Beyond tobacco- the secondary impact of substance misuse in chronic obstructive lung disease.

M Macmurdo, MBChB.[1], **R Lopez, MS, MPH.**[2,3], **B.L. Udeh, PhD, MPH.**[2,3,4], **J. Zein, MD, MBA**[1]

[1.]Cleveland Clinic Respiratory Institute.

[2.]Center for Populations Health Research, Lerner Research Institute, Cleveland Clinic

[3.]Quantitative Health Sciences, Lerner Research Institute, Cleveland Clinic;

[4.]Neurological Institute Center for Outcomes Research, Neurological Institute, Cleveland Clinic

Abstract

Background: Chronic obstructive lung disease, specifically chronic asthma and COPD, impacts more than 500 million adults worldwide, and is associated with high healthcare spending and significant disease related morbidity. While the direct impact of substance use disorder is well documented, little is known about the indirect impact of substance misuse within this patient population. The healthcare cost and indirect morbidity secondary to substance misuse in obstructive lung disease has yet to be quantified.

Objective: To determine the indirect impact of substance misuse on disease severity, healthcare utilization and healthcare costs in patients with chronic obstructive lung disease across the United States.

Methods: Utilizing data from the 2012–2015 National Readmissions Database (NRD) patients with a diagnosis of COPD or asthma were identified. Documented substance misuse, rates of hospitalization, frequency of hospital readmission, markers of admission severity and cost were assessed utilizing weighted regression analysis.

Results: 1,087,226 patients with an index admission for asthma or COPD were identified. Substance misuse was documented in 4.0% of patients. Substance misuse was associated with a 30% increase in odds of readmission and a higher cost per index admission. The additional index admission costs totaled $24 million for our cohort.

Conclusion: Substance misuse is associated with an increase in healthcare utilization and healthcare cost in patients with chronic obstructive lung disease. Targeting substance misuse in this patient population has the potential for significant cost savings to the healthcare system.

Corresponding author: Dr. Joe Zein, Respiratory Institute, Cleveland Clinic, 9500 Euclid Avenue, Cleveland, OH 44195, zeinj@ccf.org.

Introduction:

Over the past decade, focus on improving efficiency in our healthcare system has come to the forefront, particularly for patients with pre-existing chronic disease. Substance misuse, defined as either the harmful use of illicit drugs or use of prescribed drugs for unintended purposes, has been identified as an important cause of direct morbidity, mortality and ineffective healthcare utilization. Efforts to reduce these direct impacts are ongoing.

Substance misuse may also indirectly impact the health of the individual, reducing adherence with chronic disease therapy and other aspects of chronic care management. These "secondary" consequences may also impact morbidity, mortality and healthcare utilization. To date however, the secondary impacts of substance misuse in patients with pre-existing chronic disease has received little attention.

Asthma and COPD represent two of the most prevalent chronic pulmonary diseases worldwide, impacting more than 500 million adults globally[1,2] Miscategorization of asthma and COPD is common.[3] Many patients with severe asthma are incorrectly diagnosed with COPD. Additionally, asthma-COPD overlap syndromes are increasingly recognized, particularly in patients with tobacco use.[4] The link between tobacco use and worsening outcomes in chronic obstructive lung disease is well-established. The relationship between substance misuse and chronic obstructive lung disease however is less clear.

Patients with substance misuse have been shown to be more likely utilize healthcare inefficiently with more frequent Emergency Department visits, and less consistent outpatient care. [5,6] It is reasonable to assume that patients with chronic obstructive lung disease and substance misuse also have a similar healthcare utilization pattern, reducing the likelihood that their chronic disease is well managed.

Regular use of "crack" cocaine has also been associated with increased risk of developing obstructive lung disease. [7–9] Use of inhaled drugs has also been associated with an increased risk of hospitalization, and increased risk of readmission. [10–15]. Separating the impact of inhaled drug use from the impact of tobacco use in these small patient cohorts has proved challenging however.

In this study, we aim to quantify the secondary morbidity, mortality and healthcare utilization attributable to substance misuse in patients with chronic obstructive lung disease on a national scale. Utilizing national administrative data, we identify a cohort of patients with chronic obstructive lung disease, and determine the prevalence of clinician diagnosed substance misuse by drug class (benzodiazepines, opiates, amphetamines, cocaine, marijuana and polysubstance use, Supplemental Table 1). Utilizing weighted regression analysis, morbidity, mortality and healthcare utilization differences between the two groups were identified. The impact of tobacco use with or without associated substance misuse was determined, and adjusted for in final analysis.

We hypothesize that for patients with chronic obstructive lung disease, documented substance misuse will be associated with increased morbidity, mortality and healthcare utilization as compared to patients without documented substance misuse. While the direct

costs of substance misuse is known and reported, its indirect impact on chronic diseases is not. Quantifying this indirect impact including increased morbidity, mortality and healthcare utilization further supports the value of identification and treatment for substance misuse.

Methods.

Data Description.

This study utilizes data from the 2012 to 2015 Nationwide Readmissions Database (NRD). The NRD contains de-identified hospitalization and discharge data collated from 27 states across the United States as part of the Healthcare Cost and Utilization database (HCUP). Through this dataset, hospital admissions and subsequent readmissions can be tracked across the calendar year for an individual patient, along with primary diagnosis, secondary comorbidities and healthcare cost data.[16] Because the NRD transitioned from the use of international classification of diseases (ICD) 9 codes to ICD-10 coding in 2015, both ICD-9-CM and ICD-10 CM) codes were used to identify cases, substance misuse, and outcomes. Patients with a documented diagnosis of opiate, amphetamine, benzodiazepine, marijuana, cocaine misuse, 'non-specific' substance misuse or 'other mixed' substance misuse were categorized into the 'substance misuse' subset (Supplemental Table 1). Tobacco use was identified using ICD-9-CM/ICD-10-CM coding (Supplemental Table 1). Other potential confounders, including age, gender, primary expected payer, median household income national quartile per zip code, patient location, hospital location and pre-existing comorbidities were identified prior to initial data analysis.

The Elixhauser comorbidity index, a composite measure of individual patient comorbidities by ICD-9/10 CM code which was developed for use with administrative and HCUP data was calculated using the Elixhauser Comorbidity Software.[16] This score was designed to predict in hospital mortality and 30 day readmission risk within administrative data. [16] The baseline score was modified to exclude alcohol and substance misuse as these are part of our exposure of interest.[17] The HCUP Cost-to-Charge Ratio (CCR) Files were used to translate reported hospital admission charges into actual costs.[18] These secondary files allow the conversion of individual hospital charges per patient to the actual cost for care provided.[18] Costs were then inflated to 2015 USD using the Gross Domestic Product (GDP) price index.[19]

Analytic Sample.

All adult subjects (18 years or older) with a primary diagnosis of asthma or COPD were included in the analysis. Subjects were excluded if they had a secondary diagnosis of pulmonary conditions due to fumes and vapors, cystic fibrosis, pulmonary circulation disorders and or idiopathic pulmonary fibrosis (Supplemental Table 2). The index NRD admission was the first admission during a particular year with a primary diagnosis of asthma or COPD. To assess 30-day readmissions, subjects who died in the hospital during the index admission (n=9,596) and those discharged during the month of December (n=93,708) were excluded, as the NRD database only tracks readmissions per patient across the calendar year. Due to the known frequency of misdiagnosis of both COPD and asthma, we chose to combine both diagnoses into a single cohort of patients rather than analyzing

each syndrome separately.[3,20] Sensitivity analysis was performed for key outcomes by asthma, COPD and the combined diagnosis group.

Missing data.

Data were missing for the following NRD variables: median household income national quartile (1.6%), total charges/costs (1.2%), patient location (0.29%), primary expected payer (0.17%), in-hospital death (0.03%), and length of stay (0.006%).

Statistical Analysis.

Analyses were performed according to published HCUP analytic guidelines using the SURVEY procedures in SAS 9.4 software (SAS Institute, Cary, NC).[21] Descriptive statistics, including means, percentages and, standard errors were computed with analytic sample weights. Unadjusted comparisons of subjects with substance misuse vs. those without were conducted using t-tests for continuous factors and Rao-Scott chi-square tests for categorical variables.

Weighted regression analysis was used to determine the impact of substance misuse on morbidity and mortality. Weighted logistic regression was used for binary outcomes (risk of mortality and severity of illness, mechanical ventilation, respiratory failure, sepsis, shock, acute kidney injury, encephalopathy, stroke, in-hospital death, and 30-day readmission); weighted odds ratios with 95% confidence intervals are presented. Continuous outcomes (length of stay and costs) were analyzed using weighted linear regression. Length of stay and costs were log-transformed and the adjusted means and corresponding 95% confidence interval are presented. Sensitivity analysis was performed by diagnosis group utilizing weighted regression analysis. All models included substance misuse, tobacco use disorder, age, gender, primary expected payer, median household income national quartile per zip code, patient location, hospital location, rehabilitation transfer involved, AIDS, deficiency anemias, rheumatoid arthritis/collagen vascular diseases, chronic blood loss anemia, congestive heart failure, coagulopathy, depression, diabetes, hypertension, hypothyroidism, liver disease, lymphoma, fluid and electrolyte disorders, metastatic cancer, other neurological disorders, obesity, paralysis, peripheral vascular disorders, psychoses, renal failure, solid tumor without metastasis, peptic ulcer disease excluding bleeding, valvular disease and weight loss. All tests were two-tailed and performed at a significance level of 0.05.

Results:

Prevalence of substance misuse:

A total 1,087,226 (weighted n = 2,426,294) index admissions with a primary diagnosis of COPD or asthma were identified during the study period. 5% of patients received primary admission diagnoses of both COPD and asthma. Of all patients admitted with COPD and asthma, 4.01% (95%CI: 3.87, 4.15) had a diagnosis of substance misuse documented by their providers during hospitalization.

Patients with a diagnosis of substance misuse in the inpatient setting were on average 14 years younger, and more likely to be male (Table 1). Documentation of active tobacco use was significantly more common in patients with a diagnosis of substance misuse of any kind (OR 3.89 95%CI: 3.82–3.96, p < 0.001).

For patients with documented substance misuse, opiate misuse was the most common diagnosis (Table 2). Modified Elixhauser comorbidity scores were lower in patients with documented substance misuse (11.3 vs 12.0, p<0.001). However, significantly higher rates of AIDS, psychiatric disease and liver disease were seen in the substance misuse group (Supplemental Table 3).

Index Admission Outcomes.

Patients admitted with a substance misuse diagnosis of any kind were significantly more likely to have documented respiratory failure or shock during their index hospitalization (OR: 1.44 95%CI: 1.37, 1.52, p<0.001). Their likelihood of requiring mechanical ventilation was also significantly higher, with an adjusted OR of 1.44 (95%CI: 1.37, 1.52 p <0.05). (Table 3) When analyzed by type of substance misuse, the increased odds of respiratory failure and need for mechanical ventilation was strongest in patients with documented amphetamine, benzodiazepine or opiate misuse (Supplemental Table 4). Patients with documented substance misuse were more likely to have documented sepsis or encephalopathy at time of index admission. Amphetamine misuse specifically was associated with a significantly increased likelihood of shock during index admission (OR 2.45 95% CI: 1.53, 3.93, p<0.001), though this association was not seen across all substance misuse types.

Despite the association between substance misuse and increased likelihood of negative outcomes during index admissions, there was no identified difference in in-hospital mortality between patients with and without a documented history of substance misuse. After adjusting for potential confounders there was no evidence of an increased length of stay between the two groups. Patients with documented substance misuse were significantly more likely to discharge from hospital against medical advice. (OR 4.35 95%CI: 4.17, 4.52, p<0.0001).

After adjusting for potential confounders, a statistically significant increase in the cost of index admission was seen in patients with substance misuse of any kind, with an absolute cost of $6509 (95% CI: 6377.05, 6645.54) in patients with documented substance misuse, compared with $5988.84 (95% CI: 5894.95, 6084.22) in those without — an absolute 8% increase in cost per initial admission (p<0.001).

30-Day Readmission.

Out of subjects that were discharged alive between January and November, 15.4% were readmitted within 30 days. Patients with documented substance misuse were at increased odds of readmission during this time period (OR 1.29 95%CI: 1.25, 1.33 p<0.001), after adjusting for potential confounders. Patients with documented substance misuse were also more likely to be readmitted multiple times- 0.55% of patients with documented substance

misuse were observed to have three or more readmissions in this time period, compared with 0.21% of patients without documented substance misuse.

Sensitivity analysis

Sensitivity analysis was performed by diagnosis group (Table 4). The association between substance misuse and need for mechanical ventilation persisted across all diagnosis groups, though was strongest in patients with asthma alone (OR 2.33 95%CI 2.13, 2.55, P <0.001). Similar patterns of association between substance misuse and the risk of 30-day readmission were seen on sensitivity analysis by diagnosis group, though again, the association was strongest in the group with asthma alone. When analyzed for asthma alone, an increased risk of in-hospital mortality was identified (OR 1.45 95%CI 1.08, 1.95 P 0.014), though this was not seen across other diagnosis groups. Cost per hospitalization was increased across all diagnosis groups, with the greatest increase in mean cost per admission recorded in the patient group with both asthma and COPD diagnosis codes.

Discussion:

Substance misuse has a significant secondary impact in patients with chronic asthma and COPD, which persists even after adjusting for tobacco misuse, income disparities and substance misuse associated comorbidities. This secondary morbidity represents a previously undocumented burden to the individual patient, the healthcare system and society, and is not limited to inhaled substance misuse alone.

Within our cohort of patients, a documented diagnosis of substance misuse was associated with an increase in morbidity, including an increased risk of respiratory failure, need for mechanical ventilation and likelihood of sepsis on admission. Sequelae of substance misuse, including cirrhosis, AIDS and psychiatric disease, were also significantly more prevalent within this cohort.

Patients with documented substance misuse had a shorter average length of stay, likely primarily attributable to their increased risk of discharge against medical advice. Despite this decrease in length of stay, costs of initial hospitalization were higher in patients with documented substance misuse ($6,509 in total costs) compared to those without documented substance misuse ($5,988 in total costs). This difference is likely attributable to increased severity of illness seen at presentation and greater need for higher resource intensive care such as mechanical ventilation, and persisted with sensitivity analysis.

Documented substance misuse was associated with a significantly increased risk of 30 day readmission, and an increased likelihood of multiple readmission events. These readmissions in particular represent a substantial burden to the healthcare system, and to the individual patient. In addition to growing Center for Medicare and Medicare services financial penalties for excessive COPD related readmissions, 30 day readmission has previously been identified as an independent predictor of 1 year mortality in patients with COPD.[22,23]

Distinguishing between asthma and COPD has been shown to be challenging, and asthma-COPD overlap is increasingly recognized. Especially when utilizing administrative data, risk

of misclassification may be high. To avoid misclassification bias and to capture these overlap patients, we chose to analyze asthma and COPD as a combined diagnosis code. While for some outcomes the strength of association seen varied by diagnosis code, the finding that substance misuse is associated with an increased risk of mechanical ventilation, respiratory failure and 30 day readmission was robust across both the COPD and asthma cohorts.

While these findings are significant, they likely represent a small portion of the true burden of secondary substance misuse related morbidity. Our study utilizes the HCUP-NRD database, which is reliant on physician-level documentation. It is well known that substance misuse is both under-documented by providers and under-reported by patients.[12,24,25] It is likely our study underestimates the true financial and clinical burden of substance misuse within this population.

Additionally, due to the limitations of documentation, we cannot comment on relationship between frequency of use and severity of disease outcomes. Broader patterns of healthcare utilization outside of hospitalization are also not captured by our study, and represent an area for further research.

Improving outcomes in chronic asthma and COPD has proved challenging. Our study highlights a previously unquantified contributor to worsening outcomes within this patient population- one that represents both a significant economic burden, and an area for intervention. Treatment of substance dependence is associated with a decrease in healthcare utilization.[6,26,27] Increasing attention to identifying patients with active substance misuse during hospitalization or in the outpatient setting could allow us to offer targeted substance use disorder treatment in addition to the traditional aspects of chronic lung disease care. Initiating treatment during hospitalization could also be considered, especially given the frequency of readmissions, and the fact that many of these patients lack access to consistent outpatient care.

Conclusion

For patients with chronic asthma and COPD, documented substance misuse is associated with an increase in morbidity, healthcare utilization and healthcare cost. This impact extends beyond inhaled substance misuse, is associated with harm to our patients, and represents an additional burden to our already strained healthcare system. Further research at the individual patient level is needed to quantify the full impact of substance misuse on chronic asthma and COPD outcomes, and identify potential areas for targeted intervention.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements:

Abbreviation list:

COPD	Chronic Obstructive Pulmonary disease
NRD	National Readmissions Database
HCUP	Healthcare Cost and Utilization Project
LOS	Length of Stay

References

1. Akinbami LJ, Moorman JE, Bailey C, et al. NCHS Data Brief, Number 94, May 2012; 2001. http://www.cdc.gov/nchs/data/databriefs/db94_tables.pdf#2. Accessed November 5, 2019.

2. Sullivan J, Pravosud V, Mannino DM, Siegel K, Choate R, Sullivan T. National and state estimates of COPD morbidity and mortality - United States, 2014–2015. Chronic Obstr Pulm Dis 2018;5(4):324–333. doi:10.15326/jcopdf.5.4.2018.0157 [PubMed: 30723788]

3. Tinkelman D, Price D, Nordyke R, Halbert R. Misdiagnosis of COPD and asthma in primary care patients 40 years of age and over. J Asthma 2006;43(1):75–80. doi:10.1080/02770900500448738 [PubMed: 16448970]

4. Krishnan JA, Nibber A, Chisholm A, et al. Prevalence and characteristics of asthma-chronic obstructive pulmonary disease overlap in routine primary care practices. Ann Am Thorac Soc 2019;16(9):1143–1150. doi:10.1513/AnnalsATS.201809-607OC [PubMed: 31162945]

5. McAdam-Marx C, Roland CL, Cleveland J, Oderda GM. Costs of opioid abuse and misuse determined from a Medicaid database. J Pain Palliat Care Pharmacother 2010;24(1):5–18. doi:10.3109/15360280903544877 [PubMed: 20345194]

6. Morse S, Bride BE. Decrease in Healthcare Utilization and Costs for Opioid Users Following Residential Integrated Treatment for Co-Occurring Disorders. Healthc (Basel, Switzerland) 2017;5(3). doi:10.3390/healthcare5030054

7. Buster MCA, Rook L, Van Brussel GHA, Van Ree J, Van Den Brink W. Chasing the dragon, related to the impaired lung function among heroin users. Drug Alcohol Depend 2002. doi:10.1016/S0376-8716(02)00193-X

8. Burhan H, Young R, Byrne T, et al. Screening Heroin Smokers Attending Community Drug Services for COPD. Chest 2019. doi:10.1016/j.chest.2018.08.1049

9. Vlies B, Lewis-Burke N, Davies L, Walker P. P247 The Prevalence of Asthma and Level of Treatment in Current or Former Heroin Smokers. Thorax 2016. doi:10.1136/thoraxjnl-2015-207770.383

10. Krantz AJ, Hershow RC, Prachand N, Hayden DM, Franklin C, Hryhorczuk DO. Heroin insufflation as a trigger for patients with life-threatening asthma. Chest 2003;123(2):510–517. doi:10.1378/chest.123.2.510 [PubMed: 12576374]

11. Levine M, Iliescu ME, Margellos-Anast H, Estarziau M, Ansell DA. The effects of cocaine and heroin use on intubation rates and hospital utilization in patients with acute asthma exacerbations. Chest 2005;128(4):1951–1957. doi:10.1378/chest.128.4.1951 [PubMed: 16236840]

12. Rome LA, Lippmann ML, Dalsey WC, Taggart P, Pomerantz S. Prevalence of cocaine use and its impact on asthma exacerbation in an urban population. Chest 2000;117(5):1324–1329. doi:10.1378/chest.117.5.1324 [PubMed: 10807818]

13. Levenson T, Greenberger PA, Donoghue ER, Lifschultz BD. Asthma deaths confounded by substance abuse. An assessment of fatal asthma. Chest 1996;110(3):604–610. doi:10.1378/chest.110.3.604 [PubMed: 8797399]

Author Manuscript
Author Manuscript
Author Manuscript
Author Manuscript

14. Choi H, Krantz A, Smith J, Trick W. Medical diagnoses associated with substance dependence among inpatients at a large urban hospital. PLoS One 2015;10(6):e0131324. doi:10.1371/journal.pone.0131324 [PubMed: 26107402]

15. Yadavilli R, Collins A, Ding WY, Garner N, Williams J, Burhan H. Hospital readmissions with exacerbation of obstructive pulmonary disease in illicit drug smokers. Lung 2014. doi:10.1007/s00408-014-9632-3

16. NRD Overview. https://www.hcup-us.ahrq.gov/nrdoverview.jsp. Accessed August 31, 2020.

17. Healthcare Cost and Utilization Project. Elixhauser Comorbidity Software, Version 3.7 https://www.hcup-us.ahrq.gov/toolssoftware/comorbidity/comorbidity.jsp. Accessed June 5, 2019.

18. Healthcare Cost and Utilization Project. Cost-to-Charge Ratio Files us.ahrq.gov/db/state/costtocharge.jsp. Accessed June 5, 2019.

19. National Income Product Accounts Tables. Section 1 Domestic Product and Income, Table 1.1.4 Price Indexes for Gross Domestic Products. Bureau of Economic Analysis https://apps.bea.gov/iTable/iTable.cfm?reqid=19&step=2#reqid=19&step=2&isuri=1&1921=survey. Accessed June 5, 2019.

20. Lacasse Y, Daigle J-M, Martin S, Maltais F. Validity of chronic obstructive pulmonary disease diagnoses in a large administrative database. Can Respir J 19(2):e5–9. doi:10.1155/2012/260374

21. Healthcare Cost and Utilization Project. HCUP Methods Series. Calculating Nationwide Readmissions Database (NRD) Variances https://www.hcup-us.ahrq.gov/reports/methods/2017-01.pdf. Accessed June 5, 2019.

22. Guerrero M, Crisafulli E, Liapikou A, et al. Readmission for Acute Exacerbation within 30 Days of Discharge Is Associated with a Subsequent Progressive Increase in Mortality Risk in COPD Patients: A Long-Term Observational Study. Loukides S, ed. PLoS One 2016;11(3):e0150737. doi:10.1371/journal.pone.0150737 [PubMed: 26943928]

23. Readmissions-Reduction-Program https://www.cms.gov/medicare/medicare-fee-for-service-payment/acuteinpatientpps/readmissions-reduction-program.html. Published 2019. Accessed January 28, 2019.

24. Polubriaginof F, Salmasian H, Albert DA, Vawdrey DK. Challenges with Collecting Smoking Status in Electronic Health Records. AMIA . Annu Symp proceedings AMIA Symp 2017.

25. Zhao J, Stockwell T, Macdonald S. Non-response bias in alcohol and drug population surveys. Drug Alcohol Rev 2009. doi:10.1111/j.1465-3362.2009.00077.x

26. Parthasarathy S, Weisner C, Hu TW, Moore C. Association of outpatient alcohol and drug treatment with health care utilization and cost: revisiting the offset hypothesis. J Stud Alcohol 2001;62(1):89–97. http://www.ncbi.nlm.nih.gov/pubmed/11271969. Accessed July 19, 2019. [PubMed: 11271969]

27. Holder HD. Cost benefits of substance abuse treatment: an overview of results from alcohol and drug abuse. J Ment Health Policy Econ 1998;1(1):23–29. http://www.ncbi.nlm.nih.gov/pubmed/11964488. Accessed July 19, 2019. [PubMed: 11964488]

Table 1:

Index admission characteristics for patients admitted with asthma and/or COPD

Factor	Overall	No Drug Misuse	Drug Misuse[1]	p-value
	(N=1,087,226)	(N=1,040,601)	(N=46,625)	
Primary diagnosis, % (95% CI)				**<0.001**
Asthma	29.8 (29.4, 30.2)	29.3 (28.9, 29.7)	42.1 (41.2, 43.1)	
COPD	70.2 (69.8, 70.6)	70.7 (70.3, 71.1)	57.9 (56.9, 58.8)	
Age in years at admission, mean (95% CI)	64.9 (64.7, 65.0)	65.4 (65.3, 65.6)	51.4 (51.2, 51.6)	<0.001
Gender, % (95% CI)				<0.001
Male	39.7 (39.5, 39.8)	39.3 (39.1, 39.4)	49.2 (48.6, 49.8)	
Female	60.3 (60.2, 60.5)	60.7 (60.6, 60.9)	50.8 (50.2, 51.4)	
Primary expected payer, % (95% CI)				<0.001
Medicare	62.9 (62.6, 63.3)	64.2 (63.8, 64.5)	33.0 (32.2, 33.8)	
Medicaid	13.8 (13.5, 14.0)	12.7 (12.5, 13.0)	38.9 (38.0, 39.8)	
Private insurance	14.6 (14.4, 14.8)	14.8 (14.6, 15.0)	9.9 (9.5, 10.3)	
Self-pay	5.0 (4.8, 5.2)	4.7 (4.6, 4.9)	11.9 (11.2, 12.6)	
Other/Unknown	3.7 (3.5, 3.9)	3.6 (3.4, 3.7)	6.3 (5.6, 7.0)	
Patient location, % (95% CI)				<0.001
Large Metro	47.9 (46.8, 49.0)	47.3 (46.2, 48.5)	61.8 (60.0, 63.6)	
Small-Medium Metro	29.1 (28.2, 30.1)	29.3 (28.4, 30.2)	25.3 (23.9, 26.7)	
Micropolitan or Noncore	22.7 (22.1, 23.3)	23.1 (22.5, 23.8)	12.0 (11.2, 12.8)	
Unknown	0.25 (0.22, 0.29)	0.23 (0.20, 0.26)	0.84 (0.71, 0.96)	
Tobacco use disorder, % (95% CI)	32.7 (32.4, 33.0)	31.5 (31.2, 31.8)	62.7 (62.1, 63.3)	<0.001
Alcohol use disorder, % (95% CI)	4.16 (4.08, 4.24)	3.6 (3.5, 3.7)	12.2 (16.7, 17.7)	<0.001

[1]Frequencies presented are unweighted counts. p values: a = linear regression; c = Rao-Scott chi-square test.

Table 2:

Frequency and prevalence of substance misuse in the inpatient cohort

Drug misuse (non-exclusive)	Inpatient (total) (N=1,087,226)
Opioids misuse	1.35 (1.30, 1.41)
Cannabis misuse	1.12 (1.06, 1.18)
Cocaine misuse	1.00 (0.93, 1.07)
Non-specific drug misuse	0.81 (0.78, 0.84)
Other, mixed, unspecified drug abuse	0.58 (0.55, 0.60)
Amphetamine misuse	0.29 (0.27, 0.31)
Benzodiazepine misuse	0.12 (0.11, 0.13)
Drug misuse	4.01 (3.87, 4.15)
Num. of drug types	
No drug misuse	92.52 (92.35, 92.69)
Single drug type	2.93 (2.83, 3.03)
Multiple drug types	1.08 (1.03, 1.12)

Table 3:

Binary outcomes in patients admitted with a diagnosis of COPD or asthma and documented substance misuse compared to those without documented substance misuse.[1]

Outcome	Adjusted Weighted OR (95% CI)	P value
Intubation/Mechanical Ventilation	1.57 (1.47, 1.67)	< 0.01
Respiratory failure	1.19 (1.14, 1.24)	<0.01
Sepsis	1.20 (1.03, 1.40)	0.017
Encephalopathy	1.80 (1.56, 2.07)	< 0.01
In hospital mortality	0.96 (0.81, 1.13)	0.63

[1.] All adjusted ORs are adjusted for tobacco use disorder, alcohol misuse, age, gender, primary expected payer, median household income national quartile per zip code, patient location, hospital location, AIDS, deficiency anemias, rheumatoid arthritis/collagen vascular diseases, chronic blood loss anemia, congestive heart failure, coagulopathy, depression, diabetes, hypertension, hypothyroidism, liver disease, lymphoma, fluid and electrolyte disorders, metastatic cancer, other neurological disorders, obesity, paralysis, peripheral vascular disorders, psychoses, renal failure, solid tumor without metastasis, peptic ulcer disease excluding bleeding, valvular disease and weight loss.

Table 4:

Sensitivity analysis of key inpatient outcomes for patients with documented asthma, COPD and overlapping asthma/COPD diagnosis codes.

	Asthma Only		COPD Only		Asthma + COPD	
Unweighted N	309,576		722,786		54,864	
Weighted N	670,396		1,639,721		116,177	
% with documented alcohol misuse (95% CI)	2.77 (2.68, 2.87)		4.77 (4.68, 4.87)		3.46 (3.27, 3.65)	
Binary Outcomes	**Adjusted[1] OR (95% CI)**	**p-value**	**Adjusted[1] OR (95% CI)**	**p-value**	**Adjusted[1] OR (95% CI)**	**p-value**
Intubation/Mechanical Ventilation	1.22 (1.06, 1.39)	*0.005*	1.20 (1.11, 1.30)	*<0.001*	1.58 (1.15, 2.18)	*0.005*
Respiratory failure	1.02 (0.93, 1.11)	0.73	1.02 (0.97, 1.06)	0.45	1.01 (0.87, 1.18)	0.86
Sepsis	0.90 (0.63, 1.29)	0.57	0.86 (0.72, 1.02)	0.075	0.91 (0.49, 1.68)	0.75
Encephalopathy	1.62 (1.15, 2.29)	*0.006*	1.70 (1.49, 1.95)	*<0.001*	0.82 (0.42, 1.61)	0.56
In hospital mortality	0.75 (0.51, 1.10)	0.14	0.93 (0.82, 1.07)	0.32	0.95 (0.45, 2.01)	0.89
30-day Readmission	1.34 (1.25, 1.44)	*<0.001*	1.18 (1.14, 1.22)	*<0.001*	1.19 (1.01, 1.39)	*0.037*
Costs	**Adjusted[1] Mean (95% CI)**	**p-value**	**Adjusted[1] Mean (95% CI)**	**p-value**	**Adjusted[1] Mean (95% CI)**	**p-value**
Alcohol misuse group	5953.52 (5784.41, 6127.58)	*<0.001*	6910.62 (6779.65, 7044.12)	*<0.001*	7184.43 (6826.29, 7561.36)	*<0.001*
No alcohol misuse group	5615.76 (5491.56, 5742.76)		6486.23 (6379.40, 6594.85)		6706.10 (6442.03, 6980.99)	

[1].Adjusted for tobacco use disorder, drug misuse, age, gender, primary expected payer, median household income national quartile per zip code, patient location, hospital location, AIDS, deficiency anemias, rheumatoid arthritis/collagen vascular diseases, chronic blood loss anemia, congestive heart failure, coagulopathy, depression, diabetes, hypertension, hypothyroidism, liver disease, lymphoma, fluid and electrolyte disorders, metastatic cancer, other neurological disorders, obesity, paralysis, peripheral vascular disorders, psychoses, renal failure, solid tumor without metastasis, peptic ulcer disease excluding bleeding, valvular disease and weight loss.