The economic perspective

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The rationale for the economic perspective on screening is presented and the particular relevance of economic evaluation highlighted. The principles of economic evaluation are described in terms of measuring and valuing the costs and outcomes associated with screening. The different types of economic evaluation are described with discussion of data sources. The problematic issues associated with time preferences and discounting and with the measurement and valuation of outcomes other than true positives are discussed. Issues associated with antenatal screening, in particular the inclusion of averted costs due to the termination of an affected pregnancy and the inclusion and valuation of the unborn child's utility, are also raised.

Rationale for the economic perspective

The principles of screening formulated by Wilson and Junger\(^1\) three decades ago are still used as a basis for reviewing the evidence for screening programmes\(^2,3\). These criteria, and other modifications of these original criteria\(^4,5\), encompass the need for economic evaluation of screening programmes in that they recognise the economic costs of the programme have to be considered in relation to the benefits of early detection. They do not, however, provide any formal structure for undertaking an assessment of the benefits and costs of introducing a screening programme. Economic principles are being increasingly applied as part of the formal evaluation of health care interventions, and methods for such assessments have been developed and refined.

Today there is widespread acceptance of the need to address the economic question, specifically whether the benefits of a proposed or existing intervention are sufficient to justify that particular use of scarce health care resources. The use of any scarce resources, be they manpower, buildings or equipment, has an opportunity cost in terms of the benefits foregone by denying those resources to other competing claims. Choices, sometimes harsh choices, have to be made in all health
care systems: none can offer patients and public all technically feasible, or even all potentially beneficial interventions.

Economics is concerned principally with allocating resources efficiently. Efficiency is not about cost cutting, but about making choices which derive the maximum total benefit from the finite resource available. In the same way as evidence-based medicine stresses the need to use the best available formal evidence on effectiveness, rather than relying simply on educated guesses or ‘gut feelings’ to make individual treatment decisions, health economics emphasises the need to assess formally the implications of choices over the deployment of resources. A number of economic evaluation techniques have been developed to aid this formal assessment and to help identify the most efficient allocation of resources.

Economic evaluation is particularly relevant to screening for a number of reasons. Firstly, screening is discretionary: the case for intervention can be made relatively dispassionately in the light of the probabilistic expectation of benefit to a proportion of those screened. Screening is not normally subject to the pressures from the social ‘rule of rescue’. Most individuals offered screening are well and it is not possible to distinguish at the outset those individuals who have the potential to benefit from treatment. In contrast, treatment of symptomatic patients offers the potential of immediate benefit to those who are identifiably ‘ill’.

Secondly, within any one screening programme a number of different strategies for screening exist. Each of these can be informed by economic evaluation. For example, choices have to be made as to the tests or screening technologies to use, the thresholds to use, and hence the specificity and sensitivity of the test, the frequency of screening, age at screening, and whether the screening test should be used universally or selectively in a group identified on the basis of known risk factors.

Thirdly, formal screening programmes require substantial investment and infrastructures. Decisions about screening programmes tend to be made, in the UK at least, at national, or regional level, rather than at the level of the individual practitioner. As a result, a number of examples of economic evaluation being undertaken to support policy decisions relate to screening. For example, decisions about whether to introduce breast screening in a number of European countries have been informed and influenced by analyses of its likely cost-effectiveness. In the UK National Health Service Breast Screening Programme, the number of mammography views taken at a woman's prevalent screen have been influenced by the findings of economic analyses. Indeed, one of the earliest examples in the UK was the decision to abandon the routine use of mass-miniature radiography screening for tuberculosis, a decision supported by an economic analysis showing that screening was no longer cost-effective with changes in prevalence and improved therapy.
Economic evaluation can contribute to decisions about whether a new screening programme for a particular disease or disorder should be introduced, and can also aid decisions about changes to existing programmes. It should be recognised, however, that economic evaluation is a way of structuring, measuring and valuing the expected consequences of alternative courses of action. It is an aid to decision making, but criteria other than efficiency will also be relevant when making value judgements as to whether or not to provide a particular screening programme. In particular, issues of equity, which are not formally addressed in most economic analyses, may have an important impact on decisions.

Principles underlying the economic evaluation of screening programmes

Economic analysis is concerned with systematically comparing both the resource use consequences (or costs) and non-resource use consequences (or outcomes) of alternative courses of action. These may be alternative screening strategies, a comparison of formal screening with the current policy, or, where no current screening policy exists, with the status quo or 'no screening' scenario. The precise methods used to identify, measure and value costs and outcomes will depend on the specific screening context, the particular economic question being posed, and the form of analysis adopted to answer that question. A number of broad principles exist that govern the way costs and outcomes are usually handled, and these are set out in detail in a number of texts and guidance manuals.

The following sections highlight some key issues in the measurement and valuation of costs and health outcomes which are important in understanding the application of economic evaluation to screening.

Measuring and valuing the costs

The resource costs relevant to an economic evaluation are those incurred and those avoided as a result of undertaking a particular programme. The perspective adopted in a particular study will determine how widely the net of costs is cast. Typically economic evaluation studies adopt a broad societal perspective, and aim to estimate all important costs no matter on which bodies or individuals they fall. This is particularly important when examining the resource consequences of a screening programme, since the burden of resource provision and the benefit of resource savings may fall on sectors of society other than the health service, such as social, educational or voluntary services.
Whatever the perspective adopted, direct costs associated with organising and operating a screening programme, such as the labour involved and the equipment and facilities, need to be estimated. While the cost per individual screened may be relatively small, the total cost of the programme may be substantial. In the case of a cervical screening programme, for example, this would include the costs associated with recruiting women to the programme; taking, transporting and reading the smears; the costs associated with informing women of the results and, for the suspected cases detected (the screen positives) the costs of further confirmatory diagnosis and treatment. In part these costs may be offset by the savings in health service costs associated with a reduced number of patients requiring diagnosis and radical treatment at a later date.

One argument often given in favour of screening is the expectation of cost savings associated with reducing the amount of treatment of advanced diseases. In the case of breast screening, for example, it was estimated in a Dutch study that 47% of the costs of screening would be offset by cost savings in the treatment of advanced disease\textsuperscript{17}. Others have been much more conservative in their estimate\textsuperscript{18}, the differences being due to different treatment patterns. The potential savings to the health service due to the reduction in advanced disease and mortality, as a result of a mass cervical screening programme was found to be relatively small compared to the total cost of the screening programme, offsetting 10% of the costs of screening plus the incremental cost of diagnosis and treatment of primary disease\textsuperscript{19}.

Screening also imposes resource costs directly on the individuals concerned. Individuals are likely, for example, to incur out-of-pocket expenses on travel and other costs (for example, child care) when they, or a member of their family, attend for screening. Individuals will also incur indirect costs in terms of the value of their time devoted to attending for screening; they may forgo productive time at work or forgo time pursuing leisure activities or doing household tasks\textsuperscript{20-23}. A recent study showed that the costs incurred by the individuals\textsuperscript{2} attending for breast screening or for further assessment following screening were of similar magnitude to those incurred by the health service\textsuperscript{23,24}. Costs incurred by individuals are likely to have an important effects on behaviour, particularly attendance rates need to be considered carefully, if only to begin to understand and to be able to influence take-up of screening services\textsuperscript{25}.

If a broad societal perspective is adopted these private costs should be included in the costs of screening. Direct valuation of these costs using earnings as a measure of the opportunity cost of the time spent being screened is controversial and raises important distributional issues\textsuperscript{12}. For example, with this approach the time lost by an active male in the work force would be valued more highly than time lost by the elderly. Less
controversial in a societal costing are the differences in ‘care’ costs falling on services other than health, for example social services or education, as a result of the reduction in disability brought about by screening.

In measuring costs, it is important to focus on the difference in costs between the options under consideration. Thus, if the policy question is whether or not to increase the frequency of screening, the costs identified should be the net additional cost of the greater frequency compared with the lesser frequency. The principle underlying costing for economic studies is to identify and measure resource use, by estimating the quantities of the resource inputs that are used in the intervention, such as the hours of particular types of manpower, use of specific equipment, types and quantities of drugs, other consumables, and applying appropriate unit costs to these units of resource. Resource use is usually valued using market prices, but adjustments may be necessary, for example, where resources are subsidised by a third party. Some unit costs will be readily available from published sources and others will need to be estimated in the context of a specific study.

In some situations, this cost calculation will be complicated by the existence of spare capacity. For example, if a local mammography service was operating below capacity, the incremental cost of screening a small additional cohort is likely to be less than the existing average cost per screen, since the current average costs will already include the costs of some specialised equipment and staff which may not need to be increased to accommodate a small increase in the number screened. Estimated costs need to reflect a particular context and question, and may well differ significantly between screening centres.

**Measuring and valuing outcomes**

Economics is not simply about costs, but about the relationship between costs and outcomes. The identification and measurement of non-cost consequences is usually the conceptually most challenging issue. Screening programmes have a number of health and non-health related effects depending on whether the result of the screen is positive or negative and whether this result is true or false.

Typically, economic studies have focused on the outcomes associated with true positive findings. The major change in outcomes associated with screening will be experienced by this group. While the identification of a true positive case can be used as a measure of screening outcome, the value of this approach will depend upon the impact of early detection or diagnosis of the condition on future life...
expectancy and/or quality of life. For most screening situations, true positive results will bring forward the time of detection and allow earlier treatment. In the case of non life-threatening conditions, such as hearing loss in childhood, earlier treatment is associated with improved future quality of life. In the case of screening programmes for conditions which are life threatening, such as cancer, or abdominal aortic aneurysms, the main outcome would be reduced mortality, although quality of life may also be affected. In both situations, improvements in quality of life are experienced mainly by the individuals concerned, but may also have implications for the quality of life of immediate family and close friends. Economic evaluation requires evidence that screening is effective in identifying true positive cases, as well as evidence that earlier diagnosis and treatment results in better long-term outcome.

However, there are likely to be other health outcomes from a screening programme. False negative screening results may not simply fail to bring forward detection, but may provide false reassurance, thereby delaying subsequent clinical diagnosis. Thus, for some individuals, there may be a measurable reduction in survival and quality of life that needs to be set against the gains experienced by individuals who are true positives.

The most immediate and widespread impact of screening may be in terms of anxiety and or reassurance. A positive screening result will inevitably be received with negative feelings, whereas a negative result is usually reassuring. However, anxiety may be experienced as a result of receiving an invitation for screening, attending the screen and the follow-up examination. This anxiety may be short-lived if the results are negative, but may remains for several months, or in some cases years, after a false positive result. Anxiety may also be experienced by non-attenders. In adults, most of these anxieties will be experienced by the individual being screened, although they may have implications for family and friends. In addition, there may be some pain or discomfort directly associated with the test or screen, and there may be small, but potentially important, risks associated with screening, for example from a radiation dose.

Information gained from a screening test may be valued even where it does not affect prognosis or subsequent treatment. For example, parents may value the information regarding the risk to their fetus of a specific disorder, even though they have no intention of terminating the pregnancy.

Thus, a number of health states are likely to be experienced by the target population of a screening programme and, in some cases, their families. Moreover, different individuals will not necessarily experience the same health state. How such outcomes of a health care programme are measured and valued in an economic evaluation will depend on the technique used.
Methods of economic evaluation

Economic evaluations are generally categorised into four main types: cost-minimisation; cost-effectiveness analysis; cost-benefit analysis; and cost-utility analysis. Each technique, or form of analysis handles costs in the same manner: resource use is identified, measured and then valued in monetary terms. The techniques differ, however, in how they measure and value the non-resource use consequences of alternative actions. Equally important is the nature and source of the evidence available on which to base these analyses. There is often a tension between the clinical science pressures to use only evidence directly obtained from clinical trials and the economist's need to model a broader picture of the consequences of interventions than such trials typically provide.

Forms of economic analysis

Cost-minimisation analysis is the simplest form. It is relevant only when there is good evidence, usually from previously published studies, to indicate that the outcomes of the alternatives being evaluated are the same in all important respects. This might be the case in comparing two different tests with identical sensitivity and specificity or alternative logistic arrangements for running a screening service. In such restricted circumstances, it is only necessary to compare the resource use, and hence costs, of the alternatives. It then makes obvious economic sense to implement the least costly alternative. In most circumstances, however, the outcomes will differ in some way and then a technique that can consider differences in both costs and outcomes is required.

Cost-benefit analysis is, in principle, the most comprehensive technique available. The criterion of efficiency is based upon a comparison of the value placed on the outcome of implementing a new programme, or changes to an existing programme, with that placed on the resource use implications. Thus, an efficient programme is one whereby the value placed on the outcome exceeds the value of the resource consumed. Where there are multiple alternatives under comparison, the implication is that priority should be given to the one with the greatest net value. This technique requires that the outcomes of a programme (for example, improvements in quality of life and survival gains) are valued in the same unit of account as resources, i.e. in monetary units. Methods to obtain monetary outcome values exist, such as 'willingness to pay' and these have been used, for example in the context of antenatal screening for cystic fibrosis, but are generally considered experimental. Thus, despite the common use of the term cost-benefit analysis, in practice true cost benefit studies are rarely
undertaken to evaluate health care programmes because of the practical
difficulty and the social dislike of putting monetary values on life and
suffering.

Cost-effectiveness analysis attempts to avoid this problem by defining
the outcome or ‘effectiveness’ of a health care programme in terms of
natural units. Ideally the outcome measure should be all embracing, and
must at least capture the main objective of the programme. No attempt
is made to value this outcome. In assessing screening programmes,
process measures such as the proportion of cases detected are often used
as the measure of effectiveness. In the case of antenatal screening,
reproductive choice over the outcome of an affected pregnancy could be
seen as an appropriate measure of effectiveness.

It obviously makes economic sense to implement the programme
which costs less and is at least as effective as the alternative, or which
costs the same but is more effective than the alternative. These so-called
situations of dominance are, however, relatively rare. What is more
usual is for one alternative to cost more but also to be somewhat more
effective. The additional costs and effects of a programme are then
presented in terms of an incremental cost-effectiveness ratio, such as the
additional cost per additional case detected. This raises the question as
to what is an acceptable incremental cost-effectiveness ratio. An
indication of what has been acceptable historically is useful but a value
judgement has to be made as to what a decision-maker or society as
whole is willing to pay for an additional unit of effect.

Cost-effectiveness analysis can be useful for determining technical
efficiency, i.e. the most efficient way of delivering a particular
programme, such as which test to use in a screening programme. It may
also be useful for comparing alternative programmes whose effects can
be measured in the same units. However, it is more limited than cost-
benefit analysis since comparison cannot be made across health care
programmes where different outcome measures are used. Moreover it is
unlikely that all the important outcomes are captured by a uni-
dimensional measure of effectiveness.

Cost-utility analysis attempts to provide a broader comparability
between different programmes than cost-effectiveness analysis by
measuring the health effects of all programmes in a generic unit.
Effectively, it is a special case of cost-effectiveness analysis whereby a
programme’s effects are measured in terms of utility. Utility reflects the
preferences of individuals or society and, in the context of health care
appraisal, refers to the relative value placed on a specific health status or
an improvement in health status. The most common measure of utility
used in such analyses is the quality adjusted life year or QALY. It
incorporates both the programme’s impact on survival as well as health
related quality of life. The quality of life associated with a health state is
measured on a scale of zero to one, where death is assigned a value of zero and full health is assigned a value of one. A number of techniques exist to elicit utility values for specific health states. These techniques include the time trade-off and standard gamble. The duration of each health state is then weighted, or multiplied, by its utility value. Where options lead to a series of health states, the weighted durations are summed to give the number of quality adjusted life years.

Where outcomes are multi-dimensional, as in the case of screening, QALYs may be more useful than uni-dimensional natural units used in cost-effectiveness analysis. As with cost-effectiveness analysis, it obviously makes economic sense to implement the programme which costs less and is at least as effective as the alternative, or which costs the same but is more effective. Where this is not the case, the additional costs and effects of a programme are then presented in terms of an incremental cost-utility ratio, such as the additional cost per QALY gained. Again this raises the question as to what is an acceptable incremental cost-utility ratio.

Cost-utility analysis is useful for addressing the most efficient way of providing a particular programme, that is technical efficiency. More controversially, QALYs can also be used to help judge relative priorities across different health care programmes. Programmes can be ranked according to their incremental (additional) cost per QALY gained and, in the context of a fixed budget for health care, those programmes offering additional QALYs at lowest additional cost per QALY should be given priority. In the UK, for example, the additional cost per QALY for breast screening, as recommended by the Forrest report, was estimated to be £3309. This was compared with the cost per QALY gained for various other health care procedures and found to fall somewhere between the cost per QALY for kidney transplant and heart transplant. It was argued that the cost per QALY gained for breast screening was not dissimilar from other health service activities undertaken at the time.

One of the main implications of these so-called 'QALY league tables' is that as the only output of the health service is health, health outcomes are the only outcomes arising from the resource use considered in these tables. This means that resource use from outside the health budget and non health outcomes, such as the productivity gains referred to earlier, are difficult to incorporate into such tables. Reservations have also been expressed with regards to the quality of data used in such studies and the difficulties of comparing studies undertaken in different years. Analysts have also been criticised for not providing an adequate account of the incremental analysis undertaken. In addition, individual cost-utility studies are often locally specific as the appropriate comparator for the decision making context may differ between localities. It may
also be inappropriate to transfer results to another area if, for example, the incidence and prevalence of the disease or level of service differs between two areas. Caution has to be exercised when using such tables. It should, nonetheless, be recognised that resource allocation does take place and that QALYs can be used to aid such decisions, but they should be viewed as being indicative rather than determinate.

Furthermore, it is not possible to conduct a cost-utility analysis if data on the effectiveness of final outcomes are not available and it is unnecessary if the programmes under comparison are all equally effective, or quality of life can be captured in easily understood natural units, or the results cannot be altered by the use of utility values.

Sources of data: trials and modelling

Economic evaluation requires good evidence on outcomes, and is often limited by the lack of evidence on clinical outcomes. For example, it is not possible to conclude whether or not screening for prostate cancer is cost-effective because there is a lack of data on the effectiveness of available screening tests and treatment options for the early detected cancers. The decision not to recommend prostate cancer screening at the present time in the UK is based on lack of proven effectiveness, rather than on cost considerations.

Ideally, the evidence on effectiveness of screening should come from population-based prospective randomised controlled trials. Such trials would ideally be long-term to trace the survival and quality of life effects of earlier detection. This implies that they need to be large, if differences in mortality are to be estimated with reasonable confidence. Ideally, economic and psychological evaluations are incorporated into the trial design, so allowing relevant data to be collected on the outcomes and resource use from individuals participating in the trial. This is the case in a UK randomised trial investigating the effectiveness of undertaking ultrasound screening of 65 year old men to identify asymptomatic abdominal aortic aneurysms. This trial, involving 66,000 men who are being followed for 5 years, will cost approximately £4.5 million.

Possibilities for setting up such trials are infrequent, not least because of the costs entailed. For some situations, the length of follow-up required may need to be even greater, and the sample size even larger, than that cited above. Where a clinical trial is not feasible, or it is not practical to incorporate an economic evaluation into a clinical trial, available data can be synthesised using modelling techniques. In such circumstances it is likely that estimates of costs and outcomes will be subject to greater uncertainty than where data comes directly from an
appropriate trial in a relevant population. Sensitivity analysis can be used to establish whether the results are sensitive to uncertainty or variation in the values of key parameters, and to assess the potential significance of parameters for which no reliable estimates are available.

Even when economic evaluation has been incorporated in a clinical trial, some modelling is likely to be necessary to allow for differences between the trial participants and the target population, to extrapolate from short-term outcomes to long-term survival and quality of life, or to estimate QALYs using a combination of within trial classification of health states and externally generated utility values. Modelling studies undertaken before a clinical trial is initiated can help identify the key parameters that need to be estimated within the planned trial. They can also ensure that there is a reasonable prospect that the screening programme in question will prove cost-effective, and hence be of policy interest, and can help to show the likely value of undertaking the planned research study.

**Problematic issues for the economic evaluation of screening**

**Dealing with time preferences and discounting**

Economic evaluation takes into account the timing of costs and outcomes. This is because both as individuals and collectively as a society we are not indifferent to when costs or benefits arise. We exhibit a degree of 'positive time preference'. That is to say that individuals and society prefer resources now rather than later and would prefer to postpone costs. This time preference is evidenced by the existence of real interest rates (after allowing for inflation) paid on money saved. This is allowed for in economic evaluation by 'discounting' future costs to estimate their 'present value' to us now. The rate of discount will vary between societies and over time. Currently in the UK, the Treasury recommends a rate of 6% per annum for discounting cost of public sector projects, and internationally a rate of 5% is common. What is less clear is the degree of time preference that relates to health benefits, measured for example as years of life or QALYs gained. Evidence suggests that both individuals and societies exhibit time preference for such benefits, preferring them sooner rather than later, but the degree of preference that should be reflected in economic evaluation is still controversial. Traditionally the argument has been to discount benefits at the same rate as costs, but in the light of recent debate the Department of Health now recommends that life years and QALYs should be discounted at 1.5–2%.
The discount rate for costs and benefits is of great significance for screening, where invariably the costs will occur before the outcomes, and where sometimes the benefits may only arise after several decades. For example, in a Dutch study, the total number of life years gained from cervical screening was estimated to be 68,300 without discounting. After discounting at a rate of 7%, the number of life years gained was reduced to 7,900, 12% of the undiscounted life years gained. On the other hand, the total additional costs amounted to 510 million Dutch Florins (DFL) before discounting and were reduced 277 million DFL after discounting at a rate of 7%, amounting to 54% of the undiscounted costs. The higher the rate of discount applied to benefits the less attractive screening will appear, particularly when compared with those treatment interventions that give immediate benefits. This means that when evaluating screening, analysts should use sensitivity analysis to examine the impact of different and differential discount rates. Similarly, those considering economic evidence should check carefully the discount rates applied in individual studies.

**Valuing outcomes other than true positives**

While there may be health outcomes and other non-cost consequences associated with the offer of screening, economic evaluations, in common with most clinical studies, have tended to focus on the main health effects for true positives. Many cost-effectiveness studies simply measure cost per case detected, while those that estimate mortality and quality of life often do so only for the detected cases. This may be an adequate approximation if other effects are very small. While anxieties and other effects associated with the invitation and screening test may be short lived, they may affect a large number of individuals and this could have significant implications for the cost-effectiveness of a screening programme. Potentially economic evaluation in terms of QALYs provides a metric in which the balance of these various effects can be judged.

The problem is that in practice our measurement instruments for utility are generally not sufficiently refined to be sure that we can reliably measure the small but real degree of disutility associated with temporary increases in anxiety that may be associated with many programmes. Some research has been undertaken to explore the use of willingness to pay and conjoint analysis to measure the relative values respondents place on aspects of services other than health effects, such as the informational value, but these approaches are still essentially in development.

However, as there is increasing debate about the limitations of screening programmes and more reservations are expressed about their
possible harmful effects\textsuperscript{27,29}, the omission of an estimate of these effects in most economic studies will become less acceptable. The issue should have a priority in any research agenda concerned with making economic evaluation more relevant to the policy questions relating to screening.

\textbf{The particular case of antenatal screening}

The cost implications of screening pregnant women for conditions which might affect their fetus are generally more complex than for programmes which screen individuals for conditions which might only affect those individuals. Antenatal screening raises the issue of saved resources, or averted costs, associated with the termination of affected pregnancies. Had the affected pregnancy not been detected through screening and terminated, costs would have been incurred throughout the affected child’s lifetime to treat the condition for which it was screened. These are costs over and above the cost of a ‘replacement’ child without the condition\textsuperscript{59}. If a health service perspective is adopted, the excess costs avoided can be considered equivalent to the health service costs of treating the condition which would otherwise have been detected clinically at a later stage. When comparing the costs of a universal antenatal screening programme with a selective antenatal programme, averted costs are only associated with those additional affected pregnancies identified and terminated as a consequence of the universal screening programme. These additional affected pregnancies, and the costs associated with them, would otherwise have been missed by a selective programme. When comparing a universal or selective antenatal screening programme with a policy of no screening, all terminated pregnancies are associated with an averted cost since the affected children would otherwise all have been detected at a later stage.

Analysts often feel morally uncomfortable about including the resource savings due to terminating a life. These averted cost are thus often excluded without explanation, or with an explanation which may be confused. For example, in a study looking at the cost-effectiveness of antenatal screening for Down syndrome, the savings associated with lifetime care were excluded on the basis that the objective of screening was not to save the costs of care, but to give couples the opportunity of choosing not to have a child with a severe abnormality\textsuperscript{60}. The savings associated with lifetime care are, however, nothing to do with the outcome or non-resource use consequences of the programme, but part of the resource or cost implications.

Saved or averted costs can also be associated with those affected pregnancies which are detected early by antenatal screening but are not
terminated. Here the saved or averted costs relate to cost reductions due to improved prognosis achieved as a result of the early detection of an affected newborn, i.e. the difference in cost between treating an early and late detected case.

Not all conditions, however, will be associated with averted costs due to the improved prognosis of an early detected affected case. The treatment for thalassaemia, for example, is not altered through early detection. In addition, for some conditions it might be that early detected cases actually cost more because the individual survives longer.

When the resource use implications for other sectors of society are considered the issue becomes more complicated: for example, the avoided excess costs associated with educational and institutional care, would need to be considered, as well as the costs of voluntary services and care incurred by the family. Furthermore, the implementation of antenatal screening may affect family size by dissuading couples from having further children, in which case, it could be argued that the cost of caring for these children is saved. Alternatively, it may actually encourage the conception and birth of unaffected children who would otherwise not have been born, as a result of the clearer indication of risk given to couples, as well as the opportunity to terminate an affected fetus.

Some analyses have considered outcome only in terms of the number of affected pregnancies and resource use only up to the detection of those affected pregnancies\(^{51,62}\). Whilst, arguably, this approach handles outcomes and resource use symmetrically, it provides neither an adequate measure of the true effect (what happens as a result of the identification of affected pregnancies) nor the full resource implications of instituting a programme of screening.

As discussed earlier, the use of the proportion of cases detected through screening as a measure of outcome is limited in as much as it does not capture all the important outcomes. This is particularly true in the case of antenatal screening, where a number of individuals are likely to be affected by screening. Antenatal screening has implications for the existing family, as well as for the future life of an affected fetus. Although this raises practical difficulties, particularly in whether and how to include the utilities of the unborn child, in theory these would be best captured in a cost-utility analysis where the QALYs associated with the different individuals are summed and the lifetime costs averted considered\(^{59}\).

Thus, although economic evaluation is particularly relevant to screening, it raises several important and challenging issues which are mainly related to outcome measurement and valuation and where further research is needed. Even where such problems exist, explicit and well presented economic analysis can help to illuminate the difficult policy decisions that have to be made.
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