PostScript

LETTERS TO THE EDITOR

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Is there an association between impaired pulmonary function and mortality in never smokers?

I read with great interest the article by Mannino *et al*[1] on the association between impaired pulmonary function and mortality, and wish to comment on two statements in the paper.

Firstly, the authors report that ''an interesting finding in (their) analysis was that, in never smokers, moderate or severe COPD did not have a significantly increased mortality risk''. In never smokers with severe COPD the point estimate for the hazard ratio forming the basis of this statement is 1.3 with 95% confidence intervals ranging from 0.7 to 3.1. However, these confidence intervals overlap with the point estimate of the hazard ratios in current smokers with severe COPD. There were only 92 participants with severe COPD in the entire sample of the population, hence the wide confidence intervals. The estimates are similar in those with moderate COPD. Furthermore, this trend was also evident in patients with mild COPD who had never smoked. In fact, in the latter group the point estimates were identical in current smokers and never smokers. The authors should therefore be cautious in concluding that never smokers with COPD do not have an increased risk of mortality. An analysis of continuous pulmonary function data in relation to mortality in never smokers independent of the GOLD classification or in all patients with COPD may result in statistically significant results. How would one interpret such a finding? The analysis in never smokers should be seen in the context of other studies reporting increased mortality risks in never smokers,[2] as they may be due to small sample size in spite of the overall large sample size in NHANES I. The authors' statement could be misinterpreted to suggest that never smokers would not require screening, a question that is not yet resolved.

Secondly, our study did report both FEV_1% in quintiles as well as continuous variables.[3]

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Toll-like receptor (TLR) 4 polymorphisms and COPD

Neutrophil and monocyte activation contribute to the pathology of chronic obstructive pulmonary disease (COPD). We hypothesised that a known polymorphism in a key lipopolysaccharide (LPS) response gene might reduce the severity of COPD through a decreased cellular response to activators inhaled in cigarette smoke. TLR4 is the protein enabling signalling to bacterial LPS and perhaps to endogenous mediators of inflammation, and is an important regulator of leucocyte function.[1] Functional polymorphisms in TLR4 have been described and their roles investigated in a number of diseases. Most studies have focused on the Asp299Gly polymorphism, with the rare allele (Gly299) causing LPS hyporesponsiveness.[2] In a study of more than 800 subjects the presence of the TLR4 polymorphism was associated with a reduced risk of atherosclerosis.[3] Smaller studies have potentially associated TLR4 polymorphisms with increased risk of sepsis[4] but, in a large study of patients with meningococcal disease, Asp299Gly was not associated with either altered risks of, or outcomes following, meningitis;[5] although a recent study has suggested that rarer polymorphisms in TLR4 may be important in this disease.[6]

We screened a population of smokers recruited on the basis of age >40 and a smoking history of at least 10 pack years for the presence of the TLR4 polymorphism by established techniques in our group.[5] Data were available on 289 subjects, of which 260 were Asp299 homozygotes and 29 heterozygotes. No Gly299 homozygotes were detected (these data correlate closely with the known frequency of the polymorphism in our region[5]). The presence of the TLR4 polymorphism did not have any significant impact on lung function (measured as forced expiratory volume in 1 second (FEV_1) before and after bronchodilator challenge).

These data do not exclude the possibility that the well characterised and relatively common Asp299Gly TLR4 polymorphism might have a small effect on the severity of COPD. To examine fully the role of this TLR4 polymorphism, large populations (>1000) will be required to give adequate power to exclude small effects on FEV_1 or reversibility. However, the current study shows that this polymorphism is unlikely to have a major impact on the severity of COPD at the population level.

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British guidelines on the management of asthma

As a nurse consultant in respiratory diseases, I am writing to express my concern in relation to the lack of guidance in the section on patient education and self-management in the recently published BTS/SIGN guideline on the management of asthma[1]. Although I fully support the importance of patient education as a key component to effective asthma management, I do have unease around the issue of inhaled steroids. I appreciate that doubling the dose of an inhaled steroid at the time of an exacerbation is of unproven value; however, anecdotally, I