Table 1—Asthma admission rates (per 1000 patients per practice) by age group and the ratio of prophylaxis to bronchodilator prescribing in east London practices

Quartile:	Prophylaxis to bronchodilator ratio for number of items					Prophylaxis to bronchodilator ratio for net ingredient cost				
	Lower	Second	Third	Upper	Test for trend (P value)	Lower	Second	Third	Upper	Test for trend (P value)
Upper limit of quartile	0.275	0.33	0.395	0.65		0.85	1.08	1.37	2.53	
Mean (SD) admission rate:										
All ages	1.61* (0.61)	1.53* (0.56)	1.25* (0.49)	1.33 (0.52)	0.04	1.68 (0.58)	1.47* (0.61)	1.36 (0.50)	1.23* (0.47)	0.01
<5	6.78 (5.79)	4.98 (3.57)	5.54 (3.41)	5.81 (2.92)	0.47	7.00 (6.09)	4.70 (2.90)	5.99 (3.21)	5.49 (3.52)	0.75
5-64	0.12 (0.05)	0.12 (0.07)	0.10 (0.05)	0.09 (0.05)	0.03	0.12 (0.07)	0.12 (0.05)	0.10 (0.05)	0.09 (0.05)	0.01
≥65	1.42 (1.78)	1.99 (2.46)	0.97 (1.12)	1.19 (1.37)	0.60	1.99 (2.70)	1.43 (1.63)	1.05 (0.97)	1.14 (1.45)	0.28
No practices	29 and 30*	30 and 31*	37* and 38	36		26	35 and 37*	37	34* and 35	

Admission rate for all ages: mean=1.43, SE=0.05, median=1.3, minimum=0.4, maximum=3.1, 25th percentile=1.0, 75th percentile=1.8; based on 1602 patients.
 Admission rate age <5: mean=6.07, SE=0.42, median=5.3, minimum=0.0, maximum=33.7, 25th percentile=3.2, 75th percentile=7.5; based on 484 patients.
 Admission rate 5-64: mean=1.08, SE=0.05, median=1.0, minimum=0.0, maximum=3.6, 25th percentile=0.7, 75th percentile=1.3; based on 958 patients.
 Admission rate ≥65 years: mean=1.34, SE=0.15, median=1.0, minimum=0.0, maximum=12.6, 25th percentile=0.0, 75th percentile=1.9; based on 160 patients.

dilator medication had on average lower admission rates for asthma. Significant trends were observed in those aged 5-64. For young children and the elderly, however, we found neither significant trends nor differences in admission rates between categories of the prescribing ratios (prescribing items ratios: for under 5s P=0.61; for the elderly P=0.17; prescribing cost ratios: for under 5s P=0.38; for the elderly P=0.62).

Comment

We have shown an association between asthma prescribing and morbidity experienced by patients with asthma, as reflected in admissions to hospital. Practices with higher prescribing ratios had lower admission rates to hospital. This relation has been reported by other workers.⁴ The diagnostic coding for asthma is probably most secure in the middle age band: the lack of association in those aged under 5 and in the elderly may reflect the presence of other conditions such as chronic cough and chronic obstructive pulmonary disease, possibly classified under the asthma code.

Prescribing studies are often crude and may be complicated by problems such as indication and compliance⁵; ours is no exception. Nevertheless, that we can relate this marker to a patient outcome such as admission rate is encouraging. While this relation is not necessarily causal (higher prescribing ratios may simply be a marker for other aspects of good asthma

care), it seems sensible to promote more appropriate prescribing for asthma, particularly in practices with low prophylaxis to bronchodilator ratios. Methods might include facilitating local asthma guidelines, practice based medical education, and financial incentives. Further studies should address other patient and practice factors that may be associated with asthma admission rates and investigate the relation between prescribing patterns and a wider range of patient outcomes.

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Case-control analysis of bone resorption markers, disability, and hip fracture risk: the Rotterdam study

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Several factors besides bone mineral mass have been related to the risk of hip fracture. Bone quality, the rate of bone loss, and non-skeletal factors have been identified as important.^{1,2} High rates of bone resorption may be associated with disruption of the trabecular

network as well as with an increased rate of bone loss. Furthermore, immobility associated with disability induces bone resorption not followed by increased bone formation.³

Urinary pyridinium crosslinks are markers of bone resorption. We investigated whether these were associated with the risk of hip fracture and also whether such an association was attributable to disability.

Subjects, methods, and results

This nested case-control analysis was conducted as part of the Rotterdam study, a prospective cohort study of the incidence of and risk factors for chronic disabling diseases.⁴ Briefly, all 10 275 residents of a district of Rotterdam aged 55 or over were invited to participate. The study consisted of an initial home interview followed by a series of medical examinations

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Table 1—Relative risks for hip fractures

	Cases	Controls	Age adjusted relative risk (95% confidence interval)†	Age and disability adjusted relative risk (95% confidence interval)†
Total pyridinoline (nmol/mmol creatinine)‡ (mean (SD))	42.8 (14.3)	34.0 (12.1)	3.3 (1.3 to 8.6)	1.6 (0.4 to 5.9)
Free pyridinoline (nmol/mmol creatinine)‡ (mean (SD))	24.6 (10.1)	18.0 (7.5)	3.0 (1.2 to 7.2)	1.9 (0.6 to 5.6)
Total deoxypyridinoline (nmol/mmol creatinine)‡ (mean (SD))	9.9 (3.3)	8.5 (3.2)	2.2 (0.8 to 6.0)	1.0 (0.3 to 3.8)
Free deoxypyridinoline (nmol/mmol creatinine)‡ (mean (SD))	5.5 (1.6)	4.4 (1.8)	1.8 (0.8 to 4.1)	1.2 (0.5 to 3.2)
Free deoxypyridinoline (nmol/mmol creatinine)§ (mean (SD))	7.6 (2.6)	6.4 (1.8)	10.2 (1.4 to 74.6)	4.5 (0.4 to 46.8)
Disability score (median (range))	1.2 (0.2-2.2)	0.5 (0.2-2.3)	8.2 (1.6-42.3)	

†Relative risks are presented per standard deviation increase in concentration of various biochemical markers. For disability, relative risk is presented per one point increase in disability index.

‡Measured by high performance liquid chromatography.

§Measured by ELISA.

carried out during two visits to our research centre. The study was approved by the medical ethics committee of Erasmus University, and written informed consent was obtained from all participants. The overall response rate was 78%.

Between January 1990 and February 1994 all 17 women residents with an incident hip fracture after baseline assessments were identified by the computerised, general practice based follow up register. Each case was individually matched to three controls selected at random from women residents in the same one year age group. All fractures were verified radiologically.

At baseline participants brought one overnight urine sample to the research centre. Samples were stored at -20°C until analysis. Analyses were performed without knowledge of the subjects' fracture status. Urine samples were unavailable for five controls. Urinary creatinine excretion was measured by standard laboratory methods. Both total and free urinary pyridinoline and deoxypyridinoline crosslinks were measured by high performance liquid chromatography and corrected for creatinine excretion. Free deoxypyridinoline concentration was also measured by a recent enzyme linked immunosorbent assay (ELISA).

We measured bone mineral density at the femoral neck by dual energy x ray absorptiometry. Disability was assessed with the disability index of the Stanford health assessment questionnaire.⁵ The lower limb disability index was the mean score (0=no impairment, 3=unable to perform) of six component questions on rising, walking, bending, and getting in and out of a car.

The associations of the levels of urinary (deoxy)-pyridinium crosslinks with incident hip fractures were expressed as relative risks by conditional logistic regression. In an additional analysis we adjusted for disability.

The mean age of the women with hip fractures was 80.5 (SD 8.6) years. Table 1 shows the relative risks for the biochemical markers. One standard deviation increase in total and free pyridinoline concentrations was associated with a substantially higher risk of hip fracture. Total and free deoxypyridinoline concentrations as measured by high performance liquid chromatography were not significantly associated with hip fracture risk. However, a significant relation was observed for free deoxypyridinoline concentration measured by ELISA. A higher disability score was similarly associated with a considerably higher risk of hip fracture. Adjustment for disability resulted in substantially lower odds ratios for all urinary crosslinks. Though cases had lower bone mineral density than controls (0.72 v 0.76 g/cm² (SD 0.14 g/cm²), relative risk per standard deviation decrease 1.3 (0.6 - 2.7)), this difference was not statistically significant.

Adjustment for bone mineral density did not affect the risk estimates.

Comment

A considerable body of evidence has accumulated over the past few years confirming the validity of pyridinium crosslinks as parameters primarily of bone resorption. Most of the pyridinium crosslinks measured in this study showed a significant association with the risk of hip fracture, though there was a considerable difference in the gradient of risk associated with each marker. This was probably due to the comparatively small sample size and the fact that the various markers measure slightly different aspects of collagen degradation. The association between urinary pyridinium crosslinks and hip fracture risk appeared to be related to disability at baseline. Other investigators have shown that immobility increases bone resorption.³ This study provides evidence that disability and consequent immobility are followed by increased bone resorption, which then leads to increased bone fragility.

We conclude that urinary pyridinium crosslinks can be used in the prediction of hip fractures. Nevertheless, it remains to be seen whether simple measurements of risk factors for hip fracture¹ may be more cost effective than the comparatively expensive measurement of resorption markers.

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Correction

Outlook for survivors of childhood in sub-Saharan Africa: adult mortality in Tanzania

An editorial error occurred in this paper by Kitange *et al* (27 January, pp 216-20). In the section of Figure 2 relating to Dar es Salaam the percentage of deaths among age group 0-4 years should be shown as 32% (not 27%).