

Short-acting bronchodilators purchase as a marker for asthma control

Dekel Shlomi , Bernice Oberman & Irit Katz

To cite this article: Dekel Shlomi , Bernice Oberman & Irit Katz (2020): Short-acting bronchodilators purchase as a marker for asthma control, Journal of Asthma, DOI: [10.1080/02770903.2020.1837157](https://doi.org/10.1080/02770903.2020.1837157)

To link to this article: <https://doi.org/10.1080/02770903.2020.1837157>



Published online: 05 Nov 2020.



Submit your article to this journal [↗](#)



Article views: 20



View related articles [↗](#)



View Crossmark data [↗](#)



Short-acting bronchodilators purchase as a marker for asthma control

Dekel Shlomi, MD^{a,b} , Bernice Oberman, MSc^c, and Irit Katz, MD^d

^aAdelson School of Medicine, Ariel University, Ariel, Israel; ^bPulmonary Clinic, Clalit Health Services, Dan- Petah-Tiqwa District, Israel;

^cThe Biostatistics & Biomathematics Unit, The Gertner Institute for Epidemiology and Health Policy Research, Ramat-Gan, Israel;

^dDepartment of Neurological Rehabilitation, Sheba Medical Center, Ramat-Gan, Israel

ABSTRACT

Background: Administrative data has been used to quantify the amount of medication use in order to identify at-risk asthma patients. In our previous study we used short-acting beta-agonists (SABA) inhalers as a marker for asthma control.

Methods: We further analyzed patient data from the SABA inhalers study in which asthma control was classified by GINA guidelines, physician assessment and the patients overall estimation. We identified all short-acting bronchodilator purchases (SABA and anticholinergic inhalers and solutions) in the year prior to administering the questionnaire relating to asthma control, and compared inhaled and systemic steroid use.

Results: Of 241 asthma patients, 83 completed questionnaires. Using the GINA guidelines criteria, 26 were symptom controlled, 46 were partially controlled and 11 were uncontrolled. Using patients' overall impression of their asthma control, mean annual short-acting bronchodilator purchases were significantly higher in the partially controlled and uncontrolled patients (10 and 8.9 respectively) than in the controlled patients (2, $p = 0.005$). Most asthma patients purchase less than half of the controller medications prescribed to them.

Conclusion: When using administrative data, 3 or more -of all types of short-acting bronchodilator purchases in one year should alert the physician to evaluate asthma control and purchase alerts should notify both physicians and patients when controller consumption is low.

Abbreviations: CHS: Clalit Health Services; GINA: Global Initiative for Asthma; HMO: Health Maintenance Organization; ICS: inhaled corticosteroids; PCP: primary care physician; SABA: short acting beta-agonist; SAMA: short-acting muscarinic antagonist

ARTICLE HISTORY

Received 22 June 2020

Revised 24 September 2020

Accepted 11 October 2020

KEYWORDS

Electronic pharmacy data; bronchodilators; inhaled corticosteroids; asthma control; GINA guidelines

Introduction

Asthma is an obstructive chronic disease which has increased in prevalence over the past decades with a higher morbidity, mortality and economic burden (1). Only a minority of asthma patients (33.5%) have reported using long-term controllers (oral or inhaler) while most patients (64.4%) use quick-relief inhalers (2). Overuse of reliever medications increases the risk for asthma attacks, hospitalizations and mortality; these events directly correlate with the amount of inhaler use (3–7).

In recent years administrative data has been more frequently used in order to evaluate the association between asthma prescriptions and disease outcomes. Using computerized databases it has been found that the dispensing of short-acting beta-agonist (SABA) canisters correlates with asthma exacerbations (8,9). Furthermore, a higher controller to bronchodilator

medication prescriptions ratio has been seen to inversely correlate with hospital admissions, emergency department visits and asthma exacerbations (10–15). A recent systemic review found some evidence that electronic alerts reduce excessive prescribing of SABAs when delivered as part of a multicomponent intervention in an integrated health care system (16).

In our previous study we extracted administrative data of SABA inhaler purchases to classify asthma symptom control using three methods: GINA guidelines using patient questionnaires, overall estimation of asthma control by the patient and the primary care physician's (PCP) estimation (17). A correlation between asthma control and the number of SABA inhalers purchased was found only when we used the patients' overall estimation of asthma control. The mean numbers of SABA inhalers purchased were 1.5, 4.4 and 6.4 per year in the controlled, partially

controlled and uncontrolled groups respectively ($p=0.03$). We suggest that when using administrative data, 2 or more SABA inhaler purchases in one year should alert the physician to perform an asthma control evaluation. Patients' classification of their asthma control had better agreement ($\kappa = 0.34$) with GINA guidelines than physician's estimation ($\kappa = 0.05$).

Since rescue medication is used also in inhalation solutions and some patients use short-acting muscarinic antagonists (SAMA) instead of SABAs, we decided to further analyze in the same study population, the purchase of all short-acting bronchodilator medications (total number of medication purchases and powered calculations of drug doses) as well as inhaled corticosteroids (ICS) and systemic steroids. In the previous study we counted only SABA inhalers as a marker for asthma control. In this study, we hypothesize that when using all types of rescue medications, a larger amount of medication would be found as a marker for asthma that is not well-controlled. This study will further quantify the medication and validate it statistically.

Methods

The study was conducted in community clinics in the Dan-Petah-Tiqwa district of 'Clalit Health Services' (CHS), the largest publically funded Health Maintenance Organization (HMO) in Israel. In Israel patients have free access to their PCP, and all drug purchases are computerized. The study was approved by the Institutional Review Board of Meir Medical Center, Kfar-Saba, Israel.

Briefly, patients and PCPs were recruited from November 2012 through August 2014 in the Dan - Petah-Tiqwa district in the center of Israel. We provided a list of patients who had purchased SABA inhalers in the previous 12 months, to PCPs who were required to grade the level of asthma control of their asthmatic patients. Asthma patients were asked to complete a multiple-choice questionnaire regarding their asthma symptoms with respect to the GINA guidelines (18) criteria for symptom control and to grade their overall asthma control during the past 12 months.

Asthma level of symptom control according to the GINA guidelines (18) was classified using patients' questionnaires by addressing their answers to the relevant questions according to the GINA guidelines. For each patient we determined asthma control using the patients' and physician's questionnaires. Thus we obtained 3 separate estimates of asthma control: (1)

PCP estimates; (2) patient overall self-estimates; (3) estimates according to GINA guidelines. A detailed description of the methods is described in the original study publication (17).

Drug calculations

At first we calculated the mean number of all short-acting bronchodilator purchases in the form of inhalers and solutions for inhalations during the course of one year and compared them between the asthma control groups. However, since the total number of doses is different between inhaler and solution packages, we calculated the power for each medication purchased according to the most frequently used doses in Israel. We used the SABA MDI of salbutamol 100 mcg and SAMA MDI of ipratropium bromide 20 mcg inhalers as the reference (200 puffs – 2 puffs each time = 100 doses) which were given power 1. The SABA turbuhaler of terbutaline 500 mcg (200 puffs- 1 puff each time = 200 doses) was given power 2. Bottles of bronchodilator solution were powered as follows; salbutamol was given the power of 0.4 (40 doses), terbutaline the power of 0.3 (30 doses) and ipratropium bromide the power of 0.2 (20 doses). Since this last drug is used mostly in combination with a SABA we added it only if the patient didn't purchase SABA solutions in the previous 3 months.

For ICS, we calculated the number of steroid inhalers with or without LABA in one year. Since some patients use nebulized steroids in solution we evaluated each month of any steroid solutions purchased to be equal to one inhaler.

For systemic steroids we calculated the number of months that patients purchased systemic steroids (parenteral or injection) in one year.

Statistical analysis

ANOVA was used to compare between groups for continuous parametric variables, and the Kruskal-Wallis rank-sum test for non-parametric variables. Normality of variables was tested using the Shapiro-Wilk Test of normality. Equality of variances between groups was checked using Levenes Test. For categorical variables we used the Chi-squared Test or Fisher's exact test where the cells were small. For correlations we used Pearson's rank test for continuous parametric variables and Spearman's rank test for non-continuous variables. Statistical analysis was performed using R software, version 3.4.1 (R Project for Statistical Computing).

Table 1. Asthma medication purchases according to symptom control classification by the GINA guidelines, physicians' and patients' assessments.

	Asthma Control				p-value
	Total	Controlled	Partially Controlled	Uncontrolled	
Asthma control by GINA guidelines					
No. of patients (%)	83	26 (31.3)	46 (55.4)	11(13.3)	
Age yrs (SD)	37.7 (11.1)	36.2 (11.3)	37.4 (11)	42.8 (10.6)	0.24
Male (%)	42 (51)	18 (69)	17 (37)	7 (64)	0.02
Short-acting bronchodilators purchase -total mean (SD)	5.69 (14.75)	1.85 (2.11)	5.22 (9.01)	16.73 (35.13)	0.46
Short-acting bronchodilators purchase -weighted mean (SD)	4.25 (8.15)	1.74 (2.12)	4.24 (6.24)	10.25 (17.4)	0.65
ICS purchase mean (SD)	3.59 (4.44)	3.85 (4.88)	3.26 (4.35)	4.36 (3.93)	0.43
Systemic steroids purchase mean (SD)	0.55 (1.9)	0.12 (0.33)	0.65 (2.04)	1.18 (3.28)	0.43
Asthma control by physicians					
No. of patients (%)	83	59	18	6	
Age yrs (SD)		35.6 (11.2)	44.3 (8.8)	38.3 (10.7)	0.014
Male (%)		31 (53)	8 (44)	3 (50)	0.83
Short-acting bronchodilators purchase mean (SD)		5.03 (15.52)	4.78 (8.77)	14.83 (20.11)	0.29
Short-acting bronchodilators purchase -weighted mean (SD)		3.81 (7.82)	4.04 (7.43)	9.22 (12.67)	0.26
ICS purchase mean (SD)		2.98 (3.85)	3.94 (4.09)	8.5 (7.8)	0.037
Systemic steroids purchase mean (SD)		0.24 (0.6)	1.33 (3.53)	1.33 (3.27)	0.81
Asthma control by patients					
No. of patients (%)	82*	41	25	16	
Age yrs (SD)		35.7 (10.7)	37.8 (11.5)	42.1 (11.2)	0.152
Male (%)		24 (59)	8 (32)	9 (56)	0.096
Short-acting bronchodilators purchase mean (SD)		1.98 (3.57)	9.96 (8.4)	8.88 (11.24)	0.005
Short-acting bronchodilators purchase -weighted mean (SD)		1.73 (2.69)	5.88 (11.13)	8.42 (10.2)	0.005
ICS purchase mean (SD)		3.05 (4.19)	4.44 (5.19)	3.5 (3.90)	0.33
Systemic steroids purchase mean (SD)		0.1 (0.3)	0.56 (1.64)	1.75 (3.71)	0.07

ICS: inhaled corticosteroids; SD: standard deviation. * 1 patient did not classify his asthma level of control.

Results

Twenty three of 39 (59%) PCPs serving approximately 30 000 patients from 11 clinics agreed to participate in the study. Using administrative data, we found a total of 475 patients (1.58%) who purchased SABA inhalers during the 12 months prior to our first contact with the PCP. Of the 475 patients, 241 patients had asthma according to the PCPs' questionnaires, however, only 83 (34%) completed patient questionnaires. Patient characteristics are summarized in Table 1 in our original publication (17).

Using GINA guidelines criteria for patient symptom control we found 26/83 (31.3%) to be controlled, 46/83 (55.4%) to be partially controlled and 11/83 (13.3%) to be uncontrolled patients. Classification according to PCP's estimation had 59/83 (71.1%) controlled, 18/83 (21.7%) partially controlled and 6/83 (7.2%) uncontrolled patients. Eighty-two of the patients graded their own overall estimation of their asthma control; 41/82 (50%) classified themselves as controlled, 25/82 (30.5%) as partially controlled and 16/82 (19.5%) as uncontrolled patients.

Rescue medication purchases - mean number

Using the all types of rescue medication purchases (SABA and SAMA inhalers and solutions) the only statistically significant differences were found when asthma control was classified by the patients. The

mean annual rescue medication purchases were significantly higher in the partially controlled and uncontrolled patients (10 and 8.9 respectively) compared to controlled patients (2, $p = 0.005$). The 75th percentile for the controlled group was 2 medications (equal to the median of the partially controlled group) while the median of the uncontrolled group was 3.

Using asthma classification by GINA criteria and by the physicians' estimation, higher medication purchases were found in the uncontrolled and partially controlled patients compared to controlled patients although they were not statistically significant. By GINA criteria the mean rescue medication purchases were 16.7 and 5.2 for the uncontrolled and partially controlled patients respectively and 1.9 for the controlled patients ($p = 0.46$). Purchases according to the physicians' estimation were 14.8 and 4.8 for the uncontrolled and partially controlled patients respectively and 5 for the controlled patients ($p = 0.29$). Table 1 summarizes the asthma medication purchases according to the level of asthma control using all 3 methods.

Rescue medication purchases - powered calculation

Once again statistically significant differences were found only when using the patients' general assessment of asthma control. The mean of all-types of short-acting bronchodilator purchases using the power calculations were 8.4 and 5.9 for the uncontrolled and

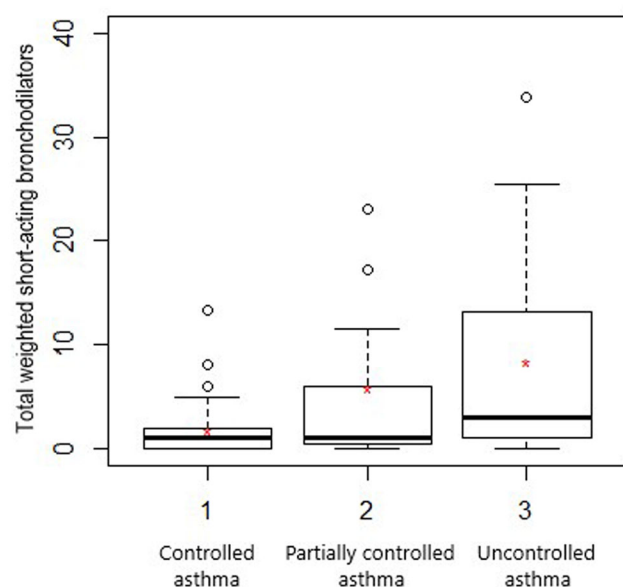


Figure 1. Short-acting bronchodilators purchased in one year according to patients' classification of asthma control (powered calculation). The box represents 25th and 75th percentile, the line in it representing the median, the asterisk is the mean, the whiskers represents 1.5X interquartile range and the dots represents external values.

partially controlled patients respectively and 1.7 for the controlled patients, $p=0.005$ (Figure 1). The calculation of -mean medication purchases, using the asthma classification by GINA criteria and by the physicians' estimation, yielded a higher but not statistically significant number of purchases in the uncontrolled and partially controlled patients compared to the controlled patients. By GINA criteria the mean powered rescue medication purchases were 10.3 and 4.2 for the uncontrolled and partially controlled patients respectively and 1.7 for the controlled patients ($p=0.65$). Purchases according to the physicians' estimation were 9.2 and 4 for the uncontrolled and partially controlled patients respectively and 3.8 for the controlled patients ($p=0.26$).

Inhaled corticosteroids purchases

A statistically significant difference was found only according to physicians' classification of asthma control. ICS purchases were 3, 3.9 and 8.5 in the controlled, partially controlled and uncontrolled groups respectively ($p=0.037$).

Small purchases were found equally between asthma control groups when we used the GINA classification – 3.9, 3.3 and 4.4 ($p=0.43$) or the patients' overall estimation- 3.1, 4.4 and 3.5 ($p=0.33$) in the controlled, partially controlled and uncontrolled groups respectively (Table 1).

Systemic corticosteroids purchases

Overall, the controlled patient group in each method of classification purchased less, albeit not statistically significant, systemic corticosteroids than the partially and uncontrolled patients (Table 1). However, in the patients' general self-assessment of asthma control classification a trend was observed in which the average purchase was 0.1 among the controlled patients, 0.56 in the partially controlled and 1.75 in the uncontrolled patients ($p=0.07$). Only 4 of 41 (0.98%) patients purchased systemic steroids in the controlled group in this classification compared to 6 of 25 (24%) and 5 of 11 (45%) in the partially controlled and uncontrolled groups ($p=0.046$).

Correlation between short-action bronchodilators, ICS and systemic steroids

Moderate correlations were found between the mean weighted short-acting bronchodilators, ICS and systemic steroids in one year when calculated for all patients regardless of asthma control. The Pearson correlation between short-acting bronchodilators and ICS was 0.35. The Spearman correlation was 0.37 between short-acting bronchodilators and systemic steroids and 0.21 between ICS and systemic steroids.

Discussion

Asthma control continues to be a major challenge for both physicians and patients. Despite improvements in asthma treatment over the last decades, most patients do not receive maintenance therapy, are not symptom controlled and use bronchodilators as their primary treatment (2,19). In order to identify asthma patients who are not controlled, we novelly, to the best of our knowledge, combined all their short-acting bronchodilator purchases (inhalers and solutions) and matched them to their asthma symptom control.

In our former study we used only SABA inhalers as a marker for asthma control (17), however, patients, mostly with more severe and uncontrolled disease, use solutions for inhalation for quick relief. Quantifying the sum of inhalers and solutions is not obvious since different inhalers and solutions contain different doses and in addition have different shelf lives after opening and thus can be used for different periods of time until their expiration date. Therefore, in this study we calculated the use of any short-acting bronchodilator medication using different methods. First, we counted all short-acting bronchodilator prescriptions in one year and compared them between

the different asthma control groups under each method of classification (GINA guidelines, PCP's and patients estimations). In the second stage we powered each drug according to the number of doses that could be derived according to common practice in Israel.

As in our former study of SABA Inhalers (17), in all of the three methods of classification, controlled patients purchased less short-acting bronchodilators than uncontrolled patients, however, the only statistically significant differences were found when using the patients' overall estimation for asthma control. Our results showed again that physicians' estimation of asthma control was further from the GINA guidelines than the patients' overall estimation. Agreement of asthma control between patients and physicians has been seen to be low in previous studies in both children and adults (20–22). Lately it has been seen that PCPs do not employ a standardization tool to monitor asthma control (23) and that an asthma-related outpatient visit to a general practitioner in the previous year is associated with a higher likelihood of inappropriate SABA use (24).

The purpose of our studies is to help PCPs detect uncontrolled asthma patients by using available and simple administrative data such as medication purchases. Since the 75th percentile for the controlled group was 2 rescue medications a year and while most patients with asthma that is not controlled purchase more rescue medications a year, we suggest that a purchase of 3 or more should alert physicians to reassess asthma control. In our previous study we used only SABA inhaler purchases and suggested that 2 or more purchases in one year should alert the physician for the need for asthma control evaluation. As we hypothesized, compared to our previous study, larger quantities and combinations of rescue medications were found to be an alert for asthma that is not controlled (3 vs. 2). However, since different patients use short-acting bronchodilators in different modalities, we believe it is better to be alerted for "over-consumption" of all types of drugs. Drug doses may be different between inhalers and solutions, however, when we used the powered calculation of all types of short-acting bronchodilators, small and not clinically significant differences were found between this analysis and the simple sum of the packages purchased in a year. Thus using the count of all purchases of all types of short-acting bronchodilator medications per year is a simple and validated marker for uncontrolled asthma.

Our results, using adjusted number of all types of short-acting bronchodilator purchases in one year as a

marker for uncontrolled asthma is different from other studies due to the different methods and different outcomes that were used. A previous study by Schatz et.al (14), that was conducted in a selected group of persistent asthma patients (selected from a database using electronic criteria) found that a purchase of 6 or more SABA canisters was associated with increased subsequent emergency hospital care. In a different study, cutoffs of 11 and 12 SABA canisters dispensed in a year were found to predict a high risk for emergency hospital care and for oral corticosteroid dispensation, respectively (8). The reason for these differences is that our study uses administrative data in order to identify all asthma patients and classify their level of control according to questionnaires, hence the smaller number of medications we found to indicate at-risk community asthma patients even if they do not seek special medical intervention.

Inhaled corticosteroid purchases were equally low (3.1–4.4 medications per year) for all asthma control levels according to GINA guidelines and patients overall impression of asthma control. Interestingly, by PCP's classifications uncontrolled patients purchase statistically significant more ICS than controlled and partially controlled patients (8.5 vs. 3 and 3.9 respectively, $p=0.037$). This observation might be explained by a bias of PCP's that recalled patients as uncontrolled when they prescribed high quantities of ICS medications. Several studies using administrative data found worse asthma outcomes for patients with a lower controller to reliever medication ratio (10–15). Since significant differences were not found, either in the number of ICS purchases between asthma control groups according to patients' overall estimation or in the short-acting bronchodilator purchases according to PCP's estimation, this ratio has no meaning in our study.

Although systemic steroid use was more prevalent in the uncontrolled patients according to the patients overall estimation of asthma control (0.98% in the controlled group compared to 24% and 45% in the partially controlled and uncontrolled groups respectively; $p=0.046$) the average number of months of systemic steroid use was low at all levels of control (0.1–1.75). Since every systemic steroid use should alert the physician to evaluate asthma control, these numbers are not clinically relevant, rather a confirmation for the consistently better classification of asthma control according to patients overall estimation.

Correlations between short-acting bronchodilators and ICS and between short-acting bronchodilators and systemic steroids were moderate (0.35 using Pearson's correlation and 0.38 using Spearman's

correlation respectively). The first finding might be in contrast to the idea that the more ICS the patient uses the less short-acting bronchodilators he needs. However, given the low amount of ICS use (mostly 3–4 medications a year), patients who need more short-acting bronchodilators are convinced to use slightly more ICS. Had they used ICS most of the year, the less short-acting bronchodilators would be needed. Furthermore, since some patients are using combined ICS + LABA in some inhalers as a reliever therapy, it may seem that patients using more ICS are less controlled. Also, as expected, the more short-acting bronchodilators used the more systemic steroids were needed.

There were several limitations in our study. First, our original group was asthma patients that were detected according to SABA inhalers purchased and not other asthma medications available. Since more uncontrolled patients usually purchase more solutions for inhalations (bronchodilators, inhaled steroids) and systemic steroids they could have increased the differences between the groups. Furthermore, some patients use LABA with or without ICS as a quick reliever which leads to lesser short-acting bronchodilator consumption, however, in our study the use of ICS including combined ICS and LABA was low and not statistically significant different between the groups.

Another limitation of the study is that asthma symptom control assessment by the GINA guidelines (18) referred to the previous 4 weeks while in our study we extended it for one year in order to match with medication purchases over the entire year. Asthma severity and control often fluctuate over time (seasons, viral infections, allergies etc.), thus patient recall of control over an entire year may be imprecise. Nevertheless, patient overall estimation of asthma control was consistently statistically significant.

Finally, patients purchase more inhalers than they actual need for rescue use such as for several locations (home, car, work etc.) or for sports activities (usually the better controlled patients). However, given the low medication purchases of the controlled asthma patients we would not expect a significant bias with respect to this behavior.

In conclusion, we found that using all short-acting bronchodilator purchases, whether inhalers or solutions for inhalation, 3 or more medication purchases in one year should alert physicians to re-assess asthma control. Most asthma patients purchase less than half of the controller medications prescribed for them. We suggest regular administrative alerts for both the physicians and patients when purchase of controllers is low.

Acknowledgements

The authors would like to thank CHS: Dan - Petah-Tiqwa district for a research grant in support of this work; Mr. Arie Reznik, former head of information systems in CHS, Dan-Petah-Tiqwa district, and Mrs. Nurit Moyal, head of the pharmaceutical monitoring department in CHS for their expert assistance in data retrieval; and the referents for information and projects in CHS, Dan-Petah-Tiqwa district, for patients' questionnaires administration.

Declaration of interest

Dr. Shlomi has received lecture fees and/or consultancy fees from TEVA, GSK, Rafa Laboratories, AstraZeneca, Boehringer-Ingelheim and Kamada.

All other authors have nothing to declare.

ORCID

Dekel Shlomi  <http://orcid.org/0000-0002-4327-1084>

References

1. Braman SS. The Global Burden of Asthma. *Chest*. 2006;130(1 Suppl):4S–12S. doi:[10.1378/chest.130.1_suppl.4S](https://doi.org/10.1378/chest.130.1_suppl.4S).
2. Centers for Disease Control and Prevention. Vital signs: asthma prevalence, disease characteristics, and self-management education: United States, 2001–2009. *MMWR Morb Mortal Wkly Rep*. 2011;60(17):547–552. [cited Oct 10]. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/21544044>
3. Spitzer WO, Suissa S, Ernst P, Horwitz RI, Habbick B, Cockcroft D, Boivin JF, McNutt M, Buist AS, Rebuck AS, et al. The use of beta-agonists and the risk of death and near death from asthma. *N Engl J Med*. 1992;326(8):501–506. doi:[10.1056/NEJM199202203260801](https://doi.org/10.1056/NEJM199202203260801).
4. Donahue JG, Weiss ST, Livingston JM, Goetsch MA, Greineder DK, Platt R. Inhaled steroids and the risk of hospitalization for asthma. *JAMA*. 1997;277(11):887–891. doi:[10.1001/jama.1997.03540350037030](https://doi.org/10.1001/jama.1997.03540350037030).
5. Schatz M, Zeiger RS, Vollmer WM, Mosen D, Apter AJ, Stibolt TB, Leong A, Johnson MS, Mendoza G, Cook EF, et al. Validation of a beta-agonist long-term asthma control scale derived from computerized pharmacy data. *J Allergy Clin Immunol*. 2006;117(5):995–1000. doi:[10.1016/j.jaci.2006.01.053](https://doi.org/10.1016/j.jaci.2006.01.053).
6. Ernst P, Habbick B, Suissa S, Hemmelgarn B, Cockcroft D, Buist AS, Horwitz RI, McNutt M, Spitzer WO. Is the association between inhaled beta-agonist use and life-threatening asthma because of confounding by severity? *Am Rev Respir Dis*. 1993;148(1):75–79. doi:[10.1164/ajrccm/148.1.75](https://doi.org/10.1164/ajrccm/148.1.75).
7. Eisner MD, Lieu TA, Chi F, Capra AM, Mendoza GR, Selby JV, Blanc PD. Beta agonists, inhaled steroids, and the risk of intensive care unit admission for asthma. *Eur Respir J*. 2001;17(2):233–240. doi:[10.1183/09031936.01.17202330](https://doi.org/10.1183/09031936.01.17202330).

8. Schatz M, Zeiger RS, Yang S-JT, Chen W, Crawford WW, Sajjan SG, Allen-Ramey F. Relationship of asthma control to asthma exacerbations using surrogate markers within a managed care database. *Am J Manag Care*. 2010;16(5):327–333. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/20469953>
9. Schatz M, Zeiger RS. Improving asthma outcomes in large populations. *J Allergy Clin Immunol*. 2011;128(2):273–277. doi:10.1016/j.jaci.2011.03.027.
10. Fuhlbrigge A, Carey VJ, Adams RJ, et al. Evaluation of asthma prescription measures and health system performance based on emergency department utilization. *Med Care*. 2004;42(5):465–471.
11. Griffiths C, Naish J, Sturdy P, Pereira F. Prescribing and hospital admissions for asthma in east London. *BMJ*. 1996;312(7029):481–482. doi:10.1136/bmj.312.7029.481.
12. Schatz M, Zeiger RS, Vollmer WM, Mosen D, Mendoza G, Apter AJ, Stibolt TB, Leong A, Johnson MS, Cook EF, et al. The controller-to-total asthma medication ratio is associated with patient-centered as well as utilization outcomes. *Chest*. 2006;130(1):43–50. doi:10.1378/chest.130.1.43.
13. Schatz M, Stempel D. Asthma quality-of-care measures using administrative data: relationships to subsequent exacerbations in multiple databases. *Ann Allergy Asthma Immunol*. 2008;101(3):235–239. doi:10.1016/S1081-1206(10)60487-5.
14. Schatz M, Nakahiro R, Crawford W, Mendoza G, Mosen D, Stibolt TB. Asthma quality-of-care markers using administrative data. *Chest*. 2005;128(4):1968–1973. doi:10.1378/chest.128.4.1968.
15. Yong PL, Werner RM. Process quality measures and asthma exacerbations in the medicaid population. *J Allergy Clin Immunol*. 2009; 124(5):961–966. doi:10.1016/j.jaci.2009.07.027.
16. McKibben S, De Simoni A, Bush A, Thomas M, Griffiths C. The use of electronic alerts in primary care computer systems to identify the excessive prescription of short-acting beta 2 -agonists for people with asthma: A systematic review. *Npj Prim Care Respir Med*. 2018;28(1):14.
17. Shlomi D, Katz I, Segel MJ, Oberman B, Peled N. Determination of asthma control using administrative data regarding short-acting beta-agonist inhaler purchase. *J Asthma*. 2018;55(5):571–577. doi:10.1080/02770903.2017.1348513.
18. GINA Report, Global Strategy for Asthma Management and Prevention | Documents/Resources | GINA [Internet]. [cited 2015 Oct 30]. Available from: <http://www.ginasthma.org/documents/4>.
19. Partridge MR, van der Molen T, Myrseth S-E, Busse WW. Attitudes and actions of asthma patients on regular maintenance therapy: the INSPIRE study. *BMC Pulm Med*. 2006;6(1):13. doi:10.1186/1471-2466-6-13.
20. Boulet L-P, Phillips R, O'Byrne P, Becker A. Evaluation of asthma control by physicians and patients: Comparison with current guidelines. *Can Respir J*. 2002;9(6):417–423. doi:10.1155/2002/731804.
21. Urrutia I, Plaza V, Pascual S. Asthma control and concordance of opinion1. Laforest L, Licaj I, Devouas1. Laforest L, Licaj I, Devouassoux G, et al. Relative exposure to controller therapy and asthma exacerbations: a validation study in community pharmacies. *Pharmacoepidemiol Drug Saf*. 2013;50(8):877–83. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/23808796>
22. Prieto L, Badiola C, Villa JR, Plaza V, Molina J, Cimas E. Asthma control: do patients' and physicians' opinions fit in with patients' asthma control status? *J Asthma*. 2007;44(6):461–467. doi:10.1080/02770900701421989.
23. Chapman KR, Hinds D, Piazza P, Raherison C, Gibbs M, Greulich T, Gaalswyk K, Lin J, Adachi M, Davis KJ, et al. Physician perspectives on the burden and management of asthma in six countries: The Global Asthma Physician Survey (GAPS). *BMC Pulm Med*. 2017;17(1):153. doi:10.1186/s12890-017-0492-5.
24. Tavakoli H, Mark FitzGerald J, Lynd LD, Sadatsafavi M. Predictors of inappropriate and excessive use of reliever medications in asthma: a 16-year population-based study. *BMC Pulm Med*. 2018;18(1):33 doi:10.1186/s12890-018-0598-4.