The economic implications of therapeutic conservatism

ABSTRACT—We review the pattern of prescribing medicines in the United Kingdom (UK) and compare it with that in other European markets. The prescribing of medicines in Britain has always been more conservative than in other major European markets such as France, Italy, Germany, and Spain, but the difference is becoming more marked. The conservative nature of the British prescription medicine market is indicated by three international comparisons. First, British doctors prescribe fewer items per patient per year than their counterparts in other European countries. Second, they are less likely to prescribe a product containing a new active chemical entity (NCE) than their counterparts in other countries. This resistance to the use of newer medicines has increased over the past decade. Third, British doctors rely on a progressively smaller number of active substances for a greater proportion of their prescriptions. As a result of these trends the pharmaceutical industry—at least as far as its British sales are concerned—is becoming more dependent on the sales of older products and on the occasional 'blockbuster' to finance its research. Declining uptake of new medicines, coupled with increasing pressure on doctors to prescribe cheaper generics instead of branded medicines, reduces the ability of pharmaceutical companies to fund their investment in research into as yet unconquered diseases. This trend could work against the interests of both patients and the British economy.

Low level of prescribing by British doctors

Compared to their European counterparts, British doctors are low prescribers of medicines (Table 1). The British patient received on average 7.6 prescriptions in 1989. In that year the French patient received 38 prescriptions, and the German patient received 12 prescriptions. Only Danish patients received fewer prescriptions than the British.

In the UK, patients under retirement age have consistently received 5.2–5.3 prescription items per head per year over the past decade, but women aged over 60 years and men aged over 65 years have been receiving increasing numbers of prescriptions. In 1988 patients over retirement age but under 75 received 17 prescription items per head; patients over 75 years received an average of 24 prescription items per year.

Table 1. Prescription items per head in EC countries

	Rxs per head 1989/90	Rxs per head 1980
France	38.0	27.6
Italy	20.1	19.9
Portugal	17.1	15.4
Spain	14.8	14.4
Germany	12.0	14.3
Belgium	9.3	10.3
UK	7.6	6.6
Denmark	6.1	6.5

Resistance to use of new medicines by British doctors

The conservatism of the British pharmaceutical market was compared with the behaviour of other national markets. Table 2 shows the value of the national markets in 'real' terms in £ sterling at the rate of exchange prevailing in December 1991, as well as the total cost of medicines per head per year and the cost of medicines introduced in the previous five years. In the subsequent Figures the percentage of the market captured by new chemical entities is expressed as a percentage of the total spend on medicines by national health authorities and/or sick funds.

Figure 1 shows the percentage of the total spend on medicines in 1987 in 11 national markets captured by products launched in the preceding five years. In Italy, 29.3% of the total national health service pharmaceutical market share by value went to products launched in the previous five years, while in the UK only 9.3% of pharmaceutical market share by value was taken by products launched in the previous five years—a lower proportion than in all other countries surveyed.

A further analysis conducted by the Association of the British Pharmaceutical Industry (ABPI), based on prescribing by British general practitioners, evaluated what proportion of prescriptions by value were for chemical entities introduced in the five years preceding each of the years 1975, 1980, 1985, 1987, 1989 and 1990 (Fig 2). In 1980 about 11% of the National Health Service (NHS) medicines bill was spent on products launched in the previous five years, but in

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Table 2. International comparison of the contribution of medicinal products introduced in previous five years on cost per head in 1991.

	Population	Consumption*		
		Total national consumption of prescribed medicines	Cost of prescribed medicines per head per year	Cost of new medicinal products introduced in previous 5 years per head in 1991
	m	£million	£	£
Italy	57.8	6,202	107	30
Japan•	123.5	24,386	198	51
USA•	249.2	34,654	139	31
Canada•	26.5	2,695	102	21
Spain	39.8	2,718	68	13
Germany	79.8	9,722	122	21
Netherlands	15.1	1,301	86	14
Belgium	10.0	988	99	17
France	57.2	6,026	105	14
UK	57.6	3,998	69	6

*Figures relate to prescription sales at retail prices, including chemists' dispensing margins.
•Estimated figures for 1991 extrapolated from 1990 based on percentage growth in first months of 1991.

1987, 1989 and 1990 the market share of the NHS medicines bill for products launched in the previous five years has shown a marked decline to less than half that amount.

In 1990 some 38% of the medicines bill was for products launched in the previous 20 years, and thus in that year 62% of the market was met by prescriptions for chemical entities already 20 years or more on the UK market. In comparison, in Germany in 1990 the top selling 20 new chemical entities introduced in the period 1986–1990 captured 25.8% of the total German prescription medicine market as against 4.8% in the UK (Fig 3).

In France between 1975 and 1990 the market penetration of new products five years after launch remained fairly steady at about 6% of the market by value, whereas it declined steadily over that period in the UK.

The real impact of these comparisons for research and development of new medicines is magnified by the much greater monetary values of the German and French national prescription medicine markets. In

Fig 1. *Sales of 1987 products introduced in the preceding five years as a share of total 1987 sales.*

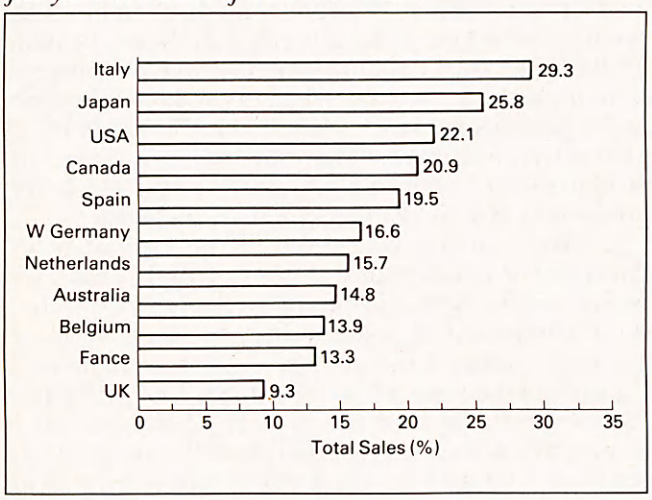
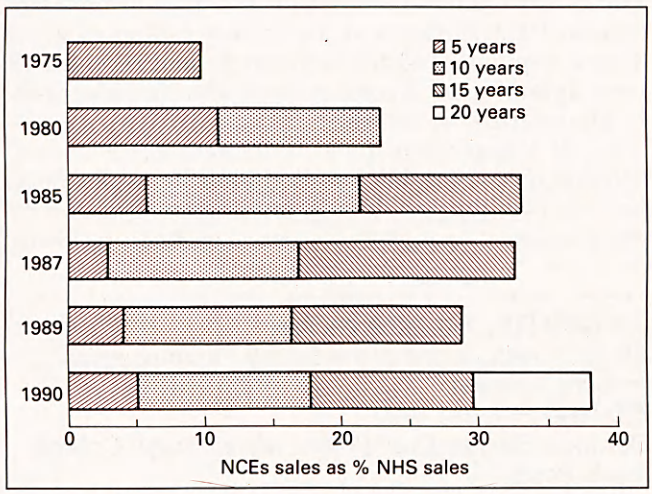


Fig 2. *New chemical entity sales as a percentage of NHS sales, UK.*



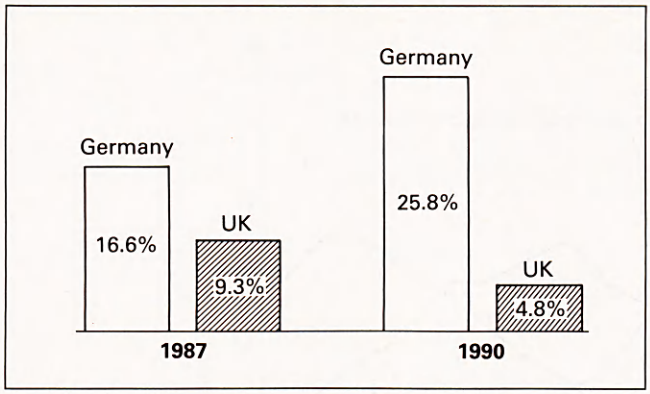


Fig 3. *Percentage of German and UK markets captured by all new chemical entities launched in the previous five years in 1987 and 1990.*

1990 the German pharmaceutical market was worth 10,125 million ECU, the French 8,900 million ECU, but the UK market only 4,742 million ECU.

The economics of the sales of a pharmaceutical product are represented in Figure 4 [1]. Some 10 years after a patent is filed the product reaches the market, but its entry on to the market and subsequent sales depend on an artificially regulated market. Entry is delayed in most developed countries by regulatory requirements, prices are depressed by price or profit control systems, and generic prescribing or generic substitution means that when the patent has expired, the originator can no longer rely on brand loyalty to maintain his market share. Nevertheless, when a new medicine enters the market it follows the general sales pattern of rise, plateau, and fall when the patent expires. The solid area of the graph represents what actually happens in the pharmaceutical market, and the line represents what would happen in a market with fewer controls.

Fig 4. *Sales by volume of a hypothetical medical product are shown in a free market economy (open area under curve), and the effect of 'environmental influences' on this hypothetical situation.* Drug regulatory authorities delay the launch of a new product and erode patent life, price or profit control measures reduce the value of sales. When the patent expires the value of the originator's sales fall as governments encourage generic prescribing or substitution. The area under the curve of sales is thus reduced (shaded area under curve).

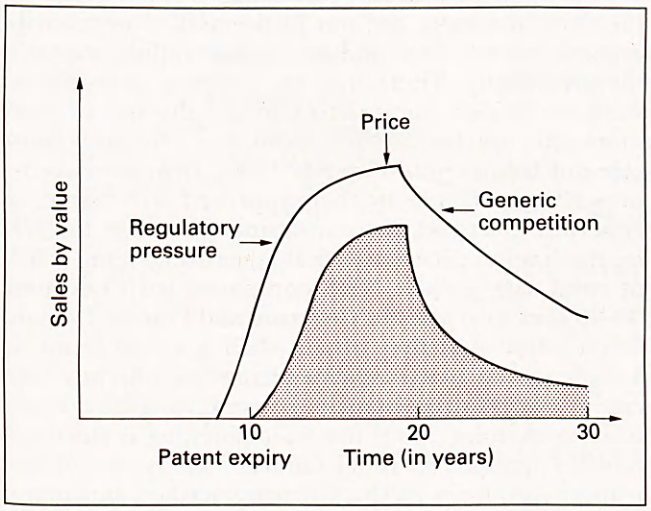


Figure 5 shows the general pattern of the penetration of the year's cohort of NCEs at intervals from 1970 to 1990 as a percentage of the total NHS medicines bill up to 1990. The aggregated sales of such cohorts of new medicines introduced after 1980 rise more slowly than those introduced in the previous decade, reach a lower peak level, and decline more rapidly.

In 1971 there were 39,000 products on the British market eligible for a Licence of Right under the provisions of the Medicines Act 1968. However, by 1991 only 1,300 active chemical substances were available in some 12,000 formulations, each holding a UK product licence. Medicines available only on a doctor's prescription, so-called 'prescription only' formulations (POM), accounted for 7,600 of them; medicines available only from a registered pharmacy but without a doctor's prescription (P), numbered 2,300; General Sales List products accounted for about another 2,000 products. In 1990 the 50 most prescribed active chemical substances, whether contained in branded or generic formulations, accounted for 44% of prescription market by value; the most prescribed 300 active substances accounted for 80% of the market. Comparable figures for the year 1980 indicated that the 50 most prescribed chemical entities represented 42% of the prescription market by value, and the top 300 achieved 70% (Fig 6). In other words, in 1990 British doctors were prescribing from a more restricted therapeutic armamentarium than in 1980, and the 1,000 or so of the less frequently used active chemical substances accounted for only 20% of the prescription market.

New medicines are cost-effective

Professor W J Louis of Melbourne, Australia, wrote in the *British Medical Journal* in February, 1989: 'New drugs have the potential to reduce substantially the costs of medical treatment, reduce investigations and prevent illness' [2]. Noting the major advances that have been made in the treatment of mental illness, Professor Spencer comments: 'There appears to be a clear association between the introduction of new psychotropic drugs and the steady improvement in both the care of the mentally ill and costs to the NHS. But the picture is not so dramatic as it might have been, and there are indications that we do not make the best use of our newer drugs' [3]. Even when there are no direct savings to the NHS, there may be evidence of

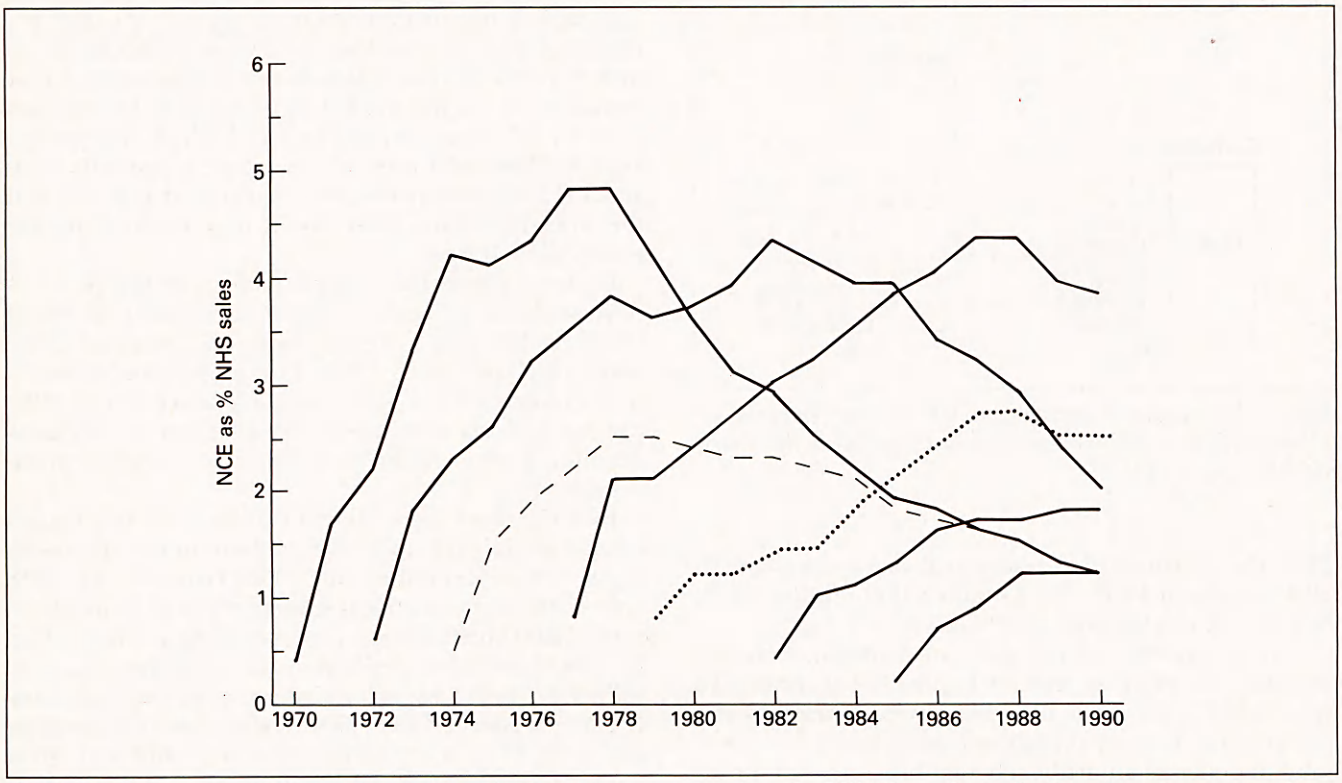


Fig 5. *Each year about 20 new chemical entities (NCEs) are marketed in the UK.* The value of sales of each year's cohort year on year after marketing was determined from 1970 to 1990. These curves are shown for the cohort of NCEs launched in 1970, 1972, 1974, 1976, 1979, 1982, and 1985, and are expressed as a percentage of the total sales of pharmaceuticals to the NHS. The penetration of newer products in the 1980s was slower, showed a lower peak and more rapid decline than in the 1970s.

better value for money from newer medicines. For example, a meta analysis of studies measuring the benefits from the use of cholesterol-lowering agents showed that 'the cost per year of life saved is approximately halved using the newer statins in place of the older cholestyramine' [4].

Initiatives to encourage doctors to prescribe cheaper medicines in the taxpayers' interests, without considering the cost-effectiveness of higher-priced medicines, may not necessarily be the right way forward in terms of achieving overall value for money in prescribing. This is revealed by an analysis of data supplied in the annual report for 1988–89 of the Prescription Pricing Authority. It shows, for example, that in the Oxford region the average expenditure on medicines for each NHS patient in that year was *lower* than virtually anywhere else in the country, although the average cost of each prescription written by doctors in the region was *higher* than in any other region in the country (Fig 7). Figures for the other regions tend to confirm the Oxford pattern of prescribing: ie, the use of more expensive modern medicines correlates with fewer medicines being prescribed on a per patient basis and lower overall expenditures per patient (Fig 8).

Implications for the future

Sales of innovative products to the British NHS are declining as a proportion of overall volume. Annual cohorts of NCEs introduced in the 1980s are achieving, on average, half the peak market share gained by annual cohorts of NCEs introduced in the 1970s.

Low levels of overall prescribing, as confirmed by the Oxford results, are not in themselves necessarily grounds for concern, and may in fact reflect responsible prescribing. There may be, however, pressures at work on British doctors to contain the use of new, more effective, but costlier, medicines. The three most relevant factors would appear to be: first, pressure to prescribe medicines by their approved INN name, ie generically; second, the constraints placed in the UK on the level of pharmaceutical advertising, namely 9% of total sales to the NHS compared with between 30–40% of total sales in Germany and France. Doctors freely admit that they obtain their greatest input of knowledge on new medicines from the pharmaceutical industry; third, financial constraints limit doctors from prescribing costly new medicines, eg erythropoietin for patients in renal failure. This is one of the leading products in the German market, but many

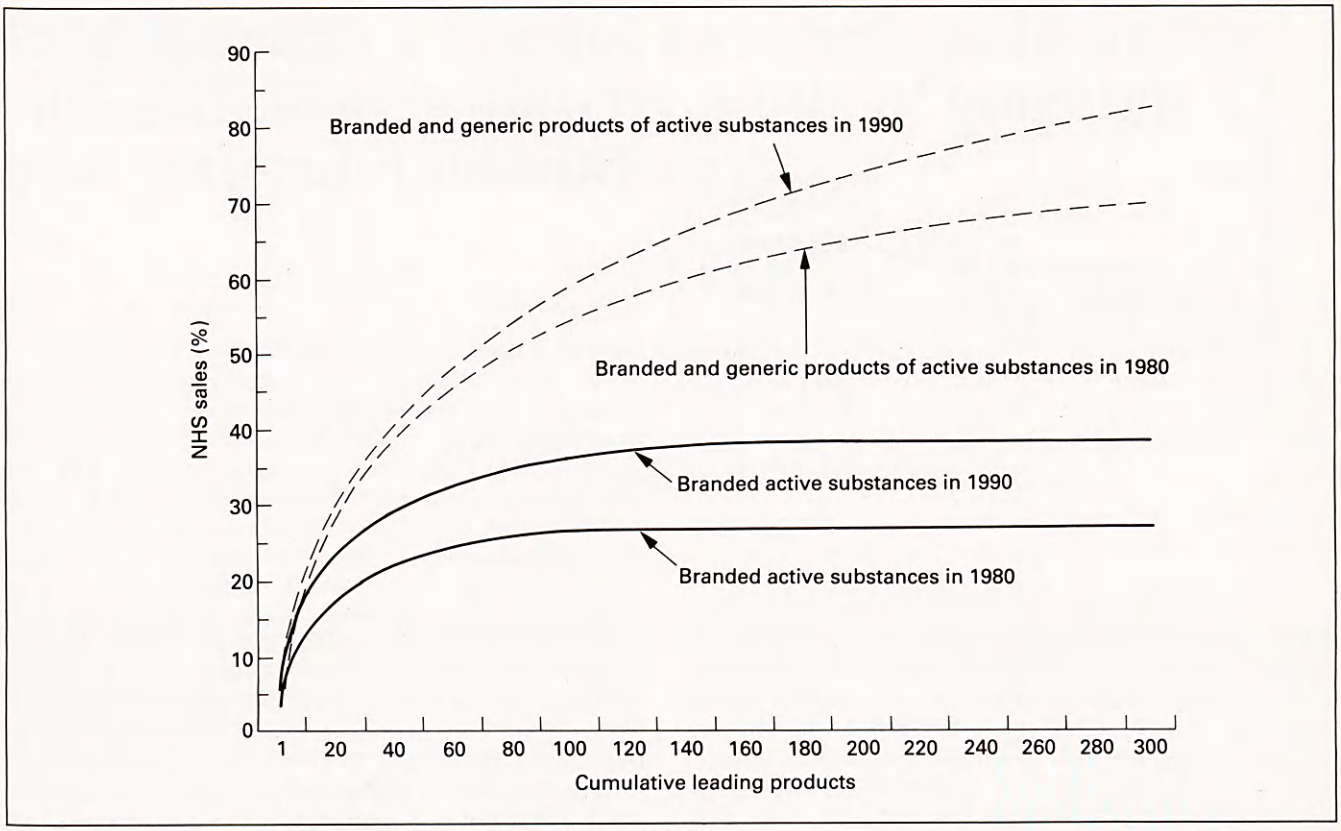


Fig 6. *Top 300 products' sales as a percentage of NHS sales, UK.*

dialysis patients who could benefit from it in Britain are denied it 'because it is too expensive'. It is therefore reasonable to assume that cost-reducing philosophies and constraints are a factor in the diminishing use of therapeutic advances in the form of new medicines in the UK. The implications of such growing conservatism, if extended to other national pharmaceutical markets, would prejudice the ability of the industry to fund research. Current research is funded out of current sales and current profits.

The cost of developing a new chemical entity was estimated at 54 million US dollars in 1976, and 230 million dollars in 1987—an increase of 425%. The British NHS medicines bill in real terms is able to

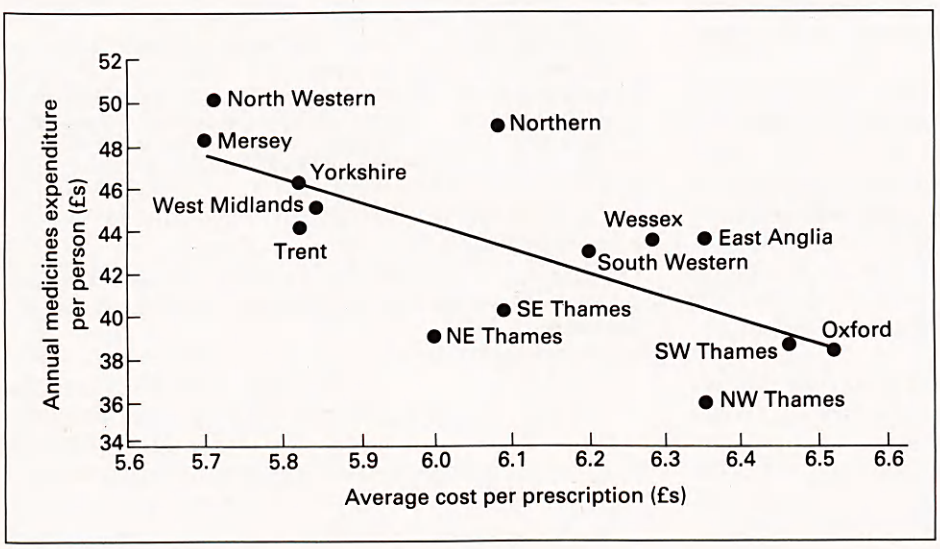


Fig 7. *Relationship between annual medicines expenditure per person and average cost of prescription, 1988.*

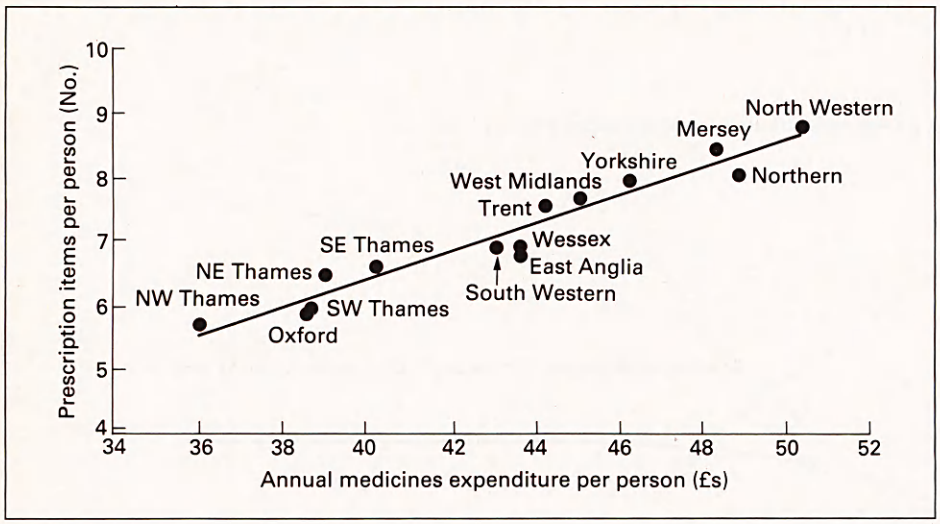


Fig 8. *Relationship between prescription items per person and annual medicines expenditure per person, 1988.*

meet its current research expenditure from the total market, but recently introduced products are not making a proportionate contribution. The current downward pressure on medicines expenditure in Europe could see a general trend towards the prescription of older, cheaper, and in many cases less cost-effective medicines. This will be to the detriment of the research-based pharmaceutical industry's ability to conduct research. More importantly, these measures will deny patients currently available modern medicines—even though they may be more effective—and undermine research into treatments for diseases where currently no adequate therapy exists. In the USA things are different. Daniel Green, writing in the *Financial Times* on 3 January 1992, pointed out that while pressures for cost containment in the USA are increasing, 'if US doctors do not prescribe the most effective drug available, even if it is only a little better than its rivals, they face the possibility of legal action from patients who do not return to complete health' [5]. Such litigious pressures do accelerate market penetration of new products.

It is therefore vital that, in addition to generating new and innovative medicines, the pharmaceutical industry convinces the prescribing doctor, the health economist, and the politician of the cost/benefit advantages of new medicines [6]. In the UK this is an area in which a highly innovative industry is failing to achieve a vital objective. For the future, it is imperative: (a) that the cost/benefits of new medicines are established and become an integral part of the education of the doctor regarding new products; (b) that industry generates fundamentally new blockbuster products whose sales provide resources for research into other, less remunerative areas (fewer than one in five NCEs marketed world-wide recoups its own research costs); (c) that patients and governments realise that in future products generated for small and specialised needs will have to be charged to health authorities or health insurance companies at a premium price, or that governments will have to generate the equivalent of orphan drug policies.

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4 Thompson D, Oster G. Cost-effectiveness of drug therapy for hypercholesterolaemia. *Pharm Econ* 1992;**2**:34–42.

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