

Relationship of Asthma Control to Asthma Exacerbations Using Surrogate Markers Within a Managed Care Database

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Asthma is a common chronic medical condition that is associated with substantial individual morbidity and cost to society.^{1,2} The traditional approach to improving disease outcomes has been by one-on-one physician–patient interactions. Computerization of medical utilization and claims data (“administrative data”) has allowed 2 more recent approaches for asthma control. The first is the use of administrative data to define asthma quality-of-care or performance measures. These measures are used by managed care organizations and others to improve the performance of their providers, with the expectation that improved performance on the measures will lead to improved asthma outcomes and lower costs.³ The most widely used asthma quality-of-care measure is the one developed by the National Committee for Quality Assurance⁴ to evaluate the performance of health plans, the Healthcare Effectiveness Data and Information Set (HEDIS) measure (“HEDIS measure”). This measure identifies patients with “persistent asthma” based on administrative data criteria and then determines the proportion of these patients who receive at least 1 controller medication dispensing the following year. Although used for approximately a decade, few studies have attempted to validate the HEDIS measure as being associated with improved subsequent outcomes. A study⁵ in children demonstrated such a relationship, but 3 studies^{6–8} in children and adults failed to show that improved performance on this measure is associated with improved asthma outcomes. After a study by Mosen et al⁹ demonstrated a relationship between the number of consecutive years of HEDIS qualification and markers of persistent asthma, the National Committee for Quality Assurance⁴ modified the definition of HEDIS persistent asthma to require that the administrative data criteria for persistent asthma be met for both the measurement year (the year the measure is being assessed) and the premeasurement year (“2-year HEDIS population”). To date, the HEDIS measure has not been systematically evaluated in this new 2-year HEDIS population.

The second use of computerized administrative data has been for population management. Patients with inadequately controlled asthma are identified based on administrative data criteria, and targeted intervention by mail, telephone, or in-person visits are instituted. In addition to the HEDIS measure of any controller use, 2 other measures have been suggested for use as quality-of-care measures or

Objective: To compare the relationship of surrogate markers of asthma control to subsequent asthma exacerbations.

Study Design: Retrospective cohort.

Methods: Administrative data were used to identify patients who met the Healthcare Effectiveness Data and Information Set (HEDIS) criteria for persistent asthma in 2006 and 2007. The following potential surrogate markers of asthma control assessed in 2007 were compared for their ability to predict asthma exacerbations in 2008 (defined as oral corticosteroid dispensing or an asthma hospitalization or emergency department visit): dispensing of any controller, unweighted medication ratio (the ratio of controller to total medication), weighted medication ratio, and the number of short-acting β -agonist (SABA) canisters dispensed. Weighted medication ratios were weighted for controller potency and for doses per container.

Results: Meeting the HEDIS criteria for persistent asthma were 8634 patients (60.5% female) aged 18 to 56 years (mean age, 42.7 years), of whom 6.5% experienced emergency hospital care and 27.3% received oral corticosteroids in 2008. The largest effect size for predicting reduced emergency hospital care was for the number of SABA canisters dispensed (odds ratio [OR], 0.49; 95% confidence interval [CI], 0.40–0.60), followed by the unweighted medication ratio (OR, 0.54; 95% CI, 0.40–0.72), and then the weighted medication ratio (OR, 0.57; 95% CI, 0.45–0.73). Dispensing of any controller was associated with a nonsignificant increased risk of emergency hospital care (OR, 1.41; 95% CI, 0.95–2.09).

Conclusions: The number of SABA canisters dispensed is most strongly related to improved asthma outcomes, followed by the unweighted medication ratio; dispensing of any controller is least related. Health plans can use the number of SABA canisters dispensed and the unweighted medication ratio for asthma population management or for provider quality-of-care assessment to reduce asthma exacerbations, which exact a high economic and humanistic cost.

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Take-Away Points

The following relationships of asthma control to subsequent asthma exacerbations were observed:

- The number of short-acting β -agonist canisters dispensed is most useful to identify at-risk patients for targeted intervention in population management.
- The ratio of controller to total medication can be used as an asthma quality-of-care marker.
- Dispensing of any controller does not seem to be a good marker for population management or for quality of care.

as measures to identify patients with uncontrolled asthma in need of intervention. The first is the medication ratio, which is the ratio of units of controllers dispensed to the total units of controllers and units of short-acting β -agonists (SABAs) dispensed. A higher medication ratio has been associated with reduced subsequent exacerbations and with better patient-reported outcomes.^{6,8,10,11} This ratio has been used in a weighted form (weighted for doses per container and drug potency)¹⁰ and in an unweighted form,^{8,11} although these 2 ways of using the ratio measure have not been directly compared to date. The second is the number of SABA canisters dispensed per year (“SABA measure”), which has been shown to be a long-term measure of asthma control.¹² To our knowledge, this SABA measure has not been compared with the HEDIS measure or the medication ratio measure as a predictor of improved asthma outcomes.

The objective of this study was to compare the ability of the HEDIS measure, the medication ratio measure (weighted and unweighted), and a SABA measure to predict asthma exacerbations (defined in 2 different ways) in the 2-year HEDIS population. Asthma exacerbations are particularly appropriate outcomes to use in validating surrogate markers of asthma control because of their large contribution to the cost of asthma care¹³ and their substantial effect on quality of life. Identifying valid asthma control measures based on administrative data that are associated with reduced asthma exacerbations should allow health plans to use these measures to provide outreach to patients in need of intervention and to offer “inreach” to providers whose patients may be at increased risk for poor asthma outcomes.

METHODS

Patients

This study was approved by the Kaiser Permanente Southern California (KPSC) Institutional Review Board. Using computerized KPSC inpatient, outpatient, pharmacy, and membership records, we identified patients aged 18 to 56 years with continuous enrollment (≤ 1 gap of < 45 days’ coverage) in 2006 and with persistent asthma in 2006 based on meeting 1

or more of the following HEDIS criteria: 4 or more asthma medication dispensings, 1 or more emergency department visits or hospitalizations with a principal diagnosis of asthma, or 4 or more asthma outpatient visits with 2 or more asthma medication dispensings. Patients with continuous enrollment in 2007 who requalified in 2007 as having HEDIS-defined persistent asthma (ie, met ≥ 1 of these criteria in 2007) who also remained continuously enrolled KPSC members in 2008 are the subjects of this study.

Outcomes and Predictors

The outcome of interest was asthma exacerbations in 2008. These were identified in the following 2 ways: (1) emergency hospital care for asthma, defined as having at least 1 hospitalization or emergency department visit for which asthma (*International Classification of Diseases, Ninth Revision, Clinical Modification* [ICD-9-CM] code 493.xx) is the primary diagnosis or is a secondary diagnosis with another respiratory diagnosis coded as the primary diagnosis, or (2) a filled prescription of an oral corticosteroid prescribed within 7 days after an outpatient encounter for asthma (ICD-9-CM code 493.xx).

Nebulized medications were excluded as potential markers of asthma control because dispensed quantities could not be reliably translated into medication units. The following candidate markers of quality asthma care or uncontrolled asthma in 2007 were evaluated as predictors of asthma exacerbations in 2008:

HEDIS Measure (Dispensing at Any Time and in Any Amount of Any Asthma Controller, as Defined by HEDIS,⁴ Which Is the Current HEDIS Asthma Quality-of-Care Measure). These controllers include inhaled corticosteroids, inhaled corticosteroid/long-acting β -agonist combinations, leukotriene modifiers, theophylline, and cromolyn sodium. They do not include SABAs, long-acting β -agonists alone, or oral corticosteroids.

Unweighted Medication Ratio (Unweighted Ratio of Controller to Total Asthma Medication). The ratio was calculated for each patient as the number of controller units dispensed during 2007 divided by the sum of the controller units and SABA inhaler canisters dispensed during 2007. For inhalers, 1 controller unit was 1 canister. For oral medications, 1 controller unit was 1 prescription of an amount lasting 30 days or less. Medication ratios range from 0 (no controllers) to 1.0 (no SABAs).

Weighted Medication Ratio (Weighted Ratio of Controller to Total Asthma Medication). This ratio was calculated

as for the unweighted medication ratio except that controllers were weighted for medication potency and for the number of doses per container to account for potentially important differences in these characteristics between products. The specific weighting algorithm for individual products is available from the authors by request. Examples of weights for common controllers among our patients are 1.0 (montelukast sodium), 1.7 (beclomethasone dipropionate hydrofluoroalkane 80), 2.0 (budesonide 180), and 4.0 (fluticasone propionate 220 and mometasone furoate 220).

SABA Measure (Number of SABA Canisters Dispensed in 2007). The total number of inhalational SABA canisters dispensed in 2007 was used for this marker.

Data Analysis

Optimal cutoffs for the medication ratio and SABA measures to predict emergency hospital care and asthma exacerbations as defined by oral corticosteroid dispensing were determined. For the medication ratios, cutoffs between 0.3 and 0.9 (at 0.1 intervals) were examined; for the SABA measure, levels of 4 to 12 canisters per 12 months were examined. These levels were chosen to include likely optimal cutoffs based on results of prior studies.¹⁰⁻¹² For each level of the predictor, odds ratios (ORs) and 95% confidence intervals (CIs) were calculated by means of simple logistic regression analysis. The optimal cutoff was determined based on (1) a significant association with a reduced risk of the outcome (upper 95% CI <1) and (2) the lowest OR associated with a significant reduction.

Optimal cutoffs for the unweighted medication ratio, weighted medication ratio, and SABA measure were then compared with the results for the HEDIS measure (dispensing of any controller) and with each other based on the magnitude of the significant effect sizes (calculated as 1 minus the OR for significant relationships). Predictor status of all patients was defined and was used in the analyses of each measure. All analyses were performed using commercially available statistical software (SAS version 9.13 for Windows; SAS Institute, Cary, NC).

RESULTS

Of 2,365,947 KPSC members 18 years and older in 2006, a total of 14,856 (age range, 18-56 years) met the HEDIS criteria for having persistent asthma in 2006 and were con-

Table 1. Risk of Emergency Hospital Care Relative to Various Cutoffs of Unweighted and Weighted Medication Ratios

Ratio Cutoff	OR (95% CI) ^a	
	Unweighted Medication Ratio	Weighted Medication Ratio
≥0.3	0.86 (0.70-1.05)	1.05 (0.82-1.34)
≥0.4	0.75 (0.63-0.90)	1.02 (0.82-1.26)
≥0.5	0.72 (0.61-0.86)	0.89 (0.73-1.07)
≥0.6	0.73 (0.61-0.87)	0.76 (0.64-0.91)
≥0.7	0.68 (0.56-0.82)	0.79 (0.67-0.94)
≥0.8	0.62 (0.49-0.77)	0.69 (0.57-0.83)
≥0.9	0.54 (0.40-0.72)	0.57 (0.45-0.73)

CI indicates confidence interval; OR, odds ratio.
^aA significant association with decreased risk of emergency hospital care is indicated by an upper 95% CI of less than 1. Cutoffs at and above the boldface values represent significantly reduced risk of asthma exacerbations.

tinuously enrolled in 2007 and 2008. Of these patients, 8634 (58.1%) requalified as having persistent asthma in 2007 (mean [SD] age, 42.7 [10.9] years; 60.5% female). Of these 8634 patients, 558 (6.5%) experienced an exacerbation as defined by emergency hospital care for asthma in 2008, and 2361 (27.3%) experienced at least 1 asthma exacerbation as defined by oral corticosteroid dispensing linked to an asthma encounter.

Medication Ratio

Emergency Hospital Care. Odds ratios for emergency hospital care decreased with increasing unweighted and weighted medication ratio cutoffs (Table 1). Odds ratios for emergency hospital care for any given ratio cutoff were lower (effect size larger) for the unweighted ratio compared with the weighted ratio. The optimal cutoff for the unweighted and weighted ratios was 0.9 or higher, with an OR of 0.54 (95% CI, 0.40-0.72) for the unweighted ratio and an OR of 0.57 (95% CI, 0.45-0.73) for the weighted ratio.

Oral Corticosteroid Dispensing–Defined Asthma Exacerbations. Odds ratios for oral corticosteroid dispensing–defined asthma exacerbations also decreased with increasing unweighted and weighted medication ratio cutoffs and for any given ratio cutoff were lower (effect size larger) for the unweighted ratio compared with the weighted ratio (Table 2). However, unweighted ratio cutoffs of 0.3 or higher and 0.4 or higher were associated with increased risk of asthma exacerbations, and only an unweighted ratio cutoff of 0.9 or higher was associated with significantly reduced risk of oral corticosteroid dispensing (OR, 0.78; 95% CI, 0.68-0.90). In contrast, weighted ratio cutoffs between 0.3 and 0.8 were associated with increased risk of asthma exacerbations as defined by oral corticosteroid dispensing, and a weighted ratio cutoff of 0.9 or higher neither significantly increased nor decreased the risk.

■ **Table 2.** Risk of Oral Corticosteroid Dispensing Relative to Various Cutoffs of Unweighted and Weighted Medication Ratios

Ratio Cutoff	OR (95% CI) ^a	
	Unweighted Medication Ratio	Weighted Medication Ratio
≥0.3	1.21 (1.08-1.36)	1.34 (1.16-1.54)
≥0.4	1.15 (1.04-1.28)	1.30 (1.15-1.47)
≥0.5	1.09 (0.99-1.19)	1.26 (1.13-1.41)
≥0.6	1.09 (0.99-1.20)	1.16 (1.05-1.28)
≥0.7	1.04 (0.94-1.15)	1.15 (1.04-1.26)
≥0.8	0.94 (0.84-1.04)	1.10 (1.00-1.22)
≥0.9	0.78 (0.68-0.90)	0.91 (0.81-1.02)

CI indicates confidence interval; OR, odds ratio.

^aA significant association with increased risk of oral corticosteroid dispensing is indicated by a lower 95% CI of greater than 1. Cutoffs at and above the boldface values represent significantly reduced risk of asthma exacerbations.

■ **Table 3.** Risk of Emergency Hospital Care and Oral Corticosteroid Dispensing Relative to Various SABA Cutoffs

SABA Cutoff, Canisters/y	OR (95% CI)	
	Emergency Hospital Care	Oral Corticosteroid Dispensing
<4	0.66 (0.56-0.79)	0.88 (0.81-0.98)
<5	0.65 (0.55-0.77)	0.83 (0.75-0.91)
<6	0.67 (0.56-0.80)	0.83 (0.76-0.92)
<7	0.57 (0.48-0.68)	0.81 (0.74-0.90)
<8	0.62 (0.52-0.74)	0.82 (0.74-0.91)
<9	0.58 (0.46-0.69)	0.76 (0.68-0.85)
<10	0.56 (0.46-0.68)	0.70 (0.63-0.79)
<11	0.49 (0.40-0.60)	0.66 (0.58-0.75)
<12	0.51 (0.41-0.63)	0.64 (0.56-0.73)

CI indicates confidence interval; OR, odds ratio; SABA, short-acting β-agonist.

^aA significant association with decreased risk of emergency hospital care or oral corticosteroid dispensing is indicated by an upper 95% CI of less than 1. Cutoffs at and above the boldface values represent significantly reduced risk of asthma exacerbations.

weighted medication ratio, and then the weighted medication ratio (Table 4). The largest effect size for predicting oral corticosteroid dispensing was also for the SABA measure, followed by the unweighted medication ratio. The HEDIS measure was associated with increased risk of emergency hospital care and oral corticosteroid dispensing, although the relationship with emergency hospital care was not statistically significant.

DISCUSSION

Asthma continues to exact a substantial humanistic and economic toll on patients and on society. Although asthma care must be individualized, population approaches to improving asthma outcomes have the potential to affect many patients.³ Valid administrative data markers of quality of care and asthma control are necessary to use such data to improve outcomes, whether by altered physician behavior (eg, rewards based on quality markers) or by targeted intervention in population management. One way to validate such measures is to test their relationship to subsequent outcomes. Of the markers evaluated in this study, the SABA measure was most strongly and consistently related to decreased subsequent risk of asthma exacerbations.

SABA Dispensing

All levels of SABA dispensing cutoffs were associated with reduced risk of emergency hospital care and oral corticosteroid dispensing—defined asthma exacerbations, although ORs were lower for emergency hospital care than for asthma exacerbations as defined by oral corticosteroid dispensing (Table 3). The optimal cutoff for emergency hospital care was less than 11, with an OR of 0.49 (95% CI, 0.40-0.60) and for oral corticosteroid dispensing was less than 12, with an OR of 0.64 (95% CI, 0.56-0.73).

Comparison of Asthma Control Markers

The largest effect size for predicting reduced emergency hospital care was for the SABA measure, followed by the un-

In contrast, the HEDIS measure was associated with increased risk of asthma exacerbations (defined in 2 different ways), consistent with prior studies^{7,8} in the 1-year HEDIS population. This study is the first comparison to date of these markers in the 2-year HEDIS population, and our results suggest that the SABA measure can be used to identify patients in need of intervention or to evaluate quality of care (level of asthma control) in a population, while the HEDIS measure seems inadequate for either purpose.

Increased SABA use is a recognized marker for uncontrolled asthma, which can be related to factors such as increased asthma severity, inadequate controller prescribing, poor patient adherence, or unaddressed comorbidities.¹⁴ As such, the value of an increased SABA use marker in population management

■ **Table 4.** Comparison of Asthma Control Markers

Measure	Emergency Hospital Care		Oral Corticosteroid Dispensing	
	OR (95% CI) ^a	Effect Size, %	OR (95% CI) ^a	Effect Size, %
HEDIS, dispensing of any controller	1.41 (0.95-2.09)	—	1.91 (1.53-2.39)	—
Unweighted medication ratio ≥0.9	0.54 (0.40-0.72)	46	0.78 (0.68-0.90)	22
Weighted medication ratio ≥0.9	0.57 (0.45-0.73)	43	0.91 (0.81-1.02)	—
SABA, No. of canisters dispensed ^b	0.49 (0.40-0.60)	51	0.64 (0.56-0.73)	36

CI indicates confidence interval; HEDIS, Healthcare Effectiveness Data and Information Set; OR, odds ratio; SABA, short-acting β-agonist.
^aA significant association with decreased risk of emergency hospital care or oral corticosteroid dispensing is indicated by an upper 95% CI of less than 1; a significant association with increased risk is indicated by a lower 95% CI of greater than 1.
^bOptimal cutoffs are less than 11 for emergency hospital care and less than 12 for oral corticosteroid dispensing.

is to identify patients who apparently need targeted intervention to address the factors responsible for their suboptimal control. Improved control should reduce direct and indirect costs of asthma, as better control has been associated with fewer exacerbations and with decreased absence from school and work.¹⁵⁻¹⁷ Patients who are receiving higher quantities of SABAs for other reasons (eg, need for canisters in multiple locations and for frequent exercise prophylaxis) are also identified by this method and account for some “false positives,” but these patients can be easily screened by telephone.

The medication ratio measure is the number of controller units dispensed during 1 year divided by the sum of the controller units and SABA inhaler canisters dispensed during that year. Our data suggest that the unweighted medication ratio measure is more closely associated with improved outcomes than the weighted medication ratio measure. The explanation for this may be related to the fact that patients who receive more potent drugs (and have higher weighted medication ratios) may have more severe disease, which attenuates the relationship between higher medication ratios and improved outcomes. Regardless of the explanation, the data suggest that, if the medication ratio measure is to be used, an unweighted measure that simply accounts for the use of controller units in relation to SABA units is best. The data also suggest that the SABA measure is more significantly and consistently related to improved outcomes than the medication ratio measure, which makes it a better choice for population management. The reason for this may be that more controller use, which is a way to increase the medication ratio, may be a marker of increased severity for some patients that works toward increasing exacerbations and counteracts the positive effects of increased controller use. In contrast, SABA dispensing is a more monotonic marker of increased severity or decreased control.

The practical implications of these results for the unweighted medication ratio measure as a quality-of-care marker are less clear. Both the HEDIS measure and the medication

ratio measure are meant to reflect the guideline recommendations of controller therapy for patients with persistent asthma. The association of any controller use with increased adverse outcomes probably reflects the greater severity of patients with persistent asthma who receive a controller versus those who do not, as well as the need for continued use of controllers to improve outcomes. Compared with the HEDIS measure, the medication ratio measure better reflects increased controller use, as well as controller effectiveness at reducing the need for SABAs. Although the medication ratio measure is less related to improved outcomes than the SABA measure, it has an advantage over the SABA measure as a quality-of-care marker. The SABA measure does not account for severity or the attempt to appropriately use controllers. A patient with severe treated disease may still require high levels of SABAs, but a high medication ratio at least reflects an attempt to use controllers to manage the illness. This would support the use of the unweighted medication ratio as a quality-of-care marker, especially because it is associated with a reduction in at least 1 important type of asthma exacerbation.

Prior studies^{8,11} of the unweighted medication ratio measure in patients with asthma have used 0.5 as the optimal cutoff. Results of the present study suggest that higher medication ratio cutoffs are associated with larger effect sizes on reduced emergency hospital care. However, a cutoff of 0.5 was associated with a significant 28% reduction in emergency hospital care in this study (Table 1). Because more patients in a population would achieve the lower medication ratio cutoff, decisions about which ratio cutoff to use as a quality-of-care marker would presumably depend on the baseline performance and the specific purpose of the quality-of-care assessment.

It is not immediately clear why a higher unweighted medication ratio was more strongly associated (more than double the effect size) with reduced emergency hospital care than asthma exacerbations as defined by oral corticosteroid

dispensing, assuming that more controller use and less SABA use should be associated with a reduction in both types of exacerbations. One possibility is that emergency hospital care as defined in this study is a better proxy for asthma exacerbation than oral corticosteroid dispensing, even with a prior asthma encounter. This would be consistent with the larger effect sizes of the SABA measure for emergency hospital care than for oral corticosteroid dispensing (Table 3). Another reason may be that some oral corticosteroid dispensings were given prophylactically, rather than for a current exacerbation. This may be especially likely in patients who are being more carefully managed overall, which may be associated with both higher medication ratios and increased prophylactic corticosteroid dispensing. A related explanation would be that oral corticosteroid dispensing identifies milder exacerbations, with weaker relationships to predictors. Again, better managed patients having more interaction with their physicians may have higher medication ratios and may be treated with corticosteroids for levels of symptom increases for which patients not as carefully managed would not receive treatment. This would serve to reduce the expected relationship between higher medication ratios and fewer asthma exacerbations.

Strengths of the present study include its large sample size, real-world managed care setting, and side-by-side comparison of several potential markers in a relevant population. One potential limitation of the study to generalizability is its inclusion of only KPSC patients, although Kaiser Permanente patients are demographically similar to the overall southern California community (Steve Derose, MD, unpublished data, October 2005), and there is no particular reason to believe that geographic variation would affect the results of this study. The KPSC system provides real-time information to providers regarding the number of SABA canisters dispensed and the medication ratio over the prior 12 months for all patients with scheduled visits. However, we do not believe that this factor should affect the relative relationships of the various markers to subsequent asthma exacerbations observed in this study. Because this cohort included only patients with persistent asthma, the results are not generalizable to patients with intermittent asthma. Similarly, because this study was limited to patients aged 18 to 56 years, the results are not necessarily generalizable to younger patients. However, a study⁸ has shown that a higher unweighted medication ratio is associated with reduced asthma exacerbations in children aged 5 to 17 years.

Another limitation is that, like all administrative data studies, this study relies on encounter coding and on medication dispensing, rather than on more direct clinical information, but that is the trade-off for the large population

being assessed. In addition, associations of the medication ratio¹¹ and the β -agonist measure¹² with patient-reported outcomes, including asthma-specific quality of life, have been reported.

In summary, this study has defined the usefulness of several administrative data asthma control markers based on their relationships to subsequent asthma exacerbations. For asthma population management, the results suggest that the SABA measure is better than the medication ratio or the HEDIS measure of controller use to identify patients who need intervention for asthma control. The study findings also indicate that the unweighted medication ratio is better than the weighted medication ratio as a quality-of-care marker. Finally, this study confirms that the unweighted medication ratio is a better quality-of-care marker than the current HEDIS measure, even in the 2-year HEDIS population. Health plans can use these markers to provide outreach to patients at risk of poor asthma outcomes and to initiate interventions such as education, medication changes, and specialty care. In addition, health plans can use these markers to offer inreach to providers whose patients may be at increased risk of adverse outcomes and to provide education regarding optimal guideline-based asthma care. Increased asthma control and decreased asthma exacerbations can reduce the economic and humanistic costs of asthma.

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