Letters

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Routine screening of children returning home from the tropics

Authors' definition of asymptomatic children is not the one usually accepted

EDITOR—Information on routine screening of children coming back from the tropics is scarce, but we do not agree with Brouwer et al's conclusion that routine screening of children without symptoms is worth while.[1]

Firstly, their definition of asymptomatic children (those seen at their scheduled appointment) is not the one usually accepted (those without symptoms). Parents of children with symptoms or signs not severe enough to seek immediate medical advice may have waited for their scheduled appointment to have the complaint investigated. In fact, 71 (28%) of the 253 so called asymptomatic children had symptoms. If a diagnosis was made in all these children, a diagnosis would have been found in only 28 (99 – 71) (15%) of the 182 (253 – 71) truly asymptomatic children; if a diagnosis was made in only half of the "asymptomatic" children with symptoms, a diagnosis would have been found in 64 (99 – 35) (35%) of the 182 truly asymptomatic children—still less than the figure given (39%). Only 98 (74%) of the 132 cases in which a diagnosis was made were treatable, which further decreases the value of screening.

Secondly, to assess the usefulness of a standard protocol for routine screening it would be necessary to estimate the positive predictive values of clinical criteria and laboratory variables for finding a diagnosis. As the authors state, the clinical examination was not very helpful. We doubt that the urea and creatinine concentrations led to any of the diagnoses found. We find that a thick smear in truly asymptomatic children is useless.

More careful analysis is needed before routine screening is advised for all children without symptoms returning from the tropics. The need for a specialised medical consultation before departure should be reinforced; children should be given vaccines for preventable diseases, including hepatitis A and B, and parents advised to seek medical help for any abnormality identified in their children. Children returning with symptoms should be investigated with laboratory tests. In this context the positive predictive values of the tests are much higher.

For truly asymptomatic children the problem is not yet solved; Brouwer et al give some background, but their proposed screening protocol is too extensive and in Switzerland would cost about Sw fr550 (£220) a child. Before routine screening for all asymptomatic children is recommended, cost efficacy and cost benefit analyses must be performed and different options compared.

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1 Brouwer ML, Tolboom JJM, Hardeman JHJ. Routine screening of children returning home from the tropics: retrospective study. *BMJ* 1999;318:568-9. (27 February.)

Authors do not prove case for routine screening

EDITOR—We are unable to agree with Brouwer et al's conclusion that routine screening of children returning from the tropics is worth while and do not believe that the intervention described is screening.[1]

Screening has been defined as "the systematic application of a test or inquiry, to identify individuals at sufficient risk of a specific disorder to warrant further investigation or direct preventive action, amongst persons who have not sought medical attention on account of symptoms of that disorder." [2] In concluding that their intervention was worth while the authors did not consider whether it met established criteria for a screening programme such as those of Wilson and Jungner (box).[3] Many of the investigations used by the authors are non-specific and poorly discriminatory. Thus the clinical or public health importance of their positive results is questionable.

The authors' belief that the patients in their study were representative of most children returning from sub-Saharan Africa is also difficult to accept. The children of expatriate workers are likely to differ greatly from most children returning to European countries from sub-Saharan Africa, most of whom are children of immigrants or refugees. Perhaps a case could be made for some sort of screening for immigrants and refugees, but that case has not been made here.

The authors' failure to consider the cost of such a programme is an important omission. In a cost constrained health service, economic evaluation should form a part of any recommendations for a new service. We are not convinced that the benefit gained from routine testing for tropical diseases of

Principles of screening[3]

- The condition should be an important health problem
- There should be an accepted treatment for patients with recognised disease
- Facilities for diagnosis and treatment should be available
- There should be a recognisable latent or early symptomatic stage
- There should be a suitable test or examination
- The test should be acceptable to the population
- The natural course of the disease, from latent phase to declared disease, should be adequately understood
- There should be an agreed policy on whom to treat as patients
- The cost of case finding (including diagnosis and treatment of cases diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole
- Case finding should be a continuing process and not a "once and for all" activity

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symptomatic and asymptomatic children returning from the tropics is justified by the large cost required to establish and run such a service. A more appropriate public health intervention would be advice to avoid exposure to tropical infections and to use appropriate chemoprophylaxis and immunisation when available.

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1 Brouwer ML, Tolboom JJM, Hardeman JHJ. Routine screening of children returning from the tropics: retrospective study. *BMJ* 1999;318:568-9. (27 February.)
2 Department of Health. *Annual report of the national screening committee*. London: DoH, 1997.
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Authors' reply

EDITOR—Blaise et al's comment that not all "asymptomatic" children were really without symptoms does little justice to paediatric reality. A workable demarcation line between being asymptomatic or symptomatic is difficult to draw. Use of a structured questionnaire leads to considerable overreporting, since parents take a safe approach and mention mild complaints for which they normally would not have consulted a doctor. In 71 of 253 asymptomatic cases symptoms of abdominal pain and diarrhoea (generally in combination) were reported, but this did not justify their classification as symptomatic. Without arguing about numbers of treatable diagnoses, we even consider 98 treatable diagnoses enough to support routine screening of children who have been in the tropics. We agree that in drafting a protocol one should also look at the predictive value of tests. Our format is similar to that advised for routine health assessment of returning adult expatriates and long term travellers in a highly recommended textbook.[1] In asymptomatic cases routine measurement of urea and creatinine concentrations, as well as a thick smear in the absence of fever or visible signs of filariasis, was indeed not useful. Screening is relatively expensive, even when some laboratory testing and chest radiography is performed only when indicated. Vaccinations for hepatitis A and B before travel certainly cut costs of hepatitis A and B serology. The remaining tests, including the tuberculin skin test, we still strongly recommend as part of a standard health assessment after travel to the tropics.

Okereke and Gelletlie compare our screening practice with that of epidemiological screening. Here we find ourselves on different wavelengths. Our screening is basically a return health assessment; the issue of public health importance does not apply. Children of expatriate workers differ greatly from most children immigrating or seeking refuge from sub-Saharan Africa. In the Netherlands we have for many years screened foreign-born adoptive children.[2] There remains an important query over whether we should routinely screen children of families who seek refuge in Western countries. This brings us back to basic questions, such as what is the cost benefit? The answer may depend, among other things, on the nutritional state of the child, the region the families came from, the conditions they had to live in while in transit, and whether the parents have been permitted official refugee status by the receiving country.

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1 Lange WR, Stich AHR, Fleischer K, Shlim DR. Expatriates and long-term travellers. In: DuPont HL, Steffen R, eds. *Textbook of travel medicine and health*. Hamilton, Ontario: Decker, 1997:291-7.
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In screening for congenital cataract, many false positive referrals will occur

EDITOR—Rahi et al's data enable the annual incidence of congenital cataracts in the United Kingdom to be estimated.[1] The incidence is roughly 3 per 10 000 live births after allowance is made for their assessment of the non-completeness of the data. This rarity does not make the condition unimportant but does raise considerable difficulties for a screening programme. This is especially so when the apparently simple screening test relies on the interpretation of a clinical sign that is difficult to elicit from many infants in the circumstances in which the test is usually performed.

The challenge for clinicians is to retain high sensitivity for detecting the abnormality without unduly reducing the specificity. In addition, they must resist the inevitable pressure to reduce their sensitivity in the light of the large number of false positive results they detect. To put this in perspective, only one in every 180 infants referred for further assessment would have the diagnosis confirmed even if the clinician achieved the impressive 93% sensitivity and 95% specificity achieved in the small study of ophthalmoscopic diagnosis in 3-30 year old subjects to which the authors refer.[2] Thus a hospital paediatrician doing 20 assessments a week would see one case in four years but would have referred one case each week throughout that time. In the community a full time general practitioner would refer one case each year but it would take six working lifetimes to see a true case.

Faced with this level of false positive results, most clinicians are likely to increase their specificity substantially, with the almost inevitable result that their diagnostic sensitivity will fall. That the current screening programme achieves about 50% sensitivity may be a cause for modest celebration. Unless an even more specific screening test is developed, attempts to reduce the number of cases missed by the current system will require the screening doctors and ophthalmologists to accept many more false positive referrals than might usually be judged acceptable clinical practice for other diagnoses.

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1 Rahi JS, Dezateux C on behalf of the British Congenital Cataract Interest Group. National cross sectional study of detection of congenital and infantile cataract in the United Kingdom: role of childhood screening and surveillance. *BMJ* 1999;318:362-5. (6 February.)
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Body mass index standards for children

1990 data will remain available

EDITOR—In his editorial Prentice suggested using the Child Growth Foundation's paediatric body mass index charts for the United Kingdom to make both prospective and retrospective comparisons of secular change pegged to the British 1990 data.[1] We can assure him that not only will the 1990 data always remain available for retrospective epidemiological research etc, but they will additionally also feature the World Health Organisation International Obesity Task Force cut offs for children when they become available.

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1 Prentice AM. Body mass index standards for children. *BMJ* 1998;317:1401-13.

❄The BMI charts are available on the *BMJ*'s website www.bmj.com

Closure of Royal Hospital Haslar is necessary

EDITOR—The new strategy for the defence medical services announced at the end of last year shows the importance attached to the medical support of the armed forces. The strategy is the outcome of a series of in-depth studies and reviews, and the implementation of a wide range of proposals is now well under way. We are already seeing improved recruiting.

In the light of this it is disappointing to read Fulford's letter prompted by the Ministry of Defence's announcement of the decision to close the Royal Hospital Haslar.[1] The views he reflects are, I believe, the result of a mistaken perception of the needs of the defence medical services and perhaps an understandable attachment to the hospital. Such views were certainly expressed during studies into the provision of secondary health care in the services and were carefully

weighed against opposing opinions. The conclusion of the studies, however, was that Royal Hospital Haslar was not viable in the long term and that its retention was less efficient and more expensive than any other option proposed. The resulting decision to close the hospital was not taken lightly, but in my judgment the closure is essential in the development of the defence medical services and deserves support.

It is natural that the residents of Gosport do not wish to lose their local hospital, but the area health authority fully understands the reasons for the closure of Haslar and is working closely with us on plans for the transition to a new Ministry of Defence hospital unit at Queen Alexandra's Hospital, Cosham. These joint arrangements will ensure the continuing provision of care and the continuing accreditation of training for service medical personnel.

Work on the other major component of our plans for the future—the new Centre for Defence Medicine—is also going well. The centre will be a professional focus of military medical expertise, with academic, research, teaching, and clinical aspects and will be established at a civilian centre of excellence. We are expecting interest from NHS hospital trusts, and I am confident that the centre will be professionally attractive to staff of the defence medical services.

I have no doubt that the strategy we are now pursuing is the correct course for the defence medical services and offers a bright future.

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1 Fulford P. The last armed service hospital. *BMJ* 1999;318:1213-4. (1 May.)

Treatment of myocardial infarction should be audited before heart failure clinics are set up

EDITOR—Cleland at al draw attention to the body of evidence favouring use of β blockers in patients with heart failure.[1] In discussing implications for clinical practice they recommend that greater emphasis be given to using these drugs as part of a preventive strategy in patients with milder symptoms. To achieve this they call for a reorganisation of services, including the establishment of heart failure clinics and specialist liaison nurses.

They fail to mention that most patients who attend these clinics would have had a myocardial infarction previously (the usual cause of systolic heart failure), all of whom should have received β blockers as part of routine secondary prevention.[2] That less than half these patients actually receive treatment in Britain represents a serious indictment of coronary care that needs rectifying before additional resources are allocated to new services.[3] Similar arguments apply to angiotensin converting enzyme inhibitors.[4]

My suggestion would be that an audit of treatment with β blockers and angiotensin converting enzyme inhibitors in patients with myocardial infarction should be a prerequisite for any trust thinking of setting up heart failure clinics with specialist liaison nurses. Treatment rates of less than, say, 66% should be acted on before resources are reallocated to the untested solutions that Cleland et al recommend. Few units achieve this modest target (certainly not mine[5]), and I suspect that this policy would result in little money being spent on heart failure clinics and specialist liaison nurses.

If the audit loop were ever completed it might lead to improvement in the secondary prevention of acute myocardial infarction. It would also ensure that most patients with heart failure or at risk of developing it were treated with β blockers and angiotensin converting enzyme inhibitors, so rendering these new heart failure services largely redundant.

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Drug and alcohol policies are rare at medical schools in UK

EDITOR—The consumption of alcohol and illicit substances is increasing among medical students in the United Kingdom[1] and is also excessive among junior house officers.[2] These findings emphasise the need for a comprehensive approach towards health promotion in medical schools, with locally negotiated and applied drug and alcohol policies being integrated within this approach. The Working Group on the Misuse of Alcohol and Other Drugs by Doctors has recommended that every medical school should have a drug and alcohol policy,[3] and in view of this I attempted to discover the number of such policies that have been implemented in the United Kingdom's medical schools.

In May 1998 I wrote to the deans at each of the United Kingdom's 26 medical schools, asking whether a drug and alcohol policy was currently implemented at their medical school. Seventeen responded, six informing me that they had written policies; these policies covered alcohol alone (three medical schools); drugs alone (two); and alcohol and drugs (one). The target population for these policies was almost exclusively medical students. Similar findings were obtained by Bhopal et al in 1994.[4] Three other medical schools stated that they adhered to the guidelines issued in the General Medical Council's document *Student Health and Conduct* regarding medical students' use of alcohol and other drugs.[5]

Although I conducted this study too early to be able to determine the effect of the working group's recommendation regarding drug and alcohol policies at medical schools, the fact that the number of such policies remains low is a cause for concern. It is also worrying that the target population for such policies remains mainly medical students despite the potentially devastating effects that drug and alcohol misuse and dependency may have on the health of all healthcare professionals and on the welfare of their patients.

The number of drug and alcohol policies implemented in the United Kingdom's medical schools should be reviewed periodically, and during this evaluation process the target population of such policies must be determined. Further research is needed to determine the quality and effectiveness of drug and alcohol policies in medical schools, with particular reference to the health and wellbeing of their target population.

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Competing interests: None declared.

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Bible is disapproving of homosexual activity but not homosexual orientation

EDITOR—In his Personal View Sheard states that "most people have a relative or friend who is lesbian or gay."[1] This is incorrect and merely reflects the misconception that homosexuality is relatively common. In fact, it is very uncommon: the national survey on sexual behaviour in 1994 found that 0.4% of men considered themselves exclusively homosexual, as did 0.1% of women.[2] Most people do not have relatives or friends who are gay.

People continue to have reservations about the acceptability of homosexuality: 72% of respondents in a survey for the *Independent* in 1997 believed that the age of consent for homosexuality should not be reduced.[3]

Sheard also implies that suggestions that homosexuality is disapproved of in the Bible come from religious bigots. But any review of Bible references to homosexuality clearly shows that they are disapproving of homosexual activity (not orientation).[4 5] Only by

trying to twist meanings and ignore inconvenient passages can one come to any other conclusion. The reason for the Bible's stance is not to "bash homosexuals"; it is to protect people from dangerous behaviour. Homosexual sexual activity is a major risk factor for HIV infection, and homosexuals have been one of the main groups suffering from and dying of AIDS. As Beard rightly says, a lifelong faithful relationship is the only way of guaranteeing safe sex; unfortunately, many homosexuals (like many heterosexuals) do not have such relationships.

Finally, the use of the word homophobia is incorrect. According to the *New Collins Concise English Dictionary*, a phobia is "an extreme abnormal fear or aversion to" something. Doctors expressing their opinion that homosexuality is not compatible with biblical Christianity are not expressing an extreme fear or aversion; they are merely restating a biblical standpoint, which is there to protect people.

Homosexuality is a difficult area, with both medical and religious aspects. Unfortunately, Beard's article has merely served as a propaganda vehicle for the Lesbian and Gay Christian Movement and has not shed any useful light on the subject.

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1 Sheard A. Homophobia in medicine. *BMJ* 1998;317:1535. (28 November.)
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Reducing antibiotic use in children with acute otitis media

Acute otitis media in children is important

Editor—Cates's paper made the point that children with acute otitis media who are not particularly ill often get better quickly; they may be managed with analgesics and a deferred prescription for an antibiotic, which is not always redeemed.[1] Unfortunately, the content of the paper did little to justify its title. Nowhere does Cates make any reference to the diagnostic criteria for otitis media in children or specify whether the same diagnostic criteria were used in both his practice and the control practice—surely the essence of a control group. We are not even told the age range of the children.

The notion of reducing antibiotic use in children with acute otitis media is not at all evidence based; indeed, the evidence is highly controversial if strict criteria for the diagnosis are upheld. This has been the subject of several meta-analyses, which have universally shown a positive if marginal advantage for the use of antibiotics in the primary management of children with acute otitis media.[2 3] How children with acute viral upper respiratory tract infections with some associated otalgia should be managed is an entirely different issue.

Any attempt to improve diagnostic accuracy in childhood middle ear infections is to be welcomed, but it is singularly unhelpful if journal editors publish papers alleging to deal with acute otitis media when the meaning of that term is not specified. I would quibble with the use of the terms "acute otitis media," "evidence based approach," and "controlled" in Cates's paper.

I have a niggling feeling that this (admittedly worthwhile) audit would not have been published in the Papers section of the journal. It seems a shame that less rigorous scientific criteria should be applied to the peer review process for a general practice paper as would be the case with laboratory based or hospital research. If this is editorial practice then it does no credit to research endeavours in general practice and should be declared. I would be interested to see the reviewer's comments as to whether the entry criteria for this study were sufficiently rigorous to justify the term acute otitis media; I would also be interested to know whether the paper was reviewed by somebody who deals daily with pyogenic middle ear infections in children and with the often catastrophic consequences of such infections. The view that acute suppurative middle ear disease is a benign self limiting condition seems to be taking hold; often it is not.

Both acute otitis media and unexplained otalgia in children are important entities, and confusing the two simply muddies the waters.

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1 Cates C. An evidence based approach to reducing antibiotic use in children with acute otitis media: controlled before and after study. *BMJ* 1999;318:715-6. (13 March.)
2 Rosenfeld RM, Vertrees JE, Carr J, Cipolle RJ, Uden DL, Giebink GS, et al: Clinical efficacy of antimicrobial drugs for acute otitis media: meta-analysis of 5400 children from thirty-three randomized trials. *J Pediatr* 1994;124:355.
3 Del Mar C, Glasziou P, Hayem M. Are antibiotics indicated as initial treatment for children with acute otitis media? A meta-analysis. *BMJ* 1997;314:526-9.

Author's reply

Editor—Children with inflamed eardrums are usually described as having acute otitis media in day to day primary care, and the same diagnostic label was used in the trials included in the Cochrane review.[1] The challenge that we face is to reduce unnecessary antibiotic use for the majority of these children, whose infection will resolve quickly (with or without antibiotics), while at the same time trying to avoid an increase in suppurative complications.

Using a handout to explain to parents that most children will get better without antibiotics and giving a deferred prescription may have met both objectives. The paper showed a large reduction in antibiotic use, and my practice partners and I have not seen any children with suppurative complications since our change in approach; nor have we noticed any increase in our follow up workload.

I certainly would not wish to imply that the potential complications of otitis media are trivial, but in our experience they are rare. In 1985 van Buchem et al reported the results of a trial in 4860 children with acute otitis media in primary care in Holland; no children were initially given antibiotics and only two developed mastoiditis, both responding to amoxicillin.[2]

Over 200 practices in the United Kingdom have requested a copy of our handout (available on the *BMJ*'s website[3]), and many have expressed an interest in trying to replicate our results. A before and after study of complications arising in children in these practices (compared with control practices that do not change policy) would have much greater power to detect any change in the incidence of these rare events than this study did. Clarke and his specialist colleagues might be well placed to carry out such a study.

Clarke says that we should have defined strict diagnostic criteria in our study. We chose not to do so because the children that we see with inflamed eardrums do not fall neatly into the two categories that he advocates. Moreover, the odds ratio analysis does not require an identical diagnostic threshold in each practice.

If further research identifies better ways to predict which children with acute otitis media will develop complications then it may be possible to target antibiotics more precisely. Until that time we commend our changed policy as a successful evidence based approach to the initial management of children with acute otitis media who are not unduly ill.

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1 Glasziou PP, Hayem M, Del Mar CB. Antibiotic versus placebo for acute otitis media in children. In: Cochrane Collaboration. *Cochrane Library*. Issue 1. Oxford: Update Software , 1997.
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Comparison of inhaled beclomethasone and budesonide

Patients do not take prescribed doses

Editor—The conclusions reached by Pethica et al in their paper concerning the relative potency of inhaled beclomethasone and budesonide are not justified because the authors have not verified an important assumption in the paper.[1] They have assumed that patients are regularly taking the dose recorded on their prescription; the data presented in their paper suggest that this is most unlikely. The total number of prescriptions issued to 5930 patients was only 16 725 (under three a year). Most formulations of inhaled steroid last 50 days at the usual prescribed dose, so patients taking regular treatment should have used around seven prescriptions in the 12 months of the study.

Prescriptions for inhaled steroids issued in practice per patient aged 30-35, July 1997 to June 1998

No of inhalers/year:	1	2	3	4	5	6	8	9	⩾10
No of patients:	20	12	4	5	2	7	2	1	6

Analysis of computerised prescriptions in my practice over the 12 months July 1997 to June 1998 shows a similar pattern: 625 patients received 2424 prescriptions for inhaled steroids (around four a year on average). Analysis of individual data on 59 patients aged 30-35 shows that 36 of the 59 were prescribed fewer than four inhalers a year (table). These patients did not receive enough medication to have taken the prescribed dose of inhaled steroid regularly over the 12 months.

The analysis carried out in Pethica et al's paper is based on the mean prescribed dose, which may bear little relation to the dose actually taken over the whole period. The total inhaled dose for each patient would be better estimated by multiplying the contents of each inhaler by the number of inhalers prescribed over the 12 months studied. Analysis should be restricted to those patients who can be shown to be taking regular inhaled steroids.

Beclomethasone is available as a 100 µg metered dose inhaler, while budesonide is available for adults only as a 200 µg metered dose inhaler. Since a dose of two puffs twice daily is commonly used when patients start inhaled steroids, there is a possibility that budesonide in adults may be started at a higher dose than beclomethasone. This could distort the findings in Pethica et al's analysis.

Before any guidelines are altered, further analysis is required of Pethica et al's data as well as confirmatory evidence from patients in other countries.

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Competing interests: None declared.

1 Pethica BD, Penrose A, MacKenzie D, Hall J, Beasley R, Tilyard M. Comparison of potency of inhaled beclomethasone and budesonide in New Zealand: retrospective study of computerised general practice records. *BMJ* 1998;317: 986-90. (10 October.)

Back titration of inhaled steroids is uncommon in New Zealand

Editor—On the basis of a retrospective analysis of prescriptions by general practitioners in New Zealand, Pethica et al suggest that budesonide is less potent than beclomethasone dipropionate.[1] This is not an appropriate way to assess the relative potencies of inhaled steroids, and the conclusions are potentially misleading. One could draw this conclusion if the patients were randomised to treatment with budesonide or beclomethasone and the dose was carefully titrated so that the minimum effective dose was used.

In clinical practice patients are not randomised to treatment, and in my experience back titration of inhaled steroids is uncommon in New Zealand. A controlled trial that compared budesonide from a Turbohaler with beclomethasone dipropionate from a metered dose inhaler and spacer found that 600 µg of budesonide had a similar effect to 1000 µg of beclomethasone.[2]

High doses of budesonide are unlikely to be used in New Zealand because budesonide is less potent than beclomethasone. However, I have observed that patients in New Zealand are often switched from a beclomethasone metered dose inhaler to a budesonide Turbohaler when their asthma is poorly controlled. This is likely to lead to the prescription of higher doses of budesonide than beclomethasone.

The use of higher doses of budesonide has also been encouraged by the availability of the 400 µg/dose Turbohaler, whereas the highest dose available from the beclomethasone metered dose inhaler is 250 µg per actuation. (Although beclomethasone is available as 400 µg per actuation from the Diskhaler, this is prescribed infrequently in New Zealand.) When high dose inhaled steroids are first prescribed 2 puffs of budesonide twice a day from a Turbohaler are clearly more convenient than 4 puffs of beclomethasone twice a day from a metered dose inhaler.

Pethica et al argue that their findings are not confounded by severity because the subjects taking budesonide were prescribed the same number of courses of prednisone as those taking beclomethasone. One could equally well argue that the reason the subjects taking budesonide did not have more exacerbations was because they were prescribed a higher dose of inhaled steroid. To exclude confounding by severity they should have assessed the severity of the asthma before treatment with inhaled steroids.

Pethica et al emphasise the use of higher doses of budesonide in all age groups. The difference in the average doses of budesonide and beclomethasone in children is easily explained when one appreciates that the lowest dose of budesonide is 100 µg per actuation compared with 50 µg per actuation for beclomethasone.

The recommendation that budesonide should be prescribed in higher doses than beclomethasone is likely to be incorrect. It is also unhelpful and could dissuade doctors from back titration in patients who are taking high doses of inhaled budesonide and have well controlled asthma.

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Competing interests: Dr Black has been reimbursed by GlaxoWellcome, Hoechst Marion Roussel, and Astra Pharmaceuticals for attending conferences and as been paid by them and Zeneca for undertaking research.

1 Pethica BD, Penrose A, MacKenzie D, Hall J, Beasley R, Tilyard M. Comparison of potency of inhaled beclomethasone and budesonide in New Zealand: retrospective study of computerised general practice records. *BMJ* 1998;317: 986-90. (10 October.)
2 Selroos O, Backman R, Forsen KO, Lofroos AB, Niemnisto M, Pietinalho A, et al. Clinical efficacy of budesonide Turbohaler compared with that of beclomethasone dipropionate pMDI with volumatic spacer: a 2-year randomised study in 102 asthma patients. *Allergy* 1994;49:833-6.

Study was inadequate

Editor—The suggestion by Pethica et al that budesonide is less potent than beclomethasone dipropionate[1] is not valid. Studies of prescription patterns may, at best, generate hypotheses. However, several important shortcomings in the authors' study exclude even this possibility.

- The authors have not shown the 28 New Zealand centres to be representative for the country. Centre effects and differences in prescription patterns are not described—for example, the doses were much higher (approximately 1000 µg) than those currently recommended[2]
- Drug compliance and actual drug exposure have not been validated
- The patients were not matched for severity of asthma before the treatment was started
- The authors claim that the data do not support confounding by severity, yet a significantly higher proportion of patients receiving budesonide accessed hospital services (7% *v* 4%, P = 0.008). Also, the proportion of patients taking budesonide who had received secondary care (56%) was considerably higher than the proportion of the entire patient population who had received secondary care (35%)
- No clinical outcome data are provided
- The authors claim that back titration was common practice among the doctors but present no data, despite access to computerised records
- As systemic effects are greater with beclomethasone dipropionate[1] the inclination to follow a back titration scheme should be greater with this drug.

Pethica et al suggest that the lower receptor affinity of budesonide compared with beclomethasone dipropionate supports a lower systemic effect in addition to a postulated lower therapeutic effect. Obviously, any prediction of therapeutic or adverse effects based on laboratory tests of topical anti-inflammatory potency is highly speculative, since such tests do not account for either physicochemical or pharmacokinetic properties of individual drugs or performance of delivery systems. It is well established that the Turbohaler inhaler performs better than a pressurised metered dose inhaler[3] and that the oral availability is less for budesonide (10%) than for beclomethasone dipropionate (around 30%).[4] In addition, in comparing topical potency, the skin blanching assay (budesonide:beclomethasone dipropionate 1.63) is at least as relevant as in vitro receptor binding affinity (budesonide:beclomethasone dipropionate 0.70).[2]

Therapeutic equipotency of budesonide and beclomethasone dipropionate through a pressurised metered dose inhaler has been documented in well controlled clinical studies. Budesonide delivered via Turbohaler is twice as potent.[3 5] Pethica et al's study can be characterised as a description of prescription habits in a selected set of centres. It cannot be used to assess relative potency,

which requires prospective, randomised, controlled clinical trials.

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Competing interests: All the authors are employees of Astra Draco, and all are shareholders in Astra.

1 Pethica BD, Penrose A, MacKenzie D, Hall J, Beasly R, Tilyard M. Comparison of potency of inhaled beclomethasone and budesonide in New Zealand: retrospective study of computerised general practice records. *BMJ* 1998;317: 986-90. (10 October.)
2 Murphy S, Bleecker ER, Boushey H, Buist AS, Busse W, Clark NM, et al. *Guidelines for the diagnosis and management of asthma.Expert panel report II.* Bethesda, MD: National Institutes of Health, 1997.
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4 Boobis AR. Comparative physicochemical and pharmacokinetic profiles of inhaled beclomethasone dipropionate and budesonide. *Respir Med* 1998;92(suppl B):2-6.
5 Makino S, Miyamoto T, Takahashi T, Nakajima S, Yamakido M, Mano K, et al. Multicentre study comparing budesonide Turbohaler with beclomethasone dipropionate (BDP) pMDI in Japanese patients with asthma. *Chest* 1996;110(suppl 4):84S.

Studies of potencies of asthma drugs have methodological limitations

EDITOR—The study by Pethica et al, by its cross sectional design, could have equally well arrived at a different conclusion.[1] The authors could have concluded from their data that higher doses of inhaled steroids given to patients with more severe asthma lead to a reduction in use of oral steroids and outpatient consultations to a level equal to that of patients with moderate asthma. Since data on inhaled steroids were obtained during the same one year period as the data on markers of the severity of asthma, it is impossible to determine which came first. It is therefore equally possible that these markers of severity were altered by the high dose inhaled steroids.

An important methodological limitation inherent in the study design may also have biased the findings. For metered dose inhalers, for example, beclomethasone was available in canisters of 50, 100, and 250 µg per puff, while budesonide was only available with 200 µg per puff. By this mere fact, the mean dose of inhaled steroids will be shifted downwards by the lower available doses for beclomethasone. Moreover, because the lower doses of beclomethasone are more likely to be prescribed for flexible regimens and the authors decided to use the minimum values for these types of prescriptions, the mean dose of beclomethasone will be shifted down further. Thus the nature of the available formulations imposed a bias in the comparison, even before the data were collected.

Another indication of bias stems from the number of prescriptions per subject per year, which is roughly equal for beclomethasone (12 305/4925 = 2.5 per year) and budesonide (3957/1532 = 2.6 per year). Since the average daily dose is 50% higher for budesonide (979 *v* 635 µg per day), the duration of use of each canister must be shorter for budesonide than for beclomethasone. Specifically, the daily dose of 979 µg for budesonide implies that fewer than 5 puffs were prescribed per day. The average of 2.6 canisters per year implies that 520 puffs were available, so that the subjects taking budesonide used their drug for around 105 days a year. These calculations are not possible for beclomethasone because of the different inhalers, but the rates indicate that the average duration of use for users of beclomethasone may be longer than for users of budesonide, which introduces another source of bias in the comparison between the two.

Some data from this study are disturbing. For example, 11 patients aged 0-2 years received 30 prescriptions of budesonide with a mean daily dose of 582 µg. Using the standard deviation of 260 and a conservative assumption of a bell shaped distribution for the dose, we note that a child used around 1100 µg of budesonide a day. Did that child use 1100 µg a day for 105 days? This seems excessive for that age and should perhaps be investigated.

This study has several methodological limitations, the most important being that the design is cross sectional so that a contrary conclusion, indicating the effectiveness of higher doses of inhaled steroids in reducing asthma outcomes, is just as tenable from these data.

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Competing interests: The authors' research into asthma is funded by Astra, Boehringer Ingelheim, and GlaxoWellcome.

1 Pethica B D, Penrose A, MacKenzie D, Hall J, Beasly R, Tilyard M. Comparison of potency of inhaled beclomethasone and budesonide in New Zealand: retrospective study of computerised general practice records. *BMJ* 1998;317: 986-90. (10 October.)

Author's reply

EDITOR—We studied prescribing in practice, seeking explanations for the higher doses of budesonide than beclomethasone. We made no assumptions about compliance but did assume that the dose reflects asthmatic state at the time of prescription. Although we believe dose adjustment to be standard practice in New Zealand, solely a dose increase in response to inadequate control of asthma gives similar data interpretation.

Variation of prescribed daily dose with device type was small, making differential compliance unlikely to explain our findings. To explain the higher prescribed doses, poorer compliance with budesonide formulations would be required, but this is not recognised. It is difficult to say which patients are compliant, either in clinical trials or observational studies. However, analysis of only patients who are compliant with treatment may leads to false conclusions, which is why an intention to treat approach is preferred.

At the time of our study it was usual to dispense up to three months of treatment. Overall in our data, beclomethasone and budesonide prescription time intervals were similar. The doses of budesonide prescribed are in line with the product information in New Zealand; no child aged 0-2 years was prescribed over 800 µg daily.

Our paper describes numerous difficulties in achieving a satisfactory trial design to compare the potency of inhaled corticosteroids in the treatment of asthma. Results indicating no difference are hard to interpret credibly in the absence of a negative control group. Insensitivity may give "no difference" results across a wide dose range.

The number of patients switching drug (103) in our study was too small to have any important effect on the results. The Diskhaler (1100 patients) was almost as commonly prescribed as the Turbohaler (1414), and both devices have 100 µg, 200 µg, and 400 µg per dose formulations. The mean prescribed daily dose in analysis restricted to these devices (Becodisk 575 µg, Turbohaler 989 µg) was similar to that found with metered dose inhalers. The 50 µg beclomethasone formulation may introduce a bias in patients under 6 years, but its exclusion from analysis had little effect on the overall results.

Analysis of use of secondary care in the previous calendar year gave similar results. Compared with beclomethasone, increased use of secondary care among budesonide patients occurred in those prescribed lower rather than higher doses. In a survey after the study all prescribers considered these corticosteroids equipotent. This makes systematic prescribing of budesonide to patients with more severe asthma implausible and favours lower potency of budesonide as the explanation for the higher prescribed doses.

Access to secondary care data for all of the included population would be preferable, and we hope it will be possible as part of the confirmation process that we consider to be required. If undetected severity bias remains, or other biases exist that we have not considered, we hope that this will be identified during this process. Pending confirmatory studies we stand by the conclusions in our paper. We would refer interested readers to the more extensive *eBMJ* correspondence.[1]

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Competing interests: BDP is a medical director of Novartis New Zealand; this company markets no inhaled corticosteroids at present, but it does market a long acting β_2 agonist. In the past five years another author of the paper has received research grants from Astra Draco, Glaxo Wellcome, Novartis, 3M Pharmaceuticals; this coauthor has received fees for consulting and reimbursement for attending a symposium from Astro Draco and Glaxo Wellcome; this coauthor has received a fee for speaking from Astra Draco and Glaxo Wellcome.

1 Electronic responses. Comparison of potency of inhaled beclomethasone and budesonide in New Zealand. *eBMJ*:317 (www.bmj.com/cgi/content/full/317/7164/986#responses).