85.9 (84.7-87.2)	89.1 (88.5-89.7)	1.3 (1.1-1.7)	0.009
Non-white	80.0 (77.2-82.7)	84.2 (82.8-85.6)	1.3 (1.1-1.5)	0.007
Sex				
Female	84.0 (82.5-85.4)	88.1 (87.4-88.9)	1.2 (1.1-1.4)	0.009
Male	85.9 (84.2-87.7)	88.4 (87.5-89.3)	1.3 (1.1-1.6)	0.009
Family Income, relative to federal poverty level (95% CI)				
<100%	71.7 (68.0-75.4)	75.6 (73.1-78.1)	1.4 (1.1-1.8)	0.007
100%-199%	76.4 (73.6-79.2)	80.7 (79.0-82.4)	1.4 (1.1-1.7)	0.007
200%- 299%	84.8 (82.1-87.5)	87.3 (85.9-88.6)	1.3 (1.0-1.7)	0.04
300%-399%	89.6 (86.4-92.7)	91.0 (89.6-92.4)	1.3 (0.9-2.0)	0.15
400% +	94.8 (93.5-96.1)	95.2 (94.6-95.8)	1.1 (0.8-1.6)	0.23
Education				
Did not graduate high school	67.2 (63.1-71.3)	71.9 (69.7-74.2)	1.4 (1.1-1.9)	0.01

High school graduate	84.1 (82.6-85.5)	86.7 (85.9-87.4)	1.2 (1.0-1.4)	0.01
College graduate or higher	93.8 (92.4-95.1)	95.3 (94.7-95.9)	1.4 (1.0-1.9)	0.03

a) All confidence intervals were computed based on a Rao-Scott-scaled chi-squared distribution for the loglikelihood from a binomial distribution using the Survey package in R.

b) Estimates were produced after adjusting for age, sex, race, region, education level, income, employment status, health insurance status, presence of child in household, marital status, unmet medical care due to cost in the past year, and not seeing a health professional in office in the past two weeks.

c) FDR-adjusted P values were computed using the Benjamini-Hochberg procedure. *P* value was defined using a multivariate regression model controlling for age, sex, race, region, education level, income, employment status, health insurance status, presence of child in household, marital status, unmet medical care due to cost in the past year, and not seeing a health professional in office in the past two weeks.

Supplement for:

Self-reported health without clinically measurable benefits among adult users of multivitamin and multimineral supplements: a cross-sectional study

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Tables:

Table S1: Interaction between demographic variable and MVM use on self-reported health

Table S1: Interaction between demographic variable and MVM use on self-reported health

Demographic Variable	MVM use:demographic variable interaction on self-reported overall health, $\beta_{\text{Interaction}}$ (95% CI)[a]	FDR Adjusted *P* value[b]
Age (18-44 years, 45-64 years, 65+ years)	1.1 (0.9-1.2)	0.50
Race (White or non-white)	1.0 (0.9-1.1)	0.50
Sex	1.0 (0.8-1.3)	0.50
Family Income, relative to federal poverty level (<100%, 100-199%, 200-299%, 300-399%, 400%+)	1.0 (0.9-1.1)	0.50
Education (Did not graduate high school, high school graduate, , college graduate)	1.0 (1.0-1.1)	0.50

a) Estimates were produced after adjusting for age, sex, race, region, education level, income, employment status, health insurance status, presence of child in household, marital status, unmet medical care due to cost in the past year, and not seeing a health professional in office in the past two weeks.

b) FDR-adjusted P values were computed using the Benjamini-Hochberg procedure. *P* value was defined using a multivariate regression model controlling for age, sex, race, region, education level, income, employment status, health insurance status, presence of child in household, marital status, unmet medical care due to cost in the past year, and not seeing a health professional in office in the past two weeks.

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	2
Methods			
Study design	4	Present key elements of study design early in the paper	6-7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6-7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-7
6Bias	9	Describe any efforts to address potential sources of bias	6-7
Study size	10	Explain how the study size was arrived at	6-7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7
		(*b*) Describe any methods used to examine subgroups and interactions	7
		(*c*) Explain how missing data were addressed	7
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	7
		(*e*) Describe any sensitivity analyses	7
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8
		(b) Give reasons for non-participation at each stage	8
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8
		(b) Indicate number of participants with missing data for each variable of interest	8
Outcome data	15*	Report numbers of outcome events or summary measures	8-10
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	8-10

		(*b*) Report category boundaries when continuous variables were categorized	8-10
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9-10
Discussion			
Key results	18	Summarise key results with reference to study objectives	10-11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	12-13
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11-13
Generalisability	21	Discuss the generalisability (external validity) of the study results	12
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	14

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.