

The authors suggest that the changes we have observed in our trial could be a speeding up of a normal maturational effect. Half of the child outcomes we measured showed changes compatible with this interpretation, but the other half do not. The latter show either continuing improvement in both groups or more change in the intervention than control group at six month follow up. We will be publishing the results of our 12 month follow up.

The authors also ask whether our results are clinically significant. The differences between intervention and control group scores at 6 months represent effect sizes of around 0.3 (of a standard deviation). In clinical terms such changes are regarded as small. However in public health terms a small change in a large group is often more important than a big change in a small group, so these differences are of public health significance.

Dr Srinivas and colleagues also ask about cost effectiveness. We did not undertake a formal economic analysis in this study, but the costs of the intervention were mainly in the staff time. Taking account of time spent in supervision, but not training, the costs fall somewhere between six and ten hours of group leader time per parent attending the course. Effectiveness in this context is more difficult to estimate and cannot be measured only in terms of immediate behavioural outcomes. The evidence that the quality of parent-child relationships has a long term impact on mental and physical health and on social well being is mounting. Estimating all the societal benefits of this intervention was beyond the scope of our study but could be very considerable.

Dr Srinivas and colleagues also suggest that our results may be invalid because they were not collected by researchers blind to intervention group. All our outcomes were based on self-report by parents, so blinding of study personnel is irrelevant. It is unfortunately not possible, in trials of health promoting interventions, to blind participants to the intervention. Although it is theoretically possible to make "blinded" observations of some of these outcomes, such approaches greatly increase the cost of studies and were not possible with the funding we had available.

Finally, and perhaps most importantly, Dr Srinivas and colleagues suggest that limited NHS resources should be concentrated where they are needed most, and not on relatively well middle classes. There will be many readers who agree with them. The pros and cons of population versus high risk approaches are much debated. The point, however, is that these approaches are not mutually exclusive and authoritative sources^{6,7} of advice on child health now recognise the need for both. The arguments in favour of population approaches to the promotion of mental health were cogently put many years ago by Geoffrey Rose,⁸ to whose paper we direct interested readers.

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Adrenal crisis due to inhaled steroids is underestimated

In response to comments by Pearce and Mabin on Professor Russell's editorial¹ on our paper.²

They doubt that our survey underestimated the true scale of the problem. I can inform them that this is not the case. Since our survey was completed we have been notified of a further seven cases (five children, two adults). All but one of the children had been taking fluticasone in similar dosages to those reported in our survey. Three of these were critically ill in intensive care and an 8-year-old girl died due to adrenal crisis. The remaining child was only 20 months old and had been given budesonide in extremely high doses of 2000-8000 mcg/day.³ Both adults had been taking fluticasone (1000 mcg/day, 2250 mcg/day).

Case reporting clearly plays a much greater role than clinical studies in post license surveillance of new drugs. In an international 20 year study of drug safety discontinuations, nearly all occurred as a result of case reporting. Despite studies the authors concluded that "it is impossible to know fully all the facts about a drugs effects both beneficial and harmful at the time of approval".⁴ Further, it is incorrect for Pearce and Mabin to say that "studies show no increased risk of hypothalamic pituitary axis (HPA) suppression with fluticasone propionate when compared with other inhaled steroids". There are many studies arguing against this assertion.⁵⁻⁹ Actually, there is a serious disparity between the results of different safety studies involving fluticasone which requires explanation. While the product monograph claims "mean plasma cortisol concentrations remained within the normal range for adults and children demonstrating that, even at high doses (2000 mcg), fluticasone propionate is well tolerated with regard to side effects",¹⁰ many studies suggest otherwise. For example, as little as 88 mcg/day of fluticasone can produce 10% adrenal suppression¹¹ and 352 mcg/day can produce 50% adrenal suppression, a considerably greater degree than the equipotent dosage of beclomethasone,⁹ leading those authors to conclude that "increasing the dose beyond this point of maximum efficacy... resulted in increasing systemic effect, especially with fluticasone metered dose inhaler with its CFC propellant"—exactly what we have reported.

Pearce and Mabin correctly state that "individuals have differing sensitivities to inhaled corticosteroids. Idiosyncratic responses to inhaled corticosteroids may occur even at licensed doses". I agree, however, such patients "disappear" in large multicentre studies, particularly when the pharmaceutical company will not make available data on individual patients.¹² This is of concern as there is evidence that fluticasone is associated with significantly more individual abnormally low cortisol values than other inhaled steroids.¹³ Also, over 75% of patients developed adrenal crisis greater than one year after starting fluticasone, and it is known that length of time taking inhaled steroids is a major factor in determining the frequency of side effects.¹⁴ How many studies of fluticasone have lasted greater than one year?

Pearce and Mabin correctly state that in recent years, when paediatricians decide that high doses of inhaled corticosteroids are necessary, more are choosing to prescribe fluticasone propionate. However, they need to explain why only 2 cases of adrenal crisis (both adults) in over 30 years of prescribing inhaled corticosteroids had ever been reported in literature before the introduction of fluticasone propionate allowing Russell to make a claim in 1994 that "there is no firm evidence that any child has ever come to harm as a result of adrenal suppression induced by inhaled corticosteroid therapy".¹⁵ Further, some cases reported in our survey had previously been taking very high doses of either beclomethasone or budesonide but only developed adrenal crisis some time after changing to fluticasone.¹⁶

Finally, it is unfair to blame doctors for prescribing fluticasone "off label". Almost half of all drug prescriptions for children in hospital are either unlicensed or off label.¹⁷ Prescribers have every right to expect a reasonable margin of safety with a drug should they decide that off label dosages are necessary in children. Bearing in mind that there have now been two reported deaths and many intensive care cases, the risks of prescribing fluticasone off label appear greatly to exceed any possible benefits for patients, and will have serious medico-legal implications for doctors, particularly when there is not a single study showing better efficacy for fluticasone compared with other available inhaled corticosteroids.¹⁸

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Moderately high doses still need to be considered for very young children

In relation to the question of adrenal suppression when using higher doses of inhaled corticosteroid, I believe there is an aspect of dose selection which has not been mentioned by previous authors.

There are limited data on the question of intra-pulmonary drug deposition in children under 3 years but the studies that have been published seem to indicate that around 1–2% of the drug released into the spacer reaches

the airways,¹ compared to 15–17% in an adult using the same device. Based on this figure, it seems reasonable to prescribe similar doses to very young children and adults alike.

I note that none of the cases of adrenal impairment have been reported in children under 3 years of age; most of them are significantly older. This could be partly because higher doses are not being used in this age group, but might also be confirmation that a smaller fraction of the drug reaches the airways.

I would argue that there are good reasons to use higher doses, at least initially, when treating very young children. The diagnosis of asthma is exceptionally difficult here, and if a “trial of treatment” is ineffective, one wishes to be reasonably confident that the reason for the negative response was not related to an inadequate dose. A negative response allows the clinician to withdraw ineffective steroid treatment in those infants who may well not have asthma at all. If there is an excellent response, the dose of steroid should be stepped down to the minimum required to control symptoms.

Finally, for clarity, the doses I am referring to are budesonide/beclomethasone 800 mcg/day or fluticasone 500 mcg/day.

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Cultural representation of newborn feeding

Nicoll and Williams¹ suggested that attitudes to breast feeding need to change: “everyone (not just women) needs to see breast feeding as normal and education needs to start early”. In Italy breastfeeding rates are low.² Numerous training initiatives have been set up to heighten awareness with the aim of promoting breastfeeding. These initiatives have been based on implementation of the Baby Friendly Hospital Initiative;³ three hospitals in the country being nominated “Baby Friendly”.

I was recently invited to discuss the importance of breastfeeding for newborns with two 4th year junior school classes (41 children in total (17 girls and 24 boys), aged between 9 and 10). Before talking to the children, I asked them to draw on a sheet of paper everything they thought was necessary for a baby to grow up healthy. All except four drew a feeding bottle next to a baby; 15 children drew a baby alone with a bottle; only three children drew a baby in his/her mother’s arms, but all these the babies were still holding a bottle. Only two drawings showed the baby with both parents and in without a bottle; the other two drawings without a bottle depicted a scene in the hospital. When I asked how many of them thought that formula milk was the same as mother’s milk, 28 out of 41 raised their hands. I believe this reflects the widespread tendency, also reported in other countries,⁴ not only to consider breastfeeding the same as artificial feeding, but “artificial” as “natural”.

In an historic and ever pertinent editorial,⁵ the *Lancet* hoped a warm chain for breastfeeding could be created, and warned about the ambivalent messages often encouraged by the marketing campaigns of formula manufacturers. I feel that the implementation of interventions aimed at supporting breastfeeding should not be limited to the healthcare system, but should cover a wider range of activities, aimed at changing the cultural representation of newborn feeding and at defending breastfeeding.

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