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Genotype is associated with smoking and other key health behaviors among individuals with alpha-1 antitrypsin deficiency-associated lung disease

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ABSTRACT

Objective: To examine the association of genotype with smoking and other key health behaviors among individuals with alpha-1 antitrypsin deficiency (AATD) associated lung disease.

Methods: Self-reported data were analyzed from 3506 individuals with AATD-associated lung disease. All data were collected upon enrollment in a disease management program designed for individuals who have been prescribed augmentation therapy. Multivariate logistic regression was utilized to examine the extent to which genotype was associated with smoking and other key health behaviors (i.e., getting a pneumonia vaccine, getting a flu vaccine, exercising, and maintaining a healthy weight). We hypothesized that MZs and SZs are more likely than ZZs to be current smokers, and that genotype is associated with additional health behaviors.

Results: MZs and SZs had higher odds of being a current smoker than ZZs (MZ versus ZZ OR = 2.73, $p < .001$; SZ versus ZZ OR = 4.34, $p < .001$). For every additional health behavior examined, MZs had higher odds of unhealthy behavior than ZZs (ORs ranged from 1.35 to 1.98, $p < .05$). SZs had higher odds of unhealthy behavior than ZZs with regard to lack of exercise (OR = 1.52, p = .003) and failure to maintain a healthy weight (underweight OR = 1.93, p = .028; overweight OR = 1.43, p = .015).

Conclusions: Among individuals who have been prescribed augmentation therapy for lung disease due to AATD, genotype is associated with smoking and additional health behaviors that are central to managing lung disease.

1. Introduction

Alpha-1 antitrypsin deficiency (AATD) is a genetic condition that increases the risk of developing lung disease [1]. The emphysema subtype of chronic obstructive pulmonary disease (COPD) is the most common health problem caused by AATD [2,3]. Various environmental exposures influence the risk of developing lung disease, but the primary factors that influence this risk are cigarette smoking and the severity of AATD [4–6].

The two most common deficient alleles are S and Z, with Z being more severely deficient [7]. The majority of identified patients with AATD-associated lung disease have the ZZ genotype [8]. The M allele is not deficient, and individuals with the MZ genotype are typically referred to as "carriers." Whether individuals with the MZ genotype are at increased risk of developing lung disease has been a controversy for decades [9]. Mounting evidence suggests that individuals with the MZ genotype are at an increased risk of developing lung disease, especially those who smoke [6,10–13]. However, the biological mechanisms that underlie the increased risk among individuals with the MZ genotype remain unknown, given that serum levels of alpha-1 antitrypsin are above the putative protective threshold in these individuals [14].

AATD-associated lung disease is currently incurable and typically has a gradually progressive course. The only specific drug therapy available for individuals with AATD-associated lung disease is augmentation therapy. Augmentation therapy involves infusions of plasma-derived alpha-1 antitrypsin, usually on a weekly basis, with the goal of slowing the rate of decline in lung function [15–21]. Guidelines for the management of AATD-associated lung disease provide specific recommendations regarding augmentation therapy, emphasize the importance of smoking cessation, and discuss additional behavioral recommendations such as vaccinations against pneumococcus and influenza, engagement in regular physical activity, and maintaining a healthy weight [18,22–24]. Disease management is an important component of treatment for AATD-associated lung disease [25,26]. A

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Abbreviation list

AATD	alpha-1 antitrypsin deficiency
BMI	body mass index
CCI	Charlson Comorbidity Index
CI	confidence interval
COPD	chronic obstructive pulmonary disease
OR	odds ratio

major focus of disease management is the promotion of behavioral recommendations for optimal management of AATD-associated lung disease (e.g., smoking cessation, engagement in regular physical activity).

No research to date has systematically examined, among a sample of individuals with AATD-associated lung disease, the extent to which individuals with the MZ genotype (hereinafter MZs) and individuals with the SZ genotype (hereinafter SZs) differ from individuals with the ZZ genotype (hereinafter ZZs) with regard to health behaviors that are critical in managing lung disease. The aim of the current study was to examine the association of genotype with smoking and other key health behaviors among individuals with AATD-associated lung disease. We hypothesized that MZs and SZs are more likely than ZZs to be current smokers. We also hypothesized that genotype is associated more broadly with health behaviors that are recommended for individuals with AATD-associated lung disease (i.e., getting recommended vaccines, exercising, and maintaining a healthy weight). Individuals who did not know their genotype also were compared to ZZs. We hypothesized that these individuals have worse health behaviors than ZZs. The assumption underlying this hypothesis is that not knowing one's own genotype may indicate a low level of engagement in managing one's health condition, which would be demonstrated via limited participation in recommended health behaviors among these individuals. Data were collected by AlphaNet, a not-for-profit organization that provides a telephone-based disease self-management program designed for individuals with AATD-associated lung disease who are prescribed augmentation therapy [25]. AlphaNet follows the majority of individuals in the United States who are prescribed augmentation therapy for lung disease due to AATD. As such, these data provide an opportunity to examine correlates of health behaviors in a large sample of geographically diverse patients.

2. Methods

2.1. Sample and procedures

Analyses were conducted under a protocol that was approved by the Western Institutional Review Board (WIRB). This report utilizes cross-sectional data collected at baseline from patients who enrolled in AlphaNet between 1/1/08 and 12/31/15. The vast majority of patients enrolled in AlphaNet's disease management program have been prescribed augmentation therapy for lung disease due to AATD. A small percentage of the patients in this program are prescribed augmentation therapy for other health conditions due to AATD, such as panniculitis. All data were collected via structured interviews that were administered via telephone.

Between 1/1/08 and 12/31/15, 5522 adults enrolled in the disease management program. To improve our ability to assess the extent to which genotype is associated with health behaviors, we limited our sample to individuals with the most frequently-reported genotypes in AlphaNet's dataset. As such, we included individuals with an MZ, SZ, or

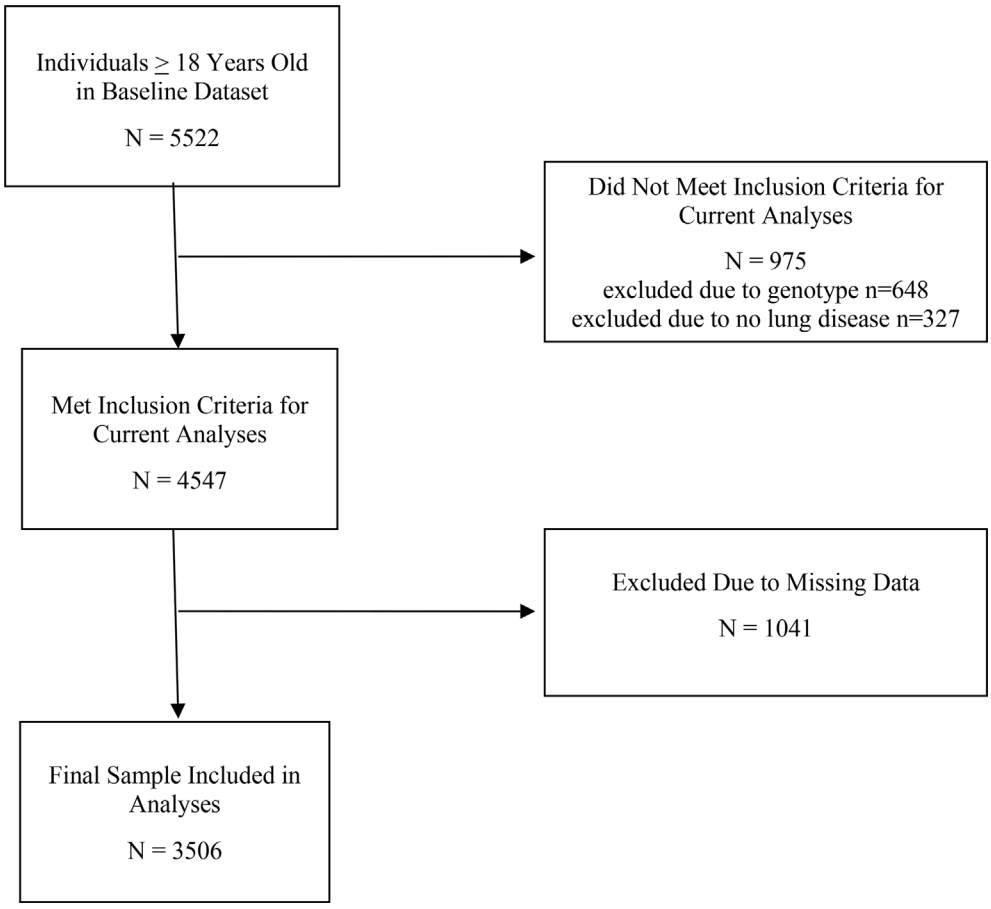

Fig. 1. Study flow diagram.