

## LETTERS TO THE EDITOR

## Authors' response

The H1N1 pneumonia cohort studied was a subset of a much larger cohort of adults hospitalised in the UK with confirmed pandemic influenza A/H1N1 2009 infection (FLU-CIN cohort, n=1046); part of that cohort has been described elsewhere.<sup>1</sup> The depth and breadth of bacteriological testing of patients recruited into FLU-CIN was at the discretion of attending physicians; only 3 of 1046 patients had evidence of bacterial co-infection recorded, probably an underestimate of the true burden of bacterial co-infection. Patients with identified bacterial co-infection were similar in age to patients without co-infection (mean age 27.0 (SD 13.1) years vs 39.5 (SD 16.4) years). The inclusion of patients with bacterial co-infection in the cohort of patients with H1N1 pneumonia would be expected to reduce any differences between the two study cohorts if patients with co-infection are indeed clinically distinguishable.

We are not aware of any publications arising from the 2009 pandemic demonstrating that patients with H1N1 pneumonia and bacterial co-infection can be reliably differentiated from patients without co-infection on clinical or demographic grounds alone. Some groups have examined the role of procalcitonin in this regard,<sup>2</sup> and ongoing investigations may provide additional information. Conclusions from studies of viruses other than H1N1/09 should be interpreted cautiously with regard to H1N1/09 disease patterns and vice versa.

**Wei Shen Lim,<sup>1</sup> Thomas Bewick,<sup>1</sup> Puja Myles,<sup>2</sup> Sonia Greenwood,<sup>1</sup> Jonathan S Nguyen-Van-Tam,<sup>2</sup> Stephen Brett,<sup>3</sup> Malcolm G Semple,<sup>4</sup> Peter J Openshaw,<sup>5</sup> Barbara Bannister,<sup>6</sup> Robert C Read,<sup>7</sup> Bruce Taylor,<sup>8</sup> Jim McMenamin,<sup>9</sup> Joanne E Enstone,<sup>2</sup> Karl G Nicholson,<sup>10</sup> and Influenza Clinical Information Network (FLU-CIN)**

<sup>1</sup>Department of Respiratory Medicine, Nottingham University Hospitals NHS Trust, Nottingham, UK;

<sup>2</sup>Division of Epidemiology and Public Health, University of Nottingham, Nottingham, UK; <sup>3</sup>Centre for Peri-operative Medicine and Critical Care Research, Imperial College Healthcare NHS Trust, London, UK; <sup>4</sup>Department of Women's and Children's Health, University of Liverpool, Liverpool, UK; <sup>5</sup>Centre for Respiratory Infections, National Heart and Lung Institute, Imperial College, London, UK; <sup>6</sup>Department of Health, Skipton House, London, UK; <sup>7</sup>Department of Infection and Immunity, University of Sheffield, Royal Hallamshire Hospital, Sheffield, UK; <sup>8</sup>Department of Critical Care, Portsmouth Hospitals NHS Trust, Portsmouth, UK; <sup>9</sup>Health Protection Scotland, NHS National Services, Glasgow, UK; <sup>10</sup>Infectious Diseases Unit, University Hospitals of Leicester NHS Trust, Leicester Royal Infirmary, Leicester, UK

**Correspondence to** Dr Thomas Bewick, Nottingham City Hospital, David Evans Building, Nottingham City Hospital, Nottingham NG5 1PB, UK; thomasbewick@doctors.org.uk

**Competing interests** None.

**Contributors** All authors contributed to the content of this reply.

**Provenance and peer review** Not commissioned; internally peer reviewed.

Accepted 13 June 2011

Published Online First 12 October 2011

*Thorax* 2011;**66**:1091.

doi:10.1136/thoraxjnl-2011-200600

## REFERENCES

1. **Nguyen-Van-Tam JS**, Openshaw PJ, Hashim A, *et al*; Influenza Clinical Information Network (FLU-CIN). Risk factors for hospitalisation and poor outcome with pandemic A/H1N1 influenza: United Kingdom first wave (May–September 2009). *Thorax* 2010;**65**:645–51.
2. **Cuquemelle E**, Soulis F, Villers D, *et al*; A/H1N1 REVA-SRLF Study Group. Can procalcitonin help identify associated bacterial infection in patients with severe influenza pneumonia? A multicentre study. *Intensive Care Med* 2011;**37**:796–800.

## H1N1 influenza pneumonia and bacterial coinfection

## ABSTRACT

The model described by Bewick *et al* seems to be able to distinguish between H1N1 influenza-related pneumonia and non-H1N1 community acquired pneumonia (CAP) based on five criteria. However, bacterial infection in the influenza group has not been accurately excluded. Therefore, this model could misidentify these patients and lead to an inappropriate treatment. We conducted a prospective observational study to compare mixed pneumonia vs viral pneumonia. In the mixed pneumonia group patients were older, had higher levels of procalcitonine and higher scores of severity. In our cohort the model proposed by Bewick *et al* would not identify patients with coinfection.

Bewick *et al*<sup>1</sup> recently published a model that identifies H1N1 influenza-related pneumonia based on five criteria.

The model seems to be able to distinguish between H1N1 influenza-related pneumonia and non-H1N1 community acquired pneumonia (CAP). However, in the H1N1 influenza-related pneumonia cohort, there is no available information about the diagnostic testing procedures applied to identify bacterial infections associated with influenza.

Mixed infection due to the influenza virus and bacterial pathogens has been well described in the pandemics that occurred in the last century.<sup>2</sup> In fact, in the last pandemic period, the incidence of bacterial infection in association with the 2009 H1N1 influenza was up to 20%.<sup>3</sup> Remarkably, this percentage is probably an underestimate of the real figure. There are important methodological limitations in the pandemic reports, mainly, bacterial diagnostic tests were not performed

in all patients and most patients received antibiotics close to the time of culture collection.

Bewick *et al* recognise that C reactive protein levels and leukocyte counts are affected by bacterial infections. It has been previously reported that clinical presentation, severity and outcome differs between pure viral pneumonia and coinfecting patients.<sup>4</sup> It is possible that the accuracy of the present model could be lower in coinfecting patients and therefore it could misidentify patients with bacterial and influenza infections. It is common practice to treat with antiviral drugs and antibiotics those patients with CAP even when only influenza has been identified. However, in the group of patients with viral and bacterial infection, a lower sensibility to detect influenza with the reported model could result in a delay in the initiation of antiviral treatment. This fact is crucial, as early antiviral treatment in severely ill patients with pneumonia has been associated with shorter length of stay, duration of ventilation and better survival rates.<sup>5</sup>

We have recently conducted a prospective observational study of patients with CAP. The aim was to determine the aetiology of CAP among patients admitted to hospital and to compare the clinical and laboratory features of patients with mixed pneumonia (bacterial and viral pneumonia) versus those with viral pneumonia. Mixed pneumonia and viral pneumonia were diagnosed in 25 and 22 patients, respectively. Patients with mixed pneumonia were older (74 vs 56 years,  $p<0.001$ ), had higher levels of procalcitonin (5.5 vs 0.8 ng/ml,  $p=0.03$ ) and higher scores of severity indices. In this cohort, the diagnostic prediction model proposed by Bewick *et al*, probably, would not identify patients with coinfection.

**Esther Calbo,<sup>1</sup> Alejandro Robles,<sup>2</sup> Anna Sangil,<sup>1</sup> Susana Benet,<sup>1</sup> Maria Eugenia Viladot,<sup>1</sup> Vanesa Pascual,<sup>1</sup> Bienvenido Barreiro<sup>2</sup>**

<sup>1</sup>Department of Internal Medicine, Infectious Disease Unit, Hospital Universitari Mútua Terrassa, Universitat de Barcelona, Barcelona, Spain; <sup>2</sup>Department of Pneumology, Hospital Universitari Mútua Terrassa, Universitat de Barcelona, Barcelona, Spain

**Correspondence to** Alejandro Robles Pérez, Department of Pneumology, Hospital Mútua Terrassa, Doctor Robert 5, Terrassa, Barcelona 08221, Spain; jander735@hotmail.com

**Competing interests** None.

**Patient consent** Obtained.

**Ethics approval** This study was approved by the Local Ethics Committee.

**Contributors** All the authors contributed equally to the conception and design of the study. ARP, ASGB, MEVB and SBG collected data. BBL analysed the data. All the authors were involved in interpretation of the results. VPG and ECS drafted the manuscript, which has been read and approved by all the authors.

**Provenance and peer review** Not commissioned; internally peer reviewed.

Accepted 23 September 2011  
Published Online First 12 October 2011

*Thorax* 2011;**66**:1091–1092.  
doi:10.1136/thoraxjnl-2011-200410

## REFERENCES

1. **Bewick T**, Myles P, Greenwood S, *et al*. Clinical and laboratory features distinguishing pandemic H1N1 influenza-related pneumonia from inter-pandemic community-acquired pneumonia in adults. *Thorax* 2011;**66**:247–52.
2. **Schwarzmann SW**, Adler JL, Sullivan RJ, *et al*. Bacterial pneumonia during the Hong Kong influenza epidemic of 1968–1969. *Arch Intern Med* 1971;**127**:1037–41.
3. **ANZIC Influenza Investigators**, Webb SA, Pettilä V, *et al*. Critical care services and 2009 H1N1 influenza in Australia and New Zealand. *N Engl J Med* 2009;**361**:1925–34.
4. **Marcos MA**, Esperatti M, Torres A. Viral pneumonia. *Curr Opin Infect Dis* 2009;**22**:143–7.
5. **Rodríguez A**, Díaz E, Martín-Loeches I, *et al*. Impact of early oseltamivir treatment on outcome in critically ill patients with 2009 pandemic influenza A. *J Antimicrob Chemother* 2011;**66**:1140–9.

## PET–CT in lung cancer: data discrepancies

The Danish study of positron emission tomography (PET)–CT versus conventional staging (CS) in non-small cell lung cancer has been reported twice now<sup>1 2</sup> and corrected once.<sup>3</sup>

However, there are discrepancies in numbers between the manuscripts,<sup>1 2</sup> which is surprising given the small number of patients (n=189) and centres (n=3). Was endoscopic ultrasonography done in 42 or 47 of 98 PET–CT patients, and in 30 or 35 of 91 CS patients? Was fine-needle aspiration done in 36 or 40 PET–CT patients, and in 24 or 29 CS patients?<sup>2</sup> Was fine-needle aspiration positive in 16 or 19 PET–CT patients? Was mediastinoscopy positive in 10 or 12 CS patients? Can the authors explain the discrepancies and show how any reconciliation of the numbers affects the findings of each manuscript?

While the total downstaging in both groups was comparable (62% vs 71%, p=0.19), the implied downstaging in the PET–CT arm as a result of modalities other than PET–CT was significantly lower (41% vs 71%; p=0.001). One would have expected the proportion of patients experiencing downstaging based on non-PET–CT investigations to be similar in both groups in a randomised study. It is possible that the apparent superiority of PET–CT is simply the result of inadequacy of non-PET–CT investigations in the CS arm.

Our concern is that the conclusions in both manuscripts have hinged upon small differences in the PET–CT and CS groups, which could simply be due to analytical errors or technical deficiencies of the sort described above. We respectfully suggest that the accuracy of the primary data from this

important study be verified independently by the journals.

**Jose M Paredes,<sup>1</sup> Jayesh Mehta<sup>2</sup>**

<sup>1</sup>University of Illinois, Chicago, Illinois, USA;

<sup>2</sup>Northwestern University, Feinberg School of Medicine, Chicago, Illinois, USA

**Correspondence to** Jayesh Mehta, Northwestern University, Feinberg School of Medicine, 676 N Saint Clair St, Suite 850, Chicago, Illinois 60611, USA; j-mehta@northwestern.edu

**Competing interests** None.

**Contributors** JMP and JM both critically analysed the manuscripts in question and co-wrote the response.

**Provenance and peer review** Not commissioned; internally peer reviewed.

Accepted 22 June 2011

Published Online First 15 July 2011

*Thorax* 2011;**66**:1092.

doi:10.1136/thoraxjnl-2011-200604

## REFERENCES

1. **Fischer B**, Lassen U, Mortensen J, *et al*. Preoperative staging of lung cancer with combined PET-CT. *N Engl J Med* 2009;**361**:32–9.
2. **Fischer BM**, Mortensen J, Hansen H, *et al*. Multimodality approach to mediastinal staging in non-small cell lung cancer. Faults and benefits of PET-CT: a randomised trial. *Thorax* 2011;**66**:294–300.
3. **Fischer BM**, Lassen U, Højgaard L. PET-CT in preoperative staging of lung cancer. *N Engl J Med* 2011;**364**:980–1.

## Authors' response

We thank Drs Paredes and Mehta for their comments on our work on positron emission tomography (PET)–CT in the staging of lung cancer.<sup>1</sup> As correctly pointed out by Drs Paredes and Mehta, there is a discrepancy in the number of patients undergoing endoscopic ultrasonography (EUS) in the two reports from our institution.<sup>2 3</sup> Although both reports concern the staging of patients with non-small cell lung cancer, they address different aspects of the disease. The paper published in the *New England Journal of Medicine*<sup>2</sup> was an intention-to-treat analysis with PET–CT as the only intervention and with the number of futile thoracotomies as the final end point. We have meticulously tried to assemble and report complete and accurate data on all included patients in both papers. Unfortunately, this was done twice, giving rise to a minor discrepancy in the number of patients undergoing PET–CT and EUS reported in the two studies. When performing the analysis previously published in *Thorax*,<sup>3</sup> we focused on information regarding the specific N-stage of each patient. In order to confirm the N-status of each patient, we compared the initial database<sup>2</sup> with (A) the database from a study on EUS performed in parallel with the study on PET–CT (as mentioned in both our previous reports) and (B) the nationwide pathology register. By doing this, we found

an additional five patients in each group who had undergone an EUS examination. In four and five patients, respectively, of the additional five patients found in each of the two groups, a fine-needle aspiration (FNA) was done during the same procedure. There was still no significant difference in the frequency of either EUS or EUS–FNA between the two groups and it had no impact on the reported results. Our findings confirm that PET–CT is an important part of preoperative staging of patients with non-small cell lung cancer, but it also underscores, as stated by Drs Paredes and Mehta and in the Discussion section of our paper, the need for a complimentary well-considered use of invasive mediastinal staging. Finally, we would be happy to welcome both Drs Paredes and Mehta to our department for a discussion of our data.

**Barbara M Fischer, Jann Mortensen, Liselotte Højgaard**

Department of Clinical Physiology, Nuclear medicine & PET, Rigshospitalet, Copenhagen, Denmark

**Correspondence to** Barbara M Fischer, Department of Clinical Physiology, Nuclear medicine & PET, Rigshospitalet, KF 4011, Blegdamsvej 9, DK 2100 Copenhagen, Denmark; malene.fischer@rh.regionh.dk

**Competing interests** None.

**Provenance and peer review** Not commissioned; internally peer reviewed.

Accepted 22 June 2011

Published Online First 15 July 2011

*Thorax* 2011;**66**:1092.

doi:10.1136/thoraxjnl-2011-200654

## REFERENCES

1. **Paredes JM**, Mehta J. PET-CT in lung cancer: data discrepancies. *Thorax* 2011;**66**:1092.
2. **Fischer B**, Lassen U, Mortensen J, *et al*. Preoperative staging of lung cancer with combined PET-CT. *N Engl J Med* 2009;**361**:32–9.
3. **Fischer BM**, Mortensen J, Hansen H, *et al*. Multimodality approach to mediastinal staging in non-small cell lung cancer. Faults and benefits of PET-CT: a randomised trial. *Thorax* 2011;**66**:294–300.

## CORRESPONDENCE

### Severity scales in community-acquired pneumonia: what matters apart from death?

Chalmers *et al*<sup>1</sup> and Loke *et al*<sup>2</sup> present excellent meta-analyses of the value of various tools in predicting mortality from community-acquired pneumonia (CAP). There is a continuing fallacious belief, however, that only patients at high risk of death are at high risk of complications. Of the 47 studies identified by Chalmers and Loke, only 16 made any assessment of the value of these scores in predicting the need for critical care. These are presented in