



Can epidemiological studies determine the productivity-related burden of COPD?

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The causal association between chronic airflow obstruction and unemployment is complex and requires further study <http://ow.ly/INtD30eqJJ>

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Chronic obstructive pulmonary disease (COPD) is one of the leading causes of death around the world [1]. Chronic airflow obstruction (CAO), measured by spirometry, is the most commonly used objective characteristic of COPD [2]. Epidemiological research has provided researchers and clinicians with critical information about the burden of COPD and its risk factors; [3–9]; however, very few studies have investigated the productivity-related burden of COPD [10–12]. The Burden of Obstructive Lung Disease (BOLD) study is one of the best designed epidemiological studies investigating prevalence and risk factors for COPD, and has been vital in improving our understanding of COPD around the world [3, 13]. In this issue of the *European Respiratory Journal*, GRØNSETH *et al.* [14] estimate the association between CAO and unemployment at 26 BOLD sites. The study demonstrates that there is greater unemployment in participants with CAO, which was partially confounded by socioeconomic factors. Importantly, the study reports no association in low and middle income countries (LMIC), which emphasises the diversity of risk factors and burden of COPD in different parts of the world.

The major strengths of the study by GRØNSETH *et al.* [14] are its rigorous design, standardised objective measures of CAO, and comprehensive methodological approach. The analysis included a large sample size (n=18710) from a diverse selection of countries and sites. While the diagnosis criteria for COPD are widely debated [15], GRØNSETH *et al.* [14] use an objective measure of lung function and identify CAO using the lower limit of normal, which is consistent with American Thoracic Society/European Respiratory Society recommendations [16]. The study presents country specific estimates and stratified results by high income country (HIC) and LMIC, which provides a unique insight into the relationship between CAO and unemployment. The analysis is thorough and adjusts for potential confounding factors as best as it can. The results presented are robust and generalisable; however, the study by GRØNSETH *et al.* [14] is not exempt from epidemiological bias and confounding.

Many aspects of COPD, including its prevalence and risk factors, differ between regions [5–9, 17]. The heterogeneous association between CAO and unemployment in HIC and LMIC countries may be explained by the differences in both risk factors for COPD, as well as the gender differences in COPD and employment between the regions [18]. Women in LMIC were disproportionately more likely to answer that they were not in paid employment and had a higher prevalence of CAO. Female gender was strongly associated with unemployment in LMIC, therefore the association between CAO and unemployment may be biased.

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Socioeconomic factors are challenging to measure and interpret [6, 17, 19, 20], especially in a large international study like BOLD, where socioeconomic status will have varying effects and interpretation depending on the socio-cultural context in each country. The heterogeneity between sites reported by the study does suggest that risk factors vary considerably by site and may also depend on unique social security infrastructure, healthcare systems and economic circumstances within each country. Furthermore education and employment are closely related, and education is a strong predictor of risk factors for COPD [11, 21–24]. In the BOLD study, participants with lower education were more likely to have CAO, therefore it is challenging to infer causal association between CAO and employment. One of the BOLD study strengths is the use of a single questionnaire at all 26 sites; however, it is also a weakness in this particular analysis since the questionnaire may not be universally socially or culturally appropriate. The BOLD survey focused on the 12-month period prior to the survey, but this question *per se* does not address the research question of whether having CAO leads to disability that decreases working opportunities. Moreover, reductions in working hours, or changes in employment due to disease were not considered. The study also chose a retirement age of 65 years, which may not be appropriate in all settings. The ideal study design to answer the question would include prospective and longitudinal follow-up of incident cases to understand how CAO affects employment.

Like many epidemiological studies it is difficult to draw any causal inferences from the cross-sectional study by GRØNSETH *et al.* [14]. There is no way to disentangle whether CAO led to unemployment, or whether the individual level risk factors that led to the unemployment also caused the CAO. The unadjusted results were found to be confounded by age, education level, smoking history and sex; suggesting that in part these socioeconomic factors explain the observed associations. The odds ratios for education and age are much larger than for CAO, suggesting that these factors have a greater effect on unemployment than CAO.

It is also not surprising that the results by GRØNSETH *et al.* [14] do not reflect existing literature. Previous studies were limited in not having an appropriate control group [21], or were missing a control group entirely [22]. Interestingly, a similar analysis of the Latin American PLATINO study showed that the association between CAO and unemployment was strongly confounded by socioeconomic factors [23]. Not surprisingly, the CAO prevalence (11.3%) did not align with physician diagnosed COPD (3.9%). Previous studies investigating the impact of COPD on employment used doctor diagnosis of COPD [24], and found stronger associations which are likely biased because a doctor diagnosis of COPD reflects a more severe classification of disease. Therefore, the study reported by GRØNSETH *et al.* [14] is the strongest epidemiological evidence we have to date.

The limitations of the study by GRØNSETH *et al.* [14] are not unique, and the strengths of the study far outweigh its limitations. The causal association between CAO and unemployment is probably complex, and requires further investigation in order to better understand how the association is mediated, such that the economic impact of CAO can be minimised.

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