# Distinguishing asthma and chronic obstructive pulmonary disease: why, why not and how?

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## ABSTRACT

*What we need to know*

- What are the essential differences in the inflammatory process that lead to different pathological outcomes in asthma and chronic obstructive pulmonary disease (COPD)?
- What factors cause some patients with asthma to have clinical features indistinguishable from COPD, and should these patients be treated differently from those with early-onset, atopic asthma?
- What should be added to $FEV_1$ improvement after bronchodilator to enhance the ability of spirometry to distinguish between asthma and COPD?
- Why is disturbed gas exchange characteristic of stable COPD but rare in asthma?
- Why and when does COPD become a systemic disease with multiorgan dysfunction, while asthma generally does not?
- Does the response to bronchodilators in asthma and COPD predict prognosis and response to other interventions?
- Do people with asthma (airway obstruction, hyperresponsiveness and atopy) and COPD (fixed airflow limitation) have different natural histories, responses to treatment and prognoses?

*What we need to do*

- Evaluate new diagnostic tools (eg, indirect markers of inflammation) for asthma and COPD.
- Target older people in epidemiological studies to identify and describe the extent of asthma.
- Initiate community awareness programs to help older people with dyspnoea recognise they may have symptoms of asthma or COPD that should be assessed by a doctor.
- Define the clinical and physiological features of asthma and COPD in older people that indicate when and which treatments will achieve maximum benefit with least harm.
- Develop strategies for better, patient-focused care of people with severe airway disease, concentrating on device use, action plans, side effects, end-of-life decisions, exercise and independence in activities of daily living.
- Maintain research into new drugs and targets for preventing progressive loss of lung function in asthma and COPD.


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Asthma and chronic obstructive pulmonary disease (COPD) were once considered to be at opposite ends of the spectrum of airway disease. Asthma was thought to be highly responsive to treatment and essentially reversible, while COPD was characterised by fixed airway narrowing that was unresponsive to treatment. The currently accepted definitions still emphasise these features, even though there may be significant overlap between the two diseases.[1,2]

Asthma is often described as a fully reversible inflammatory process, whereas COPD is a poorly reversible disease characterised by progressive airway narrowing. Eosinophilic inflammation has been considered to be the predominant pathological feature of airway inflammation in asthma, whereas neutrophils, CD8 lymphocytes and chronic inflammatory cells are more typical of COPD.[3] However, eosinophilic infiltration can also be an important feature of COPD, particularly at the end stages of the disease or during exacerbations, and, conversely, a significant minority of patients with asthma are thought to have non-eosinophilic airway inflammation.

It is now recognised that these two diseases have many common features, and in some clinical situations they are impossible to distinguish. Some have even argued that they simply represent two different outcomes of a similar pathologic process, with different insults, genetic predisposition and environmental impacts accounting for the different manifestations. Clinically, asthma and COPD may be indistinguishable in older patients, in whom fixed and partially reversible airflow limitation may characterise asthma, or in whom greater reversibility in response to bronchodilator may be a feature of COPD. On the basis of such similarities in the inflammatory process, an argument can be made for a similar approach to treatment. However, both the response to treatment and the natural histories of the two diseases are quite different. While they share some common features, they can be distinguished in several important aspects.

## Why distinguish between asthma and COPD?

### The case *against* making a distinction

The Dutch hypothesis that asthma, chronic bronchitis and emphysema should be considered as different expressions of one disease entity has been unpopular for several decades, but is now looking increasingly appealing as a potential explanation for the spectrum of airway behaviour in asthma and COPD. The interaction between atopy, infection, environmental insults and genes is critically important in both diseases. Although one or more of these features may predominate, the summative effect critically determines the severity of the disease in both asthma

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and COPD. Both diseases result from interactions between genes and the environment. In both, smoking contributes significantly to the risk of decline in lung function and suboptimal response to anti-inflammatory medication.[4,5]

The argument in favour of considering the two diseases as one is a pragmatic one. We have not been successful in developing diagnostic algorithms to usefully distinguish asthma from COPD. While variable airflow obstruction is proposed as a defining characteristic of asthma, it doesn't always separate asthma from COPD, especially in older people with longstanding disease.[6,7] Inflammatory features may not be helpful, as the inflammatory response is heterogeneous in both diseases — an eosinophil or neutrophil infiltration can occur in both. The limitations of biopsy sampling can make it difficult to identify the predominant inflammatory pattern, and different cells may predominate at different stages of each disease.

The arguments in favour of considering the two diseases on a continuum also extend to treatment. We tend to use the same drugs, with variations in emphasis. The goals of treatment are similar — to reduce symptoms, maintain lung function and normal activity, prevent exacerbations, reduce mortality and minimise the adverse effects of treatment. Asthma is optimally treated with anti-inflammatory medications, and bronchodilators are used as needed. COPD is usually treated with bronchodilators, which provide small symptomatic benefits, and inhaled corticosteroids, which reduce exacerbations and improve quality of life.[1,6] Both diseases are treated by avoiding exposure to initiators and triggers. Acute exacerbations are frequently triggered by viral infections and are managed with maximal doses of corticosteroids and bronchodilators. Dealing with each of these simply by assessing the severity of airway obstruction and the response to treatment would be simple, would provide a clear guide to management, and would not necessarily result in poorer outcomes. This is thought to be particularly true for patients with longstanding asthma, which may be clinically indistinguishable from COPD and show much less impressive responses to asthma treatment.[4,7]

### The case *for* making a distinction

Despite their similarities, there are critical differences between asthma and COPD that influence management and prognosis. The natural histories of COPD and asthma differ significantly. Patients with COPD experience an inexorable decline in lung function, and, as their airway obstruction worsens, exacerbations become more frequent. In contrast, patients with asthma may have frequent exacerbations without decline in lung function. A defining feature of asthma is spontaneous variability of airway obstruction, and patients are often symptomatic when they have near-normal lung function. Most patients with COPD do not become symptomatic or aware of impairment until the forced expiratory volume in 1 second ($FEV_1$) has fallen to about 50% of the predicted value. This frequently delays their diagnosis and has critical consequences for their quality and quantity of life,[8,9] partly because motivation to stop smoking is increased by recognising its damaging effects. Patients with asthma do not normally experience lung function deterioration if they maintain regular anti-inflammatory medication, whereas patients with COPD continue to lose lung function despite medication. Once COPD is established, the only interventions that influence life expectancy are smoking cessation and oxygen therapy. By contrast, most patients with asthma have a normal life expectancy if they maintain regular preventive medication, and in older people, even those with severe asthma have a better outlook than those with COPD.[10] Dyspnoea in patients with COPD is predominantly triggered by exertion, but in asthma there are usually many additional triggers, including allergens, cold air and non-specific irritants.

The end stages of COPD are characterised by the development of complications, particularly pulmonary hypertension and right heart failure. Many patients with COPD develop hypercapnia and respiratory failure. These are unusual outcomes for patients with asthma, even when there is severe airway obstruction, although comorbidities in both diseases may play an important role in determining outcome.

There are crucial differences in short-term and long-term responses to treatment. Objections to making a distinction between asthma and COPD are often made on the basis of the overlap in bronchodilator responses seen in both diseases. However, this occurs mostly in people with longstanding, poorly treated asthma or those in whom both diseases are present ("mixed disease"). Airflow limitation in COPD is not *fully* reversible. Although reversibility in response to bronchodilator may be significant and $FEV_1$ may improve by more than 10%, the ratio between $FEV_1$ and vital capacity ($FEV_1$/VC) does not return to the normal range in COPD, as it usually does in newly diagnosed asthma. The histopathology of asthma and COPD is markedly different, resulting in different physiological characteristics. Emphysema is associated with dilated air spaces and a progressive fall in gas transfer, which rarely occur in asthma. The accelerated loss of lung function that characterises COPD, despite treatment, is not a common feature of asthma.

Choice of treatment also differs significantly, even though similar drugs are used in both diseases. There is strong evidence in asthma for an effect of low-dose inhaled steroids on exacerbations, quality of life, lung function, symptoms and mortality. In COPD, inhaled steroids do not affect lung function decline, and only high-dose inhaled steroids have been shown to affect exacerbation rate at the later stages of the disease. However, pulmonary rehabilitation has a significant impact on quality of life and exercise performance in patients with COPD.

Prognosis differs between the two diseases, particularly when $FEV_1$ is less than 1 L. The risk of death from COPD is closely related to the degree of impairment of ventilatory function as expressed by $FEV_1$. $FEV_1$ also predicts the likely need for long-term oxygen therapy, the increasing frequency of exacerbations and hospital admissions, and the likely development of pulmonary hypertension.

## Why the distinction is important

While accepting the diagnostic difficulties inherent in assessing older patients with airway disease, there is merit in attempting to make a firm diagnosis where possible. Optimal management of asthma and COPD must be based on distinctively different approaches that acknowledge the differences in presentation, disease progression and prognosis outlined here. Tailoring treatment to individual patients and assessing its benefits carefully will yield more specific management strategies, which will maximise quality of life, reduce adverse effects of medication, optimise physical function and better prepare patients for exacerbations and future events. Tailoring management strategies to

meet individual patients' needs should be the overriding consideration in achieving better outcomes for older patients with airway disease.

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