

Statin Use in Pneumonia

To the Editor:

In the recent systematic review by Chopra et al,¹ they conclude that although prior statin use appears to lower mortality following pneumonia, the effect is substantially diminished following subgroup stratification and adjustment for confounding covariates. We note that an important exception to this conclusion is observed in smokers (current and former), where mortality reduction from statin use was

37% (and unaffected by adjustment).¹ We describe below why this observation is important.

The best predictors of developing pneumonia are age, smoking history, and comorbid disease, particularly chronic obstructive pulmonary disease (COPD) and coronary artery disease.² The most prevalent of these comorbid diseases is COPD, which affects as many as 49% of adults (>45 years old) hospitalized with community-acquired pneumonia.² In this study, 55% of smokers with community-acquired pneumonia had COPD based on baseline spirometry ($\approx 70\%$ of all COPD cases were ever smokers; personal communication; see **Figure**).² We and others have shown that, among smokers, COPD confers a 3- to 5-fold greater risk of death from both cardiac and respiratory complications of smoking, attributed in large part to the pulmonary-systemic inflammation underlying COPD.³ It is

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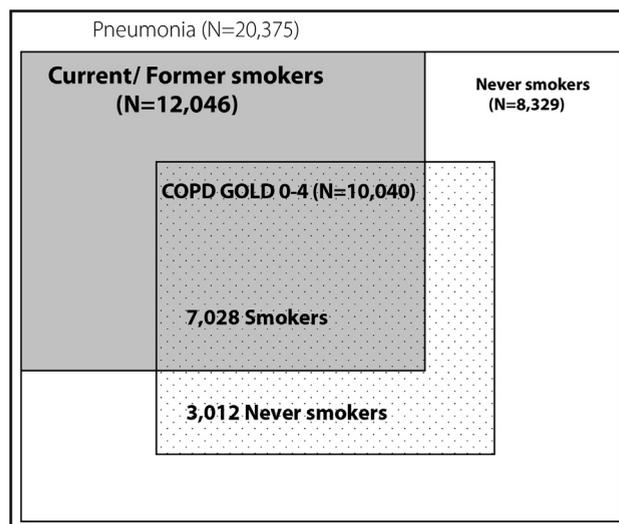


Figure Relationship between smoking status (gray box) and spirometry-defined chronic obstructive pulmonary disease (COPD; dotted box) among community-acquired pneumonia cases diagnosed in 2 US population-based cohorts followed prospectively.² According to the findings of Chopra et al,¹ statin use was associated with a mortality reduction of nearly 40% from pneumonia (after adjustment) in the subgroup including only current and former smokers (see **Figure** above). Based on data from 2 large population-based cohorts followed prospectively for 3 years identifying 20,375 cases of community-acquired pneumonia, 12,046 were current or former smokers (59%, gray box) and 10,040 had COPD (49%, dotted box) based on baseline spirometry (GOLD 0-4).² Following a personal communication (Dr David Mannino), $\approx 70\%$ of all COPD cases were smokers and 55% of all ever smokers with pneumonia had COPD.

notable that systemic inflammation, characterized by elevations of serum C-reactive protein and interleukin-6, predicts greater mortality in both pneumonia⁴ and COPD.⁵ Clinical studies show that statins substantially lower systemic inflammation, achieving reductions in C-reactive protein and interleukin-6 of over 50%.⁶ Given the close relationship between smoking, COPD, systemic inflammation, and pneumonia, we suggest that statin use might be especially beneficial in those with COPD (where 70%-80% have smoked).⁶ Indeed, observational studies of statin use in COPD have consistently reported reductions in mortality of 30%-50% following pneumonia or infective exacerbations.⁶

Based on these observations, we propose that statin-mediated attenuation of systemic inflammation might explain the findings of Chopra et al¹ (mortality reduction from pneumonia in ever smokers) and suggest that a randomized, controlled trial target COPD. Stratification by COPD status was not examined in their study, as spirometry is not routinely performed in pneumonia, or in smokers generally (explaining why 50%-80% of COPD goes undiagnosed). We conclude that subgroups of the population in which systemic inflammation is common (eg, COPD) are likely to benefit most from statin use.

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