

Implementing the Treatable Traits approach in Asthma

Content has been reproduced with permission from the Centre of Excellence in Treatable Traits, originally developed as part of the Centre of Excellence in Treatable Traits

(<https://treatabletraits.org.au>)

Case: A 75 year old male with severe asthma, past smoking and persistent symptoms. Where to next?

History: Henry is a 75 year old man with adult onset asthma causing frequent episodes of dyspnea, wheeze and limitation to his activities, especially in the past 5 years. He has a 35 pack-year history of smoking, and ceased smoking in his 50s. Henry's respiratory symptoms began in his late 60s. Now he reports daily symptoms of breathlessness, chest tightness and wheeze despite prescription of inhaled corticosteroid/long-acting beta₂ agonist (ICS/LABA) as fluticasone/salmeterol. He also reports a persistent cough productive of grey/white sputum, and comorbid gastroesophageal reflux disease (GORD), anxiety and chronic back pain. Body mass index is 31 kg/m². Lung function testing with spirometry shows his FEV1 is 1.85L (73% predicted), increasing to 2.33 (92% predicted) after inhaled salbutamol 200ug. Vital capacity is 3.75 (108% predicted) after bronchodilator. Gas transfer is 92% predicted.

Treatable Traits Assessment

A multidimensional assessment was performed to assess treatable traits across 3 domains: ABC: Airway, Behavioural/risk factor, and Comorbidity. Most traits can be assessed and managed in primary care. The asterisk (*) indicates traits where specialist management is indicated.

Airway traits

Trait	Trait Identification Marker	Targeted Treatment
Airflow obstruction	FEV1 75%	Increase LABA, add LAMA
Mucus hypersecretion	Daily sputum	Consider low dose macrolide*
Emphysema	KCO 96% predicted	Not present, a relevant negative finding given smoking history
Eosinophilic inflammation	Blood eosinophils 450 to 1000 Cells/ul	Increase ICS, add biologic* (eg anti IL5 monoclonal antibody)
Exacerbation Prone	History of frequent exacerbations	Written asthma action plan, increase ICS, bronchodilators, add biologic*

FEV1: Forced Expiratory Volume in 1 second, LABA: Long Acting Beta₂ Agonist, LAMA: long acting muscarinic antagonist, KCO: Carbon Monoxide Transfer Coefficient, ICS: inhaled corticosteroids, IL: interleukin

Behavioural traits

Trait	Trait Identification Marker	Targeted Treatment
Exercise intolerance	Reduced 6 minute walk test distance	Pulmonary rehabilitation*
Smoking	35packyear history	Has stopped smoking
No asthma action plan	Direct questioning identifies no asthma action plan	Written asthma action plan
Inhaler device technique	Observed poor technique	Education, use of valved holding device (spacer)
Adherence	Direct empathetic questioning	Adherence aiding strategies as part of education

Comorbidity

Trait	Trait Identification Marker	Targeted Treatment
Gastroesophageal reflux disease	Symptoms, questionnaires e.g. GERDQ,	Anti-reflux measures, antacids, proton pump inhibitor
Anxiety	Symptoms, questionnaires e.g. HADS	Psychological interventions e.g. Cognitive Behavioural Therapy
Nasal polyps	History, nasendoscopy*	Relevant negative
High body mass index (BMI)	31kg/m ²	Weight reduction measures

GERDQ: Gastroesophageal reflux questionnaire, HADS: Hospital Anxiety and Depression Scale

Treatable Traits Summary

75 year old male with persistent airflow obstruction and frequent exacerbations. Treatable traits assessment identifies multiple traits requiring further intervention across the Airway, Behavioural, and Comorbidity domains. Management options include increase ICS/LABA; add long acting muscarinic antagonist (LAMA); consider biologic therapy; provide written asthma action plan; pulmonary rehabilitation, dietary advice re weight loss, anxiety management; treat GORD. There are many possible treatment options now available that have been identified by using a treatable traits approach.

Discussion points

Diagnosis

Does Henry have asthma or COPD? Many clinicians would diagnose Henry as having COPD. This is supported by the presence of airflow obstruction, 35 pack year smoking history, symptoms, and the late onset of symptoms and disability. Treatment for COPD would focus on adding LAMA, and referring for pulmonary rehabilitation. It would do little to address his multiple exacerbations. This could deny him the benefits of treating eosinophilic airway inflammation with increased ICS and biologics.

Some clinicians would diagnose asthma based on the bronchodilator reversibility and blood eosinophil count. Management would focus on self-management skills (inhaler technique, action plan) and increasing ICS/LABA, or possibly changing to SMART (Single inhaler maintenance and reliever therapy).

Some may emphasise the need to make a single clear and definite diagnosis and spend a lot of time and effort weighing up the various characteristics to decide if the diagnosis they would apply was asthma or COPD.

These approaches address only some of the issues and are not comprehensive. This indicates the limitations of the asthma and COPD diagnoses. These diagnostic labels are now considered to be umbrella terms, and starting points in the patient management process. It is necessary to conduct additional assessments to provide patients with the best outcomes. Treatable traits is a framework to permit these additional assessments and treatments.

Setting: primary vs specialist care

Many of the treatable traits assessments and interventions can be conducted in primary care. Primary care structures can facilitate this, such as mental health plans to address anxiety/depression, and chronic health care plans to bring together the many facets of the patient's condition. These existing primary care structures can be used to implement aspects of treatable traits.

When to refer a patient with asthma or COPD is a question that is often asked. Treatable traits facilitates this by identifying when the next level of care is required for a particular trait. For example, with T2 (eosinophilic inflammation), if the ICS/LABA dose is increased in primary care, but Henry remains symptomatic, with exacerbations and a blood eosinophil count >300 Cells/ul., then this is a flag to refer Henry for specialist assessment for biologic therapy. In this case, assessing the T2 trait identifies an approach that can be used in primary care (ICS/LABA), and flags when next level care is required.

Where to start?

Henry has many active treatable traits. Should I start by treating all of them? Or can you prioritise some traits over others? In 2 clinical trials(1, 2), treating all traits via a case manager who coordinated the treatments and their implementation with the patient, led to a clinically significant improvement in health-related quality of life in over 50% of individuals. Traits can also be prioritised in several ways. These include: prevalent traits, traits associated with future exacerbation risk (3),

patient preference (4), setting [eg treatments accessible in a particular setting], traits with high treatment efficacy (colloquially called more 'bang for buck') (5).

Reference

1. McDonald VM, Higgins I, Wood LG, Gibson PG. Multidimensional assessment and tailored interventions for COPD: respiratory utopia or common sense? *Thorax*. 2013;68(7):691-4.
2. McDonald VM, Clark VL, Cordova-Rivera L, Wark PAB, Baines KJ, Gibson PG. Targeting treatable traits in severe asthma: a randomised controlled trial. *The European respiratory journal*. 2020;55(3).
3. McDonald VM, Hiles SA, Godbout K, Harvey ES, Marks GB, Hew M, et al. Treatable traits can be identified in a severe asthma registry and predict future exacerbations. *Respirology (Carlton, Vic)*. 2019;24(1):37-47.
4. McDonald VM, Higgins I, Simpson JL, Gibson PG. The importance of clinical management problems in older people with COPD and asthma; do patients and physicians agree? . *Prim Care Respir J* 2011;20(4):389-95.
5. Hiles SA, Gibson PG, Agusti A, McDonald VM. Treatable traits that predict health status and treatment response in airway disease. *JACI in Practice* 2020;Oct 8:S2213-2198(20)31096-5. doi: 10.1016/j.jaip.2020.09.046. Online ahead of print.