

Abstract

Background: Severe asthma is a heterogeneous disease characterized by impairments across pulmonary, extrapulmonary, and behavioral domains. The treatable traits approach provides a personalized framework by identifying modifiable traits that may contribute to poor asthma control and impaired quality of life. Alpine altitude climate treatment (AACT), combines environmental exposure reduction with multidisciplinary pulmonary rehabilitation, and has been shown to improve outcomes in patients with severe asthma. Although most patients improve, the magnitude of response still varies considerably between patients. This study aimed to identify treatable traits across pulmonary, extrapulmonary, and behavioral domains and to evaluate their association with improvements in asthma control, asthma-related quality of life, and treatment response following AACT.

Methods: A retrospective cohort study was performed using routinely collected clinical data from adults with severe or uncontrolled asthma who completed AACT at the Dutch Asthma Center Davos between 2017 and 2025. Baseline demographic characteristics and 27 predefined treatable traits were assessed across pulmonary, extrapulmonary, and behavioral domains. Primary outcome was change in Asthma Control Questionnaire (ACQ-6) score. Secondary outcomes included change in Asthma Quality of Life Questionnaire (AQLQ) score and response status. Associations between baseline treatable traits and treatment outcomes/response status were evaluated using univariable and multivariable linear and logistic regression analyses.

Results: A total of 613 patients were included (74.4% female; mean age 46.4 ± 14.4 years). Patients demonstrated a substantial baseline disease burden, with a mean of 11.4 ± 3.6 treatable traits per patient. Following AACT, significant improvements were observed in asthma control (Δ ACQ-6 -1.2 ± 1.2 , $*p < 0.001$) and asthma-related quality of life (Δ AQLQ 1.4 ± 1.1 , $*p < 0.001$). Overall, 96.1% of patients met the predefined responder criteria, including 37.0% classified as super-responders. A lower total number of treatable traits was associated with greater improvements in both Δ ACQ-6 and Δ AQLQ in univariable analyses. In multivariable analyses, baseline SABA overuse was independently associated with greater improvement in ACQ-6, whereas allergic rhinitis was associated with less improvement. Traits in the behavioral domain were associated with greater improvement in AQLQ, while inadequate self-management and endocrine comorbidity were associated with smaller improvements in quality of life. Logistic regression demonstrated that allergic rhinitis was associated with lower odds of being a super-responder (OR 0.60, 95% CI 0.39–0.93), whereas incorrect inhalation technique (OR 2.96, 95% CI 1.43–6.11) and SABA overuse (OR 1.58, 95% CI 1.05–2.37) were independently associated with higher odds of super-response.

Conclusion: Patients referred for AACT exhibited a high burden of treatable traits across pulmonary, extrapulmonary, and behavioral domains. AACT resulted in clinically meaningful improvements in asthma control, quality of life, and other clinical outcomes. While overall trait burden was associated with treatment response, several behavioral and extrapulmonary traits appeared more informative than pulmonary characteristics in predicting outcome. These findings support the implementation of a multidimensional treatable traits approach and emphasize the importance of comprehensive assessment beyond airway inflammation alone to optimize personalized management in severe asthma