# Supplementary files: ACOS

## Methods

**ACOS**

ACOS was deemed present if there was a diagnosis of COPD in line with GOLD, in addition to either two major ACOS criteria; very positive bronchodilator reversibility (increase in FEV1 >15% and 400ml), eosinophilia in the sputum, or a personal history of asthma, or one major and two minor ACOS criteria; a personal history of atopy, or positive bronchodilator reversibility (increase in FEV1 >12% and >200ml on two or more occasions).(23) Lack of follow up reversibility testing meant that the BDR minor criteria were accepted if met on one occasion. Serum IgE was not performed routinely in the ADAPT protocol, such that we were unable to assess this on all patients; hence high total IgE was excluded from the ACOS criteria in this instance to avoid bias.

## Results

**ACOS**

ACOS occurred in 4/48 (8.33%) of patients whose eosinophil count was always >0.2, 2 (0.57%) of those with a count intermittently >0.2and 10 (4%) of those whose count was never >0.2; this difference was significant (p<0.001). ACOS patients did not exhibit any difference in FEV1 decline, exacerbations or mortality from those without ACOS (all p>0.5). Multivariate analyses were not possible due to the low number of ACOS patients.

## Discussion

There has been great recent interest in ACOS as a potential subgroup within COPD, perhaps due to the potential for different therapeutic choices – such as a lower threshold for ICS. A unified definition of ACOS does not currently exist, and of the definitions that are available, many use criteria that are not frequently tested in standard COPD practice. The Spanish consensus definition includes sputum eosinophils and serum IgE as major and minor diagnostic criteria respectively ([23](#_ENREF_22)) but data pertaining to these fields was limited as they are not performed as standard practice in our cohort’s protocol. Whilst some data on IgE was available, there was potential for this to be biased, as it was an optional test which could have been done due to a clinical suspicion of asthma or allergy. In addition serial reversibility testing, again a key criterion in the Spanish definition ([23](#_ENREF_22)), is not routinely done. Consequently, we adapted the definition to include post bronchodilator increase in FEV1 >12% and >200ml on a single occasion, rather than two. Even with these caveats, which might have been expected to increase the apparent prevalence of ACOS, the frequency of ACOS was low and might represent under-diagnosis. Although multimodal ACOS criteria have been proposed in order to gain maximum diagnostic specificity, our data suggests that when considering cross-sectional features outside those that define ACOS, and particularly when considering FEV1 decline, several blood eosinophil counts would be adequate to determine ICS use, thus avoiding the need for sputum induction and subsequent sputum eosinophil count in the classical ACOS definition.