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

end-of-life care may be more appropriate, but there are many other important issues that explain the observed outcomes. End of life in chronic obstructive pulmonary disease (COPD) exacerbations is a difficult area of care for which the guidelines are currently vague and where our own data have shown that in large-scale studies all predictors of outcome combined only explain a minority of the variance in outcome.[3] Finally studies of patient choice when offered IMV for respiratory failure in COPD have shown patient preference for intervention beyond that considered appropriate by intensivists in many cases.[4] In essence, this is an area where prospective research is required to better understand both the wishes of patients and the costs and benefits of interventionist or palliative choices.

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Childhood immunisation with conjugate vaccines and prevention of pneumonia

Principi and Esposito[1] describe that widespread use of *Haemophilus influenzae* b (Hib) and pneumococcal conjugate vaccine (PCV7) has nearly eliminated pneumonia due to the first pathogen and significantly reduced the number of cases due to the second pathogen. So, they advise a strong recommendation of these vaccines worldwide. However, the Indonesia probe-trial cited by them actually found more cases of pneumonia admitted to hospital among those vaccinated, and meningitis admissions were not reduced significantly either. The trial did not support a major role for Hib vaccine in overall pneumonia prevention programmes, but in view of high incidences of Hib meningitis and pneumonia found in the study, the authors mentioned that inclusion of Hib vaccine in routine immunisation programmes in Asia deserves consideration. But if we further analyse this statement, the following points need attention. The cost of these newer vaccines precludes their routine and universal use in most developing countries. In addition, the shift of the disease epidemiology due to an increase in the less common serotypes not covered by the vaccine is being reported. Children in Gambia receiving both vaccines continued to have 13.4 episodes of severe pneumonia per 1000 child years.[2] In western countries, the wisdom of having introduced the Hib vaccine is also now being questioned. The vaccine has effectively reduced the incidence of Hib disease, at the same time resulting in an increase of non-Hib and non-serotype strains, causing invasive disease in the post-Hib vaccine era.[3] In the Dallas study, PCV7 reduced the incidence of invasive pneumococcal disease (IPD) by reducing the incidence of vaccine-type disease, but at the same time increasing non-vaccine serotypes (particularly 19A) that are more resistant to antimicrobials.[4] PCV7 covers 65–80% of serotypes associated with IPD in western countries, but the serotype coverage is lower in developing countries. The new generation vaccines (PCV10 and PCV13) are expected to cover 50–80% of IPD not only in western countries but also worldwide.[5] In addition to the PCV7 serotypes, PCV10 covers against strains 1, 5 and 7F and PCV13 covers against strains 1, 3, 5, 6A, 7F and 19A. Both these vaccines also offer broader coverage against pneumococcal strains prevalent in developing countries. So, further surveillance of the changing ecology of these organisms, and study of the true burden of disease in developing countries (also including the cost–benefit ratio of vaccinating each child), is needed before proceeding to universal immunisation.

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Authors' response

We thank Dr Das for his letter[1] regarding our paper on the management of severe community-acquired pneumonia in children.[2] He questions our suggestion that both *Haemophilus influenzae* type b (Hib) conjugate and pneumococcal conjugate (PCV) vaccines could be given to Asian children living in developing countries on the grounds that the incidence of infections due to Hib and the pneumococcal serotypes included in PCV is low. He also states that there is no clear demonstration that either vaccine is effective, and the risk of replacement phenomena is a significant limitation.

Regarding the burden of Hib infection, data show that Hib is significantly more important in Asia than previously thought mainly because a number of cases are not identified by the short-term administration of low-dose antibiotics used in many countries, which often prevents the microbiological diagnosis of Hib infections.[3] Studies carried out in Indonesia and Bangladesh indicate that the clinical efficacy of Hib vaccine is much greater than that calculated on the basis of the reduction in bacteriologically confirmed cases,[3] thus suggesting a higher incidence of Hib diseases and the theoretical efficacy of vaccination. Furthermore, the available data (including data from Asia) indicate that the Hib vaccine has an 18% overall effect on radiologically confirmed pneumonia.[4]

The emergence of new *H influenzae* serotypes after Hib vaccine administration (including those that cannot be typed) has been documented in some, but not all geographical areas. Furthermore, their relevance is marginal when set against the advantage of vaccination. All the studies have shown that the reduction in invasive Hib diseases is significantly greater than the increase in those due to new serotypes.[5] The same is true of PCV, whose role in