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**Title:** The effect of COPD and FEV1 decline on health-related quality of life: A longitudinal, population-based study

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**Body:** It is widely recognized that health-related quality of life (HRQL) is impaired in COPD patients but there is a lack of research on the impact of COPD on HRQL over time. We examined the effects of COPD and FEV1%pred change on HRQL in a longitudinal dataset. In the population-based KORA F4 study (2008) and its 3 years follow-up, 1049 participants aged 41-61 years at baseline performed spirometry and reported information on HRQL (SF-12) and comorbidities. COPD definition and GOLD grades were based on prebronchodilator values. Using adjusted linear mixed models, we compared the physical and mental component summary score (PCS-12 / MCS-12) between COPD groups over time. The effect of FEV1%pred change on HRQL was quantified via multilevel growth models. At baseline, 94 subjects (9%) were classified as having COPD, 66 of these at GOLD grade 1. In the follow-up, 133 participants had COPD, 98 at grade 1. Adjusted mean PCS-12 at baseline was 49.0 for subjects without COPD, 47.6 for GOLD 1 and 48.0 for GOLD 2 or higher (GOLD 2+). PCS-12 was nearly constant over time for subjects without COPD or with COPD GOLD 1 (-0.7%, -0.5%), but decreased by 8.4% for GOLD 2+ within 3 years. The negative effect of COPD on HRQL persisted when comorbidities were considered. No significant effects were found for MCS-12. Multilevel models showed a significant cross-sectional association of FEV1%pred levels with PCS-12 scores ( $\beta=0.072$ , CI: 0.04-0.10), but no significant longitudinal effects. Our findings underline the need to prevent COPD disease progression as this is associated with substantial loss in HRQL. Longer

follow-up studies are needed to investigate the direct effect of FEV1 decline on HRQL.