Clinicians recognize that 15% or more patients aged 40 years and older with features of chronic airflow obstruction present a diagnostic challenge and are diagnosed as having both asthma and COPD\(^1,2\). These patients may be considered as having the Asthma COPD Overlap Syndrome.

Although estimates differ, most reports recognize that patients with this diagnosis have a more severe clinical course with a higher risk of exacerbations, health resource utilization, relative corticosteroid refractoriness and possibly more rapid disease progression than either asthma or COPD. In recent years, several approaches to diagnosis and phenotyping such patients have been proposed, some from the perspective that COPD is the overarching condition\(^3\), while others favour a more inclusive starting point to categorization\(^2\). The recent GINA/GOLD 2014 ACOS document presents a simple 5-step approach for primary care physicians to recognize and initiate investigation and management of adult patients presenting chronic respiratory symptoms that, in some, might lead some to a diagnosis of ACOS. Initial steps are recognition of chronic airways disease (Step 1) and syndromic categorization into asthma or COPD (Step 2). The diagnosis of ACOS is suggested if 3 or more features of both asthma and COPD are present. Rather than attempting to define the ACOS, the document proposes a description of ACOS for clinical use as follows: “ACOS is characterized by persistent airflow limitation with several features usually associated with asthma and several features usually associated with COPD. ACOS is therefore identified by the features that it shares with both asthma and COPD\(^5\).” Step 3 is spirometry, and although this may serve as a guide, it has limited value in distinguishing between these entities since all may have fixed airflow obstruction and reversibility with bronchodilator. However, the document presents a table of the spirometric features that favour one diagnosis over the others. Step 4 is commencement of initial treatment based on the diagnosis reached in the prior steps (asthma, COPD or ACOS), recognizing that in many settings specialist referral for further investigation may take time or be unavailable. Step 5 is referral for specialist opinion and further diagnostic categorization through assessments of lung physiology, biomarkers and further trials of treatment.

At a research level, insights have been obtained from epidemiology (e.g. the BOLD data and national databases), health utilization databases and clinical cohort studies. Cluster analysis and phenotyping has resulted in several different classifications that reflect differences in the source of the data and methods employed. It has become clear that ACOS is an overarching clinical category comprising many phenotypes that differ from population to population, depending to some extent on local risk factors for chronic airways disease. Recent studies in both asthma and COPD patients have examined the genetic basis for these different conditions. For example, Hardin et al\(^5\) has reported a SNP in the genes CSMD1 and SOX5 in non-Hispanic whites with ACOS in the COPDGene cohort, and confirmed more frequent exacerbations, less emphysema and more airway wall thickness in these patients. These researchers have previously demonstrated several variants downstream from the SOX5 gene associated with COPD, and speculated that if present in patients with asthma these variants might predispose to the development of fixed airflow obstruction. In contrast, a recent GWAS study from the Netherlands was not able to confirm common genetic components in cohorts of patients with asthma or COPD\(^6\).

The importance of recognizing ACOS and for encouraging research in this field is that patients with this presentation are a source of confusion among physicians and their patients, and have been excluded from clini-
Defining and characterizing ACOS phenotypes will likely provide an incentive to perform clinical trials on such patients, and may lead to the development of new potential treatments for this form of airways diseases. The current approach, more through trial and error than evidence, is to use increasing doses of ICS (and oral corticosteroids) together with long-acting LABAs and LAMA. The role of anti-inflammatory drugs like selective PDE-4 and CRTH2 inhibitors, and biologicals that target eosinophilic and/or neutrophilic inflammation is unclear and requires research.

### Bibliography


