

systematic sampling, but is avoided in trials with patients prospectively randomised and analysed on an intention-to-treat basis. We emphasise that we did not perform any stage-based subanalyses, but compared the whole CMLND population with the systematic sampling group.

The exclusions after randomisation clearly should not have occurred, but were adequately reported. In all, 25 patients had small-cell cancer or a non-malignant pathology, 48 had incomplete primary resection, 5 turned out to have metastatic deposits from other sites and 15 were excluded because of upstaging to IIIB or IV only. The exclusions were well matched, with 52 occurring in the CMLND group and 41 in the systematic sampling group. We therefore believe this had little effect on the overall analysis.

It should also be mentioned that in one of the trials, only patients with cT1N0 adenocarcinoma of  $\leq 2$  cm diameter were randomised. Mechanistically, the authors hypothesised that this is the group least likely to benefit from CMLND; however, their inclusion in the pooled analysis still resulted in a clear benefit in favour of CMLND. In fact, the pooled hazard ratio of 0.78 is superior to that of adjuvant chemotherapy meta-analyses<sup>4</sup> that have created such enthusiasm in lung cancer circles of late. Therefore, we are concerned that as a result of this editorial, groups treating lung cancer may not demand from their surgeons that which they are demanding from their medical oncologists—an evidence-based improvement in survival with an adjuvant intervention.

We also await the results of the ACOSOG Z30 trial,<sup>5</sup> which will address this question for patients in clinical stage I. This will also allow a pooled analysis of 1959 patients, which should be able to put this question to rest after 50 years of controversy. Until then, the level I evidence is that CMLND should be performed as part of the surgical treatment of patients with stage I–IIIA non-small-cell lung cancer.

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## Authors' reply

We thank Dr Wright for his comments, but respectfully disagree. Although it is certainly possible that complete mediastinal lymph node dissection (CMLD) might improve survival in non-small-cell lung cancer (NSCLC), all three of the studies performed to date were limited by stage migration and other biases. Although overall exclusions were matched, we do not know whether exclusions due to upstaging were necessarily matched between study arms. In fact, limited data from the studies suggest that they were not. In the study by Wu *et al*,<sup>1</sup> after post-randomisation exclusions, there were more patients with stage I (42% *v* 24%) and fewer with stage IIIa (28% *v* 48%) in the lymph node sampling group than in the CMLD group. Furthermore, the authors of one of the other three included studies concluded that stage migration might have resulted in an observed survival benefit for patients undergoing CMLD,<sup>2</sup> and a previous systematic review on CMLD in NSCLC also concluded that stage migration existed for two of the three included studies.<sup>3</sup>

In addition, there are other limitations. For example, because the study by Sugi *et al*<sup>4</sup> included only patients with peripheral NSCLC  $< 2$  cm, the results are not generalisable to all patients with early-stage disease. The study by Wu *et al* had unequal follow-up between study arms.<sup>1,3</sup> The study by Izbicki *et al*<sup>2</sup> had significantly more patients with squamous cell carcinoma in the lymph node sampling group (53%) than in the CMLD group (32%,  $p = 0.03$ ). Finally, two of the three studies were unblinded during follow-up.<sup>1,4</sup> Even if a small survival benefit exists, this must be weighed against the substantially higher morbidity for patients undergoing CMLD reported in two of the three included studies.<sup>2,4</sup> The results of the ACOSOG Z30 trial should help address these trade-offs.<sup>5</sup>

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## CORRECTION

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The authors of the article entitled "Tiotropium for stable chronic obstructive pulmonary disease: a meta-analysis" (Barr RG, Bourbeau J, Camargo CA, *et al*. *Thorax* 2006;**61**:854–62), published in the October issue, have noticed an error in figure 1. Reference 26 in figure 1 should refer to a paper not in the reference list: Witek TJ Jr, Mahler DA. Minimal important difference of the transition dyspnoea index in a multinational clinical trial. *Eur Respir J* 2003;**21**:267–72. Where reference 26 is cited in the text this correctly refers to the paper listed in the reference list.