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EDITORIAL

Detecting mild COPD: don't waste resources

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Chronic obstructive pulmonary disease (COPD) is a major and growing challenge worldwide, with evidence of under-recognition, inaccurate diagnosis, lack of emphasis on smoking cessation treatment, and inaccessibility to pulmonary rehabilitation, its most effective treatment. In this context, what are we to make of the review by Price and colleagues, previously published early online, and now in this issue of the *Primary Care Respiratory Journal* (*PCRJ*)?[1] Despite the thoroughness and laudable aims of their approach, the authors make what we consider to be an unwelcome case for earlier diagnosis and earlier treatment of this disease. It is unwelcome because medical services are already having difficulty providing optimal care for patients with clinically-important COPD. Very few countries have the capacity to expand COPD case-finding to include patients with borderline abnormal spirometry results for whom there is no evidence that treatment has any effect.

As far as we are aware, the only effective intervention in early COPD is smoking cessation. The rationale for detecting COPD early to enhance smoking cessation rates is attractive but is not supported by the evidence. There is evidence from prospective randomised studies that confronting smokers with spirometry results does not improve smoking cessation rates.[2-5] Two large, uncontrolled studies from Poland showed benefits in smoking cessation associated with giving a spirometry-based diagnosis of COPD, but no effect was demonstrated in those with mild airway obstruction.[6,7] A more positive note was struck by Parkes *et al.*, who showed that informing patients of their lung age based on spirometry, followed by counselling, improved smoking cessation results irrespective of severity.[8] These findings need confirmation, because an earlier similar trial and a systematic review of the impact of biomedical risk assessment as an adjunct to smoking intervention suggest otherwise.[9,10] All smokers (regardless of spirometry testing) should be helped to quit, using pharmacotherapy proven to help those who are unable to quit without it.[11]

The concern is that we cannot predict progression of early COPD to clinically-important COPD. The majority of smokers who fall into GOLD stage I (mild COPD) do not rapidly progress to develop clinically-important COPD, even if they continue to smoke.[12] Furthermore, when compared to smokers with normal spirometry results, people in GOLD stage I have the same frequency of respiratory symptoms and no decrease in exercise capacity.[13]

GOLD stage II ("moderate" COPD) is a broad category which includes adults with probable normal spirometry (65-80% predicted forced expiratory volume in one second [FEV_1][14]) or mild restriction (FEV_1/forced vital capacity [FVC] ratio above the lower limit of the normal range but with a low FEV_1 and low FVC), with both often being associated with abdominal obesity.[15] Although even a mildly low FEV_1 is an independent predictor of mortality, the majority of these deaths are due to cardiovascular disease, not COPD. We consider it a disservice to these people (smokers and never-smokers alike) to be mislabelled as having moderate COPD. Somewhere below the middle of the GOLD stage II category (FEV_1 below 65% predicted), the likelihood that smokers have clinically important COPD increases substantially, with dyspnoea on exertion due to airflow limitation (which might respond to bronchodilator therapy) and a significantly increased risk of subsequent rapid loss of lung function (disease progression). Spirometry and bronchodilator responsiveness only

Table 1. Summary of outcomes from the sub-group analyses in the TORCH and UPLIFT trials and the SPRUCE trial.

	FEV_1 ** (post-BD)	Dyspnoea (SGRQ)*	Exacerbations	Hospital admission	FEV_1 loss ml/year
SPRUCE	+40ml	No difference	7% vs 17%	none	n/a
TORCH	+100ml	-2.3 units	.57 vs .82	0.2 ***	-44 vs -60
UPLIFT	+100 ml	-2.7 units	.56 vs .70	.08 vs .10	-43 vs -49

*SGRQ = St George's Respiratory Questionnaire; **Post-BD = post bronchodilator; ***Events per year per patient

predict 10% of the variability in the subsequent loss of lung function in continuing smokers in GOLD stage II[12] and there are currently no good biochemical markers (from blood, exhaled breath, or induced sputum) of COPD disease activity.[16]

Before anyone embarks on a COPD screening or case-finding programme they should be mindful to fulfil the criteria laid out by Wilson and Lunger in 1968.[17] These criteria include a stipulation that there should be an accepted treatment recognised for the disease and that earlier treatment is effective. Across the whole range of COPD treatments, evidence supporting intervention with drugs in early or mild COPD (GOLD stage I) is limited, if not absent. Even with respect to short-acting bronchodilators, the evidence quoted by Price and colleagues[1] from the guideline of the National Institute for Health and Clinical Excellence (NICE) in the UK,[18] in the summary statement of the American Thoracic Society with the European Respiratory Society,[19] and the recommendations of the Canadian Thoracic Society COPD guidelines,[20] is based on interventions in patients with severe to very severe disease. Large studies of COPD inhalers have shown no differences in annual loss of lung function.[21-23] Many studies of COPD inhalers show modest mean reductions in dyspnoea and small absolute reductions in exacerbation rates in patients with an FEV_1 below 50% predicted. These patients were all symptomatic, all on treatment, and all recruited for these studies by pulmonary specialists. The results should not be extrapolated – as Price and colleagues have done[1] – to patients with mild COPD with spirometry results above 65% predicted, who are seen predominantly by primary care providers.

Wishful thinking about COPD is reaching epidemic proportions, and despite their best intentions the review by Price and colleagues[1] is an example. The authors cite three trials which they say demonstrate the advantages of maintenance therapy (prescription of daily inhalers) in early COPD.[24-26] The first two are subgroup analyses from the TORCH and UPLIFT trials, and the third is their own SPRUCE trial. The majority of participants in the GOLD stage II components of the TORCH and UPLIFT trials had a baseline FEV_1 in the lower half of GOLD stage II, and in the case of SPRUCE, most participants were in GOLD stage III. The TORCH and UPLIFT studies each included more than 2000 patients with COPD from pulmonary specialist offices worldwide and followed them for three or four years. The SPRUCE study, performed in 44 primary care practices in the UK, was small and short (n=178 followed for three months). COPD outcomes measured in these studies included short-term changes in FEV_1, quality of life dyspnoea scores, exacerbation rates, hospital admission rates, and annual rate of FEV_1 decline (see Table 1).

From the patients' standpoint there was little to offer in these studies in terms of improvement in dyspnoea, the major manifestation of disease in COPD. GOLD stage II participants in the active treatment arms of the TORCH and UPLIFT studies reported statistically significant better quality of life (St George's Respiratory Questionnaire - SGRQ) than those using placebo inhalers, but the improvement was well below the minimum clinically important difference for the SGRQ (-4.0 units).[27] The SPRUCE study showed no improvement in dyspnoea for patients randomised to take tiotropium for three months. The mean FEV_1 increases in these studies (+40 to +100 ml) were in the range of the mean 77 ml increases seen after salbutamol in a large population-based sample of relatively healthy adults.[28] We see no reason to encourage patients to take a long-acting bronchodilator if their dyspnoea is not relieved soon after taking the drug. The rate of decline in post-bronchodilator FEV_1 in the TORCH study was 16ml per year better in the combination inhaled long-acting β-agonist and corticosteroid intervention group. In UPLIFT, the rate of decline in post-bronchodilator FEV_1 was 6ml per year better in the tiotropium group compared to the placebo group, an annual advantage of 0.3% in the rate of decline in lung function. After ten years of faithfully taking an inhaler every day, these patients would only have 3-4% better lung function (on average).

Finally, since there is no evidence of benefit for the use of inhaled corticosteroids in the mild or moderate stages of COPD, it is surprising that Price and colleagues mention these drugs in this context.

Interest in the early detection and treatment of COPD may have arisen from the awareness of the growing challenge of COPD worldwide. However, we believe this optimism to be misplaced because there is no evidence that inhalers in early COPD have benefits which outweigh the costs and risks. Promoting interest in early COPD risks the diversion of limited health resources away from interventions such as smoking cessation treatment, which is highly effective.[29]

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