

Drivers of health care costs for adults with persistent asthma



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Clinical Implications

- Global Initiative for Asthma step-care level 4 or 5, frequent asthma exacerbations, excessive rescue bronchodilator use, and elevated blood eosinophil count are among the independent cost predictors associated with increased asthma-related total health care costs for adults aged 18 to 64 years with persistent asthma.

TO THE EDITOR:

Yearly direct costs for adults with asthma from 2005 to 2009 were estimated at \$59.7 billion in the United States.¹ Understanding the driving forces associated with direct costs of patients with asthma may guide efforts to reduce costs and/or prevent their future increase. In addition to the usual factors related to asthma and its costs, reports highlight that a high blood eosinophil count is an independent risk factor for increased current and future asthma exacerbations in adults²⁻⁴ and children^{5,6} with persistent asthma.

To identify the independent risk factors of direct costs in adults with persistent asthma, we conducted a retrospective study of a previously characterized adult cohort with persistent asthma enrolled in the Kaiser Permanente Southern California managed-care organization.² Administrative and health care utilization data and associated costs data were collected to determine predictors associated with direct all-cause health care total costs (referred to as “all-cause costs”) and direct asthma-related health care costs (referred to as “asthma costs”) (see Figure E1, A, in this article’s Online Repository at www.jaci-inpractice.org).⁴ The study cohort included 2392 patients aged 18 to 64 years with persistent asthma who met the Healthcare Effectiveness Data and Information Set (HEDIS) 2-year criteria for persistent asthma in 2009 and 2010 (see this article’s Online Repository at www.jaci-inpractice.org for HEDIS definition, which includes all severities of persistent asthma and exclusions) and had a blood eosinophil determination in 2010 (Figure E1, B).²

The components of all-cause and asthma costs in 2011 (in 2014 US \$) are detailed in this article’s Online Repository at www.jaci-inpractice.org. Generalized linear models with gamma distribution and log-link function were used to estimate the direct all-cause and asthma costs as noted previously.⁴ The adjusted marginal costs and 95% CIs of the predictors in 2010 were reported.⁴ The predictive models included independent variables measured in 2010 as predictors (Figure 1 legend) and all-cause and asthma costs in 2011 as outcome variables.² The cost analyses were conducted with Stata 14 (StataCorp LP, College Station, Texas). All tests were 2-tailed with significance at alpha 0.05.

The unadjusted mean $\pm$ SD all-cause and asthma costs per patient were greater for the baseline year (\$6556 $\pm$ \$7834 and \$2602 $\pm$ \$2172, respectively) (see Table E1 in this article’s Online Repository at www.jaci-inpractice.org) than for the outcome year (\$5559 $\pm$ \$7007 and \$2277 $\pm$ \$2241, respectively) (Table 1), possibly representing improvement in asthma-targeted Kaiser Permanente Southern California intervention. The unadjusted total all-cause and asthma costs and many of its components were significantly greater for patients at Global Initiative for Asthma (GINA) step-care level 4 or 5 and 2 or more previous year asthma exacerbations compared with lower step-care levels and history of fewer exacerbations (Table 1). Total asthma costs, but not all-cause costs, were significantly greater at higher eosinophil counts compared with lower eosinophil counts at cutoff points of 300 cells/mm³ and 400 cells/mm³ ($P < .01$ for both analyses) (see Table E2 in this article’s Online Repository at www.jaci-inpractice.org).

After adjustment for covariates, the following predictors contributed to a significant increase in all-cause costs, in decreasing order: Charlson comorbidity index (CCI) 2 or more versus 0 (\$4156); GINA step-care level 4 or 5 versus 1, 2, or 3 (\$1633); females (\$1262); pulmonologist visit (\$1211); chronic oral corticosteroid (OCS) use, defined as 2.5 mg/d or more average cumulative daily dosage⁷ (\$1155); asthma medication ratio (AMR) 0.5 or more (see Online Repository) (\$1001); and 7 or more short-acting β_2 -agonist (SABA) canisters dispensed (\$726) (Figure 1, A). The cost predictors significantly associated with total asthma costs, in decreasing order, were GINA step-care level 4 or 5 versus 1, 2, or 3 (\$1226), AMR 0.5 or more (\$869), 7 or more SABA canisters dispensed (\$824), 2 or more asthma exacerbations (\$602), chronic OCS use (\$421), an allergist visit (\$338), CCI 2 or more versus 0 (\$334), blood eosinophil count 400 cells/mm³ or more (\$293), non-Hispanic (\$288), and an age increase per every 10 years (\$180) (Figure 1, B). Sensitivity analysis based on the eosinophil cutoff point of 300 cells/mm³ revealed similar results for both all-cause and asthma costs, except for eosinophil count no longer being a significant predictor (\$175.0; 95% CI, \$12.4-\$362.5; $P = .067$).

Factors indicating more severe disease (ie, more comorbidities [CCI], higher GINA step-care level, chronic OCS use, AMR 0.5 or more, and 7 or more SABA dispensed canisters) were predictors for both all-cause and asthma costs; pulmonologist visits added to all-cause costs. However, 2 or more asthma exacerbations, allergist care, elevated blood eosinophil count, non-Hispanic ethnicity, and age were predictors for asthma, but not all-cause costs. The increase in both all-cause and asthma costs associated with chronic OCS use may be attributable to the higher medical care utilization experienced in patients with chronic OCS use.⁷ Consistent with our² and others^{3,8} findings that high blood eosinophil counts were associated with future asthma exacerbations,² the present analyses also found a significant increase in asthma costs associated with a blood eosinophil count of 400/mm³ or more. Our study did not find eosinophil count a significant predictor of the all-cause costs (either at ≥ 400 cells/mm³ or at ≥ 300 cells/mm³). An analysis of asthma patients 12 years or older based on claims data reported a 2.2-fold increase in total annual all-cause costs associated with elevated

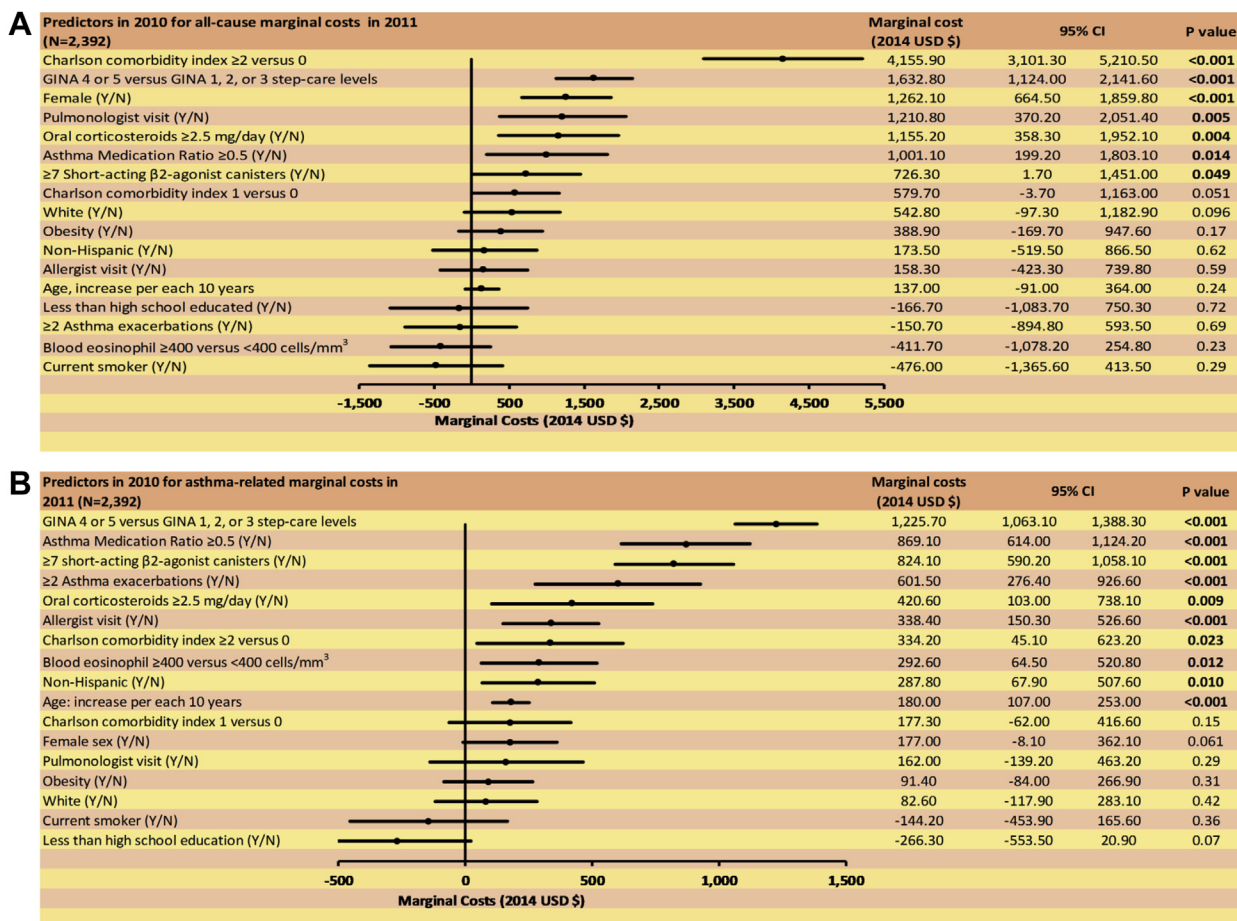


FIGURE 1. Adjusted average direct marginal cost per patient in 2011 by baseline predictor in 2010 in adults with persistent asthma. **A**, All-cause health care costs. **B**, Asthma-related health care costs. All the cost estimates were derived from generalized linear models with a gamma distribution and a log-link function.⁴ The predictors in 2010 were age, sex, ethnicity, high school education, obesity, current smoking, CCI, blood eosinophil count (binary at 400 cells/mm³ cutoff point), GINA step-care level, 2 or more asthma exacerbations, 2.5 mg/d or more OCS cumulative daily dosage (representing chronic OCS use), 7 or more SABA canisters dispensed, AMR 0.5 or more, allergist visit, and pulmonologist visit. *N*, No; *Y*, yes.

blood eosinophil counts (defined as ≥ 400 cells/mm³) (\$17,963 for elevated eosinophil count vs \$8,268 for nonelevated eosinophil count).⁹ In the same study, increasing age and CCI were also significantly associated with all-cause costs.⁹ Chastek et al¹⁰ reported unadjusted total asthma-related costs in a follow-up year of \$1775 for a persistent asthma cohort and \$5174 for a severe asthma cohort from a commercial or Medicare Advantage managed-care claims data set, comparable to the costs found in the present study of \$2277 and \$4107, respectively (Table 1). Substantially greater total annual all-cause costs have been noted in other studies.^{9,10} Differences in total all-cause costs between our study and others may be attributable to (1) differences in study design: (a) the present cost outcomes were captured in the *third* and outcome year after requiring patients to have at least 2 years of persistent asthma, (b) nonasthma drug costs, patient copays, and deductibles were not captured, and (c) many chronic diseases were excluded; (2) differences in disease management in integrated health care systems versus fee-for-service plans; (3) differences in sociodemographic and geographic parameters in

underlying populations because the present study did not include children younger than 18 years or those older than 65 years with their inherent increased frequency of comorbidities; (4) differences in asthma severity; (5) differences in approaches of monetizing resource utilization counts, as well as charges; and (6) differences in reimbursement of services across different years in each study. We previously reported that patients with eosinophil determinations compared with those without eosinophil determinations evidenced different demographic characteristics, more comorbidities, and more burdensome asthma.² Therefore, the study findings apply to patients with persistent asthma who had a blood eosinophil determination and generalization to those without a blood eosinophil determination should be with caution.

In summary, the present study was the first to capture the marginal costs of important phenotypic features associated with all-cause and asthma costs in a large 2-year HEDIS-defined cohort of adults with persistent asthma. Modifiable cost drivers in patients with asthma who require more intensive attention to

TABLE I. Unadjusted average direct costs per patient in the follow-up year in 2011 (in 2014 US \$) (mean $\pm$ SD) by type of utilization in adults with persistent asthma related to GINA step-care level and asthma exacerbations in baseline year 2010: (A) all-cause, (B) asthma-related

All-cause and asthma-related direct costs (US \$)	Total cohort (N = 2392)	1 or more asthma exacerbation in 2010			P value*	2 or more exacerbations in 2010			P value*
		Step-care level 1 or 2 (N = 137) (5.7%)	Step-care level 3 (N = 248) (10.4%)	Step-care level 4 or 5 (N = 400) (16.7%)		Step-care level 1 or 2 (N = 42) (1.8%)	Step-care level 3 (N = 81) (3.4%)	Step-care level 4 or 5 (N = 163) (6.8%)	
A. Total all-cause	5559 $\pm$ 7007	4528 $\pm$ 5851	4381 $\pm$ 4437	7086 $\pm$ 7264	<.001	4723 $\pm$ 4057	4734 $\pm$ 5201	7430 $\pm$ 7004	<.001
Inpatient visits	1623 $\pm$ 5710	1549 $\pm$ 4594	1032 $\pm$ 3220	2051 $\pm$ 5725	.10	1661 $\pm$ 3771	1433 $\pm$ 3906	2204 $\pm$ 5839	.64
Hospital outpatient visits	122 $\pm$ 408	109 $\pm$ 373	122 $\pm$ 354	148 $\pm$ 544	.67	93 $\pm$ 295	142 $\pm$ 370	163 $\pm$ 569	.54
ED visits	149 $\pm$ 440	307 $\pm$ 689	236 $\pm$ 761	258 $\pm$ 357	.004	263 $\pm$ 407	237 $\pm$ 396	203 $\pm$ 398	.10
Outpatient visits	1700 $\pm$ 1927	1596 $\pm$ 1929	1574 $\pm$ 1480	2048 $\pm$ 2557	.001	1470 $\pm$ 1168	1529 $\pm$ 1161	2058 $\pm$ 1606	.02
Laboratory†	101 $\pm$ 172	77 $\pm$ 154	82 $\pm$ 142	99 $\pm$ 164	.03	46 $\pm$ 104	78 $\pm$ 133	88 $\pm$ 152	.03
Radiology†	95 $\pm$ 236	55 $\pm$ 120	100 $\pm$ 233	91 $\pm$ 210	.09	63 $\pm$ 128	69 $\pm$ 197	84 $\pm$ 187	.23
Asthma medication‡	1768 $\pm$ 1548	835 $\pm$ 890	1235 $\pm$ 1063	2477 $\pm$ 1875	<.001	1126 $\pm$ 1028	1247 $\pm$ 1081	2630 $\pm$ 1917	<.001
B. Total asthma-related	2277 $\pm$ 2241	1573 $\pm$ 2060	1849 $\pm$ 1872	3483 $\pm$ 3432	<.001	2412 $\pm$ 2639	2251 $\pm$ 2655	4107 $\pm$ 4051	<.001
Inpatient visits	141 $\pm$ 1096	348 $\pm$ 1601	177 $\pm$ 1172	387 $\pm$ 1938	.29	690 $\pm$ 1914	464 $\pm$ 1910	689 $\pm$ 2576	.71
Hospital outpatient visits	1 $\pm$ 41	0 $\pm$ 4	2 $\pm$ 15	6 $\pm$ 99	.50	0 $\pm$ 0	2 $\pm$ 16	13 $\pm$ 155	.52
ED visits	15 $\pm$ 88	24 $\pm$ 75	30 $\pm$ 90	29 $\pm$ 129	.20	38 $\pm$ 88	51 $\pm$ 118	54 $\pm$ 184	.55
Outpatient visits	352 $\pm$ 566	367 $\pm$ 495	406 $\pm$ 477	585 $\pm$ 987	<.001	559 $\pm$ 707	488 $\pm$ 555	720 $\pm$ 803	.03
Asthma medication	1768 $\pm$ 1548	835 $\pm$ 890	1235 $\pm$ 1063	2477 $\pm$ 1875	<.001	1126 $\pm$ 1028	1247 $\pm$ 1081	2630 $\pm$ 1917	<.001

ED, Emergency department.

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

*P value: Kruskal Wallis test.

†Standalone laboratory or radiology not associated with an encounter.

‡Nonasthma medication was not captured.

improve asthma care include attention to comorbidities, frequent asthma exacerbations, excessive SABA dispensing, chronic OCS use, and elevated blood eosinophil counts.

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REFERENCES

1. Jang J, Gary Chan KC, Huang H, Sullivan SD. Trends in cost and outcomes among adult and pediatric patients with asthma: 2000–2009. *Ann Allergy Asthma Immunol* 2013;111:516–22.
2. Zeiger RS, Schatz M, Li Q, Chen W, Gossage D, Khatri D, et al. High blood eosinophil count is a risk factor for future asthma exacerbations in adult persistent asthma. *J Allergy Clin Immunol Pract* 2014;2:741–50.
3. Price DB, Rigazio A, Campbell JD, Bleecker ER, Corrigan CJ, Thomas M, et al. Blood eosinophil count and prospective annual asthma disease burden: a UK cohort study. *Lancet Respir Med* 2015;3:849–58.
4. Zeiger RS, Schatz M, Dalal AA, Qian L, Chen W, Ngor EW, et al. Utilization and costs of severe uncontrolled asthma in a managed-care setting. *J Allergy Clin Immunol Pract* 2015;4:120–9.
5. Zeiger RS, Schatz M, Li Q, Chen W, Khatri DB, Gossage D, et al. The association of blood eosinophil counts to future asthma exacerbations in children with persistent asthma. *J Allergy Clin Immunol Pract* 2015;3:283–7.
6. Tran TN, Khatri DB, Ke X, Ward CK, Gossage D. High blood eosinophil count is associated with more frequent asthma attacks in asthma patients. *Ann Allergy Asthma Immunol* 2014;113:19–24.
7. Zeiger RS, Schatz M, Li Q, Chen W, Khatri DB, Tran TN. Burden of chronic oral corticosteroid use by adults with persistent asthma. *J Allergy Clin Immunol Pract* 2017;5:1050–60.e9.
8. Casciano J, Krishnan JA, Small MB, Buck PO, Gopalan G, Li C, et al. Burden of asthma with elevated blood eosinophil levels. *BMC Pulm Med* 2016;16:100.
9. Casciano J, Krishnan J, Dotiwala Z, Li C, Sun SX. Clinical and economic burden of elevated blood eosinophils in patients with and without uncontrolled asthma. *J Manag Care Spec Pharm* 2017;23:85–91.
10. Chastek B, Korner S, Nagar SP, Albers F, Yancey S, Ortega H, et al. Economic burden of illness among patients with severe asthma in a managed care setting. *J Manag Care Spec Pharm* 2016;22:848–61.

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METHODS

The HEDIS definition for persistent asthma required 1 of the following criteria to be met in both calendar years 2009 and 2010: an asthma hospitalization; an asthma emergency department (ED) visit; 4 or more asthma outpatient visits and 2 or more asthma drugs dispensed; or 4 or more asthma drugs dispensed.^{E2,E3}

The AMR was defined as the number of dispensed asthma controller units (inhaled controller medication canisters or 30-day supplies of oral controller medications) divided by the total number of controller units and SABA canisters dispensed. The AMR is a validated administrative-data quality marker predictive of future asthma emergency ED or hospital care.^{E4} An AMR of 0.5 or more is the minimum quality measure cutoff point set by HEDIS to define adequate controller medication dispensing.^{E5}

Cost determination

The components of all-cause and asthma costs in 2010 (baseline year) and 2011 (outcome year) (in 2014 US \$) included all inpatient, hospital outpatient, ED, and outpatient visits and laboratory, radiology, and asthma medication (non-asthma medications were not captured). The asthma costs in 2010 and 2011 (in 2014 US \$) included asthma hospitalizations and ED visits with principal diagnosis of asthma, outpatient visits with an asthma *International Classification of Diseases, Ninth*

Revision diagnosis code, laboratory and radiology associated with asthma-specific visits, and asthma medication.

Economic burden (ie, direct health care costs) was characterized on the basis of setting of care. Burden was characterized in terms of annual visits during follow-up to ED, inpatient stays, and office-based visits, each of which was further classified as specific to asthma or defined as “all cause” if nonasthma. Length of hospital stay was defined as the number of nights between the date of admission and the date of discharge. Medical expenditures were calculated by multiplying units of service by standardized resource-based relative value multipliers. Resource-based relative value multipliers are based on Current Procedural Terminology codes and are published under the Physician Fee Schedule in the Federal Register. All expenditures were tallied up to the visit level. Thus, the analytic file contained annual cost outcomes for the following: (1) all-cause inpatient stays, (2) all-cause ED visits, (3) all-cause office visits, (4) all-cause laboratory visits, and (5) other ancillary costs related to radiology, and hospital-based outpatient visits. We also identified a subset of these outcomes specific to asthma that included (1) asthma-related inpatient stays with a principal diagnosis of asthma, (2) asthma-related ED visits with a principal diagnosis of asthma, (3) asthma-related office visits with asthma *International Classification of Diseases, Ninth Revision* coding, and (4) asthma-related pharmacy expenditure.^{E6}

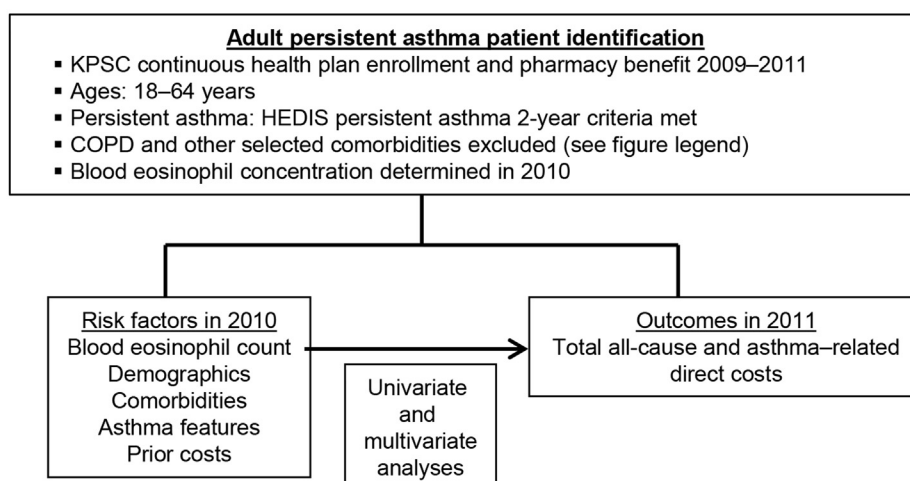
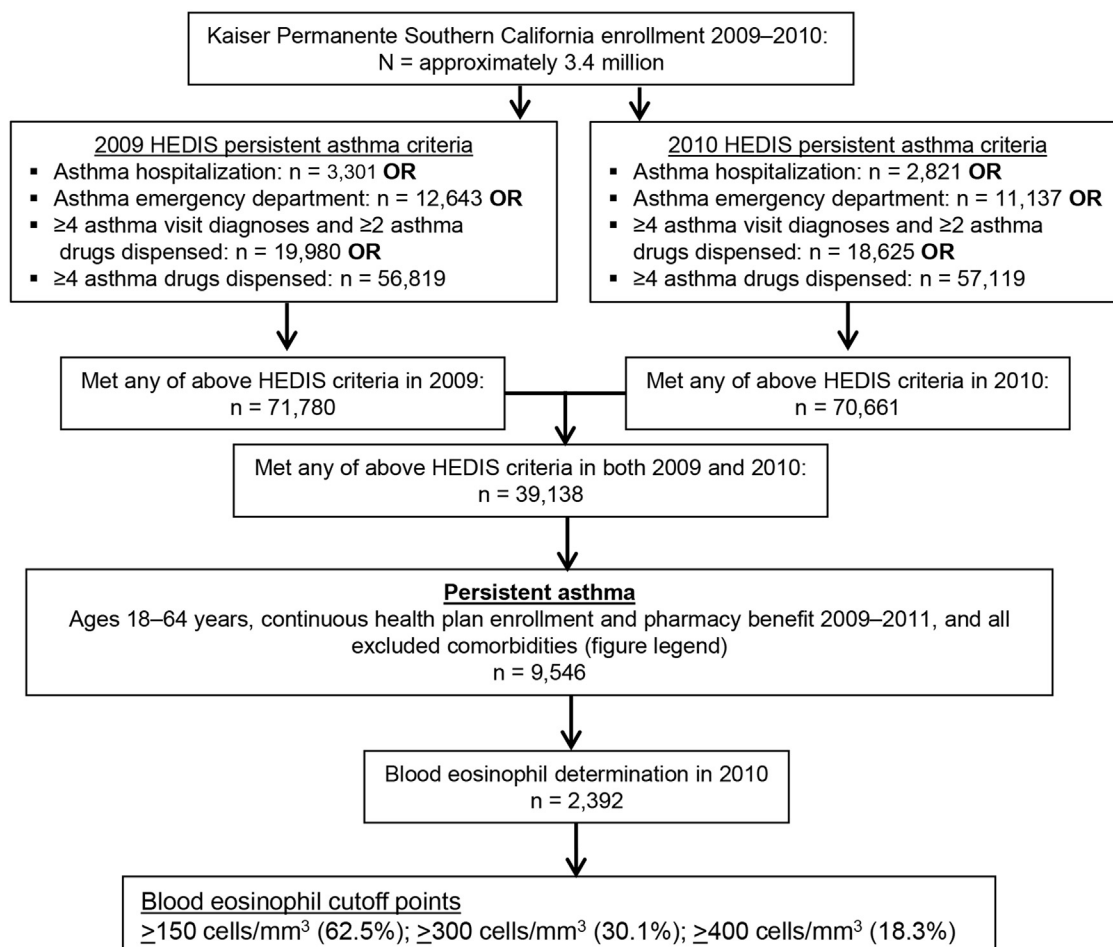
A**Study design****B Persistent asthma cohort with blood eosinophil level identification from administrative data**

FIGURE E1. Study design and patient identification from administrative databases. Modified with permission from Zeiger et al.^{E1}

A, Study design schemata. *Exclusions: encounter diagnoses of chronic obstructive lung disease, emphysema, cystic fibrosis, chronic bronchitis, bronchiectasis, Churg Strauss, Wegener, sarcoidosis, pulmonary hypertension, cerebral palsy, transplantation of major organs (2004–2010), other clinically relevant nonasthma pulmonary disorders such as autoimmunity, immune deficiency, immunosuppression treatments (procedural codes), cancer, HIV, drug addiction, and major psychiatric disorder (2009–2010). **B,** Algorithm for patient identification of adults aged 18 to 64 years with persistent asthma stratified by blood eosinophil cutoff points. *COPD*, Chronic obstructive pulmonary disease; *KPSC*, Kaiser Permanente Southern California.

TABLE E1. Unadjusted average direct costs per patient in the baseline year in 2010 (in 2014 US \$) (mean $\pm$ SD) by type of utilization in adults with persistent asthma related to GINA step-care level and previous-year exacerbations: (A) all-cause, (B) asthma-related

All-cause and asthma-related direct costs (US \$)	Total cohort (N = 2392)	1 or more asthma exacerbation in 2010				2 or more exacerbations in 2010			
		Step-care level 1 or 2 (N = 137) (5.7%)	Step-care level 3 (N = 248) (10.4%)	Step-care level 4 or 5 (N = 400) (16.7%)	P value*	Step-care level 1 or 2 (N = 42) (1.8%)	Step-care level 3 (N = 81) (3.4%)	Step-care level 4 or 5 (N = 163) (6.8%)	P value*
A. Total all-cause	6556 $\pm$ 7834	6036 $\pm$ 6994	5509 $\pm$ 4411	8347 $\pm$ 7352	<.001	5654 $\pm$ 5915	5914 $\pm$ 4862	9198 $\pm$ 7432	<.001
Inpatient visits	2203 $\pm$ 6940	2896 $\pm$ 6348	1736 $\pm$ 3521	2674 $\pm$ 6358	.30	2322 $\pm$ 5067	2027 $\pm$ 3778	3065 $\pm$ 6421	.89
Hospital outpatient visits	135 $\pm$ 438	195 $\pm$ 729	94 $\pm$ 327	108 $\pm$ 303	.06	74 $\pm$ 192	93 $\pm$ 374	101 $\pm$ 297	.12
ED visits	236 $\pm$ 480	307 $\pm$ 689	236 $\pm$ 761	258 $\pm$ 357	<.001	595 $\pm$ 1021	422 $\pm$ 576	305 $\pm$ 506	.02
Outpatient visits	1869 $\pm$ 1583	2896 $\pm$ 6348	1736 $\pm$ 3521	2674 $\pm$ 6358	<.001	1782 $\pm$ 1425	1889 $\pm$ 1315	2526 $\pm$ 1710	<.001
Laboratory†	111 $\pm$ 180	84 $\pm$ 170	101 $\pm$ 169	96 $\pm$ 145	.06	61 $\pm$ 90	98 $\pm$ 145	80 $\pm$ 109	.37
Radiology†	98 $\pm$ 221	85 $\pm$ 259	113 $\pm$ 268	92 $\pm$ 201	.06	79 $\pm$ 287	89 $\pm$ 206	79 $\pm$ 164	.16
Asthma medication‡	1904 $\pm$ 1517	666 $\pm$ 666	1313 $\pm$ 939	2892 $\pm$ 1741	<.001	740 $\pm$ 746	1297 $\pm$ 867	3042 $\pm$ 1896	<.001
B. Total asthma-related	2602 $\pm$ 2172	1661 $\pm$ 1668	2527 $\pm$ 2084	4543 $\pm$ 3227	<.001	2186 $\pm$ 1965	3182 $\pm$ 2697	5571 $\pm$ 3934	<.001
Inpatient visits	207 $\pm$ 1165	348 $\pm$ 1442	516 $\pm$ 1741	762 $\pm$ 2214	.23	609 $\pm$ 1639	1036 $\pm$ 2410	1331 $\pm$ 2914	.55
Hospital outpatient visits	1 $\pm$ 16	5 $\pm$ 20	3 $\pm$ 29	3 $\pm$ 23	.01	12 $\pm$ 32	5 $\pm$ 38	6 $\pm$ 34	.03
ED visits	28 $\pm$ 106	123 $\pm$ 205	87 $\pm$ 177	70 $\pm$ 151	<.001	187 $\pm$ 298	126 $\pm$ 202	106 $\pm$ 191	.10
Outpatient visits	462 $\pm$ 565	461 $\pm$ 521	608 $\pm$ 491	816 $\pm$ 907	<.001	639 $\pm$ 555	719 $\pm$ 489	1086 $\pm$ 988	<.001
Asthma medication	1904 $\pm$ 1517	666 $\pm$ 666	1313 $\pm$ 939	2892 $\pm$ 1741	<.001	740 $\pm$ 746	1297 $\pm$ 867	3042 $\pm$ 1896	<.001

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

*P value: Kruskal Wallis test.

†Standalone laboratory or radiology not associated with an encounter.

‡Nonasthma medication was not captured.

TABLE E2. Unadjusted average direct costs per patient in the follow-up year in 2010 (in 2014 US \$) (mean $\pm$ SD) by type of utilization in adults with persistent asthma related to blood eosinophil cutoff points: (A) all-cause, (B) asthma-related

All-cause and asthma-related direct costs (US \$)	EOS $\geq$ 300 cells/mm ³ (N = 719)	EOS < 300 cells/mm ³ (N = 1673)	P value*	EOS $\geq$ 400 cells/mm ³ (N = 437)	EOS < 400 cells/mm ³ (N = 1955)	P value*
A. Total all-cause	5539 $\pm$ 7260	5568 $\pm$ 6897	.36	5222 $\pm$ 6291	5634 $\pm$ 7156	.66
Inpatient visits	1716 $\pm$ 6114	1583 $\pm$ 5528	.54	1371 $\pm$ 5100	1680 $\pm$ 5837	.66
Hospital outpatients	115 $\pm$ 358	125 $\pm$ 427	.59	110 $\pm$ 360	125 $\pm$ 418	.54
ED visits	150 $\pm$ 500	149 $\pm$ 412	.49	118 $\pm$ 276	156 $\pm$ 469	.60
Outpatient visits	1532 $\pm$ 1516	1772 $\pm$ 2075	.004	1470 $\pm$ 1510	1751 $\pm$ 2005	.002
Laboratory†	101 $\pm$ 198	101 $\pm$ 159	.24	99 $\pm$ 220	102 $\pm$ 159	.02
Radiology†	83 $\pm$ 214	101 $\pm$ 245	.03	85 $\pm$ 224	98 $\pm$ 239	.07
Asthma medication‡	1841 $\pm$ 1517	1736 $\pm$ 1561	.02	1969 $\pm$ 1598	1723 $\pm$ 1534	<.001
B. Total asthma-related	2394 $\pm$ 2152	2227 $\pm$ 2277	.01	2565 $\pm$ 2353	2213 $\pm$ 2211	<.001
Inpatient visits	170 $\pm$ 1070	129 $\pm$ 1107	.005	222 $\pm$ 1261	123 $\pm$ 1055	.003
Hospital outpatient visits	1 $\pm$ 8	2 $\pm$ 49	.11	1 $\pm$ 7	1 $\pm$ 45	.10
ED visits	24 $\pm$ 121	11 $\pm$ 68	<.001	25 $\pm$ 105	13 $\pm$ 83	.003
Outpatient visits	358 $\pm$ 532	350 $\pm$ 581	.79	348 $\pm$ 491	353 $\pm$ 582	.89
Asthma medication	1841 $\pm$ 1517	1736 $\pm$ 1561	.02	1969 $\pm$ 1598	1723 $\pm$ 1534	<.001

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

*P value: Wilcoxon rank-sum test.

†Standalone laboratory or radiology not associated with an encounter.

‡Nonasthma medication was not captured.

REFERENCES

- E1. Zeiger RS, Schatz M, Li Q, Chen W, Gossage D, Khattry D, et al. High blood eosinophil count is a risk factor for future asthma exacerbations in adult persistent asthma. *J Allergy Clin Immunol Pract* 2014;2:741-50.
- E2. National Committee for Quality Assurance. HEDIS technical specifications. Washington, DC: National Committee for Quality Assurance; 2008.
- E3. Mosen DM, Macy E, Schatz M, Mendoza G, Stibolt TB, McGaw J, et al. How well do the HEDIS asthma inclusion criteria identify persistent asthma? *Am J Manag Care* 2005;11:650-4.
- E4. Schatz M, Zeiger RS, Vollmer WM, Mosen D, Mendoza G, Apter AJ, et al. The controller-to-total asthma medication ratio is associated with patient-centered as well as utilization outcomes. *Chest* 2006;130:43-50.
- E5. National Committee of Quality Assurance. 2015. Available from: <http://www.ncqa.org/HEDISQualityMeasurement.aspx>. Assessed January 5, 2017.
- E6. Zeiger RS, Schatz M, Dalal AA, Qian L, Chen W, Ngor EW, et al. Utilization and costs of severe uncontrolled asthma in a managed-care setting. *J Allergy Clin Immunol Pract* 2015;4:120-9.

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