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# THE ECONOMIC IMPACT OF MEDICINES

## Introduction

The objective of medical care is to improve people's health. This includes avoiding illness whenever possible, alleviating suffering and disability when illness does occur, and prolonging life, particularly through the prevention of premature deaths.

In a utopian situation, it might be possible to devote unlimited resources to these objectives. However, in the real world, resources for health care will always be limited, no matter how it is organised or financed. Difficult choices will therefore have to be made between competing demands for the same scarce funds and manpower. Thus, it is increasingly recognised that the discipline of economics has a major role to play in planning and organising health services.

Economists cannot, however, make the final judgement about how resources should be allocated. Such decisions will involve value judgements about relative priorities as well as technical considerations and are the proper domain of politicians, health service managers and representatives of patients themselves. But economists can offer analysis of the relative costs and benefits of alternative choices in order to assist decision makers. In this connection, new techniques for measuring patients' quality of life have been devised, and these are starting to supplement the traditional measures of mortality and morbidity. On the cost side, a growing body of research literature has highlighted how new treatments may improve cost effectiveness, how they save costs in other sectors of the health service, and how much the patients' recovery may add to the economic wealth of the nation.

Without ever forgetting that the objective of the health service is to improve wellbeing, it is important also to look at the financial savings which new treatments may yield. Potential savings to the health service itself are obviously of particular importance to health service managers and to doctors who may be facing cash-limited budgets. A number of examples of such savings were given in OHE Briefing No 25 and this present Briefing adds to those with further examples from a number of countries. In particular, it draws attention to cases where an expensive medicine may more than pay for itself by reducing other health care costs.

Sometimes later generations of medicines are more expensive than those they replace but they generate savings in the overall costs of treatment that more than cover their additional direct costs. Such medicines release health service resources to provide otherwise unaffordable treatments. Thus they represent real savings to the health service even though they do not directly reduce total expenditure. In other words, these examples of savings in health service costs through the use of modern medicines increase the total amount of treatment which is available from a given budget, rather than resulting in a reduction in the total annual cost of the health service. Without such savings the improvements in health which are actually achieved would have cost much more. In that way, the savings to be discussed in this paper contribute directly to increasing the welfare of patients within the limits set by the available resources.

## Cardiovascular Disease

The first group of diseases for which recent economic data have been published are the cardiovascular disorders. A study from Sweden examined the cost-effectiveness of the B-blocker metoprolol compared to a placebo in preventing recurrence of myocardial infarction. The metoprolol—100 mgm twice daily—was given to 154 patients below the age of 75 who had suffered an initial infarct, and the placebo was given to 147 matched controls over a three year period. To be included the patients had to be in sinus rhythm, without complete bundle branch block, and without contraindications to B blockade.

The result showed a lower incidence of recurrent disease and the reduced need for further medical intervention in the treated group. This resulted in a lower cost for the treatment group than in the placebo group. Taking only direct health care costs into account (including the cost of medication) the treated patients cost on average 12,310 Sweden Crowns over the period, compared to 17,120 Swedish Crowns for the control patients. Taking indirect costs from loss of employment into account, the figures were 118,610 Crowns and 137,220 Crowns respectively. Thus there was a net saving per patient, taking both direct and indirect costs into account, of roughly 19,000 Swedish Crowns (£1930). The authors of the study conclude that the results 'suggest that B-blocker treatment given as secondary prophylaxis after myocardial infarction is highly cost effective'. (Olsson *et al*, 1987).

A second study from the United States looked at the economic benefits of secondary prophylaxis in myocardial infarction patients from a different point of view. This calculated the cost of treatment with a B-blocker in terms of the price per additional year of life purchased by the preventive therapy. The authors concluded that on the most likely assumption, based on an overview of the available literature, each extra year of life resulting from a reduction in the risk of reinfarction would cost $13,000 in low-risk patients, $3,600 in medium-risk patients and $2,400 in high-risk patients. The definition of high-risk patients was those who had unstable angina or ventricular tachycardia in the hospital or

who had two or more of the features listed in Footnote 1. Low-risk patients satisfy the criteria in Footnote 2. Medium-risk patients are those who do not satisfy the criteria for either high-risk or low-risk.

The authors point out that the figures for the cost per year of expected life saved compare favourably with the 'price per year of survival' for other types of therapeutic intervention (Goldman *et al*, 1988).

Apart from the prophylaxis against second episodes of myocardial infarction, considerable interest has recently attached to the use of various agents to reduce mortality immediately after an infarction. A recent study carried out at the University of Oxford has calculated that for 55 year old male victims the average reduction in mortality using the new compound anistreplase instead of the older and cheaper thrombolylic streptokinase represents a cost per quality-adjusted life year (QALY) for the years of life saved of £1,087.[3] They concluded that this represents good value for money in comparison with other modern treatments. For example, it compares with an estimated £7,000 per QALY for heart transplant patients and as much as £17,500 for low-risk patients receiving a coronary artery bypass graft (Fenn *et al*, 1989).

A great deal of attention and debate has also surrounded the recent introduction of new compounds to lower cholesterol levels and hence to reduce the risks of coronary heart disease. The degree of economic benefit from such treatment depends on the level of risk for the individuals concerned. The economic arguments for the use of the newer cholesterol lowering agents (lovastatin and simvastatin) compared to older preparations have been advanced by Martens *et al* (1988) in the Netherlands, who developed a model of coronary heart disease incidence and mortality among persons of varying age, sex and cholesterol levels. They showed savings of 80 per cent or more compared to the use of previous therapies. For example, for men aged 35-39 years and pre-treatment levels of 8 mmol/l of cholesterol, the costs of simvastatin therapy are 31,500 Dutch Guilders per year of life saved compared to 131,200 Dutch Guilders for cholestyramine therapy (Martens and Finn, 1990).

Earlier evidence has shown the cost-effectiveness of preventing strokes through the control of hypertension in England and Wales (Teeling Smith 1988). In addition, it has been calculated that the cost per QALY for the lives consequently saved as a result of casefinding and treatment of hypertension under the National Health Service is £600 (Teeling Smith, 1990). Table 1 shows how this figure compares to estimates of the costs per QALY for other medical interventions at 1983-84 prices. It is clear that for the prevention of both myocardial infarction and stroke there appears to be good evidence of the cost-effectiveness of pharmaceutical treatment.

**Table 1** 'League table' of costs and QALYs for selected health care interventions (1983-1984 price)

| *Intervention* | *Present value of extra cost per QALY gained (£)* |
|---|---|
| GP advice stop smoking | 170 |
| Antihypertensive therapy to prevent stroke (ages 45-64) | 600 |
| Pacemaker implantation for heart block | 700 |
| Hip replacement | 750 |
| CABG for severe angina LMD | 1,040 |
| GP control of total serum cholesterol | 1,700 |
| CABG for severe angina with 2VD | 2,280 |
| Kidney transplantation (cadaver) | 3,000 |
| Breast cancer screening | 3,500 |
| Heart transplantation | 5,000 |
| CABG for mild angina 2VD | 12,600 |
| Hospital haemodialysis | 14,000 |

CABG = Coronary Artery Bypass Graft LMD = Left Main Disease
2VD = Two Vessel Disease

*Source:* Teeling Smith, 1990

## Prophylaxis Against Infection

The next major area to be considered is the control of infection. Briefing Number 25 catalogued seven studies which showed the pay-off obtained by the use of antibiotics to reduce the risks of post-operative infection. It pointed out that there appeared to be no studies contradicting this conclusion, and that the latest and most effective antibiotic agents could provide the greatest pay-off (Mendell Brown *et al*, 1984). A further very impressive analysis to show the savings obtained in antibiotic prophylaxis prior to surgery has since been published in the British Medical Journal (Mugford *et al*, 1989). This reviewed 58 controlled clinical trials involving the use of antibiotics prior to caesarean section, covering a total of 7777 women. From the analysis of these trials, the authors concluded that the probability of wound infection was reduced by between 50 and 70 per cent. For 41 women recorded as suffering from infection, the average extra costs of hospital care were estimated at £716 per case.

It was concluded that routine antibiotic prophylaxis would reduce the average costs of post-natal care (at 1988 prices) by between £1300 and £3900 per 100 cases, depending on the cost of the antibiotic used and its effectiveness. No attempt was made in this case to compare the effectiveness of different antibiotics to be used: the authors simply concluded that 'as well as reducing serious post-operative infection and the associated unpleasant symptoms such a policy also results in reduced hospital costs. In Britain, where obstetricians seem to be conservative in their use of antibiotics for prophylaxis compared with doctors in North America and Australia, there is scope for extending the use of antibiotics, even if they are adopted routinely only for women at increased risk of developing infection'.

Another study from Sweden (Persson *et al*, 1988) compared different methods of reducing post-operative infection in total joint replacement. It took into account the cost of re-operations which became necessary after deep infections. It compared the costs of reducing infections using four techniques: prophylactic antibiotics; cement impregnated with gentamycin; the 'Charnley enclosure' to achieve a sterile environment for the surgery; and exhaust-ventilated suits for the theatre staff. Figure 1 shows that antibiotic prophylaxis was the cheapest approach even if as many as 250 operations were being performed each year. The most expensive chemotherapy approach (prophylactic antibiotics plus impregnated cement) was still the cheapest if fewer than 100 operations per year were performed. Figure 2 relates the cost of prophylaxis to the cost of re-operation. The straight line shows how the cost of re-operation falls as infections are reduced, and the rising curve shows the increase in costs of prevention as more and more measures are introduced. The third curve, indicating the resultant overall cost, shows that lowest total cost for 100 operations per year occurs when the re-operation rate is reduced to below one per cent using systematic antibiotic prophylaxis alone.

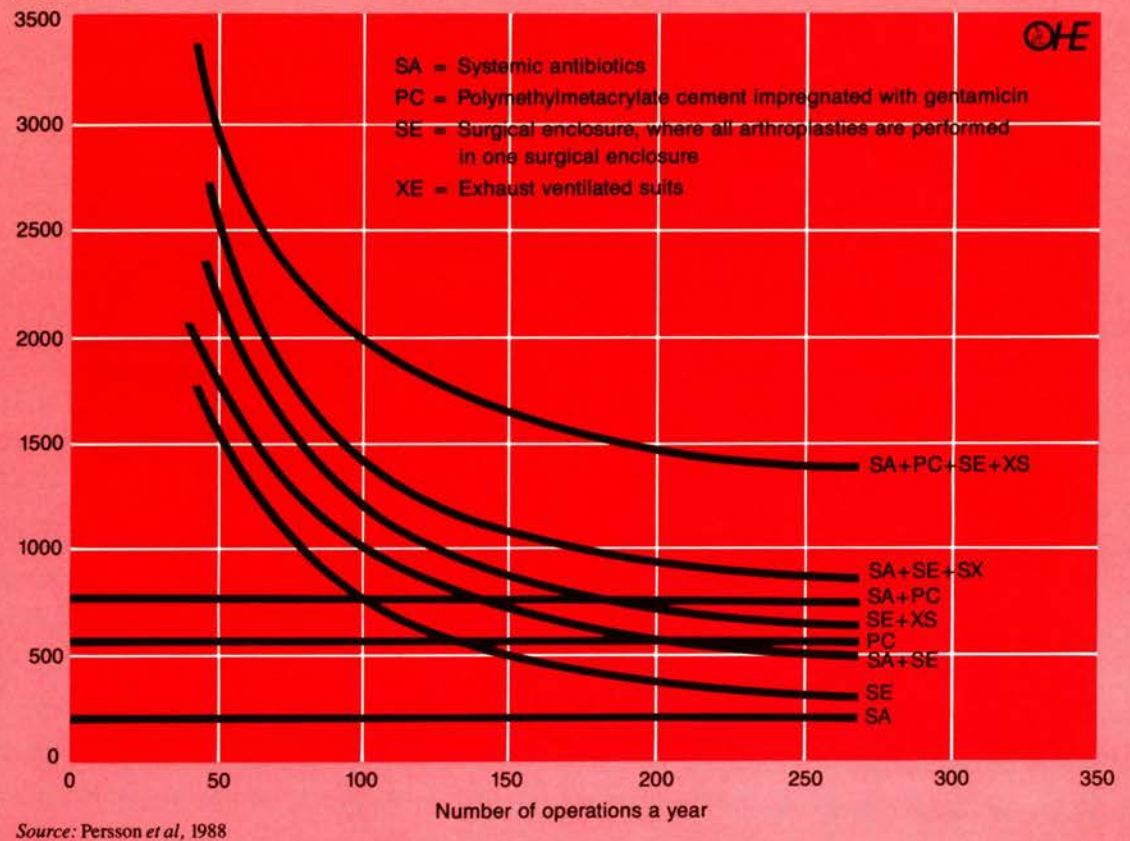
Returning to the issue of whether more expensive medicines can be more cost-effective overall, a study from the United States concerning the use of antibiotics to control serious infections confirms that it may be more economical to prescribe a higher cost medicine (Weinstein *et al*, 1986).

1 Left ventricular ejection fraction of 20 to 39 per cent; 10 or more premature ventricular contractions per minute: rales that are more than bibasilar: or qualifying characteristics for the New York Heart Association functional classes II, III or IV one month before the current myocardial infarction.

2 Patients who have had an infarction and who (1) have no severe ischemia or pump failure in the hospital, ejection fractions above 35 per cent, and no severe ischemia on symptom-limited exercise testing; (2) have results of exercise thallium scintigraphy that are normal or that show only a fixed perfusion defect in the infarct zone, or (3) have ejection fractions above 40 per cent, fewer than 10 premature ventricular contractions per hour during monitoring, no more than basilar rales, and qualifying signs for New York Heart Association function Class I one month before the infarction.

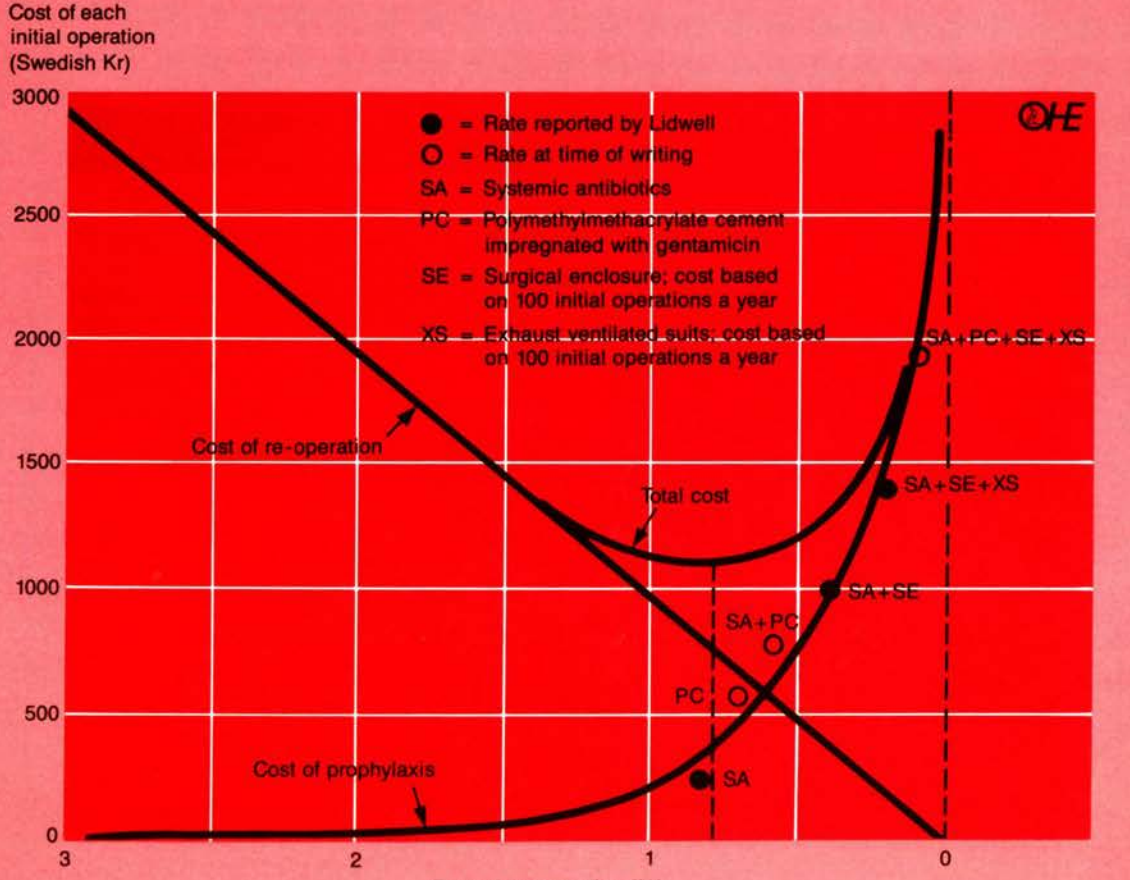
3 A QALY is an economist's unit which adjusts the value of a year of life saved by taking account of the quality of the patient's life. Thus a patient with a 50 per cent degree of wellbeing compared with perfect health would score only half a QALY for that year.

**Figure 1** Relation between cost of prophylaxis for each initial operation and number of operations a year



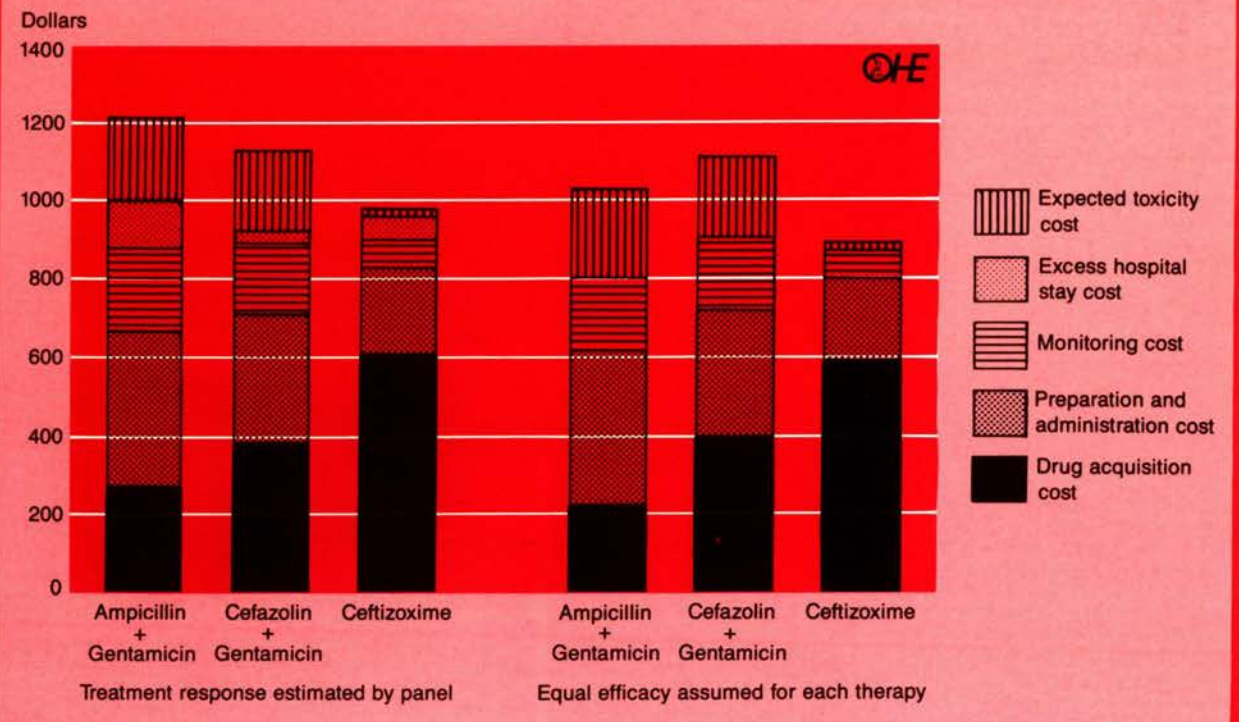

*Source:* Persson *et al*, 1988

**Figure 2** Total cost of deep sepsis with various rates of infection




*Source:* Persson *et al*, 1988

**Figure 3** The costs of sepsis calculated relative to expected hospital stay with the most effective regimen




*Source:* Weinstein *et al*, 1986

The authors evaluated the financial and health implications of treatment choices for three serious classes of infection: hospital-acquired pneumonia, intra-abdominal infection, and sepsis of unknown origin. Statistics were obtained from a review of clinical literature and published data, as well as by written questionnaire from a panel of infectious disease experts, and from the costs actually incurred at a tertiary-care hospital. For pneumonia and sepsis, the third-generation cephalosporin evaluated (ceftizoxime) was found to be less expensive than other treatments, when costs for preparation and administration, monitoring, and toxicity were added to drug acquisition costs. The lowest cost regimen for intra-abdominal infection was metronidazole plus gentamicin. Small differences in efficacy would easily outweigh differences in toxicity, however, and could justify the use of more expensive regimens (eg., mezlocillin plus gentamicin for hospital-acquired pneumonia, and cefoxitin plus gentamicin for intra-abdominal infection). If all models of treatment are assumed to be equally efficacious, then the third-generation cephalosporin was both lowest in cost and, owing to its low toxicity, greatest in net health benefits. Figure 3 shows the comparative cost elements for three dosage regimens for the treatment of sepsis. This again indicates that the higher cost of medication resulted in the lowest overall cost, whether the treatments were assumed to be of equal efficacy or their efficacy was estimated by an expert panel.

This conclusion has been supported by recent evidence relating to the third-generation cephalosporin, ceftriaxone. A 'total socio-economic product performance' profile was produced for this product. In this case, the product's once-daily dosage was shown to lead to a fall in daily treatment cost, a greater proportion of outpatient treatment, and a reduction in (packaging) disposal costs. Ceftriaxone was also compared with three other cephalosporins in terms of the daily treatment costs at ex-factory prices for 1990, as follows: ceftriaxone 2g daily, DM 48; cephalosporin A, 3x2g daily, DM 56.25; and cephalosporin C, 4x1mg daily, DM 67.5. The potential costs saving with ceftriaxone in West Germany in 1990 (daily treatment costs, 'personal costs', and inpatient/outpatient substitution) is DM 95 million per year (Sproll, 1990).

**Table 2** Comparative costs (£)

| | *Injectable papaveretum* | *Sublingual buprenorphine* |
|---|---|---|
| Medicament | 0.111 | 0.240 |
| Consumables | 0.114 | 0.001 |
| Notional staff costs | 0.225 | 0.241 |
| Pharmacy | 0.090 | 0.082 |
| Ward | 0.573 | 0.394 |
| Total | 0.663 | 0.476 |

*Source:* Wittrick, 1987

## Analgesia

Another example where a more expensive preparation results in a lower overall cost of treatment arises with the use of the analgesic, buprenorphine. A study in 1986 at Hull Royal Infirmary compared the use of sublingual buprenorphine with papaveretum in post-operative pain. All the tasks associated with their use were carefully costed. The fact that buprenorphine is not subject to legislative controls affecting potentially addictive substances which involve costly handling expenses made it a more economic treatment than the standard injectable analgesic papaveretum. The comparative costs are shown in Table 2, and although sublingual buprenorphine is more than twice as expensive as injectable papaveretum it works out significantly cheaper overall in its use (Wittrick, 1987).

## Anaesthesia

The potential economic benefits from a newer preparation are also suggested in a United States paper comparing the reduced demands on recovery room resources with the anaesthetic propofol as compared to anaethesia using more conventional thiopentone-isoflurane. The study covered a total of one hundred patients, and at each of two sites patients were randomly allocated between the two anaesthetics. The estimated mean direct patient care required was reduced in the propofol group by 18.8 per cent and by 6.5 per cent in the two different series of cases covering 40 female patients undergoing laparotomy in Illinois and 60 mixed patients receiving a variety of procedures in Chicago respectively (Mavais *et al*, 1989).

## Hepatitis B

An example of the overall cost-benefit from the use of a pharmaceutical comes from a study of the use of hepatitis B vaccination in Belgium (Lahaye *et al*, 1987). In this case the study compares not just hospital costs, but the cost of compensation payments to those who suffer the disease. The vaccination was carried out on staff in hospitals and medical care institutions on a selective basis. By the end of 1986, 40,000 people had been vaccinated. Table 3 shows the difference between the numbers of cases actually compensated under its Fund for Occupational Diseases, and the numbers which might have been expected without vaccination, using two different statistical methods of forecasting. The cost of vaccination was 160 million Belgian Francs, and the estimated savings in benefit payments to patients developing or dying from hepatitis B was either 260 million Belgian francs or 200 million, depending on the method used to estimate the reduction. Hence there was a financial benefit for the Fund for Occupational Diseases, which conducted the vaccination programme, of between 40 and 100 million Belgian Francs.

A more theoretical analysis from Japan estimates even more dramatic savings. Before the vaccine was developed, the total expense required to treat 20,000 patients suffering from hepatitis B for 20 years was Y20,300 million. After the vaccine is innoculated, the number of patients is limited only to the infection of non-positive persons, and the expense decreases to Y2,800 million. This difference, Y17,500 million, is considered to be the overall effect of the vaccine. The cost of vaccination is Y1,360 million (the assumption that an antibody disappears in five years is taken into account) and the net benefit amounts to Y16,100 million. Thus, as Figure 4 shows, the costs of hepatitis B are reduced by 86 per cent, at a cost of only 6.7 per cent of the original cost of the disease (Institute of Statistical Research, 1988).

## Asthma

Turning now to asthma, a study from the United States (Ross *et al*, 1988) has measured the effects of including cromolyn sodium in the routine treatment plan for 27 patients, against a control group of 26 receiving a placebo. Figure 5 shows the reduction in the rate of hospital admissions for the cromolyn group. Figure 6 shows the similar picture for the rates of emergency room visits. In each case it is clear that the use of hospital facilities is significantly reduced by the active treatment.

The authors concluded that 'dramatic savings in costs of emergency room visits and hospitalisation when cromolyn sodium was included in therapy were effected at a small increase in the overall cost of medications'.

A study now being undertaken in Britain over an eighteen month period is designed to establish the extent of savings in health service costs for a group treated prophylactically with nedocromil sodium compared to the costs of a matched control group receiving a placebo (Elegant, 1989).

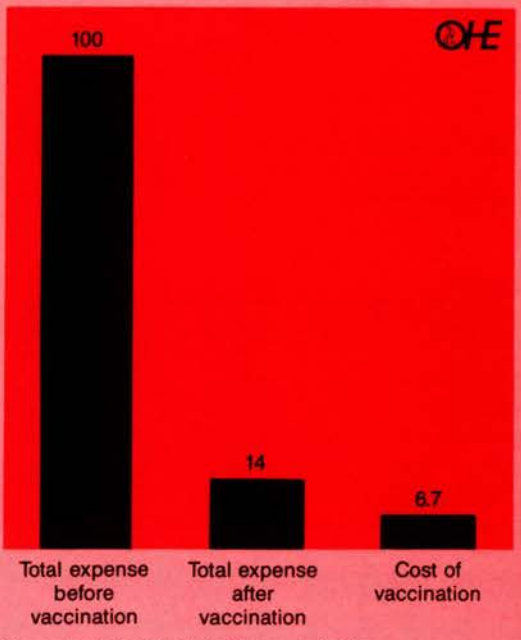
**Table 3** Differences between observed number of compensated hepatitis B cases and expected number of infections by linear and hyperbolic extrapolation

| | *Expected number of HB infections* | | *Number of compensated cases* | *Difference with:* | |
|---|---|---|---|---|---|
| | *Linear* | *Hyperbolic* | | *Linear* | *Hyperbolic* |
| 1981 | 241 | 231 | 171 | 70 | 60 |
| 1982 | 259 | 238 | 157 | 102 | 81 |
| 1983 | 277 | 242 | 82 | 195 | 160 |
| 1984 | 294 | 245 | 81 | 213 | 164 |
| 1985 | 318 | 247 | 55 | 263 | 191 |
| 1986 | 339 | 249 | 40 | 290 | 209 |
| Total | 1,719 | 1,452 | 586 | 1,133 | 866 |

*Note:* The linear extrapolation assumes a continuous growth in numbers of cases, and seems most valid from the data. However, the statistics for 1975-1981 have been fitted to a hyperbolic curve which gives a lower estimate for the number of cases to be expected.

*Source:* Lahaye *et al*, 1987

**Figure 4** Estimated change in the cost of hepatitis B in Japan as a result of introduction of vaccination: Index net cost before vaccination as 100

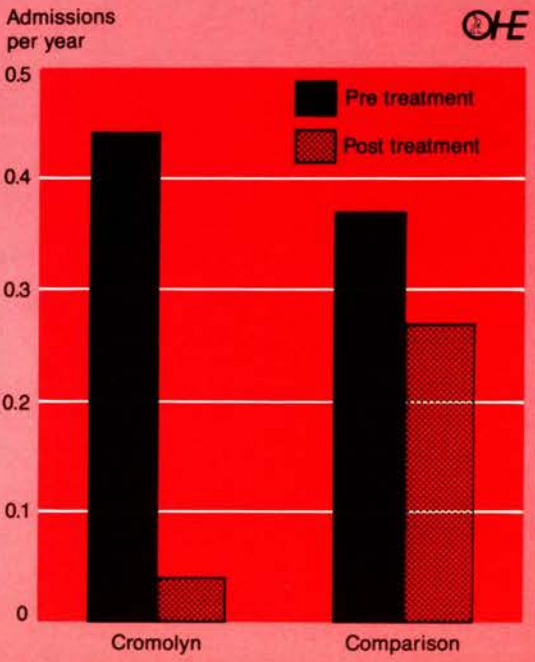



*Source:* Institute of Statistical Research, 1988

## Acne

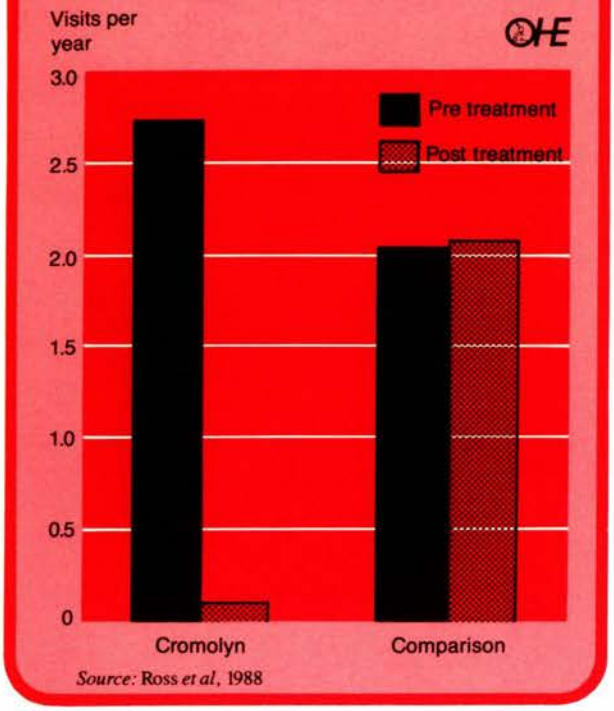
Not all of the savings in the costs of health care from the use of effective medication concern major illness. A study from France has calculated the savings in the costs of acne from the use of isotretinoin. With previous conventional treatment, the costs were calculated as 20,000 French Francs per case; with the new substance isotretinoin the costs were reduced to 3,300 French Francs. The new medicine must, however, be used with discretion as it has teratogenic effects, and should therefore not be taken by women of childbearing age unless effective contraceptive measures are being applied (Balardrie, 1986).

**Figure 5** Rate of hospital admissions for the treatment of acute asthma, before and after treatment by the study practice




*Source:* Ross *et al*, 1988

**Figure 6** Rate of emergency room visits for the treatment of acute asthma, before and after treatment by the study practice




*Source:* Ross *et al*, 1988

## Periarthritis

Another dramatic contrast in costs of treatments of a relatively 'minor' condition was recently reported in Britain (Dacre *et al*, 1989). In this case the costs of the treatment of 'frozen shoulder' (periarthritis) with physiotherapy were compared to the costs of an injection of triamcinolone. An observer-blind trial of 62 consecutive patients compared the treatment by injection with treatment by a six-week course of physiotherapy, and with treatment by both injection and physiotherapy. The three groups all showed significant improvement, which was identical in each of the groups. The authors point out that the cost of physiotherapy was £48.50, against the cost of the injection of £2.10.

## Conclusion

This Briefing underlines the savings accruing to health services which can result from the effective use of pharmaceuticals. However, two further points must once again be emphasised. The first is that these savings will not show up as a reduction in total spending. The resources released by the savings will almost invariably be used to treat otherwise untreated cases. They therefore provide an increase in wellbeing rather than financial economies. This leads on to the second point. The purpose of medical care is to increase wellbeing. It is clear that in all countries, with greater affluence, the population expect to enjoy a better quality of life. Foreign travel, home entertainment, enjoyable leisure (including sport) and better homes are all aspects of this improved quality. But better health is rated by many people as even more important than any of these other more material gains. As such it should occupy a high priority in the allocation of future resources.

Health care resources will, however, always be limited. It is therefore important to use them as effectively as possible. This Briefing highlights how the discriminating use of pharmaceuticals has an important part to play in improving the cost-effectiveness of health care as a whole thereby contributing to the maximisation of wellbeing within the limits of available resources.

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