PostScript

LETTERS TO THE EDITOR

If you have a burning desire to respond to a paper published in *Thorax*, why not make use of our "rapid response" option?

Log on to our website (www.thoraxjnl.com), find the paper that interests you, and send your response via email by clicking on the "eLetters" option in the box at the top right hand corner.

Providing it isn't libellous or obscene, it will be posted within seven days. You can retrieve it by clicking on "read eletters" on our homepage.

The editors will decide as before whether to also publish it in a future paper issue.

Trends in sales of inhaled corticosteroids and asthma outcomes in Singapore

Asthma has become a major health problem in Asia, with a prevalence in many Asian countries approaching that of developed nations. The regular use of inhaled corticosteroids (ICS) has been shown in cohort and ecological studies to decrease hospital admission rates by up to 80%.[1 2] Asthma related mortality has also been shown to decline with ICS use, even at low doses.[1 3 4] Conversely, increased use of short acting β_2 agonists (SABA) has been associated with increased mortality.[5] This study assessed the possible relationship between changes in the use of ICS and SABA and hospital admission and mortality rates for asthma in Singapore.

An ecological population based study was performed from 1994 to 2002 in patients aged 5–64 years. Figures on mortality and hospital admission rates for asthma were obtained from the Ministry of Health, Singapore. The diagnosis codes used were in accordance with the International Classification of Diseases–Clinical Modification, Ninth Revision (ICD-9: 493). Overall and age specific death rates were calculated for the 5–34 and 35–64 year age groups, and overall and age specific hospital admission rates were calculated for
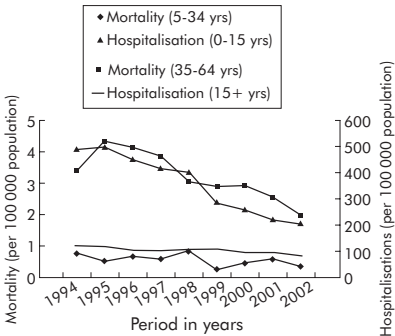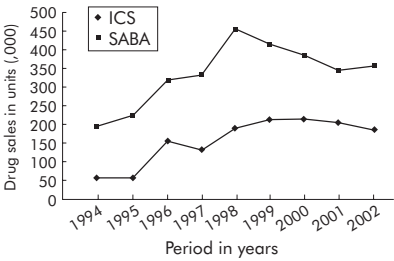
Figure 2 Annual drug sales in units ($\times 10^3$) in Singapore from 1994 to 2002.

children aged 0–14 years and for those aged 15 years and older. Data on the sales of ICS and SABA were obtained from Intercontinental Medical Statistics (Asia) Pte Ltd and presented as canister counts. A Poisson regression analysis using the generalised linear model procedure in S-Plus Version 6 for Windows was carried out to estimate the association between the asthma health outcomes and sales of ICS and SABA.

From 1994 to 2002 asthma deaths declined in both age groups (5–34 years and 35–64 years) by 52.5% and 56.7%, respectively. Throughout the study period the hospital admission rates for both age groups declined significantly (trend test: p<0.001 for 0–15 years and p = 0.001 for >15 years; fig 1). Rising trends for sales of ICS and SABA were observed (fig 2).

The rates of asthma deaths and hospital admissions were also assessed by comparing the periods 1994–1997 (P1) and 1999–2002 (P2). The mean annual asthma mortality decreased significantly from 2.30 to 1.52 and from 0.66 to 0.44 per 100 000 population for those aged 5–64 years (p = 0.0003) and 5–34 years (p = 0.0348), respectively. Mean annual hospital admission rates also decreased substantially for all ages over the P1 and P2 periods, falling from 175.3 to 122.9

per 100 000 population (p<0.001). In parallel, a corresponding increase was observed in mean annual drug sales for ICS from 100.7 units ($\times 10^3$) in P1 to 204.3 units ($\times 10^3$) in P2 (p = 0.0003). The mean sales of SABA also increased but the change in usage was not statistically significant (p = 0.0507).

Poisson regression analysis confirmed the negative association between the use of ICS and both asthma mortality and hospital admission rates (p<0.05), with and without adjustment for the sales of SABA in all age groups (table 1). The association with the use of SABA was not significant in the same model. The rate ratios of asthma mortality for those aged 5–64 years and hospital admission for all ages were 0.96 (p = 0.0461) and 0.98 (p = 0.0006) for every 10 000 units of ICS sold after adjusting for the sales of SABA (model 2 in table 1).

Being an ecological study, we recognise that other factors such as improvements in patient education and medical facilities may also have contributed to the observed improvement in morbidity and mortality. Despite this, the data presented here support the current evidence that an overall increase in ICS use has a positive impact on asthma related morbidity and mortality in our population, and highlight the importance of ICS prophylaxis as the most cost effective form of asthma treatment available today.

D L Lim
Department of Paediatrics, National University of Singapore, Singapore

S Ma
Epidemiology and Disease Control Division, Ministry of Health, Singapore

X S Wang
Department of Paediatrics, National University of Singapore, Singapore

J Cutter, S K Chew
Epidemiology and Disease Control Division, Ministry of Health, Singapore

Figure 1 Age standardised mortality and hospital admission rates for asthma in Singapore from 1994 to 2002.

Table 1 Poisson regression analysis of asthma mortality and hospitalizations by age group, associated with the sales of ICS and SABA*

| | Model 1† | | Model 2 (Model 1+SABA)‡ | | | |
| | ICS | | SABA | | ICS | |
Health outcome	β_1	p value	β_2	p value	β_1	p value
Asthma mortality						
5–34 years	−0.0029	0.0179	−0.0002	0.2782	−0.0030	0.0394
35–64 years	−0.0023	0.0098	0.0023	0.2351	−0.0046	0.0431
5–64 years	−0.0023	0.0196	0.0002	0.1826	−0.0037	0.0461
Hospital admissions for asthma						
0–14 years	−0.0039	0.0003	0.0003	0.1676	−0.0041	0.0004
15+ years	−0.0014	0.0030	−0.0003	0.1515	−0.0013	0.0165
All ages	−0.0024	0.0002	−0.0771	0.0529	−0.0024	0.0006

*All models included an adjustment for extra-Poisson due to year to year variability.
†Model 1: Mortality: log (expected number of age-specific deaths due to asthma) = $\beta_0 \times$ log (age specific population size) + $\beta_1 \times$ steroids. Hospital admissions: log (expected number of age specific hospital admissions due to asthma) = $\beta_0 \times$ log (age specific population size) + $\beta_1 \times$ ICS. Thus, exp($\beta_1 \times 10\,000$) is the rate ratio of asthma mortality/hospital admissions per 10 000 units of medication sold.
‡exp($\beta_1 \times 10\,000$) of ICS in model 2 is the adjusted rate ratio of asthma mortality/hospital admissions per 100 000 units of medication sold when SABA sales are held constant.

T K Lim
Department of Medicine, National University of
Singapore, Singapore

B W Lee
Department of Paediatrics, National University of
Singapore, Singapore

Correspondence to: Dr B W Lee, Department of
Paediatrics, National University of Singapore,
Singapore; paeleebw@nus.edu.sg

References

1 **Suissa S**, Ernst P. Inhaled corticosteroids: impact on asthma morbidity and mortality. *J Allergy Clin Immunol* 2001;**107**:937–44.
2 **Bjor O**, Braback L. A retrospective population based trend analysis on hospital admissions for lower respiratory illness among Swedish children from 1987 to 2000. *BMC Public Health* 2003;**3**:22.
3 **Suissa S**, Ernst P, Benayoun S, *et al*. Low-dose inhaled corticosteroids and the prevention of death from asthma. *N Engl J Med* 2000;**343**:332–6.
4 **Suissa S**, Ernst P. Use of anti-inflammatory therapy and asthma mortality in Japan. *Eur Respir J* 2003;**21**:101–4.
5 **Spitzer WO**, Suissa S, Ernst P, *et al*. The use of beta-agonists and the risk of death and near death from asthma. *N Engl J Med* 1992;**326**:501–6.

Non-invasive monitoring of CO_2 levels in patients using NIV for AECOPD

Non-invasive ventilation (NIV) is the treatment of choice for persistent hypercapnic ventilatory failure during acute exacerbations of chronic obstructive pulmonary disease (AECOPD), despite optimal medical treatment.[1][2] Assessment of the partial arterial pressure of carbon dioxide ($PaCO_2$) is the "gold standard" for the evaluation of the adequacy of alveolar ventilation in this setting. However, repeated intermittent invasive arterial puncture carries inherent risks, including pain.[3] Transcutaneous measurement of carbon dioxide ($TcPCO_2$) theoretically appears more appropriate for monitoring $PaCO_2$. This measurement is based on the observation that CO_2 has a high tissue solubility and diffuses through the skin. While available data as to the precision of $TcPCO_2$ measurements have given conflicting results,[4–6] no study has attempted to assess simultaneous recordings of $TcPCO_2$ and $PaCO_2$ in patients requiring NIV for AECOPD.

We prospectively studied the agreement between $TcPCO_2$ and $PaCO_2$ measurements in 22 consecutive patients with AECOPD admitted to the respiratory support unit (RSU) from the emergency department with persistent ventilatory failure ($PaCO_2 \geqslant 6$ kPa) requiring NIV treatment. Paired arterial blood gas samples taken from the radial artery and $TcPCO_2$ measurements were made on arrival in the RSU and 1 and 4 hours after commencing NIV. Patients were also given bronchodilators by nebuliser, corticosteroids, and antibiotics. Each subject gave their informed consent following a detailed presentation of the study objectives and protocol.

Thirteen women and nine men of mean (SD) age 72 (10) years and mean (SD) body weight 67 (13) kg were enrolled in the study. On arrival at the RSU, mean (SD) systolic blood pressure (BP) was 138 (33) mm Hg and diastolic BP was 70 (14) mm Hg. No patient received vasopressor or inotropic support. Arterial pH on arrival at the RSU was 7.27 (0.06). $TcPCO_2$ measurements were performed with a capnograph (Tosca Monitor; Linde Medical Sensors, Basel, Switzerland). The monitor measures $TcPCO_2$ using a Stow-Severinghaus electrode with a single ear sensor which works at 42°C to enhance blood flow in capillaries below the sensor. $TcPCO_2$ is measured by determining the pH of an electrolyte solution. The change in pH is proportional to the logarithm of the change in $TcPCO_2$. Reassembly of the sensor—which constitutes an electrolyte solution, a spacer, and a gas permeable Teflon membrane—has to be done every 14 days. The monitor displays when the sensor needs a new membrane. The system is equipped with an integrated unit for fully automatic calibration before measurements. In vitro response times are typically below 50 seconds.

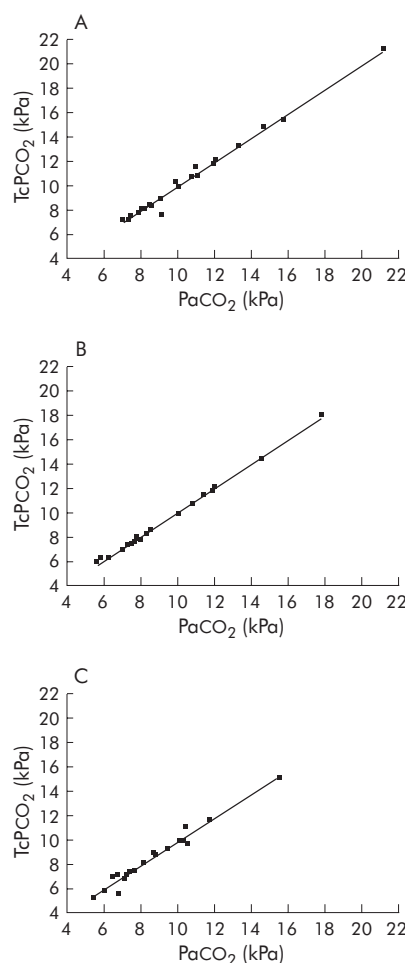Agreement between transcutaneous and arterial values for CO_2 was tested over a

Figure 1 Correlation between $TcPCO_2$ and $PaCO_2$ measurements in 22 subjects (A) on arrival in the RSU and (B) 1 hour and (C) 4 hours after commencing non-invasive ventilation for an acute exacerbation of COPD.

Figure 2 Bias of $TcPCO_2$ compared with $PaCO_2$ (d) and SD of bias (s) in 22 subjects (A) on arrival in the RSU and (B) 1 hour and (C) 4 hours after commencing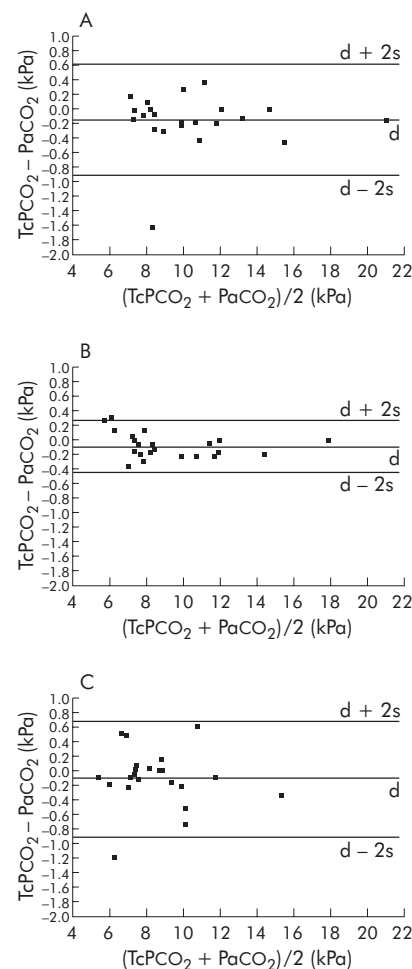 non-invasive ventilation for an acute exacerbation of COPD. Values of ($TcPCO_2 - PaCO_2$) are plotted against the mean values of $TcPCO_2$ and $PaCO_2$ as described by Bland and Altman.[7]

range of 5–22 kPa and calculated using Pearson's coefficient of correlation. Both measurements were highly correlated on arrival in the RSU ($r = 0.99$, p<0.0001) and 1 hour ($r = 0.99$, p<0.0001) and 4 hours after commencing NIV ($r = 0.98$, p<0.0001; fig 1). However, in two of our measurements—interestingly, at a lower $PaCO_2$—the agreement was less strong. We also calculated the bias and the limits of agreement between the parameters as described by Bland and Altman;[7] 95% of the values were within the limits of agreement on arrival in the RSU and 1 and 4 hours after commencing NIV (fig 2). There were no adverse effects from or patient discomfort with the heating electrode.

These findings suggest that $TcPCO_2$ measurements are appropriate for clinical application in estimating the ventilatory response to NIV in patients with hypercapnic ventilatory failure due to AECOPD. However, a larger and more detailed study is needed to confirm these preliminary findings. $TcPCO_2$ measurements allow real time estimation of CO_2 levels over a prolonged period and therefore facilitate proactive rather than reactive ventilator manipulations. Moreover,