ASSOCIATION BETWEEN TAKING ASTHMA MEDICATION AND TOTAL DIRECT HEALTHCARE COSTS AMONG PATIENTS WITH ASTHMA

by

Ira Dave

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Approved by:

Dr. Larissa R. Brunner Huber

Dr. Ahmed A. Arif

Dr. Sarah B. Laditka

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ABSTRACT

IRA DAVE. Association between taking asthma medication and total direct healthcare costs among patients with asthma. (Under the direction of DR. LARISSA R. BRUNNER HUBER)

Asthma is one of the most common chronic and financially burdensome diseases in the United States. Previous studies have focused on comparing healthcare costs between asthma patients and non-asthma patients. This study is unique as it compares healthcare costs among asthma patients based on whether they take daily asthma medication. In addition, this cross-sectional study investigates whether the daily asthma medication-healthcare cost association differs by age or race/ethnicity. Medical Expenditure Panel Survey (MEPS) 2012-2013 data was used for this secondary data analysis (n=1,336). Prescription taking status and total healthcare costs were self-reported by the study participants. A two part linear regression model was used to calculate total healthcare costs for the asthma patients. Healthcare costs for patients taking daily asthma prescriptions were higher than for patients not taking daily asthma prescriptions ($15,149 vs $7,485; $p \leq 0.0001$) after controlling for confounders. Race/ethnicity and age were effect modifiers of the association. Additional studies are needed to investigate possible factors associated with these higher costs. Specifically, future studies should further evaluate the racial/ethnic and age disparities seen in this study. This information could assist medical and public health practitioners in better understanding some of the issues responsible for high healthcare costs and helping them to plan strategies to minimize these costs among asthma patients.

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INTRODUCTION

Asthma is a chronic obstructive inflammatory disease characterized by recurring periods of wheezing, chest tightness, shortness of breath, and coughing (1, 2). Asthma is one of the most common chronic diseases in the United States. The etiology of asthma is unclear, however, there are some known triggers such as allergens (e.g. pollen, mold, animal dander, and dust mites), exercise, occupational hazards (e.g. isocyanates, flour/grain, adhesives, metals, resins, colophony, fluxes, latex, animals, aldehydes, and wood dust), tobacco smoke, air pollution, airway infections, some medications such as aspirin and acetaminophen, extreme weather conditions, and stress (3-6).

There is no cure for asthma. However, it can be effectively managed by medication (2). Most asthma patients use two types of medication: relievers such as short- acting inhaled beta 2-agonist and anticholinergics for quick relief of asthma symptoms, and preventers such as inhaled corticosteroids, antileukotrienes or leukotrienes, oral corticosteroids, and immunomodulators for long-term control and prevention of asthma (6).

Adherence to these medications plays an important role in managing asthma and its symptoms, but people are sometimes reluctant to take the medications due to their high costs or the side effects (7). Non-compliance rates for asthma medication among children and adults have been reported to be approximately 30% to 70%. (7). Non-compliance could result in severe complications of asthma including frequent visits to the emergency room, hospitalizations, and even death (7).

In 2013, the prevalence of asthma in the United States was 7.3% (5); in 2015, an estimated 18.7 million Americans suffered from asthma (6). The highest prevalence of 9

million is observed in ages 35-64 years (5). The prevalence of asthma differs by race/ethnicity with the highest rates observed among non-Hispanic Blacks (11.0%) followed by American Indians/Alaskan Natives (9.4%) (8). In comparison, prevalence rates are lower among non-Hispanic Whites (7.7%), Hispanics (6.5%), and Asians (5.2%) (8).

In 2015, in the United States, asthma-related healthcare use included 14.2 million physician's office visits, 479,000 hospitalizations, 1.8 million emergency department visits, and an average length of stay in the hospital of 3.6 days (9). Consequently, asthma creates a large economic burden on the healthcare industry.

The objective of this study is to evaluate total direct medical expenditures for asthma patients who take their daily asthma maintenance prescriptions compared to those asthma patients who do not take their daily asthma maintenance prescriptions using 2012-2013 Medical Expenditures Panel Survey (MEPS) data. Additionally, this study investigated whether race/ethnicity and age are effect modifiers of this association. Although past studies have evaluated asthma-related healthcare costs in the United States (10-12), recent changes in coverage due to the Affordable Care Act (ACA) may have led to changes in healthcare utilization since 2012. Thus, it is important to re-evaluate these costs to provide up-to-date data to healthcare practitioners and public health practitioners for targeted evidence-based interventions to at-risk populations.

LITERATURE REVIEW

This chapter will focus on the 1) background and significance of asthma; 2) prevalence and risk factors of asthma in the United States; 3) adherence to taking prescription medication and asthma-related cost; 4) direct medical costs of asthma; and 5) differences in direct medical cost with respect to race/ethnicity and age.

Background and Significance

According to the Global Asthma Report, asthma ranks as the 14th most important disorder (defined as the extent and duration of the disability) in the world (13). According to the National Heart, Lung, and Blood Institute, asthma is a common chronic disease affecting the lungs that cause inflammation and narrowing of the airway. Asthma attacks are characterized by difficulty in breathing, which occasionally can be extreme and lead to a medical emergency (14). Common symptoms of asthma are shortness of breath, coughing, recurring wheezing (a whistling sound when breathing), and chest tightness (2). Other symptoms of asthma may include sleeplessness, daytime fatigue, presenteeism (attending work while being sick therefore decreasing productivity) and absenteeism from work (15). Around the world, approximately 235 million people suffer from asthma (15). While asthma is common throughout the world and occurs in all countries regardless of their level of development or standard of living, fatality due to asthma is more common in developing and under-developed countries (15).

Asthma is also a costly disease (13). A study done by the American Lung Association reported that asthma leads to 14.2 million days of absenteeism from work and activity limitation, and approximately $56 billion in healthcare costs annually (14). Another study conducted to examine the direct and indirect costs of asthma for working

age adults (ages 18-64 years) in the United States from 2002-2006 found that the indirect cost for absenteeism was $166 greater for patients with asthma ($p=0.04$) and the average cost of short-term disability was $248 ($p<0.001$) greater for patients with asthma (17). Since this study only included subjects from self-insured employers and did not include people without insurance or those on Medicaid, generalizability may be limited (17).

Prevalence and Risk Factors for Asthma in the United States

Asthma represents a significant public health issue in the United States. The prevalence of asthma in the United States has been increasing. In 2004, the prevalence of asthma was 30 million, and it increased to 39 million in 2011 (17). These numbers constitute a huge burden on society. Among adults, females have higher rates of asthma than males (females: 100.1 per 1,000, and males: 61.8 per 1,000) but this trend is reversed among children (boys: 101.7 per 1,000 and girls 87.8 per 1,000) (14, 17).

Asthma is a complex and multifactorial disease. There are several established risk factors for asthma including race/ethnicity; environmental risk factors such as tobacco and air pollution; obesity; occupational risk factors such as exposure to cereal grains, wood dust, chemicals, and dyes; and microbes (19, 20).

Racial/ethnic disparities are evident in asthma (14). In 2011, in the United States, non-Hispanic Blacks (118.0 per 1,000 persons) had the highest prevalence rate for asthma compared to non-Hispanic Whites (80.4 per 1,000 persons), Hispanics (72.3 per 1,000), and non- Hispanic others (70.2 per 1,000) (18). The reasons for these racial/ethnic disparities are unknown; however, it is possible that differences in environmental exposures (e.g. higher indoor allergens in urban areas, secondhand smoke) may be partly responsible for the higher prevalence among non-Hispanic Blacks (51). Also, some

minority groups have a genetic predisposition to asthma which may explain the observed disparities (51).

With respect to environmental factors, being an active smoker is a risk factor for developing asthma (19). Tobacco smoke has also been seen to adversely affect asthma and worsen asthma symptoms (19). A study by Burke et al. reported that exposure to prenatal maternal smoking increases the incidence of asthma in offspring by 85% (21). Environmental pollution is also an important risk factor for asthma. The United States government has been taking steps to reduce both indoor and outdoor pollution. However, pollution remains a risk factor for developing asthma as well as triggering symptoms of asthma (22). In a study conducted in Seattle, Washington by Schwartz et al. on emergency room (ER) visits of eight hospitals for asthma-related visits, the researchers reported a significant association between asthma-related ER visits and the particulate matter count in the previous day (23).

Obesity is a co-morbidity for asthma and has a significant impact on asthma risk and prognosis (18). Obesity and asthma share common underlying immunologic and inflammatory mechanisms (18). Microbes are also a risk factor for asthma. As asthma patients have impaired mucosal and systemic immune defenses and atopy, they are more susceptible to viral and bacterial infections (18). Bacterial colonization of the airway plays an important role and contributes to the development and progression of asthma (18).

Association Between taking Asthma Medication and Total Direct Healthcare Costs among Patients with Asthma

Chronic conditions like asthma require being adherent to asthma medication for the full effect of therapy to take place (28). Express Scripts, one of the largest pharmacy benefit management service providers in the United States for self-insured employers and government agencies, published in a recent report that the cost of asthma medications/therapy increased by 0.4% ($55.96) from 2010 to 2011 (29). The average cost per prescription has also increased by 6.4% ($92.82) (29). In addition, the 2012 trend report indicated that 53.8% of adult asthma patients and 80.2% of pediatric asthma patients were non-adherent to their medication therapy (29). As a result, the use and refilling of asthma medications decreased 7.3% in 2013 (29).

Studies have found that cost concerns, low income, multiple chronic diseases, and/or no prescription coverage are some of the factors associated with non-compliance (30-32), which could lead to an increase in emergency department visits, nursing home admissions, and poor health outcomes (33-35).

Direct Medical Cost for Asthma Patients

Total direct medical expenditures for asthma include expenditures for prescription medications, emergency room (ER) visits, office- based visits (OBV), in-patient (IP) visits, out-patient (OP) visits, and other miscellaneous (OM) items (11). A cross-sectional study of medical costs burden among 10,374 non-elderly patients aged 18-64 years with asthma was conducted using 2003-2009 Medical Expenditure Panel Survey (MEPS) data to evaluate the total and out of pocket expenditures associated with asthma (12). Four groups were considered according to whether the individuals used treatments for asthma and whether they had an asthma attack in the past year. People who received treatment for asthma and had an attack in the previous year had the highest total spending

at $9,155 while people not receiving treatment and who had no attack in the past year had the lowest total spending ($5,835; p ≤0.5). The study concluded that due to high expenditure costs, the financial burden of asthma is high even when asthma is self-managed (12).

Another cross-sectional study was conducted using incremental direct medical expenditures of treating asthma in the United States using MEPS 2004 for children (<18 years) and adults (≥18 years) (11). The total sample size for adults and children was 34,403. The statistical analysis was conducted using generalized linear regression models adjusted for covariates such as age, gender, race/ethnicity, education, insurance, geographic region, and comorbidities. The annual total expenditures were reported to be $1,004.6 per person among children (p= 0.002) and $2,077.5 per person for adults (p≤0.0001) (11).

Another cross-sectional study using 2002-2007 MEPS data calculated the direct medical cost and productivity loss due to asthma morbidity and mortality at individual and national levels among 206,871 individuals (36). The study concluded that the incremental direct cost for asthma from 2002-2007 was $3,259 per person per year after adjusting for age, race/ethnicity, geographic location, education, sex, income, and insurance. Additionally, the study reported that asthma resulted in 2.62 more lost days of work per person each year. Also, the total costs due to asthma in 2007 in the United States was estimated to be $56 billion.

A case-control study of 26,738 individuals was conducted to analyze the effects of direct and indirect costs of asthma in United States working adults aged 18-64 years using data extracted from MarketScan Research Databases (17). Propensity score

matching was done for patients with and without asthma using demographic characteristics such as age, sex, geographic region, and insurance type. Clinical characteristics were matched as well. The study reported that direct costs for patients with asthma were $3,762 vs. $ 1,773 for people without asthma. Although this study had a large sample size, it only included patients who were self-insured. Thus, results may not be generalizable to individuals with Medicaid or those who do not have insurance.

Differences in Direct Medical Costs with Respect to Race/Ethnicity

A population-based study was conducted on adults frequently using emergency rooms to assess associated hospital charges for acute asthma (37). The data for this study were obtained from the Healthcare Cost and Utilization Project State Emergency Department and Inpatient Database for California and Florida. The sample consisted of 86,224 patients between the ages of 18 to 54 years with at least one asthma-related emergency department (ED) visit. The study population was divided into three groups: patients with one ED visit, patients with two ED visits, and patients with three or more ED visits. Multinomial logistic regression model was used to examine associations between patient level factors (i.e. age, sex, race/ethnicity, insurance, geographic location, state, and comorbidities) and ED visits. The study concluded that 25.6% (95% CI: 25.3-25.9) of the patients had multiple emergency department visits and that individuals who were non- Hispanic Black, Hispanic, and/or of low socioeconomic status were more likely to make multiple visits. Thus, non-Hispanic Blacks and Hispanics were more likely to have higher direct costs related to ED visits for asthma compared to non-Hispanic Whites (37). It should be noted that the results cannot be generalized to the

entire United States population due to the fact that only data for California and Florida were considered.

A cross-sectional study was conducted to examine if asthma related healthcare utilization differed for partly controlled and uncontrolled asthma and how these associations differed among racial/ethnic groups. The study population included 2,493 respondents from the Asthma Insights and Management Survey who were at least 12 years of age. The respondents were categorized into well controlled, partly, and uncontrolled asthma patients (these categories were defined according to Global Initiative for Asthma [GINA] guidelines) (38). The cost of healthcare utilization did not differ significantly among whites and non-whites with well- controlled asthma ($830 vs $650; p= 0.36). The cost of healthcare utilization for partly- controlled asthma (whites: $1,420 and non-whites: $1,960; p = 0.31) and uncontrolled asthma (whites: $4,950 and non-whites: $6,170; p value= 0.38) also did not differ by race. One limitation of this study was that it only considered race to be white or non-white. Thus, other important racial/ethnic differences may have been obscured.

Differences in Direct Medical Cost with Respect to Age

As previously mentioned, the prevalence of asthma differs by age (14, 17), and the cost of asthma also varies within different age groups. There is little research on differences in medical cost for asthma patients with respect to age. A report by the Utah Health Department found that total medical costs for asthma in Utah increased with age (47). While total medical costs for individuals between18 to 49 years were similar (approximately $10 million), the costs for people 50 to 64 years were higher at $15 million. There were several limitations to this study. First, the study lacked information

on individuals over the age of 64 years. Second, the results were at the population- level; therefore, it is difficult to understand the cost per patient. Finally, the findings may not be generalizable to the entire United States population since the study only included data for Utah.

Summary

In summary, many previous studies have concluded that the burden of asthma due to cost has increased incrementally (11, 12, 16, 17, 36). However, some of the prior studies did not include people without insurance or people with public insurance, which is a very important factor to consider when examining the burden of asthma (17). The use of MEPS data for the current study improves upon this limitation since MEPS includes public and private insurance, as well as people without insurance. Also, given that many studies were conducted over five years ago (11, 17, 36), this study provides timely information on healthcare related costs for asthma which is important so steps can be taken to decrease these costs if possible. Additionally, studies have demonstrated that racial/ethnic minorities and the age group 35- 64 years have the highest prevalence of asthma. Thus, it is important to better understand these disparities so that public health initiatives and programs can be tailored towards the people who need it most. Therefore, the purpose of this study was to examine the association between taking asthma prescription medication and total direct healthcare costs among United States adults with asthma using 2012-2013 MEPS data. Furthermore, this study evaluated whether race/ethnicity and age were effect modifiers of this association.

HYPOTHESIS

This cross-sectional study evaluated total direct medical expenditures among asthma patients aged 18 years and above using data from the 2012–2013 Medical Expenditure Panel Survey (MEPS).

The specific hypotheses addressed were:

1. Asthma patients who take their daily maintenance prescriptions have lower total direct medical expenditures than asthma patients who do not take their daily asthma maintenance prescriptions
2. Race/ethnicity is an effect modifier of the prescription taking status and total direct medical expenditures association.
3. Age is an effect modifier of prescription taking status and total direct medical expenditures association.

METHODS

Data Source

The Medical Expenditure Panel Survey (MEPS) is a national representative survey of the United States non-institutionalized population (39). It is designed to provide researchers with timely information about healthcare utilization and associated costs in the United States. MEPS is a probability survey, which collects data on the use of health services by Americans. MEPS provides national estimates of healthcare use, expenditures, sources of payment, and insurance coverage for the United States civilian non-institutionalized population (39). The Agency of Healthcare Research and Quality (AHRQ) has conducted the MEPS annually since 1996 in collaboration with the National Center for Health Statistics (NCHS), and the most recent data available are for 2014 (40). Data collected from MEPS are available to the public online at http://www.meps.ahrq.gov/mepsweb.

MEPS includes several survey components: the Household Component, the Medical Provider Component, and the Insurance/Employer Component. The Household Component is the main survey, and forms the basis for the Medical Provider Component and Insurance Component portions (41). The MEPS-Household Component is a nationally representative survey of the United States civilian non-institutionalized population, drawn from a nationally representative subsample of households that participated in the prior year's National Health Interview Survey (conducted by the NCHS) (41). The Household Component collects medical expenditure data at both the person and household levels (41). Specifically, the Household Component collects detailed data on demographics, health status, healthcare services used, payments,

satisfaction with care, and insurance. The Household Component uses an overlapping panel design in which, for each panel, data are collected through a preliminary contact followed by a series of five in-person interviews over the course of 2.5 years (2 interviews per year) (42).

Data are collected from each household using computer assisted personal interviewing (CAPI) technology. The data collection process is launched every year with a new sample of households, thus providing overlapping panels of survey data when combined with the ongoing panel. The purpose of the MEPS Medical Provider Component portion is to confirm or supplement information received from participants of the MEPS Household Components (44). Data collected include financial and medical characteristics of healthcare and pharmacy events as reported by Household Component participants. These data consist of dates of visits, procedure codes and diagnoses, charges, and payments (44). Medical Provider Component data collection involves telephone contacts with the providers, and mailed or faxed questionnaires (44).

The Insurance Component uses multiple data collection methods. Private offices and state and local government offices are screened initially by telephone to confirm the mailing address and to establish a point of contact. Offices that offer insurance are mailed survey questions. A second mailing is sent if responses to the first mailing are not received within three weeks. If the office still does not respond, a computer assisted telephone interview is conducted.

Study Design and Sample

This current secondary data analysis is a cross-sectional study of 2012-2013 MEPS, Household Component data. A total of 38,974 people participated in the 2012 MEPS (response rate: 56.3%) and 36,940 individuals took part in the 2013 survey (response rate: 52.8 %) (44). For this study, individuals were excluded if they were younger than 18 years (n=21,778), did not have an asthma diagnosis (n=50,739), or were missing information on asthma medication use (n=2,035). In addition, 26 participants were excluded because of non- positive weights, as MEPS recommends excluding individuals with non-positive weights. Thus, data for 1,336 participants were included for analysis (11).

Conceptual Model

This study used the Andersen Behavioral Model (ABM) of health services use proposed by Andersen et al. to identify determinants of the use of healthcare services among adults in the United States. The ABM was developed in 1960 and was modified to understand the individual's use of health services. The three characteristics of individual's healthcare use are: predisposing, enabling, and need factors (45). The model is depicted in Figure 1.

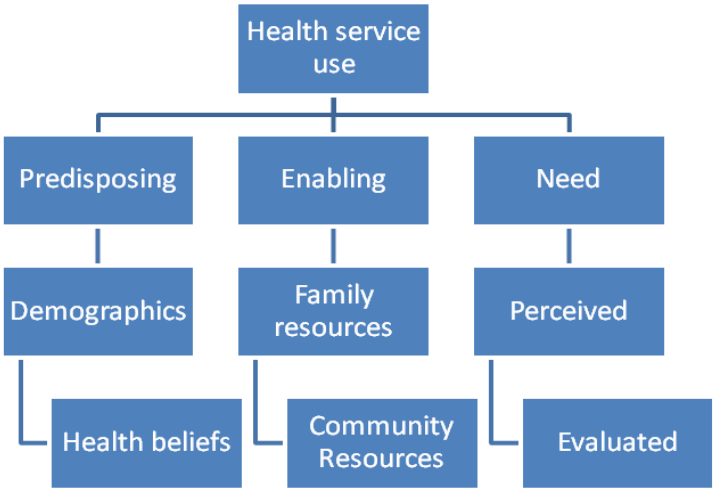

Figure 1: Andersen Behavior Model

Adapted from- Andersen R, Newman JF. Societal and individual determinants of medical care utilization in the United States. Milbank Memorial Fund Quarterly Health Society. 1973; 51(1): 95-124.

Predisposing factors are characteristics of an individual that exist independent of diseases and include demographic characteristics (e.g. age, gender, and marital status), social structure characteristics (e.g. education, race/ethnicity, occupation, and smoking status), and health belief characteristics (e.g. personal attitudes regarding medical care, medical professions, and illness) (45). Predisposing characteristics mainly motivate the individual to use health services (51). Enabling factors are those factors that give individuals the ability to secure health services. These factors are income, health insurance, and availability of services (e.g. Metropolitan Statistical Area) (45). Need factors represent the subjective acknowledgement of need of an individual for healthcare services (45). These factors are a patient's symptoms or need for health care as perceived by the patient or the professional judgment of need for health care (e.g. self-rated health status).

This study used demographic characteristics (i.e., age, gender, race/ethnicity, marital status, education) as predisposing characteristics; source of payment (i.e., private, public, no insurance), and income as enabling characteristics; and perception of health by patient or physician (i.e., asthma attack in last 12 months) as a need factor.

Exposure

Study participants with an asthma diagnosis were asked the following question: "Are you now taking daily asthma preventive medication to protect your lungs and keep you from having attacks? Include both oral medicine and inhalers. This is different from inhalers used for quick relief." Individuals who stated they were taking daily maintenance medication were considered exposed while individuals who were not taking that type of medication were considered as unexposed.

Outcome

Total direct medical expenditures was the outcome variable and included expenditures for medications, emergency room visits, office based visits, inpatient visits, outpatient visits, and other medical equipment and services as reported by participants on the Household Component of MEPS. It was important to consider total direct medical expenditures since asthma can impact other aspects of a person's health and well-being and possibly contribute to other comorbidities (12). Therefore, all the components were added to calculate the total direct medical expenditures variable. This variable was a non-negative continuous variable.

Covariates

The covariates included in this study were self-reported by participants on the Household Components portion of MEPS. Covariates included in this study were age,

sex, marital status, education, race/ethnicity, income, health insurance, region, asthma attack in last 12 months, and the D'Hoore adaptation of Charlson's comorbidity index. (11). The D'Hoore adaptation of Charlson's comorbidity index is a continuous variable that considers 17 conditions (i.e. myocardial infraction, congestive heart failure, peripheral vascular disease, dementia, cerebrovascular disease, chronic pulmonary disease, connective tissue disease, ulcer disease, mild liver disease, diabetes, hemiplegia, moderate or severe renal disease, any tumor, leukemia, moderate or severe liver disease, and metastatic tumor) (46). This index has very good predictive power for mortality and is an efficient approach to risk adjustment for studies that consider total direct medical expenditures (11, 46). Furthermore, race/ethnicity and age were examined as effect modifiers. The categories for race/ethnicity were non-Hispanic White, non-Hispanic Black, Hispanic, and Others. The categories for age were 18-24 years, 25- 40 years, 41-64 years, and 65 years and above.

Statistical Analysis

Univariate Analysis

Summary statistics were calculated to describe the study population. Specifically, frequencies and percentages were calculated to analyze the distribution of the study population with respect to the exposure (daily asthma prescription medication status).

Bivariate Analysis

A two-part model utilizing a smearing technique was used to perform the bivariate analysis. Since total medical expenditure has a non- normal distribution, this variable was transformed via log transformation. Log transformation makes the variable normally distributed and reduces the effect of outliers. Then linear regression was

conducted using the log transformed total medical expenditure variable (outcome) and the asthma prescription variable (exposure). Then the predicted value and the residual value were exponentiated and retransformed. The mean of the exponentiated residual value was calculated, and this mean value is called the smearing factor. This smearing factor was then multiplied with the exponentiated predicted value to calculate the final value, the marginal expenditure value (47). Smearing techniques are non-parametric solutions for the log transformed expenditure value that convert it into original dollar values.

Multivariate Analysis

Similar to the bivariate analysis, a two-part model was conducted for the multivariate analysis as well. However, in this model we also controlled for confounding factors. The confounding factors included were: age, sex, race/ethnicity, marital status, health insurance, asthma attack in last 12 months, and D'Hoore's adaptation of Charlson's comorbidity index. Factors that were statistically significant at the $p<0.05$ level in the bivariate analyses were included with the exception of race/ethnicity which was retained in the final model despite having one category with a $p>0.05$.

Furthermore, a separate model was run to calculate if the healthcare expenditures for the patients taking daily asthma maintenance prescriptions was due to the added cost of prescriptions compared to the patients not taking daily prescription medications. A new cost variable was calculated by subtracting the costs for all prescriptions (as there was no variable that had only the costs for asthma medications) from the total direct medical costs and then the two part model analysis was conducted. This analysis provided the true medical cost for all patients.

Effect Modification

Race/ethnicity and age were analyzed as effect modifiers of the daily asthma prescription taking status and total direct medical costs association. Race/ethnicity was categorized into the following categories: non-Hispanic White, non-Hispanic Black, Hispanic, and Other. Age was categorized as 18-24 years, 25-40 years, 41-64 years, and 65 years and older. The multivariate analysis was subsequently conducted separately for each racial/ethnic and age category to assess if total direct medical expenditures varied by race/ethnicity or age. All analyses were conducted using complex sampling procedures in SAS 9.3 to account for the sampling design employed by MEPS (SAS Institute. Inc., Cary, NC).

Power and Sample Size

The total sample size for the study was 1,362 participants. The effect size for the study was 0.185 at 95% power in total cost between the two groups (Table 7) (12). The power calculation was done using G power software. The sample size of the study was sufficient to assess differences in total direct medical costs between asthma patients who take their daily asthma maintenance medication and those who do not take their daily asthma maintenance medication.

Table 7: Power calculation for the study (12)

Parameter for sample size calculation	Scenario
Effect size	0.185
Error Probability	0.05
Power	0.95
Ratio of groups	1
Calculated total sample size	1362

Human Subject Protection

Since this study was a secondary data analysis, no contact was made with study participants. The information in the dataset was confidential as it does not include any identifying information. MEPS Household Component data are available in the public domain. Specifically, the de-identified data can be downloaded directly from the MEPS/ AHRQ website (49).

RESULTS

Univariate Analysis

Among the total study population, 60% of participants were taking asthma maintenance medication daily or almost daily (Table 1). About half of the sample were between the ages of 41 to 64 years (48.4%) and non-Hispanic White (49.1%). The majority of study participants were female (71.7%) and had a high school diploma or GED (59.6%). Over 85% of the study population had at least one comorbidity, and 61% of the study population had an asthma attack in the last 12 months.

The racial/ethnic distribution was similar for participants who were taking daily asthma maintenance medication (non-Hispanic White: 71.2%; non-Hispanic Black: 14.6%; Hispanic: 7.4%; and other: 6.6%) and participants who were not taking a daily asthma maintenance medication (non-Hispanic White: 68.7%; non-Hispanic Black: 15.1%; Hispanic: 9.6%, and other: 6.4%). Participants who were taking and not taking daily asthma maintenance medication were also similar with respect to gender, income, and insurance status. However, the two populations were different with respect to comorbidities. Among patients taking daily asthma medications 4.2% reported no comorbidities while among patients not taking daily asthma medications, 31.3% reported no comorbidities.

Bivariate Analysis

The study participants who did not take daily asthma maintenance medication had statistically significant lower total direct medical cost compared to the participants who took daily asthma medication ($ 6,413 vs $12,154; $p \leq 0.0001$; Table 2). Age was statistically significantly associated with total medical costs (18- 24 years: $3,894; 25-40

years: $6,430 [p= 0.02]; 41- 64 years: $12,205 [p ≤0.0001]; and 65 and above: $11,967 [p ≤0.0001]). With respect to race/ethnicity, non- Hispanic black and Hispanic race/ethnicity were statistically significantly associated with cost ($10,008 [p= 0.04] and; $9,583 [p= 0.02], respectively).

Compared with men, women had statistically significantly higher total direct medical expenditures ($10,910 vs $7,457; p ≤0.0001). Participants who were divorced/ separated/widowed or single had lower total direct medical expenditures compared to married individuals (singles=$8,534.98, p=0.011; divorced/separated/widowed=$8,634, p ≤0.0001; married= $8,634.98). The participants who had a high school education or less than a high school education had higher total direct medical expenditures compared to participants who had more than a high school education (High school/ GED= $9,939 p=0.45; less than high school= $11,412, p=0.85; more than high school= $8,722), although these results were not statistically significant. Income level and region did not have a statistically significant relationship with total direct medical expenditures.

There was a statistically significant association between insurance status and total direct healthcare costs. Participants with public insurance had the highest total direct medical expenditures ($13,069 p= ≤0.0001) followed by private insurance ($9,056; p= ≤0.0001), and no insurance ($3,963). There was also a statistically significant association between Charlson's comorbidity index and total direct healthcare costs. Participants with three or more comorbidities had the highest total direct medical costs ($21,364; p= ≤0.0001) followed by cost for patients with two comorbidities ($20,940, p= ≤0.0001), and one comorbidity ($11,305, p= ≤0.0001) total direct healthcare costs were lowest for participants with no comorbidities ($6,103).

Multivariate Analysis

After adjusting for sex, age, insurance status, Charlson's comorbidity index, race/ethnicity, and having an asthma attack in the past 12 months, the expenditure values seen in the unadjusted model increased in magnitude. Specifically, participants not taking asthma medication had statistically significant lower costs for direct medical expenditures compared to participants taking daily asthma medication ($7,485 vs $15,149; $p \leq 0.0001$ Table 3).

Medical Cost

Medical cost represents all medical costs with the exception of prescription costs. After adjusting for sex, age, insurance status, Charlson's comorbidity index, race/ethnicity, and having an asthma attack in the past 12 months, medical cost for patients not taking asthma medication was still lower than for patients taking asthma medication daily, and this finding was statistically significant ($4,965 vs $9,691; $p \leq 0.0006$, Table 4).

Effect Modification

There was a statistically significant interaction between preventive medication taking status and race/ethnicity ($p \leq 0.0001$). Thus, race/ethnicity was an effect modifier of the relationship between asthma prescription taking status and total healthcare costs (Table 5). Among non-Hispanic Whites, the total direct expenditures for participants taking asthma medication was $13,228 while participant's not taking asthma medication had an expenditure of $6,425. While the direction of this association persisted among other racial/ethnic groups, the total direct expenditures for participants taking asthma medication were markedly higher. Specifically, among non- Hispanic blacks, participants

who were taking asthma prescription medication daily had a total direct expenditure of $20,480; participants who did not take asthma prescription medication daily had an expenditure of $9,803. Among Hispanics, the expenditure was $24,388 for participants taking asthma medication and $6,871 for participants not taking asthma medication. Among "others", the expenditure among participants taking medication was $24,452 and for the participants not taking medication the expenditure was $7,485.

There was also a statistically significant interaction between preventive medication taking status and age ($p \leq 0.0001$). Age was an effect modifier for the relationship between daily asthma prescriptions taking status and total healthcare costs (Table 6). Among 18-24 year olds, the total direct expenditure was $10,774 for participants taking asthma medication and $3,381 for those individuals not taking asthma medication. While the direction of this association persisted among other age groups, the total direct expenditures for participants taking asthma medication were higher (25-40 years: $13,079 for taking medications vs. $5,369 for not taking medications; 41-64 years: $16,139 for taking medications vs. $10,009 for not taking medications; and 65 and older: $12,845 for taking medications vs. $9,541 for not taking medications).

DISCUSSION

Summary of main findings

The current study found asthma patients who were taking daily asthma maintenance medication daily had higher total direct medical expenditures compared to asthma patients who were not taking daily asthma maintenance medications, and this finding was statistically significant after adjustment for confounders ($p \leq 0.0001$). Furthermore, the association between taking asthma maintenance medication and total healthcare costs differed by race/ethnicity and age.

Very few studies have compared differences in total healthcare costs among patients with asthma. Most studies have compared healthcare expenditures between asthma patients and non-asthma patients (10, 11). One study that compared healthcare costs for patients with and without asthma used 2003-2005 MEPS data and found that total healthcare expenditures for asthma patients were $9,204 compared to $4,921 for non-asthma patients (10). Another study compared the healthcare cost for 997 patients with and 9,323 patients without asthma using 2004 MEPS data (11). The study concluded that healthcare costs were higher for asthma patients compared to non-asthma patients ($2,077 vs $1,004.6). These findings were similar to the current study with respect to the direction and magnitude of healthcare costs for patients despite the current study comparing cost within a population of patients with asthma.

Another cross-sectional study was conducted using 2002-2007 MEPS data to calculate the total direct costs due to asthma at the individual level (36). The exposure was having asthma or having any prescribed medication for asthma. The study concluded the total direct costs for asthma in 2002-2007 was $3,259 higher per person per year after

adjusting for confounders when compared to the cost for patients without asthma. The findings of the current study were similar although the current study only considered individuals with asthma.

As mentioned, few studies have analyzed healthcare costs within a population of individuals with a diagnosis of asthma (12, 36). A study conducted using 2003- 2009 MEPS data included 10,374 non-elderly asthma patients and they were divided into four groups based on receiving treatment and having an asthma attack in the last year. Patients who received treatment for asthma and had an attack in the last year had total healthcare expenditures of $9,155 while patients who did not receive treatment and did not have an attack in the last year had healthcare costs of $5,835 ($p \leq 0.5$) (12). The current study's findings were similar in magnitude with the aforementioned study even though the exposure for the current study was slightly different (taking daily asthma maintenance medication versus receiving any treatment for asthma).

Although study findings were contrary to the main hypothesis of the study (i.e. that asthma patients taking daily preventive medications would have lower total medical costs when compared to asthma patients who do not take daily asthma preventive medications), another study has found similar associations (12). Reasons for these opposite findings could be due to uncontrolled confounding related to smoke exposure. For example, a patient exposed to environmental tobacco smoke may require more medical attention and thus accumulate more healthcare related costs.

Based on results from stratified analyses, race/ethnicity and age are effect modifiers for the association between asthma prescription taking status and total healthcare costs. Although the directions of the findings were similar among the groups,

the magnitude was most pronounced among non-Hispanic blacks, Hispanics, and the 41-64 years age group. While studies have examined race/ethnicity and age as exposures to investigate differences in healthcare costs (37, 47), to my knowledge, no studies have evaluated whether these variables modify the association between prescription taking status and total healthcare costs. It is possible that the observed variations may be due to differences in living conditions or access to care (51) or differences in severity of disease in these populations (5).

Strengths and Limitations

Non-Differential Misclassification

The exposure, taking daily prescription medication for asthma, was self-reported by participants. Since this question is not validated with medical records, misclassification is possible. For example, if a patient is taking multiple medications for a number of conditions, she/he may confuse another medication with asthma medication. Also, there is no information about adherence to the medication. Therefore, non-differential misclassification of the exposure is possible and would most likely bias the results towards the null.

Non-differential misclassification of the outcome, total direct medical expenditure, is also possible since this information was also self-reported by participants and was not confirmed by medical or insurance records. It may be difficult for participants to remember the payments for services when multiple visits and prescriptions are involved. Also, the participants are asked to enter the exact amount for their expenditures and it is possible they may round these values. If this type of misclassification occurred, it would most likely bias the association towards the null.

Selection Bias

As the response rate for MEPS was moderate (2012 response rate: 52.8% and 2013 response rate: 56.3%) (44), selection bias is possible. People who agreed to participate in the study may differ from people who did not participate as extremely ill asthma patients may have declined to participate. If participation was related to both the exposure and outcome, an over or underestimate of the true association may occur.

Information Bias

Information bias was likely minimized in this study through the use of CAPI. Additionally, participants were only asked to recall information for the last 3 to 6 months which helps to further minimize bias.

Temporal Bias

Since this study is a cross-sectional study, temporal bias could occur. In cross-sectional studies it is difficult to maintain the temporal sequence because the exposure and outcome information is collected simultaneously.

Confounding

The confounders that were assessed in this study were restricted to the variables available in the MEPS database. This study did control for multiple potential confounders including age, race/ethnicity, sex, education, health insurance, income, region, and D'Hoore's adaptation of the Charlston comorbidity index, asthma attack in last year. However, there may be other unknown confounders of the exposure-outcome association. Failure to control for these unknown confounders could result in an over or underestimation of the true association.

Generalizability

Because of the complex sampling design used by MEPS, the sample is representative of the general population. Assuming internal validity, the results of this study may be generalized to asthma patients aged 18 years and above living in the United States.

Strengths

The MEPS database has been used for a number of health use, prescription use and expenditure studies (12, 11). Since this study was performed on the most recent complete MEPS dataset (2012- 2013), this study provides the most up-to-date information on total direct healthcare expenditures among asthma patients. The use of nationally representative data aids in better understanding the burden of asthma among adults in the United States. Furthermore, the current study's findings are unique as this study analyzed whether age and race/ethnicity modified the daily asthma maintenance medication-total health expenditures association. Lastly, most studies have compared healthcare expenditures between asthma and non-asthma patients. In comparison, this study considered total healthcare cost among asthma patients based on whether they took daily asthma maintenance medications.

Implications and Future Research

High medical expenditures for asthma patients are a major public health issue for the United States. Asthma is a financially burdensome disease and needs to be properly managed to keep it under control. Asthma can be managed by adherence to medication as directed by physicians. However, as the current study's finding indicate, healthcare costs

are high for asthma patients taking daily prescription medication. Costs are also high among racial/ethnic minority groups and older asthma patients.

The reasons for these disparities could be due to socioeconomic status differences among minority groups in the United States. For example, area of residence, environmental exposures, and access to care may impact some minority groups more than others (51). Also, with increasing age, comorbidities also increase. These comorbidities might lead to higher costs for older asthma patients.

Given that this was the first study to investigate whether the asthma maintenance medication-total healthcare expenditures association differed by race/ethnicity or age, additional studies are needed. Future studies should examine in detail reasons for the racial/ethnic and age disparities seen among asthma patients. Also, studies should focus on ways to reduce comorbidities among asthma patients since these comorbidities could be an important reason for high healthcare costs. Finally, future studies may also investigate reasons for non-adherence to daily maintenance medications among asthma patients. Together, this information could assist medical and public health practitioners in better understanding some of the issues responsible for high healthcare costs and help them to plan strategies to minimize these costs among asthma patients. For example, programs that could help asthma patients to manage their asthma symptoms via self-management education, and to reduce other risk factors such as unhealthy living conditions, smoking, and other comorbidities, may be effective in assisting populations in minimizing their healthcare costs.

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APPENDIX A: TABLES

Table.1: Demographic information of study participants, 2012-2013 MEPS

Characteristics	All patients	Participants who take their preventive medication		Participants who do not take their preventive medication	
	Total Unweighted N (%)	Unweighted N	Weighted %	Unweighted N	Weighted %
Total participants	1336 (100%)	822	60.2	514	39.7
Age	1336 (100%)				
18-24 years	138 (10.4%)	52	7.0	86	16.3
25-40 years	313 (23.4%)	143	15.3	170	36.6
41- 64 years	647 (48.4%)	432	5.10	215	38.4
65 and above	238 (17.8%)	195	26.5	43	8.5
Race/ethnicity	1336 (100%)				
Non- Hispanic White	656 (49.1%)	404	71.2	252	68.7
Non- Hispanic Black	380 (28.4%)	239	14.6	141	15.1
Hispanics	207 (15.5%)	123	7.4	84	9.6
Others	93 (7.0%)	56	6.6	37	6.4
Region	1336 (100%)				
Northeast	275 (20.6%)	183	21.2	92	18.5
Midwest	299 (22.4%)	194	24.8	105	23.2
South	443 (33.2%)	278	34.8	165	30.9
West	319 (23.8%)	167	19.0	152	27.2
Gender	1336 (100%)				
Male	378 (28.3%)	237	30.4	141	28.3
Female	958 (71.7%)	585	69.5	373	71.6
Income	1336 (100%)				
Less than or equal to $10,000	204 (15.3%)	129	10.3	75	11.8
$10,001- $25,000	289 (21.6%)	188	17.8	101	15.9

Table 1 (continued)

Characteristics	All patients	Participants who take their preventive medication		Participants who do not take their preventive medication	
$25,001- $50,000	319 (23.9%)	187	24.1	132	24.4
More than $50,001	524 (39.2%)	318	47.7	206	47.8
Insurance	1336 (100%)				
Private	760 (56.9%)	454	66.6	306	67.8
Public	451 (33.7%)	312	27.3	139	20.0
No insurance	125 (9.4%)	56	5.9	69	12.1
Marital status	1336 (100%)				
Single	376 (28.1%)	203	20.4	173	29.8
Married	554 (41.5%)	343	46.7	211	45.4
Divorced/ Separated/ Widowed	406 (30.4%)	276	32.8	130	24.6
Education	1336 (100%)				
Less than high school	246 (18.4%)	158	13.0	88	12.2
High school graduate/ GED	796 (59.6%)	502	63.6	294	54.8
More than high school	294 (22.0%)	161	23.3	132	32.9
Charlson's Comorbidity	1336 (100%)				
Zero comorbidity	200 (14.9%)	47	4.2	153	31.3
One comorbidity	778 (58.2%)	507	63.9	271	53.0
Two comorbidity	238 (17.8%)	174	19.1	64	11.8
Three or more comorbidity	120 (9.1%)	94	12.6	26	3.6
Asthma attack in last 12 months	1336 (100%)				
Yes	822 (61.5%)	321	39%	501	61%
No	514 (38.5%)	176	34%	338	65.7%

Table 2: Unadjusted linear regression analysis of total direct medical expenditure and the patients who take their prescription for asthma and patients who do not take their prescription for asthma, 2012-2013 MEPS.

Variables	**β**	**(95% CI)**	**SE**	**Expenditure value**	**P-value**
Prescription medication					
Yes	Ref			$12,154.02	
No	-1.25	-1.52 to -0.98	0.1358	$6,413	<0.0001
Age					
18-24	Ref			$3,894.35	
25-40	0.69	0.114 to 1.26	0.29	$6,430.37	0.0192
41-64	1.63	1.13 to 2.14	0.25	$12,205.68	<0.0001
65 and above	2.01	1.45 to 2.57	0.28	$11,967.86	<0.0001
Race/ ethnicity					
Non-Hispanic Blacks	-0.312	-.608 to -0.0148	0.1504	$10,008	0.04
Hispanics	-0.48	-0.88 to -0.077	0.2045	$9,583	0.02
Others	0.2055	-0.34 to 0.75	0.2762	$12,313.82	0.46
Non- Hispanic Whites	Ref			$9,673	
Gender					
Male	Ref			$7,457.61	
Female	0.736	0.431 to 1.042	0.155	$10,910.89	<0.0001
Marital status					
Single	-1.09	-1.45 to -0.72	0.185	$8,534.98	0.0116
Married	Ref			$8,634.98	
Divorced/ Separated/ Widowed	0.33	0.075 to 0.595	0.0116	$12,994.55	<0.0001
Education					
Less than high school	-0.0248	-0.29 to -0.24	0.135	$11,412.12	0.85
High school/ GED	-0.14	-0.507 to 0.228	0.186	$9,939.26	0.45
More than high school	Ref			$8,722.72	
Table 2 (continued)					

Variables	β	(95% CI)	SE	Expenditure value	P-value
Income					
≤ $10,000	Ref			$9,651.15	
$10,001- $25,000	0.466	-0.16 to 1.09	0.32	13,287.53	0.142
$25,000- $50,000	0.34	-0.278 to 0.96	0.34	$9,333.63	0.28
≥ $50,0001	0.35	-0.278 to 0.97	0.35	$8,532.76	0.27
Region					
Northeast	0.20405	0.142 to 0.55	0.175	$9,698.54	0.246
Midwest	0.262	-0.085 to 0.609	0.176	$11,552.24	0.1375
South	0.107	-0.260 to 0.475	0.186	$9,262.45	0.5653
West	Ref			$9,521.62	
Insurance					
Private	1.43	0.86 to 2.00	0.288	$9,056.17	<0.0001
Public	1.71	1.125 to 2.29	0.297	$13,069	<0.0001
Uninsured	Ref			$3,963	
Charlston comorbidity index					
Zero Comorbidity	Ref			$6,103.35	
One Comorbidity	1.12	0.86 to 1.37	0.129	$11,305.19	<0.0001
Two Comorbidity	1.67	1.31 to 2.03	0.183	$20,940.28	<0.0001
Three or more Comorbidity	1.83	1.52 to 2.13	0.154	$21,364.45	<0.0001
Asthma attack in last 12 years					
Yes	Ref			$12,333	
No	-0.36	-0.64 to -0.079	0.1407	$8,534.02	0.0121

Table 3: Multivariate adjusted linear regression of total direct medical expenditure and the patients who take their daily prescriptions for asthma compared to patients who do not take their daily prescription for asthma, 2012-2013 MEPS.

	β	95% CI	SE	Expenditure Variable	P-value
Patients taking medication	Ref			$15,149	
Patients not taking medication	-0.789	-1.02 to -0.555	0.11	$7,485	<0.0001

Adjusted for: gender, age, insurance status, Charlson's comorbidity index, race, and having an attack in past 12 months.

Table 4: The medical cost analysis for asthma patients taking medication for asthma and those not taking medication for asthma, 2012-2013.

Medical cost	β	SE	95% CI	Expenditures	P-value
Patients taking medication	Ref			$9,691	
Patients not taking medication	-0.4739	0.135	-0.7406 to -0.2073	$4,965	0.0006

Adjusted for: gender, age, insurance status, Charlson's comorbidity index, race, and having an attack in past 12 months

Table 5: The effect modification between prescription taking for asthma medications and direct medical expenditures by race/ethnicity, 2012-2013 MEPS.

	For non- Hispanic whites				
	β	**95% CI**	**SE**	**Expenditure value**	**P-value**
Patients who are taking medication	Referent			$13,228	
Patients who are not taking medication	-0.85	-1.16 to -0.544	0.156	$6,425	<0.0001

	For non- Hispanic Blacks				
	β	**95% CI**	**SE**	**Expenditure value**	**P-value**
Patients who are taking medication	Referent			$20,480	
Patients who are not taking medication	-0.59	-1.01 to -0.18	0.208	$9,803	0.005

	For Hispanics				
	β	**95% CI**	**SE**	**Expenditure value**	**P-value**
Patients who are taking medication	Referent			$24,388	
Patients who are not taking medication	-1.05	1.04 to -1.05	0	$6,871	<0.0001

	For others				
	β	**95% CI**	**SE**	**Expenditure value**	**P-value**
Patients who are taking medication	Referent			$24,452	
Patients who are not taking medication	-0.627	-1.53 to 0.280	0.45	$9,628	0.1724

Table 6: The effect modification between prescription taking status for asthma medications and direct medical expenditures by age, 2012-2013 MEPS.

	For age group 18- 24 years				
	β	**95% CI**	**SE**	**Expenditure value**	**P-value**
Patients who are taking medication	Referent			$10,774	
Patients who are not taking medication	-1.65	-2.44 to -0.858	0.39	$3,381	<0.0001

	For age group 25- 40 years				
	β	**95% CI**	**SE**	**Expenditure value**	**P-value**
Patients who are taking medication	Referent			$13,079	
Patients who are not taking medication	-1.02	-1.08 to -0.964	0.029	$5,369	<0.0001

	For age group 41- 64 years				
	β	**95% CI**	**SE**	**Expenditure value**	**P-value**
Patients who are taking medication	Referent			$16,139	
Patients who are not taking medication	-0.59	0.809 to -0.377	0.109	$10,009	<0.0001

	For age group 65 and above				
	β	**95% CI**	**SE**	**Expenditure value**	**P-value**
Patients who are taking medication	Referent			$12,845	
Patients who are not taking medication	-0.32	-0.809 to -0.162	0.245	$9,541	0.1897