Background: Although C-reactive protein (CRP) levels are increased in chronic obstructive pulmonary disease (COPD), it is not certain whether they are associated with adverse clinical outcomes.

Methods: Serum CRP levels were measured in 4803 participants in the Lung Health Study with mild to moderate COPD. The risk of all-cause and disease specific causes of mortality was determined as well as cardiovascular event rates, adjusting for important covariates such as age, sex, cigarette smoking, and lung function. Cardiovascular events were defined as death from coronary heart disease or stroke, or non-fatal myocardial infarction or stroke requiring admission to hospital.

Results: CRP levels were associated with all-cause, cardiovascular, and cancer specific causes of mortality. Individuals in the highest quintile of CRP had a relative risk (RR) for all-cause mortality of 1.79 (95% confidence interval (CI) 1.25 to 2.56) compared with those in the lowest quintile of CRP. For cardiovascular events and cancer deaths the corresponding RRs were 1.51 (95% CI 1.20 to 1.90) and 1.85 (95% CI 1.10 to 3.13), respectively. CRP levels were also associated with an accelerated decline in forced expiratory volume in 1 second (p<0.001). The discriminative property of CRP was greatest during the first year of measurement and decayed over time. Comparing the highest and lowest CRP quintiles, the RR was 4.03 (95% CI 1.23 to 13.21) for 1 year mortality, 3.30 (95% CI 1.38 to 7.86) for 2 year mortality, and 1.82 (95% CI 1.22 to 2.68) for 5 year mortality.

Conclusions: CRP measurements provide incremental prognostic information beyond that achieved by traditional markers of prognosis in patients with mild to moderate COPD, and may enable more accurate detection of patients at a high risk of mortality.
At the fifth annual visit a venipuncture was carried out on participants who attended their LHS clinics. At year 5, 5413 participants were alive and were eligible for venipuncture. Of these, 4803 provided serum samples (89% of eligible participants). At this visit the participants were also asked to consent for additional follow up (LHS 3). During the follow up of LHS 3, the vital status and hospitalisation records of participants were captured biannually. If a participant had been admitted to hospital, copies of essential documents were obtained from hospital record rooms. Records that made significant mention of respiratory disease, cardiovascular disease, or cancer were forwarded to the mortality and morbidity review board of the study for definitive coding. The mortality and morbidity review board was also responsible for classifying the causes of death for all participants who died during the study. They reviewed death certificates, necropsy reports, relevant hospital records, and summaries of interviews with attending physicians or eye witnesses. These data were supplemented by linkages with a National Death Index which provided the date and cause of death for all US study participants through the end of 2001. Vital status was successfully determined for 98.3% of the participants. Mortality end points were classified into: coronary heart disease, lung cancer, other cancer, cardiovascular disease events, defined as either fatal or non-fatal cardiovascular disease hospital admissions, we used the same model as for all-cause mortality. Multiple regression modelling was used to determine the relationship between CRP quintiles and the rate of decline in FEV1. We have previously shown in this cohort that the slope of FEV1 decline over the first 5 years of follow up reliably predicts the rate of decline over much longer periods of follow up (over 11 years). Because CRP was non-normally distributed, for certain analyses we log transformed CRP values to achieve normality.

To determine whether the predictive (discriminative) power of baseline CRP levels decayed over time, we ran a series of logistic regression models in which we determined all-cause mortality rates from 1 to >5 years of follow up. From these models we determined the area under the receiver operating characteristic curve (also known as C statistic) of baseline CRP. The C statistic can range from 0.5 (model discrimination no better than by chance) to 1.0 (perfect model discrimination). We then constructed a multiple logistic regression model in which sex, race, age (in quintiles), BMI (in quintiles), biochemically validated smoking status, and percentage predicted FEV1 (in quintiles), together with serum CRP levels, were included as potential covariates to predict 1 year mortality. We used a stepwise selection process to select variables that had a p value of 0.20 or less in the univariate model and 0.10 or less in the multivariate model. Discrimination of the model was assessed by the C statistic and calibration was assessed using the Hosmer and Lemeshow χ² statistic (p>0.05 for all models). We also did this for longer term mortality but the discriminative power of baseline measurements diminished significantly over time.

Continuous variables are presented as mean (SD) unless otherwise specified. All analyses were performed using SAS software version 9.1 (SAS Institute, Carey, NC, USA).

### Table 1: Characteristics of participants in the Lung Health Study according to quintiles of baseline CRP levels

<table>
<thead>
<tr>
<th>CRP (mg/l)</th>
<th>Age (years)</th>
<th>Men (%)</th>
<th>Whites (%)</th>
<th>Pack-years of smoking</th>
<th>Continued smokers</th>
<th>Intermittent smokers</th>
<th>Daily cough</th>
<th>Daily sputum</th>
<th>BMI (kg/m²)</th>
<th>FEV₁ (l)</th>
<th>FEV₁ (% predicted)</th>
<th>Diastolic BP</th>
<th>Systolic BP</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Quintile 1 (n = 960)</strong></td>
<td></td>
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<tr>
<td>0.21 (0.17–0.39)</td>
<td>52 (7)</td>
<td>568 (59%)</td>
<td>922 (97%)</td>
<td>37 (18)</td>
<td>470 (49%)</td>
<td>296 (31%)</td>
<td>317 (33%)</td>
<td>273 (28%)</td>
<td>24.1 (3.6)</td>
<td>2.80 (0.63)</td>
<td>80 (9)</td>
<td>76 (9)</td>
<td></td>
</tr>
<tr>
<td><strong>Quintile 2 (n = 961)</strong></td>
<td></td>
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<tr>
<td>0.73 (0.62–0.86)</td>
<td>53 (7)</td>
<td>617 (64%)</td>
<td>956 (97%)</td>
<td>39 (18)</td>
<td>509 (53%)</td>
<td>275 (28%)</td>
<td>341 (35%)</td>
<td>287 (30%)</td>
<td>25.2 (3.6)</td>
<td>2.80 (0.64)</td>
<td>79 (9)</td>
<td>78 (9)</td>
<td></td>
</tr>
<tr>
<td><strong>Quintile 3 (n = 961)</strong></td>
<td></td>
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</tr>
<tr>
<td>1.39 (1.21–1.61)</td>
<td>54 (7)</td>
<td>660 (69%)</td>
<td>933 (97%)</td>
<td>41 (18)</td>
<td>536 (53%)</td>
<td>269 (28%)</td>
<td>344 (36%)</td>
<td>306 (32%)</td>
<td>25.6 (3.5)</td>
<td>2.74 (0.63)</td>
<td>79 (9)</td>
<td>79 (9)</td>
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</tr>
<tr>
<td><strong>Quintile 4 (n = 961)</strong></td>
<td></td>
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</tr>
<tr>
<td>2.58 (2.17–3.06)</td>
<td>54 (7)</td>
<td>630 (65%)</td>
<td>925 (92%)</td>
<td>42 (20)</td>
<td>577 (56%)</td>
<td>267 (28%)</td>
<td>333 (35%)</td>
<td>287 (30%)</td>
<td>26.3 (4.0)</td>
<td>2.61 (0.59)</td>
<td>79 (9)</td>
<td>79 (9)</td>
<td></td>
</tr>
<tr>
<td><strong>Quintile 5 (n = 960)</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>2.70 (2.49–3.02)</td>
<td>55 (6)</td>
<td>548 (57%)</td>
<td>897 (92%)</td>
<td>42 (19)</td>
<td>577 (60%)</td>
<td>244 (23%)</td>
<td>332 (37%)</td>
<td>313 (33%)</td>
<td>26.6 (4.2)</td>
<td>2.61 (0.59)</td>
<td>77 (9)</td>
<td>77 (9)</td>
<td></td>
</tr>
</tbody>
</table>

- CRP: C-reactive protein; BMI: body mass index; FEV₁: forced expiratory volume in 1 second; BP: blood pressure.
- *p* for trend
- Geometric mean (interquartile range).
- Continuous variables are presented as mean (SD) and dichotomous variables are presented as number of participants (% column totals) unless otherwise indicated.
values were two tailed and those below 0.05 were considered to indicate statistical significance.

RESULTS

The mean (SD) age of the participants was 53 (7) years. Their FEV₁ was 2.75 (0.63) l (78 (9)% predicted), BMI was 25.6 (3.9) kg/m², and the mean smoking history was 40 (19) pack-years. Of the participants, 3023 (63%) were men, 4623 (96%) were white, 2601 (54%) were continued smokers, 1351 (28%) were intermittent quitters, and the rest were sustained quitters on the basis of salivary cotinine measurements at visit 5. The geometric mean serum CRP level was 1.32 mg/l (interquartile range 0.62–3.06). During the follow up period, 329 (6.8%) participants died; 87 (26%) from cardiovascular disease, 99 (31%) from lung cancer, 26 (8%) from respiratory failure, and the rest from other causes (n = 117; 36%). During the follow up period, 821 participants were admitted to hospital for cardiovascular diseases (17%). The median duration of follow up was 7.5 years from the date of venipuncture (visit 5).

The clinical characteristics of the study participants divided into quintiles of CRP are summarised in table 1. Participants in the higher CRP quintiles were slightly older and heavier. Moreover, participants who had higher CRP levels were more likely to be continued or intermittent smokers than those with lower CRP levels. The prevalence of cough or sputum production was similar between the groups. The risk of mortality over the follow up period increased as a function of CRP quintile. Both cancer and cardiovascular causes of mortality increased along the CRP gradient (table 2).

Similarly, the risk of fatal and non-fatal coronary heart disease and cardiovascular diseases also increased along the CRP quintile gradient. However, the risk of respiratory deaths was similar between the groups.

After adjustment for potential confounders (see Methods section for details), the risk of all-cause mortality increased significantly as a function of serum CRP levels (table 3). Similarly, the risk of fatal and non-fatal coronary heart disease and cardiovascular diseases and cancer specific mortality increased along the CRP gradient. Respiratory causes of mortality, however, were not significantly related to serum CRP levels. To determine whether the relationship between CRP and all-cause mortality was threshold-dependent or continuous, we plotted a cubic spline curve. Figure 1 shows that the relationship between CRP and all-cause mortality is linear over the range of CRP that is prevalent in patients with mild to moderate COPD (0–6 mg/l).

Table 4 summarises the rate of decline in FEV₁ (percentage predicted) as a function of serum CRP levels. The highest quintile had the fastest decline, while the lowest quintile had the slowest decline in all smoking categories. This relationship was not materially modified by smoking status (p = 0.140).

For 1 year mortality, the C statistic for CRP (in quintiles) was 0.69 (95% CI 0.58 to 0.81). Quartiles of age had a C statistic of 0.70 (95% CI 0.57 to 0.82), while FEV₁ (in quintiles) had a C statistic of 0.65 (95% CI 0.53 to 0.77). In a multiple regression model (described in the Methods section), age (p = 0.002), race (p < 0.001), BMI (p = 0.005), and CRP levels (p = 0.003) were the only variables that significantly predicted 1 year mortality. When combined, these variables had a C statistic of 0.82 indicating excellent discriminative power. The discriminative power of CRP decreased over time. The C statistic of CRP alone was 0.64 (95% CI 0.56 to 0.72) for 2 year mortality, 0.63 (0.59 to 0.69) for 3 year mortality, 0.59 (95% CI 0.54 to 0.65) for 4 year mortality, 0.60 (95% CI 0.55 to 0.64) for 5 year mortality, and 0.59 (95% CI 0.55 to 0.62) for >5 year mortality. Comparing the highest with the lowest CRP quintile, the RR was 4.03 (95% CI 1.23 to 13.21) for 1 year mortality, 3.30 (95% CI 1.38 to 7.86) for 2 year mortality, 2.77 (95% CI 1.46 to 5.27) for 3 year mortality, 1.98 (95% CI 1.22 to 3.24) for 4 year mortality, and 1.82 (95% CI 1.22 to 2.68) for >5 year mortality.

DISCUSSION

In this large prospective study of over 4800 individuals with mild to moderate COPD, serum CRP levels were found to be a significant predictor of all-cause mortality. The risk increased linearly along the CRP gradient, even after adjustments for

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Table 2 Clinical outcomes of participants in the Lung Health Study according to quintiles of baseline CRP levels

<table>
<thead>
<tr>
<th></th>
<th>Quintile 1 (n = 960)</th>
<th>Quintile 2 (n = 961)</th>
<th>Quintile 3 (n = 961)</th>
<th>Quintile 4 (n = 961)</th>
<th>Quintile 5 (n = 960)</th>
<th>p for trend†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean CRP (mg/l)*</td>
<td>0.21</td>
<td>0.73</td>
<td>1.39</td>
<td>2.58</td>
<td>7.06</td>
<td></td>
</tr>
<tr>
<td>Total deaths</td>
<td>47 (4.9)</td>
<td>50 (5.2)</td>
<td>61 (6.4)</td>
<td>65 (6.8)</td>
<td>106 (11.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CHD deaths</td>
<td>7 (0.7)</td>
<td>5 (0.5)</td>
<td>8 (0.9)</td>
<td>9 (0.9)</td>
<td>22 (2.3)</td>
<td>0.001</td>
</tr>
<tr>
<td>CVD deaths</td>
<td>13 (1.4)</td>
<td>7 (0.7)</td>
<td>17 (1.8)</td>
<td>17 (1.8)</td>
<td>33 (3.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fatal/non-fatal CHD</td>
<td>68 (7.1)</td>
<td>85 (8.8)</td>
<td>86 (9.0)</td>
<td>119 (12.4)</td>
<td>145 (15.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fatal/non-fatal CVD</td>
<td>120 (12.5)</td>
<td>133 (13.8)</td>
<td>147 (15.3)</td>
<td>187 (19.5)</td>
<td>237 (24.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cancer deaths</td>
<td>21 (2.2)</td>
<td>32 (3.3)</td>
<td>29 (3.0)</td>
<td>37 (3.9)</td>
<td>50 (5.2)</td>
<td>0.001</td>
</tr>
<tr>
<td>Lung cancer deaths</td>
<td>13 (1.4)</td>
<td>23 (2.4)</td>
<td>15 (1.6)</td>
<td>20 (2.1)</td>
<td>28 (2.9)</td>
<td>0.053</td>
</tr>
<tr>
<td>Respiratory deaths</td>
<td>8 (0.8)</td>
<td>3 (0.3)</td>
<td>6 (0.6)</td>
<td>3 (0.3)</td>
<td>6 (0.6)</td>
<td>0.578</td>
</tr>
</tbody>
</table>

CHD, coronary heart disease; CVD, cardiovascular disease.
*Geometric mean value for each quintile of CRP.
†Linear trend from quintile 1 to quintile 5.
Variables presented as number of participants (% column totals) unless otherwise indicated.

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Figure 1 Risk for all-cause mortality as a function of baseline C-reactive protein levels in the Lung Health Study cohort. The curve was fitted using a cubic spline technique.

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Cigarette smoking increases CRP levels, and findings of this study are consistent with the hypothesis that high sensitivity CRP measurement and decay over time. Combined with age, race, and BMI, CRP levels produced a C statistic of 0.82 for all-cause mortality, suggesting the potential usefulness of serum CRP levels in estimating the prognosis of patients with COPD. In addition, serum CRP levels were significantly associated with cardiovascular events (both fatal and non-fatal) and respiratory deaths, indicating that serum CRP provides incremental prognostic information to these traditional markers of morbidity and mortality. Its discriminatory power for all-cause mortality was greatest during the first year of measurement and decayed over time. Combined with age, race, and BMI, CRP levels produced a C statistic of 0.82 for all-cause mortality, suggesting the potential usefulness of serum CRP levels in estimating the prognosis of patients with COPD. In addition, serum CRP levels were significantly associated with cardiovascular events (both fatal and non-fatal) and with cancer specific causes of mortality.

The results of the current study have several implications. Firstly, the findings are consistent with the hypothesis that COPD is a multi-component disease and that systemic inflammation is associated with overall morbidity and mortality in these patients. Secondly, high sensitivity CRP assays are now widely available for commercial use so clinicians taking care of COPD patients can use CRP values, in addition to FEV₁, to potentially identify patients at high risk of future morbidity and institute early interventional strategy to modify the risk. Thirdly, CRP data may be useful to clinicians to promote smoking cessation as COPD is largely mediated by cigarette smoking. Public awareness of health problems related to cigarette smoking and public health campaigns for smoking cessation have made a significant impact in lowering smoking rates. Nevertheless, 20–25% of the adult population continue to smoke. Since active cigarette smoking increases CRP levels, the findings of this study can be used by health professionals to demonstrate to patients the importance of smoking cessation and in taking up healthy lifestyle choices (such as regular exercise and weight reduction) which together can reduce CRP levels.

CRP is a circulating pentraxin that is largely (but not exclusively) produced by hepatocytes as part of an acute inflammatory signal and propagate chronic inflammatory disorders. Transgenic mouse models of CRP, however, have demonstrated that CRP is a stable biomarker for low grade systemic inflammation, there is no consensus on whether it plays a critical role in mediating chronic inflammatory disorders such as atherosclerosis. In vitro studies have shown that CRP can activate the classical complement cascade, upregulate adhesion molecules and chemotactant chemokines, and induce the synthesis of inflammatory cytokines such as interleukin (IL)-8 and IL-6 which collectively can amplify the initial inflammatory signal and propagate chronic inflammatory disorders. Transgenic mouse models of CRP, however, have produced inconsistent results. Notwithstanding the ongoing controversy regarding the potential causal role of CRP, serum CRP levels correlate well with future risk of morbidity and mortality in the general population and in select patient populations such as those with underlying ischemic heart disease or stroke.

There are several limitations to this study. Firstly, the LHS cohort comprised patients who had mild to moderate COPD. It is possible that these results may not apply to individuals without COPD or to those with more advanced disease. Although cardiovascular disease is the leading cause of hospitalisation and one of the leading causes of mortality in mild COPD, respiratory insufficiency and pneumonia become more important in severe COPD. Whether CRP has a similar discriminative value in patients with more advanced COPD is unknown. Secondly, CRP levels were measured only once in the LHS cohort so we could not evaluate the effect of changes

### Table 3 Adjusted risk of clinical outcomes in the Lung Health Study cohort according to quintiles of baseline CRP levels

<table>
<thead>
<tr>
<th>Quintile</th>
<th>Quintile 2</th>
<th>Quintile 3</th>
<th>Quintile 4</th>
<th>Quintile 5</th>
<th>p for trend†</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause mortality</td>
<td>1.0</td>
<td>0.98 (0.65 to 1.46)</td>
<td>1.14 (0.78 to 1.68)</td>
<td>1.13 (0.77 to 1.65)</td>
<td>1.79 (1.25 to 2.56)</td>
</tr>
<tr>
<td>CHD deaths</td>
<td>1.0</td>
<td>0.66 (0.78 to 2.60)</td>
<td>0.93 (0.34 to 2.60)</td>
<td>1.20 (0.37 to 4.29)</td>
<td>2.20 (0.90 to 5.38)</td>
</tr>
<tr>
<td>CVD deaths</td>
<td>1.0</td>
<td>0.43 (0.17 to 1.09)</td>
<td>1.08 (0.52 to 2.34)</td>
<td>0.90 (0.43 to 1.89)</td>
<td>1.69 (0.86 to 3.33)</td>
</tr>
<tr>
<td>Fatal/CHD/CVD</td>
<td>1.0</td>
<td>0.98 (0.71 to 1.35)</td>
<td>1.02 (0.74 to 1.40)</td>
<td>1.26 (0.93 to 1.71)</td>
<td>1.56 (1.15 to 2.10)</td>
</tr>
<tr>
<td>Cancer deaths</td>
<td>1.0</td>
<td>0.91 (0.71 to 1.17)</td>
<td>1.02 (0.80 to 1.31)</td>
<td>1.18 (0.93 to 1.49)</td>
<td>1.51 (1.20 to 1.90)</td>
</tr>
<tr>
<td>Lung cancer deaths</td>
<td>1.0</td>
<td>1.39 (0.80 to 2.43)</td>
<td>1.20 (0.68 to 2.11)</td>
<td>1.43 (0.83 to 2.47)</td>
<td>1.85 (1.10 to 3.13)</td>
</tr>
<tr>
<td>Respiratory deaths</td>
<td>1.0</td>
<td>1.66 (0.83 to 3.28)</td>
<td>1.00 (0.47 to 2.11)</td>
<td>1.31 (0.64 to 2.66)</td>
<td>1.76 (0.89 to 3.45)</td>
</tr>
</tbody>
</table>

CRP, C-reactive protein; CHD, coronary heart disease; CVD, cardiovascular disease.
*Geometric mean value for each quintile of CRP.
†Linear trend from quintile 1 to quintile 5.
All values are mean (95% CI) and have been adjusted for sex, race, age (in quintiles), body mass index (in quintiles), pack-years of smoking (in quintiles), biochemically validated smoking status (continued smokers, sustained quitters, or intermittent quitters), rate of decline in FEV₁ (in quintiles), and predicted FEV₁ (in quintiles).

### Table 4 Annual change in FEV₁ (% predicted) in the Lung Health Study cohort according to quintiles of CRP levels and smoking status

<table>
<thead>
<tr>
<th>Quintile</th>
<th>Quintile 2</th>
<th>Quintile 3</th>
<th>Quintile 4</th>
<th>Quintile 5</th>
<th>p for trend†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean CRP (mg/l)*</td>
<td>0.21</td>
<td>0.73</td>
<td>1.39</td>
<td>2.58</td>
<td>7.06</td>
</tr>
<tr>
<td>All participants</td>
<td>0.43 (1.69)</td>
<td>0.63 (1.50)</td>
<td>−0.58 (1.62)</td>
<td>−0.81 (1.53)</td>
<td>−0.93 (1.54)</td>
</tr>
<tr>
<td>Sustained smokers</td>
<td>1.00 (1.60)</td>
<td>1.07 (1.44)</td>
<td>−1.03 (1.57)</td>
<td>−1.30 (1.42)</td>
<td>−1.25 (1.52)</td>
</tr>
<tr>
<td>Intermittent smokers</td>
<td>0.10 (1.60)</td>
<td>0.30 (1.37)</td>
<td>−0.38 (1.48)</td>
<td>−0.50 (1.52)</td>
<td>−0.64 (1.44)</td>
</tr>
<tr>
<td>Sustained quitters</td>
<td>0.43 (1.57)</td>
<td>0.15 (1.41)</td>
<td>0.37 (1.47)</td>
<td>0.12 (1.37)</td>
<td>−0.15 (1.44)</td>
</tr>
</tbody>
</table>

*Geometric mean value for each quintile of CRP.
†Linear trend from quintile 1 to quintile 5.
The interaction term for smoking status and CRP quintiles was not significant (p = 0.140).
Data are expressed as mean (SD) and are calculated from (FEV₁ % predicted in year 1 − FEV₁ % predicted in year 5)/5 years.
in CRP on health outcomes in COPD patients. However, it is
assuring that CRP levels measured at multiple time points
have been stable in many studies. 26–28 Moreover, any random
fluctuations in CRP levels would have produced non-
differential misclassification, leading to a dilution of the
association between CRP and health outcomes. Consistent
with this notion, the highest discriminative power of CRP
was observed with 1 year mortality and its discriminative
power decayed with longer duration of follow up. These data
suggest that baseline CRP levels are best used to predict
prognosis over a short period of time. Thirdly, we did not
measure markers of systemic inflammation other than CRP.
We chose CRP because it is a stable molecule with a half life
of 18–24 hours, it is raised in COPD, it is easy to measure, and
because it has been shown to provide prognostic information
in the general population. 26–29 The importance and usefulness
of other markers of systemic inflammation in COPD are
much more controversial. Moreover, their assays are not
widely available commercially, making them less useful for
clinical purposes. Fourthly, it is controversial whether CRP is
an effector molecule in the pathogenesis of cardiovascular
events or merely a marker of systemic inflammation. The
work is needed to identify the potential pathogenic role of
CRP and other inflammatory mediators in COPD and the
relationship with inflammation-sensitive plasma proteins.

Validation of the present findings using a separate COPD
population is needed to rule out overfitting, 30 we cannot fully
discount this possibility. Carefully minimising the number of
covariates evaluated in the analytical model to mitigate the
risk of statistical overfitting, 30 we cannot fully discount this
possibility. Validation of the present findings using a separate
COPD cohort is needed in the future.

In summary, the results of the current longitudinal study
indicate that the serum level of CRP is a significant predictor
of future risk of death, cancer deaths, and cardiovascular
events in patients with mild to moderate COPD and provides
incremental information beyond that of smoking, FEV1, and
other traditional risk factors in COPD. These data suggest
that CRP could be used routinely in clinical practice to risk
stratify patients with COPD. In those with raised CRP levels,
physicians should consider aggressive treatments—for
example, smoking cessation programmes, other lifestyle
interventions, and possibly some pharmacological agents—to
reduce the risk of morbidity and mortality in such patients.

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