

Prescribing behaviour in general practice: the impact of promoting therapeutically equivalent cheaper medicines

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SUMMARY

Background. The volume and cost of prescribing varies considerably between practices. This variation is at least in part due to the prescribing behaviour of individual doctors, who are often faced with a range of therapeutically equivalent generic and brand-name drugs.

Aim. To assess the impact on general practitioners' prescribing behaviour of promoting therapeutically equivalent lower cost prescribing in conjunction with an incentive scheme.

Method. Annual prescribing data from before (1992–93) and after (1993–94) implementation of the incentive scheme were compared retrospectively for general practices in the former Northern Regional Health Authority. Main outcome measures were the practices' 1993–94 rates of prescribing relative to those in 1992–93 for 18 drugs prescribed by brand name, of which 10 were targeted in the promotion, and for 14 drugs or classes of drugs either with equivalent cheaper alternatives or of limited clinical value (10 targeted and four not).

Results. For 17 of the 18 drugs, brand name prescribing rates were significantly lower in 1993–94. Reductions in rates were greater for the 10 drugs appearing in the scheme's promotional literature. For other cost-saving measures, total prescribing rates were lower for seven classes of drugs, unchanged for one, but higher for the other six, all of which had been targeted. According to the growth in their overall per capita prescribing costs between the two study years, the 499 practices were categorized as low, average or high. Overall costs and individual prescribing rates for the majority of drugs studied were similar for these three practice groups in 1992–93. In 1993–94, practices' changes in prescribing volume differed between the groups, with the lowest increases in the low cost-growth group for all but one of the 32 classes of drugs.

Conclusion. Generic substitution was more easily implemented than more complex hints regarding cost-saving substitutions. Practices with smaller overall cost growth were making greater use of cost-beneficial prescribing strategies, whether promoted or otherwise. Simple messages may improve the cost-effectiveness of prescribing in the UK. With information support and encouragement, many prescribers appear to have modified their prescribing habits.

Keywords: prescribing patterns; prescribing costs; generic substitution.

Introduction

There is considerable variation between general practices in the volume and cost of their prescribing. Although this partly reflects differences in the demography and morbidity of the patients they care for, an important factor is the behaviour of the prescribing doctor. This includes their threshold for deciding to prescribe, the choice of drug within a particular therapeutic group, and whether that drug is prescribed by generic or branded name.

In April 1993, the former Northern Regional Health Authority (NRHA) introduced an incentive scheme for non-fundholding practitioners to encourage more economical prescribing. Details of the scheme are reported elsewhere.¹ Fundholding practices already had similar incentives, in that savings derived from prescribing economies could be used to improve patient care in the practice. In support of the scheme, all practices in the region, including fundholders, were circulated with hints as to how they could change their prescribing in a way that might produce financial savings with no detriment to patient care. The promotional material included advice on generic prescribing of 10 drugs that had potential for high cost-savings, and recommendations on a range of therapeutically equivalent but cheaper substitutions together with simple explanations supporting the proposed changes.

In order to implement the incentive scheme, practices' prescribing volumes for targeted generic drugs and suggested substitutes for other drugs were monitored, as were overall practice prescribing costs. This study reports on changes in the prescribing of these drugs and in practices' overall prescribing costs. To assess whether the promotional hints appeared to have contributed to these changes, we also studied the generic prescribing of a further eight drugs, and the total prescribing for four other therapies, either with equivalent cheaper alternatives or of limited clinical value.

Methods

Prescribing data and registered populations for all 520 practices in the region were obtained for the periods April 1992 to March 1993 and April 1993 to March 1994. Practices were excluded from the study if they were not operative throughout the two years, or if list sizes were unavailable or inaccurate, or had changed substantially over the period. In total, 499 practices were studied, including all 38 practices who were fundholders throughout the two-year period.

Practice list size for each year was taken as the average of quarterly figures. Prescribing data were supplied by the Prescription Pricing Authority (PPA) as follows.

- Total number of items and number prescribed by brand name
 - for 10 drugs promoted generically in conjunction with the regional incentive scheme: allopurinol, amoxicillin, atenolol, cimetidine, co-amlozide, dothiepin, ibuprofen,

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methyl dopa, naproxen, salbutamol inhalers (brands, group A), and

- for eight further drugs: amitriptyline, inhaled beclomethasone, cephalixin, diclofenac, erythromycin, flucloxacillin, frusemide, propranolol (brands, group B).

2. Total number of prescription items

- for 10 drugs or classes of drugs with promoted cheaper therapeutic equivalents: H₂-blockers (ranitidine, nizatidine, famotidine), indapamide, paracetamol with 30 mg codeine (Tylex[®], Solpadol[®], Kapake[®], but not co-codamol), co-amoxiclav, co-trimoxazole, ciprofloxacin, cephalosporins (cefixime, cefuroxime, cefpodoxime), minocycline, diuretics with potassium [British National Formulary² (BNF) section 2.2.8], topical non-steroidal anti-inflammatory drugs (NSAIDs; all BNF section 10.3) (alternatives, group A), and
- for four further drug groups with equivalent cheaper alternatives or of limited clinical value, which were not specifically targeted: combination diuretics (BNF section 2.2.4), cerebral and peripheral vasodilators (BNF sections 2.6.3 and 2.6.4), compound antidepressants (BNF section 4.3.3), appetite suppressants (BNF section 4.5) (alternatives, group B).

Prescribing by brand name, failure to prescribe cheaper but therapeutically similar alternatives, and use of drugs of limited clinical value are largely determined by practitioner behaviour, although patient demand (rather than patient morbidity) plays some part. The frequency of such prescribing can be used to quantify this behaviour. For comparisons, both between practices and between time periods, standardized prescribing rates were defined as items per 100 registered patients per year. To give a perspective on these annual rates, approximate equivalent prescribing frequencies for a full-time GP with 2000 patients (NRHA average is 1900) would be:

Items/100 patients	Items/doctor
0.2	4 'quarterly'
0.5	10 'monthly'
2	40 'weekly'
10	200 'daily'
40	800 'three or four times per day'

To examine the relationship between changes in prescribing and growth in drug expenditure, each practice was classified into one of three cost-growth bands. These were defined by the increase in net ingredient cost (NIC) per patient from 1992 to 1993 and from 1993 to 1994. Across the former Northern Region as a whole, the increase was £4.10 per patient (6.3%). In terms of cost growth, practices with an increase of less than £2 were classified as 'low' (143 practices), practices with an increase of £2–6 as 'average' (153 practices) and practices with an increase of more than £6 as 'high' (203 practices). The cost-growth band gives some indication of a practice's attitude to review of their prescribing habits in the presence of incentives. In the short time-frame of this study, differential changes in patient morbidity are unlikely to be a significant factor.

Analysis

Changes in prescribing rates are more realistically assessed on a percentage (multiplicative) than on an additive scale. Comparisons between the 1992–93 and 1993–94 rates for each drug or class of drugs were therefore assessed using the logarithm of relative rates.³ If practices had no prescribing for a drug in both years, they were excluded from analysis for that drug. (Number of practices excluded out of 499: brand methyl dopa 95, flucloxacillin 79, compound antidepressants 71, brand indapamide 52, brand allopurinol 44, appetite suppressants and brand

frusemide 38, brand amitriptyline 19, cefuroxime/cefpodoxime/cefixime 14, brand cephalixin 12, all other drugs ≤ 5.) If practices had no prescribing in only one of the two years, the numbers of items were incremented by one in both years, in order to calculate log-relative rates.

Across all practices, significant rate changes were identified using the Wilcoxon signed rank test.⁴ Non-parametric ANOVA (Kruskal–Wallis) was used for comparisons of initial (1992–93) rates between the three practice bands. Differences in relative prescribing rates between bands were analysed using weighted ANOVA for log-relative rates, with weights inversely proportional to the estimated variance in each practice (see Appendix).

Results

Initial levels of prescribing

Although practice bands were defined by the growth in their per capita prescribing costs from 1992 to 1993 and from 1993 to 1994, this classification might possibly reflect different initial profiles for drug prescribing rates or overall costs. As a lower cost increment might be easier to achieve from a higher baseline, the baseline rates of the three bands were first compared. In 1992–93 all the bands had similar levels of NIC per patient (average £64.48), and similar prescribing rates for each of the branded drugs, and for all the non-preferred or unnecessary drugs except co-amoxiclav and minocycline (Kruskal–Wallis test, $P < 0.01$ for these two drugs). Table 1 shows average practice rates in descending order of magnitude. For co-amoxiclav, the difference between 5.04 and 6.68 items per 100 patients annually for low and high cost-growth bands corresponds to about 30 items for a full-time practitioner, i.e. less than one prescription per week difference. For minocycline, the difference between average practice rates in the three bands corresponds to about five items per practitioner annually.

Relative rates across all practices

Practice rates of branded prescribing per 100 patients were significantly lower in 1993–94 than in 1992–93 (Wilcoxon signed rank test, $P < 0.01$) for all drugs studied, except inhaled beclomethasone (significant increase) and diclofenac (no change). For the 10 drugs promoted generically in the regional incentive scheme (brands A), 1993–94 branded rates were typically 70–80% of those in 1992–93; for the others (brands B) the relative rates were higher at 85–90%. Estimates of the relative rates are given in Table 2, with the regionally promoted generics appearing first. Comparison of the 10 relative rates for group A brands with the eight in group B shows greater reductions in group A (Mann–Whitney test, $P < 0.002$).

There were significant reductions in prescribing for indapamide, co-trimoxazole, combination diuretics, diuretics with potassium, cerebral and peripheral vasodilators, compound antidepressants and appetite suppressants (Table 3). Prescribing of topical NSAIDs was unchanged, but there were significant increases, ranging from 4% to 33%, in rates for targeted H₂-blockers, paracetamol with 30 mg codeine, co-amoxiclav, ciprofloxacin, targeted cephalosporins and minocycline.

The low rates of prescribing initially (Table 1) mean that some changes are small in terms of prescribing frequency. For example, the reduction in indapamide prescribing in practices with an average 1992–93 rate is typically only 0.112 (= 1.18 × 0.095) items per 100 patients annually, or roughly two items per practitioner.

Figure 1 illustrates the range of variation between practices in their relative rates for various classes of drugs. Many of the

Table 1: Prescribing rates for individual drugs or drug groups, in 1992–93, before the incentive scheme.

Drug	Branded items per 100 patients (1992–3)	Drug or drug group	Total items per 100 patients (1992–93)
● Salbutamol inhaler	17.0	● Combination diuretics	19.3
● Beclomethasone	14.4	● Ranitidine/famotidine/nizatidine	12.6
● Amoxicillin	8.8	● Topical NSAIDs	10.3
● Diclofenac	5.3	● Co-amoxiclav	5.8*
● Dothiepin	4.8	Diuretics with potassium	4.1
● Atenolol	4.5	Cerebral and peripheral vasodilators	3.9
● Erythromycin	4.3	● Co-trimoxazole	3.9
● Ibuprofen	3.3	● Paracetamol + codeine	3.4
● Co-amilozone	3.3	● Minocycline	1.53**
● Cimetidine	3.2	● Ciprofloxacin	1.27
● Propranolol	3.0	● Indapamide	1.18
● Cephalixin	2.6	● Cefixime/cefuroxime/cefepodoxime	1.02
● Naproxen	2.1	Appetite suppressants	0.94
● Amitriptyline	1.09	Compound antidepressants	0.50
● Frusemide	1.08		
● Allopurinol	1.05		
● Flucloxacillin	0.72		
● Methyldopa	0.72		

Rates shown are averages of all 499 practice rates. ● Group A drug, featured in NRHA cost-effective prescribing hints. Rates differed (Kruskal–Wallis, $P < 0.05$) between low, average and high cost-growth bands of practices only for *coamoxiclav ($P = 0.002$): 5.04, 5.38, 6.68 (low, average and high bands respectively) and **minocycline ($P = 0.006$): 1.57, 1.32, 1.66 (low, average and high bands respectively).

Table 2: Rates of branded prescribing in 1993–94 relative to those in 1992–93.

Drug	All practices	Cost-growth bands		
		<£2 /patient (n=143)	£2-£6 /patient (n=153)	>£6 /patient (n=203)
Group A (included in prescribing hints)				
Salbutamol inhaler	0.921	0.834	0.913	0.998
Amoxicillin	0.692	0.560	0.673	0.794
Dothiepin	0.810	0.708	0.794	0.895
Atenolol	0.802	0.692	0.801	0.868
Ibuprofen	0.827	0.681	0.839	0.906
Co-amilozone	0.783	0.674	0.787	0.849
Cimetidine	0.697	0.549	0.686	0.799
Naproxen	0.747	0.640	0.758	0.829
Allopurinol	0.749	0.597	0.727	0.842
Methyldopa	0.757	0.677	0.730	0.819
Group B				
Beclomethasone	+ 1.017	0.993	0.996	1.053
Diclofenac	o 0.995	0.886	0.958	1.100
Erythromycin	0.867	0.815	0.844	0.914
Propranolol	0.894	0.818	0.881	0.955
Cephalixin	0.887	0.743	0.935	0.949
Amitriptyline	0.873	0.826	0.849	0.920
Frusemide	0.892	0.731	1.009	0.927
Flucloxacillin	0.828	0.753	0.784	0.919

Estimates are derived from weighted means of log(relative rates) across all practices, and also within each cost-growth band of practices. Relative prescribing rates for 'all practices' decreased significantly (Wilcoxon signed rank, $P < 0.01$), except for + (significant increase) and o (no change). Relative rates for low, average and high cost-growth bands differed for all drugs ($P < 0.01$).

extreme observed values derive from practices in which the numbers of items were small, either because they had few patients or because their prescribing rates were low. The distribution for branded cimetidine prescribing (Figure 1a) was typical of many of the branded drugs featured in the regional hints — median relative rate 0.70. Figure 1b illustrates the general increase in prescribing rates for targeted H₂-blockers, with only 71 (14%) practices achieving reductions of 10% or more (i.e. with relative rates below 0.9).

Comparisons of prescribing change between practice bands

Relative prescribing rates for each of the branded drugs differed significantly ($P < 0.01$) between the practice bands. Estimates based on weighted means of log-relative rates are shown in Table 2. In all cases, the average reduction in prescribing rates was greatest in the low cost-growth practice band and smallest in the high cost-growth band. Figure 1a shows the differing distribution

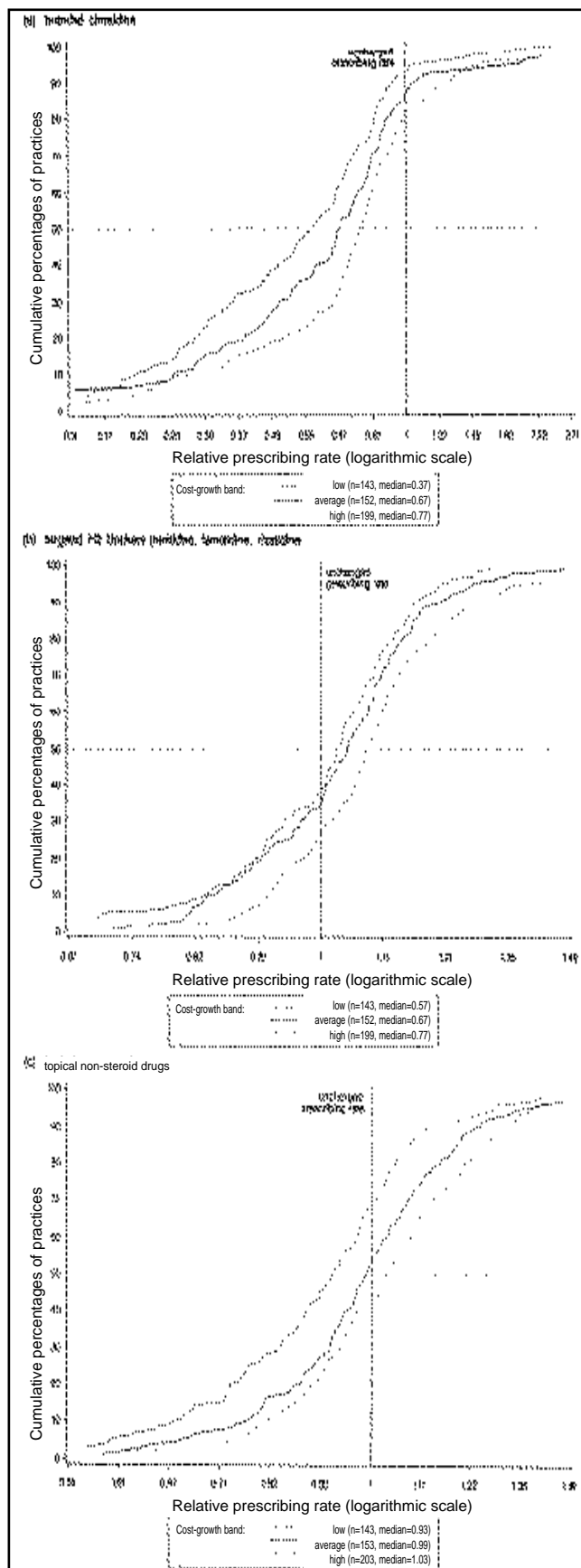


Figure 1. Prescribing for 1993-94 relative to 1992-93 rates: cumulative distribution of practices.

of cimetidine relative rates in the three practice bands.

For prescribing of non-preferred or unnecessary drugs, the picture was largely similar with significantly lower reductions, or greater increases, in the high cost-growth band (Table 2). The exceptions were compound antidepressants and appetite suppressants, for which the pattern was similar but not statistically significant, and indapamide, for which there was uniform reduction in rates across the three bands. For topical NSAIDs, the different profiles of practices in the three bands can be seen in Figure 1c (median relative rates 0.93, 0.99 and 1.03), although prescribing is unchanged when all practices are considered together (median relative rate 0.98).

Total prescribing of drugs promoted in generic form

Although branded prescribing declined, this might have been against a background of reduced per capita prescribing for the drugs in any form, either generic or branded. Table 4 shows the average practice rates for total prescribing in 1992-93, which together with the corresponding figures for branded forms (from Table 1) indicate the prevailing level of generic prescribing. Analysis of log-relative rates showed significant increases from 1992 to 1993 and from 1993 to 1994 for total prescribing of allopurinol, amitriptyline, amoxicillin, atenolol, beclomethasone inhalers, cephalixin, diclofenac, dothiepin, flucloxacillin, frusemide and salbutamol inhalers; no change for cimetidine, erythromycin and ibuprofen; and significant decreases for coamilofide, methyldopa, naproxen and propranolol. For each drug, the estimated relative rate for 1993-94 (Table 4) was higher than that for its branded form alone, indicating an increase in the percentage prescribed generically.

Discussion

Over the past few years, much effort has been directed towards limiting growth in expenditure on prescribed drugs in UK general practice. Some studies suggest that making practices responsible for their drugs budgets through fundholding can slow the rise in prescribing costs.^{5,6} More recent reports are equivocal about this in the longer term.⁷ The Audit Commission evaluation of general practitioner prescribing⁸ highlighted four aspects in which more rational drug use may result in improved patient care, reduction in drug cost or, in some instances, both of these. First, there should be more prescribing by generic name. Secondly, there should be more use of drugs from a preferred list (formulary) of drugs whose therapeutic efficacy is generally held to be similar but whose costs are lower; for example, bendrofluzide should be substituted for indapamide. Both these strategies will usually lower costs, but prescribing volume will remain unchanged. Two other strategies are avoidance of drugs of limited clinical value, such as appetite suppressants, and reducing prescribing in therapeutic areas in which there is believed to be current overprescribing, such as antibiotics or hypnotics and anxiolytics. These types of prescribing changes will reduce both volume and cost.

This study shows differences in prescribing behaviour modification between groups of practices, and this is particularly marked with respect to branded prescribing. Practices with lower cost-growth have made greater prescribing changes in line with hints provided, suggesting that these hints are among the measures adopted to limit cost growth and possibly achieve their financial incentive targets. All 38 fundholders were in this group. Differential reductions between practice bands for group B branded drugs may be attributable to spillover practice initiatives, such as setting practice computer systems to issue generic prescriptions automatically, or to greater receptiveness to other 'good prescribing' initiatives.

Table 3: Relative prescribing rates in 1993–4 compared with 1992–3 for drugs with cheaper therapeutic equivalents.

Drug or drug group	All practices	Cost-growth bands		
		<£2 /patient (n=143)	£2-£6 /patient (n=153)	>£6 /patient (n=203)
Group A (included in prescribing hints)				
Combination diuretics	0.935	0.899	0.926	0.969
Ranitidine/famotidine/nizatidine	1.040 +	1.005	1.027	1.075
Topical NSAIDs	0.985 o	0.928	0.975	1.037
Co-amoxiclav	1.075 +	1.016	1.040	1.128
Co-trimoxazole	0.805	0.770	0.779	0.847
Paracetamol + codeine	1.327 +	1.254	1.281	1.407
Minocycline	1.141 +	1.077	1.117	1.204
Ciprofloxacin	1.238 +	1.126	1.158	1.406
*Indapamide	0.905	0.908	0.917	0.896
Cefixime/cefuroxime/cefepodoxime	1.280 +	1.151	1.109	1.459
Group B				
Diuretics with potassium	0.828	0.799	0.829	0.849
Vasodilators	0.933	0.889	0.926	0.969
*Appetite suppressants	0.828	0.783	0.828	0.861
*Compound antidepressant	0.960	0.926	0.955	0.991

Estimates are derived from weighted means of log(relative rates) across all practices, and also within each cost-growth band of practices. Relative prescribing rates for 'all practices' decreased significantly (Wilcoxon signed rank, $P < 0.01$), except for + (significant increase) and o (no change). Relative rates for low, average and high cost-growth bands differed ($P < 0.01$), except for *(indapamide, appetite suppressants, compound antidepressants).

Table 4: Prescribing rates in 1992–3 and relative rates in 1993–4, for both total and branded items.

Drug	Items/100 patients (1992–93)		Estimated relative rates for 1993–4	
	Total	Branded	Total	Branded
Group A (included in prescribing hints)				
Salbutamol inhaler	23.1	17.0	1.074	0.921
Amoxicillin	26.4	8.8	1.113	0.692
Dothiepin	8.7	4.8	1.047	0.810
Atenolol	16.5	4.5	1.049	0.802
Ibuprofen	11.2	3.3	1.005	0.827
Co-amilofide	3.9	3.3	0.882	0.783
Cimetidine	9.6	3.2	1.014	0.697
Naproxen	5.2	2.1	0.925	0.747
Allopurinol	4.2	1.05	1.045	0.749
Methyldopa	1.7	0.72	0.868	0.758
Group B				
Beclomethasone	15.7	14.4	1.078	1.017
Diclofenac	8.2	5.3	1.156	0.995
Erythromycin	10.7	4.3	1.019	0.867
Propranolol	6.1	3.0	0.973	0.894
Cephalexin	4.7	2.6	1.135	0.887
Amitriptyline	4.4	1.09	1.075	0.873
Frusemide	11.3	1.08	1.140	0.892
Flucloxacillin	4.4	0.72	1.056	0.828

Prescribing rates are averages of all 499 practice rates. Relative rate estimates are derived from weighted means for log(relative rates) across all practices.

Observed reductions in the numbers of items prescribed by an individual practice may have been achieved by prescribing larger quantities (defined daily doses⁹) per item, with no reduction in the overall quantity or cost for the drug in question. However, this cannot explain why the greatest reduction in item volume is seen in practices with the lowest overall cost-growth, or why there are greater reductions in prescribing rates for brands than for their generic counterparts. Also, temporal changes within a practice in its policies over prescription length (quantity/item) would equally affect both targeted (group A) and non-targeted (group B) drugs.

Although generic prescribing is commonly described in per-

centage terms, changes in the ratio of generic to total items may derive from changes to numerator, denominator or both. Thus, the generic percentage may increase even when the volume of brand name prescribing has risen. We believe that assessment of practitioner behaviour using absolute rates of branded prescribing avoids the problems associated with statistical analyses of ratios and their interpretation,¹⁰ and presents a clearer picture of the changes achieved.

No two drugs are subject to exactly the same prescribing influences, so it is difficult to assess whether the generally greater reductions for brands in group A as opposed to those in group B are directly attributable to the circulated literature. Our

analysis was opportunistic, and the influence of 'cost-effective' promotional material would require a planned study with some practices in an incentive scheme randomized to receive the material and others not. However, there are indications that practitioners made greater changes where the potential had already been identified for them.

Despite hints targeting non-preferred drugs and suggesting alternatives, many showed increased rates. The low cost-growth band of practices performed significantly better, suggesting that they had taken more heed of the potential cost-savings these measures might deliver. Higher prescribing rates in 1993-94 for minocycline, co-amoxiclav, ciprofloxacin and the targeted cephalosporins were disappointing in view of the equally effective but cheaper alternatives suggested (oxytetracycline/tetracycline; amoxycillin). Some of these products were the subject of heavy promotional activity by pharmaceutical companies at the time of this study.

Many of the regionally promoted hints also received other publicity. Except for co-amilozide and dothiepin, the group A generics all appeared in the Audit Commission⁸ 'top 20' generic savings, as did erythromycin, flucloxacillin, frusemide and propranolol in group B. Substitution of preferred alternatives to ranitidine, indapamide, combination diuretics and combination analgesics, and the limited clinical value of topical NSAIDs, vasodilators and appetite suppressants were also highlighted in that report.

In conclusion, practices implemented generic substitution more successfully than the less straightforward hints regarding cost-saving substitutions, and those practices with lower overall cost-growth appear to have adopted cost-beneficial prescribing strategies more readily than their peers. Across practice groups the pattern, but not the magnitude, of response was similar for the majority of prescribing measures examined, whether for branded or other non-preferred drugs, and irrespective of their appearance in the regional prescribing hints. We believe that, with encouragement, many prescribers can adapt their prescribing habits, and that simple messages may improve the cost-effectiveness of prescribing in the UK.

References

1. Eccles MP, Soutter J, Bateman DN, *et al.* Influences on prescribing in non-fundholding general practices. *Br J Gen Pract* 1996; **46**: 287-290.
2. British Medical Association, Royal Pharmaceutical Society of Great Britain. *British National Formulary No. 26*. London: BMA and the Pharmaceutical Press, 1993.
3. Keene ON. The log transformation is special. *Stat Med* 1995; **14**: 811-819.
4. Armitage P, Berry G. *Statistical methods in medical research*. (3rd edn.) Oxford: Blackwell Scientific Publications, 1994.
5. Maxwell M, Heaney D, Howie JGR, Noble S. General practice fundholding - observations on prescribing patterns and costs using the defined daily dose method. *BMJ* 1993; **307**: 1190-1194.
6. Bradlow J, Coulter A. Effect of fundholding and indicative prescribing schemes on general practice prescribing costs. *BMJ* 1993; **307**: 1186-1189.
7. Stewart-Brown S, Surender R, Bradlow J, *et al.* The effects of fundholding in general practice on prescribing habits three years after introduction of the scheme. *BMJ* 1995; **311**: 1543-1547.
8. Audit Commission. *A prescription for improvement: towards more rational prescribing in general practice*. London: HMSO, 1994.
9. World Health Organization Collaborating Centre for Drug Statistics Methodology. *Anatomical therapeutic chemical (ATC) classification index (including defined daily doses (DDDs) for plain substances)*. Oslo, Norway: WHO, 1994.
10. Pearson K. Mathematical contributions to the theory of evolution - on a form of spurious correlation which may arise when indices are used in the measurement of organs. *Proc R Soc Lond* 1897; **60**: 489-497.

Appendix

Assume X_1 and X_2 , the numbers of items prescribed each year, have Poisson distributions with means $N_1\lambda$ and $N_2k\lambda$, where N_1 and N_2 are practice populations, λ is the rate for 1992-93 and k is the relative rate for 1993-94. Then $\log(\text{relative rate}) = \log(k)$ is estimated by $\log(X_2) - \log(N_2) - \log(X_1) + \log(N_1)$ with approximate variance $(1/X_1 + 1/X_2)$.

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