Comment on: Morbidity and mortality associated with the restrictive spirometric pattern: a longitudinal study

We read with interest the paper by Guerra et al reporting the demographic/clinical characteristics and prospectively assessing the prognosis of subjects with a restrictive spirometric pattern enrolled in the TESAO-D population-based study. The manuscript has the merit of following up a large number of patients for 14 years and investigating how selected co-morbidities are relevant to survival.

The results of this study deserve comparison with those published in 2008 by our research group on 1265 subjects aged 65–97 years. First, in an older population (mean age 73.4 years) we found a comparable prevalence of restriction at spirometry (12% vs 10.9%), although restriction is an age-related phenomenon and, thus, is expected to be much lower in the younger population (ie, 6.6% in a population aged 42.2 years). Second, the study by Guerra and colleagues strongly reproduces the increased mortality risk rates (MRRs) observed in our work: for all (HR 1.89; 95% CI 1.27 to 3.32) status are strong independent predictors of restriction and frailty. Clarifying these issues will allow the implementation of both guided screening and preventive interventions.

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Authors’ response

We appreciate the interest shown in our study by Scarlata and colleagues. We agree with them that, in line with several previous reports,3,5 the prevalence of the restrictive spirometric pattern was strikingly similar in the TESAO-D and SARA2 studies, despite the substantial difference in age distribution between the two populations (the TESAO-D report included subjects ≥21 years and the SARA study subjects ≥65 years of age).

however, a direct comparison of the TESAO-D and SARA2 studies, despite the substantial difference in age distribution between the two populations (the TESAO-D report included subjects ≥21 years and the SARA study subjects ≥65 years of age).

In conclusion, the paper by Guerra and colleagues has the merit of confirming that the restrictive spirometric pattern is highly prevalent and is associated with a clinical profile and risk factors differing from those of obstructive lung disease. However, research is needed to expand our knowledge of the mechanisms underlying restriction as well as to explain the link between restriction and frailty. Clarifying these issues will allow the implementation of both guided screening and preventive interventions.

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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 TESAO-D2 and SARA2 studies, despite the substantial difference in age distribution between the two populations (the TESAO-D 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 TESAO-D 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 TESAO-D 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. Firstly, 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 airflow 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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Validation of using Hospital Episode Statistics data on monitoring disease trends

We read with interest the article by Koshy et al. The findings are important in documenting changes in admission rates of childhood pneumonia and empyema since the introduction of heptavalent pneumococcal conjugate vaccine (PCV7). We are concerned that undue emphasis has been placed on Hospital Episode Statistics (HES) data to define the aetiology of childhood pneumonia, particularly ‘bacterial pneumonia’.

Given the magnitude of the case numbers reported, it would appear that the analyses are based on all pneumonia codes collectively. This would also (although it is not clear from the article) include ‘unspecified pneumonia’, which describes pneumonia of any aetiology. Our analysis of the national HES data on childhood pneumonia (1997–2006) showed that 91% of cases were coded as unspecified pneumonia. This may be of significance given that much unspecified pneumonia in children is likely to be viral; in routine clinical practice it can be difficult to differentiate between viral and bacterial pneumonia.

The authors also assert that ‘PCV7 offers protection against the most common serotypes accounting for most of the bacterial pneumonias in children’. The references provided do not support this statement. There are international variations in serotype distributions of laboratory-confirmed pneumococcal disease. There are no published data on the serotype distribution of pneumococcal pneumonia for UK children.

We have evaluated the accuracy of HES data for paediatric pneumonia in the North East of England. The incidence was previously established in a prospective study, and we repeated it prospectively between 2008 and 2009. Of 50 subjects identified during prospective recruitment, 14 (28%) had misattributed codes and were not identified in the coding list. These patients were coded, for example, as unspecified acute upper respiratory tract infection (I06.9), dyspnoea (R06.0) and cough (R05), despite a clinical diagnosis of pneumonia. Among those identified by HES codes, pneumonia (N=5) and lower respiratory tract infection (N=2) were coded as secondary diagnoses. These figures suggest that reliance on primary diagnostic codes on the basis of HES data could underestimate the levels of pneumonia. There are no reasons to think that levels of miscoding have changed over time.

This article does not describe trends in bacterial pneumonia as stated throughout the paper but all causes of pneumonia. We suggest that use of HES data should be limited to analysis of changes in the overall incidence of pneumonia.

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Authors’ response

Elemaeid and colleagues raise important points about potential diagnostic misclassification and under-ascertainment using the Hospital Episodes Statistics (HES) database, as well as the absence of national pneumococcal serotype data for children. The HES database covers all NHS hospital activity in England and has been widely used to report disease trends. It also provides the opportunity to estimate the clinical impact of major clinical policies on disease burden, but, as with any large epidemiological dataset, has inherent weaknesses at the individual level.

Our study aimed to focus on common community-acquired bacterial pneumonia trends to evaluate the impact of the heptavalent pneumococcal conjugate vaccine (PCV7). We agree that pneumonia is a clinical diagnosis and that it is difficult to differentiate between bacterial and viral causes. Furthermore, a significant proportion of cases (5–40%) of community-acquired pneumonia can be of mixed aetiology. Hence, we applied broad pneumonia definitions. We aimed to focus on bacterial pneumonias and so excluded specific pneumococcal IC-10 codes (eg, ‘viral pneumonia, not elsewhere classified’)—all J12 codes. The codes we searched are listed in the Appendix.

The authors highlight a useful point that some children diagnosed with pneumonia may have symptoms and/or signs recorded in the primary diagnosis field. Hence, we acknowledge under-ascertainment is possible for some pneumonia admissions. HES coding is dependent on the recording of the ‘reason for admission’ by clinicians and the subsequent coding by the trained staff, and we included this as a potential limitation in our discussion. We agree that such levels of miscoding are unlikely to have significantly changed over time. Therefore, this would suggest that the pneumonia admission trends that we observed are likely to represent real changes.

We used the Health Protection Agency cumulative weekly incidence reports of PCV7 and non-PCV7 isolates for children under 5 years, together with the national serotype surveillance for all ages, as the best available source of information on pneumococcal serotypes causing invasive pneumococcal disease. Admittedly, this covers a broader spectrum of invasive diseases. In
Authors' response

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