respiration [2]. My major concern relates to large-scale screening programmes for sleep apnoea in patients with heart failure before solid evidence of treatment effect on central sleep apnoea regarding patient-related outcomes is obtained, *i.e.* survival, symptoms or quality of life.

O. Oldenburg and co-workers argue that the apnoea/hypopnoea index could be used as a surrogate end-point, since a diagnosis of central sleep apnoea is associated with an impaired prognosis [3–5]. Oxygen, continuous positive airway pressure and ventilators all reduce the frequency of central apnoeas, *i.e.* the central apnoea/hypopnoea index. However, other authors have not observed any increased mortality among patients with central sleep apnoea [6, 7]. Surrogate end-points also infer a risk of false interpretation. One such example was anti-arrhythmic treatment studies on patients suffering acute myocardial infarction with arrhythmia as the outcome. Reduction of the number of ventricular arrhythmia was later shown to be associated with an increased mortality rate [8].

I am certainly in agreement with O. Oldenburg and co-workers that we need high-quality treatment studies in patients with congestive heart failure and sleep apnoea. My concern is that we should wait for the results of these studies before starting large-scale screening programmes.

K.A. Franklin
Respiratory Medicine, University Hospital Umeå, Umeå, Sweden.

STATEMENT OF INTEREST

None declared.

REFERENCES

1 Franklin KA. Sleep apnoea screening in heart failure? Not until benefit is proven! *Eur Respir J* 2007; 29: 1073–1074.
2 Javaheri S, Parker TJ, Liming JD, *et al.* Sleep apnea in 81 ambulatory male patients with stable heart failure. Types and their prevalences, consequences, and presentations. *Circulation* 1998; 97: 2154–2159.
3 Hanly PJ, Zuberi-Khokhar NS. Increased mortality associated with Cheyne–Stokes respiration in patients with congestive heart failure. *Am J Respir Crit Care Med* 1996; 153: 272–276.
4 Lanfranchi PA, Braghiroli A, Bosimini E, *et al.* Prognostic value of nocturnal Cheyne–Stokes respiration in chronic heart failure. *Circulation* 1999; 99: 1435–1440.
5 Javaheri S, Shukla R, Zeigler H, Wexler L. Central sleep apnea, right ventricular dysfunction, and low diastolic blood pressure are predictors of mortality in systolic heart failure. *J Am Coll Cardiol* 2007; 49: 2028–2034.
6 Andreas S, Hagenah G, Moller C, Werner GS, Kreuzer H. Cheyne–Stokes respiration and prognosis in congestive heart failure. *Am J Cardiol* 1996; 78: 1260–1264.
7 Roebuck T, Solin P, Kaye DM, Bergin P, Bailey M, Naughton MT. Increased long-term mortality in heart failure due to sleep apnoea is not yet proven. *Eur Respir J* 2004; 23: 735–740.
8 Epstein AE, Hallstrom AP, Rogers WJ, *et al.* Mortality following ventricular arrhythmia suppression by encainide, flecainide, and moricizine after myocardial infarction. The original design concept of the Cardiac Arrhythmia Suppression Trial (CAST). *JAMA* 1993; 270: 2451–2455.

DOI: 10.1183/09031936.00107307

Is 13 g·dL^{-1} the threshold to correct anaemia in COPD?

To the Editors:

I read with interest the recent article by COTE *et al*. [1], wherein the authors have beautifully highlighted the prevalence and association of abnormal haemoglobin with clinical outcomes in a cohort of stable chronic obstructive pulmonary disease (COPD) outpatients. However, there are certain points regarding their study that need discussion.

First, there may be overestimation of the anaemia prevalence, as patients with cancer, thyroid disease, liver disease, gastrointestinal haemorrhage or blood loss and vitamin B12 or folic acid deficiency were not excluded in the study and the prevalence of these diseases increases with age.

Secondly, the type and severity of anaemia was not categorised in the study. It was presumed that all the patients had anaemia of chronic diseases, and a wide range of other causes of anaemia in elderly people could have been missed.

Thirdly, the clinical symptoms of anaemia vary with the degree of severity of anaemia and, in the study, there was no correlation between severity of anaemia and increased dyspnoea and reduced exercise capacity.

Fourthly, it is important to note that anaemia of chronic disease (as in COPD) can be a reflection of a more progressive underlying disease [2, 3]. However, the study by COTE *et al*. [1] could not associate this.

Finally, treatment of the underlying disease is the therapeutic approach of choice for anaemia of chronic diseases [2] and, in cases where the treatment of the underlying disease is not feasible, alternative strategies are necessary. Blood-transfusion therapy has been associated with increased survival rates in anaemic patients with myocardial infarction [4], but transfusion itself has also been associated with multiorgan failure and increased mortality in critically ill patients [5]. Erythropoietic agents are approved for use in patients with anaemia of chronic disease as their beneficial effect involves counteracting the antiproliferative effects of cytokines [3], along with the stimulation of iron uptake and heme biosynthesis in erythroid progenitor cells [2].

Present data indicate that for patients receiving erythropoietic agents, target haemoglobin levels should be 11–12 $g \cdot dL^{-1}$ [6], and, in the study by COTE *et al*. [1], haemoglobin <13 $g \cdot dL^{-1}$ was the cut-off level to define anaemia. Overcorrection of anaemia to normal haemoglobin levels [7] and insufficient treatment [8] have each been associated with unfavourable clinical courses. This elegant study by COTE *et al*. [1] has opened a new debate on ideal targeted haemoglobin levels in chronic stable chronic obstructive pulmonary disease patients.

A. Singh
Christian Medical College and Hospital, Ludhiana, India.

STATEMENT OF INTEREST

None declared.

REFERENCES

1 Cote C, Zilberberg MD, Mody SH, Dordelly LJ, Celli B. Haemoglobin level and its clinical impact in a cohort of patients with COPD. *Eur Respir J* 2007; 29: 923–929.
2 Weiss G. Pathogenesis and treatment of anaemia of chronic disease. *Blood Rev* 2002; 16: 87–96.
3 Spivak JL. Iron and the anemia of chronic disease. *Oncology (Huntingt)* 2002; 16: Suppl. 10, 25–11.
4 Goodnough LT, Bach RG. Anemia, transfusion, and mortality. *N Engl J Med* 2001; 55: 1272–1274.
5 Vincent JL, Baron JF, Reinhart K, *et al.* Anemia and blood transfusion in critically ill patients. *JAMA* 2002; 288: 499–507.
6 Rizzo JD, Lichtin AE, Woolf SH, *et al.* Use of epoetin in patients with cancer: evidence-based clinical practice guidelines of the American Society of Clinical Oncology and the American Society of Hematology. *J Clin Oncol* 2002; 20: 4081–4107.
7 Henke M, Laszig R, Rube C, *et al.* Erythropoietin to treat head and neck cancer patients with anaemia undergoing radiotherapy: randomised, double-blind, placebo controlled trial. *Lancet* 2001; 162: 1255–1260.
8 Besarab A, Bolton WK, Browne JK, *et al.* The effects of normal as compared with low hematocrit values in patients with cardiac disease who are receiving hemodialysis and epoetin. *N Engl J Med* 1998; 119: 584–590.

DOI: 10.1183/09031936.00062607

From the authors:

We are very pleased that A. Singh found our work on the association of haemoglobin levels and outcome of interest. We certainly appreciate these observations, which we hope to address in this response.

There is no question that the exact prevalence of anaemia due specifically to chronic obstructive pulmonary disease, as opposed to that attributable to any comorbid conditions, can only be teased out by completing a study specifically designed to that effect. However, in our study we did exclude patients with any condition likely to influence survival over the 3 yrs (cancer, liver disease or important gastrointestinal blood loss), and more importantly assessed comorbidity using the validated Charlson score [1, 2]. As illustrated in the results and tables, using multivariate analysis, anaemia predicted outcomes in a manner independent of the comorbidity score. In other words, the relationship was independent of comorbidity.

Regarding the second comment, on the nature of the anaemia, this study was not designed to evaluate and determine the cause of the anaemia. Of course there could have been other causes different from anaemia of chronic diseases, but the literature supports this as the most frequent cause of anaemia in an otherwise stable population of elderly patients. As for the relationship between the degree of anaemia and clinical symptoms, the two figures (figs 1 and 2) illustrated the levels of haemoglobin and dyspnoea and the 6-min walk distance. If this data had been plotted in the form of a scatter plot, there would have been a significant correlation.

As for the fourth point of A. Singh, we believe that ours was the first study to address comorbidity using a validated score and thus it is not entirely true that we did not evaluate comorbidity.

The final statement by A. Singh relates to the actual treatment of anaemia, which was not the aim of our study. We agree with most of the comments of A. Singh except the implication that the threshold used to define anaemia in our study was not the correct one. We would like A. Singh to send such comments to the World Health Organization whose definition of anaemia we used [3], as this definition does not imply that we have to target it for therapy. We do agree that our study helps bring this topic to the scientific community so that it can be jointly debated by all.

C.G. Cote
Bay Pines VA Hospital, Bay Pines, FL, USA.

STATEMENT OF INTEREST

None declared.

REFERENCES

1 Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987; 40: 373–383.
2 Charlson M, Szatrowski TP, Peterson J, Gold J. Validation of a combined comorbidity index. *J Clin Epidemiol* 1994; 47: 1245–1251.
3 World Health Organization. Nutritional Anemias: Report of a WHO Scientific Group. WHO Technical Report Series 405. Geneva, World Health Organization, 1968; pp. 1–37.

DOI: 10.1183/09031936.00069907