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**Title:** Comorbidities and burden of COPD: A population based case-control study

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**Body:** Introduction COPD is associated with a burden of disease and a high mortality worldwide. Recently, the importance of COPD-comorbidities has been recognized. Studies postulated an association with inflammatory conditions sharing pathogenic pathways and worsening overall prognosis. Aims Investigate the prevalence and clustering of comorbidities of COPD, and estimate their impact on clinical outcomes. Methods In this population-based case-control study, a Swiss nation-wide database enclosing every hospital entry (years 2002-2010: n = 12'888'075) was analyzed using the R statistical software. Statistics included non-parametric tests, linear models, and exploratory multivariate approaches for the identification of clusters of COPD comorbidities. Results In 3% of all hospitalizations an active diagnosis of COPD was recorded. In 21% of these cases, COPD was the main reason for hospitalization. Patients with a diagnosis of COPD had more co-morbidities (7 [IQR 4-9] vs. 3 [1-6]; p < 0.001), were more frequently re-hospitalized (annual hospitalization rate 0.33 [IQR 0.20-0.67] vs. 0.25 [IQR 0.14 - 0.40]/year; p < 0.001), had a longer hospital stay (8 [IQR 4-15] vs. 5 [2-11] days; p < 0.001), and had higher in-hospital mortality (5.8% [95% CI 5.7%-5.8%] vs. 3.4% [95% CI 3.3%-3.4%]; p < 0.001) compared to matched controls.

**Conclusions** A set of comorbidities was associated with worse outcome. We could identify COPD-related clusters of comorbidities.