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**Title:** Mortality risks of COPD for nonsmokers and smokers from a prospective cohort study of 390,269 subjects in Taiwan – Assessing involvement beyond the lungs

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**Body:** Background COPD is known to increase mortality in respiratory diseases, but is less known for its extra-pulmonary and lung cancer effect, particularly among nonsmokers Objectives To assess the risks of COPD subjects among smokers and nonsmokers and to quantify its mortality effect beyond the lungs. Method The cohort consisted of 390,269 adults, between 1994 and 2008, went through a fee-for-service, standard panel of health screening program. COPD was defined by Gold criteria. Mortality and cancer incidence were identified in an average of 8.5 years of follow-up. Cox proportionate model was used to calculate the hazard ratios (HR) Results More men (4.6%) than women (3.8%) and more smokers (5.3%) than nonsmokers (3.7%) had COPD, with a mean age of 50. The excess all-cause mortality for smokers (HR: 2.51) was three times larger than nonsmokers (HR: 1.53), when compared to those without COPD. Not only smokers (4.5-fold) but also nonsmokers (1.4-fold) had lung cancer mortality significantly increased, implying the independent effect from COPD. Other than lung cancer and respiratory diseases, COPD had increased risks for CVD (HR: 1.76), including ischemic heart disease (HR: 1.63) and stroke (HR: 1.80), and kidney diseases (HR: 2.32). The extra-pulmonary causes constituted 77% for non-smokers and 58% for smokers. Conclusion Three quarters of the excess deaths among nonsmoking COPD subjects died from causes beyond the lungs. They had increases in stroke, heart, renal and infectious diseases, in addition to lung cancer. These extra-pulmonary risks, under-appreciated by clinicians and unaware of by the patients, are major challenges to overcome.