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Et al.

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# Factors Associated With Dietary Supplement Use Among Prescription Medication Users

Paula Gardiner, MD; Robert E. Graham, MD, MPH; Anna T. R. Legedza, ScD; David M. Eisenberg, MD; Russell S. Phillips, MD

**Background:** We examined the patterns of nonvitamin dietary supplement (NVDS) use among adult prescription medication users in the United States.

**Methods:** Using the 2002 National Health Interview Survey, we analyzed factors associated with NVDS use and prescription medication use in the prior 12 months with descriptive,  $\chi^2$ , and logistic regression analysis.

**Results:** In the United States, 21% of adult prescription medication users reported using NVDSs in the prior 12 months. Of the respondents who used both prescription medications and NVDSs in the prior 12 months, 69% did not discuss this use with a conventional medical practitioner. Among adults who used prescription medications in the prior 12 months, the most commonly used supplements included echinacea, ginseng, ginkgo, garlic, and glu-

cosamine chondroitin. Prescription medication users with menopause and chronic gastrointestinal disorders had the highest rates of NVDS use (33% and 28%, respectively), and prescription medication users with coronary heart disease and history of myocardial infarction had the lowest rates of use (12% each). In the adjusted analysis, factors associated with increased use of NVDSs by prescription medication users included being female, being Hispanic, having more years of education, living in the West, lacking medical insurance, and having chronic conditions. Elderly respondents were less likely to use NVDSs.

**Conclusion:** One in 4 prescription medication users took an NVDS in the prior 12 months, yet the majority did not share this with a conventional medical professional.

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CCORDING TO THE OFFICE of Dietary Supplements of the National Institutes of Health, a dietary supplement is intended to supplement the diet and contains 1 or more dietary ingredients (including vitamins, minerals, herbs or other botanicals, amino acids, and other substances) or their constituents. Analyses of the National Health Interview Survey (NHIS) have estimated that 10% to 19% of the US population use nonvitamin dietary supplements (NVDSs) for health conditions.<sup>2,3</sup> Rates of dietary supplement use vary by age, sex, and race/ethnicity, but substantial numbers of all patient groups report using dietary supplements, particularly among those with chronic or recurrent illnesses who also receive care by conventional health care professionals.4,5 Patients with chronic illness are also frequent users of prescription medications. Despite increasing concern about potentially harmful interactions between dietary supplements and prescription medications based on case reports and clinical observation, little clinical evidence is available to help the health care professional know which of their patients are at risk.6

Few studies have examined the use of NVDSs among US adult prescription medication users. Using data from a nationally representative survey, we examined overall prevalence and patterns of NVDS use by prescription medication users, disclosure rates of NVDS use among prescription medication users to health care professionals, prevalence of use of specific herbs and other dietary supplements taken by prescription medication users, chronic medical conditions in which NVDS use and prescription medication use occurs together, and factors associated with NVDS use by prescription medication users.

### **METHODS**

### DATA SOURCE

We analyzed data from the sample core component and the Alternative Health/Complementary and Alternative Medicine supplement to the 2002 NHIS, which was administered as part of the sample adult questionnaire of the 2002 NHIS. The NHIS is an in-person household survey conducted by the Census Bureau for the National Center for Health Statistics and is the principal source of information in the United States on the health of the civilian, noninstitutionalized, household population.

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One adult (≥18 years) was randomly selected from each household to complete this portion of the survey. There were 31 044 completed interviews, with a 73.4% final weighted response rate. The sampling methods for the NHIS are described elsewhere.8

## **USE OF HERBS AND DIETARY SUPPLEMENTS** AND PRESCRIPTION MEDICATIONS

The Alternative Medicine Supplement solicited information from US adults on 19 nonconventional health therapies. Respondents were asked "During the past 12 months, did you use natural herbs for your own health or treatment?" Of those who said yes, respondents were asked a series of questions about specific health problems or conditions. Respondents chose from a list of 35 dietary supplements used for health reasons (29 supplements were plant based; 6 supplements were not plant based) (Figure). Respondents were asked if they disclosed this use to conventional medical professionals. Finally, respondents were asked if they used prescription medications in the prior 12 months. In the NHIS adult core, respondents were asked a series of questions about specific health problems or conditions. We chose to include in our analysis 23 medical conditions that had high potential of drug-NVDS interactions. These conditions are listed in **Table 1**. In addition, from Table 1, we created a "chronic conditions" variable that included 13 chronic conditions for which patients regularly use prescribed medication in an attempt to ascertain concurrent use of NVDS and prescription medication (Table 1).

#### OTHER HEALTH-RELATED FACTORS

We considered sociodemographic information on the respondents' age (<25 years, 25-34 years, 35-44 years, 45-54 years, 55-64 years, and ≥65 years), sex, marital status (defined as married or not married), education (less than high school, high school graduate, some college, and college graduate), annual family income  $(<\$15\,000, \$15\,000-34\,999, \$35\,000-64\,999, \ge \$65\,000,$ and other), race/ethnicity (Hispanic, non-Hispanic white, non-Hispanic black, non-Hispanic Asian, and non-Hispanic other [Pacific Islander/Native Hawaiian and American Indian/Alaskan native]) and region of US residence (Northeast, Midwest, South, and West). We analyzed health care utilization data on the following: health insurance status (insured vs not insured), usual source of medical care (place for routine and preventative care), and utilization of health services (last visit to health professional). We also included self-perceived health status (excellent, very good, good, fair, and poor), and lifestyle/behavioral factors included use of a health club, wellness program, or fitness facility in the last year and smoking status.

## STATISTICAL ANALYSIS

Population estimates were calculated using NHIS weights, which are calibrated to US 2000 census totals for sex, age, and race/ ethnicity of the 2002 US population. Descriptive statistics were used to examine the prevalence of NVDS use and nonuse among prescription medication users, disclosure by prescription medication users of NVDS to medical professionals, the most common herbs and dietary supplements used by prescription medication users, and medical conditions for which NVDSs and prescription medications were used together. We limited our analysis of NVDS use for specific medical conditions to herbs with high rates of popular use and/or high reported drug-herb interactions in the literature. 9,10 We used  $\chi^2$  tests and logistic regression to compare proportions of characteristics in NVDS users vs nonusers among those who took prescription medi-

#### **Dietary Supplements**

Fish Oil Ginger Supplements Melatonin Soy Supplements Bee Pollen Ragweed/Chamomile Glucosamine Chondroitin Kava Kava S-adenosylmethionine Valerian (SAMe) Saw Palmetto Progesterone Cream Evening Primrose Echinacea Black Cohosh Ginsena Ma Huang (Ephedra) Ginkgo biloba Licorice

Garlic Supplements

St John's Wort

Peppermint

Milk Thistle Guarana Comfrey

Feverfew Dong Quai/Don Gui Tong Hawthorn Cascara Sagrada Yohimbe Bladderwrack Senna Wild Yam Cream Chaparral

Vitex/Chasteberry

#### Examples of Common Uses of Herbs Listed With Examples of Latin Names

Echinacea: To Reduce Colds and Flu Symptoms (Echinacea angustifolia) Garlic: To Lower Cholesterol and Blood Pressure and to Act as an Antimicrobial/ Antifungal Agent (Allium sativum)

Ginseng: To Increase Stamina and Energy (Panax ginseng) Ginkgo: Known for Its Memory-Enhancing Properties (Ginkgo biloba) St John's Wort: To Treat Mild to Moderate Depression (Hypericum perforatum)

Figure. Nonvitamin dietary supplements recorded in the National Health Interview Survey

cations in the prior 12 months. We used logistic regression analysis to assess which variables were significantly (P<.05) associated with NVDS use among prescription medication users. We selected variables for testing in our logistic model based on the results of previous national studies and entered these variables into the final model simultaneously.3 Given the problem of missing income data, we included a variable named "other" for those with missing income data to avoid limiting the number of respondents available for the logistic regression analysis. Variables tested in our model are listed in Table 2. All analyses were performed using SAS-callable SUDAAN version 8.1 (Research Triangle Institute, Research Triangle Park, NC)<sup>11</sup> to account for the complex sampling design of the NHIS.

### **RESULTS**

# COMPARISON OF RESPONDENTS USING PRESCRIPTION MEDICATIONS WITH OR WITHOUT NVDSs

Of the 31 044 NHIS respondents, 67% used a prescription medication in the prior 12 months (weighted for US population 134 606 105). Of the respondents who used prescription medications in the last year, 21% also used an NVDS during the same period. Of the respondents who did not use a prescription medication in the prior year. 16% used an NVDS. A comparison of the characteristics of all respondents who reported use of prescription medications vs those who used a prescription medication as well as an NVDS vs those who used prescription medications but had not used an NVDS is given in Table 2. When we compared dietary supplement users with nondietary supplement users among respondents taking prescription medications, NVDS users were more likely to be Hispanic, non-Hispanic Asian and non-Hispanic other, uninsured, younger, female, highly educated, live in the West, have high self-perceived health status, be a former smoker, use a fitness center, and have no usual source of primary care. As given in Table 2, approximately 1 in 4 prescription medication users aged 45 to 55 years used NVDSs. Nearly 30% of college-educated respondents and

Table 1. Use of Specific Nonvitamin Dietary Supplements (NVDSs) Among Respondents With Chronic Conditions and Prescription Medication Use in the Prior 12 Months\*

Chronic Condition	No. of Patients With Chronic Conditions and Prescription Medication Use	Any NVDS Use, %	Echinacea Use, %	Ginseng Use, %	Ginkgo Use, %	Garlic Use, %	St John's Wort Use, %
Medical condition in the prior 12 mo							
Menopause	1030	33.1	12.3	5.5	6.1	5.6	4.0
Insomnia	4671	26.3	9.1	6.0	5.4	5.0	4.1
Liver disease	367	25.9	8.0	5.5	6.5	4.3	1.8
Chronic pain†	4863	25.8	8.8	5.8	5.3	5.3	3.2
Depression/anxiety†	4314	25.3	8.5	6.4	5.7	4.7	4.6
Weak or failing kidneys	405	18.8	4.5	2.6	2.2	3.5	3.5
Ever been told that you had a medical condition							
Chronic gastrointestinal conditions‡	1598	28.3	9.2	5.8	5.8	5.0	3.7
Asthma†	2641	24.9	10.4	6.3	4.8	4.7	3.5
Irregular heart beat	2570	23.0	7.5	4.3	3.8	5.2	2.9
Gastrointestinal ulcer	2042	22.7	7.0	5.2	5.4	4.3	3.1
Thyroid problems†	2082	22.1	8.0	3.8	5.1	5.6	2.4
Arthritis†§	6032	21.6	6.4	4.0	4.4	4.4	2.4
Cancer	1975	20.2	6.5	3.4	3.7	4.0	1.9
Seizure disorder†	381	19.6	8.2	6.2	5.0	5.3	4.7
Hyperlipidemia†	5610	19.6	6.4	3.4	3.8	4.7	2.0
Hypertension†	7096	17.0	5.5	3.2	3.4	3.7	1.9
Diabetes†	2040	15.3	3.3	2.6	2.1	2.9	1.2
Stroke†	731	14.0	3.2	2.8	3.4	3.4	1.7
Congestive heart failure†	541	12.9	1.9	2.0	2.9	3.1	0.3
Coronary heart disease†	1209	11.9	2.1	2.5	1.9	3.7	1.0
Myocardial infarction†	965	11.7	1.9	2.0	1.8	3.5	0.4
Medical condition in the last 3 mo							
Severe headache and/or migraine	3691	27.6	11.0	6.9	5.5	5.4	4.1
Back pain	6425	25.6	9.6	6.1	5.3	4.7	3.1

<sup>\*</sup>Data sources: National Health Interview Survey 20028; weighted percentages were extrapolated from the US census (2000) for the adult civilian, noninstitutionalized, household population.

respondents who lived in the West used an NVDS and a prescription medication. Nearly 1 in 5 respondents with no usual source of health care and no insurance used NVDSs along with their prescription medication. Finally, 21% of patients with chronic conditions reported using a dietary supplement and prescription medication.

# DISCLOSURE AND USE OF SPECIFIC NVDSs AND PRESCRIPTION MEDICATION USE IN THE PRIOR 12 MONTHS

Of the respondents who used both prescription medications and NVDSs in the prior 12 months, 69% did not discuss this use with a conventional medical practitioner.

Among prescription medication users, menopausal women (33%) and those with chronic gastrointestinal disorders (28%) and severe headache or migraine (28%) had the highest rates of NVDS use. Prescription medication users with congestive heart failure (13%), coronary heart disease (12%), and history of myocardial infarction (12%) had the lowest rates of NVDS use (Table 1).

Among prescription medication users with depression, 5% used St John's wort and 6% used ginseng. Among prescription medication users with high cholesterol levels or irregular heart beat, 5% used garlic. Of the pre-

scription medication users with asthma, 10% used echinacea (Table 1).

# FREQUENCY OF SPECIFIC NVDS USE AMONG PRESCRIPTION MEDICATION USERS

**Table 3** demonstrates the frequency of use of the 35 single NVDSs by respondents who had used prescription medications in the prior 12 months. Table 3 includes the rates of specific herb use among respondents who used both NVDSs and prescription medication in the prior 12 months.

# FACTORS ASSOCIATED WITH NVDS USE AMONG PRESCRIPTION MEDICATION USERS

Among prescription medication users, NVDS use was more frequent among respondents who were female, cigarette smokers or former smokers, and Hispanic or non-Hispanic other; had a high school education or above; lived in the West compared with the Northeast; and had chronic conditions. Among prescription medication users, factors associated with decreased use included age older than 65 years, decreased use of a fitness center, and living in the Midwest or South. Finally, NVDS use was significantly more likely among respondents who were

<sup>†</sup>The "chronic conditions" variable included 13 chronic conditions for which patients used daily prescribed medication.

<sup>‡</sup>Irritable bowel syndrome, inflammatory bowel disease, and severe constipation.

<sup>§</sup>Arthritis, gout, and lupus.

Table 2. Comparison of Respondents Using Prescription Medications With or Without Nonvitamin Dietary Supplements (NVDSs)\*

Characteristic	Overall Respondents Using a Prescription Medication in the Prior 12 Months, % (n = 20 214)	Respondents Using a Prescription Medication and No NVDS in the Prior 12 Months, % (n = 16 012)	Respondents With Concurrent Use of a Prescription Medication and an NVDS in the Prior 12 Months, % (n = 4202)†	Conditional Use Among Prescription Medication Users, % of Respondents Also Using an NVDS, % (n = 4202)
Race/ethnicity		, ,	, ,,	,
White	78.5	78.7	77.5	20.3
Black	10.4	11.0	8.4	16.6
Asian	2.5	2.2	3.7	30.2
Other‡	0.9	0.7	1.3	31.2
Hispanic	7.7	7.4	9.1	24.1
Age, y	40.0	10.0	40.4	22.2
≤24	10.6	10.6	10.4	20.2
25-34	14.9	14.5	16.7	23.0
35-44	19.0	18.6	20.8	22.5
45-54	19.7	18.7	23.3	24.3
55-64	15.0	14.8	15.8	21.6
≥65	20.9	22.8	13.0	12.8
Sex				
Male	42.1	42.2	37.7	18.4
Female	57.9	56.8	62.3	22.1
Education level				
<high school<="" td=""><td>15.4</td><td>17.1</td><td>8.6</td><td>11.5</td></high>	15.4	17.1	8.6	11.5
High school graduate	26.6	27.9	21.4	16.5
Some college	32.0	31.3	35.1	22.5
College graduate	25.2	22.9	34.5	28.1
Income, \$				
<15 000	12.9	12.6	14.2	22.6
15 000-34 999	18.6	18.0	21.0	23.1
35 000-64 999	14.7	13.8	18.3	25.4
≥65 000 ≥65 000	6.4	5.8	8.8	28.2
Other	47.4	49.8	37.7	16.3
Region	77.7	43.0	31.1	10.5
Northeast	19.4	19.2	20.2	21.4
Midwest	25.3	25.9	23.1	18.7
	37.6	39.1	32.0	17.4
South				
West	17.7	15.8	24.8	28.7
Insurance: medical	0.1.0	0.1.0	00.7	00.4
Yes	91.9	91.6	90.7	20.4
No	8.6	8.5	9.3	22.2
Usual source of medical care	0.1.1	0.10	00.0	00 =
Yes	94.1	94.3	93.9	20.5
No	5.8	5.7	6.1	21.5
Last visit to a health professional				
≤6 mo	84.0	83.8	84.7	20.7
$>$ 6 mo to $\leq$ 1 y	11.4	11.5	10.8	19.5
>1 y or never saw	4.5	4.5	4.4	20.1
Self-perceived health status				
Excellent, very good, or good	83.9	83.1	87.1	21.3
Fair or poor	15.9	16.8	12.8	16.4
Smoking status				
Current	21.3	21.5	20.7	19.9
Former	26.4	25.9	28.4	22.1
Never	52.0	52.3	50.7	20.0
Chronic conditions§				
Yes	69.1	68.9	69.9	20.8
No	30.9	31.1	30.1	20.0
Use of fitness center	55.0	V / / /	55.1	20.0
Yes	63.3	61.6	69.8	29.0
No	35.6	37.2	29.4	18.3
140	00.0	01.2	23.4	10.0

<sup>\*</sup>Data sources: National Health Interview Survey (NHIS) 2002<sup>8</sup>; weighted percentages were extrapolated from the US census (2000) for the adult civilian, noninstitutionalized, household population. Data were available for greater than 95% of the NHIS population except for the variable "income." We did not have complete information on 9581 respondents

complete information on 9581 respondents.

†Outcome variable combined respondents who answered yes to "during the past 12 months, did you use herbs for your own health or treatment?" and yes to "during the past 12 months, did you use prescription medications?"

<sup>‡</sup>American Indian/Alaskan Native or Pacific Islander/Native Hawaiian.

<sup>\$</sup>Chronic condition variable includes respondents with diabetes, hypertension, asthma, arthritis, depression/anxiety, coronary heart disease, hyperlipidemia, stroke, myocardial infarction, seizure disorder, congestive heart failure, thyroid problems, and chronic pain.

Table 3. Frequency of Specific Nonvitamin Dietary Supplement (NVDS) Use Among Prescription Medication Users\*

Dietary Supplement	Among Prescription Medication and NVDS Users, Respondents Reporting Specific NVDS Use, % (n = 4202)	Among All Prescription Medication Users, Respondents Reporting Specific NVDS Use, % (n = 20 214)
Echinacea	40.6	7.8
Ginseng	22.6	4.4
Ginkgo biloba	20.5	3.9
Garlic supplements	19.4	3.7
Glucosamine chondroitin	16.0	3.1
Black cohosh	13.0	0.7
St John's wort	12.3	2.4
Peppermint	11.5	2.2
Fish oil	11.2	2.3
Ginger supplements	10.5	2.0
Soy supplements	10.1	1.9
Ragweed/chamomile	8.7	1.7
Bee pollen	6.7	1.4
Kava kava	6.4	1.2
Valerian	6.1	1.2
Saw palmetto	5.7	1.1
Melatonin	5.2 4.3	1.0 0.9
Evening primrose Licorice	4.3 3.9	0.9
	3.8	0.8
Ma huang (ephedra) Milk thistle	3.5	0.7

<sup>\*</sup>Data sources: National Health Interview Survey 20028; weighted percentages were extrapolated from the US census (2000) for the adult civilian, noninstitutionalized, household population. See the Figure for a description of the common uses for some of the herbs listed in this table.

uninsured in the adjusted model (adjusted odds ratio, 1.23; 95% confidence interval, 1.06-1.43) (**Table 4**).

# **COMMENT**

Of the estimated 135 million people who used prescription medications in the last year, 21% also used an NVDS in the prior 12 months. Of the respondents who used prescription medications and NVDSs in the prior 12 months, 69% did not discuss NVDS use with a conventional medical practitioner. Among adults who used prescription medications in the prior 12 months, the most commonly used dietary supplements included echinacea, ginseng, ginkgo, and garlic. In general, prescription medication users with chronic but not life-threatening conditions (menopause, chronic gastrointestinal conditions, headaches, and insomnia) tended to have high NVDS use, while those with chronic and life-threatening conditions (cardiovascular disease, stroke, and diabetes) had the lowest rates of NVDS use. When we examined NVDS use among respondents with chronic conditions associated with regular daily prescription medication use, we found that 21% of those respondents also used NVDSs. In the adjusted analysis, factors associated with increased use of NVDS by prescription medication users included being female, being Hispanic or non-Hispanic other, having more years of education,

Table 4. Factors Associated With Nonvitamin Dietary Supplement Use Among 20 214 Prescription Medication Users \*

Characteristic	Bivariate Logistic Regression, OR (95% CI)	Adjusted OR (95% CI)
Race/ethnicity		
White	1.00	1.00
Black	0.78 (0.70-0.88)	0.90 (0.79-1.02
Asian	1.71 (1.34-2.17)	1.31 (1.00-1.72
Other†	1.79 (1.18-2.70)	1.74 (1.17-2.60
Hispanic	1.25 (1.11-1.41)	1.37 (1.20-1.57
Age, y	,	,
≤24	1.00	1.00
25-34	1.18 (0.99-1.40)	1.00 (0.84-1.19
35-44	1.14 (0.97-1.34)	1.03 (0.87-1.22
45-54	1.27 (1.08-1.49)	1.10 (0.93-1.30
55-64	1.09 (0.92-1.29)	1.02 (0.84-1.23
≥65	0.58 (0.49-0.69)	0.66 (0.54-0.81
Sex	4.00	4.00
Male	1.00	1.00
Female	1.26 (1.16-1.37)	1.41 (1.29-1.54
Education level	1.00	1.00
<high graduate<="" school="" td=""><td></td><td>1.47 (1.26-1.71</td></high>		1.47 (1.26-1.71
High school graduate Some college	1.52 (1.31-1.76) 2.23 (1.93-2.57)	1.47 (1.26-1.71
College graduate	3.00 (2.60-3.47)	2.55 (2.16-3.02
Income, \$	0.00 (2.00 0.47)	2.00 (2.10-0.02
<15 000	1.00	1.00
15 000-34 999	1.03 (0.90-1.19)	1.00 (0.86-1.15
35 000 64 999	1.17 (1.01-1.36)	1.04 (0.89-1.21
≥65 000	1.34 (1.14-1.59)	1.07 (0.89-1.28
Other	0.67 (0.59-0.76)	0.78 (0.68-0.89
Region		
Northeast	1.00	1.00
Midwest	0.85 (0.75-0.96)	0.86 (0.75-0.97
South	0.78 (0.69-0.87)	0.82 (0.72-0.92
West	1.48 (1.31-1.68)	1.43 (1.25-1.62
Insurance: medical	1.00	1.00
Yes No	1.00	1.00
Usual source of medical	1.12 (0.98-1.28)	1.23 (1.06-1.43
care		
Yes	1.00	1.00
No	1.06 (0.89-1.27)	1.03 (0.84-1.26
Last visit to a health	, , ,	,
professional		
≤6 mo	1.04 (0.85-1.26)	1.05 (0.84-1.30
>6 mo to ≤1 y	0.97 (0.78-1.20)	0.97 (0.77-1.22
>1 y or never saw	1.00	1.00
Self-perceived health status	1.00	1.00
Excellent, very good, or good	1.00	1.00
Fair or poor	0.73 (0.65-0.81)	1.00 (0.88-1.14
Smoking status		(2.22
Never	1.00	1.00
Current	0.99 (0.90-1.09)	1.13 (1.02-1.26
Former	1.13 (1.03-1.25)	1.30 (1.17-1.45
Use fitness center	, , , ,	,
	1.00	1.00
Yes		
yes No	0.55 (0.50-0.59)	0.65 (0.59-0.72
	0.55 (0.50-0.59)	0.65 (0.59-0.72
No	0.55 (0.50-0.59) 1.00	0.65 (0.59-0.72 1.00 0.76 (0.68-0.84

Abbreviations: CI, confidence interval; OR, odds ratio.

<sup>\*</sup>Data sources: National Health Interview Survey 2002\*; weighted percentages were extrapolated from the US census (2000) for the adult civilian, noninstitutionalized, household population.

<sup>†</sup>American Indian/Alaskan Native or Pacific Islander/Native Hawaiian.

<sup>‡</sup>The chronic condition variable includes respondents with diabetes, hypertension, asthma, arthritis, depression/anxiety, coronary heart disease, hyperlipidemia, stroke, myocardial infarction, seizure disorder, congestive heart failure, thyroid problems, and chronic pain.

living in the West, being a cigarette smoker or former smoker, having chronic conditions, and lacking medical insurance. Respondents older than 65 years, those who reported less use of a fitness center, and those living in the Midwest or South were less likely to use an NVDS.

Amid increasing numbers of clinical reports describing interactions between prescription drugs and NVDS, concern has grown regarding the troubling possibility that adverse effects of NVDS are underreported. 9,12 Few studies have examined the prevalence of drug-herb/dietary supplement use patterns. <sup>13-15</sup> In our analysis, 1 in 5 prescription medication users in the United States used NVDS in the prior 12 months. Although we cannot be sure these data reflect NVDS prescription medication combinations taken concurrently, more than 27 million of those living in the United States might be taking an NVDS and a prescription medication at the same time. In 1997, an estimated 15 million people took herbal remedies and high-dose multivitamins concurrently with prescription medications, with 18.4% reporting the concurrent use of at least 1 herbal product, a high-dose vitamin, or both. 16 Kaufman et al, 17 in a national survey, noted that 16% of prescription drug users also reported use of 1 or more herbal products/ supplements within the prior week. In another analysis of the 2002 NHIS, the rate of NVDS use among elderly respondents who used prescription medications was 12.8%. 18 However, our results are inconsistent with several ambulatory care studies that found rates of concurrent prescription medication and NVDS use up to 43%. 13,14,19,20 In agreement with our findings, other studies also found that factors associated with NVDS use included being middle-aged, being female, having greater than a high school education, <sup>7,18</sup> being uninsured, <sup>21</sup> living in the West, <sup>22</sup> and using prescriptions. 17

In our study, 69% of respondents who used prescription medications did not tell any of their conventional medical professionals about their NVDS use. In 1997, Eisenberg et al<sup>16</sup> reported that 60% of NVDS and prescription medication users did not disclose this information to their primary care providers. In other national and smaller cross-sectional surveys, approximately 35% to 44% of those who take dietary supplements regularly did share this information with a health care provider. <sup>16,23</sup>

As shown in Table 1, prescription medication users with chronic but not life-threatening conditions tended to have high NVDS use. Those with chronic and possible life-threatening conditions tended to have the lowest rates of NVDS use. In the adjusted model, patients with chronic conditions requiring daily prescription medications had the higher rates of NVDS use.

There are certain patients with chronic illness who may be more susceptible to NVDS and prescription medication interactions, such as those with liver disease and kidney disease because of their limited ability to metabolize NVDSs or prescription medications. Despite this, we found that 26% of patients with liver disease and 19% of patients with kidney disease were using NVDSs and a prescription medication in the prior 12 months. Unfortunately, there is little evidence to provide clinicians with guidance on the safety of NVDS use in patients with liver and kidney disease. In addition, there is concern about potential interactions among patients taking prescrip-

tion medications with narrow therapeutic indexes of safety such as valproic acid, warfarin, and digoxin.<sup>24</sup> In our analysis, patients with seizure disorders, irregular heart beats, and congestive heart failure had relatively high NVDS use (20%, 23%, and 13%, respectively).

Many of the herbs and dietary supplements asked about in the NHIS such as chamomile and peppermint are safe for consumption. Yet, among the herbs and dietary supplements asked about in the NHIS, several are known to have well-documented drug-herb interactions. For example, an estimated 1.2 million prescription medication users with depression used St John's wort in the prior 12 months. St John's wort has been shown to lower the plasma concentration (and/or the pharmacological effect) of a number of drugs including alprazolam, amitriptyline, cyclosporine, digoxin, fexofenadine, indinavir, irinotecan, methadone, nevirapine, simvastatin, tacrolimus, theophylline, warfarin, phenprocoumon, and oral contraceptives. 25,26 Induction of P-glycoprotein and/or cytochrome P450 (CYP) enzymes (particularly CYP 3A4) by St John's wort could explain such pharmacokinetic interactions. Therefore, physicians must be aware that patients taking St John's wort run the risk of having subtherapeutic blood levels of drugs such as antirejection and human immunodeficiency virus medications. When combined with serotonin reuptake inhibitors, St John's wort may cause serotonergic syndrome.<sup>27</sup>

Although many of the 35 NVDS listed in the NHIS are safe for consumption, several may have underlying toxic effects and are particularly dangerous for patients with underlying chronic diseases such as heart disease or liver failure. For example, ephedra was used by approximately 4% of the users of both prescription medications and NVDSs. Subsequent to the 2002 NHIS, in 2003 the US Department of Health and Human Services banned the sale of ephedra after concluding that the risks associated with the use of ephedra for weight loss and sports enhancement outweighed the potential benefits.<sup>28</sup> However, ephedra is back on the market in weight loss supplements because the ban was overturned.29 Kava kava, used by approximately 6% of the users of both prescription medications and NVDSs, has been linked with hepatotoxicity and prompted regulatory agencies in the United States, Germany, Switzerland, France, Canada, and the United Kingdom to take action ranging from warning consumers about the potential risks to removing kavacontaining products from the marketplace.<sup>30</sup>

There are several limitations to our analysis. First, the survey is based on self-reported data; thus, subjects may be underreporting or overreporting their use of NVDSs. Second, we are unable to ascertain the exact proportion of respondents taking NVDSs and prescription medication concurrently. However, when we examined the rate of NVDS use among respondents with chronic conditions associated with regular medication use, the rate was also 21%. Third, the term *natural herbs*, which was used in the NHIS question (rather than dietary supplement, herbal product, or nonvitamin dietary supplement) may have been misunderstood by respondents. Respondents who took a dietary supplement such as glucosamine may not have responded positively to the question do you take a "natural herb," thus underreporting nonherbal di-

etary supplement use. Fourth, the survey listed only 35 NVDSs, although there are thousands of NVDSs sold as sport supplements, weight loss products, combination dietary supplements, or ethnic traditional medicines in the United States, which may lead to underreporting. Finally, many dietary supplements have unique common names based on the region or cultural background of the respondents, and the 35 dietary supplements may not include supplements unique to any one culture, perhaps leading to an ethnocentric and medicocentric bias in the survey instrument, which may have contributed to an underestimation of the prevalence of NVDS use, especially among nonwhite ethnic groups

Given the high frequency of NVDS and prescription medication use, physicians need to be cognizant of potential adverse effects or interactions associated with any prescribed medication or NVDS. Dietary supplements have complex mechanisms of actions and complicated pharmacokinetics, which need to be better understood. Health care professionals must regularly ask their patients with chronic conditions and prescription medications about NVDS use. More research on drug-herb interactions and postsurveillance studies are critically needed.

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