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Authors’ reply
We are most grateful for the response to our call for an international registry for idiopathic pulmonary fibrosis (IPF) from the European IPF Network collaborators.1 This most timely registry should be the forerunner of similar disease-specific approaches to problem-solving in health care. The concept of biomaterial collection in conjunction with clinical data should encourage participation from scientists with an ability to contribute to knowledge of the pathogenesis of IPF. We feel this most positive beginning should be a stimulus to other groups, particularly in North America and the Asia-Pacific region, to follow this European initiative.

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Competing interests: None.

REFERENCE

Strategies to screen for adrenal suppression in children with asthma: there is no consensus among UK centres

Inhaled corticosteroids were designed to avoid the numerous adverse effects of oral corticosteroids in the treatment of asthma. In children, inhaled corticosteroids have been proved to be highly effective and it was initially thought that the risk of adrenal suppression was low.2 As a result, high “off-licence”3 doses (eg, >1000 μg/day of fluticasone propionate) were recommended in difficult cases by national guidelines.4 The efficacy and safety of such high doses has been seriously questioned by the reporting of around 30 cases of life threatening acute adrenal crisis, including one death, in children maintained on inhaled corticosteroids (largely high dose fluticasone propionate).5 Current guidelines therefore caution that doses >400 μg/day of fluticasone propionate or equivalent should be prescribed by a specialist who should be aware of the potential for adrenal suppression.6 A range of tests, varying in invasiveness and complexity, including early morning urinary cortisol, low and high dose synacthen tests and the potentially hazardous insulin–hypoglycaemia test, exist to assess adrenal function in children. It is uncertain, however, which test is most appropriate to detect clinically relevant adrenal suppression in children with asthma.7 There are other important questions, such as the reproducibility of individual results, threshold doses above which to test, how often to repeat tests or indeed should we test at all?6

We therefore investigated current practice in screening children with asthma for adrenal suppression in the UK. A postal questionnaire was sent to each of the 23 tertiary paediatric respiratory centres of which 14 responded. Only eight (57%) centres have an official policy and of these in only 25% is it extended to regional hospitals. In children prescribed fluticasone propionate, seven (50%) centres test at >500 μg/day, three (21%) at >1000 μg/day and in four (29%) it varies. For beclomethasone, seven (50%) test at >200 μg/day, two (14%) at >500 μg/day and in five (36%) Oral prednisolone and nasal sprays were taken into account by eight (57%) and four (29%), respectively. A low dose synacthen test is performed by seven (50%), three (21%) high dose synacthen test, one (8%) morning cortisol and in three (21%) it varies. Five different abnormal cortisol responses are used. Tests are repeated annually by 10 (71%), two (15%) test 6 monthly and only once, respectively. Steroid cards are issued by eight (57%) of the centres. In total eight (57%) of the respondents regarded adrenal suppression as a significant problem and nine (64%) have changed their practice over the past 5 years.

We therefore conclude that there is no national consensus in the UK on screening of children with asthma for adrenal suppression. Specific areas of divergence include: the threshold dose to start testing, which test to perform, how to interpret the results and when it should be repeated. Further studies and discussions are required to establish an evidence base about how best to screen for this potentially life threatening problem.

Irrespective of the screening policies used in different centres, it is vital that the assumption is made that a child may be adrenally suppressed unless there is clear evidence that this is not the case. Issuing of steroid information cards to children and families is one method of reinforcing this fact. Only just over half of responding centres pursue such a policy. It should be noted however that there is little published evidence to show benefit, or equally detriment, from the use of steroid cards.

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LETTERS
International registry for idiopathic pulmonary fibrosis

We have read with great interest the recent review by Wilson et al stating the case for an international registry for idiopathic pulmonary fibrosis (IPF).1 This timely proposal prompts us to inform the community that, effective from 1 January 2008, the European Commission is funding a new network entitled ‘European IPF Network: Natural course, Pathomechanisms and Novel Treatment Options in Idiopathic Pulmonary Fibrosis’ (euIPFnet; www.pulmonary-fibrosis.net). Among many other scientific goals, the euIPFnet will establish a European-wide, internet-based registry (euIPFnet) and biobank (euIPFnetbank) for IPF which, in principle, will be open to all interested colleges. The opening of this registry is scheduled for mid 2008 (please follow news on www.pulmonary-fibrosis.net). Key features of this registry will be the collection of all relevant baseline and follow-up clinical data from patients with IPF as well as bronchoalveolar lavage fluid, blood and tissue specimens. Rigorous multidisciplinary verification of the diagnosis will be undertaken by external experts. We plan to quantify the frequency of respiratory infections, extent of pulmonary hypertension, quality of life and response to treatment modalities. Using the collected biomaterials, we intend to investigate novel surrogate parameters of disease progression, establish new disease-specific markers and identify novel candidate genes relevant to the pathophysiology of IPF. Our goals exactly identify novel candidate genes relevant to the establishment of new disease-specific markers and surrogate parameters of disease progression, biomaterials, we intend to investigate novel treatment modalities. Using the collected infections, extent of pulmonary hyper-quantify the frequency of respiratory as bronchoalveolar lavage fluid, blood and

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Predicting risk of asthma in wheezing infants

Devulapalli et al’s paper attempts to answer the commonly encountered clinical question, “What is the risk of asthma in this wheezy infant?” While welcoming this attempt, we wish to put this into perspective and draw comparison with our similar work on the Isle of Wight Birth Cohort published 5 years ago.

Findings that children with asthma at 10 years often had recurrent bronchial obstruction (RBO+ve) at 2 years are not new. We previously reported that recurrent chest infections at 2 years (causing airway obstruction and wheeze) increases the risk of asthma development at 10 years by more than fourfold. A simple risk score such as that of Devulapalli et al., not reliant on invasive testing, is an attractive concept. However, there are significant shortcomings in this work. For wide acceptability, the factors contributing to the risk scores should be unambiguous. The proposed risk score relies on “severity”, which is difficult to define and measure in this context. Hospitalisations for wheezing in infancy do not necessarily reflect a set degree of severity. Secondly, the outcome variable of diagnosed asthma is potentially contentious given the subjective nature of that label. The reasons for not including an objective measure such as bronchial hyperresponsiveness to consolidate asthma diagnosis is not clear. Alternatively, a phenotypic analysis using “wheeze” rather than “asthma” may be less prone to subjective bias. We have demonstrated that most childhood asthma originated in infancy as “early onset persistent wheeze”. We feel that a phenotypic understanding is vital in asthma where analysis of isolated events in time could convey a misleading snapshot of a complex disease. Finally, any case control study is prone to misclassification based on response evaluation and investigator bias. Reliance on such methodology to create a risk score could draw into question the potential validity of that tool.

The authors fail to compare their “risk score” with our published risk scores to show that theirs is indeed an improvement on what has already been known. We proposed a simple and practical risk scoring system for outcome of early life wheeze comprising four factors (family history of asthma, recurrent chest infections at 2 years, absence of nasal symptoms in infancy and atomic sensitisation at 4 years), showing independent significance for persistence of early wheeze to age 10 years in our cohort. The presence of all four was associated with a positive predictive value of 83.3 and a negative predictive value of 63.9 for persistent disease, compared with corresponding values of 54.3 and 86.8 with the score outlined by Devulapalli and colleagues.

The ability to accurately predict outcome of early life wheeze is clearly desirable. However, any new proposal should be considered in the context of existing work. Comparisons should be made in terms of sensitivity and specificity, and common ground should be sought to eventually develop a predictive scoring system, which is practical, valid and clinically useful. We are certainly not there yet!

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Competing interests: None.

REFERENCES

Authors’ reply
We wish to reply to Drs Raza, Kurukulaaratchy and Arshad who commented on our recent article. Our primary aim for making a severity score was to try to predict the prognosis of early life obstructive airways disease, independent of invasive examinations or measurements, and easily applicable for use in other studies and in primary care. Thus it is not clear to us why Raza et al find the factors used in our severity score difficult to define, including our use of hospitalisations for obstructive airways disease. In our view, hospital admission because of bronchial obstruction is an objective measure of severity, which is easily verified and recorded.

They question the use of diagnosed current asthma as the outcome, suggesting that this may reduce the validity of the tool and criticise that bronchial hyperresponsiveness (BHR) was not used to consolidate the diagnosis of asthma. We disagree with both of these comments. In fact, as was clearly stated, exercise induced bronchoconstriction (EIB), a measure of BHR is part of our well defined term “current asthma” used for the 10 year follow-up study of our birth cohort, including studies on “asthma prevalence,” lung function at birth versus asthma at 10 years of age asthma genetics. Our definitions of asthma and current asthma are stricter than in many other studies including, but not limited to, “wheeze” alone, requiring at least two out of three criteria (symptoms/medication or the presence of EIB in the last year or during the investigation) to acquire a definition of asthma. While “wheeze” as the outcome may be appropriate in English speaking countries, it is not a term used in most other languages. Consequently, it appears less stringent, more prone to subjective reporting but nonetheless seems to be more frequent in our and other studies than a history of asthma and current asthma. Furthermore, the authors themselves have also used the term “asthma” when reporting from their own birth cohort study.

Raza et al further criticise the fact that we did not cite their paper, describing their risk score for persistent wheeze at the age of 10 years. Although this may be an omission, our aim was not a retrospective risk assessment of persistent wheeze but prospectively to assess the risk for current asthma at 10 years in children with recurrent bronchial obstruction at 2 years. Furthermore, as the authors themselves demonstrated in their cohort, the positive predictive value (PPV) for wheeze at 10 years from the score applied at 4 years was much higher than when applied at 2 years (PPV = 0.475), which is considerably less than our 2 year score. The severity score applied is probably age specific, highlighted by our own score which was not found to be useful at 1 year of age.

In our view, the comments of Raza et al do not diminish the validity of our severity score, but we stress that the present as well as any other scores must be confirmed in other studies in different populations before any general acceptance can be reached.

C S Devulapalli, K C L Carlsten, O Håland, M C Munthe-Kaasa, M Pettersen, P Mowinckel, K-H Carlsten
Ullevål University Hospital, Oslo, Norway

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