

# Alpha-1 Clinical Demographics and Outcomes: Data from the Alpha-1 Therapy, Evaluation and Research (AL1TER) Patient Registry Program

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## Rationale

Alpha-1 Anti-Trypsin Deficiency (AATD) is a genetic disorder in which reduced levels of alpha-1 anti-trypsin (AAT) lead to unchecked neutrophil elastase activity in the lungs, causing severe pulmonary damage and dysfunction. Patients can be infused with recombinant AAT in the home, which can reduce disease progression. The Alpha-1 Therapy, Evaluation, and Research (AL1TER) Patient Registry collects patient demographic and clinical profile data as well as quality-of-life outcomes on alpha-1 patients.

## Methods

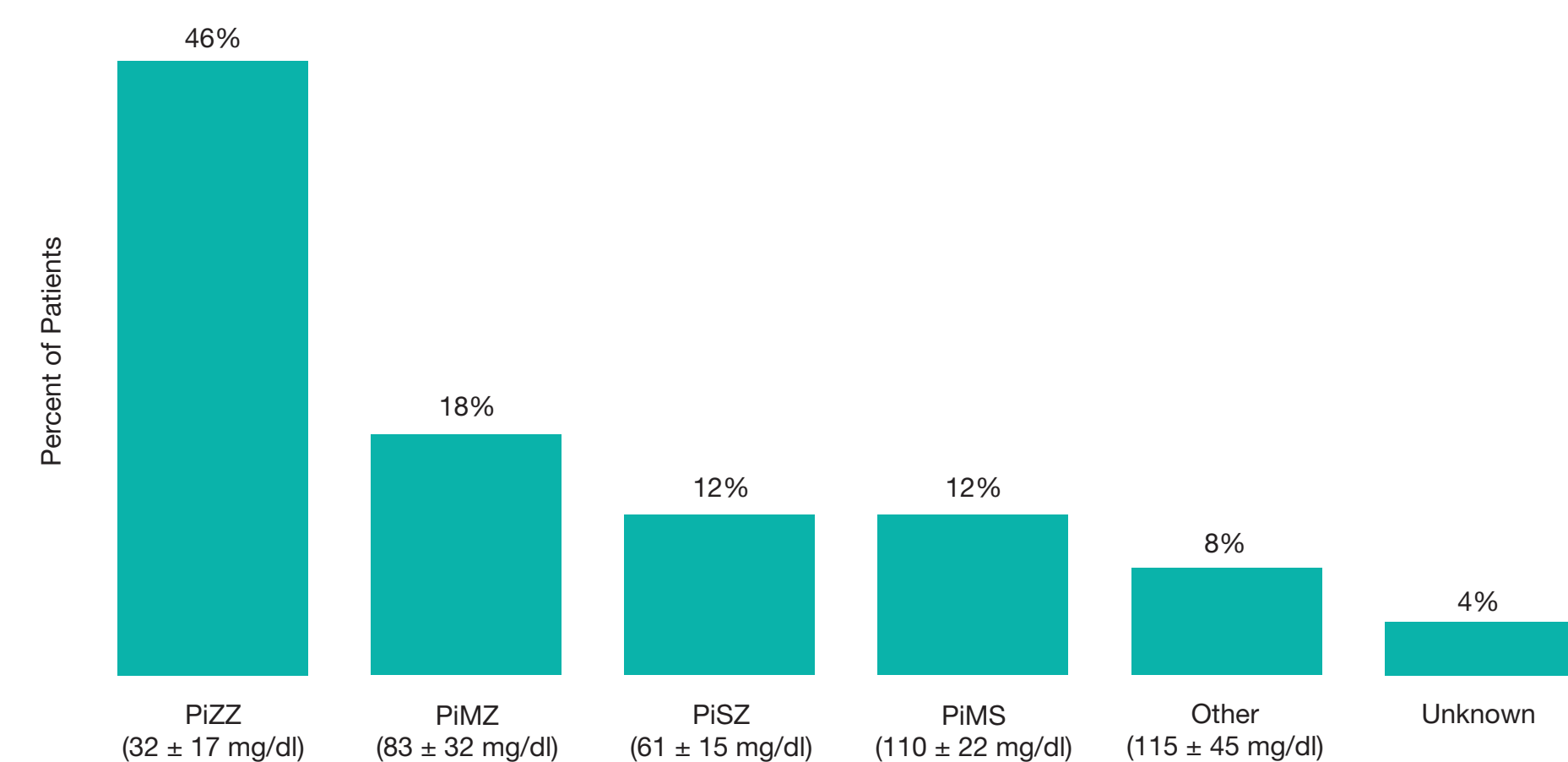
All active Coram patients from October 13, 2013, were eligible to participate. After being consented with a Western Institutional Review Board-approved form, patient referral, pharmacy, and nursing information was collected. Patients were asked to complete a baseline questionnaire about their symptoms, diagnosis, and demographics, as well as a life quality index questionnaire (LQIQ) and the St. George Respiratory Questionnaire. Patients were mailed follow-up questionnaires every six months after enrollment.

## Results

As of April 2016, 68 patients were enrolled. The gender distribution of participants was 44% male and 56% female.

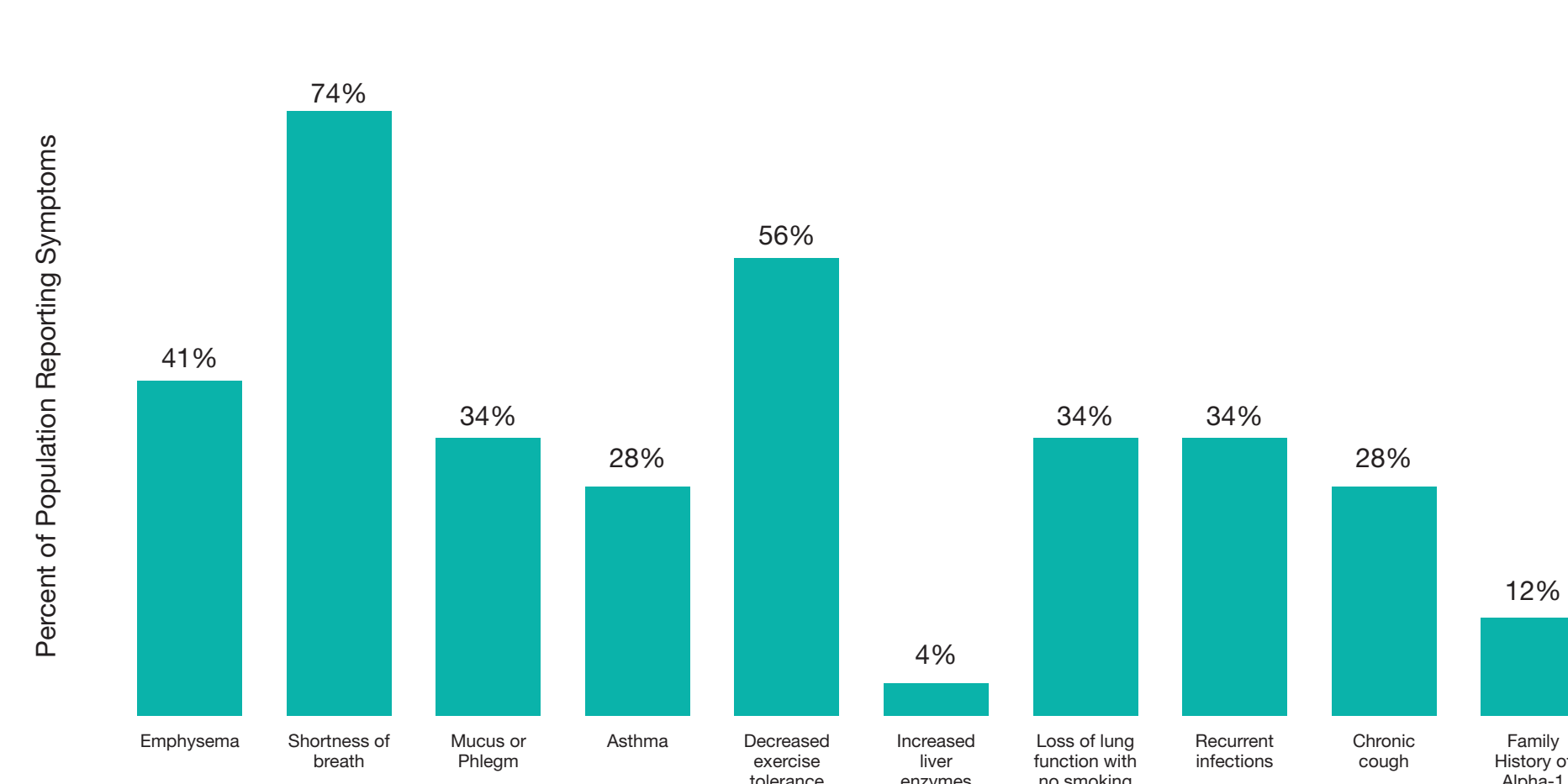
Forty-six percent (N=31) of patients were PiZZ; 18%, PiMZ; 15% (N=12); PiMS, 12% (N=8); PiSZ, 12% (N=8). The rest were some other variant (8%, N=6) or unknown (4%, N=3). The overall mean AAT level was 32 ± 17 mg/dl for PiZZ. PiSZ's averaged 61 ± 15 mg/dl. PiMZ averaged 83 ± 32 mg/dl. PiMS's averaged 110 ± 22 mg/dl. See Figure 1.

Figure 1. Alpha-1 Phenotype Distribution in AL1TER Registry



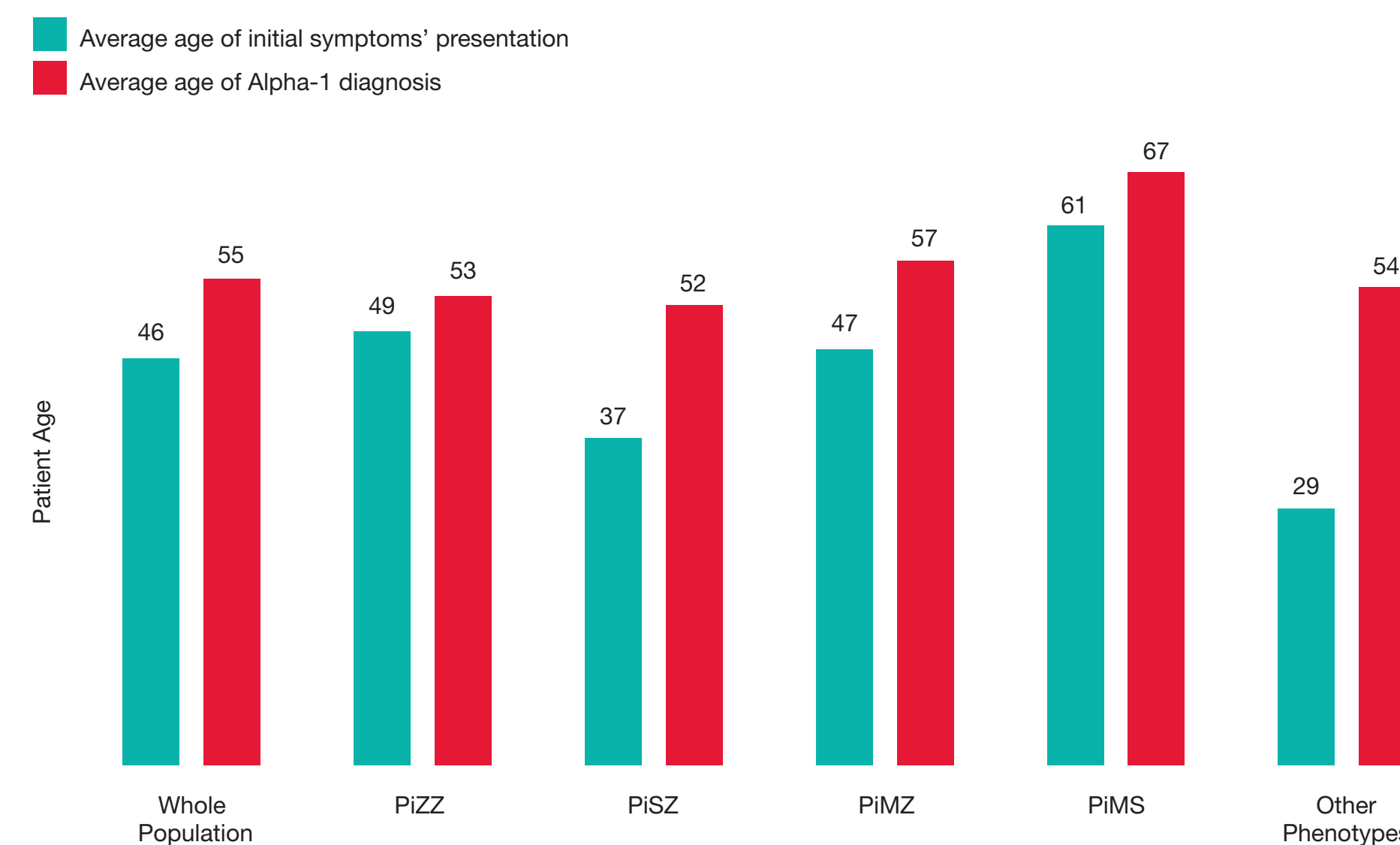
The most common symptoms across all patients leading to an AATD diagnosis were: shortness of breath (74%); decreased exercise tolerance (56%); and emphysema (41%). Interestingly, 34% of the population reported recurrent respiratory infections as a significant initial symptom leading to diagnosis. See Figure 2.

Figure 2. Patient-Reported Symptoms Leading to Diagnosis of Alpha-1



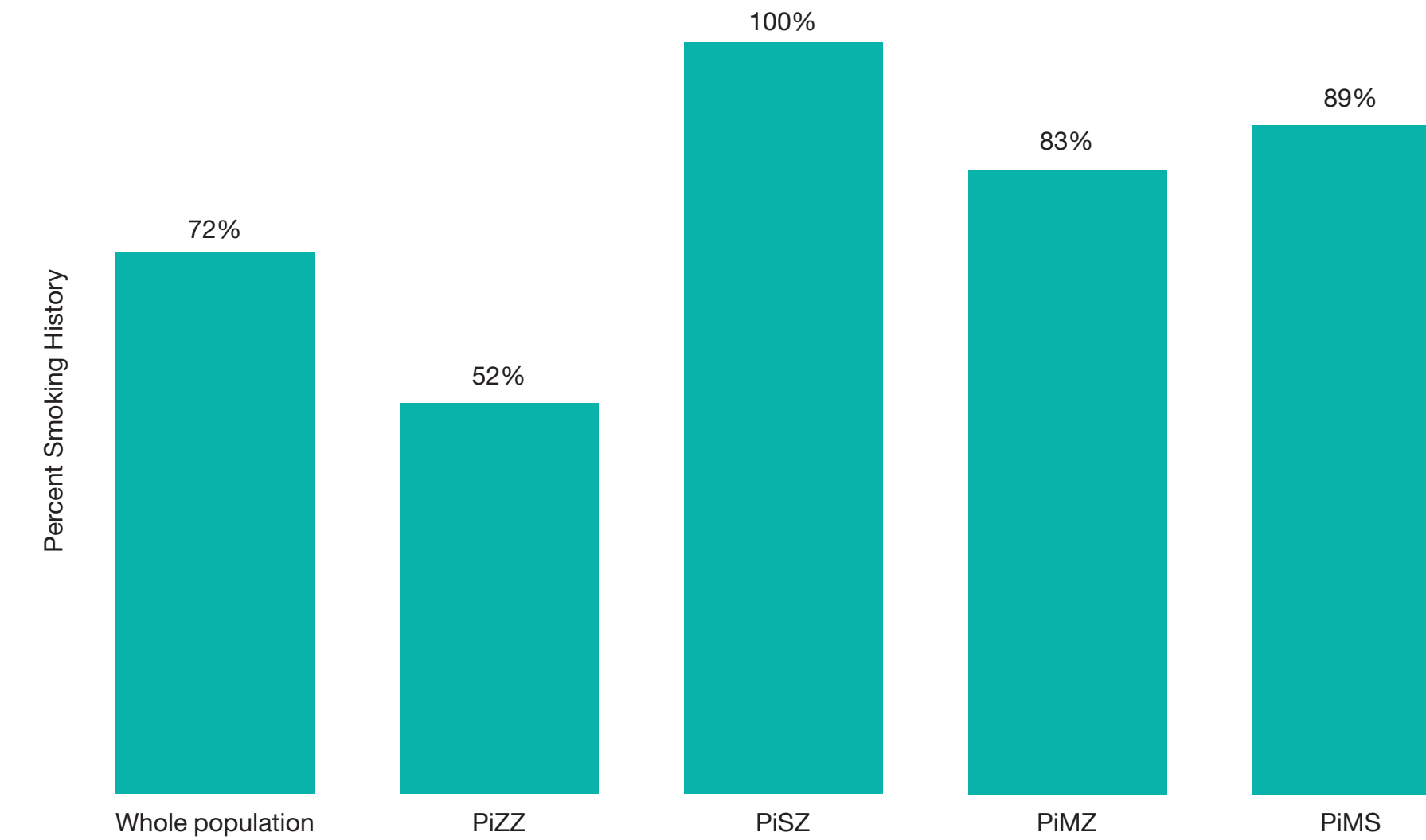
We analyzed patient reported data on the age at which their symptoms first presented and the age at which they were diagnosed with alpha-1. Within the overall population, the average age at symptom development was 46 years old (range was 5-72 years old). The average age for diagnosis with alpha-1 was 55 years old (range was 28-76 years old). This data also shows a fairly lengthy delay between initial symptom presentation and diagnosis, averaging 9 years. See Figure 3.

Figure 3. Average Age at Initial Symptom Presentation and of Alpha-1 Diagnosis



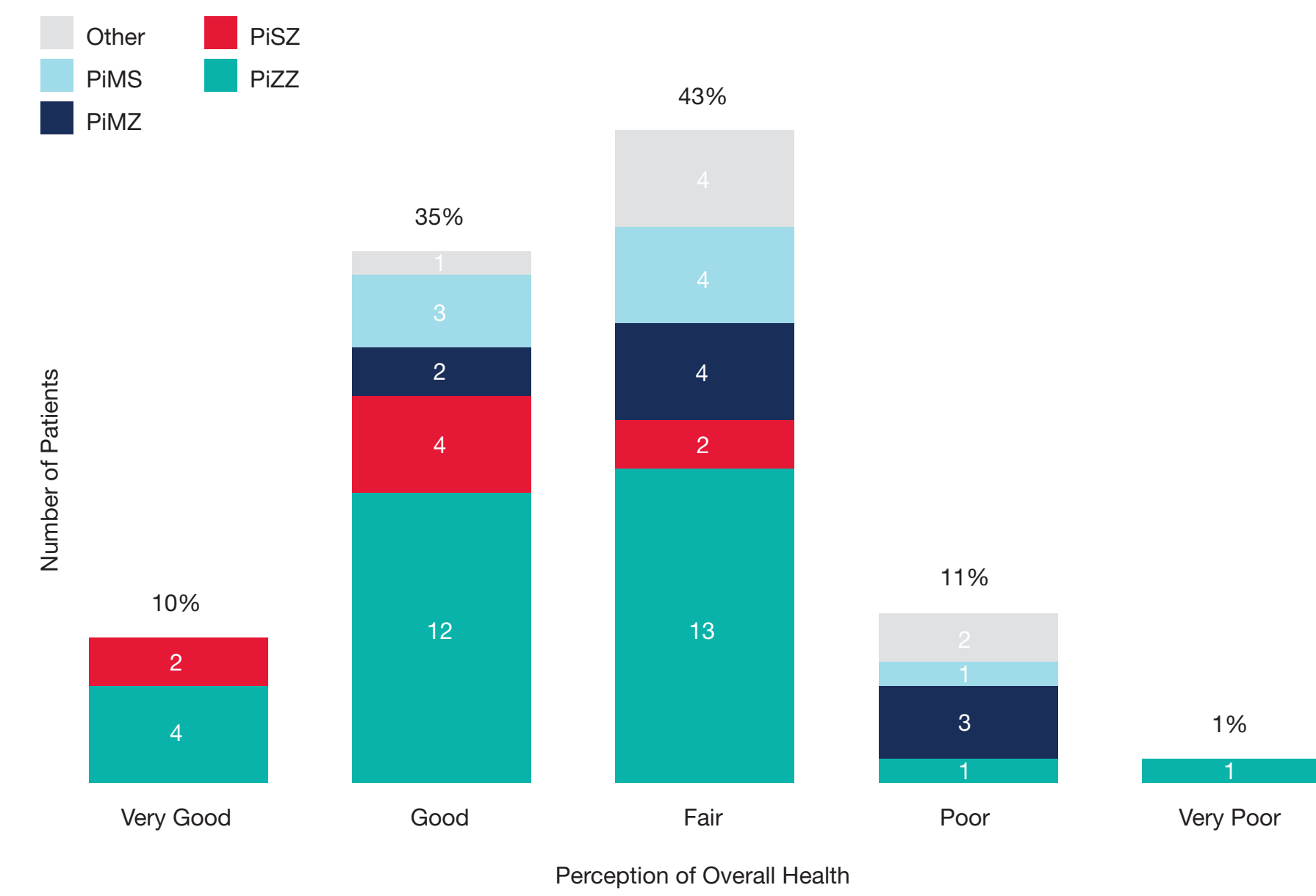
A majority (72%) of patients had a history of smoking, with most averaging 1-3 packs per day over the course of 24.5 years. PiZZ patients had the lowest incidence of smoking history, but 52% still reported being former smokers (Figure 4). Heterozygote patients had much greater incidence of being former smokers, indicating that smoking history was a significant contributing factor to their diagnosis and treatment for alpha-1. See Figure 4.

Figure 4. Frequency of Smoking History in Alpha-1 Patients



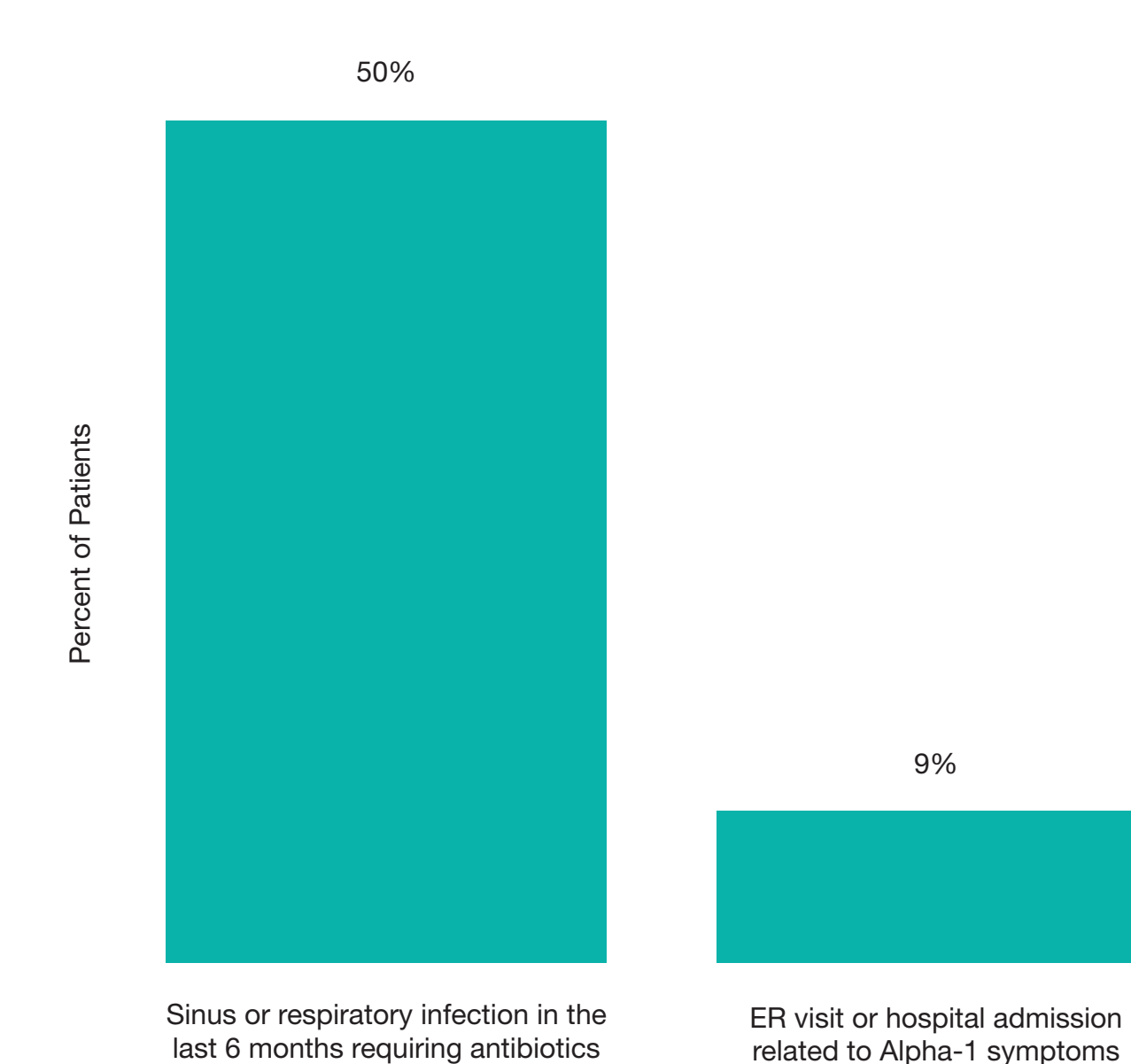
Using the St. George Respiratory question asking patients to rate their current health, at baseline, 45% of the enrolled patients stated that their overall health was "good" or "very good"; 43% "stated fair"; and 12% said "poor" or "very poor." See Figure 5.

Figure 5. Perception of Health by Phenotype Baseline Questionnaire



Initial patient follow-up questionnaires were mailed six months after enrollment in the registry. Patients were asked if they had a respiratory or sinus infection in the last six months that required antibiotics; 50% (6/12) replied yes. The questionnaires also asked if they had been to the ER or admitted to the hospital for any of their alpha-1 symptoms. Only 1 out of 11 (9%) patients responded yes. See Figure 6.

Figure 6. 6-Month Follow-Up Health Survey



## Conclusions

Alpha-1 can remain undiagnosed for long periods of time in symptomatic patients because of the heterogeneous presentation and variability in presentation, as well as patient history. Our analysis shows that in our treated population:

The majority of patients were PiZZ homozygotes with significant reduction in AAT level.

Heterozygotes with a history of smoking accounted for a significant percentage of treated patients.

Prior history of smoking was prevalent in this population, with 72% of the total population having a history of smoking. Patients averaged 1-3 packs per day and averaged almost 25 years of smoking history.

Shortness of breath was the most common symptom leading to diagnosis in the group, followed by decreased exercise tolerance. Recurrent chest infection was also an extremely common symptom in this population, and an issue that remained post-treatment.

Patients' perception of their health was generally good, with more than 75% stating their health was fair or better at the time of their enrollment in the study.

Follow-up quality-of-life surveys showed that a significant portion (50%) of patients reported a respiratory or sinus infection requiring antibiotics. There was a low incidence of patients going to the ER or being hospitalized due to alpha-1 associated symptoms.

Longer-term data on patients' perception of health while on treatment should provide a qualitative assessment of therapy effectiveness and its impact on patients' willingness to continue treatment.