LETTER

Authors' response

We appreciate the interest shown in our study by Scarlata and colleagues.[1] We agree with them that, in line with several previous reports,[2 3] the prevalence of the restrictive spirometric pattern was strikingly similar in the TESAOD[4] and SARA[5] studies, despite the substantial difference in age distribution between the two populations (the TESAOD report included subjects ≥21 years and the SARA study subjects ≥65 years of age).

However, a direct comparison of cause-specific mortality between the two studies should be interpreted with caution because of the different assessment of the restrictive spirometric pattern, which was evaluated at a single point in time in the SARA study and prospectively in the TESAOD study. Not all subjects with the restrictive spirometric pattern at baseline will have a consistent restrictive spirometric pattern (the one that was used for comparison in the letter by Scarlata *et al*) over time. Actually, in TESAOD only one out of three such subjects did. The remaining two-thirds either had an inconsistent restrictive longitudinal pattern or developed airflow limitation at some point during the follow-up. Profiles of cause-specific mortality risk differed notably across these three longitudinal groups. For example, hazard ratios for mortality by cardiac disease were 2.0, 2.7 and 1.6, respectively.

We believe that the most novel contribution of our study does not lie in confirming the mortality risk associated with the cross-sectional restrictive spirometric pattern, but rather in assessing spirometric patterns prospectively, for two main reasons. First, our data indicate that up to 38% of subjects with a restrictive spirometric pattern at enrolment developed airflow limitation during the study follow-up. These subjects were more likely to be smokers, to have a physician-confirmed diagnosis of asthma at enrolment, and—unlike those with recurrent or inconsistent restrictive patterns—to die of COPD during follow-up. These results suggest that an underlying airway obstruction may be present in a significant proportion of cases with spirometric restriction assessed at a single time point, and this may explain the finding (apparently conflicting with ours) of an increased pulmonary mortality risk associated with spirometric restriction in the SARA study. Second, the prospective analyses of our study demonstrate that, among subjects who do not develop an obstructive pattern over time, both the recurrent and the inconsistent spirometric restriction increase all-cause mortality risk by a substantial magnitude.

Although what causes increased mortality in these groups remains to be determined, our findings do suggest that this pulmonary condition predisposes to (or at least is linked to) other extrapulmonary conditions such as cardiovascular disease and diabetes. Thus, these comorbidities may be in the causal pathway from spirometric restriction to mortality and we therefore elected not to include them among covariates in our Cox proportional hazards models. We definitely agree with Scarlata and colleagues that further research is required to understand the factors that are related aetiologically to spirometric restriction, the molecular mechanisms that drive its effects on all-cause and cause-specific mortality, and the possible implications of these findings for early identification of subjects at risk.

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