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# A high-risk airway mycobiome is associated with frequent exacerbation and mortality in COPD

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The airway mycobiome in COPD is important, and associates with exacerbations, survival and systemic immune responses <https://bit.ly/32WA5kI>

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## ABSTRACT

**Introduction:** The chronic obstructive pulmonary disease (COPD) bacteriome associates with disease severity, exacerbations and mortality. While COPD patients are susceptible to fungal sensitisation, the role of the fungal mycobiome remains uncertain.

**Methods:** We report the largest multicentre evaluation of the COPD airway mycobiome to date, including participants from Asia (Singapore and Malaysia) and the UK (Scotland) when stable (n=337) and during exacerbations (n=66) as well as nondiseased (healthy) controls (n=47). Longitudinal mycobiome analysis was performed during and following COPD exacerbations (n=34), and examined in terms of exacerbation frequency, 2-year mortality and occurrence of serum specific IgE (sIgE) against selected fungi.

**Results:** A distinct mycobiome profile is observed in COPD compared with controls as evidenced by increased  $\alpha$ -diversity (Shannon index;  $p<0.001$ ). Significant airway mycobiome differences, including greater interfungal interaction (by co-occurrence), characterise very frequent COPD exacerbators (three or more exacerbations per year) (permutational multivariate ANOVA; adjusted  $p<0.001$ ). Longitudinal analyses during exacerbations and following treatment with antibiotics and corticosteroids did not reveal any significant change in airway mycobiome profile. Unsupervised clustering resulted in two clinically distinct COPD groups: one with increased symptoms (COPD Assessment Test score) and *Saccharomyces* dominance, and another with very frequent exacerbations and higher mortality characterised by *Aspergillus*, *Curvularia* and *Penicillium* with a concomitant increase in serum sIgE levels against the same fungi. During acute exacerbations of COPD, lower fungal diversity associates with higher 2-year mortality.

**Conclusion:** The airway mycobiome in COPD is characterised by specific fungal genera associated with exacerbations and increased mortality.