RESEARCH
Research Paper

Dietary Supplement and Prescription Medication Use Among US Military Service Members With Clinically Diagnosed Medical Conditions: The US Military Dietary Supplement Use Study

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ABSTRACT

Background Use of prescription medications (PMs) with dietary supplements (DSs) can be hazardous because of potential adverse interactions, but patterns of dual use in military service members (SMs) has not been examined.

Objective Investigate dual use of filled PMs (FPMs) and DSs, factors associated with dual use, and dual use among SMs with clinically diagnosed medical conditions (CDMCs).

Design Cross-sectional. Data on FPMs and CDMCs were obtained from medical surveillance records. Between December 2018 and August 2019, participants completed a questionnaire on DS use in the previous 6 months.

Participants A stratified random sample of 26,880 SMs from all military services.

Main outcome measures Prevalence of dual use of FPMs with DSs within a 6-month period, demographic/lifestyle factors associated with dual use, and prevalence of dual use among SMs with CDMCs.

Statistical analysis Prevalences were calculated as percents, χ^2 statistics examined differences across various strata of demographic and lifestyle characteristics, and univariable and multivariable logistic regression determined the odds of using FPMs with DSs for various CDMCs.

Results About one-half (49%) of SMs had dual use of FPMs with DSs in the 6-month period. Dual use was higher among women; increased with older age, more formal education, higher body mass index, and more physical activity; was highest among American Indian SMs and lowest among Asian SMs; was higher among former tobacco users; and was highest among Army personnel and lowest among Marine Corps personnel. The overall prevalence of dual use in the 6-month period was higher among those with a CDMC than those without (62% vs 19%), and this relationship was maintained for 20 International Classification of Diseases, Revision 10, code groupings covering virtually all CDMCs.

Conclusion This is the first study to document a high prevalence of dual FPMs and DSs in SMs, especially among those with CDMCs.
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DIETARY SUPPLEMENTS (DSS) ARE COMMERCIALLY available products consumed as an addition to the usual diet and include vitamins, minerals, amino acids, herbs (botanicals), and a variety of other products.[1] More than half of adults in the United States (US)[2,3] and more than 70% of military service members (SMs)[4-6] use DSs. DS use appears to be increasing over time among SMs,[7] although use has been more stable among civilians, at least between 1999 and 2012.[8] Importantly, SMs are more likely than civilians to use weight loss and pre-/postworkout supplements that contain multiple compounds with potential or documented adverse effects.[4,9]

Some DSs are potentially hazardous and combining prescription medications (PMs) with some DSs can be dangerous. Studies have estimated that among patients taking both DSs and PMs, 12% to 20% had potential drug-supplement interactions.[10-13] Interactions can occur when a DS or compound in the DS competes with a PM through mechanisms

involving absorption, distribution, metabolism, or excretion resulting in a change in the drug's concentration at the site of action. Alternately, the DS or compound within may have a direct effect on the PM and antagonize or exacerbate clinical effects.[14]

Although some evidence is available on use of PMs with DSs in the general population,[15-18] we are not aware of any study that has examined dual use among US military SMs. In addition, studies of the civilian population examining use of PMs with DSs among those with medical conditions have used self-reports of these conditions, not actual clinical records where conditions are diagnosed by medical care providers. The purposes of the current study were to: (1) investigate the prevalence of dual use of PMs with DSs in a 6-month period; (2) explore factors associated with dual use; and (3) compare the prevalence of dual use among SMs with and without clinically diagnosed medical conditions (CDMCs).

RESEARCH SNAPSHOT

Research Question: What is the prevalence of use of prescription medications (PMs) with dietary supplements (DSs)? What demographic and lifestyle factors are associated with dual use among US military service members (SMs)? How prevalent is PM and DS use among SMs with clinically diagnosed medical conditions (CDMCs)?

Key Findings: About 49% of SMs used PMs with DSs in a 6-month period. Dual use was higher among women; increased with older age, more formal education, higher body mass index, and more physical activity; was highest among American Indian SMs and lowest among Asian SMs; was higher among former tobacco users; and was highest among Army personnel. Dual use was higher among those with a CDMC than those without (62% vs 19%).

MATERIALS AND METHODS

This cross-sectional investigation involved a web-based survey of DS use that investigators combined with electronic medical and pharmacy records of US military SMs. It was part of a larger study designed to investigate the effects of DSs on SM health.[7,19] The Naval Health Research Center's institutional review board approved the investigation, and SMs electronically consented to participate by signing an informed consent document. Investigators adhered to policies and procedures for protection of human subjects as prescribed by Department of Defense Instruction 3216.01, and the research was conducted in adherence with provisions of 32 Code of Federal Regulations Part 219.

Sampling Frame and Solicitation Procedures

Details of the sampling frame, solicitation of SMs, participant recruitment flowchart, sample size determination, and response bias have been previously reported.[7] Briefly, investigators requested from the Defense Manpower Data Center a random sample of 200,000 SMs stratified by gender (88% male and 12% female) and branch of service (Army 36%, Air Force 24%, Marines 15%, and Navy 25%). Recruitment of SMs in this random sample involved a maximum of eight sequential contacts. The prospective participant was first sent an introductory postal letter with a $1 pre-incentive designed to increase the response rate.[20,21] The letter also included a description of the survey, a link to a secure website, and a unique number that could be used to access the survey and electronically sign the consent form. A follow-up e-mail message after 10 days and postcard after 3 weeks were sent as a reminder to those who did not initially complete the survey. If no response was received after sending the postcard, up to five additional e-mail reminders were sent over 8 months, after which contact with the SM ended. All postal and online contacts stated that at any time the SM could decline participation and be removed from the contact list. Recruitment began in December 2018 and no further recruitment was conducted or surveys accepted after August 2019.

Survey Description

The online survey used a standardized, web-based procedure to obtain the type and frequency of DS use and characterize participants. Supplement use questions included 96 generic DSs (eg, multivitamins/multiminerals, individual vitamins and minerals, proteins/amino acids, herbal products) and 67 brand-name products. The brand-name products included some that were included in previous armed forces DS surveys,[4,6,22,23] but were updated based on recent data on DSs sold in the Army, Marine Corps, and Air Force Exchange Systems and General Nutrition Center stores on or near military installations. There were also open text fields on the questionnaire where SMs could include supplements not on the provided lists. SMs were asked to estimate how frequently they consumed particular DSs in the past 6 months (never, once a month, once a week, 2-6 times per week, or daily). The Figure provides DS category definitions used in this study. To characterize participants, the survey included questions on demographics (gender, age, ethnicity, race, height, weight), lifestyle factors (cigarette smoking, smokeless tobacco use, physical activity), and military service branch (Air Force, Army, Marine Corps, Navy). Race and ethnicity were categorized according to the National Institute of Health classifications.[24]

Medical and Pharmacy Data

Once participants were identified by completing the informed consent and survey, the list of participants was sent to the Armed Forces Health Surveillance Branch of the Defense Health Agency. From the Defense Medical Surveillance System relational database,[25,26] the Defense Health Agency returned medical encounters and filled PMs (FPMs) of the consenting participants for the 6-month period prior to survey completion. Medical data consisted of International Classification of Diseases, Revision 10 (ICD-10), Clinical Modification codes.[27] The medical data included CDMCs (ICD-10 codes) occurring within military treatment facilities (ie, Standard Ambulatory Data Record, Standard Inpatient Data Record, and Comprehensive Ambulatory/Professional Encounter Record), as well as those occurring outside these facilities (civilian care) and paid for by the US Department of Defense (reimbursable) (ie, Tricare Encounter Data—

Category	Definition
Dietary supplement	Any substance defined by the DSHEA[a]
Multivitamin/multimineral	DS[b] containing 2 or more vitamins and/or 2 or more minerals with no additional supplement ingredients
Protein or amino acid	Amino acid mixtures, protein powders, and similar products where the intent is to provide a single or complex protein source
Individual vitamin or mineral	DS[b] that is a single vitamin or mineral supplement, such as vitamin D or calcium
Herbal supplement	DS[b] that includes 1 or more herbal ingredients with no nutrient or other supplement ingredient; also includes plant-derived ingredients
Purported prohormone	Steroidal hormone or herbal substitute for hormones marketed as a DS and included in the Supplement Facts panel on the label
Combination product	DS[b] with mixtures of ingredients from any of the above categories including two or more categories and multiple ingredients; includes products marketed as weight loss, pre- or postworkout supplements, and muscle/body-building products
Joint health product	Substance that purports to improve the functioning of body joints such as glucosamine (with or without chondroitin) or methylsulfonylmethane
Other dietary supplement	Other DS[b] that do not fit into the categories above

Figure. Dietary supplement categories and category definitions in the us military dietary supplement study. [a]DSHEA = Dietary Supplement Health and Education Act; [b]DS = dietary supplement.

Institutional and Tricare Encounter Data—Non-Institutional). Pharmacy data within the 6-month surveillance period were provided by the Defense Health Agency from the Pharmacy Data Transaction Service as American Hospital Formulary Service codes.[28] This included prescriptions filled at military medical treatment facilities, retail pharmacies in the United States, or through mail-order programs.

Statistical Analysis

All statistical analyses were conducted using the Statistical Package for the Social Sciences.[29] Body mass index (BMI) was computed from the questionnaire responses as weight/height^2 (kg/m^2). Weekly duration of aerobic and resistance training (minimum per week) was calculated by multiplying reported weekly exercise frequency (sessions per week) by the reported duration of training (minutes per session). Supplements that SMs recorded as "other" were individually examined and placed into their appropriate categories.

Prevalences (as a percent) with standard errors were calculated for dual use of FPMs and DSs within the 6-month period. We used χ^2 statistics to examine differences across various strata of demographic factors, lifestyle characteristics, and military services. A baseline stratum of each variable was defined with a prevalence ratio = 1.00 and other strata of that variable were compared with the baseline stratum. Effect sizes for χ^2 were calculated as $\sqrt{(\chi^2/n)}$, where χ^2 is the chi-square statistic and n the sample size. Small, medium, and large effect sizes were defined as 0.10, 0.25, and 0.40, respectively.[30]

CDMCs were categorized by 20 code groups representing ICD-10 codes from A00 though Y99[27] (eg, infections/parasitic diseases [ICD-10 codes A00-B99], neoplasms [ICD-10 codes C00-D49], disease of blood and blood forming organs [ICD-10 codes D50-D89]). Within each code group, prevalences (%) with standard errors were calculated for DS use, FPMs, and dual DSs and FPMs within the 6-month period. Univariable and multivariable logistic regression determined the odds of dual use within each CDMC code group. Univariable logistic regression included only the presence or absence of the code group (dependent variable); multivariable analysis adjusted for the presence or absence of the code group (dependent variable) by all demographic and lifestyle factors (independent variables).

The prevalence of CDMCs by FPMs and DSs (Figure) categories was also calculated. FPMs were arranged into the first tier American Hospital Formulary Service code groupings (eg, antihistamines, anti-infectives, autonomic drugs) covering most drugs used by SMs in this cohort. American Hospital Formulary Service code groups that included FPMs with fewer than 100 SMs were not included. These codes were antineoplastics (code 10, n = 67), diagnostic agents (code 36, n = 80), local anesthetics (code 68, n = 2), oxytocics (code 76, n = 19), devices (code 94, n = 2), and pharmaceutical agents (code 96, n = 69). We used χ^2 statistics to compare (1) the risk of a CDMC within each DS category (Figure) with any FPM and (2) the risk of a CDMC within each FPM category with use of any DS.

RESULTS

From the sample of 200,000 SMs, 73% (n = 146,365) were successfully contacted (ie, no returned postal mail), and of these, 26,680 (18.2%) signed the informed consent and completed the survey. The mean ± standard deviation age of the participants was 33 ± 8 years.

Table 1 displays the participant characteristics (demographic and lifestyle factors) and the prevalence of dual FPM and DS use. In the 6-month survey period, almost half (49%) of SMs had dual use. Women were more likely than men to have dual use. Prevalence of dual use increased with older age, more formal education, higher BMI, and more aerobic or resistance exercise training. Dual use prevalence did not differ by ethnicity, but was highest among American Indian SMs and lowest among Asian SMs. Dual use prevalence was similar among smokers/smokeless tobacco users and those who had never been a smoker/smokeless tobacco user, but higher among those who had quit either type of tobacco. Prevalence of dual use was highest among Army personnel and lowest among Marine Corps personnel. Those

Table 1. Dietary supplement use and filled prescription medications by demographic and lifestyle factors in representative cohort of military service members in the US Military Dietary Supplement Use Study

			Dietary Supplement and Prescription Medication Use in 6-mo Period	
Variable	Strata	Sample size, n (%)	Prevalence (% ± SE[a])	Prevalence ratio (95% CI[b])
All SMs[c]	None	26,680 (100.0)	49.1 ± 0.3	—
Gender	Men	23,037 (86.4)	46.1 ± 0.3	1.00
	Women	3641 (13.6)	67.7 ± 0.8	1.47 (1.43-1.51)
Age	18-24 y	4660 (17.6)	40.3 ± 0.7	1.00
	25-29 y	5580 (21.0)	45.5 ± 0.7	1.13 (1.08-1.18)
	30-39 y	11,030 (41.6)	50.3 ± 0.5	1.25 (1.20-1.30)
	≥40 y	5275 (19.9)	57.7 ± 0.7	1.43 (1.37-1.49)
Formal education	Some high school/high school graduate	3879 (14.5)	38.7 ± 0.8	1.00
	Some college	11,378 (42.7)	50.2 ± 0.5	1.30 (1.24-1.36)
	Bachelor's/graduate degree	11,417 (42.8)	51.5 ± 0.5	1.33 (1.27-1.39)
Ethnicity	Not Hispanic or Latino	22,452 (84.1)	48.9 ± 0.3	1.00
	Hispanic or Latino	4227 (15.8)	49.8 ± 0.8	1.02 (0.99-1.05)
Race	American Indian	228 (0.9)	54.4 ± 3.3	1.12 (0.99-1.26)
	Asian	1340 (5.0)	45.2 ± 1.4	0.93 (0.87-0.99)
	Black	3237 (12.1)	51.2 ± 0.9	1.05 (1.01-1.09)
	Hawaiian	163 (0.6)	46.0 ± 3.9	0.94 (0.80-1.12)
	More than 1 race	1559 (5.8)	51.2 ± 1.3	1.05 (0.99-1.11)
	Other	937 (3.5)	49.7 ± 1.6	1.02 (0.96-1.09)
	White	19,216 (72.0)	48.7 ± 0.4	1.00
Body mass index[d]	<25.0	7857 (30.0)	44.6 ± 0.6	1.00
	25.0-29.9	13,897 (53.1)	49.3 ± 0.4	1.11 (1.07-1.14)
	≥30.0	4424 (16.9)	56.7 ± 0.7	1.27 (1.23-1.32)
Smoking	Never smoked	16,706 (64.3)	48.2 ± 0.4	1.00
	Smoked but quit	4767 (18.3)	53.7 ± 0.7	1.11 (1.08-1.15)
	Smoker	4511 (17.4)	48.1 ± 0.7	1.00 (0.96-1.03)
Smokeless tobacco	Never used	20,378 (87.9)	48.7 ± 0.4	1.00
	Used but quit	2047 (8.8)	53.0 ± 1.1	1.09 (1.04-1.14)
	User	756 (3.3)	49.2 ± 0.9	1.01(0.97-1.05)
Aerobic exercise	≤90 min/wk	7286 (27.3)	46.4 ± 0.6	1.00
	91-180 min/wk	7285 (27.3)	48.5 ± 0.6	1.04 (1.01-1.08)
	181-300 min/wk	5869 (22.0)	50.0 ± 0.7	1.08 (1.04-1.12)
	>300 min/wk	6240 (23.4)	52.0 ± 0.6	1.12 (1.08-1.16)
Resistance exercise	<45 min/wk	7776 (29.1)	44.3 ± 0.6	1.00
	46-135 min/wk	6257 (23.5)	47.5 ± 0.6	1.07 (1.03-1.11)
	136-300 min/wk	6581 (24.7)	51.6 ± 0.6	1.17 (1.13-1.21)
	>300 min/wk	6066 (22.7)	54.0 ± 0.6	1.22 (1.18-1.26)
Service branch	Air Force	9788 (36.7)	48.6 ± 0.5	1.00
	Army	7935 (29.7)	53.6 ± 0.6	1.10 (1.07-1.14)
	Marine Corps	3194 (12.0)	42.4 ± 0.9	0.87 (0.83-0.91)
	Navy	5763 (21.6)	47.4 ± 0.7	0.98 (0.94-1.01)

[a]SE = standard error.
[b]CI = confidence interval.
[c]SMs = service members.
[d]Body mass index calculated as kg/m^2. Categories as defined by Center for Disease Control and Prevention.[48]

Table 2. Prevalence of dietary supplement use, filled prescription medications, and dual use in representative cohort of military service members in the US Military Dietary Supplement Use Study (n = 26,680)

CDMC[a] (ICD-10[b] code group)	Cases (n)	Prevalence of dietary supplement use (% ± SE[c])	Prevalence of filled prescription medications (% ± SE)	Filled Prescription Medication and Dietary Supplement Use in a 6-mo Period		
				Prevalence (% ± SE)	Logistic Regression Odds Ratio (95% CI[d])[e] Unadjusted (univariable)	Logistic Regression Odds Ratio (95% CI[d])[e] Adjusted for demographics and lifestyle factors (multivariable)
Any ICD-10 code (A00-Y99)	18,775	74.8 ± 0.3	71.7 ± 0.3	61.8 ± 0.4	6.92 (6.50-7.38)	6.72 (6.28-7.19)
Infectious/parasitic diseases (A00-B99)	1870	75.7 ± 1.0	94.1 ± 0.5	71.1 ± 1.0	2.73 (2.47-3.03)	2.70 (2.42-3.02)
Neoplasms (C00-D49)	1069	75.6 ± 1.3	84.5 ± 1.1	64.1 ± 1.5	1.90 (1.67-2.16)	1.61 (1.40-1.84)
Diseases of blood and blood organs (D50-D89)	261	78.9 ± 2.5	90.8 ± 1.8	72.0 ± 2.8	2.70 (2.06-3.54)	2.46 (1.81-3.33)
Endocrine, nutritional and metabolic diseases (E00-E89)	2427	78.1 ± 0.8	91.5 ± 0.6	72.0 ± 0.9	2.92 (2.67-3.21)	2.45 (2.22-2.71)
Mental, behavioral diseases (F01-F99)	3364	78.1 ± 0.7	92.9 ± 0.4	72.9 ± 0.8	3.20 (2.95-3.47)	2.95 (2.70-3.21)
Diseases of nervous system (G00-G99)	3976	76.6 ± 0.7	91.4 ± 0.4	70.2 ± 0.7	2.84 (2.64-3.06)	2.50 (2.30-2.70)
Diseases of eye and adnexa (H00-H59)	4578	74.7 ± 0.6	78.9 ± 0.6	59.0 ± 0.7	1.69 (1.58-1.80)	1.61 (1.50-1.73)
Diseases of ear and mastoid process (H60-H95)	1364	74.7 ± 1.2	86.9 ± 0.9	66.5 ± 1.3	2.14 (1.91-2.42)	2.01 (1.78-2.27)
Diseases of circulatory system (I00-I99)	1395	74.6 ± 1.2	94.8 ± 0.6	70.8 ± 1.2	2.64 (2.35-2.98)	2.30 (2.02-2.61)
Diseases of respiratory system (J00-J99)	4308	76.3 ± 0.6	96.1 ± 0.3	73.6 ± 0.7	3.51 (3.26-3.77)	3.47 (3.21-3.76)
Diseases of digestive system (K00-K95)	1817	76.4 ± 1.0	95.3 ± 0.5	72.8 ± 1.0	2.98 (2.68-3.32)	2.77 (2.48-3.11)
Diseases of skin and subcutaneous tissue (L00-L99)	2834	75.3 ± 0.8	90.1 ± 0.6	67.9 ± 0.9	2.40 (2.21-2.60)	2.29 (2.10-2.50)
Diseases of musculoskeletal system (M00-M99)	9688	76.6 ± 0.4	86.5 ± 0.3	66.5 ± 0.5	3.09 (2.93-3.26)	2.88 (2.72-3.04)
Diseases of genitourinary system (N00-N99)	1778	77.3 ± 1.0	93.3 ± 0.6	72.6 ± 1.1	2.92 (2.62-3.25)	2.19 (1.95-2.46)
Pregnancy-related conditions (O00-O9A)	250	88.0 ± 2.1	95.2 ± 1.4	83.6 ± 2.3	5.36 (3.83-7.50)	3.02 (2.10-4.34)
Congenital abnormalities (Q00-Q99)	216	75.8 ± 2.9	89.1 ± 2.1	67.0 ± 3.2	2.13 (1.66-2.73)	1.86 (1.44-2.42)
Signs, symptoms, abnormal labs NOS[f] (R00-R99)	9132	76.1 ± 0.8	91.2 ± 0.3	69.5 ± 0.5	3.66 (3.47-3.86)	3.45 (3.26-3.66)
Injury and poisoning (S00-T88)	2795	75.5 ± 0.8	88.4 ± 0.6	67.0 ± 0.9	2.29 (2.11-2.49)	2.26 (2.10-2.47)
External causes of morbidity (V00-Y99)	1403	74.9 ± 1.2	88.5 ± 0.9	66.5 ± 1.3	2.14 (1.91-2.40)	2.16 (1.91-2.44)

[a]CDMC = clinically diagnosed medical condition.
[b]ICD-10 = International Classification of Diseases, Revision 1.0.[27]
[c]SE = standard error.
[d]CI = confidence interval.
[e]Odds of filled prescription medications with dietary supplement use.
[f]NOS = not otherwise specified.

who had quit smoking had a higher incidence of CDMCs than those who had never smoked (73.6% vs 70.4, $P < .01$).

Table 2 shows the prevalence of DS use, FPM, and dual use in the 6-month period by CDMC code groups. Among those with CDMCs of any type (codes A00 through Y99), 75% were DS users, 72% had an FPM, and 62% had dual use. DS use was highest among SMs diagnosed with a pregnancy-related condition; however, for other CDMCs DS use was similar, ranging from 75% to 79% of the sample. Prevalence of FPMs ranged from 79% (diseases of the eyes and adnexa) to 95% (pregnancy-related conditions) within the different CDMC code groups. The prevalence of dual use of DSs and FPMs within CDMC code groups ranged from 59% (diseases of the eyes and adnexa) to 84% (pregnancy-related conditions). The odds of dual DSs and FPM use in the 6-month period was significant within all CDMC code groups in both univariable (unadjusted) and multivariable (adjusted) models.

Table 3 compares the risk of a CDMC by the DS categories in the Figure with any FPMs. The risk of a CDMC was higher for all DS categories with any FPM: risk was 3.08 to 3.73 times higher if the SM reported use in a particular DS category and had an FPM. Table 4 compares the risk of a CDMC by different categories of FPMs and use of any DS. The risk of a CDMC was higher for all FPM categories with any DS use: risk was 2.87 to 90.91 times higher if the SM had an FPM with any DS use.

DISCUSSION

The present study involving a large sample of SMs (>26,000) found that 49% of those with FPMs were also DS users within the 6-month surveillance period. Dual use was higher among women; increased with older age, more formal education, higher BMI, and more physical activity; was highest among American Indian SMs and lowest among Asian SMs; and was higher among former tobacco users. Army personnel had the highest prevalence of dual use and the Marine Corps the lowest. Dual use was over 3 times higher among those with a CDMC compared with those without (62% vs 19%). When 20 individual ICD-10 code groupings were examined, dual use was higher in each one, even after controlling for age, gender, education, BMI, tobacco use, physical activity, and military service.

Prevalence of FPMs and Concomitant FPM and DS Use

Comparisons between the current study and others examining DS and PM use is complicated by methodology, the nature of the sample, how DSs are defined, and possible changes over time in both DS and PM use. In the current study, with an average 33-year-old sample, dual use prevalence in a 6-month period was 49%. Studies involving nationally representative samples from over 20 years before reported that 18%[15] and 16%[16] of participants concomitantly

Table 3. Prevalence of a clinically diagnosed medical conditions by dietary supplement use category with any filled medical prescription in a representative cohort of military service members in the US Military Dietary Supplement Use Study (n = 26,680)

Dietary supplement category and any filled medical prescription (n)	CDMC[a]	Prevalence (% ± SE[b])	Prevalence ratio, CDMC/no CDMC (95% CI[c])	Effect size
Any dietary supplement use and filled medical prescription (n = 13,093)	Yes	61.8 ± 0.4	3.27 (3.12-3.42)	0.39
	No	18.9 ± 0.4		
Multivitamin/multimineral use and filled medical prescription (n = 8121)	Yes	38.6 ± 0.4	3.48 (3.27-3.71)	0.27
	No	11.1 ± 0.4		
Individual vitamin/mineral use and filled medical prescription (n = 5876)	Yes	28.1 ± 0.3	3.73 (3.44-4.05)	0.23
	No	7.5 ± 0.3		
Protein/amino acids use and filled medical prescriptions (n = 7026)	Yes	32.9 ± 0.3	3.08 (2.88-3.29)	0.23
	No	10.7 ± 0.4		
Combination product use and filled medical prescription (n = 7690)	Yes	36.3 ± 0.4	3.25 (3.05-3.47)	0.25
	No	11.2 ± 0.4		
Prohormone use and filled medical prescription (n = 857)	Yes	4.1 ± 0.1	3.38 (2.73-4.17)	0.07
	No	1.2 ± 0.1		
Herbal use and filled medical prescription (n = 3757)	Yes	18.0 ± 0.3	3.72 (3.36-4.12)	0.17
	No	4.8 ± 0.2		
Joint health product use and filled medical prescription (n = 1785)	Yes	8.5 ± 0.2	3.45 (2.99-4.00)	0.11
	No	2.5 ± 0.2		
Other dietary supplement use and filled medical prescription (n = 5542)	Yes	26.5 ± 0.3	3.70 (3.41-4.03)	0.22
	No	7.2 ± 0.3		

[a]CDMC = clinically diagnosed medical condition.
[b]SE =standard error.
[c]CI = confidence interval.

Table 4. Prevalence of a CDMC[a] with both a filled prescription medication and any dietary supplement use (CDMC n = 18,775, no CDMC n = 7905) in a representative cohort of military service members in the US Military Dietary Supplement Use Study (n = 26,680)

Variable[b]	CDMC	Prevalence (% ± SE[c])	Prevalence ratio, CDMC/no CDMC (95% CI[d])	Effect size
Any prescription and any dietary supplement (n = 13,090)	Yes	61.75 ± 0.35	3.27 (3.11-3.42)	0.39
	No	18.91 ± 0.44		
Antihistamines (AHFS[e] code 4) and any dietary supplement (n = 2563)	Yes	12.62 ± 0.24	5.15 (4.44-5.95)	0.16
	No	2.45 ± 0.17		
Anti-infectives (AHFS code 8) and any dietary supplement (n = 4137)	Yes	19.73 ± 0.29	3.60 (3.27-3.97)	0.18
	No	5.48 ± 0.26		
Autonomic drugs (AHFS code 12) and any dietary supplement (n = 3418)	Yes	17.15 ± 0.28	6.80 (5.92-7.82)	0.20
	No	2.52 ± 0.18		
Blood formation, coagulation, thrombosis agents (AHFS code 20) and any dietary supplement (n = 143)	Yes	0.75 ± 0.06	29.41 (7.35-125.00)	0.05
	No	0.03 ± 0.02		
CV[f] drugs (AHFS code 24) and any dietary supplement (n = 1930)	Yes	9.60 ± 0.21	5.99 (5.00-7.14)	0.14
	No	1.61 ± 0.14		
CNS[g] agents (AHFS code 28) and any dietary supplement (n = 8294)	Yes	40.60 ± 0.36	4.78 (4.42-5.15)	0.32
	No	8.50 ± 0.31		
Electrolyte, caloric, water agents (AHFS code 40) and any dietary supplement (n = 392)	Yes	1.98 ± 0.10	7.81 (5.00-12.35)	0.07
	No	0.25 ± 0.06		
Respiratory tract agents (AHFS code 48) and any dietary supplement (n = 2426)	Yes	12.19 ± 0.24	7.04 (5.92-8.33)	0.17
	No	1.73 ± 0.15		
Eye, ear, nose throat preparations (AHFS code 52) and any dietary supplement (n = 4106)	Yes	20.00 ± 0.29	4.50 (4.05-5.00)	0.20
	No	4.44 ± 0.23		
GI[h] drugs (AHFS code 56) and any dietary supplement (n = 3656)	Yes	18.45 ± 0.28	7.58 (6.58-8.77)	0.21
	No	2.43 ± 0.17		
Hormones and synthetics (AHFS code 68) and any dietary supplement (n = 1431)	Yes	6.74 ± 0.18	3.22 (2.75-3.79)	0.09
	No	2.09 ± 0.16		
Antitoxins, globulins, toxoids, vaccines (AHFS code 80) and any dietary supplement (n = 861)	Yes	4.56 ± 0.15	90.91 (33.33-250.00)	0.12
	No	0.05 ± 0.03		
Skin and mucous membrane agents (AHFS code 84) and any dietary supplement (n = 2714)	Yes	13.73 ± 0.25	7.93 (6.67-9.35)	0.18
	No	1.73 ± 0.15		
Smooth muscle relaxants (AHFS code 86) and any dietary supplement (n = 179)	Yes	0.94 ± 0.07	25.00 (7.87-76.92)	0.05
	No	0.04 ± 0.02		
Vitamins (AHFS code 88) and any dietary supplement (n = 878)	Yes	4.44 ± 0.15	8.00 (5.92-10.75)	0.10
	No	0.56 ± 0.08		
Miscellaneous therapeutic agents (AHFS code 92) and any dietary supplement (n = 1087)	Yes	5.05 ± 0.16	2.87 (2.41-3.42)	0.08
	No	1.76 ± 0.15		

[a]CDMC = clinically diagnosed medical condition.
[b]n = number of participants using listed AHFS category with any dietary supplement.
[c]SE = standard error.
[d]CI = confidence interval.
[e]AHFS = American Hospital Formulary Service.[28]
[f]CV = cardiovascular.
[g]CNS = central nervous system.
[h]GI = gastrointestinal.

used PMs and DSs, but in those studies,[15,16] DSs were more narrowly defined than in the current study. Data from the 2005-2008 National Health and Nutrition Examination Survey (NHANES) involving 20- to >60-year-olds and using a more inclusive definition of DSs found that 34% used DSs with PMs.[17] Another nationally representative sample[18] of

older adults (57-85 years of age) found that concomitant DS and PM use increased from 54% in 2004-2006 to 66% in 2010-2011, suggesting concomitant use is increasing over time, at least in older adults. However, the definition of DSs was not clear in that study.[18] Also it should be noted that we do not know if the DSs and PMs were consumed at exactly the same time since SMs only reported DS use within the 6-month surveillance period and not the exact date the DSs were consumed.

Demographic and Lifestyle Factors Associated With Dual Use

Data from NHANES 2005-2008[17] indicated that women were more likely than men to concomitantly use DSs and PMs and that concomitant use increased with age and formal education, in general agreement with the current study. PMs are provided by health care professionals for specific medical conditions, and DS users most often cite general health enhancement as the primary reason for use.[6,22,31,32] Women, older individuals, and those with more formal education often believe using DSs with their PMs is a way to further enhance their health. Women are more likely than men to make behavioral changes to improve health,[33-35] and individuals who have achieved higher educational levels are generally more proactive, more health conscious, prone to engage in health-promoting behaviors, and more likely to explore multiple channels of information related to their health.[36-40]

Associations between dual use and BMI, lifestyle factors, and military service are unique to the current study, have not been investigated previously, and will need to be confirmed by future research. One intriguing finding was that those who had quit tobacco use had a higher dual use prevalence than users or nonusers. Those who had quit smoking had a higher prevalence of CDMCs and FPMs. Smokers have numerous reasons for giving up smoking, but the primary reason is health concerns.[41] Health enhancement is also the primary reason for using DSs,[6,22,31,32] and these motivations may work synergistically in former smokers to increase the use of DSs along with PMs. A similar mechanism may be involved in the higher dual use among former smokeless tobacco users.

It should be noted that in contrast to most civilian occupations, the military have strict physical fitness and body weight/body fat standards,[42] and SMs are tested twice a year to ensure they meet the requirements. Individuals who do not meet the criteria for fitness or body weight/body fat can receive adverse performance reports and can be discharged from service for repeated failures to achieve the standards. This may prompt some individuals who have difficulty meeting these requirements to use DSs marketed for weight control and/or improving physical performance, thus increasing the likelihood of combining DSs with PMs.

Dual PM and DS Use Among SMs With CDMCs

A study[17] using data from 2005 to 2008 NHANES examined concomitant DS and PM use among individuals with self-reported medical conditions. Nine types of self-reported conditions were examined including arthritis, heart/vascular conditions, respiratory conditions, liver problems, thyroid problems, cancer, diabetes, kidney problems, and osteoporosis. The authors demonstrated that the odds of concomitant DS and PM use (adjusted for gender, age, education, and income) was 1.67 to 2.42 times higher among those with a CDMC and was higher regardless of the category of PM or DS examined. The current study of SMs involved medical conditions from clinical records as well as a broader range of conditions. Results indicated that the adjusted odds of dual use were 1.60 to 3.45 times higher within the 20 categories of CDMCs and was higher for all categories of PMs and DSs examined. Both studies indicated that among those with medical conditions (self-reported or from clinical records), dual use of DS and PM was considerably higher for a very broad range of PMs and DSs.

There are potential risks of interactions when individuals concomitantly use PMs and DSs. Studies using convenience samples have estimated that 12% to 20% of patients taking PMs have potential interactions with DSs.[10-13] In a nationally representative sample, major potential drug interactions increased from 8% in 2005-2006 to 15% in 2011, but this included interactions between two PMs as well as between PMs and DSs.[18] Potential drug-DS interactions may be even higher in some populations. For example, in a study of seniors ($\geq$60 years) in US and Mexico border towns (El Paso and Juarez) 32% had a potential drug-DS interaction.[43] The most commonly reported interactions are between herbal supplements and PMs,[10-12,43] and many combination products contain herbal substances.[9,44] In the current study, 18% of SMs with a CDMC were using herbals and with FPMs, and 36% of combination product users also had FPMs. Interactions between some minerals (iron, potassium, calcium) and PMs have also been reported[11,18] and 28% of SMs with a CDMC had vitamin/mineral use with FPMs.

Strengths and Limitations

The current study recruited a very large stratified random sample of SMs from all branches of service. A standardized DS questionnaire was used that was based on questionnaires used in previous military studies.[45] The military medical database used contains virtually complete information on encounters with medical care providers, and the pharmacy database is also complete with regard to medications dispensed to SMs. However, there were some study limitations. First, DS data were self-reported and suffered the usual weaknesses associated with this method including recall bias, social desirability, errors in self-observation, and inadequate recall.[46,47] Second, the FPMs examined in the present study were only those prescribed by medical care providers and obtained through pharmacy channels. Medications that SMs obtained over the counter without a prescription were not included. However, all prescriptions provided to active duty SMs (even those that can be obtained over the counter) are free so SMs are likely to use the medical care route to obtain these medications. Third, filling a prescription does not imply conformity with the prescription regimen and data on actual SM compliance were not available. Fourth, although the pharmacy database provided the exact date a SM obtained a prescription, the exact date the SMs ingested their DSs was not known. Thus, estimates of dual use could be improved by querying the exact dates of DS consumption in future studies. Fifth, compared with the requested stratified sample (12% female, and 36% Army, 24% Air Force, 15% Marines Corps, 25% Navy), respondent demographics differed slightly (Table 1). Nonetheless, two genders (conceptualized as

binary; men/women) and all service branches were well represented. Finally, gender could only be reported as "male" or "female" on the questionnaire. Participants completing the questionnaire who identify as "nonbinary" or had other gender identities would have been misclassified and individuals in the sample with other gender identities may have felt excluded.

CONCLUSIONS

This study demonstrated for the first time in a representative military sample that 49% of SMs had dual use of DSs and FPMs in a 6-month period. Dual use was higher in some demographics including women; older SMs; those with more formal education, higher BMI, or higher amount of physical activity; American Indian SMs; and former tobacco users. Importantly, dual use was over 3 times higher among those with a CDMC compared with those without one (62% vs 19%), in agreement with a previous study in a civilian sample using self-reported medical conditions.[17] Although this study quantified the prevalence of dual PM-DS use in a 6-month period, it did not determine the particular combinations of these substances that were harmful. Future studies should examine specific PM-DS interactions to determine the potential for adverse effects in this population.

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STATEMENT OF POTENTIAL CONFLICT OF INTEREST

No potential conflict of interest was reported by the authors.

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ADDITIONAL INFORMATION

The questionnaire is available from the author on request.

AUTHOR CONTRIBUTIONS

J. J. Knapik designed the research, analyzed data, wrote the paper, and had responsibility for final content; D. W. Trone designed the research, conducted research, provided essential materials, and had responsibility for final content; R. A. Steelman analyzed data and had responsibility for final content; E. K. Farina designed research and had responsibility for final content; H. R. Lieberman conceptualized the study, designed the research plan and had responsibility for final content. All authors have read and approved the final manuscript.