rate, quality of life and mortality. They acknowledge that the rate of FEV₁ decline was highest in CS, and lowest in CE in both tiotropium and placebo (other treatments) subgroups. We thank the authors for highlighting this finding in their abstract, and feel that this particular finding deserves some comment.

The authors compare their study to the Lung Health Study (LHS) [3] in respect to effect of smoking status on the rate of FEV₁ decline. The LHS and UPLIFT® studies have many similarities: large study groups, smoking cessation programme at entry, long-term follow-up and three smoking status subgroups. However, it is most interesting that the UPLIFT® trial is complementary to LHS [4]. LHS participants were younger, with a mean age 48.5 yrs *versus* 61–66 yrs in UPLIFT®. The majority of LHS participants were in the mild/moderate stage of COPD (mean FEV₁ at 78% of predicted, range 55–90%), whereas no mild stage patients were included in the UPLIFT® trial (mean FEV₁ at 40% pred, range 20–70%); 96% of participants were in the moderate or severe stage.

Interestingly, mean FEV₁ decline per year in the first 5 yrs of follow-up in LHS continuing smokers was 62 mL·yr⁻¹ *versus* 59 mL·yr⁻¹ in the UPLIFT® CS subgroup. Continuing ex-smokers in LHS lost 31 mL·yr⁻¹ *versus* 33 mL·yr⁻¹ in the UPLIFT® trial; almost superimposed figures. Thus, smoking cessation was highly effective across the entire spectrum of COPD severity.

The UPLIFT® trial demonstrated that complete smoking cessation results in clinically significant reduction in FEV₁ decline in COPD patients with more advanced stages of the disease, irrespective of treatment. A useful future objective for the authors would be to perform statistical analysis of differences in FEV₁ decline in the three subgroups of smoking status.

This new piece of evidence resolves reservations that spectacular effects of smoking cessation on FEV₁ decline demonstrated in the LHS may be limited to COPD patients with mild forms of the disease [5]. Another important message from the TASHKIN *et al.* [1] study is that only CE patients had improved survival, irrespective of treatment modality, another finding in conjunction with the results of LHS after 14.5 yrs follow-up [6]. The majority of COPD patients have cardiovascular comorbidity. Successful smoking cessation would also reduce risk for myocardial infarction or stroke.

Complete smoking cessation remains a much more effective method to stop accelerated FEV₁ decline in COPD than any pharmacological agent tried so far.

The results of the UPLIFT® trial support the idea of early detection of COPD by high-risk population screening [7] or a case finding method [8]. Early diagnosis gives a unique opportunity to target that group with the full array of antismoking initiatives. All available resources should be applied to help smokers with COPD to quit smoking as a first-line treatment. Spirometry testing of smokers combined with smoking cessation clinics increase smoking cessation rate [9]. Our observational study demonstrating that 17% of smokers with spirometric signs of airflow obstruction stop smoking has recently been confirmed by large randomised

controlled investigations [10]. We strongly believe that early detection of COPD combined with primary and secondary prevention measures are the best methods to reduce the burden of the disease [11].

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REFERENCES

- 1 Tashkin DP, Celli B, Kesten S, *et al.* Long-term efficacy of tiotropium in relation to smoking status in the UPLIFT trial. *Eur Respir J* 2010; 35: 287–294.
- 2 Tashkin DP, Celli B, Senn S, *et al.* A 4-year trial of tiotropium in chronic obstructive pulmonary disease. *N Engl J Med* 2008; 359: 1543–1554.
- 3 Anthonisen NR, Connett JE, Kiley JP, *et al.* Effects of smoking intervention and the use of an inhaled anticholinergic bronchodilator on the rate of decline of FEV₁. The Lung Health Study. *JAMA* 1994; 272: 1497–1505.
- 4 Scanlon PD, Connett JE, Waller LA, *et al.* Smoking cessation and lung function in mild-to-moderate chronic obstructive pulmonary disease. The Lung Health Study. *Am J Respir Crit Care Med* 2000; 161: 381–390.
- 5 Pride NB. Smoking cessation: effects on symptoms, spirometry and future trends in COPD. *Thorax* 2001; 56: Suppl. 2, ii7–10.
- 6 Anthonisen NR, Skeans MA, Wise RA, *et al.* The effects of a smoking cessation intervention on 14.5-year mortality: a randomized clinical trial. *Ann Intern Med* 2005; 142: 233–239.
- 7 Zielinski J, Bednarek M, Gorecka D, *et al.* National Program of early detection and prevention of COPD in the years 2000–2002. *Pneumonol Alergol Pol* 2005; 73: 116–121.
- 8 Buffels J, Degryse J, Heyrman J, *et al.* Office spirometry significantly improves early detection of COPD in general practice: the DIDASCO Study. *Chest* 2004; 125: 1394–1399.
- 9 Bednarek M, Gorecka D, Wielgomas J, *et al.* Smokers with airway obstruction are more likely to quit smoking. *Thorax* 2006; 61: 869–873.
- 10 Parkes G, Greenhalgh T, Griffin M, *et al.* Effect on smoking quit rate of telling patients their lung age: the Step2quit randomised controlled trial. *BMJ* 2008; 336: 598–600.
- 11 Soriano JB, Zielinski J, Price D. Screening for and early detection of chronic obstructive pulmonary disease. *Lancet* 2009; 374: 721–732.

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From the authors:

We thank J. Zielinski and co-workers for their comments and concur with their conclusion that the significant and substantial benefits of complete smoking cessation and sustained abstinence with respect to reduction in the annual rate of decline in forced expiratory volume in 1 s (FEV₁) that were noted in the mostly middle-aged participants in the landmark Lung Health Study [1–3] were similarly observed in older patients with more advanced chronic obstructive pulmonary disease (COPD),

as demonstrated in the Understanding Potential Long-Term Improvements in Function with Tiotropium (UPLIFT®) trial [4]. The authors are correct in highlighting the notable differences between the Lung Health Study and UPLIFT® study populations with respect to age and disease severity. It is of interest, however, that, in the Lung Health Study, a *post hoc* sub-analysis of the annual rates of decline by smoking category (continuing smokers, intermittent smokers and sustained quitters), baseline lung function (range 90–55% predicted FEV₁) and age (range 35–70 yrs) showed that baseline disease severity (FEV₁ % predicted) was not predictive of the annual change in FEV₁ in mL·yr⁻¹ within any smoking category, whereas older subjects who were either continuing or intermittent smokers had a slightly more rapid annual decline in lung function than younger subjects in the same smoking categories, although among quitters age did not influence FEV₁ decline [2]. These findings suggested that smoking cessation leads to generally comparable benefits (in terms of slowing disease progression) across the spectrum of middle to older age and mild to moderate disease severity. The UPLIFT® trial results appear to confirm and extend the findings from the Lung Health Study to an older and more severely diseased COPD population.

J. Zielinski and co-workers suggest that the UPLIFT® data be formally analysed further to compare the rates of decline among the three smoking categories. Unfortunately, such a subgroup analysis would be problematic, since the three subgroups are defined by post-randomisation smoking status and are not comparable with respect to such baseline variables as age, Global Initial for Chronic Obstructive Lung Disease stage, FEV₁ % predicted and sex [4].

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REFERENCES

- 1 Anthonisen NR, Connett JE, Kiler JP, *et al.* Effects of smoking intervention and the use of an anticholinergic bronchodilator on the rate of decline in FEV₁. The Lung Health Study. *JAMA* 1994; 272: 1497–1505.
- 2 Scanlon PD, Connett JE, Waller L, *et al.* Smoking cessation and lung function in mild-to-moderate chronic obstructive pulmonary disease: The Lung Health Study. *Am J Respir Crit Care Med* 2000; 161: 381–390.
- 3 Anthonisen NR, Connett JE, Murray RP. Smoking and lung function of Lung Health Study participants after 11 years. *Am J Respir Crit Care Med* 2002; 166: 675–679.
- 4 Tashkin DP, Celli B, Kesten S, *et al.* Long-term efficacy of tiotropium in relation to smoking status in the UPLIFT trial. *Eur Respir J* 2009; 103: 963–974.

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Polyacrylate nanoparticles: toxicity or new nanomedicine?

To the Editors:

Nanotoxicology is now becoming a very important field in view of the unique physicochemical properties of nanomaterials that may lead to adverse biological effects on occupational, environmental and consumer matters. However, a conclusion on the toxicity of nanomaterials should be carefully drawn taking into account the complexity of determining the toxicity of nanoscale materials. Until now, studies on the adverse outcomes of nanomaterials, such as carbon nanotubes and nanoparticles, were limited to the experimental stage. Although there were some reports on human cell lines, the research was limited to *in vitro* studies; *in vivo* studies were completely limited to animals. Very recently, researchers from Beijing Chaoyang Hospital, Beijing, China, have reported the first case of the clinical toxicity of polyacrylate nanoparticles in humans [1]. The main evidence

involves pathological examination of patients' lung tissue and observations by transmission electron microscopy. Nonspecific pulmonary inflammation, pulmonary fibrosis and foreign-body granulomas of pleura were displayed. Round nanoparticles ~30 nm in diameter were observed to lodge in the cytoplasm and karyoplasm of pulmonary epithelial and mesothelial cells and also in chest fluid. Based on these clinical observations and analysis, the authors conclude that long-term exposure to polyacrylate nanoparticles could result in serious damage to human lungs. Here, we note that their work may provide important evidence for concerns about the toxicity of nanoparticles in humans and may afford promising opportunities to develop a new clinical therapeutic treatment for such nanoparticle-based diseases. However, we would like to point out that there are not enough data to strongly suggest that the clinical symptoms of the patients result from the toxicity of