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Costs of Medical Care Among Augmentation Therapy Users and Non-Users with Alpha-1 Antitrypsin Deficiency in the United States

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Abstract

Background: This study is the first to utilize a large claims database to estimate medical costs of patients with alpha-1 antitrypsin deficiency (AATD) in the United States.

Methods: Adult AATD patients were identified from the OptumLabs™ Data Warehouse. Insurer and patient out-of-pocket costs were categorized into the following cost buckets, stratified by augmentation therapy use: physician visits (PV), emergency department visits (ED), inpatient stays (IP), augmentation therapy (AUG), other prescription drug costs (RX), and other costs (OTH). Costs were weighted and adjusted to 2017 U.S. dollars using the medical care component of the consumer price index.

Results: The study cohort consisted of 9117 AATD patients followed for 53,872 person years observed between 1993 and 2015. The annual costs among AATD patients totaled $127,537 among augmentation therapy users and $15,874 among non-users. The major drivers of annual costs to the insurer among the 7975 patients not on augmentation therapy were: PV: $5352 (37.7%) and IP: $4506 (31.8%). Among the 1142 augmentation users, major annual cost drivers to the insurer were PV: $15,064 (12.3%) and AUG: $82,002 (66.7%). Annual patient out-of-pocket costs were $4601 (AUG: $2084 [45.3%]; RX: $940 [20.4%]) and $1689 (PV: $727 [43.0%]; RX: $589 [34.9%]) among augmentation therapy users and non-users, respectively. Averaged across the entire cohort, the average annual costs per AATD patient were $22,975, paid by insurers ($21,100) and patients ($1875).

Conclusions: Annual medical costs among patients with AATD are $127,537 and $15,874 among augmentation therapy users and non-users, respectively, with 75.3% of the cost difference attributable to AUG.

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Introduction

Alpha-1 antitrypsin deficiency (AATD) is a rare, genetic disorder that commonly affects lungs, causing chronic obstructive pulmonary disease (COPD) and more specifically, the emphysema subtype of COPD.[1] AATD is also associated, albeit less frequently, with cirrhosis, liver cancer, vasculitis and skin disease.[2] Although not all AATD-affected patients develop lung problems, for patients who do present with respiratory disease,[3,4] augmentation therapy has become the gold standard for management. Augmentation therapy is an intravenous administration of plasma derived alpha-1 antitrypsin protein, which may assist with avoiding or delaying additional lung damage.[5-9]

Relatively few papers have examined the medical costs of AATD. This is likely because the disease is rare, therefore, finding a sufficiently large cohort for whom cost data are available is challenging. While the true prevalence of AATD remains elusive,[10,11] this condition affects 1 in 2000–5000 people worldwide with substantial variations across regions.[2,12,13] The most recent U.S. study that investigated AATD costs is more than a decade old and estimated costs through patient surveys.[14] However, it is now possible to estimate costs of patients with AATD in a more precise and rigorous manner, utilizing a large national insurance claims database in the United States.

The purpose of this analysis is to present descriptive, real-world differences between augmentation and non-augmentation users without imposing any assumptions about patients' health status or cost of comorbid conditions management. The aims of this study were to calculate medical costs of patients with AATD to the insurer and to the patient (Aim 1), then to evaluate changes in these costs over time (Aim 2). This study is the first to present direct medical costs using claims data to calculate insurance and out-of-pocket payments among a large commercially insured cohort of AATD patients in the United States.

Methods

Study Design

This retrospective analysis of the direct medical costs of AATD uses data from the OptumLabs™ Data Warehouse (OLDW), which includes de-identified claims data for privately insured and Medicare Advantage enrollees in a large, private, U.S. health plan.[15] The database contains longitudinal health information on enrollees, representing a diverse mixture of ages, ethnicities and geographical regions across the United States. The health plan provides comprehensive insurance coverage for physician and hospital services, as well as prescription drugs for a subset of patients.[15]

Identification of Patients

AATD patients were identified based on a diagnosis claim for AATD (International Classification of Diseases, 9th and 10th Revisions: ICD-9: 273.4; ICD-10: E88.01), an augmentation therapy claim either in a facility or home setting (Current Procedural Terminology/ Healthcare Common Procedure Coding System: J0256, J0257, S9346) or a pharmacy claim for augmentation products (190 distinct National Drug Code codes) during the years 1993 through 2015. The index date was the date of the first AATD-related claim. Only adult AATD patients at least 18 years of age at index date were included in the analysis. Patients over 65 years of age for whom Medicare was the primary payer were excluded from the analysis, in order to avoid bias resulting from unobserved costs.

Data Analysis

Patient demographics and clinical characteristics collected from enrollment and claims files at index

date included: age, gender, race/ethnicity and census region. The Deyo-Charlson Comorbidity Score and presence of COPD/liver disease were calculated by capturing relevant comorbidities within 365 days before the index date.

Insurer and patient out-of-pocket costs were calculated and categorized into the following cost buckets: physician visits (PV), emergency department visits (ED), inpatient stays (IP), augmentation therapy (AUG), other prescription drugs costs (RX), and other costs (OTH). Patients' out-of-pocket costs comprised the sum of copayments, coinsurances and deductibles. RX costs are only available for patients who had pharmacy insurance coverage through the same payer, all other buckets represent the entire sample as no patients have RX coverage without medical coverage. Descriptive statistics for costs are reported as the mean and standard deviation. When examining the demographic and baseline characteristics of the sample, individuals who ever used augmentation therapy (≥1 facility/pharmacy/home claim for augmentation infusion) were compared to never users. For the cost comparisons, individuals were considered to be non-users until their first claim for augmentation therapy, and were considered to be augmentation users thereafter. Therefore, the non-user cohort comprised a mix of never users and not-yet users (eventual users prior to their first augmentation claim).

Costs were compared between augmentation users and non-users using nonparametric Wilcoxon rank sum tests. All costs are presented annually, and were weighted based on patients' period of insurance coverage and were adjusted to 2017 U.S. dollars using the medical care component of the consumer price index.[16] Data were analyzed using STATA 14/MP (StataCorp, Texas). Institutional review board approval was obtained from the Institutional Review Board of the University of Maryland in Baltimore on July 27, 2016 (HP-00068329).

Discussion

Population Characteristics
The study cohort consisted of 9117 AATD patients (identified among over 21 million enrollees) and followed for 53,872 person years observed between January 1, 1993 and December 31, 2015. Figure 1 presents the number of person years of claims data on AATD patients in the database over time. For the

Figure 1. Person Years Observed for Alpha-1 Antitrypsin Deficiency Patients Over Time by Insurance Type
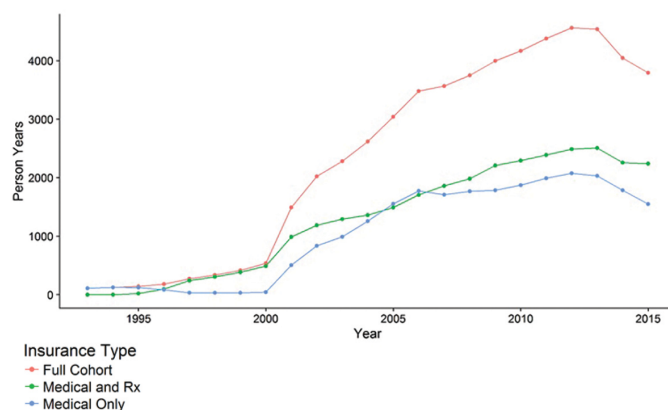
The red line represents person years observed for the entire cohort, thus the sum of the green and blue lines representing the patients who did and did not have prescription drug coverage, respectively. Prescription drug estimates are based on the person years represented in the green line and all other costs come from the cohort represented by the red line.

entire cohort, the mean duration of follow-up was 5.91 years. Among augmentation therapy users and never users, the average follow-up was 5.00 and 6.04 years, respectively. Not-yet users were followed on average for 2.00 years before the initiation of augmentation therapy and 3.00 years after augmentation therapy was started (users).

Table 1 lists the demographic and clinical characteristics of the cohort at index date. Of note, only 1142 AATD patients (12.5%) ever used augmentation therapy during the observation period. Compared to never users, patients who ever received augmentation infusions were statistically different in terms of distribution across age and Deyo-Charlson Comorbidity Score categories, race/ethnicity and census regions (*p*<0.001). A higher proportion of augmentation therapy users had COPD as compared to never users.

Aim 1: Costs to Insurer and Patient
Table 2 summarizes the mean direct medical costs per person year. All cost buckets were statistically different between augmentation therapy users and non-users (all *p*<0.001). Within the full cohort, the main cost drivers for the insurer were PV, AUG, and IP,

Table 1. Demographic and Clinical Characteristics of Commercially Insured Alpha-1 Antitrypsin Deficiency Patients at Index Date

Variable	Full Cohort		Augmentation Cohort		Non-Augmentation Cohort		P Value[a]
	N=9117	Col %	N=1142 (ever users)	Col %	N=7975 (never users)	Col %	
Age Categories, n							< 0.001
40≤	1808	20	119	10	1689	21	
41-53	2601	29	459	40	2142	27	
54-64	2850	31	416	36	2434	31	
≥65	1858	20	148	13	1710	21	
Gender, n							0.252
Male	4414	48	571	50	3843	48	
Female	4703	52	571	50	4132	52	
Race/Ethnicity, n							< 0.001
White	5569	61	731	64	4805	60	
African American	432	5	43	4	387	5	
Hispanic/Asian[b]	545	6	26	2	519	7	
Unknown/missing	2571	28	342	30	2264	28	
Census region, n							<0 .001
Northeast	1178	13	106	9	1072	13	
Midwest	2421	27	345	30	2076	26	
South	3951	43	507	44	3444	43	
West	1551	17	181	16	1370	17	
Charlson Comorbidity Score,[b] n							< 0.001
0	2100	23	50	4	2050	26	
1	2863	31	545	48	2318	29	
2	1202	13	159	14	1043	13	
3	841	9	134	12	707	9	
4	536	6	78	7	458	6	
≥5	1544	17	155	14	1389	17	
COPD,[b] n							< 0.001
Present	4963	54	1040	91	3923	50	
Moderate/Severe Liver Disease,[b] n							< 0.001
Present	507	6	32	3	475	6	

[a]Calculated between augmentation and non-augmentation cohorts using chi-square test.
[b]Calculated by capturing relevant comorbidities within 365 days before the index date.

with relatively large variations as depicted in standard deviations (Table 2). Averaged across the entire cohort, the annual direct medical cost per person year totaled $22,975. However, the annual costs of patients with AATD differed drastically depending on augmentation therapy use status and amounted to $127,537 among users and $15,874 among non-users (*p*<0.001).

Insurers' annual expenditures did not differ substantially between never users and not-yet users (users prior to their initiation of augmentation therapy); these totaled $14,128 versus $15,357, respectively. Patients' out-of-pocket costs were higher for never users as compared to not-yet users: $1693 versus $1592, respectively. When comparing costs among not-yet users with users after excluding augmentation therapy cost, augmentation users incurred an additional

Table 2. Average Annual Health Plan and Patient Out-of-Pocket Costs by Cost Buckets

	Full Cohort		Augmentation			
			Users		Non-Users	
Person Years	53,872		3423		50,449	
Health Plan's Cost Bucket	**Mean**	**SD**	**Mean[a]**	**SD**	**Mean[a]**	**SD**
Physician Visits	$5969	$19,960	$15,064	$35,821	$5352	$18,233
Emergency Department	$ 648	$4122	$1072	$5949	$619	$3966
Inpatient Stays	$4912	$34,092	$10,902	$57,668	$4506	$31,827
Augmentation Therapy	$5210	$26,157	$82,002	$66,873	$0	$0
Other Prescription Drugs[b]	$2748	$9885	$6155	$9967	$2511	$9835
Other	$1613	$13,075	$7741	$31,548	$1197	$10,599
Total	$21,100	$57,291[c]	$122,936	$96,036[c]	$14,185	$45,558[c]
Out-of-Pocket Cost Bucket	**Mean**	**SD**	**Mean[a]**	**SD**	**Mean[a]**	**SD**
Physician Visits	$731	$1362	$ 783	$1283	$727	$1368
Emergency Department	$64	$286	$56	$320	$64	$284
Inpatient Stays	$178	$886	$257	$1210	$173	$860
Augmentation Therapy	$132	$941	$2084	$3146	$0	$0
Other Prescription Drugs[b]	$612	$928	$940	$1066	$589	$913
Other	$158	$875	$481	$1452	$136	$816
Total	$1875	$2603[c]	$4601	$4541[c]	$1689	$2270[c]

Data are presented as cost per person-year (SD) in 2017 U.S. dollars.

[a]All cost buckets were statistically different between augmentation Users and Non-users (*p*<0.001)
[b]Based on 29,794.8 person years in full cohort; 27,858.8 person years in Non-Users and 1936.0 person years for Users
[c]SD for totals were calculated for patients who had both medical and prescription drug insurance

SD=standard deviation;

$26,502 ($43,451 versus $16,949, respectively) in average total annual costs.

The proportion of the direct medical cost per person year (and the proportion of the total cost) paid by the insurer for augmentation non-users was: PV: 37.7%; ED: 4.4%; IP stays: 31.8%; RX: 17.7%; OTH: 8.4%. For the 1142 patients who began augmentation therapy, these costs were: PV: 12.3%; ED: 0.9%; IP: 8.9%; AUG: 66.7%; RX: 5.0%; OTH: 6.3%. Direct medical costs per person year paid by the insurer for augmentation users were higher than non-users in all buckets.

The annual out-of-pocket costs for AATD patients are summarized in the lower panel of Table 2. Statistical differences were observed between augmentation therapy users and non-users for every cost bucket (*p*<0.001). Within the full cohort, the main cost drivers of out-of-pocket expenditures were PV and RX, followed by IP. Out-of-pocket costs (and proportion of total cost) per person year paid by the AATD patients not on augmentation therapy were: PV:

$727 (43%); ED: $64 (3.8%); IP stays: $173 (10.2%); RX: $589 (35%); OTH: $136 (8%). Among the 1142 users of augmentation therapy, these costs were: PV: $783 (17%); ED: $56 (1.2%); IP: $257 (5.6%); AUG: $2084 (45.3%); RX: $940 (20.4%); OTH: $481 (10.45%). The mean annual out-of-pocket cost for AATD patients was equal to $1875. The difference in annual out-of-pocket costs was $4601 versus $1689 among augmentation therapy users and non-users, respectively. Never users and not-yet users until their first augmentation therapy claim are not substantially different from the insurer or patient's cost standpoints. The never users incurred an annual cost of $11,638, and not-yet users incurred $10,410 from the insurers' perspective. From a patient's perspective, never users totaled $1108 and not-yet users amounted to $910 annually (disaggregated data not shown).

The annual costs among AATD patients with prescription drug coverage are only slightly higher as compared to patients without prescription drug

coverage (data not shown). Thus, Table 2 presents totals for all buckets with the caveat that RX costs were only available for a subset of patients.

Aim 2: Changes in Costs Over Time

The overall average costs of care by bucket over time are presented in Figure 2. Generally, buckets increase over time at fairly consistent rates; however, in the last 10 years inpatient and physician visits stayed relatively flat while augmentation therapy and drug costs have continued to increase to the insurer and to a lesser extent to patients.

Changes in average insurer and patient expenditures, among augmentation therapy users, over time are presented with corresponding observed person years in Figures 1 and 2. The years used for comparison show the newest year of data (2015) as well as the year preceding a substantial increase in the number of diagnosed patients (2000).

From the insurers' perspective, increases in annual expenditures, among augmentation therapy users, were noted for all cost buckets except for ED visits and IP stays which actually decreased in cost between 2000 and 2015 (Table 3). The largest increase in

Figure 2. Average Cost Among Patients with Alpha-1 Antitrypsin Deficiency Per Person Year by Cost Bucket, 1993 – 2015
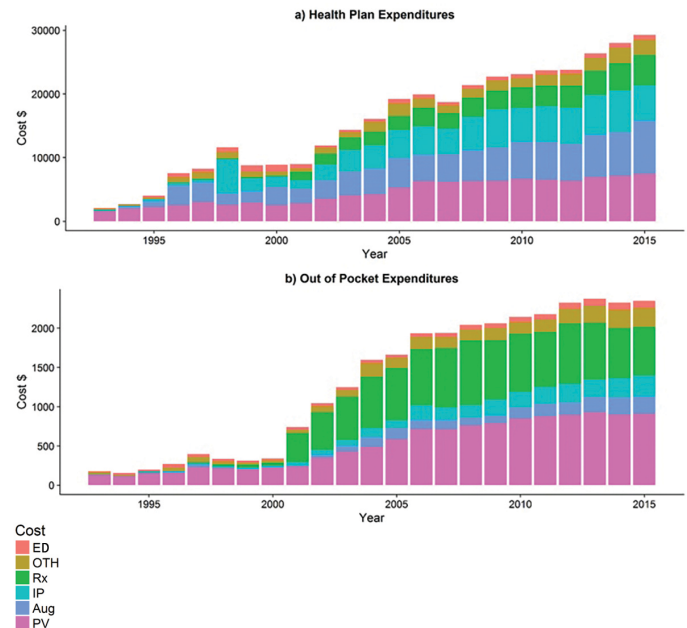
Table 3. Changes in Average Annual Health Plan and Out-Of-Pocket Costs by Augmentation Therapy Use From 2000 to 2015

Year	2000		2015		Change[a] (%)	
Augmentation Therapy Use	Users	Non-Users	Users	Non-Users	Users	Non-Users
Health Plan's Cost Bucket						
Physician Visits	$10,333	$2180	$11,747	$7023	**+14**	**+322**
Emergency Department	$6663	$869	$1003	$778	**-85**	**-10**
Inpatient Stays	$24,233	$509	$6573	$5424	**-73**	**+1066**
Augmentation Therapy	$62,841	$0	$85,975	$0	**+39**	**N/A**
Other Prescription Drugs[b]	$100	$191	$6939	$4216	**+6939**	**+2207**
Other	$7243	$329	$7983	$1769	**+10**	**+538**
Out-of-Pocket Cost Bucket						
Physician Visits	$242	$224	$694	$933	**+287**	**+417**
Emergency Department	$81	$23	$50	$96	**-62**	**+417**
Inpatient Stays	$26	$21	$385	$255	**+1481**	**+1214**
Augmentation Therapy	$121	$0	$2271	$0	**+1877**	**N/A**
Other Prescription Drugs[b]	$67	$41	$630	$575	**+940**	**+1402**
Other	$345	$19	$339	$231	**-2**	**+1216**

Data are presented as cost per person year (SD) in 2017 U.S. dollars.

[a]Year 2015 versus year 2000
[b]Based on 493 person years in 2000 and 2241 person years in 2015

expenditures was observed for prescription drugs. Among AATD patients not on augmentation therapy, insurers' expenditures increased for all cost buckets except for ED visits.

Discussion

The goal of this study was to estimate medical costs of AATD to both payers and patients. Overall, the analysis showed that the annual direct medical costs for AATD patients were $22,975 with an average of $21,100 to insurers and $1875 to patients. This study is the first to utilize a large claims database and the data represents the first U.S.-based longitudinal estimates of costs among patients with AATD. To the authors' knowledge, this AATD medical costs analysis reflects the largest ever reported cohort of AATD patients (9117).

A summary of preceding cost reports related to AATD and AATD-associated diseases are presented in Table 4. The first cost estimates published in the United States included total health care costs, including RX, AUG and out-of-pocket expenditures.[17] As noted by the authors, previously reported costs were likely underestimated due to unavailability of cost information on other cost buckets (e.g., physician visits). After adjusting for inflation, RX and AUG costs among augmentation users reported in 2001 were lower as compared to findings reported in our study. The second U.S. analysis was a follow-up to the first study and included formerly missing information on several cost buckets.[14] After adjusting for inflation, the total health care costs for augmentation users in 2003 were also lower, while the prescription drug costs were slightly higher for augmentation users in light of findings reported in this analysis.

A recent European study provides some cost estimates for comparison. The annual costs of augmentation therapies in the United States were lower than in Europe ($82,002 versus $94,755; Tables 2 and 4).[18] However, European AATD patients receiving augmentation therapy incurred lower annual direct medical costs ($103,508) as compared to American patients receiving augmentation therapy ($122,936). The health care expenditures among augmentation non-users also were lower in Germany (the mean direct annual costs in the cohort not receiving augmentation therapy were €6099, equal to $7337 in 2017 U.S. dollars[18]). These differences can be at least partially explained by differences in financing mechanisms between the German and American health care systems,[19,20] variations in the length of follow-up observed in each study, and distinct cohort definitions (AATD-associated COPD cohort in German study versus overall economic burden of AATD irrespective of AATD-associated comorbidities in this report).

The rationale regarding cost comparisons at 2 points in time is as follows: before a substantial increase in the number of diagnosed patients (2001), the authors believe that only very severe cases were diagnosed with AATD in the 1990s and early 2000s. Over time, along with increasing recognition, less severe cases were identified and disease management programs in the United States became available, resulting in decreased hospitalizations due to better management of mild/moderate exacerbations of COPD, possibly accounting for observed cost reductions.

This cohort sheds light on the use of augmentation therapy among a large group of patients in whom AATD has been diagnosed. Not surprisingly, Table 1 shows that the vast majority (91%) of augmentation users had a diagnosis of COPD. The 9% of augmentation users who did not have a COPD diagnosis likely reflects the use of augmentation therapy for other health conditions associated with AATD (e.g., bronchiectasis, panniculitis), use of augmentation therapy in a manner inconsistent with guidelines, and possible issues with misdiagnosis or misclassification in this dataset. Among the individuals in this cohort who did not use augmentation, 50% had a diagnosis of COPD. This finding may reflect the application of older prescribing guidelines for augmentation therapy (i.e., guidelines prior to 2015 recommended the use of augmentation therapy for only a subset of cases of AATD-associated COPD), and also likely, it is indicative of limited utilization of augmentation therapy due to patient preference, cost, and other barriers to the use of this treatment regimen.

The fact that only 12.5% of our cohort used augmentation therapy during the study period may be explained in part by the fact that follow-up averages only 5.91 years per patient and is shorter for augmentation users than never users (mean follow-up of 5.00 versus 6.04 years). Another cross-validation of our results stems from a utilization study among a cohort of Medicare AATD patients with COPD, in which it was found that only 13% of AATD patients were using augmentation therapy.[21]

Table 4. Summary of Previously Published Studies on Costs of Alpha-1 Antirypsin Deficiency and Alpha-1 Antirypsin Deficiency-Associated Diseases

Years	Data Source/ Perspective/ Location	Cost Category	Mean Cost (SD)	Mean Cost (SD) [2017 USD]	Reference
1997-1999	Survey/Patient's+ Payer's/United States	**Total Direct Health Care Costs Among AATD Patients**	$30,948 (55,580)[a]/ $20,673[b] (38,970)	$60,761 (109,122)[a]/ $40,588[b] (76,511)	14
		Current AUG user	$40,123 (52,909)[a]	$78,775 (103,878)[a]	
		Former AUG user	$39,610 (96,511)[a]	$77,768 (189,483)[a]	
		Never AUG user	$3553 (7531)[a]	$6976 (14,786)[a]	
		Prescription Drug Costs	$1062 (2611)[a]/ $642[b] (1480)	$2085 (5126)[a]/ $1260[b] (2906)	
		Out-of-Pocket Costs	$1866 (2708)[a]/ $1625[b] (1801)	$1866 (3664)[a]/ $3190[b] (3536)	
1997-1999	Survey/Patient's+ Payer's/United States	**Total Direct Health Care Costs Among AATD Patients**			17
		All patients	$46,114 (49,664)	$90,537 (97,507)	
		a	$48,462 (51,173)	$95,147 (100,469)	
		b	$39,672 (43,732)	$77,889 (88,860)	
		Prescription Drug Costs	$6,456 (15,867)	$12,675 (31,152)	
		Augmentation Therapy	$28,075 (31,017)	$55,120 (60,897)	
2010-2013	Survey/Societal/ Germany	**Total Health Care Costs Among AATD Patients with COPD**			18
		AATD-associated COPD Patients with AUG	€ 78,930 (4202)	$103,508 (5168)	
		AATD-associated COPD Patients without AUG	€ 5096 (5655)	$6683 (6956)	
		Prescription Drug Cost Among AUG Users	€ 2056 (1080)	$2696 (1328)	
		Prescription Drug Cost Among Non-AUG Users	€ 1558 (976)	$2043 (1200)	
		Augmentation Therapy	€ 72,255 (N/A)	$94,755 (N/A)	

[a]Pi*ZZ phenotype patients
[b]non-PI*ZZ phenotype patients

AATD=alpha-1 antirypsin deficiency; AUG=augmentation therapy

This cost analysis revealed that never users and not-yet users until their first augmentation therapy claim are not substantially different from the insurer or patient costs standpoint. However, some AATD patients identified in this study might have been diagnosed based on their family history of the disease, while they were actually symptom-free. This is more likely to be the case for individuals who did not receive augmentation therapy.

A major limitation of this study is the lack of data regarding smoking status and phenotype information. While this analysis did not focus on AATD-associated COPD, the severity of COPD, forced expiratory volume in 1 second scores, Tiffeneau index or patient's weight were not accounted for due to unavailability of these data. Another limitation relates to generalizability. Only commercially insured patients of one large health plan were included in this analysis, hence AATD

patients receiving health care services through public or other payers are not represented.

The distribution of patient characteristics (e.g., census region) may mirror differences in coverage by the insurer, not true differences in geographical distribution of AATD patients nor augmentation therapy use across the United States. While cost reductions were observed for ED visits and IP stays among augmentation users over time, the design of this study does not allow for sound conclusions regarding the effects of augmentation therapy on inpatient stays and other health expenditures. The impact of augmentation therapy on health outcomes and costs were analyzed in 3 cost-effectiveness studies comparing augmentation therapy use with conventional health interventions.[22-24]

The estimates obtained in this study can be utilized by various stakeholders: patient advocacy groups, insurers, pharmaceutical manufacturers and researchers. First, the results can be used by patient advocacy groups to further their goals of increased recognition of AATD and affordable treatments. Second, insurers can utilize cost data for budget impact projections to assure appropriate allocation of resources for AATD patients. Third, pharmaceutical manufacturers and researchers should gain insight into the current costs of the disease and look for new methods of alpha-1 antitrypsin protein production and delivery to lower costs associated with the use of augmentation therapy.

The purpose of this analysis was to present descriptive, real-world differences between augmentation and non-augmentation users without imposing any assumptions about the patient's health status or cost of comorbid conditions management. Because costs of patients with AATD might be related to management of associated comorbid conditions, the authors did not intend to control for differences in comorbid status clinically associated with AATD with the use of multivariate analyses. Additionally, this analysis does not aim to show a causal relationship between AATD and annual costs. Instead, it presents real-world differences between use of augmentation therapy (or lack of thereof) and costs among AATD patients irrespective of AATD-associated conditions to payers and decision-makers on an aggregate level.

The results of this study highlight the feasibility of rare disease research using claims databases and are intended to fuel active discussions in the rare disease policy arena. Further contributions to an increasing awareness of AATD among physicians are warranted; even today, AATD remains an under-recognized and under-diagnosed disorder.[5,25] Future studies should evaluate both cost-effectiveness and affordability of AATD treatments and delineate cost differences between AATD-associated COPD and non-AATD-associated COPD using claims for large AATD patient samples in the United States, to contrast with survey studies based on small cohorts conducted in Europe.[18]

Conclusions

Annual medical costs of patients with AATD are $127,537 and $15,874 among augmentation therapy users and non-users, respectively. Based on past expenditures showing increases in direct medical costs of care among AATD-affected individuals and their insurers, future increases in their health care spending may be expected.

Further studies are needed to assess the impact of augmentation therapy on health outcomes and costs to both patients and insurers. This will require study designs that utilize cohorts derived from real-world sources such as insurers' databases to enhance data from clinical trials, which typically have much smaller numbers of patients.

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