LETTERS TO THE EDITOR

COPD exacerbations

We read with interest the paper by Cotton and associates¹ on early discharge for patients with exacerbations of chronic obstructive pulmonary disease and the accompanying editorial by Killen and Ellis.² In both publications the 1991 study of our RespiCare home care programme was referenced,³ and both asserted that our programme was not cost effective. In fact, our study reached the opposite conclusion—namely, that the RespiCare programme was shown to be cost effective.

Actual direct care charges in US dollars were used in our calculations of both pre-programme and on-programme costs. Additionally, administrative costs of operating RespiCare were added into the on-programme costs. Our findings showed that, while hospitalisation costs substantially decreased during the programme, home care costs increased. However, the decrease in hospital costs more than offset the subsequent increase in home care costs, with a total cost savings of \$328 US dollars per patient per month or \$3956 per year being realised for those on the RespiCare programme. Although the emphasis of the work was on improvements in clinical outcome, the cost savings were a significant and important aspect of our study.

I hope this clarifies any misunderstanding created by the recent articles.

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- 1 Cotton MM, Bucknall CE, Dagg KD, *et al* Early discharge for patients with exacerbations of chronic obstructive pulmonary disease: a randomised controlled trial. *Thorax* 2000;55:902-6.
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CFC transition

The editorial by Mark Everard¹ provided an interesting viewpoint about inhaler therapy and delivery systems. However, the selective quotation of published trial evidence introduces the potential for bias in his conclusions. This is particularly apparent in the discussion on the ability of patients to use pressurised metered dose inhalers (pMDI) correctly. Like many other reviews in this field, selective citation of published papers leads to conclusions that alternative inhaler devices are used more effectively than pMDIs.

We have recently completed an NHS sponsored systematic review of the published literature on the clinical and cost effectiveness of inhaler devices. One aspect, a systematic review of the clinical efficacy of pMDIs

versus dry powder inhalers (DPIs),² found that eight of the 14 clinical studies included in the review cited papers showing poor pMDI technique, including two citing the same paper as Everard by Crompton.³ The British Thoracic Society asthma guidelines⁴ also stress such problems: "Many patients are unable to use MDIs correctly... addition of a spacer device will reduce coordination problems". Another aspect of the review was inhaler technique. Analysis of studies in which more than one type of inhaler device was assessed (six studies) showed that the "ideal" inhaler technique was found in 59% (95% CI 51 to 67) for DPI, in 43% (95% CI 36 to 50) for pMDI alone, and in 55% (95% CI 49 to 61) for pMDI with spacer. If the same outcome is considered after a period of inhaler technique teaching (20 studies), then the results are 65% (95% CI 59 to 71) for DPI, 63% (95% CI 60 to 67) for pMDI alone, and 74% (95% CI 53 to 88) for pMDI with spacer. There is marked heterogeneity within these studies and thus selective citation could show any one to be better than another.

We agree that clinical testing of all inhaler devices is critical in informed decision making, but the editorial by Everard may imply that pMDIs are worse than other devices thus encouraging the use of perhaps even less well evaluated devices and at a greater financial cost—an outcome we are sure was not intended by the author.

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Hyperventilation syndrome

I have recently come across the paper by Malmberg *et al*¹ and the accompanying editorial by Gardner² of orthostatic increase of respiratory gas exchange in hyperventilation syndrome. Gardner concludes that "the physiological basis for these responses requires investigation and may provide useful insights into mechanisms by which postural changes can influence control of breathing and respiratory sensations".

Should the work of Yates *et al*³⁻⁵ have not yet come to your notice, I present it to you for your consideration. I have found it to be fascinating and relevant work with regard to altered breathing patterns in patients with changes of posture, and also it has founded an understanding of why many patients with

vestibular and balance disorders also hyperventilate. The rehabilitation of these patients appears to be improved when the hyperventilation component is recognised and the breathing pattern re-educated.

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Obesity and lung function

The paper by Schachter *et al*¹ in the January 2001 issue of *Thorax* is interesting in that it has a number of unusual and, it is suggested, inexplicable findings that appertain to various indices of ventilatory capacity. With all due deference, we would suggest that there is an explanation for these unusual findings.

Firstly, mild, moderate and severe obesity are all associated with an incremental reduction in both the forced expiratory volume in 1 second (FEV₁) and the forced vital capacity (FVC).²⁻⁴ Secondly, in normal subjects and in those who have pure restrictive impairment, the FVC and FEV₁ are within 2-3% of each other when expressed as a percentage of predicted. The FVC cannot be significantly smaller than the FEV₁ when expressed as a percentage of predicted except in certain neurological diseases. It is noted that the criterion for acceptance of the spirometric volumes was "two measurements of the FEV₁ within 100 ml of each other", suggesting the FVC was ignored. Table 3 in the paper by Schachter *et al* shows that, when expressed as a percentage of predicted, the FVC in every instance is less than the FEV₁. In most groups there is a relatively small difference except for those who are moderately or severely obese.

The reason for the disparity in the FEV₁ and the FVC is that the FVC manoeuvre was likely to be incomplete, especially in those who are overweight. Some normal large men over 74 inches in height take 12-16 seconds to complete their FVC manoeuvre. Unfortunately, these days few physicians spend any time doing routine spirometric testing themselves as they rely on their technicians. "Shoe leather" epidemiologists such as Archie Cochrane and Ian Higgins have been replaced by computer addicted statisticians who are thrown into ecstasy by what they can do with a computer, but who fail to realise that their original data may be flawed.⁵ Were Dr Schachter and her colleagues to review their tracings, we suspect that they would find that at least some of the FVC manoeuvres had been aborted prematurely. If only flow-volume loops are relied on, it needs to be borne in mind that it is difficult—and, indeed, usually impossible—to know whether the FVC manoeuvre has been completed.

The other surprise in the study is that the smaller the FVC when expressed as a

percentage of predicted, the higher the FEF_{25-75} . What is abundantly clear, however, is that, when the FVC manoeuvre is incomplete, then the FEF_{25-75} is "pushed" further up the steeper portion of the FVC curve so that the FEF_{25-75} is artefactually increased—that is, the more premature the termination of the FVC, the higher the FEF_{25-75} .^{6,7}

The findings of wheeze in those who are obese is not surprising, especially in cigarette smokers. When a markedly obese subject exercises on the treadmill wheezes are frequently heard, providing he can continue for a sufficient length of time. In a subject who has asthma the FEV_1 is generally reduced appreciably more than is the FVC. The exact opposite applies in overweight patients included in the study by Schachter *et al.* It can be seen from table 3 that the FVC in both the moderately obese and the severely obese is significantly lower than the FEV_1 measurement. Finally, one would expect the most obese subjects to become short of breath much more quickly, especially if some of them had exercise induced asthma. This would explain the much more frequent medication usage.

We suggest the disparate reduction in the FVC and FEV_1 seen in obese subjects has little to do with asthma, but is a direct effect of their obesity and the fact that some of the FVC measurements have been significantly underestimated.

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- Schachter LM, Salome CM, Peat JK, *et al.* Obesity is a risk for asthma and wheeze but not airway hyperresponsiveness. *Thorax* 2001; 56:4-8.
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AUTHOR'S REPLY I am pleased to note that Drs Ahmad and Morgan were able to pick up on one of the main points of our paper—that reduced lung function and respiratory symptoms in obese people may well be an effect of their obesity and are not necessarily an indication of asthma. However, they imply that the differences in spirometric function that we observed were due to technical error rather than to an effect of obesity. As a physician who has spent a substantial amount of time measuring routine spirometric parameters on over 300 severely obese patients, I disagree with their suggestion.

As with a number of previous studies,¹⁻³ we found that moderate and severe obesity were associated with an incremental reduction in both FEV_1 and FVC. In our normal subjects the FEV_1 and FVC, expressed as percentage predicted, were within 2.6% of each other. The mean absolute values for FEV_1 and FVC

in this group were 3.5 l and 4.0 l, respectively. The mean FEV_1 /FVC% in all groups was 85.8-87%, which is well within the normal range for this age group.

Our results show that most patients with severe obesity have FVC within the normal range, although it is reduced when compared with patients with normal body mass index. We do not have other measurements of lung volumes to confirm further the presence of restriction, but these findings are consistent with those of other studies.

It is unlikely that our results are due to a systematic underestimation of FVC in the obese groups. In my experience, obese patients who are otherwise healthy do not usually have evidence of airway obstruction or a need for prolonged expiration times to complete their FVC manoeuvres. Their spirometric tracings show that the expiration reaches a clear plateau within 2-3 seconds in the same way as is seen in non-obese subjects.

The technical staff involved in the collection of the data are extremely well trained and the measurement methods are well standardised. The same two senior researchers were present at all studies and trained and supervised all other staff involved. Our senior researchers and technicians are very experienced, having performed many large epidemiology studies involving thousands of subjects. The FVC manoeuvre was performed to a minimum of 3 seconds. The criterion for acceptance of the spirometric volumes included both FEV_1 and FVC and required both parameters to be repeatable to within 100 ml. These procedures are stricter than the ATS guidelines which allow for 5% variability between blows. If it appeared that the patient was obstructed, then FVC was performed until expiration was complete.

In reporting our results we did not attempt to draw any conclusions from the very small differences between the percentage predicted FEV_1 and FVC values. Instead, we limited our discussion to the more substantial differences between groups based on body mass index—the hypothesis that we set out to test.

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BCG re-vaccination

The most recent guidelines on the control and prevention of tuberculosis¹ recommend that "individuals working as health care workers, irrespective of age, who are previously unvaccinated and who are negative or Heaf grade 1 on tuberculin testing, should receive BCG vaccination". The algorithm in fig 2 suggests that a health care worker without a BCG scar or documentation of prior BCG should be vaccinated if Heaf testing is negative or grade 1. Presumably the algorithm, but not the text, could apply to those previously vaccinated, but without a document or a scar.

Not infrequently, health care workers present for pre-employment screening with no BCG scar, a possible or doubtful history of prior BCG vaccination, almost always without documentation. The previous guidelines² recommended that "individuals with a negative or grade 1 Heaf reaction should receive BCG vaccination" and "those without a satisfactory reaction require a further tuberculin test and, if this is negative, a second vaccination". The latter advice does not appear in the 2000 guidelines.

It is sometimes argued that the risk of developing a nasty local reaction at a BCG re-vaccination site is not warranted by the additional protection against occupationally acquired tuberculosis, which may or may not be derived from repeated BCG vaccination. In practice, we tend to favour this approach and avoid (re-)vaccinating those who may have been previously vaccinated. This is contrary to the 1994 BTS guidance, but the 2000 guidelines are less clear on the issue of re-vaccination. Has the Joint Tuberculosis Committee changed its view?

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- Joint Tuberculosis Committee of the British Thoracic Society. Control and prevention of tuberculosis in the United Kingdom: Code of Practice 2000. *Thorax* 2000;55:887-901.
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AUTHORS' REPLY The Joint Tuberculosis Committee has not changed its view on the re-vaccination of health care workers with BCG. In 1994 BCG vaccination was only recommended for those without a prior BCG vaccination (usually with absence of a typical scar) who were tuberculin negative.¹ In the 2000 evidence based guidelines BCG vaccination was again recommended only for those who did not have a definite BCG scar (as recorded by an experienced person) or documentary evidence of a prior BCG and were tuberculin negative.² These recommendations are consistent. There is no evidence that re-vaccination in health care workers or others who have been given BCG vaccination effectively gives any additional protection. The only issue is what is to be taken as evidence of BCG vaccination. The best proof is a typical scar, but documentary evidence is also accepted. In the absence of either, in someone who states that they have been vaccinated, a risk-benefit assessment is effectively made.

The risk of vaccination in someone who has been vaccinated already is that they have an accelerated BCG reaction. Conversely, if a health care worker has not actually been vaccinated, they have no protection against tuberculosis if tuberculin negative, with an increased risk being shown.³ The Joint Tuberculosis Committee's judgement of this risk benefit analysis in 2000—as in 1994—was that, if BCG vaccination could not be proven to have been given, it should be given to tuberculin negative health care workers.

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Reliability of PEF diaries

The paper by Kamps *et al* reported that peak expiratory flow (PEF) diaries kept by asthmatic children were unreliable.¹ They found that about 25% of readings recorded by an electronic meter were not identical to those written in the diary. The Vitalograph 2110 meter was used for this study with subjects recording the best of three blows on each occasion. However, the 2110 meter does not necessarily record the highest value indicated. Rather, it records the highest value for good quality blows in preference to poor quality blows, even if the poor blow is a higher value. A good quality blow is one in which PEF is achieved between 40 and 290 ms of starting, a poor blow being one in which the time to achieve PEF is outside this window. Thus, the value recorded by an electronic meter is not necessarily the best value as observed by the subject.

Several members of our department staff have reliably kept serial PEF records using the Vitalograph 2110 electronic meter. We found that, even though the observers were "experts", 6–20% of readings recorded by the electronic meter were different from the maximum value recorded in the written diary. In one instance the value recorded by the meter was 146 l/min lower than the highest value recorded by the observer. In instances where the electronically stored reading was different from the maximum recorded written value, the value recorded by the meter was still among those noted by the observer. Furthermore, as blows are performed in quick succession, some subjects have reported occasional difficulty in recalling the last one or two digits of the best value. Inaccuracies can also arise when the clock of the logging meter shows the wrong time.

Of the 25% or so recordings that were reported as being incorrect in the study by Kamps *et al*, it is possible that a significant proportion could have genuinely been observed by the subjects but not recorded as such by the meter. It is wise to be as critical of electronically stored data as the traditional hand written record.

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- 1 Kamps A, Roorda R, Brand P. Peak flow diaries in childhood asthma are unreliable. *Thorax* 2001;**56**:180–2.

AUTHORS' REPLY We thank Dr Anees and colleagues for their valuable comments on

our paper. With regard to their first point, we were aware of the fact that the Vitalograph only records good quality PEF manoeuvres. Because of this, we tested the Vitalograph devices before handing them out to the patients in our study and found that 3.6–10.7% of PEF readings were different from the maximum recorded value in the (reliably kept) written diary. In order to minimise this problem we made sure that all patients were carefully instructed on how to perform "good quality" PEF manoeuvres on the Vitalograph. Although Anees *et al* are right that the technical performance of the Vitalograph may partly explain the incorrect PEF entries, this cannot fully explain the high prevalence of incorrect entries observed in our patients (22–32%).

Moreover, the large number of missing and invented PEF values (20–40%) were certainly not due to the technical characteristics of the Vitalograph, as these PEF values were simply not blown. We therefore feel that our conclusion that peak flow diaries are unreliable remains valid.

Monitoring of PEF with an electronic PEF meter may not only be preferable for excluding missing and invented PEF values, but also because only good quality PEF manoeuvres are recorded.

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Lung cancer survival

We read with great interest the article by Gregor and colleagues on the management and survival of patients with lung cancer in Scotland diagnosed in 1995.¹ The results were disappointing, but we congratulate them for their recognition of present conditions and for reporting the scientific analysis. In the 1990s several new chemotherapeutic drugs for lung cancer emerged, although the results of the large phase III studies were disappointing.^{2,3} It is fair to say that standard treatment for advanced lung cancer, especially for non-small cell lung cancer, is not yet established. Several well designed clinical trials have been reported in first class medical journals, but the prognosis of lung cancer is still poor. Published regimens for selected patients to define new study protocols may be inappropriate for use in clinical practice. Many of our patients are ordinary people who have several underlying illnesses and may be too sick to be enrolled into clinical trials, and it is they who need treatment which can be applied in common practice. There is no disagreement on the point that the level of evidence obtained from the retrospective study of heterogeneous patients is low; however, we believe that a

study with well analysed data of patients who are otherwise not eligible for randomised control trials also has clinical significance and would benefit such patients. We hope that the first class medical journals such as *Thorax* continue to encourage, not only randomised control trials, but also case reports or retrospective studies to complement the area where strong evidence is unobtainable.

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NOTICES

Respiratory Medicine

A conference on Respiratory Medicine will be held at the Royal College of Physicians of Edinburgh on 26 October 2001. For further information contact Ms Eileen Strawn, Symposium Coordinator. Telephone 0131 225 7324. Fax 0131 220 4393. Email: e.strawn@rcpe.ac.uk. Website: www.rcpe.ac.uk.

Pharmacology of Asthma

A course on the "Pharmacology of Asthma" organised by Professor Peter Barnes will be held at the Imperial College School of Medicine at the National Heart & Lung Institute in collaboration with the Royal Brompton Hospital, Dovehouse Street, London SW3 6LY, UK on 26–29 November 2001. The course is suitable for physicians or scientists with an interest in the pharmacology and therapeutics of asthma. For further information please contact the Postgraduate Education Centre, Imperial College School of Medicine at the National Heart & Lung Institute, Dovehouse Street, London SW3 6LY. Telephone: 020 7351 8172. Fax: 020 7351 8246. Email: shortcourses.nhli@ic.ac.uk