Chronic obstructive pulmonary disease and the risk of 12 cardiovascular diseases: a population-based study using UK primary care data

ABSTRACT
Risks for cardiovascular diseases (CVDs) other than myocardial infarction and stroke in the general COPD population are not well quantified. We used a matched cohort study design and Cox regression to estimate relative risks for 12 separate CVDs in a large population-based cohort of patients with COPD over a 12-year period. Associations between COPD and individual CVDs were heterogeneous, with the highest relative risks observed for heart failure and diseases of the arterial circulation (in excess of 2.5 for those aged 64–75 years). Relative risks declined with increasing age but for most CVD outcomes remained unchanged over the study period.

INTRODUCTION
Investigation of cardiovascular disease (CVD) risks in people with chronic obstructive pulmonary disease (COPD) has focused on coronary heart disease, in particular myocardial infarction (MI), and stroke.1–3 Risks for other CVDs such as angina, atrial fibrillation, heart failure, MI, peripheral artery disease (PAD), pulmonary artery hypertension (PAH), stroke (subdivided into all stroke excluding transient ischaemic attacks (TIAs), ischaemic stroke, haemorrhagic stroke and TIAs) and sudden cardiac arrest—and identified incident cases using Read codes.

RESULTS
A total of 299 039 individuals with at least one specific COPD code in their primary healthcare record were identified, of whom 209 909 satisfied our inclusion criteria. The number of people identified equates to a UK COPD prevalence of 2%–3%, in line with expectations. The characteristics of the base COPD cohort are summarised in Table 1. In this population, the risk of developing CVDs generally increased with age. However, there was little evidence to suggest that incidence rates have altered substantially over the last decade (online supplementary appendix 2: figure A2.1).

Relative risks (expressed as HRs) for all CVD subtypes decreased with increasing age; the inverse relationship between relative risk for CVD and increasing age was especially pronounced for atrial fibrillation, heart failure, coronary heart disease (angina, MI) and stroke outcomes (figure 1). In the crude analysis (in which adjustment was made for matching variables only), we found no evidence of an association between COPD and any of our four stroke outcomes in the oldest age

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Characteristics of the base* COPD cohort</th>
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<tr>
<td>All subjects</td>
<td>n (% unless otherwise stated)</td>
</tr>
<tr>
<td>Men</td>
<td>n (% unless otherwise stated)</td>
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<tr>
<td>Women</td>
<td>n (% unless otherwise stated)</td>
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*In order to compute relative risk for each of our 12 CVD outcomes, a series of 12 matched cohorts were created in which subjects who experienced the CVD in question prior to their diagnosis of COPD were excluded before being matched to a COPD-free control. The base cohort thus comprises all individuals with COPD meeting study inclusion criteria, save any subsequent exclusions for a prior CVD event.
Figure 1  HRs for 12 cardiovascular disease outcomes, by age group, comparing people with and without COPD (HRs are derived from Cox proportional hazard models adjusted for sex and GP practice by matching only).
group. For all other outcomes, the excess risk was evident at all ages. For most CVD outcomes, relative risks remained unchanged over the study period (supplementary appendix 2: figureA2.2).

**DISCUSSION**

We have shown that increased risks for CVD in people with COPD are not confined to MI and stroke, but exist across the spectrum of CVD subtypes. We further demonstrated that while relative risks for CVDs vary by age, these risks do not appear to have materially altered over the 12-year period of our study, implying that people with COPD are still at a disadvantage in terms of CVD risks compared with their COPD-free counterparts.

While in line with the findings of other studies, the inverse relationship between relative risk and age is a striking feature of our analysis (figure 1),6 and suggests that in older age CVD risk is driven more by the mechanisms of ageing than by COPD per se. It is not clear why relative risk for CVD should be higher among younger patients with COPD. It is possible that this high-risk group represents a subset of susceptible individuals who as a consequence of a low maximally attained lung function develop airflow limitation (and thus COPD) at a relatively early age. Factors that contribute to poor lung function in this group, such as low birth weight and environmental exposures, may well also be contributing to an increased risk for CVD in middle age.

We found a considerable degree of heterogeneity in the magnitude of the relative risks across the individual CVD outcomes studied. While COPD was associated with an increased risk of all 12 outcomes, the highest HRs were observed for AAA, PAD, PAH and heart failure. These patterns mirror those reported by Chen et al10 who also ranked diseases of the pulmonary circulation and heart failure among the more ‘high-risk’ outcomes in a meta-analysis of the prevalence of CVD comorbidities in COPD. Our heterogeneity patterns are also similar to those reported for the association between smoking and the initial (first) presentation of specific CVD outcomes by Pujades-Rodriguez et al.10

Large sample size and a representative population-based COPD cohort identified using a validated algorithm with a high positive predictive value are the key strengths of our study design. Limitations include difficulties in characterising smoking status, differential misclassification of CVD outcomes and lack of adjustment for other potential confounders (online supplementary appendix 3).

Taken together, our findings provide a strong case for a more aggressive management of CVD risks in COPD that is not confined to MI and stroke but extends to other conditions such as atrial fibrillation, heart failure and PAD. Our study also adds to the growing body of evidence that supports calls for a more integrated approach to the diagnosis and management of lung and heart disease, which targets those in middle to late-middle age.

**REFERENCES**


