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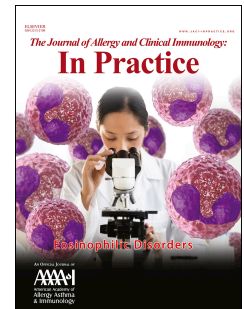
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Abstract:

Background: Out-of-pocket health care costs can cause financial burden and deferred care for many Americans. Little is known about out-of-pocket (OOP) spending for asthma-related care among the commercially insured.

Objectives: To analyze OOP spending for asthma-related care overall, across types of care, and by income.

Methods: Using enrollment, claims, and geocoded census tract data on income from a large U.S. commercial health plan from 2004-2016, we measured inflation-adjusted OOP spending for individuals with asthma ages 4-64 years (n=1,986,769). We estimated annual asthma-related OOP spending over time, and average total, asthma-related, asthma type of care, and asthma medication spending by income. We measured trends in median OOP cost per medication. Linear regression models were adjusted for patient covariates and deductible level.

Results: Asthma-related OOP spending decreased over time both for patients enrolled in high-deductible health plans and those in traditional plans. High-deductible plan enrollment increased from 7% to 54%. Compared to patients living in high-income areas, patients in the lowest income areas had similar annual total and asthma-related OOP spending, but spent 30% less on controller medications and a higher proportion of their asthma-related OOP spending on inpatient and emergency care (10% vs 3%, $p<0.001$). Asthma-related OOP spending represented a higher proportion of household income for patients in lower income areas.

Conclusion: Patients with asthma living in the lowest-income areas have greater cost burden, lower spending on controller medications, and greater spending on high acuity care than higher-income counterparts.

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70 **Highlights Box**

71 ***What is already known about this topic?*** Patients report that out-of-pocket costs are a
72 noteworthy burden and barrier to asthma treatment, but comprehensive data on asthma-related
73 out-of-pocket costs are limited.

74 ***What does this article add to our knowledge?*** The majority of asthma-related out-of-pocket
75 spending was on medications, but patients in lower-income areas had greater spending on high
76 acuity care and greater cost burden as a percent of income than those in higher-income areas.

77 ***How does this study impact current management guidelines?*** Understanding asthma-related
78 out-of-pocket spending can impact how clinicians make asthma management plans with patients
79 and inform strategies that reduce cost burden while optimizing medication adherence and timely
80 care.

81

82 **Key words:** Out-of-pocket spending; Asthma; Health insurance

83

84

85 **Abbreviations:** OOP (Out-of-pocket), HDHP (High-deductible health plan), LDHP (Low-
86 deductible health plan), ICS (inhaled corticosteroids), LTI (leukotriene inhibitors), ICS-LABA
87 (ICS-long-acting beta agonists), ICE (Index of Concentration at Extremes), ACG (Adjusted
88 Clinical Group)

89

Introduction

The annual economic cost of asthma in the U.S. is estimated to be over \$80 billion per year when accounting for medical costs and asthma-related mortality.(1) A substantial portion of asthma costs are attributed to prescription medicines and office based visits.(1) While the increasing economic burden of asthma on society has been well-described, trends in the burden of out-of-pocket (OOP) spending for asthma care on individuals is less frequently described.

High OOP costs for medical care can lead to patient financial distress and forgone care, especially for low income patients with asthma.(2–7) Out-of-pocket (OOP) spending by commercially insured patients is driven by insurance benefit design and prices for health care services. Trends over the last 15 years of increased patient cost sharing, primarily through high-deductible health plans (HDHPs), and growing OOP prices for medications raise concerns about the cost burden of asthma care and its impact on medication adherence and outcomes among patients with asthma.(8,9)

However, while patients report that OOP costs are a noteworthy burden and barrier to asthma treatment,(10,11) comprehensive data on asthma-related OOP costs across types of asthma care, plan types, and income groups are limited. Existing studies have examined OOP spending for asthma medications among children and its association with asthma outcomes during the 2000s.(5) Others have studied OOP spending generally, not specific to asthma care, for patients with asthma, finding higher total OOP spending and high medical cost burden (e.g, spending more than 10% of income on healthcare) for those in HDHPs,(12) and finding more than half of overall OOP costs spent on prescription drugs across all classes for patients with asthma.(13) Studies of total asthma care costs (not OOP), and reports of cost-related burden and barriers to receiving asthma care are concentrated among low-income families(1,14–16) and

those with more severe asthma,(17) but objective measurement of asthma-related OOP cost burden in the last decade for low-income or higher severity asthma patients is lacking.

In this study we sought to determine how much commercially insured patients in the United States spend out of pocket for asthma-related care, and how asthma-related OOP spending varies with type of health plan and income. We also report on the distribution of asthma OOP spending by type of asthma care. Understanding asthma-related out-of-pocket spending will inform (1) the development of strategies to reduce financial burden from asthma care and avoid cost barriers to needed asthma care and (2) recommendations providers give patients about asthma management in order to maximize adherence to medications and minimize forgone care.

Methods

Data Source and Population. We used administrative enrollment, claims, and geocoded census tract data from a large national commercial and Medicare Advantage health insurance claims dataset from January 2004 – December 2016. We selected all patients who had 24 or more months of continuous enrollment in a commercial health plan during the study period, and who had an encounter with an asthma diagnosis (defined as one outpatient, emergency department or hospitalization claim with a corresponding ICD-9 code 493.xx or ICD-10 codes J45.2x, J45.3x, J45.4x, J45.5x, J45.90x, J45.990, J45.991, J45.998) in any diagnosis position while continuously enrolled. We included patients age 4-64. We excluded enrollees with a diagnosis code for another serious comorbid pulmonary condition (cystic fibrosis, immunodeficiency, bronchiectasis, pulmonary hypertension, or idiopathic pulmonary fibrosis) following methods published previously.(18,19)

For each included individual, we excluded all person-months prior to the patient's first encounter with an asthma diagnosis. We excluded person-months when the patient was enrolled in more than one health plan (0.1% of person-months), when the patient was assigned to more than one unique family identifier (0.1% of person-months), and when the patient's deductible level was missing (1% of person-months). We aggregated monthly enrollment to the calendar year level and excluded patient-years when the patient had fewer than 12 months of enrollment (33% patient-years excluded); we required 12 months enrollment so we could observe the full year of patient spending. We excluded person-years where a patient was 65 years or older by the end of the calendar year (1% excluded). All spending was adjusted to July 2016 U.S. dollars using the monthly Medical CPI.(20)

Outcomes. Primary outcomes were (1) annual OOP spending on all asthma-related health care, (2) annual total OOP spending (e.g., on all medical care), and (3) annual asthma-related OOP

150 spending categorized by type of service. Out-of-pocket spending was measured as the sum of
151 patient paid deductible, coinsurance and copayment amounts on a medical or pharmacy claim.
152 Annual OOP spending on asthma-related medical care was measured as the sum of OOP
153 spending on medical services with ICD codes for asthma, asthma medications, spacers for
154 asthma inhalers, and nebulizer machines. Annual total OOP spending was measured as the sum
155 of OOP spending on all claims in the year. To control for extreme spending values in our
156 analysis, we set all negative spending values to \$0 (less than 0.01% of all patient-years), and
157 trimmed (i.e., winsorized) the top 1% of patient spending amounts to the value at the 99th
158 percentile for each of the first two outcomes.

159 We disaggregated asthma-related OOP spending into five service categories, including
160 emergency department services, inpatient services, outpatient services, asthma medications, and
161 asthma related durable medical equipment (e.g., spacers and nebulizers) (see Online Repository).

162 We also disaggregated asthma-related medication OOP spending into four medication
163 types: (1) controller medications (including inhaled corticosteroids (ICS), leukotriene inhibitors
164 (LTI), and ICS-long-acting beta agonists (ICS-LABA)), (2) albuterol/non-albuterol rescue
165 medications, and (3) oral steroids. From this disaggregation we excluded 316,084 prescriptions
166 for other controller medications (LABA, Xanthine, Mast Cell Stabilizers), and for biologics (2%
167 of all prescriptions filled) because of very small sample sizes of patients per year and because for
168 the study period (except 2016) there was only one biologic available for treatment of moderate to
169 severe asthma. We measured median OOP spending per standardized prescription by medication
170 type. Controller medications were standardized to a 30-day supply; albuterol inhalers, non-
171 inhaler albuterol medications, and non-albuterol rescue medications were standardized per
172 dispensed prescription; oral steroids were standardized to a 5-day supply.

Covariates. Patients' insurance plans were categorized as a HDHP if the annual individual deductible was \$1,000 or more per year. We directly measured deductible levels when available, and otherwise imputed deductible using aggregated OOP spending and other predictors among employees within the same plan and employer (see Online Repository).(21) Patient age and gender were extracted from the enrollment data, and age was measured as age at the end of each calendar year. Patient gender was missing for 526 person-years (0.01% of the sample).

Asthma severity was measured using the Johns Hopkins Adjusted Clinical Group (ACG®) System (version 11.1) persistent asthma designation, (22) which aligns with the Health Effectiveness Data and Information Set (HEDIS) definition (asthma diagnosis in one inpatient stay or ED visit, or in 4 outpatient visits plus two asthma medication fills, or four asthma medication fills within a 12 month period) and was measured monthly looking back at the prior 12 months. Patients who had persistent asthma for the majority of months in a year were classified as having persistent asthma that year; all other patient-year observations were classified as intermittent asthma. We used the ACG System to calculate the mean monthly ACG morbidity score for each person-year; this measure was missing for 146,223 person-years (2.2% of the sample). We measured whether there was another person insured on the same health plan (e.g., a family member) with asthma.

We assigned patients into income quintiles using a census-tract level Index of Concentration at the Extremes (ICE) score for income,(21,23,24) which is a metric used for monitoring health across populations. The ICE score is calculated for each census tract as the difference in the number of people with a household income greater than \$100,000 per year and the number of people with a household income less than \$25,000 per year, divided by the total population. We used the 2010-2014 five-year population estimates from the US Census American Community Survey,(25) which is the middle of our study period. The census tracts are

sorted into ICE income quintile by score where the cut-points for ICE score between quintiles were selected based on the income distribution in the US (e.g, cut-points assign the 20% of census tracts nationally with the lowest scores to the the first quintile, the 20% of census tracts with the highest scores nationally to the top, or fifth quintile).(24) Patients in our sample were matched to their census tract and the corresponding income quintile. We refer to those living in areas with highest poverty concentration (i.e., the first quintile) as “lower-income” and those living in areas with the lowest poverty concentration (e.g., the fifth quintile) as “higher income.” We excluded 25,873 patient-years (0.4% of sample) where the patient’s census-tract income quintile was missing.

We identified whether the patient lived in a metropolitan, metropolitan-suburban, or non-metropolitan, non-suburban county each year using patient zip code and the 2013 Rural-Urban Continuum Codes (see Online Repository).(26) This measure was missing for 92,375 patient-years (1.4% of the sample).

Statistical analysis. We used descriptive statistics to characterize the sample, and to report unadjusted trends in median OOP spending per medication type per year.

We estimated the average, asthma-related annual OOP spending per patient in 2004-2016, and the proportion of patients each year who had no asthma-related OOP spending (e.g., \$0) using linear and logistic regression respectively. We stratified and report the results from this analysis by patient’s asthma severity and health plan type (HDHP or not), and adjusted for patient age, gender, income quintile, mean monthly ACG score, presence of another family member with asthma, and rural-urban continuum classification. See Online Repository for unadjusted data (Figure E1).

We estimated our three primary outcomes —patient annual asthma-related OOP spending, patient annual total OOP spending, and patients’ asthma-related spending by type of

service—across ICE income quintiles. We also estimated total asthma medication spending by medication type across ICE income quintiles. We used multivariate linear regression models adjusting for patient age, gender, plan type, asthma severity (intermittent vs persistent), mean monthly ACG score, presence of another family member with asthma, rural-urban continuum classification, and secular trends (e.g. year fixed effects).

For ease of interpretation, we did not use a two-part model nor was our base specification logarithmic-transformed since linear models have been shown to adequately predict medical spending, compared to more complex functional forms.(27) Standard errors were clustered by family in all models to adjust for correlations in spending within families. Results are presented as predicted values of spending by patient ICE quintile.

We estimated models stratified by whether the patient was enrolled in a HDHP and models that pooled patients across plan type. When results from the pooled analyses were similar to those from stratified analyses we present the pooled results; model results stratified by HDHP enrollment are in the Online Repository. Analyses were performed using Stata software, version 14. This study was approved by the Institutional Review Board at Harvard Pilgrim Health Care.

Results

The study sample included 6,530,667 person-year observations, representing 1,986,769 unique patients with asthma (Table 1). Across the study sample (e.g., person-years), 62.1% had persistent asthma, and 34.3% were enrolled in HDHPs. The sample was majority female (55.0%), mean age was 33.4 years, and 20.3% lived in neighborhoods classified in the lower two ICE income distributions. Additional sample characteristics in Online Repository Table E1.

Asthma-related OOP Spending Trend Over Time. Patients with persistent asthma had higher asthma-related spending than those with intermittent asthma, and those in HDHPs had greater asthma-related spending than did other patients (Figure 1). Within each severity–health plan group (e.g., within the population of patients with persistent asthma in HDHP), regression-estimated, annual asthma-related OOP spending decreased over the study period ($p<0.001$ for all groups). However, the proportion of the sample enrolled in a HDHP increased from 7% in 2004 to 54% in 2016, and patients in HDHPs experienced higher OOP spending compared to those in non-HDHPs. In all years, approximately 30% of patients with persistent asthma did not have any annual asthma-related OOP spending; between 70%-80% of patients with intermittent asthma had no annual asthma-related OOP (Figure 1). The trends in unadjusted asthma-related OOP spending and trends among patients with any asthma-related spending in a year were similar (Online Repository Figures E1 and E2).

Variation in Asthma-Related OOP Spending by Income. After adjusting for differences in patient covariates, on average patients in a HDHP spent approximately \$600 more in total OOP spending, and \$30 more on asthma-related OOP spending per year than did patients in a low or no-deductible health plan (Table 2). Within health plan type (e.g., within patients in HDHPs), both total OOP spending and asthma-related OOP spending amounts were very similar across income quintiles; a higher proportion of patients in the lowest income quintile was enrolled in an

HDHP. Total and asthma-related out-of-pocket spending represented a significantly larger proportion of income for patients in the lowest income quintile.

Patients in higher income quintiles spent a higher proportion of their asthma-related OOP spending on medications than did patients in lower-income quintiles. For the lowest-income quintile patients, 63% of asthma-related OOP spending was for prescription drugs, with 27% on outpatient care, 6% on inpatient care and 4% on ED care (Figure 2). For patients in the highest-income quintile, 78% of asthma-related OOP spending was for prescription drugs, 18% on outpatient care, with 2% on inpatient and 1% on emergency care (for all between quintile differences, $p<.001$). This pattern of utilization across quintiles was similar whether patients were in an HDHP or not; patients in a HDHP spent a higher proportion of OOP on outpatient care and higher-acuity care than did patients in low or no-deductible plans (Online Repository Figure E3).

The study sample includes 17,483,339 prescriptions filled between 2004-2016. Compared to patients in the highest income quintile, patients in the lowest income quintile spent an average of \$19 (30%) less on all controller medications per year (\$47 lowest-income quintile vs \$66 highest income quintile, $p<0.001$) (Figure 3). Less spending by lower-income patients was seen across all types of controllers, including ICS, LTI, and ICS-LABA. The magnitude of spending on other types of medications was similar for patients across ICE income quintiles, including for rescue medications (\$21-\$23 per year). However, because low-income quintile patients spent lower total amount on medications, spending on rescue medications represented a larger proportion of the sum of spending on controllers and rescue medications for lower income patients than that for patients in the highest income quintile (32% vs 24%, $p<0.001$) (Online Repository Figure E6).

Out-of-pocket spending per Medication Type. On average, 52% of dispensed asthma prescriptions each year were for controller medications, 26% were for albuterol inhalers, 13% for oral steroids, 4% for non-inhaler albuterol, and 2% for non-albuterol rescue medications (Online Repository Figure E4). Median cost per prescription varied substantially (Figure 4). Among controller medications, the median OOP cost per fill for ICS-LABA ranged from \$30-\$50 and, from 2013 forward, was more than two times that for other controller medications. The median cost per albuterol inhaler ranged from \$10-\$25 for the majority of the study period, except in 2009 when it rose to \$44. Non-albuterol rescue medication OOP cost declined steadily over the study period. The median cost per fill for oral steroids was consistently just below \$3 for all enrollees. Online Repository Figure E5 presents median cost per standardized prescription stratified by plan type.

Discussion

This national study of OOP costs for patients with asthma with commercial insurance has three key findings. First, trends in per-patient asthma-related OOP spending decreased over time within both high-deductible health plans and low-deductible plans; enrollment in high-deductible plans increased from 7% to 54% from 2004-2016. Second, asthma-related OOP spending was higher for those in HDHPs than those in plans with low or no deductible, but within plan type, it was similar for those with low and high incomes. Third, the majority of OOP asthma spending for all patients was on asthma medications, but patients living in the lowest-income areas had greater spending on high acuity care and lower spending on controller medications than those living in higher income areas.

It is notable that average out of pocket spending for asthma care was similar across income quintiles within the same plan type. This is in addition to lowest-income patients being slightly more likely to be enrolled in a HDHP. Taken together, these findings suggest that the increased OOP cost burden reported by low-income patients with asthma may be due both to higher absolute OOP spending (for those in HDHPs), and to experiencing the same level of OOP costs as a greater relative burden.

The majority of OOP asthma spending was on asthma medications. Median OOP cost per medication was flat or declined for most types of medication, except for ICS-LABA which increased and remained high over the study period, and albuterol inhalers which experienced a temporary one-year spending increase in 2009. This increase for albuterol inhalers occurred when the inhalers regained their branded status due to a ban on inhalers that used chlorofluorocarbons.⁽²⁸⁾ The decrease in cost per albuterol inhaler starting in 2010 may reflect a decision by the health plan to revert back to lower-cost sharing despite the higher medication cost, as some carriers chose to do.⁽¹⁸⁾

We examined spending for controller medications and albuterol and found that lower-income patients spent less on controller medications than do other patients. We also find that lower income patients had greater spending on higher-acuity (i.e. inpatient, emergency department) asthma-related services than other patients. Residents of lower-income quintiles may have needed more high-acuity services (for example, if they had greater exposure to environmental factors that trigger asthma exacerbations), leaving them less disposable income to spend on medications that year. Income constraints could lead lower-income residents to forgo asthma controller medications, resulting in lower medication spending. Increased OOP requirements for important asthma medications has been associated with decreased use.(5,12,13)

Several important limitations should be noted. This study is observational. Although we adjusted for differences among patients that we could measure in claims data and through geocoding, unobservable differences across patient cohorts over time, or across patients living in different income quintiles, may remain. Our results do not account for changes in OOP spending due to changes in asthma severity or plan type over time. Because we lack data on patient paid health plan premiums, results also do not reflect total patient spending. Moreover, high-deductible health plans have lower premiums than traditional plans; this difference in premiums will offset some of the differences in OOP spending across the two health plan types but we are unable to measure the magnitude of the offset. We lack data on the OOP maximum for each patient's plan and cannot determine how asthma utilization and costs may differ after hitting their OOP maximum. The majority of HDHPs in our study exempted medications from the deductible and instead required co-payments, so differences with low/no deductible plan patients might be greater for patients in HDHPs that include medications in the deductible.

Other limitations are that we cannot observe when patient cost-sharing is offset by coupons or copay assistance or when spending is paid using Health Savings Account (HSA)

contributions which are tax-advantaged (both which would decrease the estimates reported here). We also do not observe patient spending on asthma-related care that is not covered by insurance and paid entirely out-of-pocket (which would increase spending above these estimates). Our income categories are not intended to be patient-level measures of socioeconomic status; rather, they are intended to capture a mix of socioeconomic effects of the neighborhoods where patients live. Our sample likely includes a higher proportion of patients from large employers than among the overall commercially insured population because those plans it is much more likely to have a January - December benefit year and to have complete calendar year data. Our sample of patients was slightly more likely to live in Metropolitan areas than the US population overall (92% vs 85%).(26) Thus our estimates of patient OOP spending may be higher than that for the US overall because asthma exacerbations are worse in urban settings.

Conclusion

Our finding that the majority of asthma-related OOP spending is on medications and that low income patients experience greater cost burden of asthma care as a percent of income can inform the decision making of clinicians, policy makers, and health plans. Understanding the cost burden among low income patients with asthma could guide providers to help patients prioritize high-value asthma medications and treatments and suggest strategies to find lower-priced alternatives. This evidence of the types of asthma care, types of medications, and types of health plans for which asthma-related OOP cost burden is greatest can inform clinical decisions, insurance benefit design and subsidies, and drug pricing to reduce the cost patients face for important asthma care.

Table 1. Sample Characteristics, 2004-2016 (person-year level observations)

Total person-years, n	6,530,667
Total persons, n	1,986,769
Person-years per person, mean (SD)	39.4 (30.2)
Age (y) at the end of calendar year, mean (SD)	33.4 (18.1)
Age group, n (%)	
4 - 17 years old	1,056,830 (16.2%)
18 - 30 years old	911,411 (14.0%)
31 - 40 years old	1,867,748 (28.6%)
41 - 50 years old	1,194,181 (18.3%)
51 - 64 years old	1,500,497 (23.0%)
Female, n (%)	3,589,359 (55.0%)
Enrolled in a HDHP, n (%)	2,237,358 (34.3%)
Persistent asthma, n (%)	4,052,419 (62.1%)
Had 1+ other family member with asthma, n (%)	1,715,282 (26.3%)
Monthly ACG score, mean (SD)	1.12 (1.69)
ICE income quintile, n (%)	
1 (low)	495,075 (7.6%)
2	829,204 (12.7%)
3	1,113,812 (17.1%)
4	1,562,669 (23.9%)
5 (high)	2,529,907 (38.7%)
Rural-Urban Continuum Classification, n (%)	
Metropolitan	6,007,295 (92.0%)
Metropolitan Suburban	305,559 (4.7%)
Non-metro, non-suburban	125,438 (1.9%)

Notes: HDHP = High-Deductible Health Plan; ACG = Johns Hopkins Adjusted Clinical Group (ACG®) System (version 11.1); ICE = Index of Concentration at Extremes; quintiles defined in methods section. Table includes all person-year observations included in the study sample. All person-years represent a full year (or 12 calendar months) of enrollment, and where the patient was no older than 64 years old by the end of the calendar year. Count of female patients excludes 526 person-years (0.01% of sample) with missing data. Mean monthly ACG score excludes 146,223 person-years (2.2% of sample) with missing data. Rural/Urban continuum classification excludes 92,375 persons-years (1.4% of sample) with missing data.

Table 2. Total and asthma-specific OOP spending by income quintile as percent of median income, by HDHP enrollment (regression adjusted)

Income quintile	Average median household income	Patients in Low or No Deductible Health Plans			Patients in HDHPs		
		Average annual total OOP spending	Average annual asthma-related OOP spending	Asthma-related OOP spending as percent of average median income	Average annual total OOP spending	Average annual asthma-related OOP spending	Asthma-related OOP spending as percent of average median income
1 (lowest)	\$29,574	\$972	\$94	0.32%	\$1,537	\$121	0.41%
2	\$41,546	\$1,003	\$98	0.24%	\$1,553	\$125	0.30%
3	\$52,187	\$996	\$99	0.19%	\$1,561	\$126	0.24%
4	\$66,506	\$1,000	\$100	0.15%	\$1,578	\$130	0.20%
5 (highest)	\$106,944	\$1,023	\$103	0.10%	\$1,628	\$134	0.13%

Notes: OOP = Out-of-pocket; HDHP = High-Deductible Health Plan. Median household income is in the patient's census tract, derived from the 2010-2014 American Community Survey, and adjusted to \$2016 using the All Items CPI. Average total and asthma-related OOP spending was estimated using a linear regression. Models were stratified by HDHP enrollment and adjusted for patient age, gender, asthma severity, income quintile, year, mean monthly ACG score, presence of another family member with asthma, and rural-urban continuum classification, with standard errors clustered by family. Sample sizes: for the low or no deductible health plan enrollees model, N=4,140,730 patient-years; for the HDHP enrollees model, N=2,152,426 patient-years. All spending amounts are adjusted for inflation to July 2016 dollars using the Medical CPI.

Figure 1. Annual asthma-related OOP spending by asthma severity and health plan type, 2004-2016

Notes: OOP = Out-of-Pocket; HDHP = High-Deductible Health Plan; LDHP = Low-Deductible Health Plan.

Both panels (a) and (b) include 6,293,156 person-years. Estimates in \$2016 and adjusted for patient age, gender, income quintile, year, ACG score, family member with asthma, and rural-urban status. Differences in spending over the time period were jointly statistically significant F-statistic $p < 0.001$.

Figure 2. Distribution of average annual asthma-related OOP spending by service category, by income quintile

Notes: OOP = Out-of-pocket; HDHP = High-Deductible Health Plan; LDHP = Low-Deductible Health Plan; ER = Emergency Room; DME = Durable Medical Equipment. N=6,293,156 person-years. Estimates in \$2016 and regression adjusted for patient covariates and deductible level; standard errors clustered on family.

¹ Spending on DME, ² on medications, ³ on outpatient services, ⁴ on inpatient services, ⁵ on ER.

Figure 3. Distribution of asthma-related medication out-of-pocket spending by medication type, by patient income quintile

Notes: OOP = Out-of-pocket; ICS= inhaled corticosteroids; LTI = leukotriene inhibitors; ICS-LABA = ICS-long-acting beta agonists. N= 6,293,156 person-years. Estimates in \$2016 and regression adjusted for patient covariates and deductible level.

Figure 4. Median Out-of-pocket cost per standardized prescription fill, by medication type, 2004-2016

Notes: OOP = Out-of-pocket; ICS= inhaled corticosteroids; LTI = leukotriene inhibitors; ICS-LABA = ICS-long-acting beta agonists. N= 17,483,339 prescriptions. Prescriptions in \$2016 and standardized: controller medications (ICS, ICS-LABA, and LTI medications) to 30-day supply, oral steroids to 5-day supply, all others per dispensed prescription.

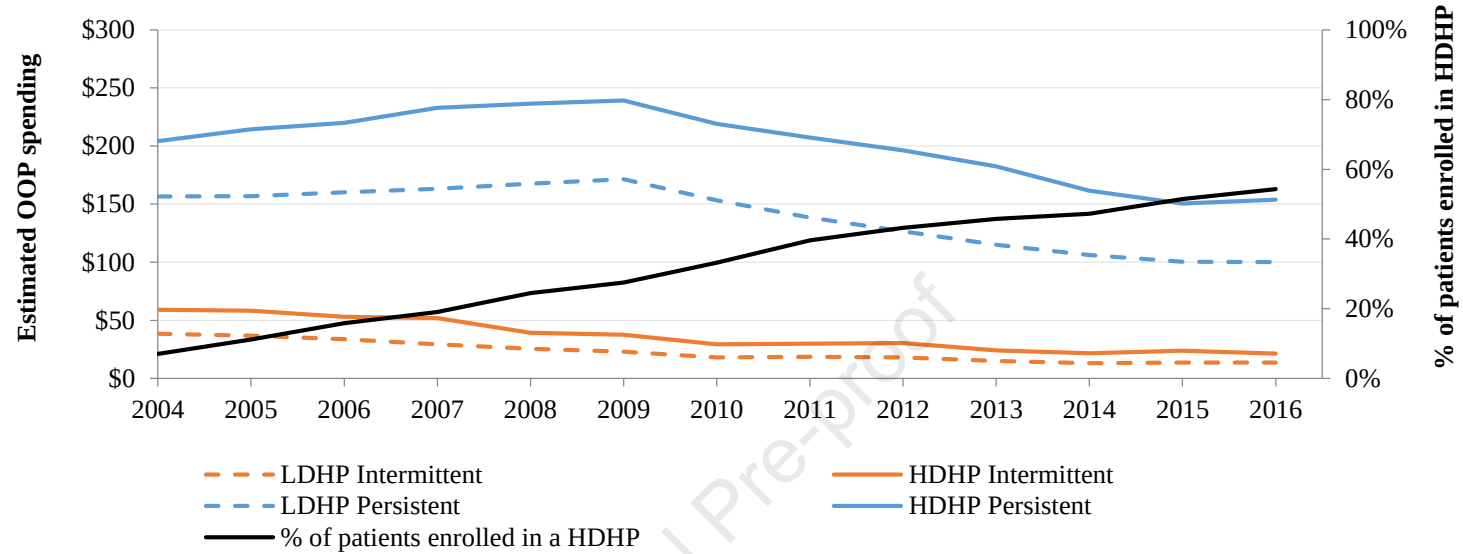
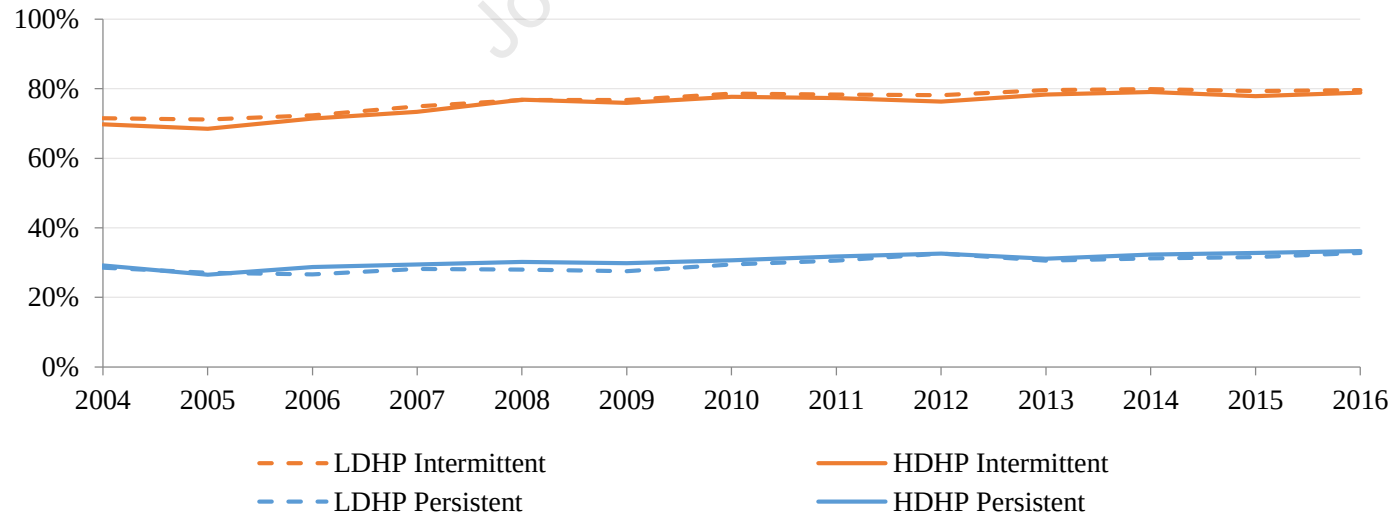
References

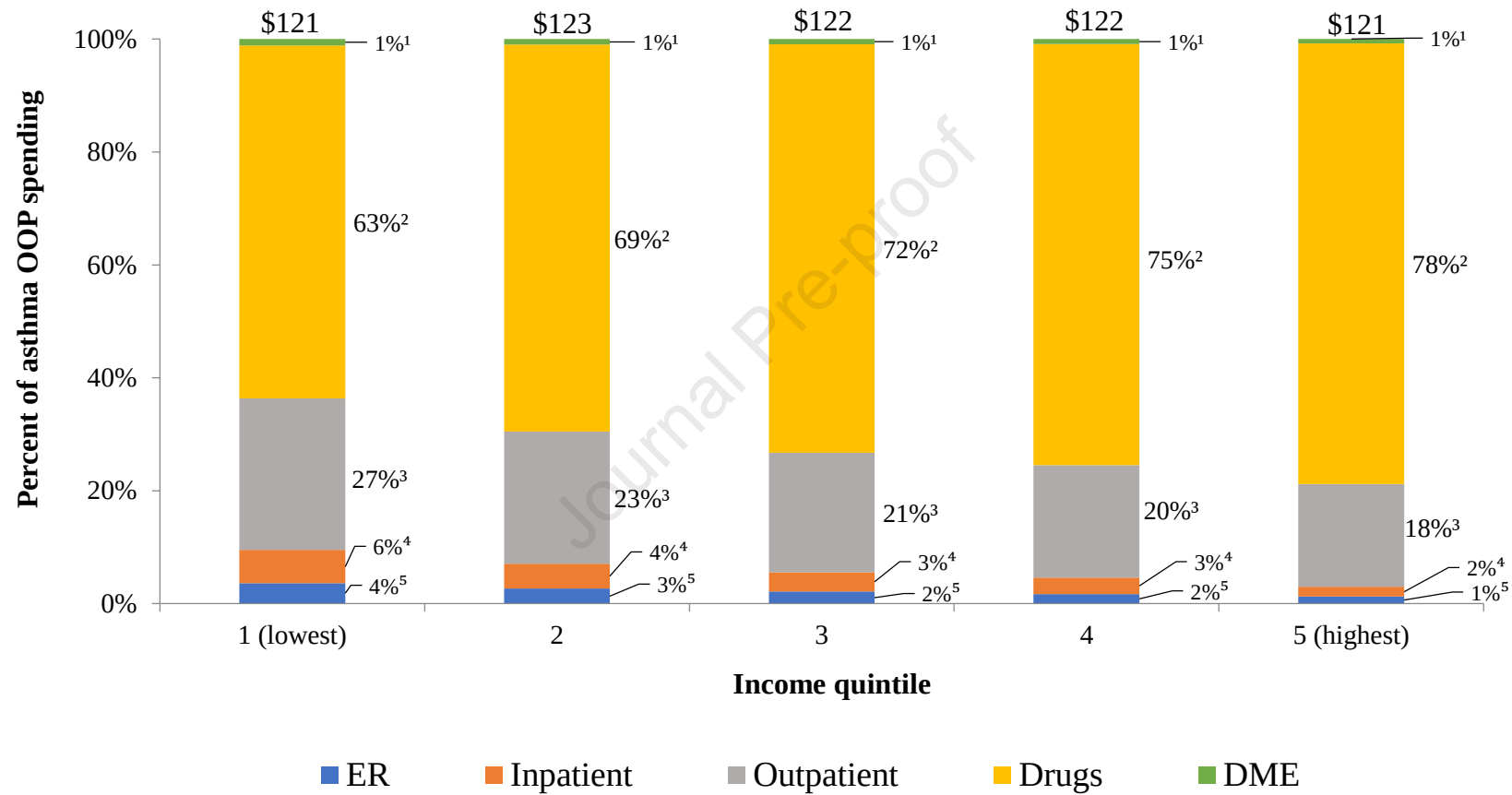
1. Nurmagambetov T, Kuwahara R, Garbe P. The Economic Burden of Asthma in the United States, 2008 - 2013. *Ann Am Thorac Soc*. 2018;
2. Goldman DP, Joyce GF, Escarce JJ, Pace JE, Solomon MD, Laouri M, et al. Pharmacy benefits and the use of drugs by the chronically ill. *J Am Med Assoc*. 2004;291(19):2344–50.
3. Blais L, Couture J, Rahme E, LeLorier J. Impact of a cost sharing drug insurance plan on drug utilization among individuals receiving social assistance. *Health Policy (New York)*. 2003;64(2):163–72.
4. Campbell JD, Allen-Ramey F, Sajjan SG, Maiese EM, Sullivan SD. Increasing pharmaceutical copayments: Impact on asthma medication utilization and outcomes. *Am J Manag Care*. 2011;17(10):703–10.
5. Karaca-Mandic P, Jena AB, Joyce GF, Goldman DP. Out-of-pocket medication costs and use of medications and health care services among children with asthma. *JAMA*. 2012;307(12):1284–91.
6. Ungar WJ, Paterson JM, Gomes T, Bikangaga P, Gold M, To T, et al. Relationship of asthma management, socioeconomic status, and medication insurance characteristics to exacerbation frequency in children with asthma. *Ann Allergy Asthma Immunol*. 2011;106(1):17–23.
7. Galbraith AA, Ross-Degnan D, Zhang F, Wu AC, Sinaiko A, LeCates RF, et al. Association of Controller Use and Exacerbations for High-Deductible Plan Enrollees with and without Family Members with Asthma. *Ann Am Thorac Soc*. 2021;epub.:1–13.
8. Miller GE, Vistnes JP, Rohde F, Keenan PS. High-deductible health plan enrollment

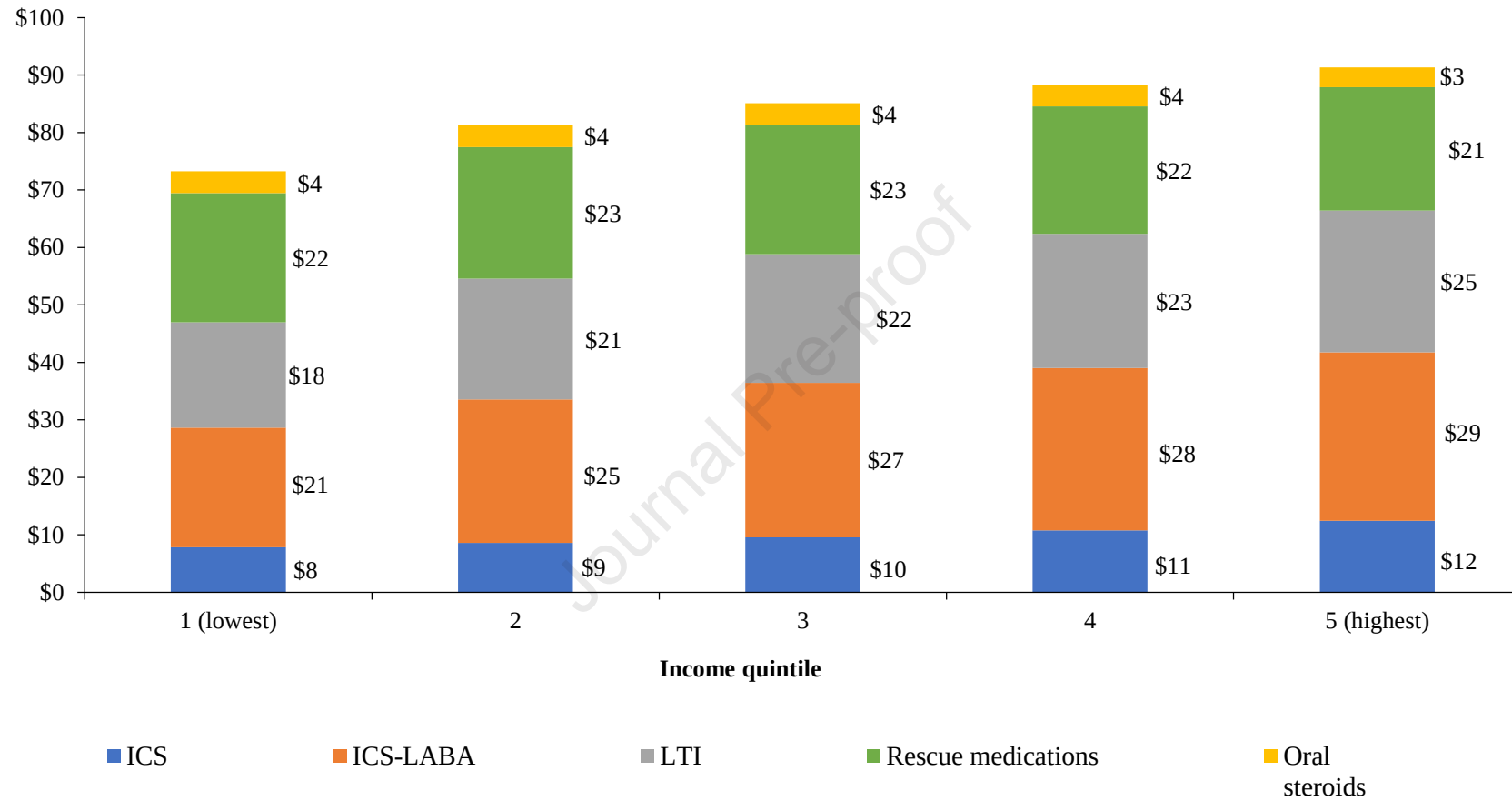
- increased from 2006 to 2016, employer-funded accounts grew in largest firms. *Health Aff.* 2018;37(8):1231–7.
9. Aaron MB, Sinaiko AD. Spending and Out-of-Pocket Prices for Brand-Name Drugs among Commercially Insured Individuals in Massachusetts, 2015-2017. *JAMA Netw Open.* 2021;4(3):2015–7.
 10. Gelhorn HL, Balantac Z, Ambrose CS, Chung YN, Stone B. Patient and physician preferences for attributes of biologic medications for severe asthma. *Patient Prefer Adherence.* 2019 Mar;13:1253–68.
 11. Hanania NA, Hawken N, Gilbert I, Martinez FJ, Fox KM, Ross MM, et al. What Symptomatic Patients with Asthma and Chronic Obstructive Pulmonary Disease (COPD) Find Important in Their Maintenance Inhaler Therapy: A Focus Group Study. :2.
 12. Segel JE, Kullgren JT. Health Insurance Deductibles and Their Associations With Out-of-Pocket Spending and Affordability Barriers Among US Adults With Chronic Conditions. *JAMA Intern Med.* 2017 Apr;177(3):433.
 13. Carrier E, Cunningham P. Medical Cost Burdens Among Nonelderly Adults With Asthma. *Am J Manag Care.* 2014;20(11):8.
 14. Inselman JW, Jeffery MM, Maddux JT, Shah ND, Rank MA. Trends and Disparities in Asthma Biologic Use in the United States. *J Allergy Clin Immunol Pract.* 2020 Mar;8(2):549-554.e1.
 15. Fung V, Graetz I, Galbraith A, Hamity C, Huang J, Vollmer WM, et al. Financial barriers to care among low-income children with asthma: Health care reform implications. *JAMA Pediatr.* 2014;168(7):649–56.
 16. Wang T, Srebotnjak T, Brownell J, Hsia RY. Emergency Department Charges for Asthma-Related Outpatient Visits by Insurance Status. *J Health Care Poor Underserved.*

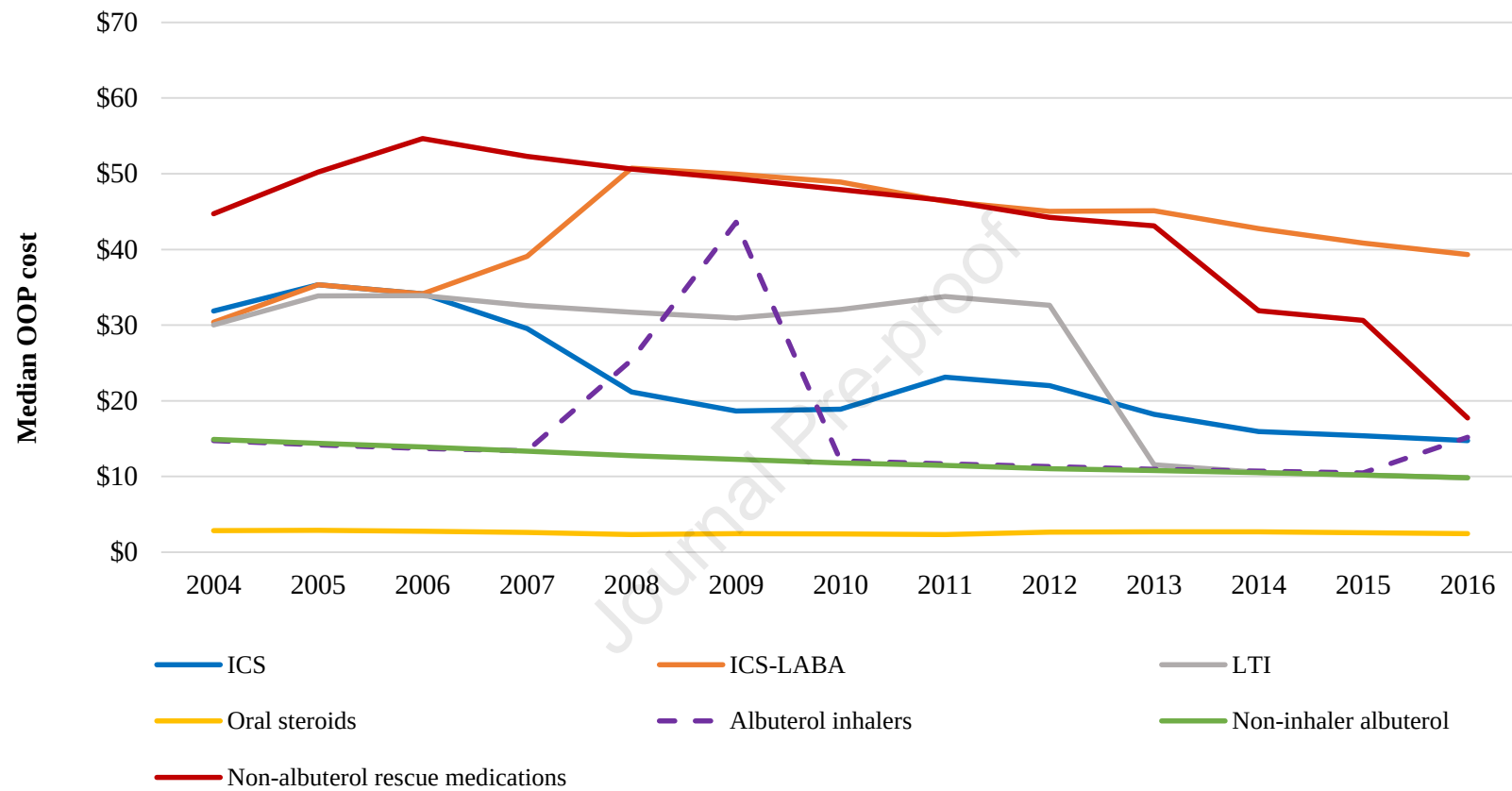
- 2014 Feb;25(1):396–405.
17. Ivanova JI, Bergman R, Birnbaum HG, Colice GL, Silverman RA, McLaurin K. Effect of asthma exacerbations on health care costs among asthmatic patients with moderate and severe persistent asthma. *J Allergy Clin Immunol*. 2012;129:1229–35.
 18. Galbraith AA, Fung V, Li L, Butler MG, Nordin JD, Hsu J, et al. Impact of Copayment Changes on Children’s Albuterol Inhaler Use and Costs after the Clean Air Act Chlorofluorocarbon Ban. *Health Serv Res*. 2018;53(1):156–74.
 19. Tse SM, Li L, Butler MG, Fung V, Kharbanda EO, Larkin EK, et al. Statin exposure is associated with decreased asthma-related emergency department visits and oral corticosteroid use. *Am J Respir Crit Care Med*. 2013;188(9):1076–82.
 20. U.S. Bureau of Labor Statistics. Consumer Price Index for All Urban Consumers: Medical Care in U.S. City Average [CPIMEDSL] [Internet]. FRED, Federal Reserve Bank of St. Louis. [cited 2020 Feb 20]. Available from: <https://fred.stlouisfed.org/series/CPIMEDSL>
 21. Wharam JF, Zhang F, Wallace J, Lu C, Earle C, Soumerai SB, et al. Vulnerable and less vulnerable women in high-deductible health plans experienced delayed breast cancer care. *Health Aff*. 2019;38(3):408–15.
 22. The Johns Hopkins ACG System Version 11.1 Technical Reference Guide. Baltimore, MD: Johns Hopkins University; 2016.
 23. Wharam JF, Zhang F, Eggleston EM, Lu CY, Soumerai S, Ross-Degnan D. Diabetes outpatient care and acute complications before and after high-deductible insurance enrollment: A natural experiment for translation in diabetes (NEXT-D) study. *JAMA Intern Med*. 2017;177(3):358–68.
 24. Krieger N, Waterman PD, Spasojevic J, Li W, Maduro G, Van Wye G. Public health monitoring of privilege and deprivation with the index of concentration at the extremes.

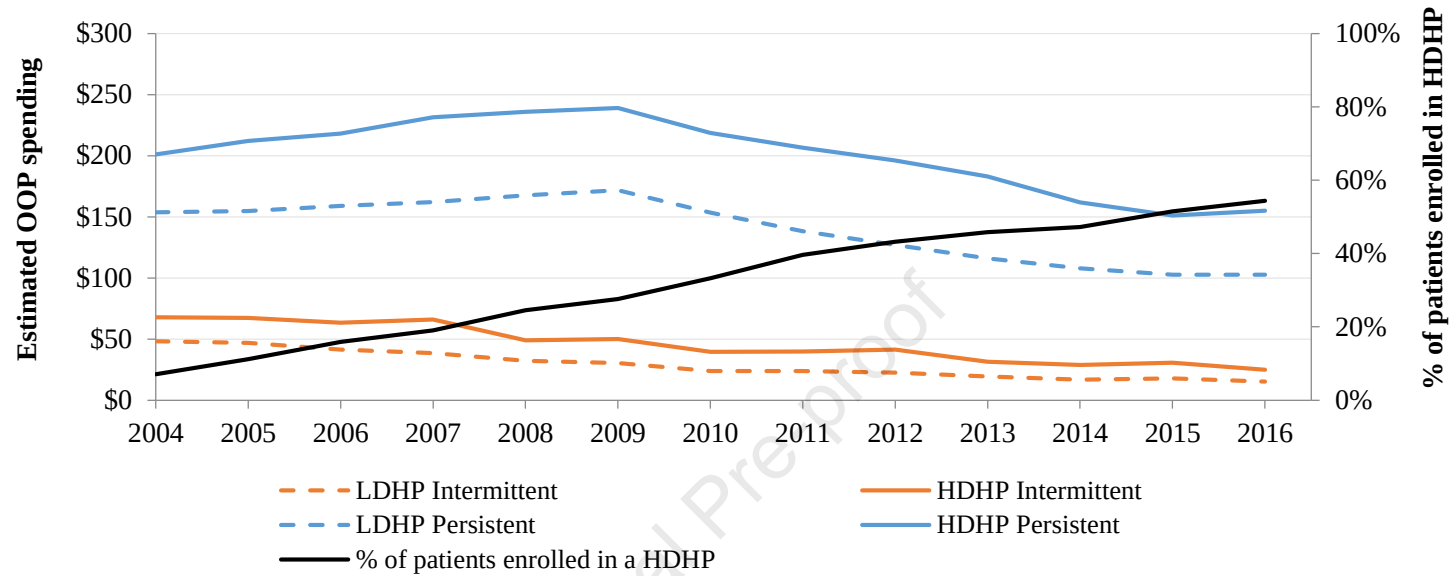
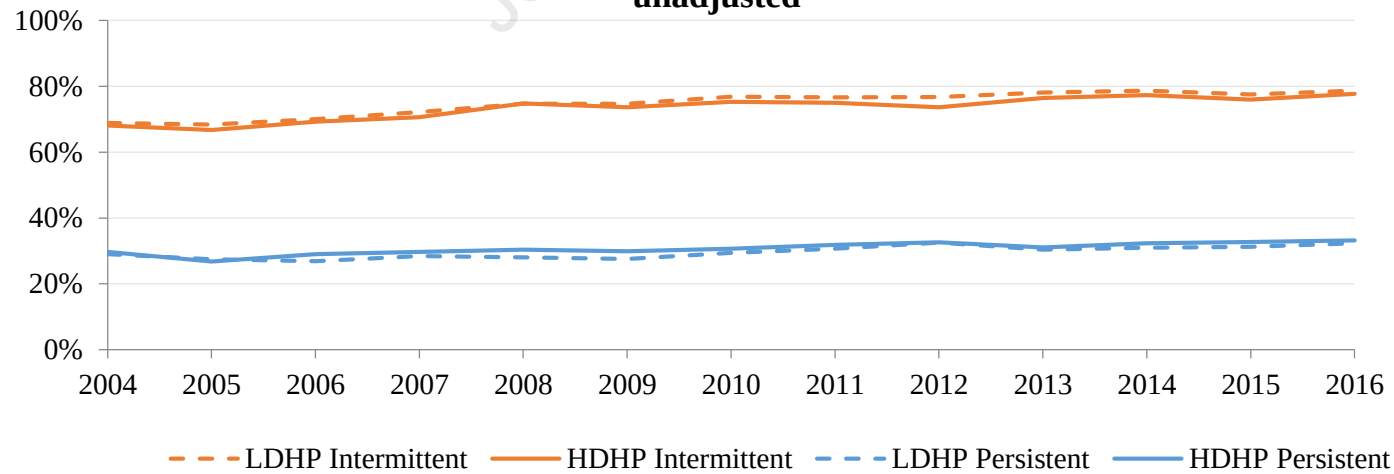
- Am J Public Health. 2016;106(2):256–63.
25. US Census Bureau. American Community Survey (ACS). 2021.
 26. US Department of Agriculture Economic Research Service. Rural-Urban Continuum Codes [Internet]. 2020 [cited 2021 Feb 19]. Available from:
<https://www.ers.usda.gov/data-products/rural-urban-continuum-codes/>
 27. Buntin MB, Zaslavsky AM. Too much ado about two-part models and transformation? Comparing methods of modeling Medicare expenditures. J Health Econ. 2004;23(3):525–42.
 28. US Food & Drug Administration. Transition from CFC Propelled Albuterol Inhalers to HFA Propelled Albuterol Inhalers: Questions and Answers. 2018.

(a) Annual trends in OOP spending on asthma-related medical care, estimated**(b) Predicted probability of having no OOP spending on asthma-related medical care****Figure 1**

**Figure 2**

**Figure 3**

**Figure 4**

(a) Annual trends in OOP spending on asthma-related medical care, unadjusted**(b) Percent of patients with no OOP spending on asthma-related medical care, unadjusted****Figure E1**

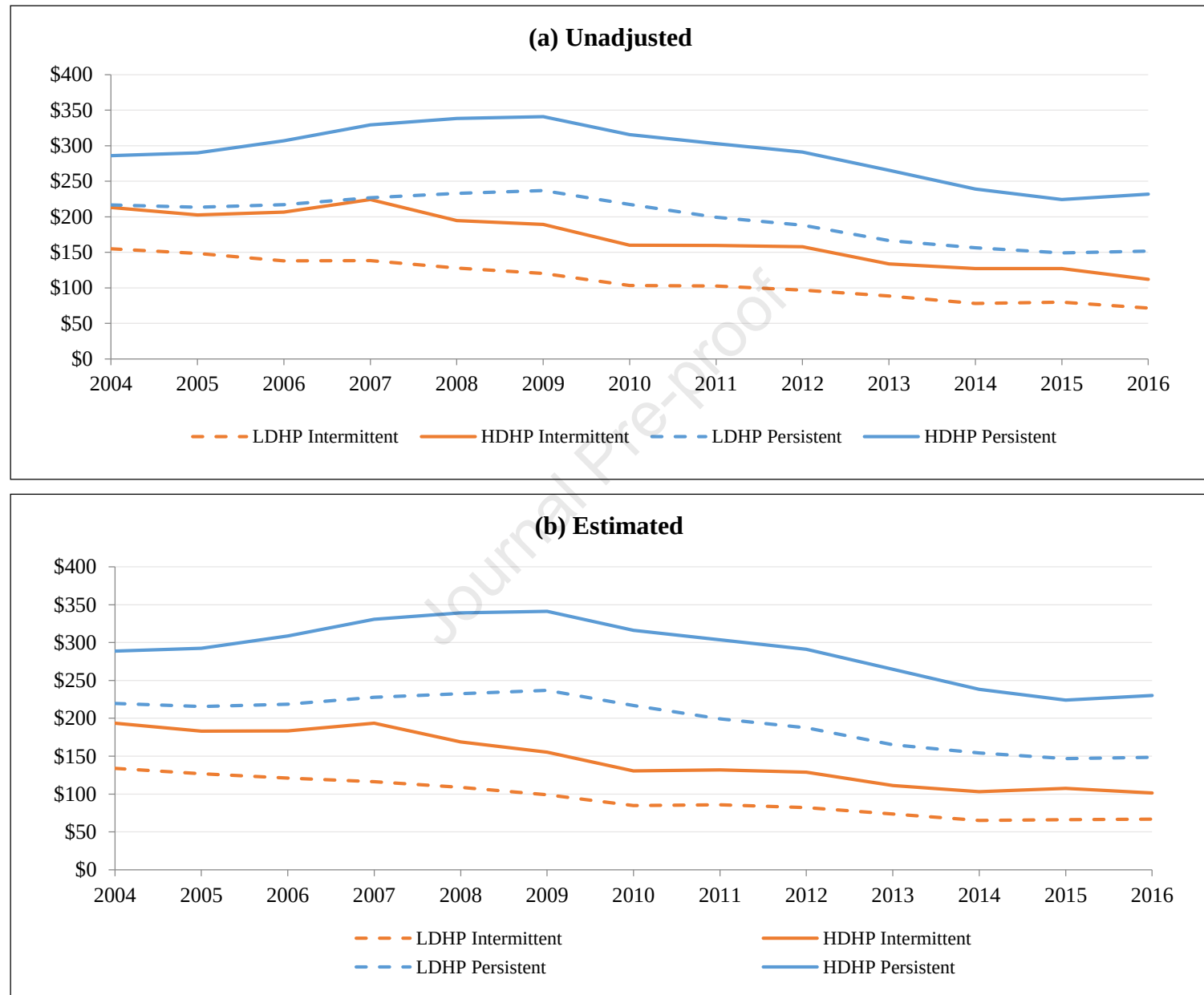


Figure E2

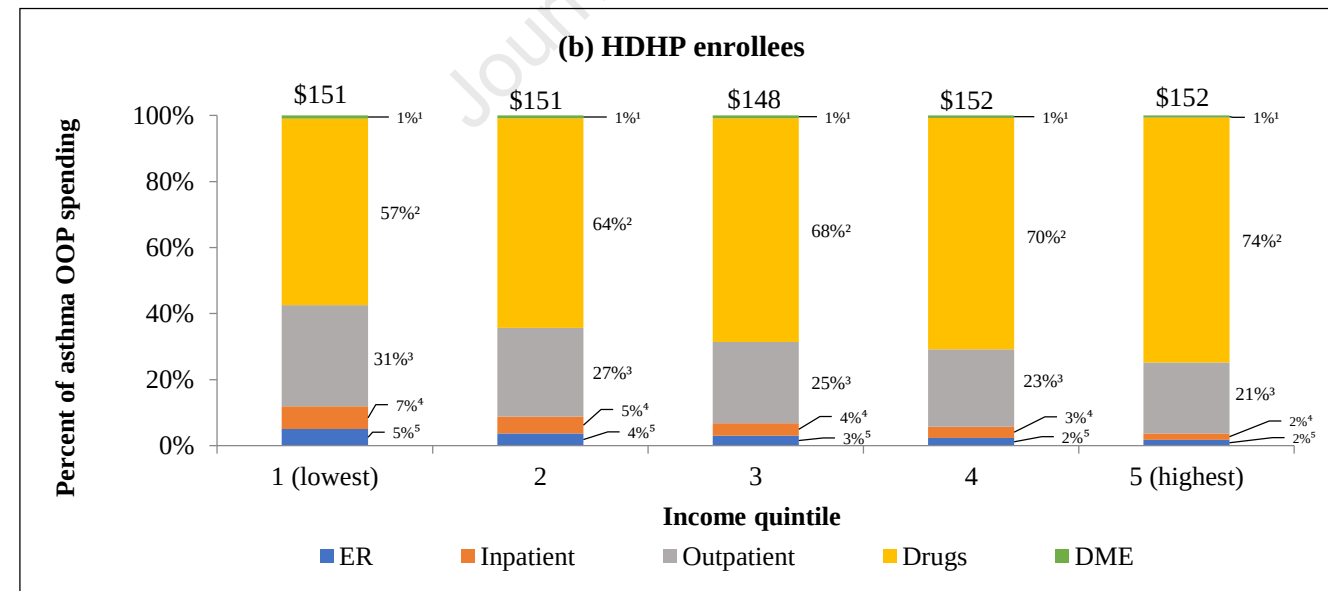
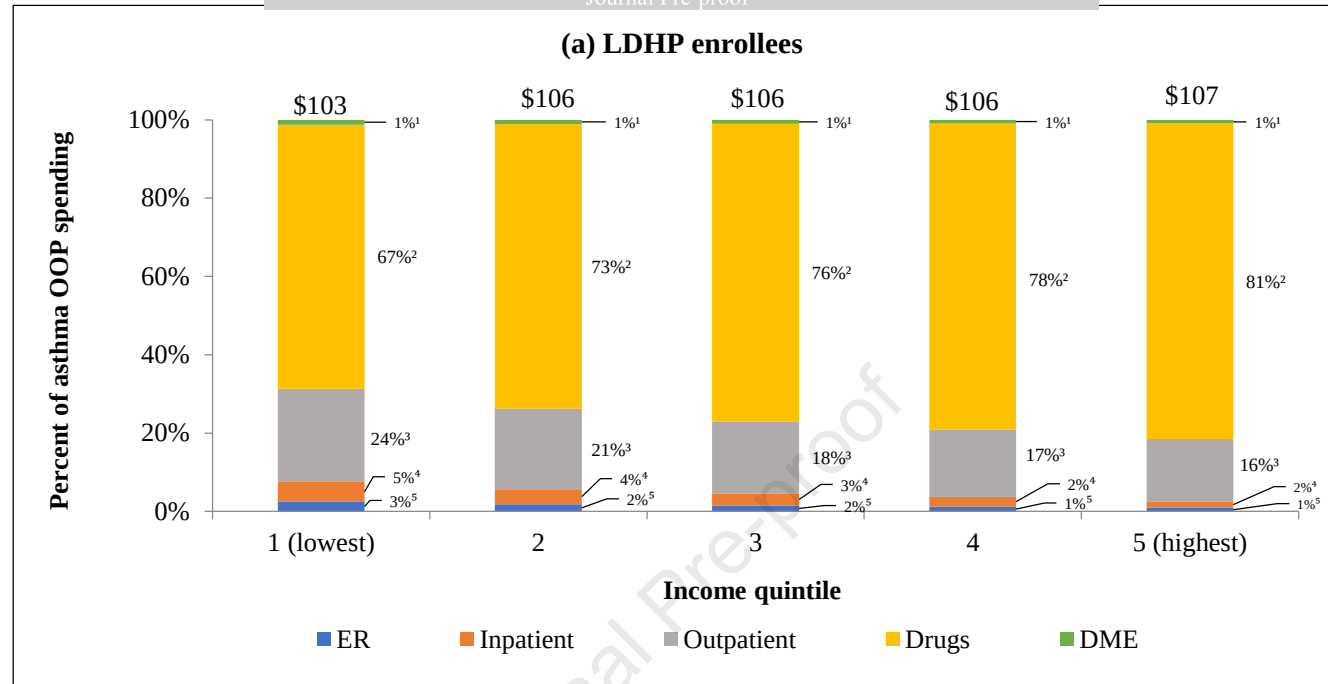
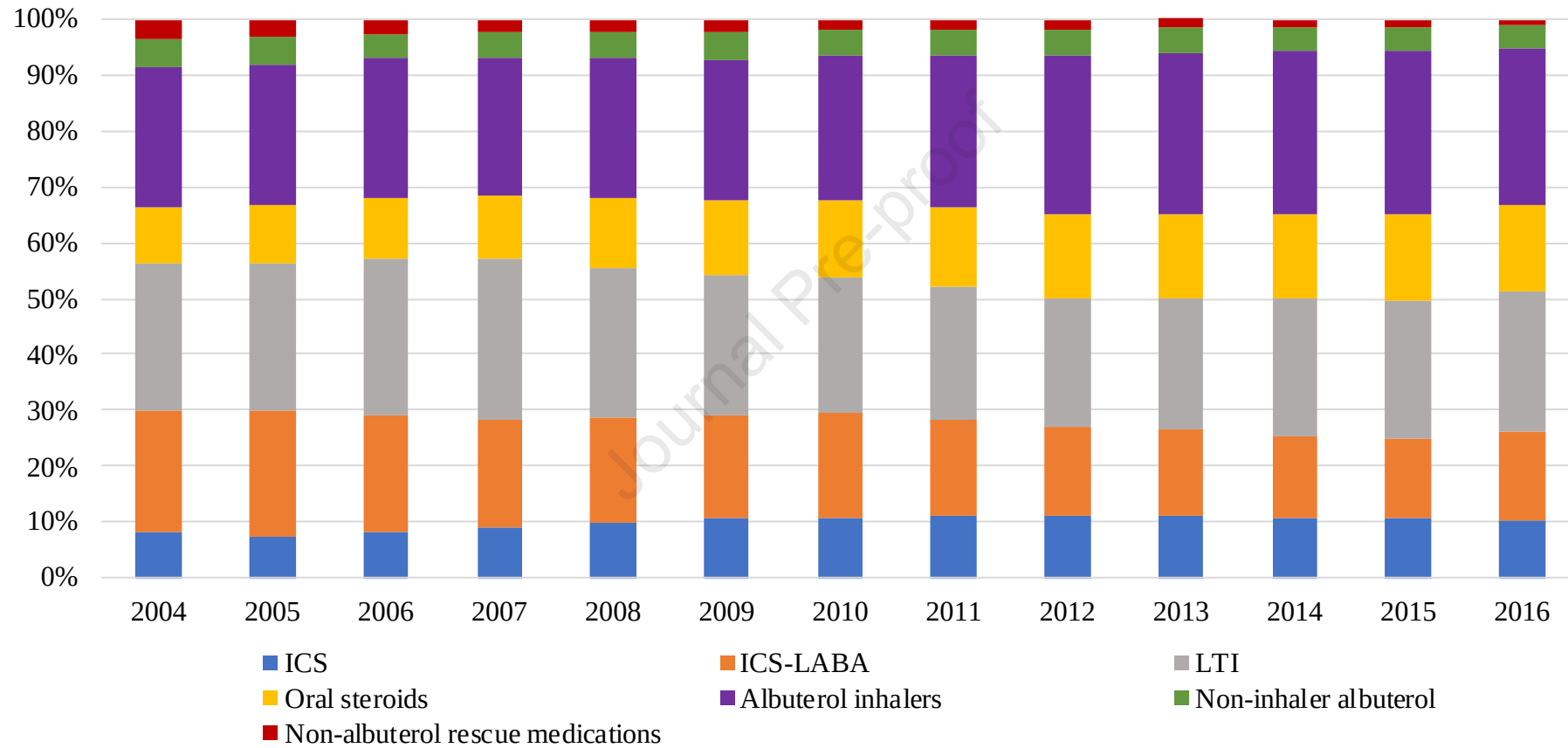
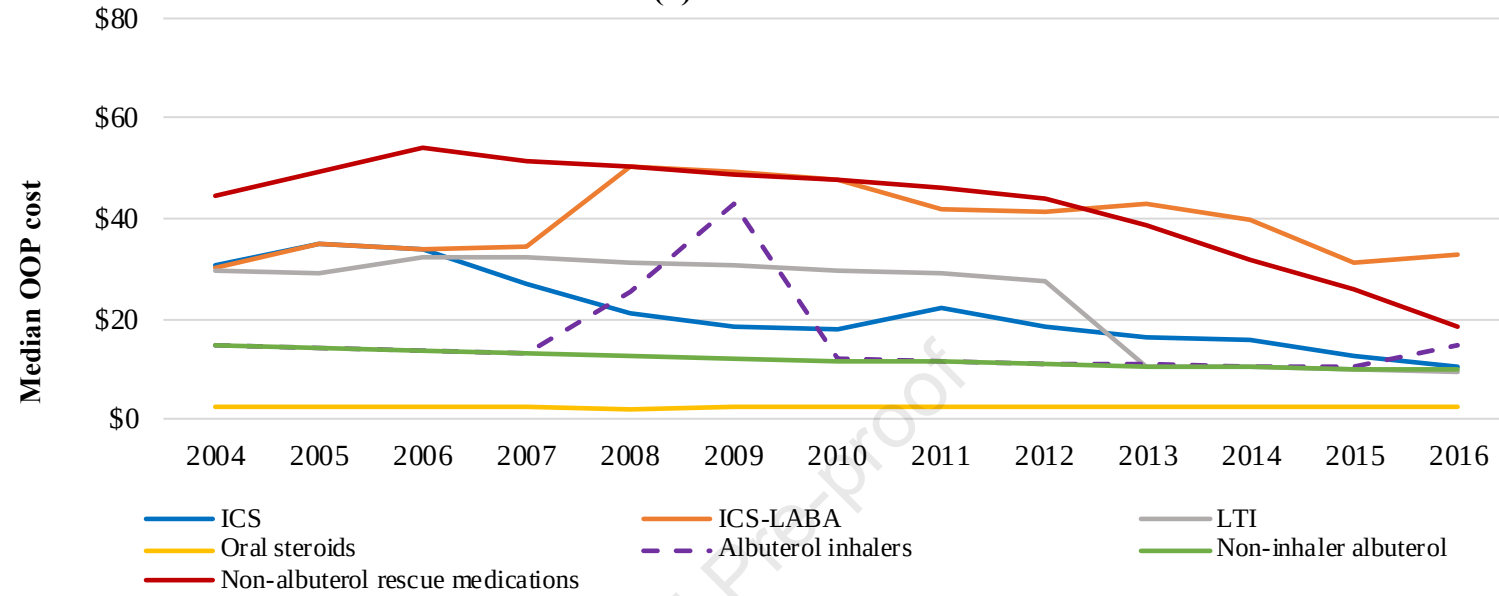


Figure E3

**Figure E4**



(b) HDHP enrollees

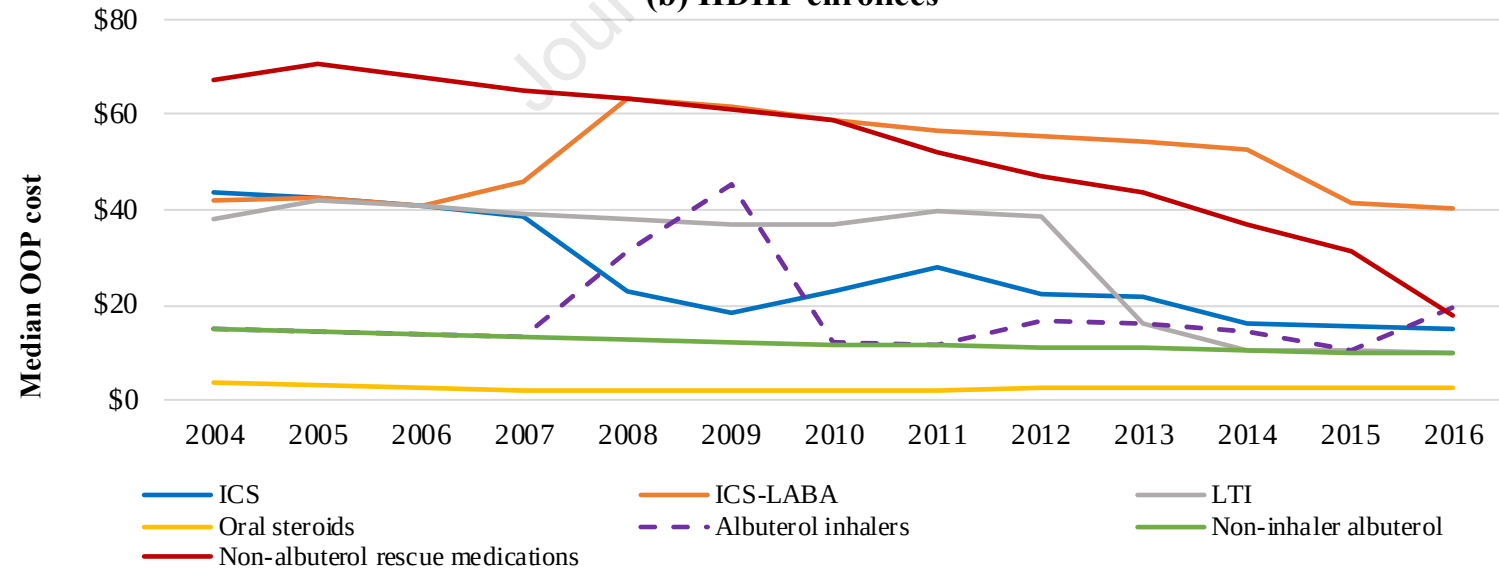
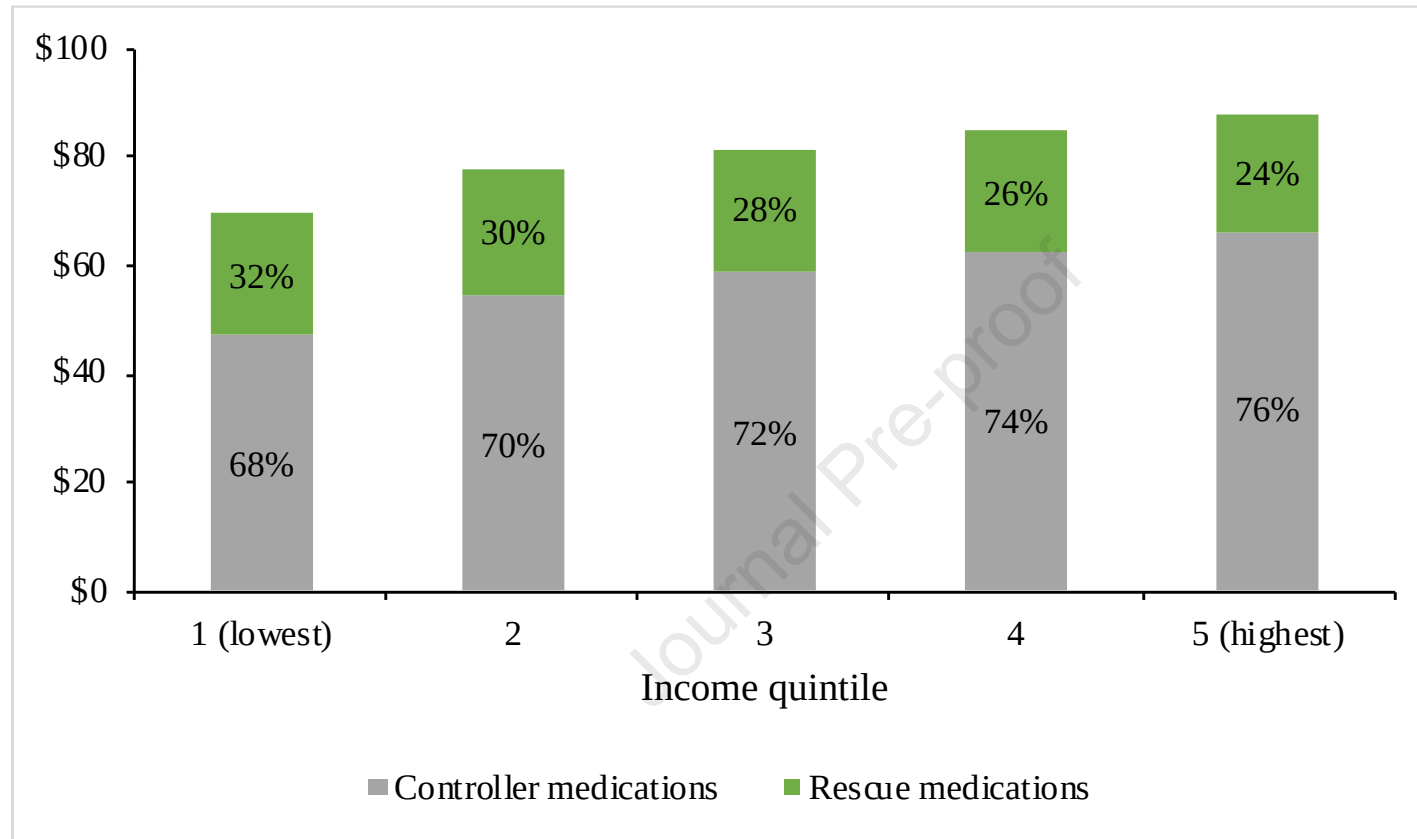


Figure E5

**Figure E6**

Online Repository

Out-of-Pocket Spending for Asthma-Related Care Among Commercially Insured Patients, 2004-2017

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Additional Methods

1. Defining service categories for asthma out-of-pocket spending

Asthma-related inpatient services were defined as a hospitalization with a principal diagnosis of asthma; OR a diagnosis of asthma in any position AND a diagnosis of one of the following related conditions: acute respiratory infections (ICD-9 codes 460-466.xx), chronic obstructive pulmonary disease and allied Conditions (ICD-9 codes 490-496.xx), other conditions originating in the perinatal period (ICD-9 codes 764-779.xx), other diseases due to viruses and chlamydiae (ICD-9 codes 070-079.xx), other diseases of respiratory system (ICD-9 codes 510-519.xx), pneumonia and influenza (ICD-9 codes 480-488.xx).

Asthma-related outpatient visits were defined as office visits with a principal diagnosis of asthma.

Asthma-related emergency department (ED) visits were defined as an ED visit with a principal diagnosis of asthma; OR a diagnosis of asthma in any position AND a diagnosis of one of the following related conditions: acute respiratory infections (ICD-9 codes 460-466.xx), chronic obstructive pulmonary disease and allied Conditions (ICD-9 codes 490-496.xx), other conditions originating in the perinatal period (ICD-9 codes 764-779.xx), other diseases due to viruses and chlamydiae (ICD-9 codes 070-079.xx), other diseases of respiratory system (ICD-9 codes 510-519.xx), pneumonia and influenza (ICD-9 codes 480-488.xx).

Asthma-related medications included prescriptions filled for biologics (anti-IgE), controller medications (including inhaled corticosteroids (ICS), ICS long-acting beta agonists (ICS-LABA), long-acting beta agonists (LABA), leukotriene inhibitors (LTI), mast cell stabilizers, and xanthine), oral steroids, and rescue medications (including ipratropium, short-acting beta agonists (SABA), and ipratropium short-acting beta agonists (SABA ipratropium)).

Asthma-related durable medical equipment included prescriptions filled or medical claims for spacers for asthma inhalers and nebulizer machines.

2. Index of Concentration at Extremes Variables, Description and Information

The Index of Concentration at the Extremes (ICE) calculates a score between -1 and 1 that can be used to describe concentrations of access and deprivation within an area. Values closer to -1 demonstrate a greater concentration of deprivation and those closer to 1 indicate greater access. An ICE Score of zero might indicate an equal number of both populations in the area or a very high concentration of people who do not fall into either end of the extremes. In general, the calculation is as follows:

(# of People in High Access Group - # of People in Deprived Group) / Total Population of Area

In our analysis ICE Scores for Income were calculated for all Census Tracts in the United States. More specifically, data on annual (e.g., prior 12-month) household income was obtained from the American Community Survey (ACS) 5-Year Estimates from 2010-2014 at the Census Tract Level (approximately 3,000 people per census tract). More information regarding the ACS can be found at <https://www.census.gov/programs-surveys/acs/> and <https://www.census.gov/programs-surveys/acs/guidance/estimates.html>

ICE score = (# Of People with Household Income of Greater than \$100,000/year - # Of People with Household Income Less than \$25,000/year) / Total Population

ICE scores were plotted to find the Quintiles (20% cut-offs) across the entirety of the US population. Each member in the study sample was then matched to their Census Tract and the corresponding ICE Scores and Quintiles.

3. Methods to construct measures of other covariates.

a. *Deductible level*

Patients' deductible level was missing for 1% of person-months. In these cases, we imputed missing deductible at the monthly level using aggregated OOP spending among employees within each plan offered by the employer. Our sample includes patients who had more than one health plan choice offered by their employer. However, in these cases we can still estimate the individual patient's deductible level from the available choices using the variables for *employer account*, *product type*, *benefit code*, *savings option*, and *medical product code*. For each specific plan, we use same-year annual deductible spending by all patients in the plan and other predictors to impute the deductible level for each plan. We then assign patients enrolled in this plan to this deductible level.

The analysis in this paper was done at the calendar year level (e.g., measuring annual spending between January and December). Plan-years include twelve months, but for some patients their plan-year doesn't span January to December. To measure deductible level at the patient-calendar year level (a variable needed to control for deductible in regression models of annual spending) patients were categorized as having a high-deductible health plan if the annual individual deductible was \$1,000 or more for the plurality of months per calendar year.

b. *Rural – Urban Classification*

There are 9 categories of urban/rural areas in the 2013 Rural-Urban Continuum Codes. We grouped categories 1-3, which are all counties in Metro areas, into a category for "Metropolitan." We grouped categories 4-6, which are non-metro urban counties with populations of 20,000 or more and non-metro, metro-adjacent counties of 2,500 or more into "Metropolitan suburban." We grouped categories 7-9, which are counties with population 2,500

– 19,999 and non-Metro adjacent, or all counties with population less than 2500, into “Non-Metro, Non-Suburban.”

As reported by the US Department of Agriculture Economic Research Service on its Rural Urban Continuum Codes webpage in 2020 (www.ers.usda.gov/data-products/rural-urban-continuum-codes/), the distribution of 2010 US population across our three constructed categories was 85% Metropolitan, 11% Metropolitan suburban, and 4% Non-Metro, Non-Suburban. Thus, our sample generalizes well to that in the US overall, but is slightly more Metropolitan.

Table E1 – Additional characteristics of study population, 2004-2016 (person-year level observations)

Total person-years, n	6,530,667
Total persons, n	1,986,769
Person-months per person, mean (SD)	39.4 (30.2)
Age (y) at the end of calendar year, mean (SD)	33.4 (18.1)
Age group	
4 - 17 years old	1,056,830 (16.2%)
18 - 30 years old	911,411 (14.0%)
31 - 40 years old	1,867,748 (28.6%)
41 - 50 years old	1,194,181 (18.3%)
51 - 64 years old	1,500,497 (23.0%)
Female patients, n (%)	3,589,359 (55.0%)
Person-years by year of enrollment, n (%)	
2004	292,879 (4.5%)
2005	359,166 (5.5%)
2006	430,730 (6.6%)
2007	466,776 (7.1%)
2008	505,225 (7.7%)
2009	535,398 (8.2%)
2010	550,138 (8.4%)
2011	580,326 (8.9%)
2012	594,546 (9.1%)
2013	611,087 (9.4%)
2014	534,782 (8.2%)
2015	528,314 (8.1%)
2016	541,300 (8.3%)
Enrolled in a high-deductible health plan, n (%)	2,237,358 (34.3%)
Persistent asthma, n (%)	4,052,419 (62.1%)
Had 1+ other family member with asthma, n (%)	1,715,282 (26.3%)
Monthly ACG score, mean (SD)	1.12 (1.69)
ICE income quintile, n (%)	
1 (low)	495,075 (7.6%)
2	829,204 (12.7%)
3	1,113,812 (17.1%)
4	1,562,669 (23.9%)
5 (high)	2,529,907 (38.7%)
Rural-Urban Continuum Classification	
Metropolitan	6,007,295 (92.0%)

Metropolitan Suburban	305,559 (4.7%)
Non-metro, non-suburban	125,438 (1.9%)
Census division	
South Atlantic	1,696,922 (26.0%)
West South Central	1,000,094 (15.3%)
East North Central	996,784 (15.3%)
West North Central	651,107 (10.0%)
Mountain	616,289 (9.4%)
Pacific	583,986 (8.9%)
Middle Atlantic	533,423 (8.2%)
New England	258,122 (4.0%)
East South Central	183,835 (2.8%)

Notes: HDHP = High-Deductible Health Plan; ACG = Johns Hopkins Adjusted Clinical Group® System (version 11.1); ICE = Index of Concentration at Extremes. Table includes all person-year observations included in the study sample.

Figure E1. Unadjusted trends in annual asthma-related OOP spending and the proportion of patients with \$0 asthma-related spending, by asthma severity and health plan type

Notes: OOP = Out-of-Pocket; HDHP = High-Deductible Health Plan; LDHP = Low-Deductible Health Plan. Panel (a) shows the unadjusted percent of patients with no asthma-related OOP spending in each year by asthma severity and HDHP enrollment and panel (b) shows the unadjusted per-year average spending on asthma-related health care and both panels include patient-years from 2014-2016 (N=6,530,671). All spending amounts are adjusted for inflation to June 2016 dollars using the Medical CPI.

Figure E2. Trends in annual asthma-related OOP spending limited to patients with greater than \$0 asthma-related spending

Notes: OOP = Out-of-Pocket; HDHP = High-Deductible Health Plan; LDHP = Low-Deductible Health Plan. Panel (a) shows the unadjusted per-year average spending on asthma-related health care. Panel (b) shows the estimated per-year average spending on asthma-related health care among patients with >\$0 spending on asthma-related care. Estimates based on linear regression model that included 3,322,126 patient-years and adjusted for patient age, gender, income quintile, year of enrollment, mean monthly ACG score, presence of another family member with asthma, and rural-urban continuum classification, with standard errors clustered by family. All spending amounts are adjusted to \$2016 dollars using the Medical CPI.

Figure E3. Distribution of asthma-related out-of-pocket spending across medical services, by patient income quintile and HDHP enrollment

Notes: OOP = Out-of-pocket; HDHP = High-Deductible Health Plan; LDHP = Low-Deductible Health Plan; ER = Emergency Room; DME = Durable Medical Equipment. Estimated mean spending from linear regression models stratified by service category. Models were also stratified by HDHP enrollment and adjusted for patient age, gender, asthma severity, income quintile, year of enrollment, mean monthly ACG score, presence of another family member with asthma, and rural-urban continuum classification, with standard errors clustered by family. The models for low or no deductible health plan enrollees included 4,140,730 patient-years, and the models for HDHP enrollees included 2,152,426 patient-years. All spending amounts are adjusted for inflation to \$2016 dollars using the Medical CPI.

¹ Spending on DME, ² on medications, ³ on outpatient services, ⁴ on inpatient services, ⁵ on ER.

Figure E4. Distribution of prescriptions by medication type

Notes: The figure includes data from 17,483,339 prescriptions filled between 2004-2016.

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Figure E5. Trends in median OOP spending per prescription, by health plan type

Notes: OOP = Out-of-pocket; ICS= inhaled corticosteroids; LTI = leukotriene inhibitors; ICS-LABA = ICS-long-acting beta agonists. The figures include data from 17,483,339 prescriptions filled between 2004-2016. For panel (b), standardized prescription fills were defined as follows: controller medications (ICS, ICS-LABA, and LTI medications) medications were standardized to a 30-day supply, albuterol inhalers, albuterol non-inhaler medications, and non-albuterol rescue medications were standardized per dispensed prescription, and oral steroids were standardized to a 5-day supply. All cost amounts are adjusted for inflation to \$2016 dollars using the Medical CPI

Figure E6. Distribution of proportion of controller and rescue medication out-of-pocket spending by medication type, by patient income quintile

Notes: OOP = Out-of-pocket; Controllers include ICS= inhaled corticosteroids, LTI = leukotriene inhibitors, and ICS-LABA = ICS-long-acting beta agonists. Rescue medications includes albuterol and non-albuterol rescue medications. Mean spending for each medication type was estimated using linear regression models stratified by HDHP enrollment and adjusted for patient age, gender, asthma severity, income quintile, year of enrollment, mean monthly ACG score, presence of another family member with asthma, and rural-urban continuum classification, with standard errors clustered by family. Estimated spending for all included medication types summed, then we calculated percentage spending for controllers and for rescue medications. The figures include data from 15,147,061 prescriptions filled between 2004-2016. All spending amounts are adjusted for inflation to \$2016 dollars using the Medical CPI.