

Associations of Herbs and Nonvitamin Dietary Supplements Use with Clinical Outcomes Among Adult and Pediatric Patients with Asthma in the United States



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What is already known about this topic? As one kind of complementary and alternative medicine, herbs and nonvitamin dietary supplements (NVDS) have been broadly used among patients with asthma.

What does this article add to our knowledge? Herbs and NVDS use was not associated with a patient's likelihood of having an asthma episode, but potential benefit of these supplemental medications use on asthma-related emergency department visits might exist for adult patients with asthma.

How does this study impact current management guidelines? Based on this study, herbs and NVDS use among patients with asthma needs to be considered and further evaluated.

BACKGROUND: Herbs and nonvitamin dietary supplements (NVDS) have been commonly used among patients with asthma, yet evidence of their impact on patients' clinical outcomes is limited.

OBJECTIVE: This study examined the associations of herbs and NVDS use with asthma episodes and asthma-related emergency department (ED) visits among US adults and pediatric patients with asthma.

METHODS: A cross-sectional analysis of the 2012 National Health Interview Survey data included 2,930 US adults and 1923 children with self-reported asthma. We estimated the prevalence and type of herbs and/or NVDS use and identified factors associated with their use. We then used multivariable logistic regression models to examine the associations between these supplemental medications use and asthma outcomes, controlling for patient-related covariates. All results were weighted to represent national estimates.

RESULTS: Approximately 7.20% of American children and 21.17% of adults with asthma used herbs and/or NVDS in 2012. Herb and/or NVDS users were more likely to be female, non-Hispanic white, living in the West region, having higher family income, and having comorbidities compared with nonusers.

Herbs and/or NVDS use was associated with lower likelihood of having asthma-related ED visit (adjusted odds ratio = 0.48; 95% confidence interval: 0.31, 0.75) among adult patients with asthma, but not for pediatric patients with asthma. No association between herbs and/or NVDS use and having an asthma episode was observed in either adults or children.

CONCLUSIONS: This study found high prevalence of herbs and/or NVDS use among US patients with asthma. Potential benefit of these supplemental medications use on asthma-related ED visits might exist for adult patients with asthma. © 2017 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2018;6:936-43)

Key words: Asthma; Asthma episodes; Clinical outcomes; Dietary supplements; Emergency department visits; Herb

Asthma is one of the most common allergic diseases in the world.^{1,2} It is a chronic lung disease with characteristics that are variable and recurrent and include reversible airflow obstruction and bronchospasm.^{1,2} Asthma can cause recurring periods of coughing, wheezing, tachypnea, dyspnea, hypoxemia, and mucus plugging.^{1,2} It not only affects the function of the body but also reduces patients' quality of life.³⁻⁶ During the years 2001-2010, an estimated 25.7 million Americans, including 18.7 million adults and 7.0 million children, had been diagnosed with asthma.⁷

As a chronic disease,^{1,2} asthma treatment typically involves symptom management and control by using a variety of medications such as β -agonists, corticosteroids, and leukotriene modifiers.^{2,8,9} In addition, an increasing number of Americans pursue complementary and alternative medicine (CAM) to improve quality of life.¹⁰⁻¹² Research has indicated that 40% of adult¹³ and 27% of pediatric patients¹⁴ with asthma in United States may use CAM. There are a variety of CAM that have been used for asthma management, such as herbs, dietary supplements, homeopathy, chiropractic, acupuncture, hypnosis,

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Abbreviations used

ALT- Adult Alternative Medicine file
AOR- Adjusted odds ratio
CAL- Child Alternative Medicine file
CAM- Complementary and alternative medicine
CI- Confidence intervals
ED- Emergency department
NCHS- National Center for Health Statistics
NHIS- National Health Interview Survey
NVDS- Nonvitamin dietary supplements

relaxation techniques, and Chinese, Japanese, and Indian medicines.¹⁵ There also has been considerable research investigating the motivations of patients with asthma pursuing CAM treatment. In general, patients with asthma seek CAM treatments for health promotion and disease prevention.¹⁶ As the most commonly used CAM,^{17,18} herbs and/or nonvitamin dietary supplements (NVDS) have higher prevalence (17.7% and 4.9% for adults¹⁹ and children,²⁰ respectively) and have been indicated to have potential benefits for asthma management.²¹⁻²⁴

Despite the high prevalence of herbs and/or NVDS use in patients with asthma and the potential beneficial effect on asthma management,^{17,18,21-24} there have not been any nationally representative studies to assess their impact on clinical outcomes of patients with asthma in real-world settings. Therefore, the main objectives of this study were to estimate the utilization patterns of herbs and/or NVDS use among adult and pediatric patients with asthma in United States, and to examine the associations between herbs and/or NVDS use and asthma-related clinical outcomes.

METHODS

Study sample

This was a retrospective cross-sectional study design using the 2012 National Health Interview Survey (NHIS) datasets, which is a large scale of continuing probability survey of households' representative of the civilian noninstitutionalized population in the United States. It is conducted annually by the National Center for Health Statistics, Centers for Disease Control and Prevention. The NHIS administers face-to-face interviews in a nationally representative sample of households. In 2012, more than 100,000 US individuals in 43,345 families responded to the NHIS.

For this study, we used the Adult and Child CAM files, the person file, and imputed income files in the 2012 NHIS datasets. Adult Alternative Medicine file (ALT) and Child Alternative Medicine file (CAL) are 2 NCHS-added supplementary questionnaires. These 2 core surveys collected information on various types of CAM use among respondents. The response rates for ALT and CAL in 2012 were 61.2% and 69.7%, respectively. The Sample Child Core obtains additional information on the health of one randomly selected child (the sample child) in the family. For sample children, information is provided by a knowledgeable adult family member residing in the household. In 2012, the supplement included sample children aged 4-17 years ($n = 13,275$ children). The Person File contains information on health status and limitation of activity, health care access and utilization, health insurance, sociodemographics, and income and assets. The information of family income data is in the Imputed Income File. A detailed description of the

NHIS sample design and the survey questionnaires for specific years is available from NHIS description documents.²⁵

The study population was limited to US adults (aged ≥ 18) and children (aged 4-17) with concurrent asthma. Both adult and pediatric participants were classified as having current asthma by answering "yes" to both of the following questions: "Has a doctor or other health professional EVER told you that you had asthma?" and "Do you still have asthma?" Individuals who responded "no" to "Do you still have asthma?" were considered as formerly but not currently having asthma and were excluded from the analysis. We also excluded individuals with missing or incomplete data on asthma status ($n = 20$ adults and $n = 12$ children). The final study sample size included 2,930 adults (weighted $n = 19,168,471$) and 1,923 children (weighted $n = 10,353,461$). This study was approved by the Auburn University institutional review board.

Measurements

Herbs and/or NVDS use was measured as a binary variable from the 2012 ALT and CAL files based on the question: "During the past 12 months, have you taken any herbal medication or other nonvitamin supplements listed on this card for yourself?" The individual herbs and NVDS included in the survey can be found at the NHIS website.²⁶

Asthma clinical outcomes were identified as binary variables of having asthma episodes (yes/no) and having asthma-related emergency department (ED) visits (yes/no) among patients with asthma. Two questions from the ATL and CAL files were asked to the respondents to determine whether they had asthma episodes or went to ED because of asthma in the past 12 months. The first question was: "During the past 12 months, have you had an episode of asthma or an asthma attack?" The question pertaining to the ED visit because of asthma was: "During the past 12 months, have you had to visit an ED or urgent care center because of asthma?"

The following covariates were also identified from Sample Adult File, Sample Child File, Person File, and Imputed Income Files: sociodemographic variables included sex (male and female), race/ethnicity (non-Hispanic white, non-Hispanic black, Asian, Hispanic, or others), age (18-44, 45-64, ≥ 65 in the adult sample and 4-10, 10-17 in the pediatric sample), region (Northeast, Midwest, West, and South), marital status, annual family income, drinking, smoking, physical activities status, and the status of adult family members using herbs and/or NVDS (only in pediatric sample). Comorbidity variables included the self-reported diagnosis of mental disorder, chronic obstructive pulmonary disease, emphysema, hypertension, bronchitis, influenza/phenomena, sinusitis, acid reflux/heartburn, and allergy conditions in the past 12 months (respiratory allergy, hay fever, food allergy, and eczema).

Statistical analyses

First, we estimated the prevalence of herbs and/or NVDS use, overall and by individual type, among adult and pediatric patients with asthma. Then we compared covariates between patients with asthma with and without any herbs and/or NVDS use in both adult and pediatric asthma samples using χ^2 tests. Proportions of participants with any asthma episodes and asthma-related ED visits were also compared between patients with asthma with and without any herbs and/or NVDS use in both adult and pediatric asthma samples. Proportion estimates were calculated by using NHIS weights, which were calibrated to the US 2010 census totals for sex, age, and race/ethnicity of the 2012 US population.

TABLE I. Sample characteristics for US adults with asthma and adjusted odds ratios of associations with herbs and/or nonvitamin dietary supplements (NVDS) use among adult patients with asthma (N = 2,930, weighted n = 19,168,471)

Variable	Patients with asthma				Likelihood of using herbs and NVDS	
	Herb and NVDS users		Herb and NVDS non-users		P†	AOR (95% CI)‡
	N = 594	Weighted % (21.17)	N = 2,336	Weighted % (78.83)		
Age, y					.0001†	
18-44	221	40.38	1,045	50.03		Ref
45-64	264	45.28	824	34.08		1.68 (1.26-2.25)
≥65	109	14.34	467	15.89		1.16 (0.74-1.80)
Sex					.0263†	
Male	153	30.58	792	37.67		Ref
Female	441	69.42	1,544	62.33		1.32 (1.00-1.78)
Race/ethnicity					<.0001†	
Non-Hispanic white	423	76.96	1,369	65.24		Ref
Non-Hispanic black	67	8.04	483	16.52		0.63 (0.42-0.95)
Asian	24	3.19	71	2.82		0.91 (0.50-1.66)
Hispanic	50	7.02	340	12.60		0.55 (0.34-0.89)
Others	30	4.79	73	2.82		1.43 (0.80-2.58)
Region					<.0001†	
Northeast	94	16.08	513	22.52		Ref
Midwest	127	26.27	486	22.78		1.53 (0.96-2.44)
South	156	23.92	826	35.70		1.02 (0.67-1.53)
West	217	33.73	511	19.00		2.54 (1.66-3.89)
Marital status					.0075†	
Not married and other	351	47.47	1,525	55.91		Ref
Married	243	52.53	811	44.09		0.98 (0.72-1.32)
Annual family income					<.0001†	
≤\$14,999	104	10.95	722	23.14		Ref
\$15,000-\$34,999	115	15.58	578	22.59		1.25 (0.83-1.89)
\$35,000-\$64,999	151	27.53	512	23.53		1.87 (1.20-2.91)
≥\$65,000	224	45.94	524	30.74		2.21 (1.43-3.41)
Physical activity level					<.0001†	
Low	208	33.29	1,199	50.68		Ref
Moderate	177	33.28	515	22.91		1.81 (1.29-2.53)
High	209	33.43	622	26.41		1.62 (1.18-2.23)
Drink					.0004†	
No drink	183	30.55	1,025	42.30		Ref
Social drink	309	52.33	959	42.78		1.37 (0.99-1.91)
Often drink	102	17.12	352	14.92		1.42 (0.97-2.06)
Smoking					.0104†	
Nonsmoker	321	52.83	1,222	52.85		Ref
Former smoker	172	30.52	562	24.09		1.15 (0.84-1.58)
Current smoker	101	16.65	552	23.06		0.83 (0.55-1.26)
Mental disorder					.0850	
No	332	56.46	1,366	61.53		
Yes	262	43.54	970	38.47		
COPD					.4571	
No	528	88.76	1,994	86.74		Ref
Yes	66	11.24	342	13.26		0.82 (0.48-1.42)
Emphysema					.2532	
No	566	93.82	2,113	90.91		
Yes	28	6.18	223	9.09		
Hypertension					.2900	
No	336	56.36	1,318	59.46		
Yes	258	43.64	1,018	40.54		

(continued)

TABLE I. (Continued)

Variable	Patients with asthma				Likelihood of using herbs and NVDS	
	Herb and NVDS users		Herb and NVDS non-users		<i>P</i> [†]	AOR (95% CI) [‡]
	N = 594	Weighted % (21.17)	N = 2,336	Weighted % (78.83)		
Bronchitis					.8638	
No	489	82.82	19,00	82.37		
Yes	105	17.18	436	17.63		
Influenza/pneumonia					.0498 [†]	
No	518	86.69	2,100	90.37		Ref
Yes	76	13.31	236	9.63		1.30 (0.88-1.93)
Sinusitis					.0028 [†]	
No	386	67.51	1,731	75.16		Ref
Yes	208	32.49	605	24.84		1.21 (0.91-1.62)
Flu shot					.0015 [†]	
No	226	37.81	1,039	47.13		Ref
Yes	368	62.19	1,297	52.87		1.28 (0.96-1.71)
Acid reflux/heartburn					.0698	
No	337	57.24	1,450	62.65		
Yes	257	42.76	886	37.35		
Other allergy conditions [§]						
0	212	33.45	1,153	48.56	<.0001 [†]	Ref
1	197	33.59	656	28.99		1.11 (0.83-1.47)
≥2	185	31.96	527	22.44		1.78 (1.09-2.89)

COPD, Chronic obstructive pulmonary disease.

Bold indicates statistical significance (*P* < .05).

*Weighted percent.

[†] χ^2 test significant at *P* < .05.

[‡]All covariance variables that had χ^2 test *P* ≥ .05 or small cell size (<20) were removed from the multivariable logistic regression models; adjusted odds ratios (AOR) and 95% confidence intervals (CI) were reported.

[§]Other allergy conditions included a history of respiratory allergy, hay fever, food allergy, and eczema in the past 12 mo.

We conducted a total of 5 multivariable logistic regression models to identify factors associated with any herbs and/or NVDS use among patients with asthma (model 1: adults; model 2: pediatrics), and test the associations between any herbs and/or NVDS use with asthma outcomes (model 3: having asthma episodes; model 4: having asthma-related ED visits) among adults patients with asthma. Because of the small numbers of asthma-related ED visits for pediatric patients with asthma, only 1 multivariable logistic model (model 5) was completed to access the association between herbs and/or NVDS use and the likelihood of having an asthma episode in pediatric patients with asthma. All multivariable models were adjusted for covariates that were statistically significant in the bivariable analysis at *P* < .05. We further tested the significance of the interaction term of herbs and/or NVDS use and family income in models 3 and 4 because the previous literature has indicated that individuals with higher income are more likely to prefer supplemental treatments.²⁷⁻²⁹ The results from multivariable models were weighted to represent national adult and pediatric patients with asthma. The parameter estimates from the models were presented as adjusted odds ratio (AOR) and their corresponding 95% confidence intervals (CI). Statistical significance was tested at *P* < .05.

RESULTS

Patterns of herbs and/or NVDS use among US adult and pediatric patients with asthma

The descriptions of the study sample are presented in Table I (adults) and Table II (pediatrics). In 2012, approximately

21.17% adult and 7.20% pediatric patients with asthma used at least one herb and/or NVDS in the last 12 months. Adjusted results showed that adult patients with asthma who were older, female, non-Hispanic white, residing in West region, with higher family income, having better physical activity level, and having more allergy conditions were more likely to use herbs and/or NVDS than their counterparts (Table I, all *P* < .05). In addition, pediatric patients with asthma who were older in age, non-Hispanic white, residing in West region, with higher family income, living with family members using herbs or NVDS, and not having flu shot were more likely to use herbs and/or NVDS than their counterparts (Table II, all *P* < .05).

The prevalence of top 10 types of herbs and/or NVDS use among adult and pediatric patients with asthma is shown in Table III. In 2012, the top 5 commonly used individual herbs and/or NVDS among US adults with asthma included fish oil (13.31%), probiotics or prebiotics (3.89%), glucosamine (3.98%), melatonin (3.76%), and Echinacea (3.17%). The top 5 commonly used individual herbs and/or NVDS among US pediatric patients with asthma included fish oil (2.62%), melatonin (1.91%), probiotics or prebiotics (1.50%), Echinacea (1.15%), and chondroitin (0.11%).

Associations between herbs and/or NVDS use and asthma outcomes

Compared with adult patients with asthma without any herbs and/or NVDS use (Table IV), those adults who used herbs

TABLE II. Sample characteristics and factors of herbs and/or nonvitamin dietary supplements (NVDS) use pattern for US pediatric patients with asthma (N = 1,923, weighted n = 10,321,849) and adjusted odds ratios of associations with herbs and/or NVDS use among pediatric patients with asthma

Variable	Patients with asthma			
	Herb and NVDS users	Herb and NVDS nonusers	P†	Likelihood of using herbs and NVDS AOR (95% CI)‡
	N (%)*	N (%)*		
	N = 132 (7.20)	N = 1,791 (92.80)		
Age, y				
4-10	45 (33.89)	882 (50.79)	.0032†	Ref
≥10	87 (66.11)	909 (49.21)		1.72 (1.04-2.84)
Sex				
Male	75 (59.20)	1,024 (57.93)	.8291	Ref
Female	57 (40.80)	767 (42.07)		1.14 (0.68-1.93)
Race/ethnicity				
Non-Hispanic white	67 (55.00)	705 (46.69)	.0008†	Ref
Non-Hispanic black	17 (10.36)	428 (21.93)		0.63 (0.42-0.95)
Hispanic	27 (15.83)	480 (23.24)		0.50 (0.38-1.66)
Others	21 (18.81)	178 (8.14)		1.83 (1.01-3.31)
Region				
Northeast	22 (16.37)	320 (17.34)	.0262†	Ref
Midwest	28 (26.03)	310 (20.13)		0.98 (0.48-2.00)
South	36 (27.06)	724 (41.31)		0.70 (0.33-1.46)
West	46 (30.53)	437 (21.22)		1.85 (1.32-2.59)
Family information				
Annual family income				
≤\$14,999	14 (10.56)	360 (18.22)	.0170†	Ref
\$15,000-\$34,999	23 (14.05)	468 (24.18)		1.25 (0.78-2.01)
\$35,000-\$64,999	33 (27.90)	388 (21.14)		1.73 (1.13-2.66)
≥\$65,000	62 (47.50)	575 (36.46)		2.05 (1.37-3.07)
Adults family members using herbs and/or NVDS				
No	76 (53.95)	1,638 (90.93)	<.0001†	Ref
Yes	56 (46.05)	153 (9.07)		6.77 (3.6-11.58)
Sinusitis				
No	105 (79.50)	1,555 (86.07)	.0970	
Yes	27 (20.50)	236 (13.93)		
Pediatrics visit				
≤1	23 (19.19)	413 (23.05)	.0804	
2-5	81 (59.25)	1,156 (63.90)		
≥6	28 (21.55)	222 (13.06)		
Flu shot				
No	75 (63.02)	895 (49.42)	.0104†	Ref
Yes	57 (36.98)	896 (50.58)		0.63 (0.39-0.99)
Other allergy conditions				
0	52 (39.62)	911 (50.39)	.0151†	Ref
1	37 (26.65)	518 (28.40)		0.64 (0.29-1.40)
≥2	43 (33.73)	362 (21.20)		0.63 (0.15-2.65)

Bold indicates statistical significance ($P < .05$).

Other allergy conditions included a history of respiratory allergy, hay fever, food allergy, and eczema in the past 12 mo.

*Weighted percent.

† χ^2 test significant at $P < .05$.‡All covariance variables that had χ^2 test $P \geq .05$ or small cell size (<20) were removed from the multivariable logistic regression models; adjusted odds ratios (AOR) and 95% confidence intervals (CI) were reported.

and/or NVDS had a lower rate (7.64% vs 13.43%, $P = .001$) of asthma ED visits in the past 12 months, but no difference in having asthma episodes was observed ($P = .692$). For pediatric patients with asthma, there was no difference in having either asthma-related ED visits or asthma episodes between children

with and without herbs and/or NVDS use. Multivariable results confirmed that herbs and/or NVDS use was independently associated with the lower likelihood of having asthma-related ED visits (AOR = 0.48, 95% CI = 0.31, 0.75) but not associated with the likelihood of having asthma episodes (AOR = 0.95,

TABLE III. Top 10 weighted frequencies of adult and pediatric patients with asthma who used selected types of herbs and/or nonvitamin dietary supplements (NVDS) in the past 30 days

Herb and NVDS use in past 12 mo	Adults*	Children*
	Weighted % (standard error)	Weighted % (standard error)
Fish oil (or omega 3, DHA, or EPA fatty acid)	13.31 (0.82) [†]	2.62 (0.50) [†]
Glucosamine	3.89 (0.43) [†]	0.11 (0.11)
Probiotics or prebiotics	3.98 (0.48) [†]	1.50 (0.38) [†]
Melatonin	3.76 (0.45) [†]	1.91 (0.40) [†]
Echinacea	3.17 (0.40) [†]	1.15 (0.32) [†]
Cranberry pills or capsules	2.68 (0.36)	0.07 (0.07)
Ginseng	2.37 (0.41)	0.09 (0.09)
Combination herb pill	1.97 (0.25)	0.09 (0.05)
Co-enzyme Q10	1.87 (0.29)	0.04 (0.04)
Chondroitin	1.79 (0.27)	0.11 (0.11) [†]

DHA, Docosahexaenoic acid; EPA, eicosapentaenoic acid.

*Respondents may have used more than one herb and NVDS product.

[†]Top 5 products.

TABLE IV. Associations between use of herbs and/or NVDS with asthma clinical outcomes among adult and pediatric patients with asthma*

Asthma								
Variable	Having asthma episode in last 12 mo				Having asthma-related ED visit in last 12 mo			
	N (%)†		AOR (95% CI)		N (%)†		AOR (95% CI)	
Adults patients with asthma‡								
Herb and NVDS users	Yes	No	P§		Yes	No	P§	
Yes	311 (53.09)	283 (46.91)	.692	0.95 (0.74-1.22)	52 (7.64)	542 (92.36)	.001§	0.48*(0.31-0.75)
No	1,121 (49.11)	1,215 (50.89)	Ref		342 (13.43)	1,994 (86.57)	Ref	
Pediatric patients with asthma								
Herb and NVDS users	Yes	No			Yes	No	.984	
Yes	53 (44.56)	79 (55.44)	.212	1.05 (0.58-1.90)	22 (14.81)	270 (85.19)	N/A	
No	654 (38.26)	1,137 (61.74)	Ref		270 (14.73)	1,521 (85.27)		

COPD, Chronic obstructive pulmonary disease; ED, emergency department; NVDS, nonvitamin dietary supplements.

Bold indicates statistical significance ($P < .05$).

*Other covariance variables that had χ^2 test $P < .05$ were collected into the multivariable logistic regression models; adjusted odds ratios (AOR) and 95% confidence intervals (CI) were reported.

[†]Weighted percent.

[‡]For adults, covariance variables in both asthma episode and ED visit included sex, race, age, region, marital status, family income, mental disorders, pneumonia, COPD, respiratory allergy, hay fever, allergy conditions, and interaction of herbs and/or NVDS use.

[§]Chi-square.

^{||}For children, covariance variables in asthma episode included sex, race, age, region, family income, family herbs and/or NVDS use, respiratory allergy, hay fever, and allergy conditions.

95% CI = 0.74, 1.22), controlling for all covariates, among adult patients with asthma. The interaction term of herbs and/or NVDS use and family income was not significant ($P = .785$), indicating that income did not modify the association between herbs and/or NVDS use and lower likelihood of asthma-related ED visits.

DISCUSSION

This study provides the first nationally representative profile of herbs and/or NVDS use in adult and pediatric populations with asthma. We found that approximately 7.20% American children and 21.17% of adults with asthma used herbs and/or NVDS in 2012. Although the prevalence of herbs and/or NVDS use among pediatric patients with asthma was much lower than adults, it almost doubled compared with its use in the general US pediatric population (4.9%, 2007).²⁰ The prevalence of herbs and/or NVDS use among adult patients with asthma was also

higher than its use in the general US adult population (17.7%, 2012).¹⁹ Fish oil, probiotics or prebiotics, melatonin, and Echinacea were the most commonly used herbs and/or NVDS among both adult and pediatric patients with asthma in the United States.

The high prevalence of herbs and/or NVDS use among adults and pediatric patients with asthma is worthy of attention of caregivers, providers, and policy makers. Specifically, melatonin is the second most commonly used supplement among pediatric patients with asthma. Numerous studies have reported that there may be potential benefits of melatonin in the treatment of asthma by the suppression of airway inflammation³⁰⁻³² or improvement of sleep quality.³³ However, melatonin has also been shown to have differential immunomodulatory effects based on asthma clinical phenotype, suggesting a potential adverse effect of exogenous melatonin in some patients with asthma.³² Research suggests that melatonin supplements may make asthma symptoms worse in people who already suffer from

nocturnal asthma.³⁴ Adverse effects of melatonin on some children with asthma could contribute to the overall lack of association with positive asthma outcomes observed in children (vs adults) in this study. Given the potential side effects and possible interactions between prescriptions and herbs and/or NVDS,³⁵ it is important for physicians to be aware of patients' herbs and/or NVDS use, monitor closely, and investigate its potential benefit and risk in asthma symptom management.

One of the main objectives of this study was to examine the associations between herbs and/or NVDS use and asthma-related clinical outcomes in both adult and pediatric populations with asthma. We found that the use of these supplement products among adults with asthma was associated with less likelihood (52% less) of self-reported asthma-related ED visits but similar likelihood of self-reported asthma episodes compared with those who did not use herbs and/or NVDS. No associations between herbs and/or NVDS use and asthma-related clinical outcomes among pediatric patients with asthma were observed. This is the first evidence that we are aware of to document association between herbs and/or NVDS use and asthma clinical outcomes using real-world, nationally representative population level data. Although previous research has indicated potential health benefits of dietary supplements on asthma symptoms such as reducing wheeze and cough as well as improving shortness of breath in adults with asthma,³⁶ we found no evidence of lower likelihood of having asthma episode in either adult or pediatric patients with asthma who used herbs and/or NVDS compared with those who did not use. Evidence indicated that some herb products, such as quercetin and flavonoids, have antiallergic properties by improving the immune system, inhibition of histamine release, decreasing proinflammatory cytokines, leukotrienes creation, and suppressing IL-4 production.³⁷⁻³⁹ Our findings indicate that herbs and/or NVDS use might improve the immune system of patients with asthma but not necessarily help manage asthma-related symptoms so that some more severe adverse events, such as asthma-related ED visit, can be reduced. In addition, the insignificant interaction term of herbs and/or NVDS use and family income indicated that the relationship between reduced asthma-related ED visits and herbs and/or NVDS use among adult patients with asthma was not mediated by socioeconomic factors such as income. This finding further suggested that herbs and/or NVDS use was an independent factor associated with lower asthma-related ED visits among adult patients with asthma. Given the inadequate statistical power for the pediatric group in this study, future studies with better design and larger sample size are warranted to assess the association between herbs and/or NVDS use and asthma-related outcomes among the pediatric population.

Another goal of this study was to determine the factors associated with herbs and NVDS use among adults and children with asthma. We found some significant differences in herbs and/or NVDS use among different sex, race/ethnicity, geographic region, and family income subgroups in both adults and pediatric patients with asthma. Specifically, we found that non-Hispanic black and Hispanic adult and pediatric patients with asthma were less likely to use herbs and/or NVDS compared with their non-Hispanic white counterparts. We also found that patients with asthma who were female, residing in the West region of the country, and with higher family income were more likely to use herbs and/or NVDS. Our findings are consistent with previous studies focusing on the general US adult population.^{17,40,41}

Given the high prevalence of herbs and/or NVDS use among both pediatric and adult patients with asthma in the United States found in this study, practitioners such as primary care providers, lung specialists, or integrative medicine clinicians should carefully document and closely monitor herbs and/or NVDS use in patients with asthma to ensure that these supplements are appropriate and safe to use, especially for patients with special demographic and socioeconomic profiles identified from our study.

In addition, our results indicated that those adult patients with asthma with higher physical activity level were more likely to use herbs and/or NVDS. This indicates that adult patients with asthma who use herbs and/or NVDS are more likely to have better health behaviors. Indeed, evidence has shown that dietary supplement users are more likely to be nonsmokers, physically active, and less likely to have risk factors of chronic conditions such as cardiovascular diseases.⁴² Thus, herbs and NVDS use may serve as a marker for the many possible factors that may be related to the better health behaviors and higher socioeconomic status. Such factors may also be associated with high medication adherence⁴³ or response to conventional treatment, emotional support,⁴⁴ as well as better health outcomes.

Limitations

There are several limitations with this study. First, the self-report nature of survey data usually introduces recall bias. Data in the CAL file were reported by children's adult proxies, who may or may not be their primary caregivers. The majority of variables, particularly self-reported asthma episode and ER visit, were derived from single survey questions, which may affect the precision of measurements and thereby introduces measurement bias. Second, the cross-sectional study design cannot derive causal relationships between herbs and/or NVDS treatment and asthma outcomes. The limited numbers of asthma outcome events among pediatric patients with asthma also prevented us to conduct multivariable analysis to determine the association between herbs and/or NVDS use and asthma-related ED visits in this population. Third, we combined a total of 22 types of herbs and/or NVDS into a single binary independent variable due to the limited study sample size. It is possible that asthma severity, asthma episode, and ER visit, or other adverse events could vary among different types of herbs and/or NVDS, which could be investigated among larger samples in the future. Fourth, with respect to asthma severity and interaction between NVDS and traditional medications, the NHIS does not include any item that probes the extent to which these factors affect the life of an individual with asthma. In addition, the lack of information among participants regarding reasons for taking herbs and/or NVDS or adverse reactions to them prevented us from further investigating the causal relationship between herbs and/or NVDS use and asthma management in this study sample. Finally, this study did not capture potential confounders, such as type of care (eg, specialty), medication use (type and adherence), environmental exposures, and different levels of health literacy of patients with asthma.

CONCLUSIONS

In conclusion, our findings provide the first national estimates in herbs and/or NVDS among US adult and pediatric patients with asthma. The prevalence of herbs and/or NVDS use is high among both adult and pediatric patients with asthma. We found

the lower likelihood of having asthma-related ED visits associated with herbs and/or NVDS use among adult patients with asthma. No association between herbs and/or NVDS use and having an asthma episode was observed in either the adult or pediatric sample. Practitioners should closely monitor patterns of herbs and/or NVDS among patients with asthma to help balance its benefits and risks in patient wellness and clinical outcomes. Further studies of the relationships of herbs and/or NVDS use to clinical asthma outcomes and patients' quality of life are warranted.

REFERENCES

1. US Department of Health and Human Services. National Heart, Lung and Blood Institute: Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma (EPR-3 2007). NIH Item No. 08-4051; 2007. Available from: <https://www.nhlbi.nih.gov/files/docs/guidelines/asthsumm.pdf>. Accessed October 15, 2017.
2. Bateman ED, Hurd SS, Barnes PJ, Bousquet J, Drazen JM, FitzGerald M, et al. Global strategy for asthma management and prevention: GINA executive summary. *Eur Respir J* 2008;31:143-78.
3. Zhang X. World Health Organization (WHO). General guidelines for methodologies on research and evaluation of traditional medicine; 2000. Available from: http://apps.who.int/iris/bitstream/10665/66783/1/WHO_EDM_TRM_2000.1.pdf. Accessed October 15, 2017.
4. Leynaert B, Neukirch C, Liard R, Bousquet J, Neukirch F. Quality of life in allergic rhinitis and asthma: a population-based study of young adults. *Am J Respir Crit Care Med* 2000;162:1391-6.
5. Goldney RD, Ruffin R, Fisher LJ, Wilson DH. Asthma symptoms associated with depression and lower quality of life: a population survey. *Med J Aust* 2003;178:437-41.
6. Sullivan PW, Smith KL, Ghushchyan VH, Globe DR, Lin S-L, Globe G. Asthma in USA: its impact on health-related quality of life. *J Asthma* 2013;50:891-9.
7. Akinbami LJ, Moorman JE, Bailey C, Zahran HS, King M, Johnson CA, et al. Trends in asthma prevalence, health care use, and mortality in the United States, 2001-2010. *NCHS Data Brief* 2012;94:1-8.
8. Busse W, Corren J, Lanier BQ, McAlary M, Taylor AF, Cioppa GD, et al. Omalizumab, anti-IgE recombinant humanized monoclonal antibody, for the treatment of severe allergic asthma. *J Allergy Clin Immunol* 2001;108:184-90.
9. US Department of Health and Human Services. National Institute of Health, National Heart, Lung, and Blood Institute. National Asthma Education and Prevention Program, "Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma," Full Report 2007; 2009.
10. Astin JA. Why patients use alternative medicine: results of a national study. *JAMA* 1998;279:1548-53.
11. Eisenberg DM, Davis RB, Ettner SL, Appel S, Wilkey S, Rompay MV, et al. Trends in alternative medicine use in the United States, 1990-1997: results of a follow-up national survey. *JAMA* 1998;280:1569-75.
12. Tindle HA, Davis RB, Phillips RS, Eisenberg DM. Trends in use of complementary and alternative medicine by US adults: 1997-2002. *Altern Ther Health Med* 2005;11:42.
13. Marino LA, Shen J. Characteristics of complementary and alternative medicine use among adults with current asthma, 2006. *J Asthma* 2010;47:521-5.
14. Shen J, Oraka E. Complementary and alternative medicine (CAM) use among children with current asthma. *Prev Med* 2012;54:27-31.
15. Zhang X, Organization WH. General guidelines for methodologies on research and evaluation of traditional medicine. World Health Organization; 2000:1-71.
16. Hawk C, Ndetan H, Evans MW. Potential role of complementary and alternative health care providers in chronic disease prevention and health promotion: an analysis of National Health Interview Survey data. *Prev Med* 2012;54:18-22.
17. Kennedy J. Herb and supplement use in the US adult population. *Clin Ther* 2005;27:1847-58.
18. Wu C-H, Wang C-C, Tsai M-T, Huang W-T, Kennedy J. Trend and pattern of herb and supplement use in the United States: results from the 2002, 2007, and 2012 national health interview surveys. *Evid Based Complement Alternat Med* 2014;2014:872320.
19. Clarke TC, Black LI, Stussman BJ, Barnes PM, Nahin RL. Trends in the use of complementary health approaches among adults: United States, 2002-2012. *Natl Health Stat Report* 2015;(79):1.
20. Black LI, Clarke TC, Barnes PM, Stussman BJ, Nahin RL. Use of complementary health approaches among children aged 4-17 years in the United States: National Health Interview Survey, 2007-2012. *Natl Health Stat Report* 2015;(78):1.
21. Guo C-H, Liu P-J, Lin K-P, Chen P-C. Nutritional supplement therapy improves oxidative stress, immune response, pulmonary function, and quality of life in allergic asthma patients: an open-label pilot study. *Altern Med Rev* 2012;17:42-56.
22. Gvozdjaková A, Kucharská J, Bartkovjaková M, Gazdík K, Gazdík F. Coenzyme Q10 supplementation reduces corticosteroids dosage in patients with bronchial asthma. *Biofactors* 2005;25:235-40.
23. Wendell SG, Baffi C, Holguin F. Fatty acids, inflammation, and asthma. *J Allergy Clin Immunol* 2014;133:1255-64.
24. Wen M-C, Wei C-H, Hu Z-Q, Srivastava K, Ko J, Xi S-T, et al. Efficacy and tolerability of antiasthma herbal medicine intervention in adult patients with moderate-severe allergic asthma. *J Allergy Clin Immunol* 2005;116:517-24.
25. National Center for Health Statistics. Data file documentation, National Health Interview Survey, 2012 (machine readable data file and documentation). Hyattsville, Md: National Center for Health Statistics; 2012. Available from: ftp://ftp.cdc.gov/pub/Health_Statistics/NCHS/Dataset_Documentation/NHIS/2012/srvydesc.pdf. Accessed October 15, 2017.
26. National Center for Health Statistics. NHIS survey description. 2012 National Health Interview Survey (NHIS): Public use data release. Available from: ftp://ftp.cdc.gov/pub/Health_Statistics/NCHS/Dataset_Documentation/NHIS/2012/srvydesc.pdf. Accessed October 15, 2017.
27. Kao GD, Devine P. Use of complementary health practices by prostate carcinoma patients undergoing radiation therapy. *Cancer* 2000;88:615-9.
28. Morris KT, Johnson N, Homer L, Walts D. A comparison of complementary therapy use between breast cancer patients and patients with other primary tumor sites. *Am J Surg* 2000;179:407-11.
29. Palinkas LA, Kabongo ML, Group SNS. The use of complementary and alternative medicine by primary care patients. *J Fam Pract* 2000;49:1121-32.
30. Gumral N, Naziroglu M, Ongel K, Beydilli ED, Ozguner F, Sutcu R, et al. Antioxidant enzymes and melatonin levels in patients with bronchial asthma and chronic obstructive pulmonary disease during stable and exacerbation periods. *Cell Biochem Funct* 2009;27:276-83.
31. Luo F, Liu X, Li S, Liu C, Wang Z. Melatonin promoted chemotaxis expression in lung epithelial cell stimulated with TNF- α . *Respir Res* 2004;5:20.
32. Sutherland ER, Martin RJ, Ellison MC, Kraft M. Immunomodulatory effects of melatonin in asthma. *Am J Respir Crit Care Med* 2002;166:1055-61.
33. Campos FL, da Silva-Júnior FP, de Bruin VM, de Bruin PF. Melatonin improves sleep in asthma: a randomized, double-blind, placebo-controlled study. *Am J Respir Crit Care Med* 2004;170:947-51.
34. Sutherland ER, Ellison MC, Kraft M, Martin RJ. Elevated serum melatonin is associated with the nocturnal worsening of asthma. *J Allergy Clin Immunol* 2003;112:513-7.
35. Ernst E, Posadzki P. Alternative therapies for asthma: are patients at risk? *Clin Med* 2012;12:427-9.
36. Watson RR, Zibadi S, Rafatpanah H, Jabbari F, Ghasemi R, Ghafari J, et al. Oral administration of the purple passion fruit peel extract reduces wheeze and cough and improves shortness of breath in adults with asthma. *Nutr Res* 2008;28:166-71.
37. Li J, Zhang F, Li J. The immunoregulatory effects of traditional Chinese medicine on treatment of asthma or asthmatic inflammation. *Am J Chin Med* 2015;43:1059-81.
38. Micek J, Jurikova T, Skrovankova S, Sochor J. Quercetin and its anti-allergic immune response. *Molecules* 2016;21:623.
39. Kawai M, Hirano T, Higa S, Arimitsu J, Maruta M, Kuwahara Y, et al. Flavonoids and related compounds as anti-allergic substances. *Allergol Int* 2007;56:113-23.
40. Kantor ED, Rehm CD, Du M, White E, Giovannucci EL. Trends in dietary supplement use among US adults from 1999-2012. *JAMA* 2016;316:1464-74.
41. Chao MT, Wade CM. Socioeconomic factors and women's use of complementary and alternative medicine in four racial/ethnic groups. *Ethn Dis* 2008;18:65.
42. Harrison R, Holt D, Pattison D, Elton P. Are those in need taking dietary supplements? A survey of 21 923 adults. *Br J Nutr* 2004;91:617-23.
43. Ni H, Simile C, Hardy AM. Utilization of complementary and alternative medicine by United States adults: results from the 1999 national health interview survey. *Med Care* 2002;40:353-8.
44. Shinto L, Yadav V, Morris C, Lapidus JA, Senders A, Bourdette D. The perceived benefit and satisfaction from conventional and complementary and alternative medicine (CAM) in people with multiple sclerosis. *Complement Ther Med* 2005;13:264-72.

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