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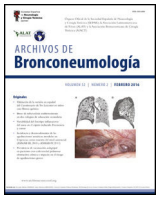

Editorial

Treatable Traits in Asthma and COPD

Introduction

Treatable Traits personalises the management of airway diseases.[1,2] This model of care packages assessment of measurable, modifiable, and clinically relevant phenotypes, and biological and molecular endotypes (traits), and applies targeted treatment directed towards the identified traits using an individualised care plan. The Treatable Traits approach recognises that chronic airway disease is a heterogeneous, multisystem illness.[2] The benefits include limiting exposure to unnecessary treatments, using objective measures to identify illness burdens, providing the most appropriate treatments for the most appropriate patients, engaging all parties in a person-centred approach, and improving health outcomes.

A Treatable Trait is defined as a "*therapeutic target identified by phenotypes or endotypes through a validated biomarker*".[1] Traits are categorised into pulmonary, extra-pulmonary, and behaviours/lifestyle risk factors domains[1,2] (Fig. 1). A 'Treatable Trait' must fulfil three criteria, that is be (1) clinically relevant, (2) identifiable and measurable and (3) treatable[2] (Fig. 1).

Prevalence

The prevalence of traits has been reported in people with asthma, severe asthma, Chronic Obstructive Pulmonary Disease (COPD) and in people with features of both. In a tertiary care setting, these studies consistently show that people with airway disease have, on average, 10 traits each,[3] that the number and type of traits identified were similar across diagnostic categories,[4] and that there are many untreated traits. This highlights the need for improved assessment and management of asthma and COPD using a treatable traits approach.

Impact

The impact of Treatable Traits on future risk has been assessed in COPD and in asthma populations. In COPD, Sarwar et al. explored the impact of traits in patients from the English Longitudinal Ageing Study. Among 406 people with COPD from this community sample, the traits that predicted future decline in lung function were smoking, being underweight, chronic bronchitis, sarcopenia, and breathlessness. Traits that predicted quality of life (QoL) decline included depression, poor family and social support, anaemia, chronic bronchitis, disability, cardiovascular disease, and arthritis.[4]

Traits that predict future attacks in asthma has also been explored. In a longitudinal cohort of 434 severe asthma patient and 102 with controlled asthma, 10 traits that predicted future attacks were identified. These included, in order of effect, being prone to exacerbations, depression, inhaler device polypharmacy, vocal cord dysfunction and obstructive sleep apnoea, systemic inflammation, eosinophilic inflammation, being underweight, anxiety, and upper airway disease. Each additional trait that was identified conferred a 13% increased risk of an attack.[5]

Traits that were associated with QoL impairment in COPD and severe asthma were frequent chest infections, dysfunctional breathing, inadequate inhaler technique, systemic inflammation, and depression. Other associated traits but to a lesser degree were airway pathogen colonisation, anxiety, mucus hypersecretion, exercise intolerance, and sarcopenia.[6]

These studies identify traits that predict future risk of QoL impairment, future attacks, and lung function decline. These studies are a good start in identifying a 'hit list' of traits that could be prioritised to minimise the impact on future outcomes.

Multidimensional Treatable Trait Approaches

There is an abundance of evidence to support the targeting of individual traits with specific interventions.[7] Implementing this model of care in a personalised way has been reported, in small studies in both COPD and asthma using multidimensional approaches to test the Treatable Traits model. In COPD, 36 adults were allocated to usual care ($n = 19$) or MDA and management according to identified traits ($n = 17$). The individualised treatment programme included tailored pharmacologic and non-pharmacological interventions implemented by a multidisciplinary team working in partnership with the patient. The intervention led to a major improvement in health-related QoL. The improvement in the St George's Respiratory Questionnaire was 14 (20.7–8.5) versus 3.5 (−3.8 to 10.8); $P = .0003$ for the intervention and control groups respectively. The intervention also led to significant improvements in airway and systemic inflammation.[8]

A randomised controlled trial ($N = 55$) in patients with severe asthma tested a similar individualised multicomponent intervention compared to severe asthma usual care. The key components included an MDA using trait identification markers to assess traits, individualised treatment targeted to each trait, and was supported by a case-manager and multidisciplinary team. The intervention led

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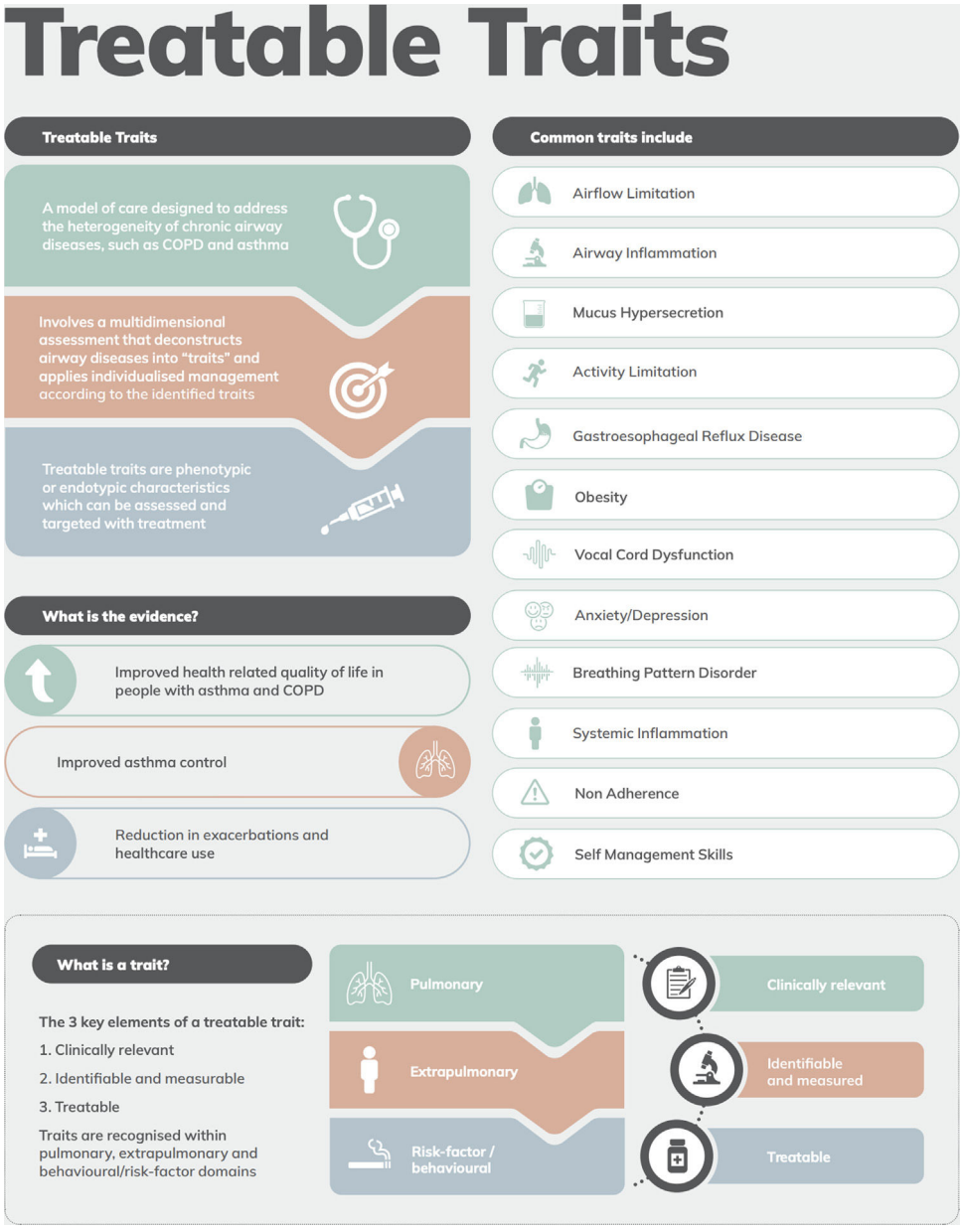

Fig. 1. A visual of treatable traits. Reproduced with permission from the centre of excellence in treatable traits, developed as part of centre of excellence in treatable traits.

to a significant between treatment group difference in the primary outcome of asthma QoL ($P < .001$).[9]

What next for Treatable Traits?

The Treatable Traits strategy, which was initially proposed in 2016[1] is now in part, included in COPD management recommendations by the Global Obstructive Lung Disease strategy[10] and by a Lancet Commission, *After Asthma; Redefining Airway Disease*.[11] Future developments include the need to establish this model of care in different resource settings. Therefore, identifying key traits that might be assessed and addressed in primary and secondary care is a priority. Another setting where treatable traits are likely to have an important impact is in acute care, during exacerbations. Key traits in this setting have been proposed.[12–14]

How we engage patients in this approach is also important. A large RCT in severe asthma that tested a composite score of Type 2 biomarkers (fractional exhaled nitric oxide [FENO], blood eosinophils, and serum periostin) compared to a standardised symptom-risk-based algorithm, with the goal of reducing corticosteroids was unable to reach its primary outcome. However, in the per protocol analysis the proportion of people that could reduce their corticosteroids was significantly greater in the intervention group. The primary reason patients were excluded from the per protocol analyses was for not following the intervention treatment advice.[15] This highlights an essential need to ensure patients and clinicians engage in shared-decision making as part of Treatable Trait interventions. Understanding the health literacy of patients in relation to Treatable Traits is an important area for future research.

Finally, much of the Treatable Traits research has been derived from cross-sectional evaluation, resulting in a lack of understanding of the stability of traits, and how stability, or lack of affects outcomes among people with COPD and asthma.

Treatable is a new paradigm for COPD and asthma management. It provides a model of care that allows individualised assessment and implementation of personalised care. Driving implementation

of this approach to practice is a priority for optimising care of people with airway disease.

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