Healthcare Costs For Patients With Severe Alpha-1 Antitrypsin Deficiency Among Augmentation Therapy Users And Non-Users And Impact Of Therapy Frequency

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Healthcare Costs for Patients with Severe Alpha-1 Antitrypsin Deficiency Among Augmentation Therapy Users and Non-Users and Impact of Therapy Frequency

By Nikita Raina

First Reader: Michaela Dinan
Second Reader: John Ko

A Thesis Submitted in Candidacy for the Degree of Master of Public Health

Yale School of Public Health
Department of Chronic Disease Epidemiology
May 2023
ABSTRACT

Background: Alpha-1 antitrypsin deficiency (AATD) is a rare disease caused by a genetic mutation in the SERPINA1 gene which causes low levels of or no working alpha-1 antitrypsin protein to be made. This results in a number of clinical manifestations, most prominently pulmonary issues such as emphysema. An intravenous infusion of human plasma-derived AAT (augmentation therapy) is sometimes prescribed to patients with emphysema, but there is a need for a greater understanding of the resulting economic burden in this patient population.

Methods: A retrospective observational cohort study was conducted using the PearlDiver Mariner Patient Claims Database to analyze healthcare costs of adult AATD patients with emphysema. Total costs for AATD-emphysema patients who have not taken augmentation therapy at any point were calculated. Augmentation therapy costs and non-therapy related healthcare costs were calculated for all augmentation therapy users, patients who received therapy on a weekly basis, and patients who received therapy monthly. Costs for each group were compared using nonparametric Wilcoxon rank sum tests, and a linear regression model was used to further assess the association between treatment frequency (weekly vs. monthly) and non-therapy related healthcare costs.

Results: Non-augmentation therapy users had a total average annual cost of $17,739, whereas all augmentation users had an average non-therapy cost of $23,753. Weekly augmentation therapy users had higher augmentation therapy costs compared to monthly users due to increased frequency but also still had significantly higher remaining non-therapy costs of $32,863 compared to monthly augmentation therapy users who had non-therapy costs of $23,696.
Augmentation therapy users had a significantly higher average length of stay compared to non-users, though there was not a significant difference in average length of stay between the weekly and monthly augmentation therapy users.

**Conclusions:** Non-augmentation therapy users had a total average annual cost of $17,739, while all augmentation users had an average non-therapy cost of $23,753. Weekly augmentation therapy users had higher augmentation therapy costs due to increased frequency but also still had significantly higher remaining non-therapy costs of $32,863, whereas monthly augmentation therapy users had non-therapy costs of $23,696. Given the retrospective and observational nature of the study, it is possible that the association we observed between therapy frequency and resulting non-therapy healthcare costs is due to selection bias. Further research employing prospective study designs and approaches to assess for and mitigate potential selection bias is necessary in order to better understand how augmentation therapy influences economic burden for AATD patients with severe disease manifestations.
ACKNOWLEDGEMENTS

I’d like to thank my advisor and primary reader Dr. Michaela Dinan for her meaningful advice, help, and support throughout the whole thesis process. I’d also like to thank John Ko for his endless help and guidance, assisting me as I navigated the continuous highs and lows of independent research.

I’d also like to extend my gratitude to all my professors at the Yale School of Public Health who have each guided me and helped shape my academic experience over the past two years.
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INTRODUCTION

Alpha-1 antitrypsin deficiency (AATD) is a rare disease caused by a genetic mutation in the SERPINA1 gene which causes low levels of or no working alpha-1 antitrypsin protein to be made. This causes damage to the lungs and liver and can manifest in a variety of pulmonary issues such as chronic obstructive pulmonary disease, as well as liver disease, panniculitis, and vasculitis. The prevalence of AATD is approximately 1 in 2,000 to 1 in 5,000 individuals. However, given that this rare disease is underdiagnosed and the lack of enough large population screening studies, this prevalence is an estimation.

Augmentation therapy, an intravenous infusion of human plasma-derived AAT, is sometimes prescribed to AATD patients with lung manifestations, often emphysema. The therapy was approved by the FDA in 1987, specifically indicated for emphysema associated with severe AATD and there are now five approved treatment options in the market. Other forms of treatment are meant for managing symptoms and include bronchodilators, inhaled steroids, and oxygen, and in some very severe cases lung transplantation is considered.

While augmentation therapy is the only approved treatment for AATD patients with lung disease related symptoms, literature shows that there is mixed clinical evidence on whether it is effective for all AATD patients with emphysema. Furthermore, research has shown that prescribing patterns can also be variable, despite the fact that augmentation therapy is indicated to be an intravenous infusion on a weekly basis. A study of the National Heart, Lung, and Blood Institute Registry for Individuals with Severe Deficiency of Alpha-1 Antitrypsin found that patients shifted from weekly therapy to less frequent infusions, with only 33% of the study population remaining on weekly augmentation therapy compared to the 51% of the study population at baseline of the study. Therefore, it is important to understand how these shifts in
prescribing and treatment patterns could reflect overall health outcomes and economic burden for patients with severe AATD.

Overall, there is not a lot of existing research on medical costs and general economic burden for AATD patients primarily due to the rarity of disease and resulting underdiagnosis, making it challenging to find a large enough patient cohort with meaningful cost data. Existing literature has investigated the economic burden and healthcare resource use of AATD patients vs. non-AATD patients, use of augmentation therapy, as well as differences between AATD-associated COPD patients and non-AATD COPD patients. Furthermore, there are also studies which compare outcomes and cost of burden between AATD patients and COPD patients, as well as between non-AATD COPD patients and general COPD patients. Despite this background, there is a gap in literature when it comes to cost burden and differences within the most severe cohorts of AATD patients. There is also a gap in the understanding of prescribing patterns of the therapy, rates of adherence to the therapy, and associated costs and healthcare utilization overall for patients specifically impacted by greater severity of AATD.

This retrospective cohort study aimed to examine whether augmentation therapy in a severe AATD patient population had an impact on non-therapy related costs as well as how augmentation therapy treatment frequency affects other healthcare costs.

METHODS

Data Source

Data was obtained from the PearlDiver Mariner Patient Claims Database, comprehensive of 152 million patient lives spanning a time period of 2010 to 2021. The database includes patients of any diagnosed medical condition and allows users to query healthcare claims that have been processed in physician networks in all 50 states in the US and is has inpatient,
outpatient, and prescription records that have been billed to insurance payers including commercial insurance, Medicare, Medicare, self-pay, and government plans. Codes include ICD-9, ICD-10, CPT, and NDC.

**Study Population**

The study population consisted of adult patients with severe AATD patients enrolled in the PearlDiver claims database and active from 2010 to 2021. As AATD can present differently across patients and has a range of phenotypes and resulting treatment patterns, we defined severe disease as having AATD and diagnosed emphysema following an AATD diagnosis. These patients are also more likely to be prescribed augmentation therapy to alleviate symptoms and research has shown emphysema tends to present in more severe cases of AATD. A study of individuals in the National Heart, Lung, Blood Institute Registry of Individuals with Severe AAT Deficiency found that the most underlying cause of death for severe AATD patients was emphysema (72% of the study population)

Patients who had a primary diagnosis claim for AATD (ICD-10-E8801) and then a diagnosis of emphysema (ICD-10-J430, JF431, J432, J438, J438, or P250) following their AATD diagnosis were included in the study population. Patients were selected as having been treated with augmentation therapy if they had claims with CPT procedure codes for infusions of alpha-proteinase inhibitor (CPT-J0256, CPT-J0257, or CPT-S9346) and/or NDC codes for any of the approved therapies Aralast, Glassia, Prolastin, Prolastin-C, and Zemaira (associated codes: NDC-00053720102, NDC-00944280201, NDC-00944280202, NDC-00944281201, NDC-00944281401, NDC-00944281501, NDC-00944282202, NDC-00944288401, NDC-13533060130, NDC-13533060135, NDC-13533070001, NDC-13533070002, NDC-13533070101, NDC-13533070310, NDC-13533070501, NDC-13533070511). As AATD-related
symptoms manifest later on in life, resulting in later diagnoses\textsuperscript{4}, only adult patients were included in the study. Lastly, patients were excluded from the study population if they were not consistently active in the claims database for the year 2010 through the year 2021.

**Defining augmentation therapy frequency**

In this analysis, severe AATD patients who have not received augmentation therapy were compared to severe AATD patients who have received augmentation therapy to determine if treatment has an impact on non-augmentation therapy healthcare costs. As treatment frequency can be highly variable in this patient population, among individuals receiving augmentation therapy, patients who received treatment on a weekly basis as augmentation therapy is intended to be prescribed, were compared to patients who received treatment less frequently, on a monthly basis.

Patients receiving augmentation therapy up to every week were identified as individuals within the database for which the maximum amount of time elapsed between care records was ten days over the span of one year. The defined ten-day period versus seven-day period was to account for shifts in infusion schedule due to weekends or changes in which day of the week a patient chooses to receive their next weekly infusion. Patients receiving augmentation therapy less frequently, at every one month, were identified as individuals in the database for which the time elapsed between records was exactly one month. Patients receiving augmentation therapy at any other frequency (weekly, and between weekly and 1 month) were removed from this patient population to ensure there was no overlap between the two treatment frequency groups.

**Statistical Analyses**

All statistical analyses were run within PearlDiver’s proprietary user interface, Bellwether, which performs all statistical tests through the R Statistical package.
Key patient demographics and clinical characteristics were compared across patient groups using bivariate statistics (t-tests for continuous variables and chi-squared tests for categorical variables). Groups compared were compared in pairs. AATD-emphysema patients who have never received augmentation therapy were compared to AATD-emphysema patients who have received augmentation therapy at any given time within the study period. Among the augmentation therapy patients, patients receiving infusions weekly were compared to patients receiving therapy monthly.

Patient demographics available in the dataset included: age, sex, and region; Clinical characteristics compared included: Charlson comorbidity index (CCI) score, Elixhauser comorbidity index (ECI) score, average length of inpatient stay, asthma, liver disease, bronchiectasis, tobacco dependence, and use of bronchodilators or inhaled steroids.

Both patient CCI and ECI scores are based on scoring criteria for comorbidities within the two years preceding the patient’s last record. The CCI score is calculated based on presence of the following comorbidities (1 point applied for each condition, unless otherwise noted): myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, COPD, connective tissue disease, peptic ulcer disease, diabetes mellitus (1 point for uncomplicated, 2 points if end-organ damage), moderate to severe chronic kidney disease, hemiplegia (2 points), leukemia (2 points), malignant lymphoma (2 points), solid tumor (2 points, 6 points if metastatic), liver disease (1 point mild, 3 points if moderate to severe), AIDS (6 points). The ECI score is calculated based on the presence of the following comorbidities: congestive heart failure, cardiac arrhythmias, valvular disease, pulmonary circulation disorders, peripheral vascular disorders, hypertension, paralysis, other neurological disorders, chronic pulmonary disease, diabetes, hypothyroidism, renal failure, liver disease,
peptic ulcer disease excluding bleeding, AIDS/HIV, lymphoma, solid tumor without metastasis, rheumatoid arthritis/collagen vascular diseases, coagulopathy, obesity, weight loss, fluid and electrolyte disorders, blood loss anemia, deficiency anemia, alcohol abuse, drug abuse, psychoses, and depression.

Patients using bronchodilators or inhaled steroids for AATD symptom management were identified as having any of the following codes: USC-28131, USC-28132, USC-28410, USC-28420, USC-28430, USC-28431, USC-28432. Tobacco use was defined as having any one of the ICD-10 codes on record: ICD-9-D-3051, ICD-9-D-V1582, ICD-10-D-F17220, ICD-10-D-F17221, ICD-10-D-F17223, ICD-10-D-F17228, ICD-10-D-F17229, ICD-10-D-F17290, ICD-10-D-F17291, ICD-10-D-F17293, ICD-10-D-F17298, ICD-10-D-F17299, ICD-10-D-Z720. The number of patients with liver disease and bronchiectasis in each group was also examined as they are common other clinical manifestations associated with AATD. Liver disease included any ICD-10 code defining general liver disease, as well as mild or severe liver disease, and bronchiectasis was identified with the code ICD-10-D-J479.

Healthcare costs are reported in the form of total reimbursement costs within the database for all health services, patient visits, and prescriptions. In order to calculate total annual reimbursement costs for each patient group, a report in PearlDiver was created showing the longitudinal tracking of all patients, comprehensive of all procedures, diagnoses, and prescription information (where available). The index date for each patient group was defined as the first instance of an emphysema diagnosis claim, which in this study population followed an existing AATD diagnosis. Analysis for all annual costs began on the index date and ended one year following the index date for each patient. Augmentation therapy related CPT and NDC codes
were filtered out from the longitudinal tracking report to obtain segmented costs for augmentation therapy related reimbursements and non-therapy related reimbursements.

The costs were compared in pairs (between augmentation therapy users and non-users; and patients receiving weekly versus monthly treatment) using non-parametric Wilcoxon rank sum tests. For the patients on augmentation therapy, linear regression modeling was used to assess the relationship between treatment frequency (weekly vs. monthly) and non-augmentation therapy related healthcare costs. Available covariates were added to the model including age range, sex, region, CCI and ECI scores, and tobacco dependence.

Average length of stay across groups in the study cohort was also compared using t-tests to determine if there was a significant difference in stays for inpatient visits based on augmentation therapy use and frequency.

RESULTS
Population Characteristics

Within the PearlDiver database, there were 4,996 adult AATD-emphysema patients active in the database from 2010 through 2021. Table 1 describes the demographic and key clinical characteristics of the study population that were available within the database. Out of these patients, 3,221 patients (64% of the study population) did not receive augmentation therapy at any point and 1,775 patients (36% of the study population) had received augmentation therapy (at any frequency) within the time frame. Out of the 1,775 patients who received augmentation therapy at any frequency, 266 patients received augmentation therapy weekly, and 391 patients received therapy at a minimum of every month. Patients who underwent augmentation therapy with any gap longer than one month were excluded for further study. Of the augmentation users,
only 13% were receiving weekly augmentation therapy infusions and 22% were receiving monthly infusions.

Overall, patient demographics were balanced across all patient groups within the study cohort. When compared to patients who have never been on augmentation therapy, therapy users were statistically different for characteristics including average CCI and ECI scores, asthma, tobacco use, bronchiectasis, and use of respiratory medicines such as bronchodilators and inhaled steroids. CCI and ECI scores were both higher for non-augmentation therapy users, indicating a potential higher comorbidity burden compared to augmentation therapy users (p<0.001). Augmentation therapy non-users also had a higher percentage of patients with diagnosed asthma (41% compared to 37%, p=0.01) and had higher rates of tobacco use (79% compared to 70%, p <0.001). Non-augmentation therapy users had a lower percentage of patients with bronchiectasis compared to augmentation therapy users (13% compared to 17%, p=0.002). Non-augmentation therapy users also had a lower percentage of patients using bronchodilators or inhaled steroids for symptom management (88% compared to 94%, p<0.001). Weekly augmentation therapy users and monthly augmentation therapy users did not significantly differ from each other across any of the demographic and clinical characteristics assessed.

**Average Annual Costs**

Non-augmentation therapy users had an average annual cost of $17,739, whereas the overall average annual cost for augmentation therapy users was $91,602 (p<0.001; Table 2). Augmentation therapy costs alone for the overall therapy group was an average of $67,848 per year, indicating that augmentation therapy is the primary cost driver for this patient group.
When augmentation therapy costs were removed from the group, augmentation therapy users overall had an average annual non-therapy related cost of $23,754, higher than the average annual cost of $17,739 for non-augmentation therapy users (p<0.001).

Augmentation therapy costs were removed ahead of comparing the weekly and monthly treatment groups to determine if there were differences between non-therapy related costs depending on treatment frequency. Patients receiving weekly infusions had an average annual non-therapy cost of $32,863 and patients receiving monthly infusions had a lower average annual non-therapy cost of $23,696 (p<0.001).

To further assess the relationship between treatment frequency and impact on non-therapy related healthcare costs, a linear regression analysis was performed adjusting for age range, sex, region, CCI score, ECI score, and tobacco use. Among patients receiving augmentation therapy, weekly vs. monthly was associated with higher non-therapy related costs ($33,940 vs. $22,588; p<0.001). Patients with record of tobacco use had $8,458 lower non-therapy related costs than patients who do not have a record of tobacco use. Augmentation therapy users have a lower percentage of patients with record of tobacco use (Table 1) and therefore it could be possible that patients on augmentation therapy smoke less due to their treatment regimen, though this requires further study to confirm an association.

**Average Length of Stay for Inpatient Visits**

Augmentation therapy users overall had a significantly longer average length of stay for inpatient visits in a year of 12.2 days compared to non-augmentation therapy users who had an average length of stay of 9.0 days (p=0.029). While monthly augmentation therapy users were
seen to have a numerically higher average length of stay at 10.0 days compared to 7.1 days for weekly augmentation therapy users, this difference was not significant.

**DISCUSSION**

The goal of this study was to gain a deeper understanding of what healthcare costs are for patients with severe AATD depending on whether they are on augmentation therapy or not, in addition to whether treatment frequency has any impact on non-therapy healthcare costs. The results of the study show that augmentation therapy users had higher annual non-therapy costs compared to non-augmentation therapy users ($23,754 vs. $17,739) and that weekly therapy users had higher annual non-therapy costs compared to monthly users ($32,863 vs. $23,696). Therapy users were also found to have longer average length of inpatient stay compared to non-users (12.2 days vs. 9.0). While the study aimed to retrospectively assess the differences in costs and healthcare use in augmentation therapy vs. non-augmentation therapy patients and the impact of treatment frequency on costs, a causal relationship between therapy use and therapy frequency and costs cannot be concluded due to the observational nature of the study and likely presence of selection bias.

The results of this study are generally in line with previous research on healthcare costs for AATD patients. For example, a 2018 study conducted by Sieluk et al compared the costs of medical care among augmentation therapy users and non-users for AATD patients in the US. The average annual augmentation therapy cost for users was $82,002 and average annual cost for non-augmentation therapy users was $14,185 (treatment frequency for augmentation therapy users was not specified). These costs are comparable to the average weekly patient group augmentation therapy cost of $79,154 and $17,739.45 annual cost for non-augmentation therapy users, though the Sieluk et al study had a significantly higher patient population of 9,117 AATD
patients, compared to this study which had a patient population of 4,996 AATD-emphysema patients. Lastly, the Sieluk et al study included patients from 1993 to 2015, while this study consists of a more current analysis of costs on patients from 2010-2021.

Strengths of this study are primarily related to the use of claims data. The data within PearlDiver is longitudinal and offers the opportunity to track healthcare services and incurred costs over the specified time period. This allowed for the selection of a defined period for which all patients in the study population were consistently active for, ensuring that the average annual costs were reflective of all the healthcare each patient received within the follow-up period. Furthermore, as claims data is primarily collected for the purpose of billing and reimbursement, there is increased confidence in the data for analyzing incurred costs. This aspect of claims data also helps avoid errors and inaccuracies that can occur as a result of self-report data.

The major limitations of this study are due to the retrospective observational study design and small patient population due to the rare nature of AATD and limited prevalence. While the study was designed to only include severe AATD patients defined as having an associated emphysema diagnosis, it is likely that frequency of treatment in patients using augmentation therapy was due to these patients having worse disease manifestations and more severe symptoms, ultimately leading to the selection of sicker patients with higher costs for inclusion in this analysis. Therefore, additional research is needed to better understand the impacts of treatment frequency on costs through prospective study designs or other methodology applied to adjust for suspected selection bias. Additionally, to better understand potential cost differences in this patient population, further research into the major drivers of non-adherence to treatment or reasons behind reduced augmentation treatment frequency will be beneficial for this severe patient population to help determine the most cost-effective treatment options.
Some limitations in this study can also be contributed to the use of claims data. These include lack of clinical information that could help provide additional insight into factors contributing to healthcare costs, the potential for incomplete or missing data, variations in how providers code different healthcare services, and lack of patient characteristics and demographic data. In this study specifically, data on race and ethnicity was not available and there was not sufficient clarity in the breakdown of types of health insurance the enrolled patients had. As a result, while the database does aim to reflect the overall US population, assessing the generalizability of this study is challenging without some of these key pieces of demographic information. Another important consideration in the claims data used in this study is that augmentation therapy can be coded with CPT codes reflecting an inpatient visit or as a home-based infusion or even just using the drug NDC code corresponding to the specific augmentation therapy utilized. While this study captured all relevant augmentation therapy codes, there is potential for an over or underestimation of the costs due to the way augmentation therapy was coded for in each claim.

Lastly, smoking is a major risk factor in the development of emphysema, especially in AATD patients, and promoting smoking cessation is a major aspect of AATD symptom management to avoid further lung deterioration. Patient smoking patterns and history are hard to capture in claims data as it is typically included in self-reported data compared to a diagnosis claim. While this database provides information on tobacco use which includes records of smoking allowing for the analysis of patterns across treatment groups, the results on smoking may not be as accurate compared to if the data had been collected via self-report for all the patients in the study.
While there have been several studies comparing healthcare costs between COPD patients and AATD-COPD patients, augmentation therapy users and non-users, few studies have focused on comparing costs in the specific severe AATD-emphysema population or studied the impact augmentation therapy infusion frequency can have on non-therapy related healthcare costs, and there is not yet enough clarity on how treatment frequency can impact overall health economic burden for these patients. For this reason, it is important to have additional research into how treatment patterns affect overall health as well as resulting economic burden since augmentation therapy is a significant cost driver for these patients and may dictate how often they choose to receive their augmentation infusions.

CONCLUSION

Non-augmentation therapy users had a total average annual cost of $17,739, while all augmentation users had an average non-therapy cost of $23,753. Weekly augmentation therapy users had higher augmentation therapy costs due to increased frequency but also still had significantly higher remaining non-therapy costs of $32,863, whereas monthly augmentation therapy users had non-therapy costs of $23,696. For average length of stay for inpatient visits, augmentation therapy users had a significantly higher average length of stay compared to non-users, though there was not a significant difference between the weekly and monthly augmentation therapy users. Further research on the impacts of treatment frequency on non-therapy costs and healthcare use is required to mitigate selection bias as a result of the retrospective observational study design and limitations involving the use of claims data.
### Table 1. Demographic and Clinical Characteristics of Study Cohort

<table>
<thead>
<tr>
<th></th>
<th>A</th>
<th>B (monthly)</th>
<th>B2 (weekly)</th>
<th>p-value†</th>
</tr>
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<tbody>
<tr>
<td><strong>N</strong></td>
<td><strong>3,221</strong></td>
<td><strong>1,775</strong></td>
<td><strong>391</strong></td>
<td><strong>266</strong></td>
</tr>
<tr>
<td>Age (years)</td>
<td>62.9 (11.2)</td>
<td>61.3 (9.5)</td>
<td>61.0 (9.2)</td>
<td>61.6 (9.1)</td>
</tr>
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<td>Sex</td>
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<td></td>
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<td></td>
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<tr>
<td>Male</td>
<td>1,327 (41)</td>
<td>751 (42)</td>
<td>158 (40)</td>
<td>120 (45)</td>
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<tr>
<td>Female</td>
<td>1,894 (59)</td>
<td>1,024 (58)</td>
<td>233 (60)</td>
<td>146 (55)</td>
</tr>
<tr>
<td>Region</td>
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</tr>
<tr>
<td>Midwest</td>
<td>980 (30)</td>
<td>516 (29)</td>
<td>112 (29)</td>
<td>92 (35)</td>
</tr>
<tr>
<td>Northeast</td>
<td>579 (18)</td>
<td>321 (18)</td>
<td>74 (19)</td>
<td>51 (19)</td>
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<tr>
<td>South</td>
<td>1,263 (39)</td>
<td>670 (38)</td>
<td>145 (45)</td>
<td>81 (30)</td>
</tr>
<tr>
<td>West</td>
<td>12 (3)</td>
<td>262 (15)</td>
<td>59 (15)</td>
<td>41 (15)</td>
</tr>
<tr>
<td>Unknown</td>
<td>387 (12)</td>
<td>6 (3)</td>
<td>1 (3)</td>
<td>1 (4)</td>
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<tr>
<td>CCI Score</td>
<td>3.4 (2.5)</td>
<td>1.8 (1.8)</td>
<td>1.4 (1.5)</td>
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<td>ECI Score</td>
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<td>7.4 (4.0)</td>
<td>7.6 (3.9)</td>
<td>7.1 (3.7)</td>
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<td>Asthma</td>
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<td>Present</td>
<td>1,326 (41)</td>
<td>664 (37)</td>
<td>131 (34)</td>
<td>99 (37)</td>
</tr>
<tr>
<td>Liver Disease</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Present</td>
<td>1,057 (33)</td>
<td>591 (33)</td>
<td>131 (34)</td>
<td>88 (33)</td>
</tr>
<tr>
<td>Tobacco Use</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>2,540 (79)</td>
<td>1,236 (70)</td>
<td>281 (72)</td>
<td>181 (68)</td>
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<tr>
<td>Bronchiectasis</td>
<td></td>
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<tr>
<td>Present</td>
<td>426 (13)</td>
<td>293 (17)</td>
<td>64 (16)</td>
<td>53 (20)</td>
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<tr>
<td>Other medications*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>2,823 (88)</td>
<td>1,666 (94)</td>
<td>374 (96)</td>
<td>250 (94)</td>
</tr>
</tbody>
</table>

† P-value for t-test or χ² test.
A = AATD-emphysema patients NOT on augmentation therapy
B = AATD-emphysema patients who have received augmentation therapy
B1 = AATD-emphysema patients who have received augmentation therapy monthly
B2 = AATD-emphysema patients who have received augmentation therapy weekly
* Other medications include bronchodilators and/or inhaled steroids
**Numbers may not add up due to rounding
Table 2. Average Annual Healthcare Costs Per Patient

<table>
<thead>
<tr>
<th></th>
<th>Total Costs</th>
<th>Augmentation Therapy Costs</th>
<th>Other Costs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-augmentation therapy users</td>
<td>$17,739</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All augmentation therapy users</td>
<td>$91,602</td>
<td>$67,848</td>
<td>$23,754</td>
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<tr>
<td>Weekly augmentation therapy users</td>
<td>$112,017</td>
<td>$79,154</td>
<td>$32,863</td>
</tr>
<tr>
<td>Monthly augmentation therapy users</td>
<td>$98,511</td>
<td>$74,815</td>
<td>$23,696</td>
</tr>
</tbody>
</table>

Table 3. Average Annual Healthcare Visit and Prescription Costs Per Patient

<table>
<thead>
<tr>
<th></th>
<th>Inpatient Visits</th>
<th>Outpatient Visits</th>
<th>Physician Visits</th>
<th>Prescription Costs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-augmentation therapy users</td>
<td>$1,120</td>
<td>$6,056</td>
<td>$4,458</td>
<td>$5,105</td>
</tr>
<tr>
<td>All augmentation therapy users</td>
<td>$2,269</td>
<td>$9,549</td>
<td>$5,923</td>
<td>$6,013</td>
</tr>
<tr>
<td>Weekly augmentation therapy users</td>
<td>$2,224</td>
<td>$16,230</td>
<td>$9,339</td>
<td>$5,071</td>
</tr>
<tr>
<td>Monthly augmentation therapy users</td>
<td>$1,952</td>
<td>$8,524</td>
<td>$6,204</td>
<td>$7,016</td>
</tr>
</tbody>
</table>

Table 4. Average Length of Inpatient Stay

<table>
<thead>
<tr>
<th></th>
<th>Average length of stay in days (SD)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-augmentation therapy users</td>
<td>9.0 (12.3)</td>
<td></td>
</tr>
<tr>
<td>All augmentation therapy users</td>
<td>12.2 (18.2)</td>
<td>0.029</td>
</tr>
<tr>
<td>Weekly augmentation therapy users</td>
<td>7.1 (7.9)</td>
<td></td>
</tr>
<tr>
<td>Monthly augmentation therapy users</td>
<td>10.0 (12.6)</td>
<td>0.277</td>
</tr>
</tbody>
</table>
REFERENCES


8. PearlDiver Mariner Patient Claims Database (PearlDiver Technologies, Colorado Springs, CO, USA).


10. de SFJ. Alpha-1 antitrypsin deficiency is not a rare disease but a disease that is rarely diagnosed. *Environ Health Perspect.* 2003;111(16):1851-1854. doi:10.1289/ehp.6511
