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Temporal trends in dietary supplement prescriptions of United States military service members suggest a decrease in pyridoxine and increase in vitamin D supplements from 2005 to 2013

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ABSTRACT

Dietary supplements (DSs) can be obtained over-the-counter but can also be prescribed by health-care providers for therapeutic reasons. Few studies have documented this later source despite the fact that 79% of physicians and 82% of nurses have recommended DSs to patients. This investigation assessed prevalence and temporal trends in oral DS prescriptions filled by all United States service members (SMs) from 2005 to 2013 (n = 1 427 080 ± 22 139, mean ± standard deviation (SD)/y). We hypothesize that there would be temporal variations in specific types of DSs. Data obtained from Department of Defense Pharmacy Data Transaction System were grouped by American Hospital Formulary System pharmacologic-therapeutic classifications and prevalence examined over time. About 11% of SMs filled one or more DS prescriptions of 235 180 ± 4926 (mean ± SD) prescriptions/y over the 9-year period. Curve-fitting techniques indicated significant linear declines over time for multivitamins ($P = .004$), iron preparations ($P < .001$), antacids ($P < .001$), and vitamin B and B complex vitamins ($P < .001$). There were significant quadratic trends indicating a rise in early years followed by a leveling off in later years for replacement preparations ($P < .001$) and vitamin C ($P < .001$). There were significant

Abbreviations: AI, Adequate Intake; AHFS, American Hospital Formulary System; AFHSB, Armed Forces Health Surveillance Branch; COX, Cyclooxygenase; DS, Dietary Supplement; GC3, Generic Class 3; GERD, Gastroesophageal Reflux Disease; IOM, Institute of Medicine; NDC, National Drug Code; NHANES, National Health and Nutrition Examination Surveys; PDTS, Pharmacy Data Transaction System; PEC, Pharmacoecomomic Center; RDA, Recommended Daily Allowance; SD, Standard Deviation; SM, Service Member; TLESR, Transient Lower Esophageal Sphincter Relaxation; US, United States; USPSTF, United States Preventive Services Task Force; PPI, proton pump inhibitor; H2RA, histamine 2 receptor antagonist.

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quadratic trends (P < .001) for vitamin E indicating a decline in early years and leveling off in later years, and vitamin D indicating little change in early years followed by a large rise subsequently (P < .001). This study identified temporal trends in specific DS categories that may be associated with changing perceptions of prescribers and/or patients of the appropriate roles of DSs in medicine and public health.

1. Introduction

Dietary supplements (DSs) are commercially available products that are consumed as an addition to the usual diet. DSs include vitamins, minerals, herbs (botanicals), amino acids, and a variety of other substances [1]. Recent surveys of health care providers found that 79% of physicians, 82% of nurses, and 97% of dietitians had recommended DSs to their patients [2,3]. It is estimated that about 50% of Americans and 60% to 70% of US military personnel use DSs.[4-6]. The Dietary Supplement Health and Education Act (DSHEA) of 1994 [7] established the regulatory framework for DSs in the US. Since DSHEA became law, US sales of DSs has increased from $4 billion in 1994 to $37 billion in 2014, [8,9] a >9-fold increase over 20 years.

Individuals can obtain DSs from over-the-counter sources like drug stores, grocery stores, and retailers that specialize in these substances. In addition to these sources, DSs can be obtained from prescriptions written by medical care providers. The types of DSs that are medically prescribed and their prevalence of use likely differ from those obtained over-the-counter. The primary reason individuals report for using over-the-counter DSs is to promote general health [10-12]. DSs prescribed by medical personnel are for particular therapeutic purposes, for example to correct vitamin, mineral, or nutritive (e.g., amino acid) deficiencies [13]. DSs can also be recommended by health care providers as alternatives to other types of medications. Pharmaceutical grade DSs do not appear to carry the same potential risk for contamination or adverse effects as do some over-the-counter products [14-16].

A number of investigations have quantified the prevalence of over-the-counter DS use among civilians [5,6,17,18] and military personnel [4,10,16]. However, investigations on medically prescribed DSs are more limited. A few studies have examined population-level prescribed DS use among civilians, but these studies are based on self-reports rather than information obtained from medical records [19-21]. Other studies have examined some limited prescription data within the US military medical system [22-24].

In the US military health care system, medical care is freely available to service members (SMs) and since there are no charges for prescription medications, SMs are likely to fill prescriptions within the system. Information on prescriptions dispensed to SMs is documented by the US Department of Defense Pharmacy Data Transaction System (PDTS), thereby providing an opportunity to examine prevalence and temporal trends in prescriptions filled by all US SMs. These temporal trends may reflect patterns present in the general medical community for which such comprehensive data are not available. We hypothesized that although the overall prevalence of prescriptions would remain relatively stable over time, there would be temporal variations in specific categories of DSs. We tested this by obtained DS data from the PDTS, grouping these data by American Hospital Formulary System (AHFS) pharmacologic-therapeutic classifications, and examining changes over time in DS prescriptions.

2. Methods and materials

This was a descriptive study designed to identify patterns of oral DSs filled by the entire population of US military SMs from 2005 through 2013. SMs included only active duty personnel in the Army, Navy, Marine Corps, Air Force, and Coast Guard. DSs were defined based on the Dietary Supplement Health and Education Act of 1994 as "…a product (other than tobacco) intended to supplement the diet that bears or contains one or more of the following dietary ingredients: (*a*) a vitamin; (*b*) a mineral; (*c*) a herb or other botanical; (*d*) an amino acid; (*e*) a dietary substance for use by man to supplement the diet by increasing total dietary intake; or (*f*) a concentrate, metabolite, constituent, extract or combination of any ingredient in clause a to e" [1]. The study was approved by the institutional review board of the US Army Research Institute of Environmental Medicine in accordance with Army Regulation 70-25 (Use of Volunteers as Subjects of Research).

2.1. *Identification of dietary supplements*

To identify DSs available for prescription to SMs, 2 databases were queried. One database was the Food and Drug Administration National Drug Code (NDC) database, obtained in November 2013 [25]. At the time, the NDC database contained 65 536 listed substances. The other database was the basic and extended core formularies of the US Defense Health Agency's Pharmacoeconomic Center (PEC) [26]. Using the search engine at the PEC website [26], the following search terms were used to identify substances classified by First Data Bank as Generic Class 3 (GC3) categories of drugs which could also be DSs: vitamins, minerals, protein and amino acids, herbs and botanical ingredients, fish oil, creatine, joint support, digestive, and dietary supplements. The GC3 system utilizes 3 characters (alpha, numeric, and alpha) to represent the organ system, pharmacological class, and specific therapeutic class. A total of 34 901 listed substances were identified and the corresponding NDC numbers, GC3 numbers, and generic names were provided by a pharmacist from the Defense Health Agency Pharmacy Operations Division. A nutritionist and a physiologist/epidemiologist knowledgeable in DSs each independently examined the two databases to identify DSs. After the independent evaluations, the 2 individuals met to resolve any discrepancies. Only substances