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# Can Economics be applied to Prenatal Screening?

by Nicholas Phin

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## Abstract

This paper is a review of the economics of prenatal screening as seen from a medical point of view. The difficulties and controversies over the economic analysis are examined with specific reference to screening for Down Syndrome. The aims and principles of prenatal screening are set out and discussed before reviewing the attempts that have been made to assess the costs and benefits of screening for Down Syndrome. The major problem identified is the measurement and valuation of benefits. This makes it difficult to use cost benefit or cost utility analysis and, therefore, to say whether or not prenatal screening is worthwhile per se. Given a general social acceptance to screen for Down Syndrome, the most useful economic appraisal would be cost-effectiveness analysis of the most efficient methods of carrying out the procedure.

## Can Economics be applied to prenatal screening?

### Introduction

Economists and others argue that economic analysis is needed in health care to help society to spend its limited money to best effect. To make such an analysis one must choose the most appropriate method and work out the costs and benefits of competing health care programmes. This is not a new concept and is one of the 10 principles of screening advocated by Wilson and Jugner for the World Health Organisation in 1968.

New techniques and diagnostic methods are appearing at an ever increasing rate, prenatal screening is no exception and so we are forced to choose which prenatal screening programmes to introduce or develop. An economist might ask, "Is prenatal screening worth doing and how does it compare with competing health programmes?"

There are particular difficulties and controversies with the economic analysis of prenatal screening. Some stem from misunderstanding over what screening is or from confusion about its aims and objectives. The unique problem is that often the only "treatment" available if an affected fetus is detected is termination of the pregnancy. As two individuals are affected, termination of the pregnancy may be an acceptable treatment for

one but, in the view of some people, should not be inflicted on the other.

What are the costs and benefits of prenatal screening? Who benefits from prenatal screening, and in what way? How are these to be quantified? Which costs and benefits should be considered?

I will begin by discussing the terms "screening" and "prenatal screening" as they have been used in different ways by various authors, and then use Down syndrome, for which there are clearly defined tests and procedures, as a typical example. I will then discuss the various economic methods available, again using Down syndrome as an example, and suggest an appropriate method of economic analysis.

**What is screening?**

Screening is the identification of a group within a population who may have or be likely to develop a specific condition, by recording the presence of a known risk factor or of an altered physiological variable (for instance, serum cholesterol). Screening can also be used loosely to mean visualising on a screen by, for example ultrasonography.

Screening permits those "at risk" to be offered a definitive diagnostic test. If the diagnosis is confirmed, treatment can

be offered at an early enough stage for it to be most effective and least harmful. Those "not at risk" can be reassured that they do not need the definitive test, which may be both too hazardous and expensive to be offered to everybody.

#### **What is prenatal screening?**

Prenatal screening is any method of assessing a pregnant woman's risk of carrying a fetus affected by a particular condition. The screening test is not usually diagnostic, but merely picks out those women who should be offered a definitive diagnostic test. Prenatal screening, therefore, establishes the risk, and prenatal diagnosis establishes the diagnosis. This distinction has not always been made but is clearly spelt out in a report of the Royal College of Physicians (RCP 1989).

Screening may fail to show the abnormality being sought or it may show some other condition, or it may show no abnormality. In the first two eventualities it may be possible to treat the fetus in utero or during the neonatal period. In most conditions, however, termination of the pregnancy is all that can be offered.

#### **What are the aims of prenatal screening?**

Before any programme can be assessed its aims and objectives must be specified. One objective of screening which is seldom stated openly is the "survival of the fittest". This implies



that detecting and terminating an affected fetus benefits society by removing the need to care for it and by eradicating unhealthy traits from the population. This motivated much research into heredity but is now largely discredited. It is, however, still implicit in much of the economic analysis of prenatal screening (Hagard and Carter 1976, Glass 1975, Henderson 1982).

This argument may be reinforced by claims that prenatal diagnosis leads to fewer births with certain congenital defects. The results may seem to bear this out but are really only the net outcome of individual decisions rather than a conscious policy.

The primary aim is more aptly described as the identification of pregnancies at risk of producing an affected child, enabling parents at low risk to be reassured and parents at increased risk to seek prenatal diagnosis (RCP 1989). If the diagnosis is confirmed the parents have the option of continuing with the pregnancy or of terminating it. There should be no question of pressurising parents to opt for termination.

Screening and prenatal diagnosis are not always offered to women even though they are available and technically feasible. Some doctors feel that women should be grateful for any child. Some will only offer screening provided that women consent beforehand to termination if the fetus is affected, their

rationale being that screening becomes uneconomic if the possibility of termination is foreclosed. More often doctors may have too little organisation and initiative to screen other than haphazardly. Informal "economic" decisions made by doctors and nurses may therefore pre-empt the plans of both pregnant women and the NHS.

### **Why screen?**

Prenatal diagnosis is usually achieved by biochemical or cytological analysis of the fluid around the developing fetus. A needle is guided by ultrasonography into the abdomen to withdraw a sample of fluid. This procedure, called amniocentesis, is uncomfortable, time-consuming, and can provoke miscarriages in between 0.3 and 1.5% of women tested (MRC working party 1978, Tabor 1988). The risk of miscarriage precludes its use for all pregnancies, therefore some screening procedure is needed to identify those at risk of having an affected child.

To illustrate the issues Down syndrome is used as an example.

### **Down syndrome**

Down syndrome results from a chromosomal abnormality, trisomy 21. Although it is associated with advancing maternal age and maternal exposure to radiation the cause is unknown. The syndrome is characterised by mental retardation, and the classic "Mongoloid" faces. There are commonly heart and other

defects. Most cases require some form of special care throughout their life. As a result of improved treatment and care about 90% of children with Down syndrome survive early childhood and many survive into middle age, thus increasing the burden of care (Bell et al 1987).

### **Prenatal screening for Down syndrome**

A woman's risk of carrying a child with Down syndrome may be predicted from her age, and her serum alpha-fetoprotein, unconjugated oestriol, and human chorionic gonadotrophin concentrations, either separately or in combination. Amniocentesis is generally offered if this risk is 1/200 or more - which equals the risk of miscarrying after amniocentesis. This assumes that detecting a fetus with Down syndrome at the cost of losing one unaffected fetus are equivalent. The risk of miscarriage decreases, however, with the experience of the operator (MRC working party 1978, Leschot et al 1983). Only one unaffected fetus in over 1000 amniocenteses was aborted in Leeds (unpublished obs). It is interesting that although this risk has declined the threshold of 1/200 has not been reassessed, and this link between the risk of miscarriage after amniocentesis and the risk of having an affected child is lost.

The incidence of Down syndrome rises from 2/1000 live births among mothers aged 30-34 to 15/1000 live births at ages 40-45. If one accepts the risk of 1/200 then women over the age of 38

should be offered amniocentesis. Only about 1/3 of babies with Down syndrome are born to mothers in this age group, however; this illustrates a common dilemma in screening - most cases occur in "low risk" populations.

The other screening tests are based on the detection of different chemical products of the fetus or placenta that diffuse into the maternal circulation and so can be sampled by a simple blood test. All three products are produced during normal pregnancy so the tests are not diagnostic. The fetus with Down syndrome is relatively less mature than its normal counterpart and so the amounts detected are only abnormal in the sense that they are wrong for that particular stage of gestation. All three therefore depend upon accurate estimation of gestational age.

The concentrations of maternal serum alpha-fetoprotein and unconjugated oestriol are significantly lower in pregnancies affected by Down syndrome (Wald et al 1988, Cuckle et al 1984).

The concentrations of maternal human chorionic gonadotrophin are higher in pregnancies affected by Down syndrome (Bogart et al 1987), probably because production of the hormone continues after it would normally have stopped. It is probably the most sensitive single predictor of risk (Wald et al 1988).

The risk of having an affected pregnancy is calculated by combining the mother's age and the particular risk associated with each test (Murday and Slack 1985, Cuckle et al 1987).

Combining the results of all the tests with age increases the predictive value and can modify the assessment of risk in a high risk group, for instance, women over 38 years, so that amniocentesis need not be done.

If the mother has previously had a pregnancy affected by Down syndrome, either born or aborted, the risk to subsequent pregnancies increases to 1/20 regardless of any other factor. These women, should therefore be offered amniocentesis straight away. Certain rare versions of Down syndrome have a high rate of recurrence (50 - 100%). Prenatal diagnosis could reveal such births but I will not consider them in this analysis as they make up such a small proportion of Down syndrome births.

### Principles of Screening

Before any screening test is introduced it should satisfy certain principles (Wilson and Jugner, 1968). Often, however, tests are introduced - perhaps for research or even without any assessment; demand may then grow and create a drain on NHS resources. This may initially be tolerated, but eventually there is a crisis and assessment called for.

No screening test fulfils all the principles outlined below - which makes the economic analysis more interesting.

- 1) The condition sought should be an important health problem.

Down syndrome is the commonest chromosomal abnormality diagnosed at birth and among the commonest cause of disability. The mental retardation and organ defects that it causes create a considerable burden of lifelong care for families and society.

- 2) There should be an acceptable treatment for patients with recognised disease.

Prenatal screening is unique in that two subjects must be considered at the same time. Who is the patient, the mother or the child? If only the mother is regarded as the patient then termination may be acceptable. To some patients and professionals this is the case but there is a large group of dissenters who would not regard termination as "treatment". Is there a clash of values? Is the choice the mother's to make?

- 3) The facilities for diagnosis and treatment should be available.

Amniocentesis can be done in most district general hospitals or at specialist centres. The analysis of the samples is usually carried out at regional cytogenetic laboratories. Abortions should be available in all districts.

4) There should be a recognisable latent or early symptomatic stage.

The detection of the abnormality in utero at about 19 weeks fulfils this condition. If the age limit for abortion was reduced this might cease to be so.

5) There should be a suitable test or examination.

The use of "suitable" could refer to the yield - that is, the number of cases identified in a screened group. The yield will be influenced by the specificity and sensitivity of the test and also by the level of risk at which it is decided that amniocentesis is indicated.

If a risk of 1/300 as opposed to 1/200 is adopted:

- (i) more amniocenteses would be recommended.
- (ii) the number of amniocenteses/case detected would be higher
- (iii) the number of normal fetuses that miscarried as a result of amniocentesis would be higher.

But:

- (i) the detection rate of fetuses with Down syndrome would be higher - cases would be detected in those with a risk of between 1/200 and 1/300 that would otherwise be missed.

The level of risk at which amniocentesis is recommended is therefore important to the economic analysis.

6) The test should be acceptable to the population.

The test comprises taking one sample of blood at about 16 weeks gestation whether or not the gestational age has been confirmed by ultrasonography. This is quite acceptable.

7) The natural history of the condition, from latent to declared disease, should be adequately understood.

In other words, we must know the consequences of not detecting or not treating the disease. In this respect, Down syndrome is clearly understood, although the primary cause is not known.

8) There should be agreement about who is offered treatment.

Assuming that the patients are the mothers whose risk exceeds 1/200, treatment thresholds will have a major impact on the economics of screening.

9) The cost of finding cases (including diagnosis and treatment of patients diagnosed) should be balanced against possible expenditure on any other form of medical care.

10) The finding of cases should be a continuing process and not a "once and for all" project.

If screening fails to show an abnormality this does not imply a low risk in future, therefore, the test needs to be repeated for each subsequent pregnancy.



For many conditions that are already screened it is essential that it is done systematically, because often those who are most at risk are least likely to seek screening and diagnosis of their own accord (for instance, the condition is linked to social deprivation). This is not so of Down syndrome, the incidence of which is comparatively stable. Obviously full benefit cannot accrue if the programme is applied only partially while the capital and staffing costs are incurred in full.

This is the point to turn to economic analysis, of which there are two strands: inputs and outcomes, and choices.

#### **Inputs and Outcomes**

These are usually thought of as costs and benefits. Cost in economic terms is more than just money. The use of resources for a particular activity means that the opportunity to use the same resource for another activity is lost. This is termed "opportunity cost" and is the benefit that would be derived from a unit of resource in its best alternative use - for instance, a gynaecologist doing an amniocentesis is not free to do other work. There is also a psychological cost, in terms of the adverse feelings and emotions experienced by patients or relatives caused by such a programme - for example anxiety, and pain. These are impossible to quantify and are therefore often not considered.

A benefit is the positive aspect of a course of action or intervention - for instance, being healthy, the prolongation of life or improvement in its quality and, in relation to preventative measures, reassurance about future health.

Costs and benefits can be classified into three groups (Drummond 1980). Firstly, changes in use of resources. This includes the cost of organising and operating a programme, its capital and operating cost, and also patients' and relatives' out-of-pocket expenses. Secondly, changes in health state. These are the results of treatment, which are difficult to quantify and value. How do you value good health? How is a price put on reassurance or informed choice? Because of this economic appraisal has focused on a third area, changes in productive output, and used it as a proxy for changes in health state. "Changes in productive output" refers to the productivity or contribution to the community of patients for whom disability is relieved. There are immense difficulties applying this to a disabled fetus, which are discussed later. Although changes in productive output attracted a great deal of attention in the past, they have been largely discredited by economists and are no longer used.

By concentrating on the easily measured monetary aspects of a health treatment, economists have excluded perhaps the most important benefit of a health care programme and certainly one on which a treatment should stand or fall, changes in health state.

## Choices

Economics is also about choices and how they are made. With a finite amount of cash it is not possible to fund all treatments or programmes and therefore choices must be made: who to treat, how to treat, when to treat, and how much treatment to offer?

The criteria used to make these decisions are often based on personal values and beliefs. What makes a doctor decide when to stop actively treating terminally ill patients or to decide who should have renal dialysis? Why do some doctors offer amniocentesis to patients with a 1/300 risk of carrying a fetus with Down syndrome and others to those with a risk of 1/200?

Parents also face choices - should they accept amniocentesis and its associated risk of aborting a normal fetus? If the fetus has Down syndrome should they accept termination of the pregnancy? It has been suggested that parents think in terms of risk, burden, and outcome when making such decisions (Skinner 1983).

	Risk	Burden	Outcome	Action
Duchenne muscular dystrophy	High	Early: nil Late: heavy	Tragic	Diagnosis sought
Down syndrome	Low	Heavy	Poor	Diagnosis sought
Sickle cell trait	High	Light	Good	Diagnosis sought?

Parents often come with preconceived notions of the burdens and outcome associated with a condition and so it is important to give them a full account of the condition being screened. In this way if the risk of a particular condition is low yet the burden is great or the outcome poor, prenatal diagnosis may be sought. If the risk is high but the long term outcome is good, is prenatal diagnosis indicated?

Because economic analysis considers alternative uses of resources and to some extent the outcomes, the criteria used to make decisions must be explicit. In this way difficult problems are aired, so that informed decisions can be made.

The three main types of economic analysis that may be applied to prenatal screening are cost-benefit, cost-utility, and cost-effectiveness.

### **Cost-benefit analysis**

Cost-benefit analysis is a way of examining all costs (real costs and adverse effects) and benefits of an intervention, then translating all these into the same unit of account - usually money - and expressing the size of any overall loss or gain. This gives an assessment of the inherent worth of an intervention and allows comparison of competing alternatives regardless of any intrinsic differences.

It is a seductive notion, especially nowadays, to translate benefits into monetary terms as, if there is a net gain from a programme it can jump the queue for allocation of funds. As a result, early studies purporting to be cost-benefit analysis assumed that the objective of prenatal screening was the detection and abortion of affected fetuses. The following costs and benefits were presented and cash values were allocated where possible.

Costs - costs of screening programme including amniocentesis  
          termination of pregnancy

False positives - unnecessary amniocentesis

False negatives - false reassurance

miscarriage of normal fetus after amniocentesis

Benefits - averted costs of not caring for the affected child

improved quality of life for mother and family

a replacement child

reassurance if screening is normal

There are difficulties associated with using averted costs as a benefit. If we accept that the benefit of a treatment is a positive change in health state then averted costs seem to be irrelevant.

Using averted costs as a benefit may detract from certain important changes brought about by a treatment. The benefit of prenatal screening is not merely the future savings made in

medical resources, but may be what people would be willing to pay (in the absence of screening) to avoid the consequences of certain diseases or conditions.

Any savings made using averted costs depend on the quality of care to be provided to the disabled child. It is a paradox that screening may not be viable if the care offered to affected children is cheap, low quality, institutional care.

The economic benefit of screening using this method is also less if the termination of an affected pregnancy is followed by the birth of an unaffected child (Henderson 1982, Hagard and Carter 1976). If the object is to reduce disability then the benefit should be greater not less with the birth of an unaffected child, unless we accept that we would all be better off dead. For these (among other) reasons, counting averted costs as actual benefits is no longer acceptable to economists.

Applying cost-benefit analysis to prenatal screening when the objective is to detect abnormal pregnancies still presents problems, and the following costs and benefits remain:

Cost - costs of screening programme including amniocentesis  
false positives - unnecessary amniocentesis  
false negatives - false reassurance  
miscarriage as a result of amniocentesis

Benefit - reassurance to most mothers  
Choice of whether to proceed to amniocentesis

Most of the benefits of prenatal screening are intangible - how do you quantify the psychological benefit of not having a disabled child, or of the loss of a normal child? Regardless of which approach is used we are still left trying to put a cash value on intangibles. Financial costs are therefore meaningless, and cost-benefit analysis is not appropriate.

### Cost-utility analysis

Cost-utility analysis attempts not only to calculate the cost and benefit of an intervention but also to consider its utility. Utility refers to the value or worth of a specific degree of health - for instance if a pianist and a singer both fractured their fingers, the value of complete recovery would be greater to the pianist. Typically cost-utility analysis is expressed as cost/unit output.

Attempts have been made to value or rank health states associated with the outcomes of different interventions or programmes relative to one another. The commonest measure is the quality adjusted life year (QALY). This is an attempt not only to take account of any extra years gained but also to include the quality of those years as well.

There are obvious problems in using QALYs in prenatal screening. Quality of life is important not only for the mother and family, but also as perceived by the family for the affected fetus had it been born alive. What characteristics of

quality of life should be included in the QALY weighting? How would you "weight" different characteristics relative to each other? How do you measure these characteristics? What QALY should you use? Is the quality of life of a young mother greater or less than for an older one? How do you arrive at an overall QALY when two individual subjects are affected?

The present measures of QALY calculation do not take account of these problems in relation to prenatal screening (Gudex and Kind 1988). They were not designed for such comparison and further research is needed before QALYs can be applied.

#### **Cost-Effectiveness Analysis**

Cost-effectiveness analysis is about the best way of delivering a service. It does not, however, allow direct comparison of programmes with different objectives and cannot be used to determine the inherent worth or value of any one programme. It is important that the programme has a clear, unambiguous, objective and has only one dimension along which effectiveness can be assessed. If there is more than one, and no single alternative is superior on all counts, some sort of ranking is required thus introducing an element of utility (Drummond et al 1987).

Cost-effectiveness analysis is therefore used when the outcome is assumed to be worth having, that one of the alternative ways to achieve that outcome will be adopted regardless of cost, and



that the question "Is it worth doing at all?" is not asked, or has already received a definite "yes". Cost-effectiveness analysis might thus pose the question "Given that it is worth detecting Down syndrome and that there is a choice of tests and target populations, what is the most effective, cheapest way of doing it?"

By calculating the cost/case detected (not the cost/case aborted) for a variety of combinations of tests we can look at the options available and decide on a combination. The more tests carried out per pregnancy, the more expensive the programme - but more cases are detected yet fewer amniocenteses performed per case detected.

Age + screening test	AFP	AFP+UO	AFP+UO+HCG
detection rate (%)	31	45	57
no of amniocenteses/ case detected	79	74	54

Risk cut-off 1:200

AFP = alpha-fetoprotein. UO = unconjugated oestriol.  
HCG = human chorionic gonadotrophin.

To compare combinations we must calculate the incremental cost - that is, the cost of the additional effects gained from each combination, not just the average. This is not to be confused with the marginal cost, which is the change in total cost from single unit increases or decreases in a programme.

Cost may be only part of the analysis. The number of amniocenteses carried out may be relevant, because the more amniocenteses done the greater the likelihood that a normal fetus will be aborted, and so the number of amniocenteses/case detected could be calculated for each combination. Problems arise if the incremental costs increase as the number of amniocenteses decrease with different programmes.

Which measure is taken to be more important - extra cost and less loss of fetuses or vice versa? Either we are clear at the outset which dimension of effectiveness we wish to measure (we have made explicit valuations at the beginning) or we can choose to weight certain factors. If we choose the latter then again we are introducing an element of cost-utility analysis, showing that there is no single way of analysing health care provision.

## **Discussion and conclusions**

Economics is used to assist decision-making within allotted health care budgets. Doctors and others, however, have used economics arguments to show that society should spend more money on health care. In the case of prenatal screening, attempts have focused on showing its potential savings as a way of answering the question "Is prenatal screening worth doing?" and also to make it appear more attractive to funding bodies and influence the allocation of resources. For reasons already given it seems that economics cannot answer this question and

should not be used to decide whether or not to have a prenatal screening programme: this is a political decision. It may assist, however, in determining the extent of such a programme.

Much of the controversy surrounding the economic analysis of prenatal screening has arisen because of a fundamental misunderstanding of its aims. The averted costs of caring for a disabled child are seen as the main benefit to society and as such are easier to talk about than ethical and moral issues. Nevertheless, it should be apparent that the true benefits of screening are in detecting affected fetuses, not aborting them, giving reassurance to couples with unaffected fetuses, and giving high risk couples the option of prenatal diagnosis.

Costs and benefits are only some of the dimensions to be considered in the analysis. There is the question of equity. If amniocentesis is done simply on the basis of age - for instance 38+, which implies acceptance of a risk of 1/200 or greater, is it fair to deny amniocentesis to younger women who may be shown to have a risk greater than 1/200 on the results of serum screening tests?

This paper was concerned with Down syndrome, but similar arguments hold for other common disabling conditions such as cystic fibrosis and Duchenne muscular dystrophy. In the case of Duchenne muscular dystrophy the moral arguments are more pronounced as currently it is not the trait that is tested for in the fetus but simply sex: thus there is a 50% chance that

the aborted fetus could be normal. Development of specific genetic probes may allow the trait itself to be screened.

Different arguments apply to conditions such as haemolytic disease of the newborn and syphilis for which effective treatments are available. Such programmes can be analysed by more traditional economic methods.

Three approaches to health economics in prenatal screening have been discussed. These are summarised as follows:

The major components of prenatal screening do not lend themselves to monetary valuation, which therefore excludes cost-benefit analysis, no matter how attractive this approach may look.

Cost-utility analysis has attractions and seems to be the goal to aim for if we are seeking a method of comparing like with like and deciding on priorities. At the present time, however, the methods required are not refined enough and a lot of research is needed to work out and validate the values and weights to attach to the intangible or psychological benefits of prenatal screening programmes. Ultimately the costs of such research must be weighed against the possible benefits and will need to be submitted to economic analysis (Detsky 1989).

Prenatal screening for Down syndrome is the detection of mothers at risk, and if it is assumed to be worth doing then

cost-effectiveness analysis is currently the only viable option. There should, however, be only one dimension of effectiveness to be measured unless it can be shown that one project is superior on all counts.

A suitable outcome measurement may be the cost/case detected or the number of amniocenteses/case detected (not cost/case aborted or unit of disability averted), but one must decide whether the monetary cost (cost/case detected) or the human cost (the number of amniocenteses/case detected) is more important and at what degree of risk amniocentesis should be carried out. This introduces an element of overlap with cost-utility analysis.

Genetic engineering is evolving and with it comes the possibility of preventing the expression of deleterious genes with treatment at an early stage of development. This will not be cheap and the economic analysis of prenatal screening will require careful re-evaluation as the somewhat more expensive option of treatment as opposed to termination becomes available.

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