



Editorial

Discovering Treatable Traits in Asthma: Toward More Precise Treatment



Descubriendo los rasgos tratables en asma: hacia un tratamiento más preciso

At the beginning of the 20th century, the German physician Paul Ehrlich introduced the concept of the “magic bullet”, a revolutionary idea that had a profound impact on modern pharmacotherapy. This term referred to therapeutic compounds designed to specifically target infectious diseases, like a precisely aimed bullet. The concept marked a milestone in medicine, as it spurred the development of antibiotics that transformed the treatment of infectious diseases and laid the foundation for the future of pharmacotherapy.¹

In the second half of the 20th century, non-communicable diseases such as cardiovascular diseases, diabetes and chronic respiratory diseases, including asthma, became the leading causes of morbidity and mortality in many parts of the world. In response to this shift in the epidemiological profile, a “step-up therapy” approach was developed to treat these conditions.¹

Step-up therapy is a gradual approach that adapts treatment to disease severity. It is the model followed by current therapeutic guidelines in conditions such as asthma. However, due to the significant variability in both clinical presentation and therapeutic response, the need for a specific approach tailored to the individual characteristics of each patient was recognized. This led to the emergence of the concept of “treatable traits”, a key concept in personalized medicine for respiratory diseases.²

Treatable traits are therapeutic targets identified by phenotypes or endotypes using a validated biomarker. This approach facilitates personalized disease management while avoiding overtreatment and reducing unwanted side effects. Around 24 treatable traits have been identified in asthma patient cohorts.^{2,3}

For a trait to be considered treatable, it must meet 3 essential criteria: it must be clinically relevant, meaning it must have a significant impact on the patient's health; it must be identifiable and measurable using precise and accessible diagnostic methods; and, of course, it must be treatable, meaning that an effective therapeutic intervention must be available to address it. These treatable traits are divided into 3 main domains: pulmonary, extrapulmonary, and lifestyle.²

In the pulmonary domain, one of the most relevant traits is inflammation, which can be measured using exhaled nitric oxide fraction (FeNO) and eosinophilia in sputum or peripheral blood. These biomarkers are key to identifying patients who could benefit from biological treatments aimed at reducing inflammation.

Another important pulmonary trait is the presence of mucous plugs, which can be identified on computed tomography. The accumulation of mucus in the airways can contribute to airflow obstruction and the persistence of symptoms in asthma patients.⁴ In the extrapulmonary domain, the most prevalent treatable trait is chronic rhinosinusitis with nasal polyposis. In the lifestyle domain, one of the most obvious treatable traits is smoking. Smoking is not only one of the main causes of respiratory diseases, but it can also significantly exacerbate asthma. In fact, asthma patients who quit smoking experience show a significant improvement in disease control.⁴

Some of these traits, categorized as “super-traits”, have a crucial impact on the management of the others. Failure to treat super-traits, especially in cases of severe asthma, can lead to the progressive accumulation of further problems, creating a chaotic cascade that worsens the patient's condition. These include obesity, smoking, inflammation, and airflow obstruction, among others. Furthermore, “connected comorbidities” have been described. These are defined as conditions that commonly coexist with asthma, have a clinical impact on it, and share pathophysiological mechanisms. Proper management of these comorbidities not only improves asthma control but also optimizes outcomes related to the comorbidity itself. Additionally, treating super-traits can contribute to what are known as “marginal gains”, small incremental improvements in any process that, when combined, lead to significant overall improvement.⁴

The identification and management of treatable traits has proven effective in reducing exacerbations and hospitalizations, improving patients' quality of life scores, and reducing morbidity and mortality.^{5,6}

In studies, such as that conducted by Petsky et al., adjusting treatment based on eosinophilic inflammation (measured by induced sputum or FeNO) significantly reduced exacerbations and was shown to be superior to an approach based solely on symptoms.⁷

Similarly, the results of the NOVELTY study showed that management based on treatable traits, such as eosinophilic inflammation and chronic rhinosinusitis, improved severe asthma control, with fewer exacerbations, improved quality of life, and reduced hospitalizations compared to standard treatments.⁸

Given the positive results observed in the management of respiratory diseases such as asthma, this treatable trait approach is also beginning to be applied in other respiratory conditions, such as bronchiectasis, diffuse interstitial lung disease, and chronic cough. However, it faces challenges, such as the difficulty in accurately identifying treatable traits, the high costs of personalized treatments, and the need for a multidisciplinary approach to coordinate care and continuous patient follow-up, which may complicate its effective implementation in clinical practice.⁴

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Conflicts of interest

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Raquel García Hernández^{a,*}, María Victoria García-Gallardo Sanz^b,
Francisco Javier González Barcala^c

^a Servicio de Neumología, Hospital Universitario
San Pedro de Logroño, Spain

^b Servicio de Neumología, Hospital Universitario de Burgos, Spain

^c Servicio de Neumología, Complejo Hospitalario
de Santiago de Compostela, Spain

* Corresponding author.

E-mail address: raquelmanjarres@hotmail.com
(R. García Hernández).