

## Letters

## Population screening for lung cancer using CT

We read with interest the paper by Black and colleagues<sup>1</sup> which outlines the current status of CT screening, and value the authors' cautious interpretation of the relatively few well conducted studies regarding this controversial topic. However, when using reduction in lung cancer mortality as proof of screening efficacy with CT due to early intervention, one has to be careful in interpreting the calculation of the potential reduction in mortality. This is because the denominator used for calculating disease-specific mortality is also affected and is thus biased by the proportion of early cancers detected, especially when overdiagnosis is likely to be encountered.

We would like to highlight the recent ELCAP study to illustrate this.<sup>2</sup> Screening of 27 456 participants led to the detection of 74 early lung cancers which translated to an annual incidence of 269/100 000 persons at risk (100 000/27 456×74). The reported cure rate was 80% and mortality was 20%. Although we acknowledge that the study included participants from several countries, Centers for Disease Control and Prevention have reported annual lung cancer mortality of 83.3/100 000 men and 53.7/100 000 women.<sup>3</sup> Assuming equal gender distribution, lung cancer mortality of 68.5/100 000 is obtained. When this figure is compared with the ELCAP study, an overdiagnosis of 200/100 000 persons could be implied by CT screening alone. Considering the generally quoted dismal cure rate of 15% for 69/100 000 persons, overdiagnosis and overtreatment of such a magnitude would automatically result in a higher cure rate of 78.5% (69×15% + 200×100%) and 21.5% mortality.

It would therefore appear premature to associate the effectiveness of lung screening with a higher cure rate or reduction in mortality. Instead, a significant reduction in annual lung cancer mortality following the start of any screening method will be the proof of clinical significance. In our opinion, it should decrease lung cancer mortality statistics year after year.

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**Competing interests:** None.

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## Authors' reply

We thank Drs Grigoriu and Scherpereel for commenting on our recent publication examining the diagnostic value of soluble mesothelin in malignant pleural mesothelioma.<sup>1</sup> We agree with their comments that the numbers in our study may not have been sufficient to address the question of the prognostic value of this marker. While we have found that mesothelin levels reflect tumour burden and would therefore be expected to have prognostic value, the patients did not receive a standardised treatment regime. At our centre, patients are offered a range of surgery, chemotherapy, radiotherapy, novel immunotherapies or best supportive care treatment options. The numbers of patients in each category therefore further reduces the power of the survival analysis. However, given that patients with sarcomatoid mesothelioma have low mesothelin levels and a poor prognosis, one would not a priori anticipate a close correlation unless patients are stratified according to histology—that is, elevated mesothelin levels could indicate greater tumour bulk (worse prognosis) or greater epithelial differentiation (better prognosis). We are currently evaluating the prognostic value on patients enrolled in a standardised treatment regime. In both studies pleural effusion levels of mesothelin were not related to survival.<sup>1,2</sup> While serum mesothelin levels may indeed have prognostic value with Grigoriu and colleagues showing in their analysis of 76 patients that high serum mesothelin levels (>3.5 nM) had prognostic significance, it is unclear at this stage whether an individual's mesothelin level will have a strong clinically relevant predictive value that adds to that of the currently used prognostic indicators.<sup>3</sup>

As emphasised by Lee<sup>4</sup> in his editorial published with our paper and by Grigoriu and Scherpereel, we support the need for an international multicentre investigation into the value of soluble mesothelin in the management of patients with mesothelioma.

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## Diagnostic value of soluble mesothelin in malignant mesothelioma

We read with great interest the article by Creaney *et al*<sup>1</sup> together with the associated editorial by Lee<sup>2</sup> published in the July issue of *Thorax*. After the seminal paper by Robinson *et al* in 2003,<sup>3</sup> there has been a lot of interest in the diagnostic value of soluble mesothelin in malignant pleural mesothelioma (MPM). Dr Lee emphasised the similarity between his results and those obtained by us.<sup>4</sup> We completely agree with his statement that this new marker seemed therefore to be robust but could not be used as the sole diagnostic tool.<sup>2</sup>

We would like to comment on the finding of Creaney and coworkers that soluble mesothelin has no prognostic value. The same group of authors have previously suggested that an increasing serum level of this marker may reflect the tumour burden,<sup>3</sup> thus suggesting that soluble mesothelin may have a prognostic value. The series reported by Creaney *et al* included only 52 cases of mesothelioma, and this figure may be insufficient to arrive at a firm statistical conclusion. In our first study which included 60 patients with MPM, we were also unable to find any relationship between patient outcome and soluble mesothelin assessed either in serum or in pleural effusion.<sup>4</sup> However, when the same analysis was performed on a much larger series including almost 60% more patients with MPM,<sup>5</sup> soluble mesothelin appeared as an independent prognostic factor along with the histological subtype, while tumour stage fell short as a significant parameter probably owing to the still low number of cases. Although both the Australian and French series may be subjected to bias, these data stress the urgent need for an international multicentre investigation on the value of soluble mesothelin in the management of malignant mesothelioma before we can firmly recommend the use of this marker in clinical practice.

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**Competing interests:** None.