CGM. Both authors obtained further data from primary patient records and analysed the data. The authors co-wrote the manuscript: the table was generated by CGM; figures and statistics by CLS. Both authors approved the final version. CLS is the guarantor of the data.

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Monitoring treatment response in precapillary pulmonary hypertension using non-invasive haemodynamic measurements

Lee *et al* should be commended for showing that non-invasive haemodynamic monitoring using inert gas rebreathing (IGR) might be a valuable tool to detect treatment response in patients with precapillary pulmonary hypertension (PH).[1] Even under resting conditions, haemodynamic parameters may be more sensitive than the 6-minute walk distance. This is especially interesting as it may facilitate frequent therapy monitoring. Although pulmonary blood flow (PBF) equals cardiac output (CO) in the absence of relevant intrapulmonary shunting, it should be noted that a reliable shunt correction algorithm based on the haemoglobin value has already been implemented in the IGR device.[2] Since using solely PBF significantly increased the measurement bias as compared with the non-invasive gold standard of cardiac MRI, shunt correction should always be applied. A fixed haemoglobin concentration of 14.0 g/dl can be used, if the exact value is not known.[3] This seems to be especially important as pulmonary shunting might be altered in PH. In serial measurements, therapeutic effects and changes in CO may also be due to shunting. This may remain undetected when solely measuring PBF. In analogy to the 6-minute walk distance, IGR measurements require active collaboration, which may limit their application in patients with advanced disease, high WHO functional class or lack of motivation. In these cases, other techniques of measuring CO such as impedance cardiography or continuous-wave Doppler may become potentially valuable, although they are not sufficiently applicable under exercise conditions. There is a rather large variation when compared with IGR or cardiac MRI; however, the reproducibility is high, which is of tremendous importance in serial measurements.[4–6] Although the overall PBF values in the study at hand were between 3.1 and 6.5 l/min, we would like to mention that there is a significantly worse agreement for IGR in large heterogeneous patient collectives at extreme CO states represented by values between 2–4 and 6.4–9.6 l/min, respectively.[7] However, this seems to be negligible considering the aims of the study as the reproducibility is not affected. We agree that based on the very promising findings of Lee *et al*, non-invasive haemodynamic measurements in PH justify further studies to improve and monitor specific therapy. IGR seems to be perfectly suitable for measurements during exercise as it is the only non-invasive device to be used under these conditions.

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Authors' response

We would like to thank Trinkmann *et al* for their comments[1] on our paper, 'Use of non-invasive haemodynamic measurements to detect treatment response in precapillary pulmonary hypertension',[2] and address the point raised regarding shunt correction. We are of the opinion that the in-built shunt correction algorithm in the inert gas rebreathing device may introduce measurement bias, as the assumptions made to correct for shunt flow may not be applicable to patients with pulmonary vascular disease. In the algorithm,[3] cardiac output (CO) is derived from pulmonary blood flow (PBF), oxygen content in arterial blood (CaO_2), oxygen content in pulmonary end-capillary blood (CcO_2) and oxygen uptake (VO_2) according to the formula $CO=1/(1/PBF+(CaO_2-CcO_2)/VO_2)$. The oxygen content of arterial blood and pulmonary end-capillary blood is calculated from the formulae $CaO_2=0.000139\times$haemoglobin concentration (Hb in g/dl)$\times SaO_2$ and $CcO_2=0.000139\times Hb\times ScO_2$ respectively, where SaO_2 denotes arterial oxygen saturation measured by pulse oximetry and pulmonary end-capillary oxygen saturation (ScO_2) is assumed to be 98%. However, ScO_2 may not reach 98% in patients with pulmonary hypertension due to failure of oxygen equilibration in the alveoli combined with a low mixed venous saturation. As a result of the destruction of pulmonary capillary beds and consequently reduced pulmonary capillary blood volume, red cell transit through pulmonary capillaries is more rapid.[4] This shortens the time available for oxygen diffusion to complete across the alveolar–capillary membranes, especially as PBF increases in response to exercise. This is compounded by systemic venous blood being more deoxygenated at the start of the equilibration process due to increased peripheral oxygen extraction in a low CO state associated with pulmonary hypertension. These two mechanisms contribute to resting arterial hypoxaemia and exercise desaturation commonly seen in pulmonary hypertension patients. Applying the shunt correction algorithm would overestimate CO, especially for exercise measurements. Therefore, we advocate the use of inert gas rebreathing PBF instead of derived CO in this patient group. As Trinkmann *et al* pointed out, other non-

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invasive techniques for measuring CO such as impedance cardiography and continuous-wave Doppler have the advantage of not requiring patient collaboration and may be more suitable for patients with advanced disease. However, they are not readily applicable during exercise and there are little clinical data on their use in patients with pulmonary hypertension.

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CORRESPONDENCE

Acidosis, non-invasive ventilation and mortality in hospitalised COPD exacerbations

The national chronic obstructive pulmonary disease (COPD) audit confirms the high mortality associated with acute hypercapnic respiratory failure (AHRF) in COPD, particularly in severely acidotic patients.[1] The authors highlight the observations that significant numbers of patients eligible for non-invasive ventilation (NIV) do not receive it and that NIV is almost universally the ceiling of care with only 5% of acidotic patients receiving invasive mechanical ventilation (IMV). Comparisons are made with the outcomes of clinical trials of NIV, and there is an implication that in clinical practice NIV is not being used optimally with patients being denied potentially life-saving treatment. However, patient selection is the likely explanation for the higher mortality rates in the 'real world'. The greater mortality rates in those receiving NIV at all levels of acidosis, even after allowing for early iatrogenic acidosis due to high flow oxygen, suggests NIV is often used in patients with no chance of survival. The high mortality rate reflects the fact that for many COPD patients AHRF represents the end stage of inexorable decline.

While pH identifies patients in need of ventilatory support, other factors should be considered to determine the appropriate level of intervention. Clinicians use 'clinical judgement' and objective evidence to support this may be obtained on routine clinical assessment. Previous national audits identified performance status as an important predictor of survival in patients admitted to hospital with an acute exacerbation of COPD (AECOPD).[2 3] We have recently shown that in patients dying from AECOPD a WHO performance score (WHO-PS) ≥3 is a powerful marker of end-stage disease and a better predictor of death than pH.[4] In 2009 we prospectively studied COPD patients admitted to hospital with AHRF treated with NIV (n=65). Inpatient mortality was 33.8% and on univariate analysis, factors associated with mortality included poor performance status, long-term oxygen therapy, early warning score, severe acidosis (pH<7.20) and anaemia (table 1). On multivariate analysis only performance status (WHO-PS≥3: OR (95% CI) 39.1 (6.8 to 223.6; p<0.0001) and anaemia (OR (95% CI) 5.87 (1.27 to 26.7; p=0.023) were significant.

We acknowledge that the authors may have highlighted possible deficiencies in delivery of NIV and perhaps more patients should be considered for IMV, but we contend that of equal importance is identification of those patients in whom neither NIV nor IMV is likely to be beneficial so that they may be offered more appropriate end-of-life care.

Table 1 Univariate analysis of variables associated with mortality

Variable	OR	95% CI	p-Value
WHO-PS	3.59	1.66 to 7.76	0.001
WHO-PS≥3	37.7	7.4 to 192.5	0.000
EWS	1.45	1.05 to 1.99	0.021
Hb (g/dl)	0.58	0.41 to 0.83	0.002
Anaemia	5.53	1.81 to 16.92	0.002
LTOT	2.99	1.03 to 8.65	0.043
pH	0.003	0.00 to 1.94	0.079
pH<7.20	3.64	1.16 to 11.37	0.025

Anaemia: men Hb<13.0 g/dl; women<12.0 g/dl.
EWS, early warning score; Hb, haemoglobin; LTOT, long-term oxygen therapy; PS, performance score.

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Authors' response

We thank Mydin *et al*[1] for their interest in our article.[2] They contend that the main findings are explained by patient selection and that for many of these patients management with non-invasive ventilation (NIV) is inappropriate and end-of-life care pathways should be introduced instead.

We agree that patient selection is one of the important explanations for the difference in outcomes of observed clinical practice when compared with the randomised controlled trial (RCT) results and repeatedly emphasise this within the discussion. Patient selection alone however is unlikely to explain the poor survival observed as we also demonstrate that patients subject to pre-hospital oxygen poisoning have poorer outcomes and patients treated with NIV often have significant delays in the initiation of treatment contrary to the RCT evidence and guideline recommendations.

We have also found that patients who fit the RCT and guideline criteria for NIV do not in some cases receive this treatment while escalation to invasive mechanical ventilation (IMV) is the exception. The study also describes inadequate documentation of both escalation plans and do not resuscitate orders. So it is quite possible that some of these patients are receiving NIV when instead

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