Office of Health Economics

MEASURING THE BENEFITS OF MEDICINES; THE FUTURE AGENDA

Papers from an international symposium
held in London on 23rd and 24th October 1989

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PREFACE

George Teeling Smith

These papers were presented to an Office of Health Economics meeting in London in October 1989. The programme for the meeting was put together by a group of international experts interested in the economics of the pharmaceutical industry, and hence it reflects developments in health economics across Europe.

In his keynote speech, Sir Christopher France referred to health economics as having 'come of age' because the first health economist in the then Ministry of Health in London was appointed in 1968. It is interesting, therefore, to reflect that the Office of Health Economics had been set up by the pharmaceutical manufacturers six years earlier. Thus the meeting at which these papers were presented was a timely reminder that the pharmaceutical industry over the past 27 years has been at the forefront in stimulating discussion about the importance of cost effectiveness in medical care. Now in 1990 the industry is still ahead in undertaking economic analyses to demonstrate the fact that its medicines are often the most economical approach to therapy.

In my retirement, having directed the Office of Health Economics since its foundation in 1962, I look forward to its continuing contribution to this increasingly important field of health economics under the new leadership of Ray Robinson.

The papers in this booklet are a tribute to how far the understanding of economic analysis in the pharmaceutical field has advanced over the past 27 years.

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INTRODUCTION

Baroness Hooper

I should like to begin my remarks by drawing your attention to a famous notice which a well-known English novelist used to keep on his garden gate. The novelist concerned was Evelyn Waugh, and given that this is an international occasion, it may be that Evelyn Waugh will be known to many of you as the author of the book on which the British television series 'Brideshead Revisited' was based. The notice on his gate, which reflected his general antipathy to the human race, was 'No admittance on business'! I mention this because it seems to me that quite undeservedly the attitude of many people in the health service to health economists is one of 'No admittance on business'! That is to say, that there is still a reluctance, if not a refusal, to accept that cost-effectiveness studies, of the kind which your symposium is addressing, are actually in the interest of both health care staff and patients. Instead they seem still to be perceived as a weapon to grind them into the ground.

I think we need to reflect seriously on why such attitudes should still be prevalent. There is a perceptible feeling around that the provision of health care is not subject to the normal rules of human behaviour (on which, after all, economics is based). Or, even if it is so subject, that it is somehow immoral to stand up and say so. We have to contend with a great prejudice that we should *not* seek to associate cost with health provision, *not* recognise that doctors – just like the rest of us – have their share of human frailty, and finally *not* accept that proper human motivation is as necessary to improve quality in the health service as in any other walk of life. Our strong belief, as a government, is that we cannot accept these shibboleths and that maintaining and improving the NHS demands that we act radically to cut through this kind of pretension. This is a main aim of the NHS review. Indeed it is on the connections between the review and the cost-effectiveness issues, which form the subject of your symposium, that I would wish to dwell tonight.

It is a fundamental principle of the NHS review that 'Those who take decisions which involve spending money must be accountable for that spending'. In most walks of life such a principle would seem self-evident. Yet in the health service we have a situation where, both in the hospital services and in the family practitioner services, doctors daily take decisions which involve the commitment of large amounts of resources without any idea of the financial consequences of their actions. That is clearly not right. It is first of all unfair to the doctor concerned that he should have often to take decisions in a financial vacuum because the cost information is simply not available to him. I have heard that a private sector hospital offered to help reduce waiting lists in one area by carrying out hernia operations for £200 each, but the district health authority could not take up the offer as they were unable to quantify their own costs and establish whether the offer was good value for money. That is why in the hospital service we have decided to extend the Resource Management Initiative. In the area of the family doctor service, again we find that doctors regularly sign prescriptions without any knowledge of the financial consequences. Hence the new indicative drug budget scheme will, for the first time, provide them with regular monthly statements of their expenditure and how it compares with what might be anticipated, given the particular circumstances of their individual practices.

Decision taking in such a financial vacuum is, however, not simply unfair to doctors – it is above all else unfair to the interests of patients. Any government, in any country, of whatever political complexion, is always going to have a ceiling on the resources it can make available for health care. Equally, it has often been argued that the demand for medical care is infinite.

Certainly, it seems likely that we will always be able to think of new and desirable improvements to delivering both preventive and remedial health care. The consequence of this is obvious. If we spend more money than we need in one area of health care, we are effectively denying it to another. If, for example, we do not manage our delivery of elective surgery effectively, then we are adding unnecessarily to waiting lists and denying patients treatment which could be made available from existing resources. If family doctors refer patients unnecessarily to hospitals – and you will know that there is a large and unexplained difference in referral rates between GPs – we are simply taking up the time of hospital departments which could be better spent on patients in real need of their services. Yet even against this background, we still find those who are prepared to condemn any efforts to keep expenditure within reasonable bounds. Indeed, I was interested to see that the latest BMA leaflet on the review (and these are, of course, avidly read in the Department!) sums up the main proposals of the review by saying 'All these proposals have an underlying theme – cost containment', with the clear implication that any reasonable person would find such an objective reprehensible.

I would, however, strongly suggest to you that 'cost containment' – in the sense that we need rigorously to pursue value for every pound of the taxpayer's money spent on the health service – whilst certainly not the sole objective of the review, is in fact wholly legitimate as a purpose and one very much to the benefit of members of the health care professions and patients alike. Incidentally, I have taken the BMA's use of the term 'cost containment' at its face value. I am sure that they would not want the term to be misinterpreted by the casual reader as being shorthand for 'cuts', bearing in mind this government's record of having increased expenditure on the NHS in real terms by 40 per cent since 1979.

Neither can we forget the need for proper human

motivation. We are, of course, very fortunate in having many very fine doctors who are completely self-motivating and give well above what we could reasonably expect to the NHS. That is true in the hospital service. That is true in the family practitioner service. But we cannot ignore the fact that human frailty is a condition from which doctors in general are no more removed than the rest of us. For example, a recent study found that there were waiting lists for many of the more common items of elective surgery which were due, at least in part, to the fact that consultants found them less exciting than high-tech pioneering work and therefore had a rather low productivity rate. This is understandable, but I am sure that we would all equally accept that the reason we carry out the more pedestrian elements of our own jobs is that at the end of the day we know it is necessary. By contrast, the current system of employing and remunerating hospital consultants fails to provide the necessary spur to ensure that proper levels of work are carried out. That is why, for the first time, we are proposing in the review that all consultants should have proper and agreed job descriptions and that their distinction award system should take full account of their actual contribution to the NHS and its patients. Precisely the same considerations apply to the new contracts for GPs, which have been the subject of so much ill-focused criticism and ballyhoo, and which in fact will have precisely the effect of rewarding most of those doctors who meet today's patients' needs and thereby encourage the others to raise the standard of their services.

But so far I have spoken of only two of the factors we need to take into account in planning our health care, namely the need for cost data and for proper motivation to be injected into the system. Equally, the government is determined to raise the *quality* of the health service in this country and to ensure that options for health care provision are evaluated not simply in terms of their cost but in terms of the quality of outcome which is delivered. Thus we are in the business of seeking to deliver through the NHS review, not *cheaper* health care, but *more effective* health care. 'Cost is not the enemy – waste is the enemy.'

It is extraordinary that critics of the review should have gone to such lengths to claim the government has no interest in improving the delivery of high-quality health care. In fact we are proposing to put in place a whole string of mechanisms designed precisely to improve quality. Frankly, these would be the last changes a government would make which was intent on skimping and cheese-paring. The whole object of contractual arrangements between DHAs and hospitals is to ensure that health providers have a powerful incentive to maintain and improve standards of care for patients. If not, they will simply risk losing the contract. For the first time the true financial cost of running hospital departments to which relatively few patients are referred because they are not well regarded by other doctors will be revealed. And we can be sure that not only will they be revealed but action will be taken to correct them. I am convinced that the contractual system will lead to real improvements, where improvements are necessary, precisely because the option of continued funding for a poor-quality service will no longer exist. Incentives and disincentives do change behaviour. With their proper application in the health service, we expect to see improvements in the standards of care provided to patients and the quick resolution of problems of unsatisfactory performance, which in the past have often been allowed to drag on from year to year in a wholly unacceptable manner.

The government's proposals in the review have somewhat curiously been dubbed as 'anti-doctor', notwithstanding the fact that their intention is actually to give more power to doctors in the management and provision of services. The new procedures for medical audit, which will apply throughout the health service, are designed specifically to help 'ensure that the best quality of medical care is given to patients'. The government has recognised that medical audit is essentially a professional matter, and there has been close consultation with the profession over its implementation. Medical audit is, I suggest, a clear sign of our commitment to improving standards, and indeed were this not our objective it is more than a little difficult to see why we would be so thoroughly committed to it. Practice budgets, which give GPs funds to exercise control over the buying of a number of services including in particular a specified range of hospital services, represent another initiative to give power directly to doctors to influence the shape of the services which they think best for their patients. Self-governing hospitals will provide their medical staff with a whole new world of opportunity to determine the best way of providing health care in their individual situations.

Our plans for indicative prescribing budgets, which I appreciate may be particularly interesting to you, have the same emphasis on cost-effectiveness rather than saving money at any cost. We are proposing to provide much more extensive professional advice on prescribing to GPs than is currently the case. Budgets will be set for individual practices, not on the basis of slide-rule calculations by administrators but on the basis of a professional judgement taken in the knowledge of a practice's previous prescribing history and any special circumstances. We do not regard prescribing budgets as a substitute for educating GPs on prescribing. On the contrary. We propose to strengthen our prescribing information service to GPs, and we would see indicative budgets as complementary to educational initiatives which will help to stimulate interest in cost-effective prescribing amongst GPs and thus in the pharmaceutical industry itself. Similarly, we have made it clear that GPs

who exceed their indicative prescribing budgets will not be penalised unless a professional committee should find them guilty of over-prescribing. In other words, GPs who prescribe high-cost but necessary medicines to their patients will have nothing to fear. High-cost medicines can be very cost-effective in raising the quality of patients' lives and are under no threat from this government. By contrast, unnecessary and excessive prescribing, whether high cost or low cost, is very much *not* in the patient's interest and needs to be tackled. This is our full intention. It is, however, hardly a new perception, given that Hippocrates in ancient Greece was strongly of the view that 'Wherever a doctor cannot do good, he must be kept from doing harm'.

In conclusion, I hope that this survey of the NHS review and its deep roots in the application of cost-effectiveness will serve as an encouragement to you as health economists to know that we, as a government, value your work. We have every intention of working with health care professionals at all levels to ensure that in the future you will find the sign at the gatepost considerably more welcoming! I wish you an enjoyable and stimulating symposium.

HEALTH COSTS: ARE THEY WORTH IT?

Christopher France

I am honoured to have been invited to make a contribution to this seminar. I have no doubt that the topic – Measuring the Benefit of Medicines – is one of major importance, and I hope to demonstrate why I believe it to be so.

But I confess to finding somewhat daunting the task of delivering a keynote speech. What key am I to choose? At the broadest level, is it to be major and assertive, or minor and reflective – not to say a touch pessimistic? I suspect that, like most substantial compositions, this seminar will show some modulation. My dictionary of music defines modulation as 'The art of changing from one key to another in the course of a composition in such a way that the transition makes grammatical sense and also adds to the formal and logical progress of the music'. If 'formal and logical progress' proves to be within our reach then we shall certainly have struck the right key.

When I was thinking of a title for these remarks I began to wonder about the value of measurement in the field with which we are concerned. Is it really important for us to know about costs, and if so, why? That is why I posed the question 'health costs: are they worth it?' Formulated in this way, the question encapsulated for me two challenges and an assertion.

The challenges are these. First, how can we improve our response to the fundamental problem of measuring inputs? There are those in the audience who could speak with much more authority than I about the technical problems which this task involves. But I can certainly count myself among those who feel the frustration when inputs have defied analysis. I recently found myself being cross-examined by the Public Accounts Committee on the effort that we are putting into the prevention of coronary heart disease. One knew it to be much more than the bald figures of investment in the 'Look After Your Heart' campaign would suggest, but how to convince a sceptical audience of this?

The second challenge is to proceed to the evaluation of the measured input against an output, measured or merely desired. This is demanding indeed, but it is implicit in the title of this seminar, which requires us to measure the *benefits* of medicines. Here we have one of those splendid logical onions. Do we mean by benefit the degree of remission achieved? In absolute or relative terms? Do we address the improved quality of life which that remission secures for the patient? Or do we go beyond that to the social consequences, economic and otherwise, of securing a remission? What, in fact, are we going to measure when we seek to measure the benefits of medicine?

This brings me to the assertion. The title I have chosen deliberately uses the word 'worth'. Measurement by itself is a start, but it is insufficient. We need criteria with which to assess whether the measured movement is desirable or otherwise in terms of some end or ends which constitute the ultimate goal. Economists will appeal to the concept of 'opportunity costs', but knowing that the same resources could be used either, say, to extend the lives of the old or to improve the quality of life of the disabled young does not tell us which is the better use of resources.

I believe that it is because the need for this kind of value judgement is often obscured that measurers do not always get a good press. I am reminded of what claims to be a description of the typical accountant, which I came across when I was taking an excursion in that direction. This was the description:

> 'A man past middle age, spare, wrinkled, intelligent, cold, passive, non-committal, with eyes like a cod-fish; polite in contact but at the same time unresponsive, calm and damnably composed as a concrete pot or a plaster of paris cast; a petrification with a heart of feldspar and without charm of the friendly germ, minus bowels, passion or a sense of humour. Happily they never reproduce and all of them finally go to hell.'

A gross calumny on accountants, I am sure. But the point is that this description reflects the aridity, even infertility, which is often perceived in the process of measurement. I hope accountants, and others, may be relieved to hear that I at least do not see such a view of measurement as bringing us anywhere near the end of the story.

I think I can best begin to explain why not by sharing another quotation with you. This one comes from Enoch Powell's 1961 Lloyd Roberts lecture to the Royal Society of Medicine. Mr Powell took as his subject 'Health and Wealth'. He considered the difficulty of justifying health expenditure in economic or statistical terms. Having decided that neither was wholly adequate for the purpose, and having talked of the planner's despair (here we are certainly in the minor key), he modulated to the major, and said this:

> 'Change, improvement, progress do not mainly come about in human experience by exerting larger claims on resources, even when those resources are rapidly growing in total. They come about by individuals, groups and societies using resources more wisely, more cunningly, more effectively.'

Here is a theme which perhaps the seminar may wish to develop. We cannot judge whether the improvement in performance implicit in these words is being achieved unless we know whence we start, in which direction we are moving, whether that is the desired direction, and whether the speed at which we are moving is appropriate to our situation. That is where the cunning comes in. Mr Powell was, of course, using the word in the sense that takes us back to the roots of

the language, where it spoke of knowledge, ability or dexterity, and had not taken on the flavour of deceit. The association of words at the end of that quotation draws us firmly towards the acquisition of knowledge as a means of improving the ways in which we use our resources. This is where we find the fertility in measurement. Measuring benefit is surely an essential element in any approach to using resources more wisely, more cunningly, more effectively.

It is a worthy aspiration to seek to make these measurements of performance, whether at the macro or the micro level. But they have proved woefully elusive in practice. Perhaps you will forgive me if I take a short excursion into the history of the British National Health Service to illustrate this point.

I think it would be generally agreed that the conception of the health service lay with the Beveridge Report of 1942. But in that report a comprehensive health service was seen as part of the necessary underpinning for a dynamic system of social insurance. It was seen as having a role to play in influencing the scale of demand for such benefits – applying downward pressure to them, to use the current jargon. Admittedly, Beveridge proposed that there should be detailed study of the organisation and financing of the health service. But in his costing of a social insurance budget for 1945 he included a sum of £170 million for that service – and the projections in the same table showed that precise figure again in 1955 and 1965 despite changes upwards and downwards in other items in these forecast budgets. So the health service was seen as in some sense self-balancing. The report assumed, to quote its words, 'that there will actually be some development of the service and as a consequence of this development a reduction in the number of cases requiring it'. In other words, the health of the population would be so improved by greater use of the service that there would be no net increase in expenditure on it. If only we could rediscover these splendid certainties today!

I cannot resist another quotation from the Beveridge Report while I am at it. It is given as 'a logical corollary to the receipt of high benefits in disability that the individual should recognise the duty to be well'. I have no doubt that such an appeal to duty sounded rather different in 1942. It would be interesting to apply the concept now to such things as smoking, drug abuse and alcohol abuse.

But perhaps the objective that was in 1942 expressed in terms of duty is not all that foreign to us today. I have already mentioned the 'Look After Your Heart' campaign. This is an example of the common cause which the government expects to make with those who have a reasonable concern to protect themselves from the more damaging consequences of lifestyles which must have been beyond most imaginations in the 1940s. Of course these concerns can be exaggerated. I often find myself wondering whether those who write of the latest threats to health in our food supplies have any concept of relative risk. But be that as it may, measurement has another role to play in the achievement of a healthier society when we try to assess the risks posed by certain forms of behaviour and the benefits to be achieved by altering them.

Moving on a little in our historical excursion, a similar approach to containing the cost of the NHS was still evident 10 years later when Aneurin Bevan published his book *In Place of Fear* in 1952. The cost of the service at its inception in 1948 had been £399 million. Bevan describes his concern to see a consistent pattern of use of the new service quickly established because otherwise producing estimates for approval by Parliament would be very difficult. These were the days when fear of abuse – by people taking unnecessary dentures and spectacles, and by foreigners – were rampant. But Bevan's proud claim was that, after only one full year's experience of the new service, he 'was able to put in an estimate which was firm and accurate', to use his words. He went on, 'from that point on any increased expenditure on the service would come from its planned expansion and not from its unpredictable use and abuse. We now knew the extent to which the people would use the existing facilities and what it would cost us. The ground was now firm under one's feet.'

Perhaps the overwhelming impression one draws from this brief excursion into history is that the founding fathers of the NHS thought that they were contemplating an essentially static system. Today, we are all of us aware that the system is only too dynamic. This is demonstrated very clearly in the figures. Rounding Bevan's figures slightly, the NHS started off at an annual cost of £400 million. Forty years later the cost is some £24 billion. That is an increase of 6,000 per cent in cash terms, or nearly 440 per cent after allowing for general inflation.

Growth of spending on that scale, requiring annual Parliamentary approval, has to be explained and justified. Why is it happening? Can it be shown that the money is being used efficiently? What is it producing? Are we getting maximum value for the money? Some of these questions can be approached with greater confidence and certainty than others. I am sure this seminar will be touching on a good many of them, and I do not want to embark on what might prove to be a boring account of the facts of today's health service. But perhaps I could offer some reflections on a few of the more striking features of the landscape.

First, the dynamics of the systems. Two of the moving forces are well appreciated if not always well

understood, namely *demography* and the advance of *medical technology*. It would be a waste of your time to labour the importance of these factors. But the demands made by the growing cohort of the elderly, who are there partly because medical technology has advanced sufficiently to sustain them to even riper years, is perhaps the most prominent feature in any account of the increasing pressure on health expenditure.

But I am very conscious of a third force, namely growing public expectations. I do not mean by this just an extension into health care of the attitudes to quality, speed and variety of service that are the commonplace of a vigorous capitalist economy, though those attitudes are certainly there. It would be a subject for another seminar to consider how far they have received adequate responses from those providing health care. But I am thinking also of a phenomenon which is perhaps peculiar to a system which, like the NHS, is in the public sector, and to all intents and purposes wholly tax financed. I refer to increased intensity of the political process.

I mean two things by this. First, the politician is bombarded 24 hours a day by news and comment on radio and television often demanding his – or her – instant reaction to some local event. (If I may be permitted a personal aside, I regard the tendency of newsreaders to adopt the interrogative mode while they are still telling us of the event to which they apparently seek an instant solution as bringing us near to the ultimate black hole in this particular universe. The solution is required even before we are fully aware of the problem. Fact is swallowed by comment.)

But to end the diversion. The second element in this incessant pressure is the projection of a particular clinical event into a national challenge to the system. This turns the political chess game into a three-dimensional contest, as it were, because the responsible politician finds him or herself compelled to leave the broad uplands of policy to grapple publicly with the clinical details of an individual case.

The consequence of all this is that there is a greater premium than ever on the need to deploy resources efficiently and effectively, and to be able to demonstrate that this is being done. This brings us back to measurement. The individual case is, of course, incapable of measurement in the sense in which we are considering it. The case has a significance – and no doubt an emotional appeal – of its own, for good or ill, not least because the doctor looking after the individual patient will be judged professionally by whether he has done the best he can. But its broader significance, and in some sense a comment on the system of health care, depends very much on what can be demonstrated about the efficiency and effectiveness of that system generally. Are the resources involved being deployed in such a way as to tend towards a maximisation of the benefits to be derived from them? If not, what are the options for improving on the situation? It is far easier to pose these questions than it is to suggest an approach to answering them, let alone come up with a pat solution. The growing complexity of health care – generally, not just in the NHS – makes the task ever more demanding.

The front over which health care must be provided has undoubtedly widened beyond any expectation of 40 years ago. In the acute hospital sector, for example, technology and treatment methods have in a sense climbed on one another's shoulders to make possible things that were unthinkable then. An excellent example is the way in which advances in anaesthesia have made possible major surgery on elderly patients. Numbers of in-patients, day-patients and out-patients attendances have all increased. The use of each available bed has improved, and the average costs per case have fallen in the acute and maternity srvices. But these are intermediate outputs measurable in the performance indicators which the NHS has been developing. They may or may not be adequate as proxies for the real outputs which can be the only ultimate concern of the service.

Nevertheless, the NHS and the department may claim some progress in tackling these problems, and I believe we can give a reasonable account of our stewardships. But rightly, we shall not be allowed to rest on our laurels. The pressures which I have so briefly outlined show no signs of reducing – quite the contrary. And there is still too much evidence from comparisons of local performance of the scope for improved efficiency within the service. Although with minor exceptions the NHS does not have paying customers, in the sense that money passes in exchange for the service rendered, the patient is generally the paymaster too, because he or she (or at least some very close relative) is also the taxpayer.

I am tempted to pause here to explore the relationship between the realities of the NHS and the realities of government, something which has to be kept in good order if the health service is to thrive. It is too easy for people who are engaged in political cut and thrust in and around Westminster and Whitehall to forget the impact they can have on those delivering health care. Equally, the people at that end can forget that so long as the NHS is tax financed the political process is as real for them as the bank manager is for the local businessman. An enterprise which in 1989/90 will account for some 12 per cent of general government receipts, which includes all central taxes, local authority rates and national insurance is not accidentally bruised by the political process. It is rooted in it. But I fear it would take us too far away from our main theme, and intrude too much on your patience, to develop this

variation, which again refers to the need to address the efficient use of resources.

However, I should like to pick up one of the topics which is in a recent product of that often stormy relationship between health service and government, namely the White Paper 'Working for Patients'. The topic I have in mind is the indicative drug budget. The White Paper says of this:

> 'The objective of this scheme is to place downward pressure on expenditure on drugs, particularly in those practices with the highest expenditure, but without in any way preventing people getting the medicines they need. In this way prescribing can be improved and wasteful expenditure avoided, for the benefit of the NHS as a whole.'

So drug budgets are not intended to prevent patients receiving the medicines their doctors judge they need. Nor are they intended to prevent doctors from practising high-quality medicine – quite the reverse. Nor are they to be seen as a means of preventing newly developed medicines from being available to patients. Rather, they are intended to encourage more effective use of a particular part of NHS expenditure by encouraging practitioners to ask themselves questions about why they are proceeding in such and such a way. Sometimes the answer would undoubtedly satisfy the sternest critic. But sometimes one suspects it might not stand a moment's scrutiny. Prescribing costs per head ranged in 1986/87 from £26 in one FPC to £40 in another. Have we really asked – and answered – all the questions that are to be asked about this? Are we satisfied that other possible claims on the resources involved should take second place to sustaining differentials of this kind? These must surely be legitimate questions, and they forge a link between the work of this seminar and the changes which the NHS is now tackling.

The recent White Paper certainly provides a further indication of the importance of improved measurement. Such reforms as the internal market, the use of contracts, audit (both medical and financial) and the Resource Management Initiative will either directly generate improved information about the way the health service works or are dependent on such information for their success.

I hope I have said sufficient to justify my own belief that the measurement of health costs – and of the benefits which they generate – *is* worth it. It is certainly something with which the Department of Health is much concerned. I was fortunate to inherit a department which has for many years made an important contribution to the analysis of health care problems. 1989 sees our coming of age in the practice of the discipline of health economics, although being frugal people we have not so far arranged any celebrations to mark the event. It is 21 years since the first professional economist was appointed to the staff of the department. Since then, our Economic Advisers' Office has made an increasing, and I believe increasingly valuable, contribution to our work.

In the mid-1970s we published a consultative document on priorities in spending on health and personal social services. That was based substantially on economic analysis, and recognised the difficulties of identifying suitable output measures to provide a basis for assessing the benefits enjoyed from the considerable costs incurred in providing these services. In the same tradition, there has, over the years, been much exchange of economists between the department, universities and other institutions, and the department has provided long-term financial support to post-graduate training in health economics. All of this I welcome, just as I welcome the fact that the product of this seminar will no doubt give us further opportunity in the department to go on building vigorously on these foundations.

I hope that in striking the seminar's tuning fork, so to speak, I have not chosen a note that is either too high, in the sense of being unattainable, or too low, in the sense of being hardly worth the breath expended on it. Perhaps in conclusion I may be permitted another quotation from Enoch Powell's 1961 lecture, because it seems to me to repeat the theme which I believe is central to this seminar. Towards the end of his remarks, he said this:

> 'To attempt to measure the vitality and value of the service by the size of the absolute or relative claims it exerts upon resources is to turn our backs on the history of human progress, which has been conditioned by discovering how to do more with less and so release effort and resources from old purposes to new.'

This process of discovery involves measurement. It involves value judgements. It takes us towards what my distinguished predecessor, Kenneth Stowe, called in his recent Rock Carling Lecture 'a morass of moral and conceptual problems through which the right path is hard indeed to find'. He went on to say:

> 'Public and well-informed consideration of these issues is highly desirable and, at present, sadly lacking save in a few specialised precincts like the departments of universities studying health economics and a few specialists inside government departments.'

I see this seminar as a welcome occasion for carrying forward a part of that process of exploration, of discovery. I am sure it will do so with distinction, and I am even more sure that my department and I shall not be alone in benefiting from the contribution which it will make.

TRADITIONS OF SOCIAL INSURANCE

Rudolf Klein

My role today, I believe, is to provide some of the wider context for the papers that follow. So I shall be talking about the traditions of social insurance in Europe, and examining some of their implications for health policy today. Note, however, the plural. I do not think that there is just one tradition. I think that it is possible to identify at least two, and that many of our current policy preoccupations can be usefully interpreted in the light of the relationship (and conflict) between the two traditions.

WHAT ARE THE TWO TRADITIONS?

First, I would identify the Anglophone tradition of social efficiency, where the function of social insurance (and social policy generally) is perceived to be to foster the economy – particularly by maintaining the work ethic. Second, there is the continental European tradition of social solidarity, where the function of social insurance is seen to be to maintain social cohesion and political stability.

You will realise at once, of course, that I have oversimplified. Historically, my two models have never existed in their pure form. There is overlap between them in practice. There has also been cross-national learning over the decades, so blurring the neat symmetry of my distinction. However, I hope to be able to convince you that, analytically, the distinction earns its keep. For example, it helps to explain the British reaction to the social dimensions of the European Commission's proposals for 1992. What we are seeing there – I shall argue when I come to looking at some of the implications of 1992 for health policy – is a collision as much between two intellectual traditions as between different definitions of self-interest.

More important, using these two traditions or models allows us to explore a paradox. This is that the social solidarity model imposes severe constraints on the scope for the kind of economic analysis associated with the social efficiency tradition, while yet at the same time making it more necessary. So in the first half of this talk I shall depress you by identifying those constraints – while in the second half I shall try to cheer you up by arguing that the need for good economic analysis is all the greater because of the policy drive of the social solidarity tradition.

The Chadwickian model

In trying to delineate the Anglophone tradition, I can do no better than to quote Sir Edwin Chadwick, who laid the foundations of Britain's public health policies in the 19th century. In arguing the case for state intervention in public health, he took his stand squarely on the principle of social efficiency – precisely the same principle he had invoked when helping to design the English Poor Law. The justification of social intervention by the state was the prevention of waste and the promotion of efficiency. Speaking in 1862, he argued: 'each head of the reduction of disease may be treated by the economist as a reduction of expense – a staying of waste'. Moreover, in all this, the economist had a special role to play:

> 'Where the sentimentalist and the moralist fails, he will have as a last resource to call in the aid of the economist, who has in some instances proved the power of his art to draw iron tears from the cheeks of a city Plutus.'
>
> *Journal of the Statistical Society*, vol. 25, pp. 502–524 (London, 1862)

The Anglophone tradition of social insurance has been largely shaped, it seems to me, by this kind of utilitarian approach. It is an approach which easily uses the language of economics. It is also an approach which, to mention just very briefly another aspect of the tradition, tends to encourage the development of centralised institutions and to be intolerant of the muddle of institutional diversity.

Turning to the European tradition, I can offer you no neat quotation which will encapsulate it. I suspect, in any case, that it is a more varied one, drawing on a wider range of intellectual influences. In Britain, the influence of utilitarianism is clear and strong; in Europe, we have to look at a variety of intellectual origins – Hegel and idealist philosophy in Germany, Durkheim in France, and so on. However, I would argue that central to the European tradition – in its various incarnations – is its emphasis on social cohesion and political stability. It is a tradition which emphasised the use of social insurance to maintain the existing social fabric: hence the logic, for example, of relating benefits to earnings. Furthermore, in strong contrast to the Anglophone–utilitarian tradition, the European tradition saw society not as a collection of individuals but as a network of institutions – institutions whose function it was to integrate individuals into society. In institutional terms, the European tradition is therefore more pluralistic and less centralising. It is more tolerant of localism and differentiation.

There are other differences, with implications for the theme of this conference. In the European tradition of social insurance, the language of rights – or legal entitlements – plays a large role: it is particularly important, for instance, in the case of Germany. In the British tradition, rights are much more difficult to establish: for example, the British courts have systematically repulsed a series of attempts to establish any kind of right to health care treatment. Indeed, I think that the language of analysis in the two traditions tends to be rather different. The Anglophone tradition is hospitable to the language of economics; the European tradition tends, by way of contrast, to rely more on the

language of sociology and the law. The vocabulary of the former is that of prices and costs; the vocabulary of the latter is that of values and norms. To an extent this distinction has become blurred in recent decades, if only because of the all-pervasive influence of American ideas. However, it remains important when it comes to analysing the policy implications of measuring the costs and benefits of health care interventions, for it raises the central question of the extent to which collective social benefits – over and above the benefits to individuals – should be included in any equation.

Let me illustrate this last point by moving from the general to the specific and, by so doing, show that my analysis of the two traditions has some relevance for this conference. Economists have long had fun in demonstrating the dramatic discrepancies in the valuations implicitly put on human life, without any apparent rationale (for example, Gavin H Mooney, *The Valuation of Human Life*, Macmillan, 1977). From the individualist-utilitarian perspective, such variations are, of course, a nonsense. From a social-solidarity point of view, however, they may be eminently rational. If we think that it is one of the functions of the state to proclaim a certain set of values – the European tradition of social insurance – then it may make very good sense, if only in some circumstances, to ignore costs: to spend more on saving mountaineers from the consequences of their own folly than we might be prepared to spend on improving a dangerous road which imperils the lives of innocent drivers. For what the money is being spent on, in my example, is not on saving particular lives but in demonstrating the caring nature of the state: the very fact that it is economically irrational makes it politically highly rational. For if it was cheap to save the lives of reckless mountaineers, the demonstration effect of so doing would be weak. If we further take the view of Fred Hirsch (*Social Limits to Growth*, Routledge and Kegan Paul, 1977) that Western societies are living off a stock of shared values that is being rapidly depleted, then investment in demonstrations designed to build up that stock would seem to be amply justified.

You may now be wondering where my argument is taking me. Am I saying that it we follow the European tradition of social insurance, then we should be more concerned with political than with economic analysis? Not quite. You will have noticed that I introduced a saving clause in what I said about the justification for demonstration expenditure on projects whose benefits are measured in terms of their contribution to social cohesion rather than in terms of maximising the impact or yield of public expenditure. I said that this was justified in some circumstances. For my intention has been not to argue against the key importance of economic analysis but rather to indicate that its domain is inevitably and rightly constrained, and that good analysis will recognise the nature of those constraints. To paraphrase Pascal, *la politique a ses raisons que l'économie ne connaît point*.

Moreover, it is not just constrained within the European tradition of social insurance. It is also constrained within the Anglophone tradition in the case of health care. For Britain's National Health Service is perhaps nearer to the European tradition than any other area of social insurance. From its inception, the NHS has been seen as an instrument for creating social cohesion: an institutionalised proclamation that health care is a collective good. Economists tend to be welcome when (like Chadwick) they demonstrate a case for extra resources being devoted to health care; they tend to be less popular when they demonstrate the case for scepticism about the use of existing resources.

To recognise these social and political constraints is perhaps also to identify possible strategies for economic analysis. First, if my argument has any strength, it suggests that the economic analysis of new drugs or procedures is likely to be most influential if it precedes their general introduction or diffusion. Once there is an identifiable group of potential beneficiaries, and once there is any evidence that at least some members of that group may benefit from the new drug or procedure, then political pressures for generalising the innovation are likely to become irresistible. The case of AZT and AIDS makes the point. It also makes a further point. This is that discrimination within or among groups of potential beneficiaries is difficult. This is particularly the case in those health care systems based on legal entitlements. However, there is a more general problem. We have to ask ourselves, I think, whether economic analysis – or the social efficiency model – carries sufficient legitimacy in our societies to justify such discrimination. If analysis suggests that a new drug or procedure is more cost-effective if used for particular individuals or groups – if, say, these yield a higher QALY count – is this likely to count as sufficient justification for discrimination among potential beneficiaries? I suspect not. And I suspect further that, in this respect, 'clinical judgment' carries greater legitimacy in our societies, even though it is now under challenge. The lesson here for economic analysis seems to be that it is likely to carry more conviction if carried out in alliance with clinicians, rather than as a challenge to their judgement.

Second, the analysis suggests that economic evaluation is most likely to be influential when it is weighing up alternative means for achieving the same ends: i.e. identifying the least-cost solution. Within a social solidarity tradition this is likely to be much more acceptable – because less divisive – than evaluations which threaten to deprive groups or individuals from

the benefits (however illusory or expensive) of medical intervention.

Third, the analysis implies – rather against one's preconceptions – that economic evaluation may have the largest part to play in decentralised, pluralistic systems in the European tradition rather than in the kind of centralised tradition developed in the UK. In theory, a centralised system ought to be able to make national policy, having carefully weighed the evidence. In practice, a centralised system tends to give political visibility to what may be uncomfortable findings. So the system prefers not to collect the evidence: note, for example, the contemptuous attitude towards research of Sir Kenneth Stowe in his Rock Carling lectures (making an exception only for Martin Buxton's work on the evaluation of heart transplants). In contrast, a decentralised system in the European tradition provides many more low-visibility opportunities – and may therefore, in the long run, allow economists to play a larger role. Maybe that is what will happen in the UK as well, under the new order.

So much for the first, rather negative part of my paper: that dealing with the constraints imposed by one of the traditions of social insurance. Now let me turn to the more cheerful and positive part of my message. What I shall be arguing here is that the European tradition of social insurance – particularly as reflected in the Brussels Commission's proposals for the post-1992 era – will actually make it more imperative to use the instruments of analysis developed in the social efficiency tradition. The Chadwickian value-for-money approach will, I think, speak with an ever more developed European accent.

In making this point, I am not primarily referring to the resource pressures within European health care systems: i.e. the demands created by a rapidly evolving technology and changing demographic structures (to which Sir Christopher France has already referred, and on which others will no doubt elaborate). I am referring to what I see as increasing competition among different social programmes, where health care will not necessarily have the strongest claim.

Let me elaborate. If this conference had been held ten or even five year ago, the context would have been talk about the fiscal crisis of the welfare state or the health care cost explosion. Apocalypse was the fashion. Now we have seen that the European state have the steering capacity required to adjust social expenditure: the 1985 OECD report clearly showed the ability to restrain the rate of increase in expenditure, and the scope for continued if cautious growth in social spending. (*OECD Social Expenditure 1960–1990*. OECD, 1985.)

But the fact that we have moved away from the rhetoric of crisis does not mean that we can complacently settle back, and once again project past growth rates into the future. There is considerable evidence of cross-national moves to reassess the priorities of the welfare state, as well as the institutional means of delivering services and benefits.

The challenge to complacency emerges strongly from the documents of the Brussels Commission which, in turn, reflect what I have called the European tradition of social insurance. For what these documents stress are the social and political roles of the welfare state: the phrase 'social cohesion' provides a kind of refrain for many of the proposals. And indeed the emphasis throughout is strange for those brought up in the Anglophone tradition. It is on dealing with unemployment and labour market problems; it is on investing more in education; it is in asserting the rights of workers in their place of work. And so on.

By way of contrast, there is remarkably little about the traditional areas of the welfare state, such as health services. And therein, of course, lies the challenge. If priority in the allocation of resources is to be given to labour market policies and to education (rightly so, in my own view), it is going to become progressively difficult to assert the claims of health services for more money. Add to this the increasingly heard argument that investment in health should have priority over investment in health care (a somewhat slippery argument, in my view, but emotionally appealing), and it is clear that health may slip down the list of national priorities for resource allocation.

Hence, of course, the cross-national – and cross-ideological – trend towards the exercise of greater managerial control, and the invocation of the principle of competition. The prospect of continuing financial pressures – plus, crucially, the opportunities for organisational change created by information technology – are bringing about a marriage of the two traditions of social insurance. The tradition of social efficiency does not provide an adequate prescriptive or descriptive model of insurance. But it does, quite clearly, provide some of the tools needed if the European tradition of social insurance is to prosper.

THE COST OF 'NON-TREATMENT'

Björn Lindgren

INTRODUCTION

In 1985 per capita health-care expenditures averaged US$850 in the OECD countries, ranging from $250 in Greece to $1,800 in the US. This means that many industrialised countries spend between 6 and 9 per cent of their gross domestic products on health care. 10 per cent of the total health care bill – a little less in some countries, somewhat more in others – is spent on pharmaceuticals (Schieber and Poullier, 1987).

These figures represent the costs of treatment. But there is also a cost associated with the non-treatment of a disease, viz. due to the absence of adequate therapy. Thus a new therapy, a new medicine, may well increase the drug bill but at the same time potentially decrease the costs of hospital and other types of institutionalised care; reduce the number of sickdays; and increase life expectancy and quality.

In order to get a feel for the size of the cost of non-treatment, I shall present some of the main results of a recent study on the costs of illness in Sweden (Lindgren *et al*, 1989). The estimates include both direct health care costs and indirect costs, i.e. loss of productivity, distributed by major disease categories. These findings will then be related to some areas where there seem to be big holes in therapy today.

A full description of concepts, methods and data used, as well as additional results, can be found in Lindgren *et al* (1989). Here only a few essential concepts will be introduced. For more detailed overviews of the methodological issues involved in cost-of-illness studies, the reader is referred to Rice (1966), Lindgren (1981) or Hodgson (1983).

Cost-of-illness studies usually distinguish between direct and indirect costs. Direct costs are all the costs of prevention, detection, treatment, rehabilitation and long-term care due to the existence of diseases. The indirect costs of ill-health reflect the value of those goods and services that could have been produced had a person not fallen ill. Thus, direct and indirect costs are slightly different in character. Direct costs reflect the value of the resources shifted from other sectors of the economy into the health care sector due to the presence of illness. They do represent the sacrifice of other goods and services required to obtain health care, but they do not represent any lost resources. Indirect costs, on the other hand, represent the loss of potential productivity, an opportunity forgone for ever.

The sum of direct and indirect costs represents the opportunity cost of illness, i.e. the value of all resources which might have been realised in other uses than health care at the present state of technology, had illness not existed. The total costs may change over time because of improvements in medical technology (including the introduction of new medicines), prevalence of disease and changes in overall productivity.

Observed market prices of goods and services as well as of labour and other resource use were used when calculating direct and indirect costs. For both categories of costs, however, market prices are only approximations of the true opportunity costs. Market prices do not fully reflect opportunity costs unless a number of necessary conditions are satisfied. These are, *inter alia*, (a) that each market is in equilibrium; (b) that there is no involuntary unemployment, i.e. that the labour markets are in equilibrium; (c) that markets are competitive; and (d) that there are no externalities in the production or consumption of any goods and services (Bohm, 1987).

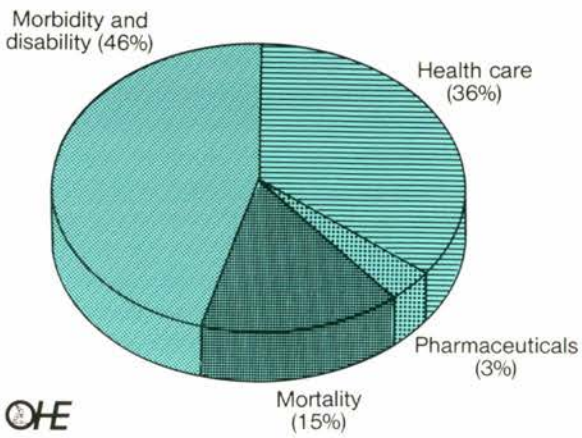
When these conditions are not fulfilled, market prices have principally to be adjusted in order to reflect opportunity costs correctly. This is seldom done in practice, however, partly because of computational problems, and partly because most market prices might at least approximately be regarded as sufficiently good measures of opportunity costs. In any case, direct and indirect costs should be treated consistently. Thus, high unemployment rates should lead to downward adjustments of both observed health care costs and estimated productivity losses.

For Sweden, the number of job vacancies has been greater than the number of unemployed people for a long time; hence full employment was assumed in the Swedish study (Lindgren *et al*, 1989). No further adjustments of market prices were made either.

Intangible costs constitute a third category of costs consisting of the psychological effects of pain, suffering, insecurity and grief associated with illness. This type of costs should, ideally, also be included in an estimate of the costs of illness, at least in principle. Research on health-related quality-of-life measures suitable for economic assessments is still in its infancy, even though important and promising work is going on; see, for instance, Brooks (1986), Drummond, Teeling Smith and Wells (1988) or Williams (1990). Moreover, there is still no consensus among health economists on the measurement of health and its changes at this aggregate level. Nor is the commensurability of intangible costs on one hand and direct and indirect costs on the other at all clear.

Consequently, most estimates of the economic impact of illness concentrate on the direct and indirect costs, and so does our study. Secondary data were used, data which are fairly easily available in official documents. The collection of primary data tailored to the measurement of the costs of illness would have been too resource-consuming. Data were provided by a number of sources, for instance by the Swedish National Social Insurance Board and the Swedish National Bureau of Statistics. Availability of data explains the choice of 1983 as the year of study (Lindgren *et al*, 1989).

1 COSTS OF ILLNESS IN SWEDEN 1983
Total: SEK 162 billion



THE COSTS OF ILLNESS IN SWEDEN

According to Figure 1, estimated total direct and indirect costs of illness were SEK 162 billion in Sweden 1983. Pharmaceuticals accounted for only 3 per cent of this total figure, and health care in total for 39 per cent. This means that the indirect costs dominated. Productivity losses due to short-term morbidity and long-term disability accounted for 46 per cent of the total costs, and premature mortality for 15 per cent.

It should be observed that mortality costs consists of the loss of present output as well as the loss of future output due to 'premature' death. (In this context 'premature' effectively means 'before normal or legal retirement age', since very little is produced by people above normal retirement age.) Adding present and future outputs (here approximated by earnings) raises the question of choosing the appropriate discount rate (Keeler and Cretin, 1983). 5 per cent was used; it is a fairly commonly used discount rate in this type of study.

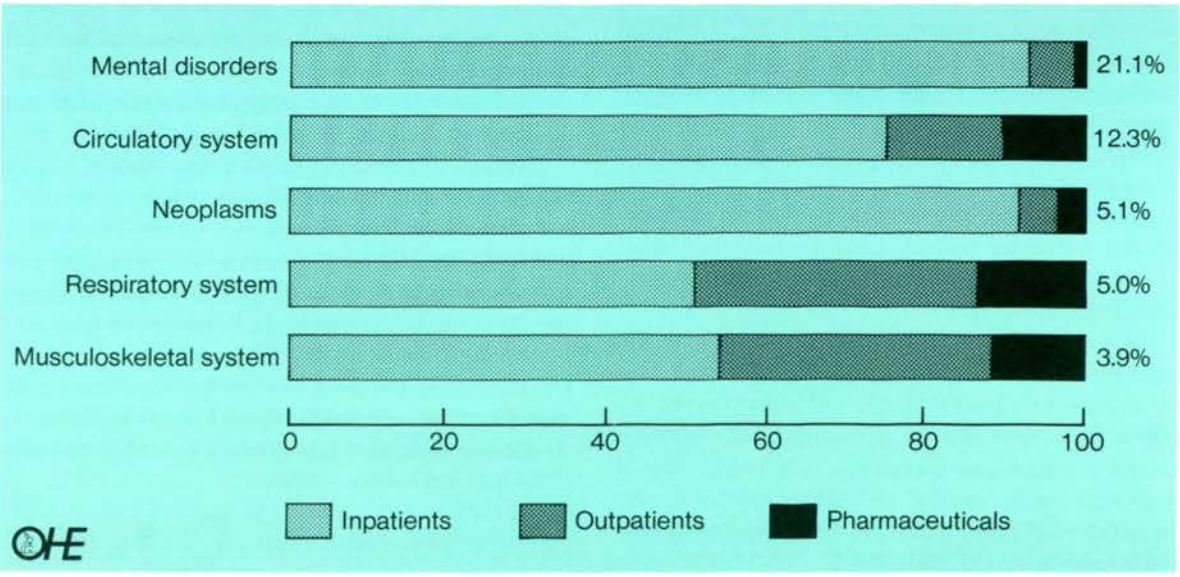
It should also be observed that the size of the whole 'cake' may in fact depend on the size of its different parts. It is fairly obvious that if 'unnecessary' or 'incorrect' drug use could be reduced and inefficient use of other scarce health care resources could be avoided, then both those particular parts of the 'cake' and the 'cake' itself can be diminished.

It is not so obvious that the 'cake' can become smaller if some of its parts are increased. It may be true, however. Sometimes, an increased use of health care may enable productivity losses to be reduced, for instance, for people at working age waiting to get their total hip replacement. Besides, the use of a new medicine may reduce both other health care costs and productivity losses. So the really interesting question here is not how to minimise the use of pharmaceuticals, but rather to minimise the total burden of illness. Then the question changes into the different problem of optimising the use of pharmaceuticals. The issue is how to use pharmaceuticals and other scarce health care resources most cost-effectively.

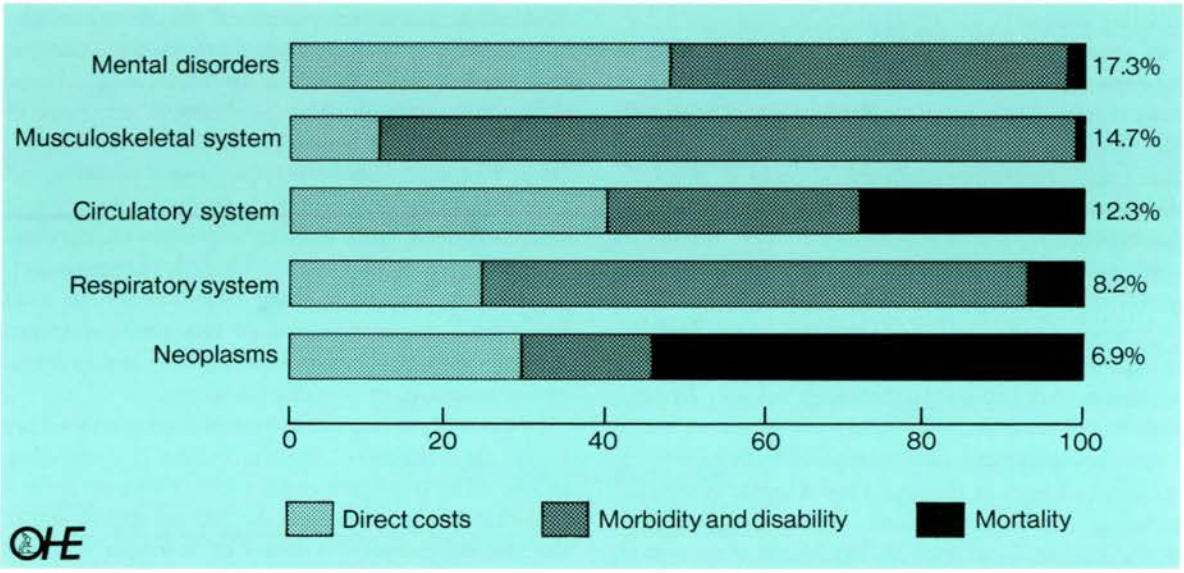
THE MOST EXPENSIVE DISEASES

Figures 2 and 3 reproduce estimates of the costs of illness in Sweden 1983 for those diseases that had the greatest economic impact. Figure 2 concentrates on the direct costs of the health care system. For each of five selected main disease categories, Figure 2 presents estimates of the direct costs as a percentage of the total direct costs in

2 DIRECT COSTS OF ILLNESS IN SWEDEN 1983
Selected main disease categories



3 TOTAL DIRECT AND INDIRECT COSTS IN SWEDEN 1983
Selected main disease categories



Sweden 1983 (column far right). The dominating disease category, according to our estimates, were mental disorders with about a fifth of the total health care bill; followed by diseases of the circulatory system (12 per cent). Cancer, diseases of the respiratory system and diseases of the musculo-skeletal system each accounted for 4–5 per cent.

About 80 per cent of the total health care costs were allocated between the 17 main disease categories in this way. The remaining 20 per cent (or SEK 12 billion) consists mainly of dental care and care for the mentally retarded.

Figure 2 also shows, for each main disease category, the distribution of the costs by type of health care: in-patient care, out-patient care and pharmaceuticals. In-patient care accounted for more than 50 per cent of the direct costs in all categories but diseases of the skin and subcutaneous tissue and symptoms and ill-defined conditions. In-patient care accounted for more than 90 per cent for treating cancer and mental disorders. Pharmaceuticals had a relatively large share of the costs for treating diseases of the respiratory system (13 per cent).

Figure 3 reproduces the main findings on the total (direct and indirect) costs of illness. Roughly the same categories dominated here also. There were some differences, however, for instance in the ranking order among the categories. Mental disorders certainly also led this league (17 per cent). Disorders of the musculo-skeletal system, however, due to their impact on the morbidity and disability costs, now ranked second (15 per cent). In fact, diseases of the musculo-skeletal system accounted for the lion's share – almost 30 per cent of the morbidity and disability costs.

Diseases of the circulatory system ranked third (12 per cent). This category had high shares of the direct costs, as well as of both morbidity/disability costs and mortality costs. Another category which dominated mortality costs was cancer; cancer and diseases of the circulatory system together account for roughly 50 per cent of all mortality costs.

The three largest categories accounted for about 45 per cent of the total costs in 1983; the same disease categories together had, actually, exactly the same share in 1975 (Lindgren, 1981).

MEDICINES AND THE COST OF 'NON-TREATMENT'

If we had been able to construct a similar table for, say, 1920 or even 1930, infectious diseases would probably have led the league. Since then, better living standards, public health measures and the discovery and introduction of antibiotics and other drugs have mastered most infectious diseases in the industrialised world. Today, infectious diseases account for only 1.6 per cent of the costs of illness in Sweden.

During the last 50 years there have been a number of pharmaceutical discoveries. Still there remain big gaps in therapy, whether treatment with drugs or by other means is involved. The costs of these therapeutic gaps – the costs of 'non-treatment' – are considerable, as have been indicated by Figures 2 and 3. This fact would have been

even more accentuated if we had been able to cover also the intangible costs associated with discomfort, pain, suffering and grief.

It should be observed, of course, that I am not suggesting that all the costs of illness as measured in our study represent the cost of 'non-treatment'. The cost of non-treatment is part of the story. And the total costs of illness must be further analysed in detail in order to identify the most important areas of non-treatment and their costs.

Mental disorders, diseases of the musculo-skeletal system, diseases of the circulatory system, diseases of the respiratory system and cancer are five of the greatest medical problems in terms of economic resource consequences. All five have substantial holes in therapy (Booth, 1989).

Among mental disorders there seem to be numerous examples of gaps in therapy. One is senile dementia, including Alzheimer's Disease. Senile dementia presently accounts for at least 25–30 per cent of the cost of mental illness in Sweden. It is an old-age problem. In an ageing population, it becomes a growing problem. Despite interesting and encouraging research, for instance on the role of nerve growth factors in preserving or regenerating nerve tissues, physicians are still powerless to change the progress of disease. Even medicines for significantly reducing the disability suffered by dementia victims, although without affecting the underlying impairment, would be a great improvement. For many other unfortunate sufferers of mental handicaps the best one can do at present is to provide for their life-long support. Little is known about the normal function of the brain and how it is disordered in conditions such as schizophrenia or manic-depressive states.

There is also a big cost of non-treatment hidden in the costs of diseases of the musculo-skeletal system. A treatment for osteoarthritis, for instance, might reduce or totally eliminate the necessity for total hip replacements – thus more or less solving the problems of waiting lists for orthopaedic surgery in Sweden and many other countries in Europe. People suffering from rheumatoid arthritis can certainly be helped by physiotherapy and modern medicines, but the aetiology of the disease is unknown and treatment remains symptomatic only. Other diseases of the musculo-skeletal system that contribute to the cost of non-treatment include fractures of the neck of the femur and osteoporosis, both considerable problems for elderly women.

Despite the progress in medical research and despite the introduction of new medicines, diseases of the circulatory system are still the major killer in the population at large in the western world. For younger age groups, only accidents, poisonings and violence and neoplasms contribute more to productivity losses due to premature mortality (30, 24 and 23 per cent respectively; Lindgren *et al*, 1989). Whereas the role played by the new medicines in the decline of stroke seems to have been established, the interpretation of the causes of the reduction in coronary heart disease mortality has not yet been made clear. New medicines which reduce blood cholesterol levels promise to diminish the risks of developing primary events of coronary heart disease. Other new medicines both reduce blood pressure and have favourable effects on the high-density lipoprotein/total cholesterol ratio. In order to prevent the development of cardiovascular disease, life-style changes in diet, physical exercise and smoking behaviour may be most important. The contribution of new pharmaceuticals may, however, still be considerable both in prevention and in treatment once the disease occurs.

Diseases of the respiratory system accounted for 8 per cent of the total costs of illness in Sweden 1983 according to our study (Lindgren *et al*, 1989). This may seem a remarkably large share, but the relative importance of this disease category in terms of economic resource consequences is to a large degree explained by absenteeism from work due to the common cold. So far, no treatment has been possible for people afflicted with the common cold. The responsible viruses seem now to have been identified; will a cure be developed?

Besides accidents and cardiovascular disease, cancer remains a major killer. So, despite all the efforts made so far, cancer in all its forms is still one of the major challenges to medical research. Although cancer treatment has been improved in recent years by new medicines and by earlier detection of the disease made possible by modern imaging techniques, much remains to be done. A whole range of medicines which can selectively kill cancer cells without affecting the normal cell population seems to be needed. In prevention, the reduction of smoking may be one of the most important measures to be taken.

CLOSING REMARKS

Three remarks conclude this paper.

Firstly, pharmaceuticals account for a fairly small share (3 per cent in Sweden) of the total costs of illness. Despite the small share, efforts should, naturally, be made to reduce 'unnecessary' drug use. On the other hand, a new medicine may well increase the drug bill at the same time as hospital costs will be decreased; the number of sick-days reduced; and life expectancy and quality increased. So, for society at large, the question is not how to minimise or, for that matter, how to maximise the costs of pharmaceuticals, but rather how to induce the optimal utilisation of existing drugs as well as how to encourage the optimal innovation rate for new drugs.

Secondly, there are still big gaps in therapy, where the lack of treatment causes much discomfort, pain and suffering as well as health care costs and productivity

losses. We have identified only a few of these gaps here, but the cost of 'non-treatment' seems to be considerable.

Thirdly, there is obviously great potential for new medicines and for the companies that will succeed in developing these new medicines.

REFERENCES

Bohm P (1987). *Social Efficiency. A Concise Introduction to Welfare Economics*. 2nd edn. London, Macmillan Education.

Booth C (1989). *Holes in Therapy*. London, Office of Health Economics.

Brooks R G (1986). *The Development and Construction of Health Status Measures. An Overview of the Literature*. IHE Report 1986: 4. Lund, The Swedish Institute for Health Economics.

Drummond M F, Teeling Smith G and Wells N (1988). *Economic Evaluation in the Development of Medicines*. London, Office of Health Economics.

Hodgson T A (1983). 'The state of the art of cost-of-illness estimates'. In *Advances in Health Economics and Health Services Research*, Volume 4 (ed. by R M Scheffler and L F Rossiter). Greenwich (Conn.), JAI Press Inc.

Keeler E and Cretin S (1983). 'Discounting of life-saving and other non-monetary effects', *Management Science*, 29: 300–306.

Lindgren B (1981). *Costs of Illness in Sweden 1964–1975*. Lund, Liber.

Lindgren B, Jendteg S, Palmgren H-Å and Mårtensson A (1989). *Vad kostar sjukdomarna de svenska medborgarna?* (What are the costs of illness to the Swedish citizens?). Lund, The Swedish Institute for Health Economics. (In press).

Rice D P (1966). *Estimating the Cost of Illness*. Health Economics Series, No. 6: Public Health Service. Washington DC, US Government Printing Office.

Schieber G J and Poullier J-P (1987). 'Recent trends in international health care spending', *Health Affairs*, 6 (Fall): 105–112.

Williams A (1990). 'Importance of quality of life', *Measuring the Benefits of Medicines: the Future Agenda* (ed. G Teeling Smith). London, Office of Health Economics. (This volume).

HEALTH CARE SYSTEMS AND ECONOMIC ANALYSIS

Martin Buxton

THE CHANGING ENVIRONMENT

The organisation, structure and incentive systems of health care programmes in many countries throughout the world have undergone major changes during the last few years, and the pace of change appears to be increasing. In the US, the far-reaching effects of the move to a system of predetermined payment per episode of care categorised by diagnostic related groups (DRGs) are still rippling through the health care system. Rather more slowly the effects of DRGs in the US are being analysed and reported (for example, Schramm and Gabel, 1988; McCarthy, 1988; Davis and Rhodes, 1988; and Kane and Manoukian, 1989). Already work on DRGs is being carried out in most European countries (Bardsley, Coles and Jenkins, 1989). Other examples of important changes are numerous: the Netherlands are now implementing the 'Dekker' proposals for regulated competition put forward in 1987 (Kirkman-Liff and van de Ven, 1989). In Sweden a government commission has been set up to make proposals for changes in the health service information system that could help to increase the efficiency of the health care sector, under the influence of Alain Enthoven (1989). New Zealand has embarked on a fundamental process of decentralisation of responsibility for decision-making to hospital boards with a population-based funding arrangement (Malcolm, 1989). In the UK, following the White Paper (Secretaries of State, 1989), the National Health Service is about to embark on a series of changes of a magnitude not seen since the establishment of the NHS in 1948. One of the most important of these is likely to be the introduction of formal contracts for particular health care services between hospitals and district health authorities (Robinson, 1989). Whatever the overall merits of these and other changes, they form the environment within which economic evaluation takes place and to which economic evaluation has to be sensitive.

A few of these changes explicitly affect the requirement for economic evaluation. The French so-called 'transparency committee' invites economic evidence in deciding on the reimbursement categorisation of new drugs, and the same criterion seems to be included in the EC directive on transparency of drug pricing (EC, 1989). More explicitly, new rules for Medicare coverage proposed by the Health Care Financing Administration in the US include for the first time cost-effectiveness as a criterion for the funding of a technology or procedure (Leaf, 1989).

But in addition to such cases as these where health care system changes introduce an explicit requirement for economic evaluation, all health service reforms subtly change the decision-making environment into which economic evaluation can feed.

TRADITIONAL CLINICAL AND ECONOMISTS' MODELS OF ALLOCATING RESOURCES

Historically, health economics has struggled against the traditional model of the clinician making decisions with respect to the treatment of his patient on the basis of trying to do anything that might benefit the patient irrespective of cost (and often, worse, simply doing all that is technically feasible regardless of likely benefit). Professor Archie Cochrane, who as a questioning epidemiologist did so much to help promote the basic ideas of economic evaluation, likened this sort of behaviour by doctors to a quote from T S Eliot (Cochrane, 1972). He suggested his colleagues acted:

> 'Not for the good that it will do
> But that nothing may be left undone
> On the margin of the impossible.'

It is hard to say whether this attitude is still a fair representation of the way in which many doctors think. Some are quite explicit about their denial of the relevance of cost. In 1980 the *New England Journal of Medicine* still felt it appropriate to publish the following views of an American MD, Loewy (1980):

> 'Of late an increasing number of papers in this and other journals have been concerned with "cost-effectiveness" of diagnostic and therapeutic procedures. Inherent in these articles is the view that choices will be predicated not only on the basis of strictly clinical considerations but also on economic considerations as they may affect the patient, the hospital, and society. It is my contention that such considerations are not germane to ethical medical practise . . . A physician who changes his or her way of practising medicine because of cost rather than purely medical considerations has indeed embarked on the "slippery slope" of compromised ethics and waffled priorities.'

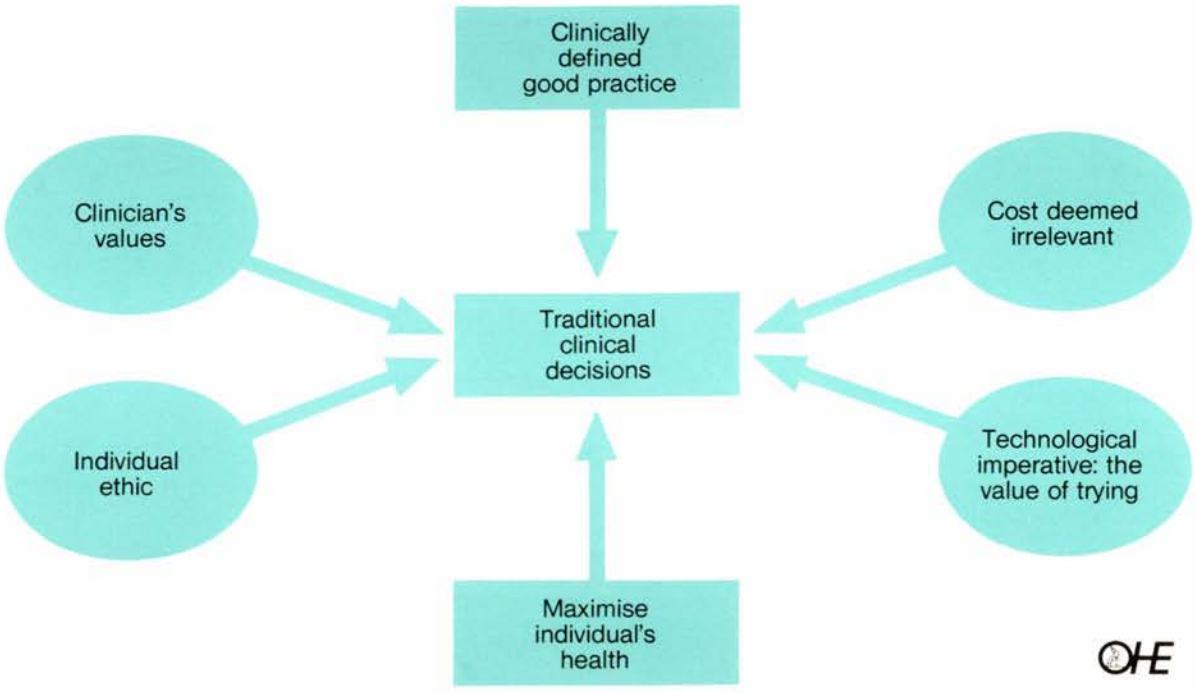
And currently in the UK, some of the professional reaction to indicative budgets for GPs seems still to imply that the cost of drugs should be an irrelevant consideration in prescribing for patients.

But referring to the professional opposition to the introduction of the 'limited list' in 1985, Sir Raymond Hoffenburg (1987) took the view that:

> 'The profession in this instance chose a weak issue on which to defend its rights; that they did so is an indication that the tenet of "clinical freedom" – in this case, to prescribe freely – is still firmly entrenched in the professional mind and its sanctity is to be safeguarded.'

Professor Bryan Jennett (1988), in supporting the role of economic evaluation, deplored the way that:

> 'under the guise of ethics' these 'clinical freedom fighters hope to legitimise their attempts to secure all possible services for *their* patients, regardless of the



expectation of benefit relative to the prospects of other patients'.

This traditional clinical decision model, the world of the clinical freedom fighters, is represented in Figure 1. It is characterised by a decision paradigm that:

- is based on 'good practice' as defined by clinical opinion;
- relies on the individual values of the doctor concerned;
- assumes an individualist ethic towards each patient;
- encourages a technological imperative to do all that is feasible;
- deems costs as irrelevant; and
- aims to maximise an individual's health.

Health care economics has traditionally argued from a completely different paradigm, but has usually focused its attention on central planning, priority-setting or regulatory decisions. Its model (Figure 2), firmly built on welfare economics, is characterised by:

- good practice defined in terms of evidence of health benefits from clinical trials;
- priorities and values reflecting society at large;
- a collective ethic for society as a whole;
- consideration of all costs falling on society;
- the viewpoint that the process of medical care has no inherent value in itself;
- the aim of maximising societal health.

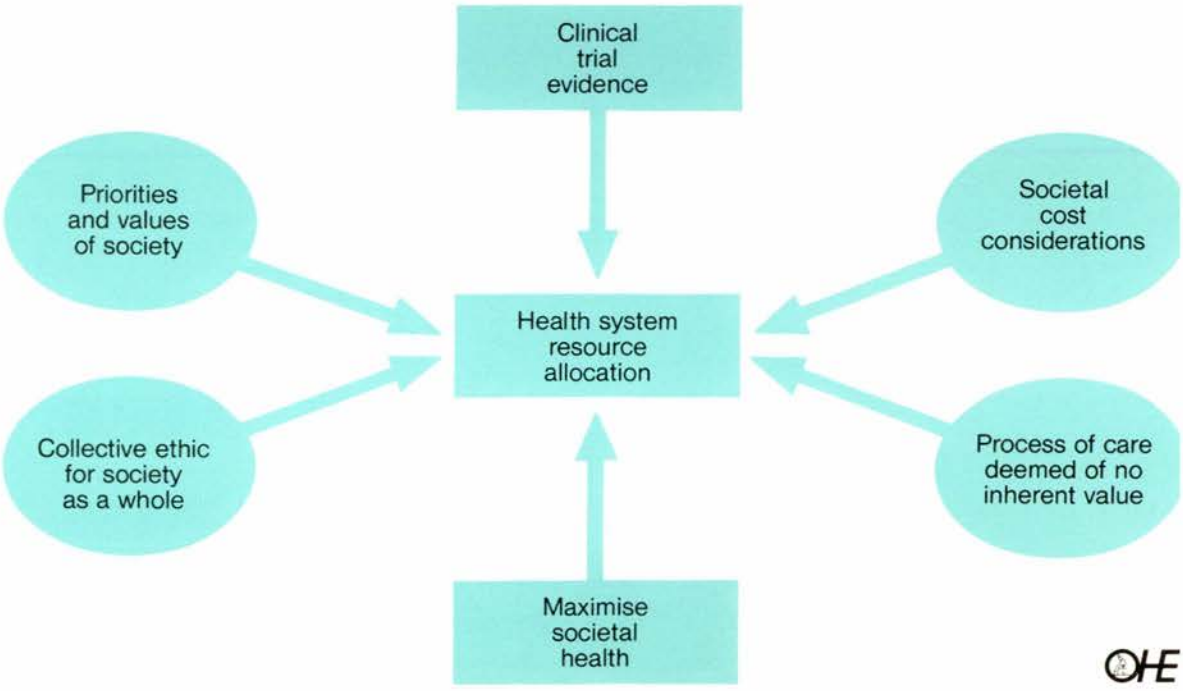
For as long as most of the applications of economic evaluation within this framework have been about decisions at the planning or regulatory level, they have been sufficiently divorced from the individual doctor/patient interaction for the disparity between the two models to be implicit, and the two models not to be in open conflict.

Few of the many economic evaluations carried out over the past decade or so have tried directly to impinge on the individual doctor/patient relationship, but have instead, at a more macro-level, constrained the range of resources available to the doctor. Economic evaluation in the UK has typically contributed to decisions about provision of screening services, or location of hospital facilities, or diffusion of new technologies. The author's study of heart transplantation in the UK fits into this mould (Buxton *et al*, 1985) and it is clear that it contributed to the rational diffusion of this expensive but effective technique (Stowe, 1988). However, the danger is that economic support for a particular technique as used at a point of time is taken as blanket support for that technique (and any number of variations on it), even when the technique is applied to different patient groups with poorer results or at greater cost (Mulcahy *et al*, 1988).

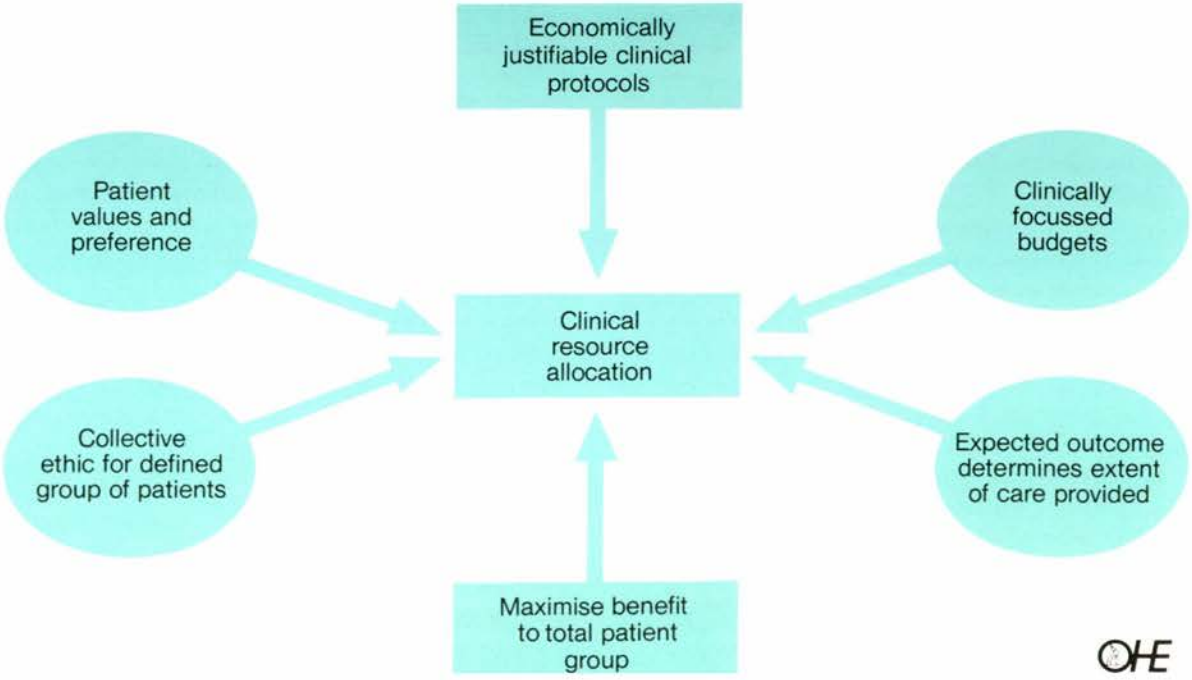
THE EMERGING CLINICAL RESOURCE MANAGEMENT MODEL

But what is, or will be, the effect of the ubiquitous health care reforms? It can be argued that in part at least they have been concerned to make individual doctors behave in a manner more like the economists' resource allocation

2 TRADITIONAL ECONOMISTS' HEALTH CARE RESOURCE ALLOCATION MODEL



3 CLINICAL RESOURCE MANAGEMENT MODEL



model, whilst at the same time reducing the need for centralised decisions on location, priorities etc. Many reforms have tried to leave with clinicians, or indeed give back to them, responsibility for decisions about appropriate care, within a framework of incentives and competition. The reformers hope that this should lead to more efficient health care systems by requiring providers to balance costs and benefits. The implied model in these changes, which I have called the 'clinical resource management model' (Figure 3), is characterised by:

- practice informed by economically justifiable clinical protocols;
- reference to patient values and preferences;
- a context of a collective ethic for a specifically defined group of patients;
- consideration of all costs falling within a clinically focused budget;
- expected outcome determining the extent of care provided;
- the aim of maximising benefit to the defined group of patients within a predetermined budget.

It would be wrong to give the impression that progress towards such a model will necessarily be fast or painless. Work in the Health Economics Research Group at Brunel monitoring the pilot sites in the Resource Management initiative which intends to put clinicians into just such a role, shows that this process is happening, but slowly and painfully (Buxton, Packwood and Keen, 1989; Packwood, Buxton and Keen, 1989). Major informational, organisational and cultural changes are required. But the common direction of change in several health care systems is towards this 'resource management model'.

It will, of course, still leave certain arbitrary budgetary boundaries within the process of care. Hospitals may not pay much attention to costs imposed on GPs. Similarly, there is a worry that hospital costs and payments for care will be analysed in terms of admissions rather than true episodes of care, and the true costs of readmissions will be ignored. Such anomalies, perverse incentives or discrepancies will need monitoring and economic analysis will be required to show their effect and to press for further changes.

But, within this new 'resource management' paradigm, the role and scope for economic evaluation will change and, indeed, is already changing. The impact on economic evaluation will be both positive and negative. On the negative side of the balance, it is likely that it will become increasingly difficult to persuade clinicians to take note of cost implications outside their own budgets. This is always true of systems with constrained budgetary responsibility: not worrying about someone else's budget is behaviour that we instantly recognise from within any large organisation. In systems where budgets have not been rigid, and constraints not too tight, then unselfish behaviour contributing to a wider benefit may well have been practised. But once budgets become tight and pressures for greater 'efficiency' are increased, then such generosity is more difficult to sustain. In the past the NHS has relied heavily on goodwill and responsible behaviour. Its efficiency hitherto has been more *despite* of the incentives built into the system rather than *because* of them. For example, given the way in which hospital doctors have been rewarded and promoted, it is amazing that so much routine patient care has been undertaken. But, as the rules of the game are drawn explicitly to achieve cost-effectiveness, rather than expecting cost-effectiveness to be a moral obligation on providers, then the more providers are likely to play the game strictly according to the limitations of the rules, to work the system as best they can, and to leave it to the 'rule-makers' to cope with the anomalies.

On the positive side of the balance, the new clinical resource management model provides exciting opportunities for economic evaluation. There is no reason to suppose that local collective health care purchasers or funders will be any less interested in the broad comparative data as to how much health benefit can be bought within a fixed budget by purchasing treatment for cancers, or cardiothoracic surgeries, or screening or prevention strategies. The broad-brush comparisons of interventions, in the now familiar cost per life-year gained (or cost per QALY) league tables, will be just as relevant for those purchasing care from providers to best meet the needs of the population for which they have responsibility as it has been to health authorities with more centralised planning.

But in addition, the changes should provide the environment in which to begin to interest clinicians in the economics of their detailed practice. Clinical managers competing for contracts, or for patients on a prospective payment basis, have the right incentive environment to become actively interested in, for example, how alternative diagnostic sequences will affect costs and benefits, or how alternative drug therapies influence the total costs of hospitalisation. In working in this area health economics needs to build on, and integrate with, the medical decision-making literature, much of which currently does not consider costs at all, nor adequately deals with the value of different outcomes to the patient. It does, however, provide a rigorous conceptual framework, which is comprehensible to clinicians, and can readily be made to incorporate these economic dimensions of costs and patient utilities.

PRESCRIBING IN HOSPITALS IN THE CHANGING ENVIRONMENT: AN ILLUSTRATIVE EXAMPLE

By way of illustration, let us consider prescribing in hospitals in the UK and the way that the changing

economic environment within hospitals has affected the nature of the relevant economic evaluation. For many years the hospital drug bill was not a key issue. With functional budgets, hospital pharmacy costs were visible and were regularly subject to budget reductions at the beginning of the financial year – in that cutting the size of the drug bill did not involve staff cuts or externally visible bed closures. But typically, by the end of the year, pharmacy budgets were overspent because of the lack of a mechanism to control them. This situation was merely exacerbated when strict cash limits on hospitals effectively controlled overall expenditure, but still no mechanism existed to effectively control the drug bill. Clinicians were free to follow their traditional model and ignore costs. Studies, such as that on the cost-effectiveness of cimetidine by Culyer and Maynard (1981), could provide important indications of relative cost-effectiveness of different drugs or treatments. However, the budget structures provided no real incentive to clinicians to pursue cost-effective therapy, if it did not happen to coincide with their preferred clinical practice. [Measures, such as minimising the quantity of drugs patients took home on discharge may have helped the hospital pharmacy budget, but did nothing to increase – indeed, would have reduced – the efficiency of the health care system as a whole.] The development of hospital formularies was (and still is) an attempt to introduce an element of control by encouraging or requiring hospital doctors to prescribe the cheaper drug, where the local clinical opinion is that one or more drugs of differing cost were clinically equivalent. The process of agreeing hospital formularies may have had considerable educational value (Petrie and Scott, 1987), but for as long as the focus of the activity was on keeping within a functional pharmacy budget, the scope and incentives for considering the overall costs of alternative therapies was severely limited. A more expensive drug, that could save nursing costs by leaving the patient better able to care for himself, might be more cost-effective, but without a mechanism to transfer from the nursing budget to the pharmacy budget it still appeared as a more expensive drug. Only when clinicians are given the opportunity to manage budgets for the various resources that contribute to the care of their patients, as under the emerging model, can such trade-offs be made. Economic evaluation will need to provide evidence on these trade-offs and the overall cost-effectiveness of alternative therapies in a way that is both intelligible to the clinicians, and directly relevant to the decision parameters of their new-found position as resource managers.

An economic evaluation that illustrates some of these points is a small study, carried out at Brunel, analysing the economic implications of using transdermal glyceryl trinitrate in reducing failures of peripheral intravenous infusions (Khawaja *et al*, 1989). This modelled the costs and outcomes (of infusion failure) using a probability tree to illustrate the cost implications of a decision to use patches. It showed that if the expected life of the infusion was greater than 48 hours, then the extra costs of the 'patch' would be outweighed by savings from avoiding the costs associated with infusion failure. To a pharmacist concerned only about the drug bill, use of patches would add to costs, in that most of the cost-avoided fall on other budgets. To a clinician with a fixed budget for his surgical patients, the use of patches would make economic as well as clinical sense, although in the short run certain cost savings (e.g. in nursing time) would not be immediately realisable. To a clinician competing for patients, the undoubted patient preference for avoiding painful infusion failure would make the case definitive.

CONCLUSIONS

Current and proposed changes in many health care systems, particularly to the extent that they move towards situations where doctors are given a predetermined budget for specific groups of patients *and* managerial control over the resources they use in the care of these patients, will encourage the development of clinically focused economic evaluation. There will still be arbitrary boundaries to budgets, which may leave anomalies and disincentives to consider certain wider cost and benefit ramifications of clinical decisions, but there will be the makings of a new 'resource management model' of clinical behaviour. Doctors will have an environment in which the resource costs of treatments and the benefits they give to patients are together relevant parameters in their clinical decision-making. The reality of this will need to be reflected in appropriate economic evaluation techniques reflecting the changed paradigm of clinical behaviour.

REFERENCES

Bardsley M, Coles J and Jenkins L [eds] (1989). *DRGs and Health Care*, 2nd Edition, King Edward's Hospital Fund for London.

Buxton M J *et al* (1985). *The Costs and Benefits of the Heart Transplant Programmes at Harefield and Papworth Hospitals*, DHSS Research Report no 12, HMSO, London.

Buxton M J, Packwood T and Keen J (1989). *Resource Manage-ment, Process and Progress*, Health Economics Research Group, Brunel University, Uxbridge.

Cochrane A L (1972). *Effectiveness and Efficiency: Random Reflections on Health Services*, Nuffield Provincial Hospital Trust, London.

Culyer A J and Maynard A K (1981). 'Cost-effectiveness of duodenal ulcer treatment', *Social Science and Medicine*, 15(c): 3–11.

Davis C K and Rhodes D J (1988). 'The impact of DRGs on the cost and quality of health care in the United States', *Health Policy*, 9: 117–131.

Enthoven A C (1989). 'Management information and analysis for the Swedish health care system', *IHE Working Paper 1989: 7*. Lund, Sweden.

European Community (1989). 'Directive sur la transparence des procédures de fixation des prix des médicaments: Directive No 89/105/CEE', *Journal Oficiel des Communautés Européennes*, 11 February.

Hoffenburg R (1987). *Clinical Freedom*, Nuffield Provincial Hospitals Trust, London.

Jennett B (1988). 'Appropriate high technology – a painless prescription?' in Binns T B and Firth M (eds), *Health Care Provision Under Financial Constraint*, International Congress and Symposium Series No 115, Royal Society of Medicine, London.

Kane N M and Manoukian P D (1989). 'The effect of Medicare prospective payment system on the adoption of new technology', *New England Journal of Medicine*, 321, no 20: 1378–1383.

Khawaja H T *et al* (1989). 'Cost-minimisation study of transdermal glyceryl trinitrate in reducing failures of peripheral intra-venous infusion', *British Medical Journal*, 299: 97.

Kirkman-Liff B L and van de Ven W P M M (1989). 'Improving efficiency in the Dutch health care system: current innovations and future options', *Health Policy*, 13: 35–53.

Leaf A (1989). 'Cost-effectiveness as a criterion for Medicare coverage', *New England Journal of Medicine*, 321, no 13: 898–900.

Loewy E H (1980). 'Cost should not be a factor in medical care', *New England Journal of Medicine*, 302, no 12: 697.

Malcolm L A (1989). 'Decentralisation trends in management of New Zealand's health services', *Health Policy*, 12: 285–299.

McCarthy C M (1988). 'DRGs – five years later', *New England Journal of Medicine*, 318, no 25: 1683–1686.

Mulcahy D *et al* (1988). 'Cardiac transplantation in severely ill patients requiring intensive support in hospital', *British Medical Journal*, 296: 817–819.

Packwood T, Buxton M J and Keen J (1989). 'Mapping resource management', *Health Services Management*, 85, no 6: 273–275.

Petrie J C and Scott A K (1987). 'Drug formularies in hospitals', *British Medical Journal*, 294: 919–920.

Robinson R (1989). 'New health care market', *British Medical Journal*, 298: 437–439.

Schramm C J and Gabel J (1988). 'Prospective payment: some retrospective observations', *New England Journal of Medicine*, 318, no 25: 1681–1683.

Secretaries of State for Health, Wales and Northern Ireland (1989). *Working for Patients*, HMSO, London.

Stowe K (1988). *On Caring for the National Health*, Nuffield Provincial Hospital Trust, London.

METHODOLOGIES FOR THE ECONOMIC EVALUATION OF MEDICINES

Michael Drummond

26 INTRODUCTION

The starting point for economic evaluation is the notion of scarcity of health care resources; that is, there are not and never will be enough resources to achieve all the worthwhile objectives that can be identified. The extent to which the available resources fall short of the apparent demand for care varies from country to country, but even in the relatively rich countries one can identify areas of unmet need or point to examples where a rapid increase in health care costs has diverted resources from other beneficial uses.

Therefore, given scarcity of resources, the real problem with the over-use of new medical technology is not the financial expenditures themselves, but the more fundamental cost or sacrifice in that benefits in other programmes, such as community care for the elderly, are forgone. This is why economists refer to the notion of opportunity cost; that is, the cost of a resource is equal to the benefits that it would have generated in its best alternative use. Therefore, when economists argue that attention should be paid to efficiency in health care they are implying that health care programmes, treatments and procedures should be compared not only in terms of their relative benefits, but also in terms of their relative costs (i.e. benefits forgone). Economics is therefore about choice in how the community uses its scarce resources.

The issue of efficiency can be explored in choices of different levels of complexity. For example, the relative costs of two alternative ways of meeting the same treatment objective could be assessed. The more efficient approach would be the one having the lower costs, provided it achieved the objective to the same degree. However, this says nothing about whether the objective is worth attaining. A broader level of choice would therefore be between competing objectives. Here the assessment of efficiency would be based on the relative benefits resulting from attainment of the respective objectives and the relative costs of the programmes to achieve them. As will be seen later, the broader choices require more comprehensive and complex forms of analysis.

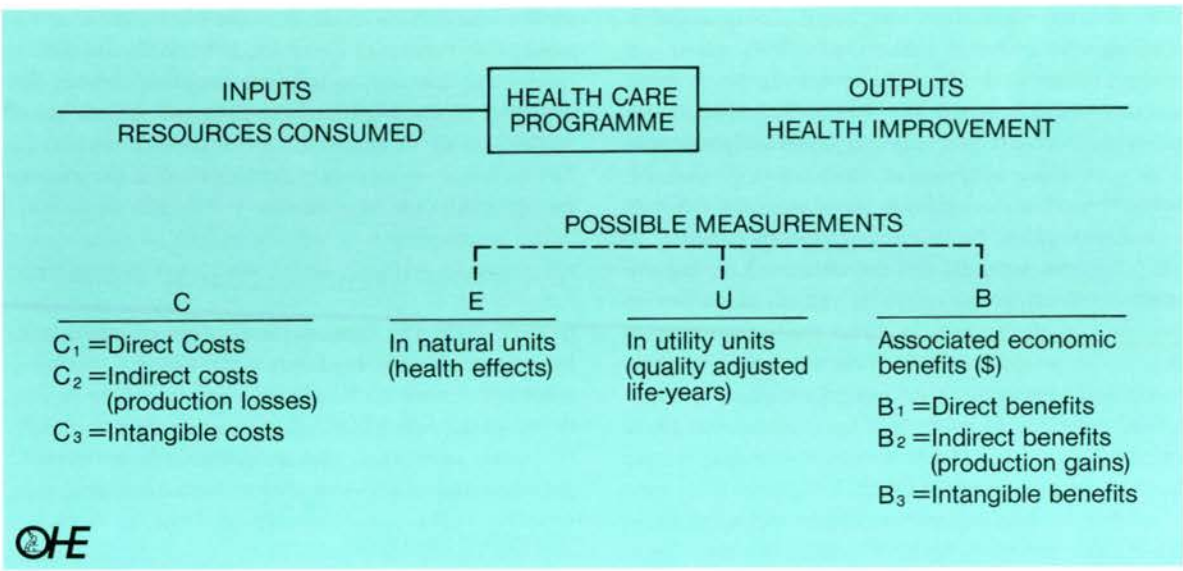
Although they accept the arguments about scarcity and the need for efficiency in principle, some clinicians are concerned that consideration of costs in clinical decision making is contrary to medical ethical principles. The first point to note is that the economic reasoning and the methods of analysis that are discussed below relate mainly to 'planning' decisions. That is, investment decisions about the kinds of facilities that should be provided, their location and the medical technologies (including medicines) that should be encouraged or discouraged from use. Against the background of the facilities made available, the clinician, in treating the individual patient, would still provide the best care at his/her disposal.

The way in which economic thinking should influence individual clinical decision making is less clear, although it should be pointed out that considering costs in decisions embodies an important ethical principle of its own; that resources should not be consumed in a given activity if they would generate greater benefits if used elsewhere. The extent to which the individual clinician considers costs in practice is likely to depend on whether he or she can identify the other uses to which the resources could be put. For example, if the clinician knows that other patients are waiting for care, he or she will tend to ration his or her time with a given patient or, in the case of in-patient care, discharge a patient earlier so that another can be admitted. Some of the policy initiatives being taken by governments such as the encouragement of pre-paid group practice, or clinical budgeting and prospective reimbursement systems for hospitals, encourage the clinical practitioner to take into account efficiency considerations

1 TYPES OF EVALUATION

Are both costs (inputs) and consequences (outputs) of the alternatives examined?

Is there comparison of two or more alternatives?	NO		YES
	Examines only consequences	Examines only costs	
NO	1A PARTIAL EVALUATION Outcome description	1B Cost description	2 PARTIAL EVALUATION Cost-outcome description
YES	3A PARTIAL EVALUATION Efficacy or effectiveness evaluation	3B Cost analysis	4 FULL ECONOMIC EVALUATION Cost–minimization analysis Cost–effectiveness analysis Cost–utility analysis Cost–benefit analysis



when making decisions. Therefore, it is likely that over time such mechanisms will have a profound impact on clinician behaviour and resource utilisation, including the use of medicines.

BASIC FORMS OF ECONOMIC EVALUATION

If it is to be argued that clinicians and other health care decision makers should take note of efficiency considerations, there is a need for evaluation methods that assess the relative costs and consequences of health care programmes and treatments.

There are a number of forms of economic evaluation, but they have a common feature that some combination of the inputs to a health care programme are compared with some combination of the outputs. Figure 1 shows how economic evaluation relates to other forms of health care evaluation, in particular efficacy or effectiveness evaluations, which are now commonplace for medicines since they are required for registration. Full economic evaluation requires that both costs and consequences of interventions are considered and that two or more alternatives are examined.

Figure 2 shows in more detail the range of costs and consequences typically considered in economic evaluations. The inputs include the direct costs of providing care (C_1) which fall mainly (though not exclusively) on the health care sector, and the indirect costs (in production losses) arising when individuals are withdrawn from the workforce to be given therapy (C_2). Although not strictly an 'input', there may also be intangible costs, in pain or suffering, associated with therapy (C_3).

In some cases it may be sufficient to compare alternative therapies solely on the basis of their comparative costs, if it can be assumed that they produce equivalent medical results. This was the case in the study by Lowson *et al* (1981) on alternative methods of providing long-term domiciliary oxygen therapy. Such a study would be called a *cost analysis* and constitute a partial form of economic evaluation. Alternatively, it might be demonstrated, by way of a concurrent controlled clinical trial, that there is no difference in clinical terms between the alternatives. Such study would be called a *cost minimisation analysis*.

However, in most cases one cannot assume or show that the treatment alternatives produce similar results, and therefore the benefit measurement issue must be tackled. The outputs of health care programmes can be assessed in a number of ways. First, they can be assessed in the most convenient natural units (health effects), such as 'cases successfully treated' or 'years of life gained'. For example, Hull *et al* (1981) compared objective diagnostic tests for deep-vein thrombosis in terms of their incremental cost per case detected, over and above normal clinical diagnosis. Oster and Epstein (1987) compared treatment options for hypercholesterolaemia in terms of their cost per life-year gained. Such analyses are known as *cost-effectiveness analyses*.

Of course, much modern medicine is concerned with improving the quality, not quantity, of life. In addition, some therapies, such as cancer chemotherapy or hypertension treatment, may bring about slight reductions in the quality of life in order to extend life. Therefore, there has been a growth in interest in *cost-*

utility analysis, where the life-years gained from treatment are adjusted by a series of utility weights reflecting the relative values individuals place on different states of health. The output measure most frequently used in cost-utility analysis is known as the quality-adjusted life year (QALY). An early example of a cost-utility analysis of medicines is that by Weinstein and Stason (1976), who calculated the cost per well-year gained from lowering blood pressure.

Finally, the outputs can be measured in money terms. Some categories are fairly easy to assess in this way, such as the savings in direct medical care costs (B_1), or the production gains from an earlier return to work (B_2). However, other more intangible benefits, such as the value to patients of feeling healthier (B_3), are obviously more difficult to express in money terms. One rare example is the work of Thompson (1986) who found that arthritis sufferers would be willing to forgo 22 per cent of their household income in return for a cure for their arthritis. However, more generally this form of analysis, known as cost-benefit analysis, has been criticised for ignoring important benefits from health care programmes and for concentrating on items that are easy to measure.

Economic evaluation has been widely applied in the health care field (Warner and Luce, 1982; Drummond *et al*, 1987). There is now a fair degree of agreement on the elements of a sound evaluation, although there remain deficiencies in the published literature. In a recent review, Drummond *et al* (1986) noted that the main deficiencies were:

- failure to specify clearly the viewpoint from which the appraisal was carried out (e.g. health care sector, government, society);
- failure to base the economic study on good medical evidence, such as that generated by controlled clinical trials;
- the unthinking use of average costs, particularly in estimating the costs of hospitalisation or the savings from shortening hospital stays;
- failure to consider patient, family and volunteer costs where these were relevant;
- inadequate allowance for uncertainty in cost and benefit estimation;
- inadequate consideration of the link between evaluation results and the decisions, in health service planning and clinical practice, to which they pertain;
- failure to consider factors other than economic efficiency (including equity considerations and the managerial procedures required to bring about a change in policy).

A recent development has been the construction of 'league tables' or 'rankings' of health care programmes in terms of their relative cost per QALY. Hence, for the first time decision-makers are formally being invited to compare alternative possibilities for health service investments in terms of their relative value for money (Torrance and Zipursky, 1984; Williams, 1985). Obviously, this approach raises important issues, not least that of the quality of the data and the analytical methods used to generate such estimates. However, this is clearly an important development in the evaluation of health care programmes.

IMPORTANT METHODOLOGICAL ISSUES

In undertaking an economic evaluation of health care programmes a number of important technical and value judgements need to be made. These are discussed in more detail elsewhere (Drummond *et al*, 1987). However, a few issues that are particularly pertinent to the evaluation of medicines are discussed below.

Viewpoint for the analysis

The broadest viewpoint for an economic evaluation is that of society, and it is recommended that, where possible, the societal viewpoint should always be investigated. However, there are other more limited, but important, viewpoints that may require exploration, such as those of the government or other third-party payers, health care managers, clinicians and patients. It is important that economic analysts are clear about the viewpoint for their study and, in particular, do not confuse the government and societal viewpoints.

Governments are most concerned about the impact of health care programmes and treatments on their revenue and expenditure. Therefore, if the government is the third-party payer for health care, such as in countries with a national health service or those with a sizeable government contribution to health care expenditure, it will no doubt be interested in the direct costs of medicines and any direct savings that result from their use. For example, from the government viewpoint it would be important to demonstrate that expensive antibiotics generate savings in reduced hospitalisation, or that antihypertensives reduce the need for long-term care for those suffering non-fatal heart attacks and strokes. To a more limited extent the government may also be interested in the indirect costs and benefits, since these relate both to the productivity of the country and to the government's own revenue and expenditure in taxation and welfare payments. (These latter costs and benefits, known by economists as transfer payments, cancel out in a societal assessment. Nevertheless, they may be important to the government itself.)

Although the health care manger is also primarily interested in direct costs and benefits, he or she may have a slightly different viewpoint because of particular

budgetary responsibilities.

For example, the administrator of a hospital will be primarily interested in his own costs or profit margin and not necessarily in the savings that medicines bring about in other parts of the health service, or to patients themselves. Indeed, the same may be true in primary care. In the UK, where family practitioner services and hospital services are financed separately, it may not immediately be recognised that an expensive medicine prescribed by family physicians could be economically justified because of the resource savings in the hospital sector. For example, reductions in the utilisation of coronary care units may result from the use of medicines for heart disease, notwithstanding the obvious benefits from the gains in life expectancy.

Some of the recent policy initiatives taken by governments in many countries are aimed at solving this kind of problem. For example, under pre-paid group practice the costs of hospitalisation are charges against the annual premium paid in advance to the practice. Therefore it is in the primary health care physicians' interest to prevent expensive hospitalisations by the use of medicines or by other means.

The clinician's perspective is important, given his or her key role in resource allocation in health care. It was mentioned earlier that under the new administrative arrangements the physician may have a financial interest in delivering efficient care. Incentives and disincentives operate in all systems, however. Under fee-for-service systems a physician's income may be affected by, for example, the number of physician visits required to administer, or monitor the use of, different medicines. The physician may also be influenced by the level of convenience or inconvenience associated with different therapies.

Finally, the patient's perspective is important since it may also affect the adoption of therapy. For example, in some countries patients pay a proportion of the costs of their medicines, although in others these costs are covered by insurance or are set at a flat rate. Also, it is well known that side-effects influence patient compliance with therapy. In economists' terms, side-effects increase the intangible costs of therapy (C_3 in Figure 2). In addition, the setting in which medicines are delivered may affect patients' costs. Logan *et al* (1981) found that the costs falling on patients were higher when antihypertensives were delivered by physicians in community care, rather than by nurse practitioners at the worksite.

In summary, whilst the societal viewpoint should be the main perspective from which to undertake economic evaluations in health care, the other subsidiary viewpoints should be considered since they may crucially affect the diffusion and use of health care programmes and medicines.

Marginal analysis

The concept of the margin is central in economics. That is, whereas efficiency requires that the total benefits of activities should exceed the total costs, it also requires that the marginal benefits (i.e. those from the next unit of treatment) equal the marginal costs. This can be deduced by logic: if the marginal benefits are greater than the marginal costs, then more benefit in total can be gained by further expansion of the programme; if the marginal benefits are less than the marginal costs there would be a net loss in expansion of the programme.

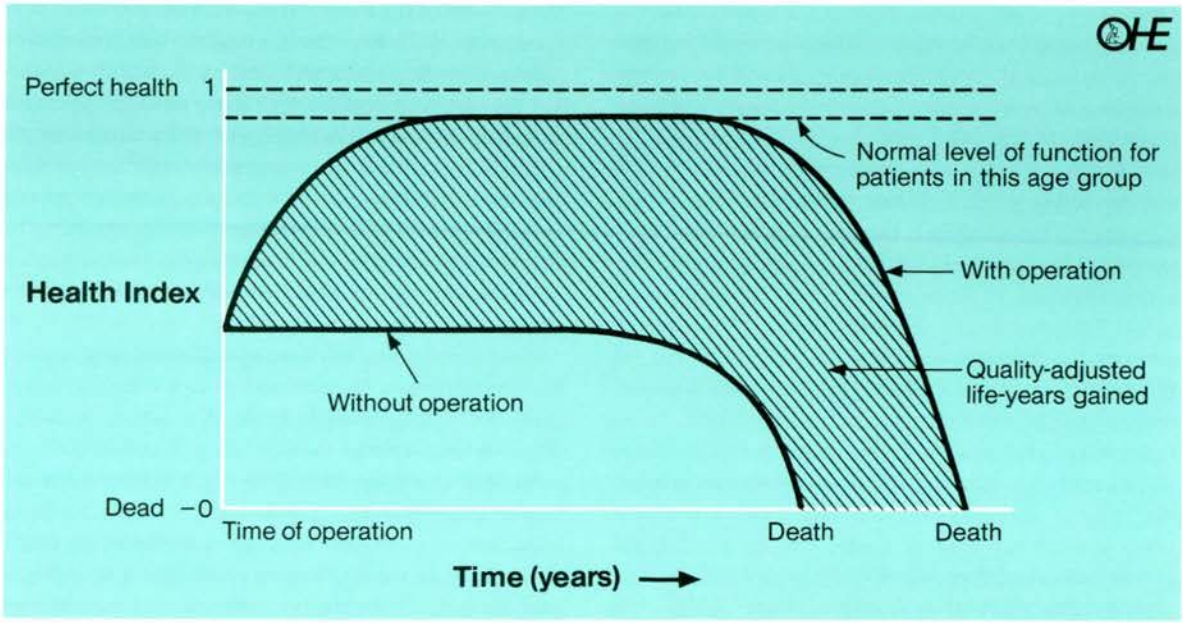
Most clinical practitioners would agree that one of the key questions in medicine is not whether procedures are totally worthless, but the extent to which diagnosis or treatment should be pursued. There are numerous examples: should C-T scans be given when headache is the only indication or should there also be associated neurological findings (Larson *et al*, 1980); should coronary artery bypass grafting be given only to patients with severe angina, or also to those suffering from mild angina with one- or two-vessel disease (Williams, 1985); should hepatitis B vaccination be given to the whole population or only to high-risk groups? (Mulley *et al*, 1982). Therefore, in evaluating the use of medicines from an economic perspective it is important to explore similar kinds of issues: for which indications should medicines be given; what is the appropriate frequency and level of dose; for how long should therapy be continued?

Another situation where marginal analysis is important is in the estimation of the savings in reduced hospitalisation. For example, average hospital costs (per day) are sometimes used to calculate the savings from shortened stays brought about by antibiotic prophylaxis. This needs to be considered carefully, as often the later days of a patient's hospital stay are less resource intensive than the earlier days. Therefore, the average costs may often overstate the real savings. Also, of course, the benefits of shortened stays are not necessarily translated into financial savings.

Measuring and valuing improvements in the quality of life

It was mentioned earlier that the main way in which the various forms of economic evaluation differ is in the extent to which they measure and value improvements in health. Since most modern medicine is concerned with improving the quality of life, rather than extending life, the measurement of quality of life has gained particular importance of late.

Of course clinical effects, that would typically be measured in a clinical evaluation and incorporated in a cost-effectiveness analysis, bear some relation to quality of life. For example, an evaluation of a surgical procedure may measure effectiveness in terms of the



number of complications or recurrences, or an evaluation of a medicine may record the number and nature of side-effects. It is implicit that it is not the side-effects themselves that are important, but the impact that they have on the patient's functioning or psychological state. The economic evaluations incorporating a quality of life measure merely take this a stage further, by assessing the impact directly and explicitly, rather than implicitly. Indeed, this is nothing particularly new. Rosser (1984) pointed out that up until the start of the twentieth century, St Thomas's Hospital in London assessed outcomes of its patients in terms of 'relieved, unrelieved, or dead'. There are two main methods by which quality of life has been measured and valued in economic evaluations: by quality of life scales (or profiles) and by utility measurement.

The quality of life scales consist of a range of attributes thought to affect the patient's quality of life, such as physical functioning, ability for self-care, social functioning and psycho-social status. One example is the Nottingham Health Profile (Hunt *et al*, 1986), which was used by Buxton *et al* (1985) in their economic evaluation of the heart transplant programme in the UK. Other well-known examples of such general scales are the Karnofsky Index (Karnofsky and Burchenal, 1949), the Sickness Impact Profile (Bergner *et al*, 1976), the General Well-Being Scale (Kaplan *et al*, 1976) and the Spitzer QL Index (Spitzer *et al*, 1981). There is a growing number of evaluations of medicines incorporating quality of life assessments, such as the comparison of anti-hypertensive agents carried out by Croog *et al* (1986). Although some of the quality of life scales embody scoring schemes, they usually do not generate a single quality of life score. This makes comparisons from one evaluation to another difficult, as does the fact that often disease-specific scales are used instead of the general scales referred to above. However, it is still possible to make comparisons of two medicines, or a medicine versus surgery, for a given condition using this type of quality of life scale.

However, economists are interested in making broader comparisons and in assessing the relative value for money from a range of health care interventions. This has led them to search for a generalisable index of quality of life which can be used in programme evaluation. The method used is to measure health utility values, which can then be combined with survival data to calculate the QALYs gained from treatment (see Figure 3). The utilities are relative valuations of states of health, standardised on a scale from 0 (dead) to 1 (perfect health). (However, it should be noted that some researchers have found states worse than death, with negative utility values.)

Whereas it is easy to accept that there is an ordinal ranking of health states, from better to worse, the methods of obtaining the health state valuations have generated considerable debate. In the UK the most widely used index is that developed by Kind, Rosser and Williams (1982). This classifies states of health by disability and distress, generating a 32-cell matrix for which relative valuations have been obtained from 70 respondents.

In North America three main measurement methods have emerged, the rating scale, the time trade-off approach and the standard gamble (Drummond *et al*, 1987). A typical rating scale consists of a line on a page with clearly defined end points. The most preferred health state is placed at one end of the line and the least preferred at the other end. The remaining health states are placed on the line between these two, in order of their preference, and such that the intervals or spacing between the placements correspond to the differences in preference as perceived by the respondent. In some studies more sophisticated 'props' are now being used to aid the respondent, such as 'health thermometers'.

Under the time trade-off approach the respondent is asked to consider the relative amounts of time he or she would be willing to spend in various health states. For example, in order to value a chronic health state, the respondent would be offered a choice of remaining in this state for the rest of his life versus returning to complete health for a shorter period. The amount of time that the individual is willing to 'trade' to return to perfect health can be used to obtain a preference value for the chronic health state. A similar approach can be used to calculate the relative values of temporary health states.

The standard gamble is the classical method of measuring cardinal preferences, being based directly on the fundamental axioms of utility theory. In order to measure preferences for chronic states preferred to death the subject is offered two alternatives – either the gamble, a treatment with two possible outcomes (death or return to normal health for the remainder of his life), or the certain outcome of remaining in the chronic state for the rest of his life. The probability of a successful outcome to the gamble is varied until the respondent is indifferent between the gamble and the certainty. This probability can then be used to calculate the preference value for the health state. Slightly different approaches are used to assess states worse than death and temporary health states.

As was mentioned earlier, there is considerable debate about the methods of utility measurement; which method is to be preferred; whose values are the most relevant, those of patients, doctors, policy makers or members of the general public? The validity and reliability of the various methods are extensively discussed by Torrance (1987) in a special issue of the *Journal of Chronic Diseases* dealing with quality of life measurement. In addition, Buxton *et al* (1986) have compared the Rosser index with the time trade-off approach.

Discounting costs and benefits

In many cases the costs and benefits of the alternative health care interventions occur at the same point in time, such as in the comparison of two medicines for the same condition. However, on some occasions the time profile of costs and benefits may differ between the alternatives, such as in a comparison of long-term medical management versus surgery. Here the costs of surgery would all be incurred now, whereas the costs of medication would stretch far into the future. In the case of preventive measures, such as screening and treatment for hypertension, or hypercholesterolaemia, a conscious decision is being made to commit resources earlier in the disease process in order to avoid medical care costs, morbidity and mortality in the future.

It is usually argued that, as individuals and as a community, we are not indifferent to the timing of costs and benefits. We prefer to have benefits sooner rather than later and to postpone costs. (In the economists' jargon we are said to have a positive rate of time preference.) Therefore, there is a need, in economic evaluation, to reflect this preference in the analysis. This is achieved by a process known as discounting of costs and benefits to present values. It is not necessary to explain the mechanics of discounting here, as other sources are available (Drummond *et al*, 1987). However, it is important to note that the effect of discounting is to give costs and benefits occurring in the future less weight in the analysis. Therefore, discounting would make the long-term medical management of a condition more attractive, when compared to surgery. Conversely, it would make a preventive programme less attractive than it otherwise might, because the averted future medical care costs would assume less numerical importance in the analysis.

Whilst most analysts acknowledge that costs and benefits occurring in the future should be discounted, there is still debate about the choice of discount rate. In some countries, such as the UK, the government advises the rate (currently 6 per cent per annum in real terms). Where no rate is advised, current practice is to discount by a range of rates from 2 to 10 per cent, and to examine how sensitive the study conclusions are to the rate chosen. The other main debate centres around whether years of life or other health benefits should be discounted in the same way as costs. This issue is not fully resolved, but current practice is to treat all categories of benefit in the same way as costs, since inconsistencies emerge if this is not done. In addition, the calculation of QALYs includes discounting.

Boundaries of the economic analysis

So far much of the discussion of economic evaluation has centred on the comparison of alternative health programmes or treatments in clearly defined applications. The boundaries of the economic analysis are therefore drawn around the costs and benefits of the alternative programmes, treatments or procedures in

question. However, another approach to economic evaluation would have as its focus the economic impact on the health care system in total. That is, instead of evaluating a medicine in one particular application, such a study would examine the total impact of its diffusion. This was the approach adopted by Bulthuis (1984) in a retrospective analysis of the impact on hospital costs of cimetidine in the Netherlands. Jönsson (1983) has pointed out that the same kind of analysis coud be performed prospectively. Here one would consider not only the costs and benefits of a medicine in clearly defined clinical applications, but also those resulting from its use in other situations where effectiveness has not been proved. One would also consider the effects of changing epidemiology of the disease and the possible application of other new treatment technologies. Such studies are more complex and are rarely carried out.

Another example of the same issue relates to medicines used in primary prevention. Should screening or case finding costs be included in an evaluation of medicines for hypertension or hypercholesterolaemia? This is difficult to resolve intellectually. On the one hand one might argue that individuals are likely to come to the notice of the health care system eventually, since most people visit their physician periodically. Therefore it is legitimate to examine the cost-effectiveness of alternative medicine interventions on the assumption that cases will be found at low marginal cost.

On the other hand one might argue that a new, more effective medicine might fuel the demands for screening for the disease in question. Therefore it is legitimate to assign the costs of case finding to the medicine. There is no simple answer to this issue. It is likely to depend mainly on the situation prevailing in a given country at a given time and the concerns of health care decision makers.

Finally, one might choose to draw the boundaries of the study to include the impact on the economy as a whole. This would recognise that the economic impact of a new medicine is not restricted to the health care system, but that pharmaceutical industry profits and investments affect employment levels, national growth rates and the balance of trade. Whereas such considerations no doubt come into play when pricing and reimbursement decisions are made, they have rarely been studied formally in the context of individual medicines. However, an earlier study documented the general contribution made by the pharmaceutical industry in seven countries (Chew *et al*, 1985).

THE FUTURE AGENDA

There is now a growth in the application of economic evaluation to medicines. Given the pressures for increased efficiency from government and other third-party payers for health care, the interest in economic evaluation is unlikely to subside. Therefore, if more economic evaluations are likely to be carried out in the future, what are the main issues that need to be resolved? These are discussed below: the need to improve quality of life measures; the need to improve the integration between economic evaluation and clinical research; and the need to improve the interpretation and use of economic evaluation results.

Improving quality of life measures

Although there is now widespread agreement that in principle quality of life is the most relevant outcome measure in the evaluation of health care interventions, there is still considerable disagreement about the reliability and reproducibility of particular measures. For example, some clinical researchers feel that the general quality of life indices or profiles, such as the Nottingham Health Profile, are not sensitive enough to detect changes in the patients' condition. Therefore, they prefer to use disease-specific scales which, while useful for comparing two treatments for the same condition, offer limited scope for generalisation across a range of conditions.

There is also disagreement about the use of utility measures, particularly within the context of clinical trials. From the economist's perspective utility measures are the most useful measures of quality of life, since they enable the calculation of the QALYs gained from health care interventions. However, many clinical researchers are sceptical about the usefulness and validity of the measures. They doubt whether respondents really understand the questions that are posed during an interview to estimate utility values by the standard gamble or time trade-off approaches. Also, they wonder how a 0.02 improvement in utility can be interpreted in clinical terms. Finally, some economists have pointed to the systematic differences in the utility estimates obtained by different measurement approaches (Buxton *et al*, 1986; Loomes, 1988) and concerns over the theoretical foundations of the QALY approach (Mehrez and Gafni, 1989).

There is no easy solution to these problems. In the short term the answer is likely to be in the increased use of a range of measures within a given evaluation. The study of oral gold therapy for rheumatoid arthritis (Bombardier *et al*, 1986) is a good example. Whilst costly, the use of multiple measures will enable the extent of convergent validity to be assessed. This will form a better basis for judging both the quality of life

measures themselves and the signs and symptoms typically used in clinical practice.

Another possibility is to map clinical symptomology data onto generic utility scales such as those developed by Rosser (Kind and Gudex, 1986) or by Torrance (Torrance *et al*, 1982). The general well-being scale (Kaplan *et al*, 1976) both incorporates descriptive quality of life data and enables the calculation of a single quality of life (utility) score. This approach needs to be investigated further and comparisons made with utility measures obtained by direct measurement.

Improving the integration between economic evaluation and clinical research

The incorporation of quality of life measures in clinical trials is one aspect of this integration. However, there is also the question of whether certain items of resource use data (C_1, C_2, B_1 and B_2 in Figure 2) could be collected alongside clinical trials. Clinical trials are clearly an important vehicle for assessing the efficiency of medicines, since they have to be performed for other purposes and offer the possibility of controlled evaluations. In addition, most major pharmaceutical companies have large medical research divisions undertaking trials.

Drummond and Stoddart (1984) discussed the advantages and disadvantages of undertaking economic analysis alongside clinical trials, outlined the data that should be collected and suggested a 'phasing policy' for economic evaluation that would minimise unnecessary work. However, many methodological issues remain unresolved. These include the issues of sample size requirements for economic analysis, the problems in extrapolating economic analysis results from one setting to another, and the problems and opportunities posed by multi-centre clinical trials (Drummond, Teeling Smith and Wells, 1988).

Improving the interpretation and use of economic evaluation results

There is no point in investing in the economic evaluation of medicines or any other health care alternatives if the results of studies cannot be interpreted and used. The development of rankings of health care interventions in terms of their incremental cost per QALY is an important development, but many methodological issues remain. These include the reliability of the mortality and morbidity data upon which such estimates are based, the importance of considering cost/QALY values at the margin, the desirability of making comparisons across a broad range of health care programmes, the differences in utility values produced by different estimation measures and the need to incorporate equity considerations. (Strict application of the cost/QALY logic would result in some groups receiving no care.) These issues are discussed more fully in Drummond, Teeling Smith and Wells (1988).

The other main issue in the use of economic evaluation results for medicines relates to the ways in which they feed into decision-making procedures. It is clearly too simplistic to regard economic evaluations as providing conclusive data for pricing and reimbursement decisions in the way that clinical trials provide these for registration decisions. The price of a drug and its reimbursement status are likely to be the result of a complex interplay of social, political and economic factors. However, economic evaluation may help determine the reasonable range of defensible prices and, with its explicit assumptions and methodology, fulfils the criteria, within the EEC, for transparency.

It may be that the most important role of economic evaluation is not in setting the initial price of a medicine, a decision often taken in the absence of comprehensive economic data, but in encouraging a rational diffusion and use of medicines. More specifically, this means determining whether or not a particular medicine should be added to a formulary and the indications for which it should be used. However, much more work needs to be done in order to demonstrate that economic evaluation has a useful part to play in these decisions in practice.

CONCLUDING REMARKS

The main objective of this paper has been to outline the methodologies of economic evaluation as they apply to medicines. Much as been achieved in recent years and there are now many such evaluations published or in progress. However, the other objective of the paper is to look to the future. It can be seen that many methodological challenges remain if economic evaluation is to be influential in decision making about the diffusion and use of medicines. This paper has outlined some of these challenges as a contribution to the future agenda.

REFERENCES

Bergner M *et al* (1976). 'The Sickness Impact Profile: conceptual formulation and methodology for the development of a health status measure', *International Journal of Health Services*, 6(3): 393–415.

Bombardier *et al* (1986). 'Auranonfin therapy and quality of life in patients with rheumatoid arthritis', *The American Journal of Medicine*, 81: 565–578.

Bulthuis R (1984). 'Cimetidine and the cost of peptic ulcer in the Netherlands', *Effective Health Care*, 1(6): 297–309.

Buxton M J *et al* (1985). *Costs and benefits of the heart transplant programme at Harefield and Papworth Hospitals*. London, Her Majesty's Stationery Office.

Buxton M J, Ashby J and O'Hanlon M (1986). 'Valuation of health states using the time trade-off approach: report of a pilot study relating to health states one year after treatment for breast cancer'. *HERG Discussion Paper No 2*. London, Brunel University.

Chew R, Teeling Smith G and Wells N (1985). *Pharmaceuticals in seven nations*. London and Mainz, Office of Health Economics and Medizinisch Pharmazeutische Studiengesellschaft eV.

Croog S H *et al* (1986). 'The effects of antihypertensive therapy on the quality of life', *New England Journal of Medicine*, 317(26): 1657–1664.

Drummond M F and Stoddart G L (1984). 'Economic analysis and clinical trials', *Controlled Clinical Trials*, 5: 115–128.

Drummond M F, Stoddart G L and Torrance G W (1987). *Methods for the economic evaluation of health care programmes*. Oxford, Oxford University Press.

Drummond M F, Teeling Smith G and Wells N (1988). *Economic evaluation in the development of medicines*. London, Office of Health Economics.

Hull R D. Hirsh J, Sackett D L and Stoddart G L (1981). 'Cost-effectiveness of clinical diagnosis, venography and non-invasive testing in patients with symptomatic deep-vein thrombosis', *New England Journal of Medicine*, 304: 1561–1567.

Hunt S M, McEwen J and McKenna S P (1986). *Measuring health status*. London, Croom Helm.

Jönsson B (1983). 'A review of the macroeconomic evaluation of cimetidine'. In A J Culyer and B Horisberger (eds), *Economic and medical evaluation of health care technologies*. Berlin, Springer-Verlag.

Kaplan R M, Bush J W and Berry C C (1976). 'Health status: types and validity and the index of well-being', *Health Services Research*, 11: 478–507.

Karnofsky D A and Burchenal J H (1949). 'The clinical evaluation of chemotherapeutic agents in cancer'. In C MacLeod (ed), *Evaluation of chemotherapeutic agents*. New York, Columbia University Press.

Kind P and Gudex C (1986). *The QALY toolkit*. Centre for Health Economics, University of York.

Kind P, Rosser R M and Williams A H (1982). 'Valuation of quality of life: some psychometric evidence'. In M W Jones-Lee (ed), *The value of life and safety*. Amsterdam, North-Holland.

Larson E B, Omenn G S and Lewis H (1980). 'Diagnostic evaluation of headache. Impact of computerised tomography and cost-effectiveness', *Journal of the American Medical Association*, 243(4): 359–362.

Logan A G *et al* (1981). 'Cost-effectiveness of a worksite hypertension treatment programme', *Hypertension*, 3(2): 211–218.

Loomes G (1988). 'Disparities between health state measures: an explanation and some implications'. Paper presented to the Health Economists' Study Group, Brunel University, July 1988.

Lowson K V, Drummond M F and Bishop J M (1981). 'Costing new services: long-term domicilary oxygen therapy', *The Lancet*, i: 1146–1149.

Mehrez A and Gafni A (1989). 'Evaluating health-related quality of life: an indifference curve interpretation for the time trade-off technique', *CHEPA Working Paper Series No 13*. McMaster University, Hamilton (Ont.), April 1989.

Mulley A G, Silversteen M D and Dienstag J L (1982). 'Indications for use of Hepatitis B vaccine, based on cost-effectiveness analysis', *New England Journal of Medicine*, 307: 644–652.

Oster G and Epstein A M (1987). 'Cost-effectiveness of anti-hyperlipidaemia therapy in the prevention of coronary heart disease; the case of cholestyramine', *Journal of the American Medical Association*, 258(117): 2381–7.

Rosser R M (1984). 'A history of the development of health indicators: a review'. In G Teeling Smith (ed), *Measuring the social benefits of medicines*. London, Office of Health Economics.

Spitzer W O, Dobson A J, Hall J *et al* (1981). 'Measuring the quality of life of cancer patients: a concise QL-index for use by physicians', *Journal of Chronic Diseases*, 34: 585–597.

Thompson M S (1986). 'Willingness to pay and accept risks to cure chronic disease', *American Journal of Public Health*, 76(4): 392–396.

Torrance G W *et al* (1982). 'Application of multi-attribute utility theory to measure social preferences for health states', *Operations Research*, 30(6): 1043–1069.

Torrance G W (1987). 'Utility approach to measuring health-related quality of life', *Journal of Chronic Diseases*, 40(b): 593–600.

Torrance G W and Zipursky A (1984). 'Cost-effectiveness of antepartum prevention of Rh immunisation', *Clinics in Perinatology*, 11(2): 267–281.

Warer K E and Luce B R (1982). *Cost-benefit and cost-effectiveness analysis in health care*. Ann Arbor (Mich.), Health Administration Press.

Weinstein M C and Stason W B (1976). *Hypertension: a policy perspective*. Cambridge (Mass.), Harvard University Press.

Williams A H (1985). 'Economics of coronary artery bypass grafting', *British Medical Journal*, 291: 326–329.

PRACTICAL USE OF ECONOMIC ANALYSIS FOR MEDICINES

Rolf Dinkel

THE CHANGING ENVIRONMENT FOR PHARMACEUTICALS

The increasing role of the political system

(1) Profound and lasting changes are occurring in the producing, delivering, prescribing, using and financing of medicines. These are deeply affecting the structures and the conditions of the pharmaceutical market. Gone are the days when the provider and user of medicines were rather insulated from the financial consequences of their decisions. Gone are the days when everything that was available for the elimination and reduction of illness was capable of being financed. Today's political system, which is concerned with the financial burden of pharmaceutical health care, is represented by:

- Government agencies (price control committees, registration authorities);
- Third-party payers (health insurance schemes, sickness benefit funds);
- Health care providers (hospitals, medical practitioners);
- Health care politicians;
- General public, society, consumer organisations;
- Media.

These groups place an ever-increasing number of hurdles before medicines which are submitted to the market or want to remain in the market. Pharmaceutical products today circulate in a supervised, controlled, political market on a worldwide basis, even in so-called 'free markets'.

(2) In this environment of growing regulatory pressure on drug costs, stronger price controls and higher price awareness, even advances in pharmacological medicine are not immune to efforts to conserve resources and increase cost-effectiveness. The political system will question more and more carefully the value of all medicines purchased. The system wants to know not only if a drug has value (i.e. whether it is efficacious), but also whether it is cost-effective. In other words, in many cases it is no longer sufficient to demonstrate the mode of action, efficacy and safety of a pharmaceutical product; one must also show that the benefit obtainable from its use will bear a positive relationship to the cost it generates.

Cost-containment measures

In its attempt to curb spiralling total costs for pharmaceuticals, the political system is:

- forcing physicians towards more economic prescribing, affecting the doctors' freedom of choice in prescribing or decreasing their latitude in choice of drugs;
- restricting reimbursement lists by setting entry criteria, drawing up negative or positive lists of indications which do or do not qualify for reimbursement, widening the number of products only partially reimbursed or delaying the appearance of products in the official list;
- reducing drug formularies, limiting the total number of products and the number per therapy class on the market;
- keeping the initial price levels for new products low, blocking price increases and enforcing price reductions;
- experimenting with transparency and price comparison lists to raise price awareness.

Relevance of socio-economic performance

In this restrictive environment the need to substantiate the economic dimension for pharmaceuticals has become a key success factor for pharmaceutical companies. To successfully introduce and market a drug depends increasingly on its economic performance in the context of costs and benefits. Successful marketing is not limited to getting market approval of a drug. In only very rare cases the economic profile has influence for this procedure. Successful marketing, however, *is* largely dependent upon the product's election for reimbursement, a favourable classification according to the proportion of cost which will qualify for reimbursement, the avoidance of being negatively listed, etc. For these decisions, economic aspects are scrutinised.

Examples from Germany and France may illustrate this key role:

One of the main provisions in Labour Minister Norbert Blüm's Health Reform Act (Gesundheitsreformgesetz) affecting pharmaceuticals was that a federal committee would be allowed to determine which products should be excluded from reimbursement on cost-benefit grounds – 'this would also include pharmaceutical products which offer no guarantee of suitable and economic treatment because their therapeutic benefit is either disputed or slight (§ 34)'.

In France, new products are only reimbursable under social security if they provide an improvement in medical care to the patient or a saving in the cost of health care. 'Products likely to lead to increased consumption or unjustified expenditure' or 'products, the price of which would not be justified, considering the present or potential market' are not reimbursed. The application file for social security has to be submitted to the Ministry of Health and must prove the merits of the new product in comparison to available treatment. Besides therapeutic factors, the economic merits of the product, including the requested unit price, are taken into consideration.

36 THE STRATEGIC RESPONSE

Being confronted with this need to justify prices and substantiate economic merits, the pharmaceutical industry – at least to a very large extent – has learned several lessons:

Need for price justification

In the past, it was tempting to suggest that the price of a medicine 'ought' to reflect some appropriate return on accumulated R&D expenditure; today, no one is entitled to automatic compensation on a 'cost plus' basis. Companies compete in a political market; therefore price-setting and price-justification is a political activity too. The price must be accepted by the political system.

Cost-effectiveness vs cost reduction

In addition, the pharmaceutical industry has realised that prize premiums can be justified only if the preparation gives greater benefits. The higher the added value, the higher the potential for prize premiums. To justify this premium, to substantiate the product's value for money, one must go beyond cost/cost comparisons which are used in 'price comparison lists' or 'transparency lists'. The economically relevant effects of using the preparation have to be taken into consideration as comprehensively as possible. The spectrum of these effects ranges from impact on the use of concomitant medication, medico-technical services, and doctors' services, through effects on the number of ambulatory or hospitalised days of illness and absence from work to qualitative influences on the mental, physical and social well-being of the patient.

Medicines which, on the face of it, are more expensive, can be more cost-effective than cheaper preparations if they lower the cost of other aspects of therapy and create a better overall cost-benefit ratio.

Two practical examples from HealthEcon's research programme:

Nitroderm TTS. In 1982, a new form of transdermal nitroglycerin was introduced to the market in the form of a patch. The most significant drawback of the patch has been its relatively high price compared to traditional oral nitrate preparations. Consequently, an economic study programme was launched by the producer. This programme consisted of a portfolio of 14 studies conducted in Europe, the United States and Australia. All 14 studies report on the same topic and reach the same general conclusion: the increased cost of prophylactically treating angina using the nitroglycerin patch would be partially or wholly offset by benefits in other fields.

In the case of a cost-benefit study in the Federal Republic of Germany, the increase in the costs of medication is more than compensated by savings in the field of doctors' services and lost productivity.

ACE inhibitor. Treatment of heart failure with ACE inhibitors is reputed to be 'expensive', since other cheaper drug therapies are available, particularly digitalis. Using the data obtained from a German health insurance company, a cost/cost-study showed that the difference on dosage costs does not in itself reflect the cost-effectiveness of these different treatment schedules. The study led to the following conclusions:

- Out-patients with heart failure treated with ACE inhibitors have significantly less contact with their physician than digitalis-treated out-patients.
  Medication costs for ACE inhibitors out-patients are not significantly different from the medication costs of the digitalis patients because of the higher cost of concomitant medications in this group.
  The total costs of treatment per year for the ACE inhibitor patients are significantly lower than those for the digitalis patients.
- In-patients treated with ACE inhibitors occasioned nearly double the medication costs of those treated with digitalis.
  However, their total yearly costs of treatment were 1600 DM lower than those of the digitalis patients.

New spheres of interest

In the past, industry has given primary importance to the practising physician as a target for marketing and information. The importance of the physician, however, has been eroded by the institutions and groups of the political system. In the future, it will be necessary to address these new target groups which share interest in the economic performance of a drug.

These groups are very heterogeneous and have differentiated interests. Segmented and specific information is needed to match their requirements.

Socio-economic analysis as strategic element

Consequently, these needs are reflected by the establishment of departments for 'Political Marketing', 'Pharma Economics' and 'Pharma Policy' within the pharmaceutical industry. Industry seems to be responding appropriately by broadening its own assessment of its products in the form of CBA, CEA, cost/cost-comparisons, including the measurement of the effects which products may have on the quality of patients' lives. Respective studies are no longer only the reactive outcome of increasing regulatory pressure. On the contrary, they are understood as a potential active strategic response to a changing market environment and its demands. They are qualified as an essential contribution to additional information needs of new partners in the health care field. They represent a strategic element, a decisive marketing component helping to achieve a suitable competitive advantage.

DEVELOPING THE ECONOMIC EVIDENCE: A PRACTICAL APPROACH

The research question

Today, firms throughout the pharmaceutical industry are sponsoring socio-economic research. The aim is to make such research an informative, scientifically valid adjunct to a firm's marketing strategy and pricing policy. But disregard of rules, concepts and procedures can make attainment of this goal questionable. The quality of study outcomes and the expected credibility will depend significantly on the existence of some basic prerequisites, an optimal design, the selection of appropriate tools and the application of standards. Some key issues should receive particular attention.

Every socio-economic analysis is grounded in the product's efficacy and safety profile. If there are parameters with potential for differentiation, the economic analysis should begin with a research question which states the objective of the evaluation. The research question should outline the perspective taken, the alternatives that are examined and the cost and benefit parameters that will be examined.

The clinical profile

Economic analyses are 'appendages' to the pharmacological and clinical profile of a product. To develop a relevant socio-economic hypothesis, the analyst must first understand the pharmacological and clinical effects of the technology. His task is to name those parameters in which the reference preparation might distinguish itself from the existing ones. Positive distinctions revealed by the results of pre-clinical and clinical studies suggest that positive conclusions, at least by economic standards, will result. Economic evaluation is, therefore, a transformation process which projects the result of pre-clinical and clinical research onto an economic dimension. So, for instance, a shorter half-life of the substance may lead to an improvement in the patient's quality of life, or an improvement in effectiveness may lead to lower cost for concomitant medication.

Consequently, weaknesses in the clinical profile cannot be eliminated by socio-economic analysis. A product which is questionable or inferior from a clinical perspective would only in exceptional cases be superior from an economic point of view.

The alternative

Another important decision for the quality of the economic study is the choice of the alternative treatment for comparison. Whereas the problem of comparison is generally solved in the clinical area by the use of placebos, in the field of economics no such acknowledged measurement basis exists. Here, ideally, evaluations should examine those alternatives that are actually available and would be realistic options, even if it is 'no treatment' or a non-drug therapy such as surgery or educational approaches.

The cost-effectiveness of a particular drug depends to a large extent on the alternative analysed. Thus the choice of alternatives should be justified. The use of relevant and realistic alternatives is a decisive contribution to the plausibility and credibility of the study findings. The following recommendations should be followed:

- Select real and acknowledged choices in daily clinical practice.
- The alternative should not be controversial with respect to efficiency.
- Select quantitatively meaningful alternatives (market leader) or 'therapy of choice'; do not ignore important competitors.
- Pay close attention to the specifications of comparability; for example, corresponding patient structure, equivalence in the treatment dosage, need for additional medication, etc.

The spheres of interest

Spheres of interest refer to the viewpoint from which the study is performed, whose interests are considered in the evaluation.

Each partner in the political system maintains its own specific perspective on costs and benefits. What signifies a cost for one is a benefit to the other and vice versa. Medicines which seem efficient to sickness funds are not necessarily efficient for society as a whole. One agency's budget may benefit, but overall cost may increase. Studies on narrower perspectives may lead to suboptimal solutions in the context of general social welfare. Every player in the game increasingly competes for the limited means available. In view of the struggle for resources, economic analysis has to find a compromise. It should evaluate new medicines from the perspective of society as a whole, but should, in addition:

- identify the interest groups affected by the new treatment, and
- calculate the cost-benefit relationship for each of these groups on the basis of those costs and consequences that are relevant to their budgets.

Only the composite of studies can avoid shifting costs from one sector of society to another.

PERSPECTIVES

Future perspectives in the practical use of economic analysis for medicines have – from my point of view – a factual and a political component.

Search for a factual standard

Whereas in the clinical field there are rigorous criteria to make a study scientifically valid, in the socio-economic field methodological soundness does not mean a prospective, randomised, double-blind, placebo-controlled, cross-over design. Socio-economic research can be conducted by using prospective or retrospective data. Prospective data might be collected in conjunction with a clinical trial – a relatively recent approach which can be expected to increase in the future – or by a specifically performed economical-clinical trial. Retrospective data might be collected from literature or from the database of a third-party payer; the study may use analytic modelling techniques or simulation programmes to simulate general population values.

Depending on the research hypothesis, the objective of the study, the financial resources and the time available, different strategies may be called for. In addition, researchers must simplify an often broadly stated 'ideal' research question into a practicable study plan. Inevitably, compromises are necessary and choices must be made. These compromises and choices present pitfalls, as shown by the inconsistent quality of economic research. Consequently, there is a perceived need among researchers and target persons for standards. There is a need to avoid and identify the pitfalls. The basic questions still to be answered are: Which form of analysis is most appropriate for a given research problem? Were the appropriate choices made for the goals set out? Are the compromises acceptable or are they contrary to 'state-of-the-art' technology?

Search for a political standard

What we need in addition to factual standards is a 'political' standard. Although the societal perspective is the optimal way of determining the value of a medicine and only this perspective considers all potential costs and consequences, many studies are performed from narrower perspectives. These narrower perspectives, be it of third-party payers or providers, will not necessarily lead to conclusions that are optimal for society as a whole. Costs and benefits of medicines are evaluated by different segments of society independently, each with its own sphere of interest in mind. What we need is a bridge – a comprehensive picture – to link these interests together for the best benefit to society as a whole. The interest of society must be claimed more energetically. This is the task which is before today's health care politicians and legislators.

SAVINGS FROM BETTER TREATMENT

Simone Sandier

Two characteristics of the health care sector are that there may be more often than for any other economic sector, there are frequent debates about the cost and the quality of the services provided.

The first reason lies in the fact that the scope of medical procedures has largely expanded during the three last decades leading to an increased span of choice among therapeutic behaviours. The second reason is that the third-party payers in charge of the financing of health care are concerned both with the amount that they pay and the usefulness of the services that they pay for.

SAVINGS FROM BETTER TREATMENT?

Advances in medical technology

- more treatments available
- what efficacy?
- what price

Collective financial coverage

- how much?
- unnecessary consumption?

OHE

From a political point of view, it is certainly more clever to announce that savings can come from better treatment than to close hospital beds or introduce some form of cost sharing to avoid over-consumption. But to what extent is it possible to save from better treatments?

There is every reason to think that medical science and medical practice aim at advancing people's well-being. We also have strong reasons to think that for ethical reasons a physician who knows for sure that a cheaper treatment will produce the same or greater improvement in the health of the patient than another treatment will prescribe or perform the first one.

But in most cases, however, faced with a condition to treat, the physician experiences difficulties in deciding the best treatment. This difficulty reflects the uncertainty of the clinical outcomes expected and the arbitrary nature of the evaluations of both the direct and indirect costs of the treatment.

First I would like to say after many others that health and costs have multiple facets which make it difficult to appreciate the quality of treatment A compared to treatment B, or to compare the benefit to cost ratio of treatment C and treatment D.

There are several considerations to be taken into account to make up one's judgement. They include medical and scientific criteria as well as the psychological and social aspects of illness.

The reduction of mortality in the short term is, of course, an important factor, but all conditions are not life threatening and not all treatments are provided to avoid death.

From a medical point of view, a treatment could be considered better than another one because it shortens the duration of the illness; or because it reduces the impairments due to the condition, or because it prevents the condition from becoming more serious. More and more treatments are aimed at increasing the length of a condition, allowing the patient with a chronic illness to live longer.

Other criteria can be considered too: economy (we will come to that point later), convenience and accessibility. Though these are secondary to technical effectiveness, they can play an increasingly great role in the choice between different therapeutic techniques.

The convenience of certain forms of treatment, for the patient or his family, is measured by such factors as lack of therapeutic complications, absense of pain, rapidity and comfort of treatment, proximity of the place of treatment to the patient's home.

WHAT IS BETTER TREATMENT?

EFFECTIVENESS	CONVENIENCE
-Reduction of mortality	-Absence of pain
-Shorter duration of illness	-Rapidity
-Reduction of impairments	-Comfort
-Stabilization of chronic diseases	-Proximity
-Prevention of aggravation	

OHE

SAVINGS, COSTS, BENEFITS

FOR WHOM?

The provider,
The patient,
The society

WHEN?

Today,
Medium, or long term

MEASURES

Monetary, non monetary
Direct and indirect, costs and benefits

OHE

The savings that a treatment can induce can be computed by comparing its costs, direct and indirect, with a valuation of its benefits. Expressing costs and benefits in monetary terms places a price on the human life, or on the productive years of life or on the quality of life without handicaps, and this raises fundamental ethical questions.

Some other remarks have to be presented. Briefly:

- The time dimension must be associated with the definition and the valorisation of the costs and benefits expected from a certain treatment. Of course, the

benefits differ according to whether the time scale is one month, six months, one year or 40 years. Changes in productivity over time can have a great impact, generally leading to a reduction of unit costs.

- How are the different benefits to be weighted against each other so as to reach an overall appraisal? In any event the weights of different outcomes may differ according to the age of the patient.
- The family, the social and economic environment of the patient may be of considerable influence on the conduct of a treatment and on the results of this treatment.

In spite of the difficulties some very interesting studies have been conducted to compare the cost of treatments. I will not insist on the very classic cases of the savings brought in by the pharmaceutical treatments of tuberculosis, or some mental illness or peptic ulcer disease. I will refer to other examples.

MYOCARDIAL INFARCTIONS 1971–1981

OHE	1971	1981	Annual rate of change
Average length of stay (days)	18.8	10.6	−5.6%
Number of lab-tests	81.0	124.8	+4.4%
Number of X-rays	3.5	2.5	−3.3%
Cost of treatment (1981 prices)	$13490	$12935	−0.4%

Anne Scitovsky, from the Palo Alto Medical Foundation, is among the first who have undertaken studies on the cost of illnesses; what is very special in her work is that it compares the treatments of the same illnesses at different points of time. In her last study she considered the cost of 16 conditions between 1971 and 1981. She found that the net effects of changes in treatment were cost savings in eight of the conditions, cost raising in seven, and that for one they were neutral. An example of savings over time from better treatment is the case of myocardial infarctions. Anne Scitovsky has found that the average length of hospital stay for myocardial infarction decreased dramatically from 18.8 days in 1971 to 10.6 days in 1981, that the use of X-rays was reduced and that the overall cost of the treatment decreased by 4 per cent in spite of an increased use of laboratory tests.

Another example of savings coming from the experience gained in treating patients is the case of AIDS. Different American studies have shown that the use of AZT, combined with more clinical experience, and a trend towards earlier treatment of HIV infection have transformed the disease from an acute condition with rapid progression to death into a chronic condition, though still incurable, that permits patients to live longer and less disabled lives. Data gathered by different authors show that the cost of treating AIDS has declined since the early epidemic and also that the average length of hospital stay has been reduced over time.

AIDS

LIFETIME COSTS

California

1985–1986	$91,000
1986–1987	$70,000
1987–1988	$63,000

AVERAGE LENGTH OF HOSPITAL STAY (WEEKS)

	New York State	San Francisco W. Bay Hospital
1982		18.2
1983	23.4	13.9
1984	21.8	12.3
1985	21.2	12.1
1986	19.2	12.2
1987		10.6

OHE

Even in those cases where a reasonably reliable conclusion can be drawn from the study of the comparative benefits and costs of two treatments of the same condition for the same category of patients, there could be various reasons why the best and less costly treatment is not applied; an example is provided by the treatments of renal failure. The duty of the planners and the financers in the health care field are to overcome the difficulties.

One question arises: can administrative measures help in the substitution of cost-efficient treatments for more expensive or less efficacious ones? Can they remove the obstacles to such a shift? Can they carry incentives to prevent the use of unnecessary or inappropriate treatment?

At a macro-economic level, international comparisons make us think that in different countries the health conditions are not treated at the same cost and in the same way. There is a wide variation of the average per capita health expenditures among countries; the respective shares of hospital care and ambulatory care and pharmaceuticals in total health expenses vary; for the same condition the length of stay in hospitals varies between countries.

There is not one unique reason for the discrepancies. General and medical culture certainly play a great role, and so does the organisation of the provision of care, and so do also the various incentives built into the methods used to pay for health care services.

First of all, the knowledge of the providers, the patients and the payer can play a great role. The knowledge must

SAVINGS FROM BETTER TREATMENT: INCENTIVES

KNOWLEDGE	PROVISION	FINANCING
Analysis: effectiveness costs benefits	Hospitals,	Coverage: Free care of copayment which services?
Education	Ambulatory care,	Methods of payment
Information	Home care, drugs	Global budget
	New technologies	Fee for service
	H.M.O	Relative scale

OHE

first be acquired through systematic evaluation of medical practice and of new technologies from a medical and economic point of view; in that field research and studies must be encouraged. Of course, when there are important and widely accepted findings they have to be disseminated through publications, courses and conferences.

Secondly, the way the provision of health care is organised can also play a role in the use of better and cheaper treatments. Some obstacles to the spread of new treatments or to cost-efficient shifts can derive from the fact that ambulatory treatments and in-patient treatment may not be provided by the same physicians; or that new technologies are tested in some settings and not in others. Some forms of organisations, like HMO where the profit is explicitly linked to the efficiency of the treatments conducted, have a great potential for using cheaper treatments. Unfortunately, they may also have incentives for providing fewer treatments too.

The type of coverage for the different types of care and the methods of payment of the providers can carry incentives or disincentives for the use of certain treatments. When care is free for the patient, the financial barriers to access medical servces are removed and treatments have more chances not to be postponed. In particular, in some countries co-payments are required from the patient for ambulatory care and pharmaceuticals, while hospital care is completely free. In this case, the co-payment can both deter the patient from using unnecessary treatment and also contribute to delay the access to care, leading finally to increase expensive hospital care.

The payment on a global budget, or a payment based on a fee for service, can influence – at least from a theoretical point of view – the behaviour of the provider. However, in a recent study conducted on the payment of physicians I found that this factor is certainly second to the power of the third-party payers which, when they are strong enough, always exert some control over the payment of physicians and counterbalance the incentives of the payment method. They control by setting the fees, by putting a cap on total income, by limiting the number of registered patients, and by setting rules to avoid a biased selection of the patients.

On a more micro level it is certain that in the case of a fee-for-service payment, the design of the scale used to classify the services could, at least in theory, play a role in promoting the use of some treatments or in preventing the over-use of others. The difficulty here is to keep up with the technological advances which allow for new services and which can change the cost of producing older ones.

A possibility to associate savings with better treatment is, of course, to get rid of inappropriate care. Robert Brook from the Rand Corporation has addressed this problem in a very scientific way. He and his colleagues have shown first that a significant part of the health care services provided were inappropriate, and second that it was very difficult to eliminate the inappropriate services without at the same time affecting the necessary ones, and perhaps the health of the population.

For example, he has shown from American data that

APPROPRIATENESS OF CARE

Rate of inappropriateness		Unappropriate care cannot be relied to:
Coronary angiography	17%	Supply of physicians
Carotid endarterectomy	32%	Free for service
Upper GI endoscopy	17%	Free care or Cost sharing
Hospital admissions		High use of services
Free care	24%	Low use regions have large amounts of inappropriate care
Cost sharing	22%	

OHE

the use of coronary angiography was inappropriate in 17 per cent of the total cases; that one out of every five admissions was inappropriate and that one of every four days of patient care was inappropriate. Of course, the criteria of appropriateness can be discussed; however, it cannot be discussed that there is evidence for inappropriate care. The problem really is to identify the reason for that and to help eliminate those services which are not relevant.

It is also Brook who has shown that the real problems are not those suggested by conventional wisdom. In particular, he has shown that inappropriate care is not necessarily related to high use of services; he observed that low-use regions still have large amounts of inappropriate care. The supply of physicians does not explain the inappropriate use of procedures either; inappropriate care exists even in non-fee-for-service settings, and also for patients with cost sharing. Brook has also shown that rationing reduces all prescription drug use. When Medicaid in the US put a limit on three paid prescriptions per month, the number of prescriptions filled was reduced by

30 per cent but both the use of essential medications and ineffective ones dropped.

In conclusion, it is quite clear that an expensive health-care system does not necessarily mean that the health of the population is better. On the other hand, the contrary is not true either. Promoting better treatments is certainly the principal aim of a health policy; if savings seem necessary too, and although they sometimes can be associated with better treatment, it should nevertheless be made clear to decision makers that the goal of savings in health care is difficult to attain without depriving access to certain categories of population. The improvement of health indicators which has occurred in many European nations, although it is not totally due to health care, could be stopped if the objective of financial savings superseded that of maintaining equity and quality of health services.

REFERENCES

Sandier S (1989). Working party on social policy: The payment of physicians in selected OECD countries. OECD.

Schieber G J and Poullier J-P (1989). 'Overview of international comparisons of health care expenditures'. HCFR Annual Supplement.

Scitovsky A A (1985). 'Changes in the costs of treatment of selected illnesses, 1971–1981', *Medical Care*, 23, no 12.

Scitovsky A A (1989). 'Use and costs of health care services of persons with aids in San Francisco in three practice settings, 1986/87'. Presented at the Vth International Conference on AIDS, Montreal.

MEASURING BENEFITS IN HOSPITAL

The choice of a strategy for thrombolytic therapy after acute myocardial infarction (MI)

Robert Launois

METHODS

The Strategies

Three strategies for preventing a risk of reocclusion have to be distinguished: the conservative strategy, the elective indications and the aggressive treatment.

The conservative strategy. Two situations are clearly identified: either the patient suffers or he does not. If there are clinical signs from persistent or recurrent ischaemia, an immediate catheterisation is done. Mechanical or surgical recanalisation should be attempted if the infarct-related artery appears occluded. If the artery is patent, a medical treatment is administered on patients who do not have significant lumen narrowing. When the stenosis is greater than 50 per cent, a CABG or a PATC is carried out.

If the patient does not suffer, he recives standard medical care and undergoes a submaximal treadmill exercise 10 days after the use of the thrombolytic and a maximal treadmill exercise two weeks later. Patients with a strongly positive test undergo angiography. Patients with a negative test are treated with standard medical care. Patients with indetermined treadmill exercises are referred for thallium scans.

The elective strategy. The patient having recurrent or persistent ischaemia is referred for immediate catheterisation and PATC or CABG. Others undergo angiography under more or less strict eligibility criteria (good enough left ventricular function, age under 70) and within variable delays. Patients can be scheduled for coronary angiography within 18–48 hours after receiving the thrombolytic or may undergo a delayed angiograph 2–7 days later or a deferred angiograph 7–42 days after fibrinolysis. Angiography is followed by medical treatment when the infarct-related coronary artery is patent and when the stenosis is less than 50 per cent. When the stenosis is greater than 50 per cent and well suitable for surgery, a CABG is carried out, otherwise mechanical revascularisation is attempted when there is no counter-indication.

The aggressive strategy. All patients receiving reperfusion therapy undergo emergency cardiac catheterisation followed by PATC or CABG.

Three thrombolytic agents out of the five presently available are commercialised in France: Streptase, Actylise and Urokinase (the last being not in common use). Since Isis II, it is clear that the concomitant administration of aspirin and SK confers additional benefits and reduces deaths. However, such a proof is not available for rTPA. Adjunction of aspirin to TPA has only been carried out in small trials and its effects cannot be measured in mortality terms. The comparison of the respective products' efficacy should therefore be limited to SK, SK plus aspirin, and TPA plus Heparin.

Efficacy: which criteria?

The efficacy of thrombolytic therapy in AMI is by now very well established, but it is not so for the three management strategies of reocclusion. Comparisons on these grounds are difficult for two reasons: the criteria for inclusion and the protocols are never the same, and the end-point results are different from study to study.

The outcome comparison of the strategy and the products used are difficult because there are no large randomised trials comparing directly the efficacy of the thrombolytic agents. They differ in terms of time of inclusion (Isis II: 24hr, Gissi: 12hr, Asset: 5hr), of age limits (Isis II and Gissi: no limitation, Asset: less than 75) and of time-window considered for evaluation (Isis II: 21 days, Gissi and Asset: 4 weeks). Therefore, a Meta-analysis has to be conducted.

As far as the end-points are concerned, the efficacy can be measured from quite different points of view. Some consider only the rate of reperfusion after 90 minutes. They believe that recanalisation leads to the improvement of the ejection fraction, which would itself be an indicator of survival. Others emphasise that only real end-points like reinfarction and mortality have to be under scrutiny. How can we choose? The outcome criteria have to fulfil three conditions: it should be global, significative from the patient point of view and scientifically validated. The rate of mortality seems to fulfil the conditions required. Mortality integrates in one figure the benefits of the treatment during the follow-up period and the consequences of the major complications. It is for sure the main concern of the patient who does not pay much attention to technical criteria and surrogate end-points; it has been measured in several large randomised trials which give effective results and not hypothetic inferences. Thus the first criterion for outcome should be avoided deaths, measured either as a reduction in the odds ratio or as a decrease in the relative mortality rate.

However, the therapeutic decisions cannot be based only on an objective index such as the two years' mortality rate. With such a measure, living six years is not better than living two. Similarly, dying in the first month is not worse than dying one year later. Clearly, the life expectancy, even if we assume that all life-years are equally valuable, is a better criterion than the one or two years' mortality rate. It is a necessary prerequisite for integrating a more detailed knowledge of patient preference with respect to the length of survival into the clinical decision-making process.

For calculating the life expectancy, we use the Deale method. According to this procedure, two rates of mortality are considered. First, the baseline, average yearly mortality rate for a French cohort of same age–sex characteristics as the population at risk of AMI. This rate can easily be found from the French tables of vital

statistics. Secondly, the myocardial infarction specific excess mortality rate was deducted from Isis II. Adding the baseline rate and the specific rate and taking their inverse ratio permits one to calculate the life expectancy of the treated patients.

Cost evaluation

It is important to calculate the actual cost of an episode of care. Average *per diem* price is inappropriate because the number and kind of services used may vary widely according to the therapeutic attitudes chosen.

To explore fully the impact on resources of a change in strategy, we tried to isolate volume and intensity of care services used in angiography, PATC and CABG. Simple calculations provide information on expensive medication and diagnostic tests received by the patient. The medical and nursing time is determined through time-and-motion studies. Such a method avoids problems of cross-subsidisation by determining which basic resources specific to a patient are used. The cost allocated by this method is naturally deducted from the total direct operating expenses of the cardiology unit.

Remaining operating costs are then broken down into two categories:

- The expenditure of cardiology for salaries of the medical and nursing staff and for medical or drug supplies is directly assigned to the unit. The average daily cost is then taken as a yearly cost divided by the number of patient-days.
- The yearly induced expenditure for diagnostic tests and X-rays routinely provided to the cardiology unit by other departments is then evaluated and divided by the number of patient-days.

Such a methodology excludes overhead costs. This viewpoint was selected because the medical team is considered as the ultimate decision-maker in terms of therapeutic decision, and the objective of the evaluation is to assist them in the decision-making process.

RESULTS

Frequency, length of stay and costs

Frequency. Finding in the literature figures about the frequency of the major procedures may be more or less difficult.

For the conservative strategy, Gissi and Tico give us precise information on the number of PATC and CABG carried out, but we cannot find any information in them about the numbers of angiograms. To complete our data, we thus studied the cardiology unit activities of a non-teaching hospital located in a suburban area near Paris. Our findings confirm the rate of PATC (3 per cent) but show a higher intervention rate for CABG (6 per cent). This latter figure is not very different from those given for CABG in TIMI II when a conservative strategy is carried out (10 per cent). However, in the so-called conservative strategy, implemented in the US, the rates of PATC and angiograms are much higher than in Europe. Thus we considered that the frequencies of the French hospital were a maximum for our country.

For the aggressive strategy, the rates of PATC and CABG found in a French teaching hospital are quite similar to those presented in TAMI and TIMI II (55 per cent of PATC against 54 per cent in TIMI II, 11 per cent for CABG against 10.3).

Length of stay. On this subject, the literature is rather poor. According to Gissi, the mean length of stay ranges between 14 and 25 days. For Isis II, the median length of stay is 10 days. Facing such a lack of precise data, a sensibility analysis was done, based upon three assumptions for the length of stay: 10, 13 and 6 days.

The length of stay and the frequency of major procedures, which depends on the complication rate, were assumed to be independent of the kind of thrombolytic used. The medical literature reveals that the risk of reinfarction is the same when SK or rTPA are used with aspirin. Such a risk seems to be less important when aspirin is added to SK. On the contrary, rTPA seems to be associated with a higher rate of intracranial haemorrhages and major bleedings. Assuming an identical length of stay for the two products introduces a bias against SK, which comes to strengthen the economical case of SK.

On this basis, the average direct costs of hospitalisation per patient treated with SK plus aspirin is about 22,000 Fr. It increases by 5 per cent with delayed elective angioplasty and by 45 per cent with aggressive reperfusion strategy.

Efficacy

Up to now, neither the aggressive strategy nor the elective strategy has clearly shown additional benefits for the patients. Even more, the aggressive strategy seems to be condemned by the convergent results of the European Co-operative Study Group, TAMI and TIMI II. The merits of the elective strategy have never been really evaluated. Only the conservative patient management strategy has a proven efficacy. Therefore, cost efficacy analysis has only been conducted for this conservative strategy.

According to the Meta-analysis of Yusuf, SK (without aspirin) and rTPA reduce the odd ratio five weeks after the fibrinolysis by 26 per cent for patients treated within five hours after the pain onset. The authors of Asset indicate a similar reduction in the relative mortality rate when rTPA is used. Such a reduction of 26 per cent applied to the rate of mortality of the non-treated group in Isis II or Gissi avoids 3.4 deaths. The association of SK and aspirin improves this result and reduces the relative

mortality rate by 51 per cent. Thus, 6.7 deaths could be avoided using this combination.

The average life expectancy of a patient surviving an acute myocardial infarction is 12.5 years. For a cohort of 100 patients, the use of SK or rTPA alone saves 42.5 years of life, compared with 83.75 for the association of SK plus aspirin.

The cost-effectiveness ratio is calculated with respect to the number of avoided deaths and the life-years gained. For patients fibrinolysed within the first five hours after pain onset, the cost per avoided death is 13,500 Fr. for SK plus aspirin compared with 270,000 Fr. for rTPA. The cost per life-year gained is 1,100 against 21,700 Fr.

REFERENCES

'Les grands essais thrombolytiques dans l'infarctus du myocarde', Symposium Atelier, Centre de Salorges, Nantes, 22–23 avril 1989. Partie I: Enseignements méthodologiques et cliniques. Partie II: Enseignements economiques. Partie III: Ateliers de perfectionnement.

Launois R et B (1989). 'Analyse coût-efficacité des strategies thrombolytiques', *Archives de Maladies du cœur et des vaisseaux*, tome 82 (Octobre), N° spécial (Ill.): 55, 62.

COST-EFFECTIVENESS ANALYSIS OF CHOLESTEROL-LOWERING THERAPY IN THE NETHERLANDS

Léon Martens and Patricia Finn

INTRODUCTION

The increase of health care expenditures as a share of gross national product in most western countries has led to an array of cost-containment measures. In many countries, particular attention has been given to the cost of pharmaceuticals. Regulations to limit expenditures on pharmaceuticals typically involve pricing, substitution of generics for brand drugs, and restricted reimbursement, i.e. establishing guidelines that identify those patients whose prescriptions will be reimbursed.

The need for guidelines for treatment, whether they are imposed by restrictive reimbursement or offered as a support for good clinical practice by consensus conferences, particularly arises in the case of the primary prevention of coronary heart disease. Epidemiological studies, such as the Multiple Risk Factor Intervention Trial (Martin *et al*, 1986) have demonstrated the positive relationship between serum cholesterol level and coronary heart disease mortality. Every increase in serum cholesterol level increases the risk for coronary heart disease death, and there is no threshold level below which this relationship does not exist. Although this finding identifies the need to lower serum cholesterol levels, debate continues concerning whether the costs of making a nationwide commitment to lower cholesterol levels are worth the benefits, especially for persons with only mildly elevated cholesterol levels.

The Dutch Cholesterol Consensus Conference (DCCC), organised in 1987, issued guidelines for the detection and treatment of persons with elevated serum cholesterol levels (Voorbereidingswerkgroep, 1987). According to these guidelines, persons with cholesterol levels above 6.5 mmol/l should receive dietary counselling. If several months of diet fails to reduce serum cholesterol levels below 8 mmol/l, drug therapy should be initiated. For persons with serum cholesterol levels between 6.5 and 8 mmol/l, drug therapy should be considered only if other coronary risk factors are present.

The DCCC has designated bile acid sequestrants such as cholestyramine as the drug of first choice for the treatment of patients with elevated serum cholesterol levels. In December 1988, the cholesterol-lowering agent simvastatin was registered in The Netherlands. Simvastatin is one of the first HMG-CoA reductase inhibitors, a group of pharmacological agents that effect dose-related lowering of serum cholesterol levels through inhibition of hydroxy-methylglutaryl-coenzyme A reductase, the rate-limiting enzyme of cholesterol synthesis. Recent clinical studies suggest that these agents may be more effective in lowering serum cholesterol levels and may be associated with fewer side-effects than are other medications such as cholestyramine (Lovastin Study Group, 1988; Tobert, 1988). These findings call for a re-evaluation of the recommendation of cholestyramine as drug of first choice.

In the following, we describe a model to estimate the cost-effectiveness of cholesterol-lowering therapy in the primary prevention of coronary heart disease. We then use these results to identify those patients who should be candidates for cholesterol-lowering therapy.

METHODS

General model

To estimate the cost-effectiveness of therapy, we developed a model of coronary heart disease incidence and mortality among persons of varying age, sex and cholesterol level. A detailed description of this model, which is based on multivariate logistic risk functions from the Framingham Heart Study, can be found elsewhere (Martens *et al*, 1989). Changes in lifetime coronary heart disease risk, life expectancy and future medical care costs for given pre-treatment cholesterol levels were estimated by combining this model with data on the effectiveness and cost of cholesterol-lowering therapy, as well as data on the cost of treating symptomatic coronary heart disease.

The cost-effectiveness of cholesterol-lowering therapy was calculated as the ratio of the net treatment costs (i.e. cost of therapy minus any savings in the cost of treating symptomatic coronary heart disease) to the net change in life expectancy due to therapy. The net change in life expectancy for a cohort of any given age and sex was calculated as the discounted sum of the changes in the proportion of persons remaining alive in each future year due to therapy. The net change in medical care costs was calculated similarly, as the discounted sum of the changes in annual medical care costs in each future year of life. Changes in life expectancies and treatment costs were discounted at a 5 per cent annual rate. All costs were adjusted to reflect 1988 price levels.

The error in cholesterol measurement

The multivariate logistic risk functions from the Framingham Study are based on a single cholesterol measurement. According to the DCCC, physicians should base the decision to initiate treatment on the average of three cholesterol measurements, which provides a better estimate of the patient's serum cholesterol level than a single measurement. Furthermore, the cholesterol measurements for the risk functions from the Framingham Study took place between 1950 and 1970, when the quality of laboratory measurement was undoubtedly less than that of current laboratories. We adjusted our model estimates for the difference in the number of cholesterol measurements and the difference in laboratory quality (see Appendix).

Cost and effectiveness of cholesterol-lowering therapy

We estimated the reduction in serum cholesterol levels that would be achieved by cholestyramine therapy using the dose-response relationship between total serum cholesterol and the daily intake of packets of cholestyramine reported in the Lipid Research Clinics Coronary Primary Prevention Trial (Lipid Research, 1984). We estimated that three packets of cholestyramine daily would lower serum cholesterol by 6.2 per cent, calculating this change as a reduction from cholesterol levels achieved by diet. We estimated that the annual costs of therapy for cholestyramine, including drug cost, physician fees and cholesterol testing, would be 1,761.36 NLG in the first year and 1,670.16 NLG in later years of therapy.*

Based on the phase III multicentre studies cited in the Marketing Authorisation Application for Zocor, we assumed that patients receiving one 10mg tablet per day would experience a 21 per cent reduction in cholesterol levels, and we assumed that those receiving one 20mg tablet of simvastatin per day would experience a 27 per cent reduction in cholesterol levels (Marketing Authorisation: unpublished). We estimated that the annual costs of therapy for simvastatin 10mg per day (including drug cost, physican fees, cholesterol testing, and monitoring of the liver function) would be 1,383.30 NLG in the first year and 1,038.30 NLG in later years of therapy. For simvastatin 20mg per day, annual therapy costs would be 1,745.30 NLG and 1,400.30 NLG in the first year and in subsequent years respectively.

RESULTS

Costs per year of life saved due to therapy

Table 1 presents estimates of the cost per year of life saved with simvastatin therapy for men and women, by cholesterol level and age at initiation of therapy.

For men and women at all ages, the costs per year of life saved decrease with increasing pre-treatment cholesterol levels. The costs of simvastatin therapy for men 35–39 years of age are 52,400 NLG per year of life saved for those with pre-treatment cholesterol levels of 7 mmol/l, compared to 19,000 NLG for those with pre-treatment cholesterol levels of 9 mmol/l.

When examined by age, costs per year of life saved are lowest when therapy is begun between the ages 35–49 years for men and 50–64 years for women. In men, the costs per year of life saved rapidly increase when therapy is begun at a later age. For example, simvastatin therapy in men with pre-treatment cholesterol levels of 9 mmol/l costs 19,000–21,500 NLG per year of life saved when begun between the ages of 35–49 years, but more than doubles to 51,500 NLG when therapy is started by age 60–64 years. Among women, the costs per year of life saved are not as sensitive to the age at which therapy is begun. When simvastatin therapy in women with pre-treatment cholesterol levels of 9 mmol/l is begun at any age between 35 and 64 years, the costs per year of life saved are 60,700–68,200 NLG.

Costs per year of life saved are greater for women than for men at all cholesterol levels and ages at initiation of therapy. These differences are more pronounced at younger than older ages. For example, for persons with cholesterol levels of 9 mmol/l, the costs per year of life saved for simvastatin therapy begun at age 35–39 years are three to four times higher among women than among men (68,200 NLG versus 19,000 NLG), Whereas at age 55–59 years, they are only twice as high (63,800 NLG versus 34,800 NLG).

The costs per year of life saved with cholestyramine therapy are presented in Table 2. For both men and women at any pre-treatment cholesterol level and age at initiation of therapy, the costs per year of life saved with cholestyramine therapy are four to five times greater than those of simvastatin therapy. For example, for men aged 35–39 years and pre-treatment cholesterol levels of 8 mmol/l, the costs of simvastatin therapy are 31,500 NLG

* 1 Dutch Guilder (NLG) equals approximately US $0.5.

1 Cost per year of life saved by cholesterol-lowering therapy with Simvastatin 20mg per day amoung Dutch men and women (Dutch Guilders)

Cholesterol	Age at initiation of therapy					
MEN	35–39	40–44	45–49	50–54	55–59	60–64
7.0	52,400	50,300	51,200	57,500	69,800	95,000
8.0	31,500	31,300	33,100	39,000	49,000	69,500
9.0	19,000	19,500	21,500	26,700	34,800	51,500
WOMEN	35–39	40–44	45–49	50–54	55–59	60–64
7.0	167,300	149,900	133,900	123,900	119,200	118,500
8.0	107,200	98,700	90,500	86,400	86,800	87,900
9.0	68,200	65,000	61,400	60,700	63,800	66,000

1 Dutch Guilder = US $0.5.

2 Cost per year of life saved by cholesterol-lowering therapy with Cholestyramine 12g per day among Dutch men and women (Dutch Guilders)

Cholesterol	Age at initiation of therapy					
MEN	35–39	40–44	45–49	50–54	55–59	60–64
7.0	218,200	215,800	225,900	261,300	324,300	445,400
8.0	131,200	134,600	147,100	178,600	229,200	326,500
9.0	80,500	85,700	97,700	124,400	165,200	243,700
WOMEN	35–39	40–44	45–49	50–54	55–59	60–64
7.0	704,100	644,400	588,800	558,000	549,600	557,600
8.0	432,400	410,800	388,000	382,400	395,700	410,700
9.0	262,500	261,000	256,600	264,300	288,100	306,900

1 Dutch Guilder = US $0.5.

3 Cost per year of life saved by Cholesterol-lowering therapy with Simvastatin 10mg per day among Dutch men and women by the presence of Diabetes Mellitus and/or Hypertension (Dutch Guilders)

Risk status	Pre-treatment serum cholesterol			
MEN	6.5	7.0	7.5	8.0
Average risk	54,600	42,600	33,300	26,000
Hypertension	44,700	34,900	27,200	21,200
Diabetes	42,500	33,200	26,000	20,300
Hypertension & diabetes	35,100	27,400	21,400	16,800
WOMEN	6.5	7.0	7.5	8.0
Average risk	129,600	107,400	89,200	74,200
Hypertension	116,700	96,800	80,400	67,000
Diabetes	47,500	39,800	33,400	28,200
Hypertension & diabetes	43,800	36,700	30,900	26,200

N.B. – 1 Dutch Guilder = US $0.5.
– Age at initiation of therapy: men 40–44 years, women 50–54 years
– The diastolic blood pressure of hypertensive persons is assumed to be controlled at 95mm Hg.

per year of life saved compared to 131,200 NLG for cholestyramine therapy.

Coronary risk factors and cost-effectiveness

Because coronary risk factors can have a multiplicative effect on coronary heart disease incidence, we also examined the cost per year of life saved with simvastatin therapy for persons with different combinations of risk factors in addition to elevated serum cholesterol levels. We considered the presence of hypertension and/or diabetes mellitus. We assumed that the diastolic blood pressure of hypertensive patients is controlled at 95mm Hg. We also assumed that in patients with cholesterol levels between 6.5 and 8.0 mmol/l, 10mg simvastatin per day will achieve the desired therapeutic effect.

Table 3 presents costs per year of life saved with simvastatin therapy 10mg per day among 40–44-year-old men and 50–54-year-old women, by the number of additional risk factors present. We used these age groups for purpose of illustration because they are the groups in which therapy is most cost-effective.

Among men costs per year of life saved decline markedly as the number of risk factors increases. For example, at pre-treatment cholesterol levels of 7.5 mmol/l, costs per year of life saved are 33,300 NLG at average risk, 26,000–27,200 NLG with either hypertension or diabetes present, and 21,400 NLG when both hypertension and diabetes are present.

Among women, the presence of diabetes mellitus causes the greatest reduction in costs per year of life saved. For example, when therapy is begun in 50–54-year-old women with pre-treatment cholesterol levels of 7.5 mmol/l, costs per year of life saved are 89,200 NLG for those at average risk. This falls to 33,400 NLG with the presence of diabetes mellitus, compared to 80,400 NLG when hypertension is present.

COMMENT

Using a model of the incidence and prevalence of coronary heart disease in The Netherlands based on logistic risk functions from the Framingham Study, we have assessed the cost-effectiveness of cholesterol-lowering therapy in the primary prevention of coronary heart disease.

Our results indicate that the costs per year of life saved among men rapidly increase when therapy is initiated at a later age. The identification of hypercholesterolaemia and the subsequent initiation of treatment should, therefore, be accomplished at an early age. For women, the costs per year of life saved do not vary substantially when therapy is started between the ages of 35 and 64 years.

Our results confirm an inverse relationship between the costs per year of life saved and the pre-treatment cholesterol level, which provides an economic rationale for the DCCC's guideline to initiate drug treatment only for persons with a serum cholesterol above a certain level. From a clinical point of view, it is rational to lower cholesterol levels in the entire population since the relationship between serum cholesterol and coronary heart disease mortality is continuous and graded (Martin *et al*, 1986). Costs per year of life saved increase rapidly, however, with decreasing pre-treatment cholesterol level.

Our results indicate that simvastatin is substantially more cost-effective than cholestyramine. Although cholestyramine is not well tolerated by many patients, its long-term safety has been established by the Lipid Research Clinics Coronary Primary Prevention Trial. When, in the course of time, the long-term safety of simvastatin becomes increasingly established, this agent can be accepted as a drug of first choice in the treatment of persons with elevated serum cholesterol levels.

According to the guidelines of the DCCC, drug treatment should be initiated when serum cholesterol levels remain higher than 8 mmol/l after several months of diet. When therapy is started in men at the age of 35–39 years who have a pre-treatment cholesterol level of 8 mol/l, cholestyramine increases life expectancy at a cost per year of life saved of 131,200 NLG. This compares unfavourably with the cost-effectiveness of other health care programmes in The Netherlands, such as screening for breast cancer (Maas *et al*, 1987), intracoronary thrombolysis (Martens and Van Doorslaer, in press), screening for cervical cancer (Habbema *et al*, 1988), heart transplantation (De Cherro *et al*, 1988), and the end-stage renal disease programme (De Cherro, 1988), the costs per year of life saved of which are approximately

10,000 NLG, 8,000–25,000 NLG, 24,000 NLG, 52,000 NLG, and 54,000 NLG respectively. When therapy is started among men with cholesterol levels of 8 mmol/l and above, simvastatin 20mg per day adds life-years at a cost of no more than 31,500 NLG, which is well within the range of generally accepted Dutch medical practices. The cost per year of life saved with simvastatin 20mg per day among women with serum cholesterol levels of 8 mmol/l ranges from 86,400 NLG to 107,220 NLG, depending on the age at which therapy is started. These cost-effectiveness ratios compare unfavourably with those of the above-mentioned health-care interventions.

According to the guidelines of the DCCC, drug therapy should be considered at post-diet cholesterol levels between 6.5 and 8.0 mmol/l when additional coronary risk factors are present. Therapy with simvastatin 10mg per day started among men aged 40–44 years, with pre-treatment cholesterol levels between 6.5 and 8.0 mmol/l, adds life-years at a cost of 16,800–44,700 NLG per life-year saved when hypertension and/or diabetes is present. These costs are well within the range of those of other generally accepted practices in The Netherlands. The cost-effectiveness of cholesterol-lowering therapy among women, however, does not appear to compare favourably to that of currently accepted medical interventions, unless therapy is limited to those with diabetes.

We think that our findings have a number of important implications for physician and policy makers. First, our results suggest than simvastatin is substantially more cost-effective than cholestyramine in the treatment of hypercholesterolaemia and that, as its long-term safety becomes more established, it should become accepted as a drug of first choice in the treatment of persons with elevated serum cholesterol levels. Our results also suggest that the costs per year of life saved of cholesterol-lowering therapy compare well with a number of other generally accepted medical practices when therapy for men is begun at an early age, and when cholesterol-lowering therapy among women is limited to women with diabetes mellitus or severely elevated serum cholesterol levels.

ACKNOWLEDGEMENTS

We would like to express our appreciation to the Department of Epidemiology and Biostatistics of the Erasmus University, Rotterdam, for providing data from the Epidemiological Preventive Study Zoetermeer, and to Joseph M Heyes, Harry Guess and Keaven Anderson for their helpful comments.

APPENDIX

The measured value x of an individual's serum cholesterol varies around an average level x_1 (the 'true' level) due to a combination of biological variation and laboratory error (Williams *et al*, 1978). The expected value for x_1 is given by the following equation:

$$x_1 = x + \frac{{\sigma_2}^2}{n\,\sigma^2}\,(\mu - x),$$

where x is the average of n cholesterol measurements, μ and σ are the mean serum cholesterol level and standard deviation respectively of the population, and ${\sigma^2}_2$ is the error variance in the cholesterol measurement. ${\sigma^2}_2$ is usually expressed in the coefficients of variation of the biological variation (CVb) and the laboratory variation (CVa).

Using $n = 3$, CVa = 3.5 per cent ('Current status': 1988), age- and sex-specific values for CVb (Williams *et al*, 1978), and the age- and sex-specific cholesterol distribution of the Dutch population,* we estimated the expected value x_1 for the true cholesterol level of Dutch men and women who have a cholesterol level x based on three measurements. We used the above formula to calculate the expected value for a single cholesterol measurement among men and women in the Framingham Study whose true cholesterol level would have equalled x_1, we then used the Framingham multivariate logistic risk functions to attribute the corresponding coronary risk to Dutch men and women with a cholesterol value x based on three measurements. Since the cholesterol measurements for these risk functions took place between 1950 and 1970, the quality of the laboratory determinations must have been considerably lower than nowadays. From longitudinal studies performed in the 1950s with a similar laboratory technique (Thomas *et al*, 1961; Thomas *et al*, 1957), we estimated that the analytical coefficient of variation was approximately 7–8 per cent. We chose to apply a conservative estimate of CVa = 5 per cent to the Framingham risk estimates.

* Data from the Epidemiological Preventive Study Zoetermeer (EPOZ) were provided by the Department for Epidemiology and Biostatics of the Erasmus University, Rotterdam, The Netherlands.

This research was supported by a grant-in-aid from Merck & Co. Inc., Rahway, New Jersey.

REFERENCES

(1988). 'Current status of blood cholesterol measurement in clinical laboratories in the United States: a report from the Laboratory Standardization Panel of the National Cholesterol Education Program', *Clinical Chemistry*, 34: 193–201.

De Charro F, Bonsel G J and Hout B A van (1988). *De kosten en effecten van harttransplantatie*. Deelrapport 9: Eindrapport. Rotterdam, Erasmus Universiteit.

De Charro F (1988). *Kosen-effectiviteitsanalyse van het nierfunktievervangingsprogramma in Nederland*. Delft, Eburon.

Habbema J D F, Lubbe J Th N, Agt H M E van, Ballegooyen M van, Koopmanschap M A and Oortmarssen G J van (1988). *Kosten en effecten van bevolkingsonderzoek op baarmoederhalskanker*. Rotterdam, Instituut Maatschappelijke Gezondheitszorg, Erasmus Universiteit.

Lipid Research Clinics Program (1984). The Lipid Research Clinics Coronary Primary Prevention Trial Results: 'I. Reduction in incidence of coronary heart disease', *Journal of the American Medical Association*, 251: 351–364.

Lipid Research Clinics Program (1984). The Lipid Research Clinics Coronary Primary Prevention Trial Results: 'II. The relationship of reduction in incidence of coronary heart disease to cholesterol-lowering', *Journal of the American Medical Association*, 251: 365–374.

Lovastatin Study Group (1988). 'III. A multicenter comparison of lovastatin and cholestyramine therapy for severe primary hypercholesterolemia', *Journal of the American Medical Association*, 260: 359–366.

Maas P J van der, Ineveld B M van, Oortmarssen G J van, Koning H J de, Lubbe J Th N, Habbema J D F, Birnie E, Geerts A, Bruyn A E de, Collette H J A, Rombach J J, Verbeek A L M, Straatman H, Hendricks J A C L and Heuvel W J A van den (1987). *De kosten en effecten van bevolkingsonderzoek op borstkanker*. Interimrapport 1987. Rotterdam, Instituut Maatschappelijke Gezondheidszorg, Erasmus Universiteit.

Marketing Authorization Application for Zocor (simvastatin). Data on file at Merck Sharp & Dohme Research Laboratories, Blue Bell, Pa., and at the Food and Drug Administration, Washington, DC.

Martens L L, Rutten F F H, Erkelens D W and Ascoop C A P L (1989). 'Cost-effectiveness of cholesterol-lowering therapy in The Netherlands: simvastatin versus cholestyramine', *The American Journal of Medicine*, 87 (suppl. 4A): 54S–58S.

Martens L L and Van Doorslaer E K A. 'Dealing with discounting: an application to the cost-effectiveness of intra-coronary thrombolysis with streptokinase', *International Journal of Technology Assessment in Health Care*. (In press.)

Martin M J, Hulley S B, Browner W S, Kuller L H and Wenthworth D (1986). 'Serum cholesterol, blood pressure, and mortality: implications from a cohort of 361,662 men', *The Lancet*, ii: 933–936.

Thomas C B and Eisenberg F F (1957). 'Observations on the variability of total serum cholesterol in Johns Hopkins medical students', *Journal of Chronic Diseases*, 6: 1–24.

Thomas C B, Holljes H W D and Eisenberg F F (1961). 'Observations on seasonal variations in total serum cholesterol level among healthy young prisoners', *Annals of Internal Medicine*, 54: 413–430.

Tobert J A (1988). 'Efficacy and long-term adverse effect pattern of lovastatin', *American Journal of Cardiology*, 62: 1J–9J.

Voorbereidingswerkgroep cholesterol consensusbijeenkomst (1987). *Consensus cholesterol: Het resultaat van een consensusbijeenkomst gehouden op 20 maart 1987 te Amersfoort*. Utrecht, Centraal Begeleidingsorgaan voor de Intercollegiale Toetsing.

Williams G Z, Widdowson G M and Penton J (1978). 'Individual character of variation in time series studies of healthy people: II. Differences in values for clinical chemical analytes in serum among demographic groups, by age and sex', *Clinical Chemistry*, 24: 313–320.

COSTS AND BENEFITS FROM 'BREAKTHROUGH' INNOVATION

Gérard Milhaud

We are grateful to George Teeling Smith, Lord Butterfield and Michel Salomon for having organised this international conference on measuring the benefits of medicines. It offers a unique opportunity to discuss both economic and therapeutic aspects. We knew for a very long time that health is priceless. It took many years for the European health care systems to understand that health has a cost. These conflicting points of view have been discussed at previous meetings, but the present conference will help to reconcile the oppositions.

Let us try to put the topic in perspective. Life expectancy was 45 years for both men and women in 1900. Progress in medicine and hygiene have extended life expectancy to 72 years for men and 81 years for women. Two therapeutic revolutions have contributed to this striking evolution. The first one in the '40s and '50s discovered chemotherapeuticals like sulfadrug, the first antibiotics, the first antihistamine agent, curare-like compounds, diuretics and tranquillisers. The cost of these medicines was moderate and economically bearable for the health care systems.

The situation has completely changed with the achievements of the second therapeutic revolution of the '70s and '80s, engendered by the understanding of the logic of the body. Progress in the synthesis of peptides as well as genetic engineering is making available very complex molecules. They held great promise for the control of disorders previously beyond our therapeutic reach. The rising cost of medicines, such as calcitonin, H_2-antagonists, calcium channel blockers, converting enzyme inhibitors, tissue plasminogen activators, human erythropoietin and HMG-CoA reductase inhibitors, has become, rightly or wrongly, a major cause of concern. Special attention is attracted on decisions between optimal therapy according to the Hippocratic oath and economically feasible therapy according to the social point of view of health economists. Where lies the border between health economy and savings on health care?

Assuming the physician prescribes medications and investigations in the best interest of his patient, how will he manage to take into account the cost to society, or to public or private health insurance? How will he cope with the concern of the health insurance systems over the rising cost of medical care, and with their efforts to control the expenses?

The analyses of health economists are clearly needed at this point in order to optimise the benefits of the social health service considered as a whole. Nevertheless, containing health care costs should not be achieved at the expense of pharmaceutical innovation.

We should remember that nearly half of the total health care expenses stems from hospital care. The cost of medicines represents only 9–14 per cent of the bill, as Mr Farrant has underlined yesterday. Yet the blame for increasing health expenses is aimed at the pharmaceutical industry. There is probably a good or a bad reason for doing so. In France, the number of hospital beds is in excess, and there is no such thing as waiting lists. Nevertheless, administrators and politicians are reluctant to take the responsibility for reducing the number of hospital beds to the real needs of the population. Is it not much easier to accuse the pharmaceutical industry – and why only the pharmaceutical industry – for the rising costs of the health care system?

Let us now discuss two examples where optimal decisions were not taken by the administration. The first example deals with antagonists of H_2 receptors inhibiting the acid secretion by the stomach. In 1988, in France, cimetidine and ranitidine represented 81 per cent of the anti-ulcer medicine cost, for over 820 million francs. This cost is high and partly due to over-prescribing. But the benefits are large; gastro-duodenal surgery for ulcer is practically no more performed, and the consequent dumping syndrome and painful osteoporomalacia have disappeared. The cost-benefit ratio of this major therapeutic breakthrough should be easy to calculate. On one hand lies the cost of medication; on the other, the cost of gastro-intestinal surgery. Taking into consideration the two costs, the balance is most likely to switch in favour of medication. But in such a case a real saving would only be achieved by closing an adequate number of surgical beds. Yet the health administration, which is so concerned about increasing expenditure on medicine, has never made such a decision. The excuse cannot be waiting lists, as they do not exist.

The next question is: why is the price of new medicines so high? One of the reasons is certainly the fact that the development has grown out of control, amounting to $100 million for the introduction on the world market of a breakthrough medicine. How much of this cost is related to the successful discovery, and how much to the many preceding failures? How much is required for the fulfilment of the requirements of the regulatory authorities, in absence of mutual recognition of marketing authorisation? These requirements are no longer directed towards the welfare and the safety of the patients. Another conference would certainly be needed to discuss costs and benefits of regulatory requirements. If the administration would really care to reduce drug expenses, the requirements could be dramatically decreased with negligible risk for the patient. In the case of AIDS, the public as well as the patients demanded and obtained immediate access to new experimental drugs. Under pressure, FDA had to yield and to change its policy. This is another example of how savings could be achieved concerning the cost of medicines.

These considerations should nevertheless not lead to the prescription of the newest and most advertised drug. Let us mention the treatment of hypertension with inhibitors of the enzyme-transforming angiotensin I to

angiotensin II. These expensive drugs are prescribed for the management of all stages of arterial hypertension and of congestive heart failure. Is their use more manageable than one of the earlier and cheaper medications? This question should be answered by an adequate survey, as the cost of the inhibitors exceeded 1.5 billion francs in France last year.

A similar situation is found in the case of the inhibitors of the HMG-CoA reductase versus the fibrates for managing hyperlipidemia or in the case of tissue plasminogen activator versus streptokinase-streptodernase for treating early stages of heart attacks.

In the near future, we will have to face another type of cost-benefit question linked to breakthrough innovation. The ageing population suffers more and more from age-related disorders, particularly from osteoporosis and bone-brittleness. The hip fracture is a serious event, as 25 per cent of the patients will die in the following six months. It is likely that treatment such as calcitonin could prevent age-related bone loss and the consequent fractures. The cost-effectiveness of large prevention schemes should be assessed, as the yearly expenses for hip fractures in France are over 1 billion francs.

In conclusion, the attempts to contain health care costs should not prevent pharmaceutical innovation. Cost-effectiveness should become of major concern for doctors, administrators and politicians. But cost-effectiveness surveys should not be restricted to the use of medicines. They should consider all aspects of the health care system. They should be extended to the administration and even to the government itself.

THE IMPORTANCE OF QUALITY OF LIFE

Alan Williams

The traditional outcome measure in medicine has been survival, and it still plays an important role in many clinical trials. This is not surprising, because most people have a strong desire to live longer. But survival is not the only outcome of interest. People are also interested in the quality of that survival, i.e. what will their actual health state be like after treatment . . . will they be disabled, disfigured or distressed, will they be in pain, will they be able to pursue their normal activities, and so on. It may well be that in some circumstances people will be willing to sacrifice some life expectancy in order to improve their quality of life, whilst others might be willing to sacrifice quality of life to extend life expectancy. The general point that I wish to establish at the outset, however, is that both life expectancy and quality of life are valued by patients, and neither will generally take absolute precedence over the other, so we need to measure both of them.

I think there is increasing recognition of this fact, and George Teeling Smith and the OHE have been very active and successful over the past few years in driving that message home, both at the level of principle and by offering the converted some practical assistance with implementation. But whilst those in the vanguard may now look upon all this with a strong sense of *déjà vu*, I regret to say that those in the vanguard are still a regrettably small minority. I still hear people saying that the treatment of life-threatening conditions must take priority over mere symptomatic relief, by which they clearly mean that we should always give absolute precedence to the prolongation of life over 'mere' improvement in its quality. Hence expensive, but very unpleasant, drug regimes or heroic surgery for terminal cancer cases, which might prolong people's lives for a few weeks, are argued to be a higher priority use for NHS resources than (say) total hip replacements, which 'merely' enable elderly women to enjoy pain-free mobility for the last ten years of their lives instead of being crippled, chairbound and in considerable pain. I also note that in clinical trials the survival rate at some arbitrary time point is still often the dominant criterion for choosing between treatments. But the use of (say) the two year survival rate to choose between treatments implies that:

- to survive less than two years is of no value to people;
- having survived two years, further survival is of no additional value;
- it does not matter with what quality of life people survive to two years;
- it does not matter who you are.

The only one of these implications I find at all acceptable is the last one, the others seem to me to be quite at odds with the truth. Although it is more difficult to estimate, the average change in life-expectancy would be superior to the survival rate if it is prolongation of life we are seeking to measure, but I will not pursue that matter further today because my main concern here is with the neglect of the quality-of-life dimension.

In 1984 I was heartened to read in a survey by Nanette Wenger and colleagues concerning the methods used to assess quality of life in clinical trials of cardiovascular therapies that: 'The emerging consensus is that both biomedical and quality-of-life outcomes require evaluation.' In the following year Wortman and Yeaton published a paper with a most encouraging title: namely, 'Cumulating quality of life results in controlled trials of coronary artery bypass surgery'. But it turned out that the only quality-of-life outcome measure they were able to use that was common to the fourteen trials they reviewed was 'percentage of patients who were angina free' at whatever follow-up dates each trial happened to use. Not much consensus emerging so far it seems. I tested the state of play in the cardiovascular field again more recently by conducting a MEDLINE search of clinical trials published in 1987 and 1988 in any of four broad fields of Cardiology, Cardiovascular Disease, Heart Disease, and Vascular Disease. As you see, I came up with 380 such trials, of which only 20 used some kind of quality-of-life measure as an endpoint. So the 'emerging' broad consensus seems to be having a rather long gestation period.

But you might object that there is more to medicine than is dreamed of by cardiologists and cardiac surgeons, and indeed there is. For a more thorough assessment of the current state of play I went through all the issues of *The Lancet* published in 1987, and there found 93 published trials of ostensibly therapeutic activities. The outcome measures used were predominantly physiological, with only 32 using some sort of quality-of-life measure (applying rather lax criteria of what a quality-of-life measure is). If stricter criteria are applied, the number falls to nine, or about 1 in 10. The physiological measures used were much as you would expect, and note that 28 trials had only such measures. Morbidity measures were the next most common, but as far as I am concerned they represent little advance on physiological measures. Next in order of frequency were mortality rates at varying follow-up dates (from a few days to several years). Note that no study estimated the change in life expectancy, which we would need to have if we were to translate the benefits into life-years gained.

As I have already indicated, on a generous interpretation of what quality-of-life measure is, 32 studies could be said to include such measures, though in many cases it was obvious that the clinical interest in such phenomena as nausea, cough frequency or length of maternal labour was more physiological than anything to do with the patient's quality of life. The content of these measures indicates a predominant interest in physical functioning and pain/distress/discomfort. Using rather stricter criteria only nine studies passed through my filter, but the

content of the quality-of-life measures used in these studies was very similar to that in the larger set.

The commonest formal indicator used was Karnofsky's Index which has a set of 10 descriptive categories based on a mixture of patients' activity levels and symptoms, and the place and type of treatment being given. Its weaknesses are, first of all, that the place and type of treatment are partly supply determined so are not good indicators of patient state, and, secondly, that the 0 to 100 rating is purely arbitrary (i.e. it is not a measure of the relative seriousness of being in each state, but an indication of the likely rank ordering of the states).

So my overall conclusion remains that quality-of-life measurement is still a minority interest and that the 'emerging consensus' still has a long was to go before it makes any significant impact upon the measurement of the effects of medicine generally.

So where do we go from here? In 1988 Nanette Wenger suggested that: 'The quality-of-life issues chosen for assessment in a clinical trial must therefore reflect the questions likely to be raised by both physicians and patients in reference to the clinical problem under consideration.' (*European Heart Journal*, 9: 233.) To which I would merely add that they should also reflect the questions likely to be raised by managers and policy makers.

Wenger had earlier noted six existing instruments for measuring quality of life, which had somewhat different focuses of interest and which made varying demands upon patients and practitioners or researchers. I myself have been using a very simple classification system devised by Rosser, which again highlights disability and distress as the key dimensions, partly because it is one of the few classification systems to go beyond description and take that important further step and elicit the relative values that people attach to being in each state. In this important respect it takes matters further than the arbitrary scale of values embodied in measures such as the Karnofsky Index.

To me this is very important because it enables us to address the trade-off issue between life expectancy and quality of life, for it indicates that (say) three years in a state rated at 0.67 is of about the same value of two years in good health (rated at 1.0). Thus someone with those values would be willing to sacrifice not more than one-third of his or her remaining life expectancy for such an improvement in quality of life. It is such quality ratings that are needed if we are to implement such composite benefit measures as the Quality Adjusted Life Year, which seem to me the most promising candidate for development on the future agenda for benefit measurement in medicine over the next decade.

But judging by the slow rate of progress over the past decade we may have to settle for something more modest over the next five years or so. Perhaps it would be best to start at ground level building a sort of 'stairway to the stars', for, as Confucius said, 'A journey of a thousand miles still begins with a single step'. Whether or not we have a thousand miles to go remains to be seen, but may I suggest the following initial steps in quality of life measurement.

In addition to whatever physiological, morbidity or mortality data is collected because it is of scientific or clinical interest, elicit some simple subjective rating of the effect on the patient's overall health-related quality of life, perhaps by the use of a visual analogue scale such as:

Worst imaginable health state	Best imaginable health state

and get that measure recorded as frequently as is feasible by the patient, the patient's relatives, and by those treating the patient (preferably independently of each other). Even such simple data offers the possibility of cross-checking (over time) the perceptions of the different parties as to how things are going, and in seeing what correlation there is between the quality-of-life assessments and whatever other clinical or scientific data on outcome is being collected. Be prepared for some surprises!

The next step up my stairway would involve using one or more of the standard descriptive systems which have been developed for use in particular clinical fields. They have the advantage of concentrating on aspects of the patient's feelings and functioning which are of particular clinical interest, and have usually been developed so as to be sensitive to quite small changes in the patient's condition. But the use of such a measure should not replace the simple overall assessment by visual analogue scale, because again there is then the possibility of cross-checking the dimensions of the standard descriptors against the overall assessment.

The third step is to move to a more versatile generic measure which usually covers a wider range of phenomena related to quality of life, but which has less fine measurement scales on each such dimension so as to keep the overall assessment task manageable. The typical result is a profile which includes a broad brush assessment of what was in the specific index, but more besides. This has two advantages to set against the disadvantage of reduced sensitivity in measuring items of particular clinical interest. These are, firstly, that it may pick up unexpected side-effects upon people's quality of life which might otherwise have gone undetected, and secondly, that it facilitates systematic comparison of the effects of rather diverse treatments of rather diverse conditions, which may be very important for priority setting within specialties or across specialties.

By the time we get to my fourth step I fear we may already have left some of the weaker souls behind, for it consists in moving from descriptions (of a profile kind) to

the use of a summary index based on actual relative valuations of the different states by patients or relatives or practitioners or by the citizenry at large. There are a few such pioneering indexes in existence at present, and it is at about this point on the staircase that vertigo usually sets in amongst the practitioners, and scaling the rest of the dizzy heights is left to the research community.

So on my fifth step I expect to find only the hardiest explorers of benefit measurement (or some would say only the foolhardiest). For at this level of ambition the objective is actually to elicit these valuations from a wide range of respondents, to see whether people's valuation of health varies systematically by age, sex, family situation, religious beliefs, occupation, experience of illness, etc. This is my own particular level of interest in the subject, and it is here that I expect most of the action on the 'future agenda' over the next 10–20 years. How people actually value the effects of medicines is the 64,000 dollar question which we can no longer run away from, difficult and mind boggling though it is.

But there is a sixth step, which is not of much immediate interest if you are a clinician or clinical researcher interested in quality-of-life measurement as a means of increasing the benefits of medicine to a particular group of patients. But it is of rather considerable significance if you are concerned with matters of equity in the distribution of the benefits of medicine between different groups in the community. The issue to be addressed on step six of my 'stairway to the stars' is: is it more important to improve the length and quality of life of some people than of other people, or is a given improvement to be regarded as of equal value no matter who gets it? You may remember that near the beginning of my talk I observed that the use of the two year survival rate implied, amongst other things, that it did not matter who you are. Two years of survival is counted equally whether it accrues to a seven-year-old or a 70-year-old, to a derelict middle-aged single alcoholic or to the young mother of several school-aged children, etc. There is some evidence that such discriminations are in fact made in practice, and that they have public support, but so far, to my knowledge, they have not been explicitly recognised or used in benefit measurement in any clinical trial. Nor, at the moment in my view, should they be. But it may be that we shall in future need to identify more clearly the different kinds of people who stand to benefit from a particular treatment, so that if priorities of this kind are to be brought to bear, the descriptive data is there to enable it to be done. Meanwhile, we need to research rather carefully these notions of fairness or equity or social worth, and discuss them and their implications rather more openly than hitherto.

There are doubtless some further steps to be taken before we actually reach the stars, but I have to confess that it is at step six that my vision grows too dim to perceive anything very clearly. There will doubtless be some amongst you who can see further ahead than me, and you will have your opportunity to say so shortly. But before you have your say I want to leave you with my 'future agenda' as a starting point for the discussion.

I have divided our future needs into three groups of activity.

- Better integration of the various ways of describing and 'scoring' degrees of disability and distress in use in various areas of medicine at present, linking them systematically to some global index.
- Wider application of the various ways of measuring quality-of-life variables systematically by the use of simple standard questionnaires which can be completed quickly by patients or observers both in clinical trials and in routine monitoring.
- Broader valuation of different health states to establish whether there are marked differences between different groups in the population and whether different methods of eliciting valuations have a significant effect.

So by way of a parting shot, (and with due acknowledgement to John F. Kennedy, one of whose telling phrases I am about to plagiarise with only slight modification) my exhortation to you all would be this – Ask not: What can quality-of-life measurement do for me? Ask instead: What can I do for quality-of-life measurement?

THE IMPORTANCE OF ECONOMIC ANALYSIS

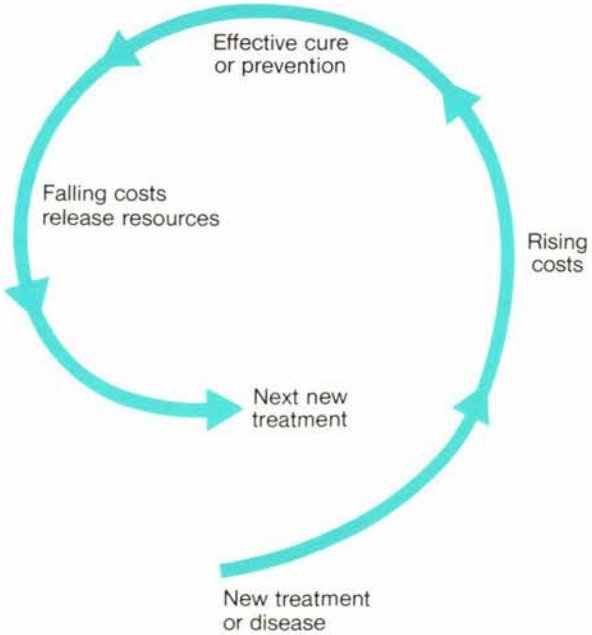
George Teeling Smith

56 THE HEALTH COST SPIRAL

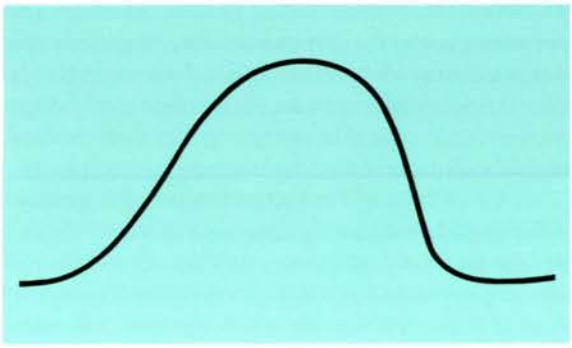
The theme of this paper can be stated in a brief paragraph. When a new disease emerges, or when a previously untreatable and rapidly fatal disease starts to respond to palliative and life-extending measures, health care costs for the disease increase. However, at the next stage, when effective curative or preventive measures are developed, its costs start to fall again and may be eliminated altogether. This does not mean that total expenditure on the health service will be reduced. As one disease is conquered, others become treatable, so that resources saved through success against one illness are released to treat another (Figure 1). And as medicine as a whole becomes increasingly sophisticated, overall costs increase. But without the savings from the development of effective medicines for 'yesterday's' diseases, it would be more difficult to treat 'tomorrow's'. That is the message of this paper: it is important to demonstrate the cost-effectiveness of past and present treatments because it is the savings which they have released which help to fund future developments in health care.

In general, the costs of ill health arise in three main ways: direct costs for the health service; lost production through premature death; and production lost through absence from work due to sickness. There are also, of course, major 'costs' to the individual and his family through suffering and disability. All of these costs can be reduced by effective treatment, but this paper concentrates mainly on the first – savings for the health services themselves. This is partly because for the disease concerned these represent real reductions in actual expenditure. It is also because health care costs are of most direct concern to health service administrators, politicians and the medical professions.

1 THE HEALTH COST SPIRAL



2 TEELING SMITH ALL-PURPOSE CURVE

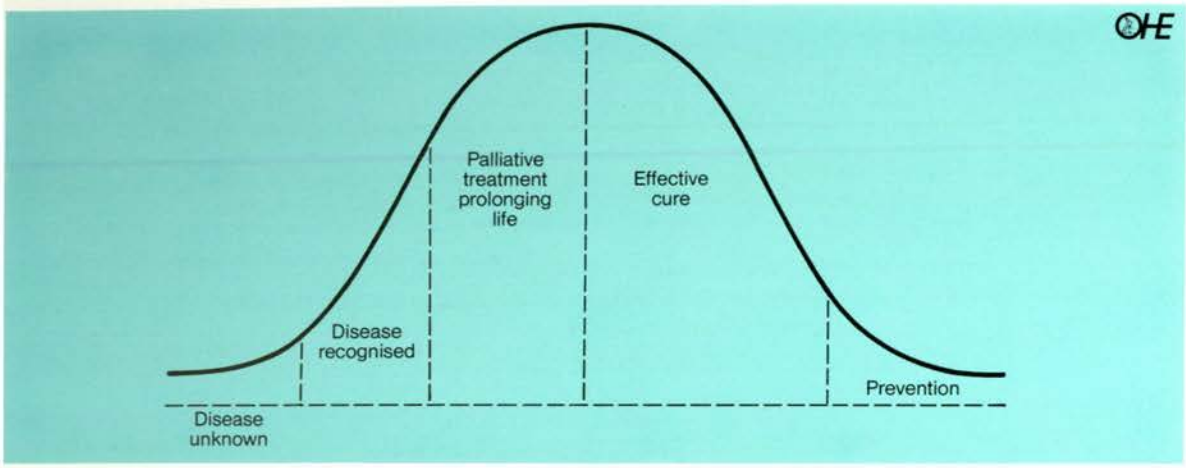


The overall theme of first rising and then falling costs over the 'lifetime' of a disease exemplifies the general theme illustrated by the 'Teeling Smith All-Purpose Curve' shown in Figure 2. The pattern of growth and decay indicated by this curve is almost universal. It applies first to all living organisms. Birth, childhood, adolescence, maturity, old age, senility and death is a natural pattern over a lifetime. It may be prematurely cut short, and individual phases may vary greatly in their length and significance, but the underlying pattern is always there.

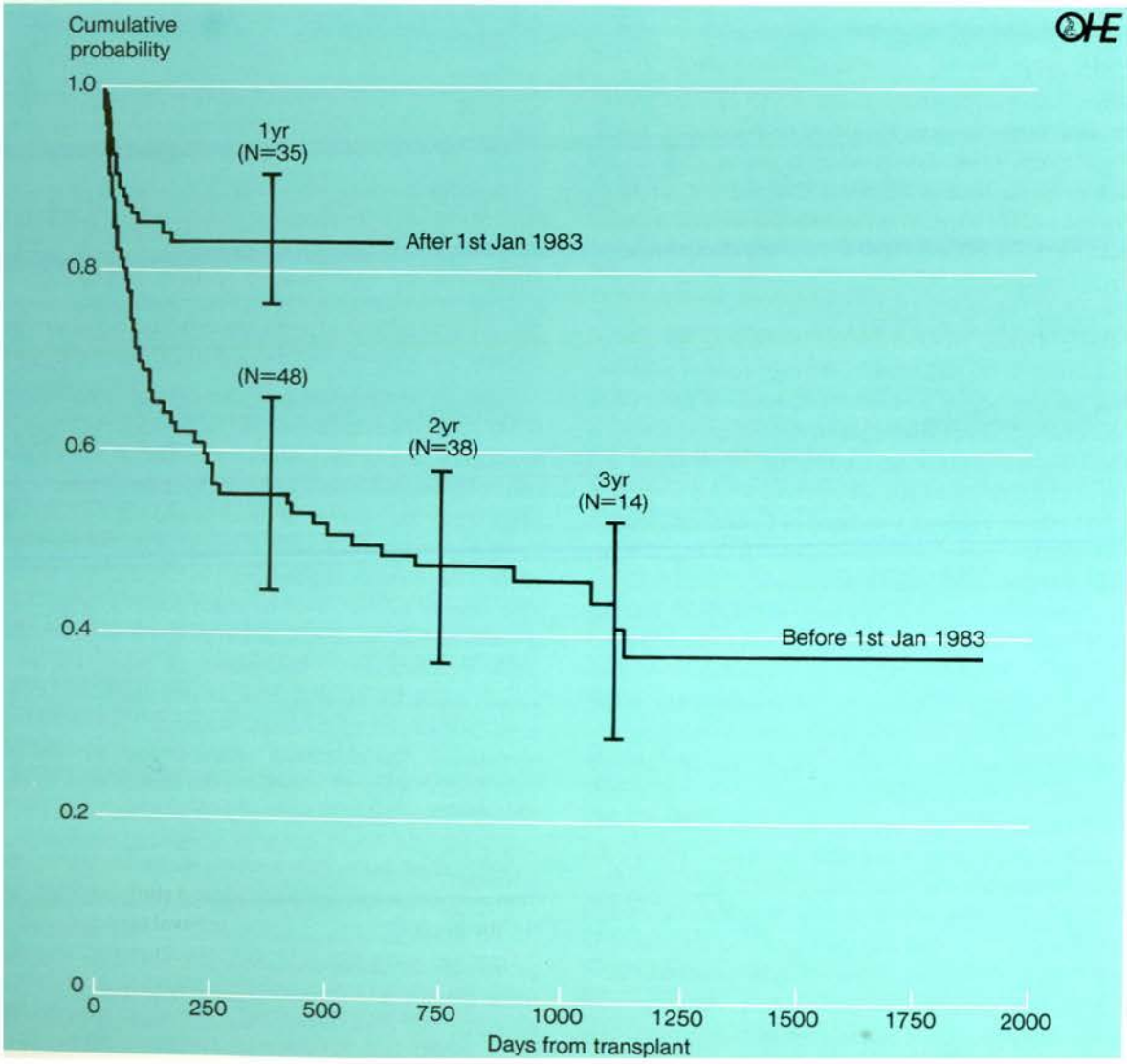
It can be argued that a very similar pattern applies to many social organisms, such as companies, whole industries, associations and even nations. In the short to medium term, most organisations display a pattern of growth, maturity and then decline. The longer-term picture is different, but that will be discussed later. The important point here is that the 'all-purpose curve' is very often typical of the pattern of costs for an individual disease. At first, costs rise and they are then reduced by effective treatment or prevention. Most often, these reductions are achieved with pharmaceutical products. This pattern is illustrated in Figure 3. The examples given in this paper will illustrate this general theme, either by showing those savings which have already been obtained, or where studies are still needed to demonstrate the economic benefits.

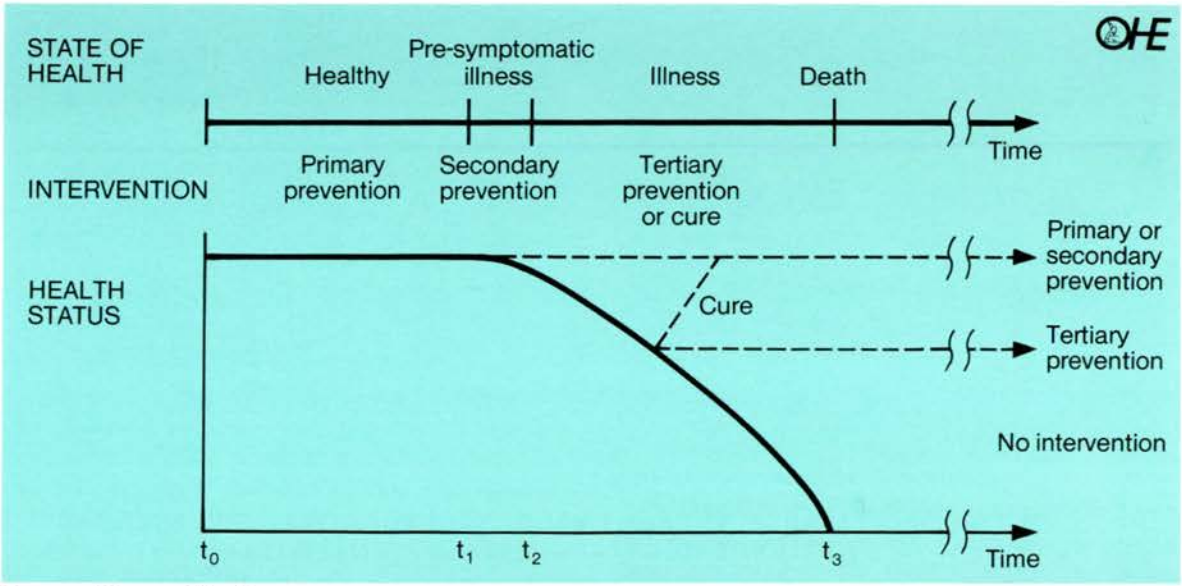
First, simply to give an example of rising costs, one can take the case of heart transplants. These were impossible, and indeed inconceivable, 30 years ago. The first transplant was performed in 1967. Now they have become an almost routine procedure provided the transplant organ is available. Figure 4 shows, in particular, the improvement in patient survival coinciding with the introduction of pharmaceutical cyclosporin to reduce graft rejection. This innovation still occurred on the rising side of the 'all-purpose curve'. A patient who died soon after surgery cost only about £10,000, but one who

3 CYCLE OF DISEASE COSTS



4 PRODUCT-LIMIT POSTTRANSPLANT SURVIVAL CURVES FOR COMBINED HAREFIELD AND PAPWORTH DATE BY TIME PERIODS (AS AT 30TH SEPTEMBER 1984).





Source: Cohen and Henderson

survives ten years costs the health service nearer £30,000, because of the costs of after-care (Buxton *et al*, 1985). Cyclosporin saves money when it allows a successful kidney graft instead of renal dialysis; but in heart transplants the alternative to successful survival is death. And for the health service death is a very cheap event.

STAGES OF PREVENTION

Returning to the basic theme, the high costs of palliative and life-prolonging medical intervention is most often reduced by preventive measures. An extreme example is the complete worldwide elimination of smallpox – a previously expensive disease which now costs nothing at all. However, Figure 5, produced by Cohen and Henderson (1988), shows that 'prevention' is a much wider concept than simply 'health promotion' or the avoidance of illness. It can occur at any stage in a disease. Primary prevention, such as immunisation, will indeed prevent the disease altogether. However, secondary prevention tackles existing disease at its pre-symptomatic stage, often preventing the symptoms from developing and avoiding damage to the body's tissues. Tertiary prevention comes into play when the disease is overt and clearly present; but it too can avoid further degeneration of the patients' vital organs. Each of these stages of prevention can reduce otherwise rising costs.

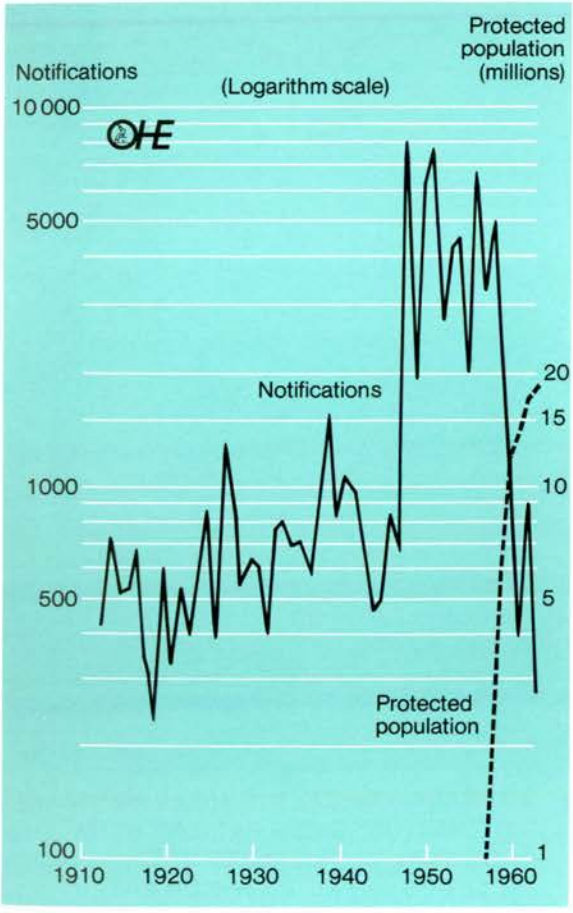
Examples of primary prevention have been the control of tuberculosis, polio, and the childhood infections. In the 1930s and 1940s, it could honestly be said that a case of tuberculosis was 'never cured'. Treatment by surgery, or long, costly periods of rest in a sanatorium, could bring about a remission, but the 'received wisdom' in my childhood was that one should never marry anyone who had had TB: it was almost certain to recur and cause an early death. Treatment was at best palliative.

The breakthrough came in the 1950s with the development of the first antitubercular compounds, and this was soon followed by an effective vaccination programme. The number of hospital beds occupied by TB patients fell from 29,000 in 1952 to just 383 in 1987. The corresponding saving in hospital costs amounted to £394 million in that year.

For polio, an early Office of Health Economics report (OHE, 1963) calculated that the UK health service would break even, setting the costs of immunisation against the costs which would otherwise have arisen for treatment, in years when the number of cases would have exceeded 3,000. Figure 6 shows a classic example of the 'all-purpose curve'. The number of polio cases in England and Wales rose steeply in the 1940s to reach 8,000 a year. The introduction of the immunisation programme in the late 1950s rapidly reduced the number of cases. The previously rising cost of the disease, and the deaths and long-term disability which it caused, were quickly reduced by vaccination. The estimated treatment costs in 1950 (at 1961 prices) were £3.4 million; the annual cost of the immunisation programme was £1.1 million. Thus there was a 200 per cent pay-off from the vaccination programme.

Examples of secondary prevention involve much more recent advances in medicines research. They include the prevention of osteoporosis through hormone replacement therapy and the consequent potential to reduce fractures; the prevention of strokes through the treatment of hypertension; the treatment of stomach ulcers to

6 POLIOMYELITIS. ANNUAL NUMBER OF CASES NOTIFIED. ENGLAND AND WALES. 1912-1962, AND TOTAL PROTECTED POPULATION (INITIAL COURSE TWO DOSES) 1957-1962.



Source: OHE 1963

prevent perforation; and the reduction of renal damage by the control of urinary tract infections.

Figure 7 shows the 'epidemic' of fractures of the neck of the femur in the 1960s and 1970s. This is the rising section of an 'all-purpose graph'. Studies are now under way to calculate the extent to which this 'epidemic' can be controlled by strengthening the bones, especially in post-menopausal women, by the use of hormone replacement therapy.

In the case of hypertension and stroke, the calculations have recently been carried out in the OHE to show the savings which have been achieved for the NHS from the reduction in the number of strokes (Teeling Smith, 1988). The number of new cases seen in general practice fell from 2.4 per 1,000 in 1951/52 to 1.75 per 1,000 in 1981/82. This represents a reduction of 7,150 cases per year. Furthermore, the number of deaths from stroke amongst the 45–64 age group was 9,240 fewer in 1985 than it would have been had there been no reduction since 1966.

Based on these figures, it is possible to estimate savings to both the health service and the economy. The total cost of stroke to the NHS for England and Wales has been estimated at £550 million in 1985 (Dale, 1988). Without the reduction between 1954/55 and 1981/82, there would have been 37 per cent more strokes in the 45–64 age group in 1982. Ignoring the further reduction to 1985, this gives a saving to the health service of £204 million on the assumption that the reduction in strokes over the age of 65 was at the same rate as for the younger group. In addition, based on reasonable assumptions about the years of working life saved among the extra survivors in the 45–64 age group for both men (retiring at 65) and women (retiring at 60), it can be calculated that an extra 49,130 years of working life will result from the reduction of stroke mortality in the year 1985, compared with 1966. At the value of average earnings in 1985, this gives a further contribution to the economy of £322 million without discounting future years' earnings. It must be emphasised that these savings are related to stroke alone.

Against these savings, there is the cost of £185 million for antihypertensive medicines for all ages. These medicines will obviously have brought many benefits apart from the reduction in strokes. However, taking the very broad cost figure of £185 million, and savings of £526 million (£322m + £204m) for stroke alone, it is clear that the hypertensive therapy is very cost-effective. The total cost of hypertension medication is more than offset by savings to the health service from stroke alone.

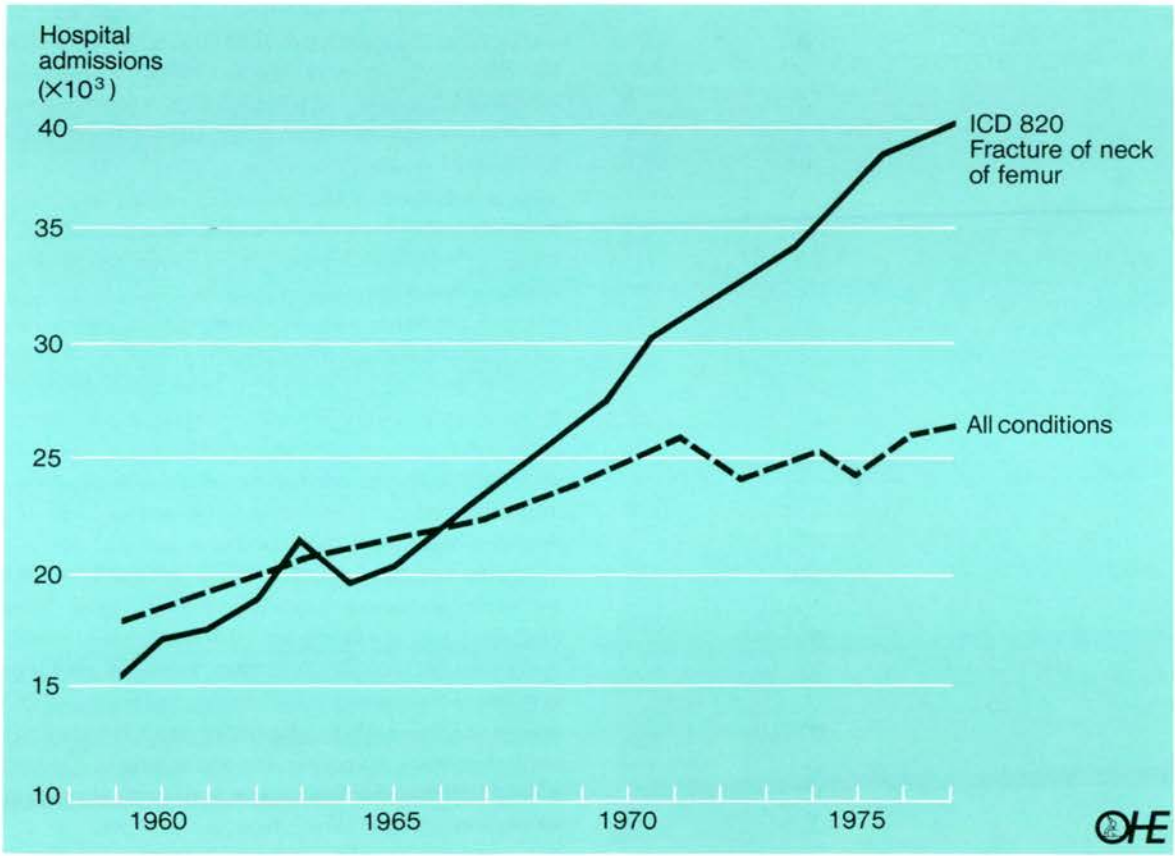
Apart from these savings for the health service and the economy, there are also benefits which can be measured in terms of what have been called 'quality-adjusted life-years' (QALYs). This is an economist's unit which calculates the number of extra years of life achieved by a successful treatment, but which discounts the value of each year by the degree of disability and distress suffered by the patient.

Figure 8 shows the 'cost per QALY' for the extra years of life achieved by different types of medical intervention. It shows that the treatment of hypertension to prevent stroke, carried out as a part of good medical 'case-finding' practice, gives very good value indeed in terms of costs per QALY (Teeling Smith, 1989). But it is interesting to note that an active screening programme to detect those with moderate to severe hypertension (diastolic above 105), as opposed to case-finding in practice, costs about 10 times as much per year of life saved (Kaplan *et al*, 1988).

A third fairly recent example of pay-off from successful pharmaceutical innovation is in the treatment of stomach ulcers with the H_2 antagonists. Figure 9 shows that in a study in the US, the cost of ulcer treatment was reduced by 70 per cent as a result of preventing the need for hospitalisation and surgery.

In the final example of the potential for 'secondary

7 ESTIMATED HOSPITAL INPATIENT ADMISSIONS (ENGLAND AND WALES) FOR FRACTURE OF NECK OF FEMUR AND ALL CONDITIONS.



Source: Lewis F. (1981)

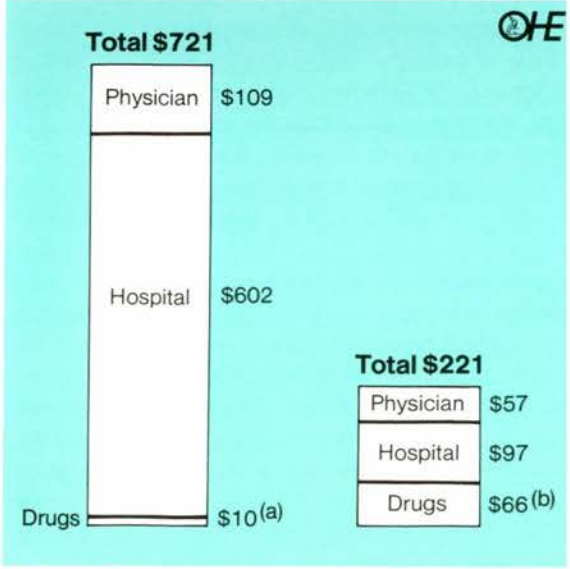
8 'LEAGUE TABLE' OF COSTS AND QALYs FOR SELECTED HEALTH CARE INTERVENTIONS (1983–84 prices)

Intervention	Present value of extra cost per QALY gained (£)
GP advise 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

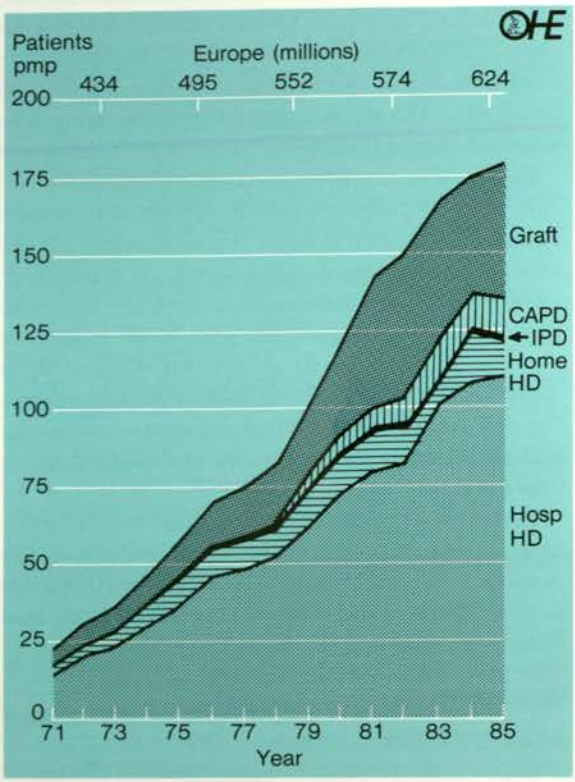
Source: Teeling Smith, 1989.

9 AVERAGE ANNUAL MICHIGAN MEDICAID EXPENDITURES PER PATIENT WITH DUODENAL ULCER. DOES NOT INCLUDES ANTACIDS WHICH ARE EXCLUDED FROM MICHIGAN MEDICAID: [b] INCLUDES COST OF CIMETIDINE THERAPY.



Source: Geweke and Weisbrod (1982)

10 NUMBER OF PATIENTS PER MILLION POPULATION (PMP) ALIVE ON A KNOWN METHOD OF RENAL REPLACEMENT THERAPY.



Source: EDTA (1988)

prevention', Figure 10 once again shows a rising sector of an 'all-purpose curve'. In this case, it is for the treatment of end-stage renal failure, by either dialysis or transplant. One cause of the renal damage which leads to kidney failure is recurrent infection of the urinary tract. Here again, studies are needed to show the way in which steady improvements in antibacterial medicines can reduce the risk of such damage.

This example leads immediately into the opportunities for tertiary prevention. Other cases of renal damage are hypertension (which has already been mentioned) and diabetes. Diabetes, of course, can also lead to blindness and to the loss of limbs through gangrene, so the scope for 'tertiary prevention' in diabetes is enormous in both financial and social terms. Figure 11 shows the estimated costs for diabetes in Sweden (Jonsson, 1983). Whereas the cost of medicines in 1978 was 128 million Swedish Kroner, the cost of treatment of complications was estimated at twice that figure – 255 million Swedish Kroner. Clearly better use of medication, reducing the incidence of complications, is once again an example of potentially cost-effective tertiary prevention.

Similarly, the control of chronic bronchitis and asthma, can have a substantial effect in reducing the incidence

11 COST OF DIABETES: SWEDEN 1978

DIRECT COSTS	MILLION (Swedish Kroner)
Medicines	128
Other 'management'	185
Complications	255
Total	568
INDIRECT COSTS	749

Source: Jonsson (1983).

of 'respiratory failure' – which is not only extremely distressing but also extremely expensive. Here again, economic studies are needed.

But it is worth, in this connection, recalling how conservative and nihilistic parts of the 'medical establishment' can be in relation to the use of medicines for secondary or tertiary prevention. In November 1954, the very influential and officially supported *Prescribers' Notes* stated categorically that Aureomycin and Terramycin were 'NOT INDICATED' for chronic chest infestions. At that time the 'received wisdom' was that the dangers of causing antibiotic resistance outweighed any benefits for bronchitic patients.

Seven years later, however, in May 1961 the same publication (then called *Prescribers' Journal*) stated that 'probably the largest consumption of tetracyclines in Britain is in patients with chronic bronchitis where the infection is often due to a mixture of bacteria. Here the tetracyclines are UNDOUBTEDLY VALUABLE' (emphasis added). This complete reversal of official advice had only been achieved because the manufacturers had had the confidence to recommend their products for use in 'tertiary prevention' in the face of persistent official opposition and criticism. That historical example still has important lessons for everyone involved in 1989.

OLD AGE

The economic – as well as the medical and social – benefits of 'preventive medication' apply especially to the growing elderly population in Western countries. Alzheimer's disease, affecting about 20 per cent of the very elderly, is one of the most obvious examples. At present, Alzheimer's patients require virtually continuous supervision, because they will wander off and endanger themselves and others if they are not kept under surveillance. There is much work being done in pharmaceutical industry laboratories to try to conquer Alzheimer's.

Osteoporosis has already been mentioned, and arthritis is another example. If preventive medication could reduce the need for hip replacements, there would be substantial savings for the health service. Depression is yet another area where further progress is needed,

although much can be done to counter the 'granny staring into an empty grate' syndrome. Once again, stroke in the elderly has already been discussed.

The extent to which the problems of the elderly need to be tackled is underlined by the continued growth of the very elderly population in Western countries. In Britain, for example, the over-85s represented 0.4 per cent of the population when the NHS was first set up in 1948. By the year 2000, it is estimated they will account for 2 per cent – a fivefold increase in the proportion. For the European Community, the numbers over the age of 60 will increase from 42.3 million in 1985 to 63 million in 2025. The high cost of health care for the elderly is illustrated by the fact that whereas in England in 1986/87, health-care expenditure for an average 16–64-year-old was £205, that for a person over 75 years of age was £1,570 (Stowe, 1989).

CONCLUSION

The conclusion from this brief review must be that economic analysis should be able to show that extra money spent on 'preventive medication' is the best way to invest in better health, particularly in the elderly.

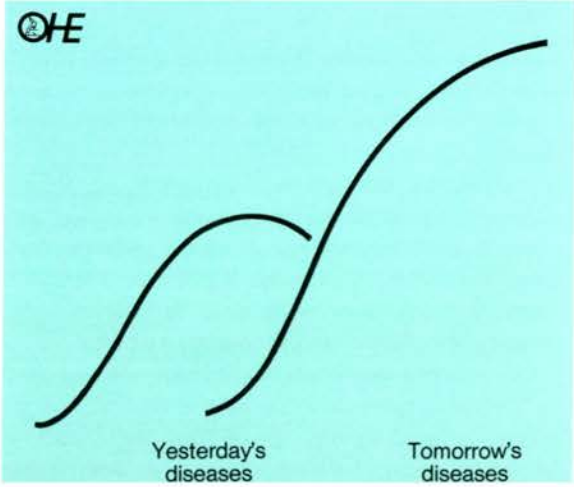
However, it must be emphasised again that the economic savings for the prevention or control of individual diseases will not reduce overall expenditure on health care. This should not be seen as a problem. It was the late Lord Vaizey who pointed out that it was illogical to worry about the 'health care explosion' when even more rapid increases in expenditure, for example on home entertainment, were seen as an 'economic triumph'. Expenditure to improve the quality of life of individuals and further to reduce premature mortality is money very well spent indeed.

Returning to the 'all-purpose curve', Figure 12 shows it in a new perspective. As medical progress brings individual diseases onto the downward part of their own particular cost curve, so new diseases will become treatable, and these other diseases will be on the upward swing of their curves. And as medicine becomes more sophisticated and as the remaining diseases become harder to tackle, the next curve will always tend to be taller than the one it replaces.

Thus, just as new living creatures emerge to replace those reaching decline and death, so new treatments will emerge as previous diseases are conquered. Health steadily improves, but always – overall – at a rising cost. As was pointed out in the introduction, the finance to fund 'tomorrow's' treatments will more readily be available when it can be shown that the control of 'yesterday's' diseases have brought substantial savings. The challenge to pharmaceutical manufacturers and their health economists is to produce the evidence to demonstrate this result.

There may perhaps still be some 'doubting Thomas's' who question the need for economic analysis of new medicines. For them, it may be useful to recall that a very creative young medical director in the pharmaceutical industry published an article in *The Lancet* in 1963 on 'The Feet of Clay of the Double Blind Trial' (Cromie, 1963). No one, surely, would question the importance of such double blind clinical trials today. In another 20 years, economic analysis, to demonstrate the financial as well as the medical and social benefits of new medicines, are likely to have become as routine as double blind clinical trials have become today.

12 THE 'ALL-PURPOSE' CURVE IN PERSPECTIVE



Buxton M, Acheson R, Caine N *et al* (1985). *Costs and Benefits of the Heart Transplant Programmes at Harefield and Papworth Hospitals*. HMSO.
Cohen D R and Henderson J B (1988). *Health, Prevention and Economics*. Oxford Medical Publications.
Cromie B W (1963). 'The Feet of Clay of the Double Blind Trial', *Lancet*, ii: 994–997.
Dale S (1988). *Stroke*. Office of Health Economics.
European Dialysis and Transplant Association (1988). Annual Report.
Geweke J and Weisbrod B A (1982). *Assessing Technological Change: the case of a new drug*. Madison, University of Michigan.
ILO (1989). *From Pyramid to Pillar*, p. 21.
Jonsson B (1983). 'Diabetes – the Cost of Illness and Cost of Control: an Estimate for Sweden (1978)', *Acta Med. Scand.* (Suppl. 671): 19–27.
Kaplan R H, Atkins C J and Wilson D K (1988). 'The Cost Utility of Diet and Exercise Interventions in Non-insulin-dependent Diabetes Mellitus', *Health Promotion*, 2, No 4 (Table 5): 337.
Lewis F (1981). 'Fracture of the Neck of the Femur Changing Incidence', *British Medical Journal*, 283: 1217–1219.
OHE (1963). *The Price of Poliomyelitis*. Office of Health Economics.
Stowe K (1987). *On Caring for National Health*. Nuffield Provincial Hospitals Trust.
Teeling Smith G (1988). 'Economics of Cardiovascular Disease'. In Sleight P (ed.), *Risk Factors and Coronary Heart Disease*. London, Mediq.
Teeling Smith G (1989). *Measurement and Management in the NHS*. Office of Health Economics.

IMPLICATIONS OF THE ECONOMIC EVALUATION OF MEDICINES

Felix Lobo

My first words are to express my gratitude to the Office of Health Economics for its very kind invitation.

I would like as well to apologise to all of you for my English being far from perfect.

SOCIAL IMPLICATIONS OF THE ECONOMIC EVALUATION OF MEDICINES

By economic evaluation of medicines I understand all kinds of analysis with the common feature that costs of treatment (including direct, indirect and intangible costs) are compared with some combination of the outputs.

I cover when I refer to 'economic evaluation': 'cost-analysis', 'cost-benefit', 'cost-effectiveness' and 'cost-utility' analysis. As this conference deals with measuring the benefits of medicines I will, of course, emphasise the last form of analysis mentioned.

The first point I would like to raise is that the political challenges involved are not acute, not pressing. Economic evaluation and measuring the benefits of medicines are rather technical questions, not controversial issues to be discussed in anger by social groups with competing interests and goals.

This is an advantage because problems that can be discussed in a calm atmosphere find their solution earlier and easier.

This is not to say that the questions analysed in this conference are, from a social point of view, totally neutral or without implications for social groups or society at large.

The task I have been given is, precisely, to identify these consequences and implications.

ECONOMIC EVALUATION OF MEDICINES AND THE RELATION BETWEEN HEALTH PROFESSIONALS, ECONOMISTS, HEALTH AUTHORITIES AND MANAGERS

Economic evaluation and particularly cost-utility analysis may foster better relations between health professionals on one side and economists, health authorities and managers on the other side.

The progress we are experiencing in cost-utility analysis will facilitate a better understanding between doctors, pharmacists, nurses and the rest of professionals responsible for the management of resources which are never unlimited.

Economics has been blamed for not being sensitive to ethics and personal well-being and for dealing only with money, costs, efficiency and economic benefits considered in a very narrow sense. Professor Allan Williams gave us, a long time ago, a wonderful lesson explaining to health professionals that it is unethical not to include economic analysis in health-related decisions.

Economic evaluation, especially cost-utility analysis, gives more ground to support Professor Williams' arguments since quality of life of the patients becomes a fundamental dimension.

Apart from this, I would like to mention two more reasons relevant to this context.

Firstly, economic evaluation makes explicit and systematic facts and arguments that would otherwise be hidden or left in confusion.

Secondly, these studies are multi-disciplinary and require direct and immediate collaboration between health and other professionals, particularly economists and accountants.

I sincerely believe that an important part of the political problems we have to face in our health systems are complicated by the cultural trap that separates health professionals and social scientists and administrators.

The analytical tools we have reviewed in this meeting launch a bridge over this trap.

This is all the more important when the tendency is towards decentralisation of decisions, more incentives and less regulation. When it is not only the central level (government, professional bodies) that matters, but a myriad of decision makers across the whole system.

THE POSITION OF PATIENTS, HEALTH PROFESSIONALS, THE PHARMACEUTICAL INDUSTRY, GOVERNMENT AND SOCIETY

Patients

It is clear that economic evaluation of medicines, particularly by means of cost-utility analysis, will be supported by patients since it implies a new interest for their well-being and quality of life.

In an ageing society emphasis on quality of life is certainly welcomed by the population.

Doctors

In health care and particularly in prescription the trend is towards greater complexity of the decision process. Nowadays doctors need the inputs provided by other professionals, and they cannot rely solely on their clinical judgement. Formularies, therapeutic substitution, review committees, indicative budgets are more and more common every day. For doctors they imply the need to rely on the judgement, opinions and information provided by other persons. Economic evaluation is certainly part of this trend, and its results may be considered as restrictions to doctors' decision making. But on the other hand, as we have seen a few minutes ago, it has an important co-operative dimension.

The pharmaceutical industry

The pharmaceutical industry has three main reasons to perform economic evaluations of medicines.

First of all, it can be an important aid in investment and marketing decisions. In my opinion it can help to avoid costly mistakes, by deciding early not to proceed with investment or marketing programmes not backed by sufficiently clear economic justification.

Secondly, economic evaluation is relevant for the industry when it has to show that medicines provide good value for money at the price actually charged. It is interesting to note that economic evaluation tends to shift the discussion about prices from production and overhead costs to the benefits for the patients.

Thirdly, economic evaluation tries to be an objective exercise where value judgements and personal opinions, however present, tend to be reduced to a minimum. This objectivity implies less uncertainties for the firm in this very sensitive area.

Governments

For governments, objectivity is important too. When prices are under public control this kind of analysis makes negotiations with pharmaceutical firms easier. It is always better for the parties involved in bargaining to discuss facts and figures than to argue on the basis of personal assumptions.

Society

It is often remembered when we come to grips with the methodological intricacies of economic evaluation that the point of view of society as a whole is not to be forgotten. I want to stress the point that government and health managers are mainly interested in the impact of therapies on their budgets and, especially in the short run, they may forget any differences that arise with their impact on society as such, especially due to the emergence of externalities.

ECONOMIC EVALUATION AND DECISION MAKING IN REGULATION

Economic evaluation and regulation

When regulatory authorities have to reach a decision about the marketing approval of a product or when deciding to finance a drug with public funds, economic evaluation may be of great interest.

But in my opinion, in the present state of affairs, it would not be wise to add economic evaluation to the regulatory process as a legal requirement. It is true that 'adding cost-effectiveness criteria to the already long and cumbersome regulatory process would likely be a problematic and controversial step' (Wilensky *et al*, 1988). The methodological problems still unsolved are another reason in support of this opinion. Regulatory authorities, on a voluntary basis, may perform economic analysis on particular occasions or, as it has been suggested, 'facilitate the collection of necessary data during clinical trials and make that information available to private groups, which would then be free to use it in their own cost-effectiveness analysis' (ibid).

Economic evaluation and price controls

The relevance of economic evaluation is not the same for all markets and products.

Where competition prevails and markets function well, efficiency is automatically guaranteed. In this case what we call economic evaluation may be redundant. The market and the price system are enough to guarantee good value for money, since we know that the price would equal marginal costs and the consumer would spend as little resources as possible in getting all the benefits of the product.

I do not see anyone caring to launch a study on the costs of QALYs gained from aspirin treatments of mild headaches.

This is very important because we expect an enlargement of the competitive segment in the pharmaceutical industry. With more and better pharmacological costs and economic information on the part of doctors; greater market share for generics; therapeutic substitution; and incentives to buy and spend economically competition is now a distinctive feature of the pharmaceutical industry – at least in some countries.

But in the case of new pharmaceutical products covered by patents and in other segments where market forces do not or cannot work, economic evaluation is likely to become more important in the process of determining prices.

If economic evaluation shows a medicine to have superior relative value compared to alternative treatments, consumers and health authorities will be willing to pay a price superior to its competitors.

If the results are the opposite, then the medicine should be priced at a lower, more competitive level.

Even when there are no alternative treatments to be compared with directly, cost-utility analysis is interesting for the purpose of determining prices, because we can use, as a reference, the cost per QALY gained in different health-care interventions, and therefore illuminate the decision process towards a higher or lower price.

In these conditions, companies can demonstrate a reasonable cost per QALY gained, and consumers and health authorities will be more willing to pay the price currently included in the calculation.

But still, in this case it would be sensible for consumers and health authorities to continue to ask if this price is commensurate with the competitive supply cost of the drug, and if it carries reasonable benefits, including the necessary rewards for R&D of drugs.

Economic evaluation and technology assessment

Due to the complexities of new medical technologies, agencies or groups specialised in the assessment of its advantages and drawbacks are being established. In the US the National Center for Health Care Technology performed this function for a few years. Now there is the Council of Health Care Technology at the Institute of Medicine.

In my opinion these kind of institutions, whether public or private but with a broad commitment to the evaluation of new health technologies, are a good setting for the economic evaluation of drugs. They can help regulatory authorities with the necessary assistance if they need this sort of analysis.

CONCLUSIONS

- Economic evaluation methods tend to integrate the different parties with an interest in health care.
- Economic evaluation methods may contribute to smooth negotiations aimed at the allocation of resources in the health system.
- Economic evaluation methods should not be made a legal requirement for regulatory decisions.
- Economic evaluation methods are not umbrellas to cover high prices, but analytical tools to arrive at pricing decisions.

REFERENCE

Wilensky, Blumberg and Neumann (1988). In Eimeren W and Horisberger B (eds.), *Socioeconomic Evaluation of Drug Therapy*, p. 35. Berlin, Springer-Verlag.