Complementary and alternative asthma BMI **Den** treatments and their association with asthma control: a population-based study

Wenjia Chen,^{1,2} J Mark FitzGerald,^{2,3} Roxanne Rousseau,² Larry D Lynd,^{1,4} Wan C Tan,^{3,5} Mohsen Sadatsafavi^{2,3}

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For numbered affiliations see end of article.

Correspondence to

Dr Mohsen Sadatsafavi; Mohsen.Sadatsafavi@ubc.ca

ABSTRACT

Objectives: Many patients with asthma spend time and resources consuming complementary and alternative medicines (CAMs). This study explores whether CAM utilisation is associated with asthma control and the intake of asthma controller medications. Design: Population-based, prospective cross-sectional study.

Setting: General population residing in two census areas in the province of British Columbia, Canada. Recruitment was based on random-digit dialling of both landlines and cell phones.

Participants: 486 patients with self-reported physician diagnosis of asthma (mean age 52 years; 67.3% woman).

Primary and secondary outcome measures: We assessed CAM use over the previous 12 months, level of asthma control as defined by the Global Initiative for Asthma and the self-reported intake of controller medications. Multivariate logistic regression was performed to study the relationship between any usage of CAMs (outcome), asthma control and controller medication usage, adjusted for potential confounders. Results: A total of 179 (36.8%) of the sample reported CAM usage in the past 12 months. Breathing exercises (17.7%), herbal medicines (10.1%) and vitamins (9.7%) were the most popular CAMs reported. After adjustment, female sex (OR 1.66; 95% CI 1.09 to 2.52) and uncontrolled asthma (vs controlled asthma, OR 2.25, 95% CI 1.30 to 3.89) were associated with a higher likelihood of using any CAMs in the past 12 months. Controller medication use was not associated with CAM usage in general and in the subgroups defined by asthma control. **Conclusions:** Clinicians and policy makers need to be

aware of the high prevalence of CAM use in patients with asthma and its association with lack of asthma control.

INTRODUCTION

Asthma is a chronic disease of the airways associated with high healthcare resource utilisation, productivity loss and reduced quality

ARTICLE SUMMARY

Article focus

How does the use of complementary and alternative medicines (CAMs) in treating asthma relate to the clinical control of asthma and the use of conventional asthma controller therapies?

Key messages

- Our study demonstrated that CAMs were commonly used to treat asthma.
- The CAM usage was inversely associated with asthma control, whereas unrelated to the use of controller medications.
- Given the uncertain benefits and potential side effects of CAMs and possible drug interactions. it is important for physicians to be aware of CAM usage among their patients and understand the reasons of use.

Strengths and limitations of this study

- This is one of the few population-based studies investigating the association between CAM usage, the use of conventional asthma therapies and asthma control. We estimated asthma control using internationally accepted standards based on measures of asthma impairment and lung function. Various subgroup and sensitivity analyses added to the robustness and credibility of our results.
- However, the study is based on self-reports and thus the results are subjected to recall bias. Also, the cross-sectional design of this study prevents the evaluation of whether CAMs played a causal role in changing the level of asthma control.

of life.¹ Proper management can lead to clinically controlled asthma which, compared with uncontrolled asthma, is associated with lower usage of healthcare resources and better quality of life.² Clinical guidelines recommend anti-inflammatory medications as the primary controller treatment for asthma. In particular, inhaled corticosteroids are considered as the foundation therapy for treating asthma. $\!\!\!^3$

In addition to conventional treatments, many patients with asthma use complementary and alternative medicines (CAMs) in an attempt to improve their asthma symptoms.⁴ The CAMs are generally defined as "a group of diverse medical and healthcare systems, practices and products that are not generally considered to be part of conventional medicine."⁵ The reported prevalence rates of CAM usage in treating asthma is quite varied, ranging from 4% to 79%.⁶ Breathing techniques, homeopathy and herbal medicines are reportedly the most popular CAMs among patients with asthma.⁶ Despite the common usage of CAMs, individuals often do not disclose CAM usage to healthcare professionals.^{7 8}

In general, the effectiveness of CAMs in treating asthma is unknown and most likely is minimal, whereas some CAMs are associated with certain risks.^{4 9 10} The resources individuals spend in seeking and using CAMs may potentially draw from the resources they possess to their support evidence-based care for asthma. Understanding the reasons behind individuals' consuming CAMs can thus help care providers offer informed advice to patients. Two of the important determining factors that make patients consume CAMs are the association between CAM usage and the level of asthma control as well as the usage of conventional controller therapies. There is evidence indicating the association between CAM usage and poor control in work-related asthma.¹¹ Nonetheless, few studies have attempted to determine the association between the usage of CAMs and controller medications as a function of asthma control. Hypothetically, CAMs can play either a complementary or a substitute role in relation with conventional therapies. In a complementary role patients use CAMs in addition to their conventional treatments in an attempt to reduce asthma-related impairment. A substitute role for CAMs indicates that individuals use CAMs as a replacement for conventional therapies if they do not perceive benefit from conventional therapies (or do not seek conventional therapies due to lack of belief in their effect or due to their prohibitive cost). The objective of this study was to explore the association between CAM use, asthma control and the use of controller medications in a random sample of adult patients with asthma. Specifically, we hypothesised that lack of asthma control will be associated with higher usage of CAMs, and that individuals use CAMs to complement their conventional therapies.

METHODS

Study participants and data

Data were collected from the baseline visit of a prospective, longitudinal cohort study with the ultimate goal of estimating the economic burden of asthma. Study participants were recruited via random digit dialling from Vancouver and Central Okanagan, two representative census subdivisions in British Columbia, Canada (population of 603 502 and 179 839, respectively, in 2011^{12}). The sample size of the original cohort was designed to provide reliable estimate of the prevalence of asthma (with 95% confidence bound being within 10% of the point estimate). Participants aged 1-85 years with a parental or a self-reported physician diagnosis of asthma, plus a parental or a self-reported record of asthmarelated healthcare resource usage in the past 5 years, were initially identified. Individuals were not eligible if they were unable to provide informed consent due to language difficulties or cognitive impairment, reported a 10 pack-year smoking history or greater, or had plans to leave the study area during the follow-up period. Pregnant women, those who planned to become pregnant in the next 12 months, and those in whom a methacholine challenge test was contraindicated were not eligible. Consenting individuals attended the study centres for the baseline visit, during which a comprehensive questionnaire was administered to gather information on the demographic and socioeconomic status, asthma-related symptoms and use of CAMs and conventional medications. Patients also underwent spirometry by a trained technician. For the purposes of this substudy, we restricted the sample to adults 18 years and older.

Demographics and socioeconomic status

The sociodemographic characteristics included age at baseline, sex, ethnicity (self-reported and defined as Caucasian, Asian which included Mandarin, Japanese, Korean, Arabic and Persian or other ethnicities), education (self-reported and categorised as less than postsecondary education vs postsecondary education) and annual household income (self-reported and categorised as low vs high at a cut-off value of \$C60 000).

CAM use

The usage of CAMs in the past 12 months was assessed with the question "In the past 12 months, have you received any alternative therapy for your asthma? Check all that apply." followed by a list including nine options: (1) massage, osteopathy or other manipulative techniques; (2) herbal treatment; (3) acupuncture; (4) homeopathy; (5) breathing exercises; (6) vitamins or other supplements; (7) chiropractic; (8) dieting programs and (9) naturopathy. The interviewer provided verbal explanation and examples to clarify the options. There was also a miscellaneous category with free text, capturing any other modality that could be considered as CAM. This free text field was evaluated by three investigators who decided whether each stated item was CAM. Approved items then entered into the analysis as the 'other' category.

Asthma control

Asthma control was defined according to the Global Initiative for Asthma criteria.³ Patients were classified as controlled, partially controlled or uncontrolled based on asthma symptoms during the past 3 months (daytime symptoms, limitation of activity, nocturnal symptoms and need for rescue medication) as well as the ratio of forced expiratory volume in 1 s (FEV1) to its predicted value. We used the NHANES III standards to calculate the predicted FEV1.¹³

Controller medication use

Asthma medications taken during the past 12 months were documented in a self-reported prescription medication chart. For each medication we evaluated the intensity of intake through questions 'How many months?' and 'How many days a week?'. Using these two questions, we measured the intake of controller medication and converted the intensity of intake to proportions of days covered (PDC).¹⁴ Low intake was defined as PDC<50%, moderate intake as $50\% \leq$ PDC<80% and high intake as PDC \geq 80%.

Statistical analysis

All analyses were performed using Stata/IC (V.12.1., College Station, Texas, USA). The criterion for statistical significance was a two-tailed p value (p) of less than 0.05. The distribution of variables across groups was compared with Pearson χ^2 tests for categorical variables and Student t tests for continuous variables. We report the frequency of use of any CAMs, individual CAM categories as well as the concomitant use of different types of CAMs.

Logistic regression was performed to evaluate the association between CAM use and asthma control, controller medication use and potential confounders. Unadjusted analysis involved performing the logistic regression with the dependent variable being any use of CAMs (vs no use), and individual covariate of interest as the single independent variable. For the adjusted analysis, we used the same logistic regression model with any use of CAMs (vs no use) as the dependent variable, with independent variables including the level of asthma control (dummycoded to represent partially controlled and uncontrolled vs controlled asthma), controller medication use (the abovementioned PDC categories) as independent variables of interest. We also controlled for sex, ethnicity, age at baseline, annual household income and education status by entering such variables as additional independent variables in the regression model. The hypothesis of the complementary versus substitute role of CAMs with regard to conventional controller medications was evaluated by interpreting the coefficient for controller medication use: a positive coefficient (indicating an OR of more than one) indicates a complementary role for CAMs, whereas a negative one (indicating an OR of less than one) points towards CAMs playing a substitute role.

Sensitivity and subgroup analyses

To investigate whether the association between controller medication use and use of CAMs was different across asthma control levels, we fitted separate regression models using the aforementioned logistic model within each level of asthma control. In addition, to more efficiently exploit the information on CAM usage provided by participants, we used a negative binomial regression model with the dependent variable being the number of different types of CAMs used by the individual (all independent variables similar to those of the logistic model described previously). In assessing the presence of asthma symptoms as part of the definition of asthma control, in addition to 'yes' or 'no' options, a third category of 'I do not know' was also available to respondents. In the main analysis it was assumed that those who chose the latter option had not experienced the corresponding symptom. In a sensitivity analysis we treated such values as missing and performed multiple imputations on these values. In another sensitivity analysis, the logistic regression analysis was repeated by removing the 'other' category of CAMs.

RESULTS

Characteristics of study participants

Among the 622 individuals who completed the baseline visit, there were 486 adults with asthma who comprised the sample for the current study. The average age was 52.3 years (SD=14.7) at study entry, and 67.3% were women (table 1). Participants were likely to be Caucasian (82.1%), have attended college (75.3%) and with annual household income greater than \$60 000 (72.2%). The mean baseline FEV1 was 2.61 (SD=0.87). The distribution of individuals across controlled, partially controlled and uncontrolled asthma was 20%, 38.5% and 41.6%, respectively. Of all adults, 42%, 15.2% and 42.8% had low, medium and high intake of controller medications, respectively.

The overall prevalence of the use of any CAMs in the past 12 months was 179/486 (36.8%; 95% CI 32.5% to 41.1%). Excluding the 'other' category, which comprised 16.3% of CAM usage, a majority of the individuals (18.3%) reported using one type of CAMs, while 7.6% used two different CAMs and 9.3% used more than two types of CAMs. The most frequent CAMs were breathing exercises (17.7%), herbal medicines (10.1%) and vitamins (9.7%; figure 1).

Association between CAM use, asthma control and controller medication intake

Results of both unadjusted and adjusted logistic regressions are provided in table 2. Only female sex and uncontrolled asthma were associated with a higher chance of using any CAMs in the unadjusted analysis. After adjustment, the same two variables, female sex (OR 1.66; 95% CI 1.09 to 2.52) and uncontrolled asthma (uncontrolled vs controlled asthma OR 2.25; 95% CI 1.30 to 3.89), were significantly associated with CAM utilisation. Partially controlled asthma and controller medication intake were not associated with CAM usage.

Variables	Overall (N=486)	Used any CAMs		
		Yes (N=179)	No (N=307)	p Value†
Age, mean(SD)	52.3 (14.7)	52.3 (13.6)	52.1 (15.2)	0.88
Gender, N (%)				
Female	327 (67.3)	134 (74.9)	193 (62.9)	0.007*
Male	159 (32.7)	45 (25.1)	114 (37.1)	
Education, N (%)				
Less than postsecondary education	120 (24.7)	43 (24.0)	77 (25.1)	0.79
Postsecondary education	366 (75.3)	136 (76.0)	230 (74.9)	
Ethnicity, N (%)				
Caucasian	399 (82.1)	143 (79.9)	256 (83.4)	0.62
Asian	67 (13.8)	28 (15.6)	39 (12.7)	
Other	20 (4.1)	8 (4.5)	12 (3.9)	
Household income, N (%)				
<\$60000	135 (27.8)	57 (31.8)	78 (25.4)	0.13
≥\$60000	351 (72.2)	122 (68.2)	229 (74.6)	
Baseline FEV1 (L), mean(SD)	2.61 (0.87)	2.51 (0.86)	2.67 (0.87)	0.06
Asthma control level, N (%)				
Controlled	97 (20.0)	26 (14.5)	71 (23.1)	<0.001*
Partially controlled	187 (38.5)	58 (32.4)	129 (42.0)	
Uncontrolled	202 (41.6)	95 (53.1)	107 (34.9)	
Controller medication intake, N (%)				
PDC <50% (Low)	204 (42.0)	66 (36.9)	138 (45.0)	0.21
50%≤PDC<80% (Moderate)	74 (15.2)	31 (17.3)	43 (14.0)	
PDC≥80% (High)	208 (42.8)	82 (45.8)	126 (41.0)	

*Significant at 0.05 level.

+p Values are associated with independent sample t test for continuous variables and χ^2 test for categorical variables.

CAMs, complementary and alternative medicines; FEV1, forced expiratory volume at 1 s; N, total number; PDC, proportions of days covered by conventional controller medications.

Subgroup and sensitivity analyses

Results of the subgroup and sensitivity analyses are reported in online supplementary appendix tables A1–A3. Controller medication use was not associated with CAM use within the strata of controlled, partially controlled or uncontrolled individuals. No change was observed in the overall study results when indeterminate answers to asthma symptoms were treated as missing values, when the multivariate logistic regression model was replaced with a negative binomial model, and when the 'other' category of CAMs were removed from the analysis.



Figure 1 Frequencies of past 12-month complementary and alternative medicine (CAM) usage in treating asthma, by CAM types.

DISCUSSION

Using a population-based sample, we described the patterns of CAM usage in adults with asthma, and further examined the association between CAM use, asthma control and controller medication intake. In our study, 37% of adults with asthma reported using any CAMs in the past 12 months. We also found that patients with uncontrolled asthma had a higher likelihood of reporting any use of CAMs, compared with patients with conasthma, after adjusting trolled for potential confounders. Our study, therefore, suggests that the use of CAMs in patients with asthma is high, and is associated with worse asthma control. In addition, we found breathing exercise, a modality often used by patients with more severe asthma, to be the most common type of CAM. This, combined with a lower baseline FEV1 (p=0.06) among CAM users compared with non-users, might indicate that CAM users tended to have more severe asthma.

However, CAM usage was unrelated to the intake of controller medication in the overall study population, as well as within the subgroups defined by asthma control. As such we could not discern any complementary or substitute role of CAMs in relation to conventional controller therapies. In addition to our limited sample size to discover such a relationship, it might be the case that users of CAMs are a mixture of those who consume

	Any CAM use, OR (95% Cl); p value			
Variables	Unadjusted†	Adjusted‡		
Age	1.00 (0.99;1.01); p=0.88	1.00 (0.98;1.01); p=0.70		
Gender				
Male	Reference	Reference		
Female	1.76 (1.17;2.65); p=0.007*	1.66 (1.09;2.52); p=0.019		
Household income				
<\$60000	Reference	Reference		
≥\$60000	0.73 (0.49;1.09); p=0.13	0.80 (0.52;1.23); p=0.31		
Education				
Less than postsecondary education	Reference	Reference		
Postsecondary education	1.06 (0.69;1.63); p=0.79	1.07 (0.68;1.69); p=0.77		
Ethnicity				
Caucasian	Reference	Reference		
Asian	1.29 (0.76;2.18); p=0.35	1.31 (0.76;2.28); p=0.32		
Other	1.19 (0.48; 2.99); p=0.71	1.14 (0.44;2.96); p=0.78		
Asthma control level				
Controlled	Reference	Reference		
Partially controlled	1.23 (0.71;2.12); p=0.46	1.26 (0.72;2.19); p=0.42		
Uncontrolled	2.42 (1.43; 4.11); p=0.001*	2.25 (1.30;3.89); p=0.004*		
Intake of controller medication				
Low	Reference	Reference		
Moderate	1.51 (0.87;2.61); p=0.14	1.22 (0.69;2.16); p=0.49		
L Bash	1.36 (0.91; 2.04); p=0.14	1.10 (0.71:1.71); p=0.67		

CAMs as a complement versus those who use them as substitute to their conventional controller therapies.

Our estimates of the prevalence of CAM usage is in line with recent survey-based estimates (Behavioral Risk Factor Surveillance System) for 38–40% for any use of CAMs in the USA.^{11 15} Our findings on the association between CAM use and sociodemographic factors (eg, age, education, household income and ethnicity) are generally consistent with published findings^{6 15–17}: several previous studies also reported a greater possibility of receiving CAMs among women with asthma as compared with men,^{6 16 17} but a recent US study did not find a statistically significant association.¹⁵ Such discrepancies may be explained by our limited sample size as well as differences in data collection methods and in the types of CAMs being reported in these studies.

Marino and Shen¹⁵ found asthma emergency room visits and disability days, as surrogates for lack of asthma control, to be positively related with CAM usage in adults. However, a Northern California study of adult patients reported no association between self-assessed asthma severity and CAM usage.¹⁶ Using a validated and internationally accepted measure of asthma control,³ our analysis showed an inverse association between asthma control and usage of CAMs. Similar results have been observed in samples of individuals with work-related asthma.¹¹ However, the link between CAM usage and adherence to asthma controller medications is inconsistent in the literature and likely confounded by asthma control. Two inner-city studies in the USA reported decreased adherence to asthma controller therapy among adult CAM users,^{18 19} whereas a recent longitudinal analysis found no effect of CAMs on future adherence to controller medication in paediatric asthma patients.²⁰

Compared with previous studies,^{11 15 16 18 19} our study has several strengths. Based on a random sample, the estimates of CAM use and the association with asthma control are population based. We estimated asthma control using internationally accepted standards based on measures of asthma impairment and lung function.³ Various subgroup and sensitivity analyses added to the robustness and credibility of our results. However, this study is not without limitations. First, both CAM usage and controller medication intake were based on selfreports and thus are subject to recall bias, which may affect the precision of measurement and thereby increase the noise in finding an association. We provided a list of nine prespecified types of CAMs to participants to ensure homogeneity in the definition of CAMs across all individuals and to increase the accuracy of recall; however, individuals might have been less likely to report other forms of CAMs. Finally, using a cross-sectional design, we were not able to evaluate whether CAMs played a causal role in changing the level of asthma control.

Despite these limitations, our findings have important clinical implications. The extent of CAM usage among the population of patients with asthma gives policy makers an estimate of the overall burden of CAM usage at the population level. The resources individuals spend consuming CAMs represent an opportunity cost because such resources could have been spent in evidence-based treatments or other activities. Given the uncertain benefits, potential side effects and possible drug interactions of CAMs,⁴ it is important for physicians to be aware of CAM usage among their patients and understand the reasons of use. We found the use of CAMs to be associated with uncontrolled asthma. Overall, CAM use might be a sign of patients' lack of satisfaction with asthma treatment, prompting the care provider to re-evaluate asthma management. Further research is required to evaluate the economic impact of CAM usage, to further examine other potential factors determining the use of CAMs such as individuals' value systems and beliefs, access to care, health literacy and quality of life, and to rigorously study the causal interactions between CAM use, asthma control and use of controller medications.

Author affiliations

¹Faculty of Pharmaceutical Sciences, Collaboration for Outcomes Research and Evaluation, University of British Columbia Vancouver British Columbia Canada

²Division of Respiratory Medicine, Faculty of Medicine, University of British Columbia, Vancouver, British Columbia, Canada

³Institute for Heart and Lung Health, University of British Columbia, Vancouver, British Columbia, Canada

 ⁴Centre for Health Evaluation and Outcome Sciences, Providence Health, University of British Columbia, Vancouver, British Columbia, Canada
⁵James Hogg Research Centre, University of British Columbia, Vancouver, British Columbia, Canada

Contributors JMF, MS, CM, LL and WH designed the Economic Burden of Asthma (EBA) study, whose data are used in the present research. MS and RR designed the case report forms. JMF and WC proposed the research question. WC conceptualised the study design, was the main analyst, and wrote the first draft of the manuscript. JMF, MS, CM, LL, RR and WH were involved in the acquisition of the data. CM and LL critically revised the manuscript. All authors approved the final version of the manuscript.

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