For Debate . . .

Can we afford screening for neural tube defects? The South Wales experience

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Abstract

Clinical and financial gains and losses accruing from five different options for screening for open neural tube defects were estimated, based principally on the results of detailed monitoring of inputs and outcomes and of process costs in the South Wales Anencephaly and Spina Bifida Study. As well as estimating the overall clinical costs of a screening service it was shown that if the prevalence, including terminations, of open neural tube defects is between 1·25 and five per 1000 births the financial cost of avoiding the birth of a seriously handicapped child who would survive for more than 24 hours is in the range £9000-£54 000 depending on the option adopted and the prevalence of the condition in the target population. Prevalence is the biggest determinant of cost.

The data should provide a basis for assessment and discussion of resource priorities in the National Health Service.

Introduction

Objective analysis of a clinical service is nearly always difficult and sometimes unpalatable but it is necessary for rational decision making and for defining strategies. This is particularly relevant in the case of prenatal screening for neural tube defects, and, in view of the complexity of medical and ethical issues raised, it is not surprising that opinion diverges widely on the desirability and practicability of a national screening programme. In 1979 the Working Group on Screening for neural tube defects (Black Report) identified four policies that might be followed with respect to screening for neural tube defects[1]: discourage further development; encourage existing development; encourage new development; and make the service generally available when resources permit. The choice of which of the above to recommend will depend on judgments of whether in personal, social, and financial terms the benefits of a policy outweigh, by an acceptable amount, the costs.

The interdisciplinary South Wales Anencephaly and Spina Bifida Group was established to make an objective assessment of various options for a neural tube defect screening programme under field conditions.[2-4] This was carried out as an operational research exercise with detailed monitoring of inputs and outcomes and careful assignment of process costs. It was designed to permit the calculation of the various costs and benefits of each of various tactical options. We used this data as a basis for the present assessment to assist regional policy makers who are concerned with the use of resources and the returns therefrom.

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Subjects and methods

SUBJECTS

The study area and population—The study was mounted in Mid Glamorgan, a non-teaching health authority with a population of 540 000 and a high prevalence of open neural tube defect. All patients (15 915 women, 98·9% of all pregnancies in the area) who made a booking at any of the National Health Service antenatal clinics in Mid Glamorgan between 1 April 1977 and 31 August 1979 were included in the study. Complete information was obtained for 15 687 (98·6%).

The screening procedure and its outcome—The screening procedure, and more detailed information on the efficacy of the serum screening test, have been published previously.[3] The proportion of open neural tube defects terminated in the screened population was 66% but for the population overall (70% screened) 56·1% (66·6% for anencephaly, 40·7% for open spina bifida). The diagnostic effectiveness of ultrasound examination was also assessed by investigating 2509 mothers at high risk. During the study diagnostic ultrasound had only a limited ability to detect open neural tube defects, but studies in progress showed that by 1983 detection rates of 100% for anencephaly and 80% for open spina bifida had been achieved. Further details have been published elsewhere.[4]

METHODS

The following five screening options were studied: (1) Diagnostic ultrasound scanning (see definition below) and amniocentesis for all mothers with serum α fetoprotein concentration confirmed to be above the 95th centile (roughly median ×2·5) after ultrasound estimation of gestational age and exclusion of multiple pregnancy. (2) As option 1, but for all mothers with serum α fetoprotein concentration confirmed to be above the 97th centile (roughly median ×3). (3) As option 2, but, in addition, with diagnostic ultrasound scanning and amniocentesis for all pregnancies with close family history (first or second degree relative) of open neural tube defect, irrespective of serum α fetoprotein concentration. (4) As option 2, but with routine ultrasound scanning (see definition below) examination at the time of the first visit to hospital. (5) Diagnostic ultrasound scanning, but no measurement of serum α fetoprotein concentration, in all pregnancies eligible for screening together with amniocentesis in all pregnancies with a suspicion of open neural tube defect on ultrasound scanning.

("Diagnostic" ultrasound scanning was defined as scanning undertaken by an experienced ultrasonographer using a high resolution scanner to exclude the presence of a neural tube defect. It is to be distinguished from "routine" ultrasound scanning, which, in this context, was scanning carried out principally to establish gestational age of the fetus and detect multiple pregnancy.[4])

Calculation of the social gains and losses associated with each of these options was based on the assumptions shown in table I, which were derived primarily from the South Wales field study. These gains and losses included:

Short term gains—Reassurance that parents gain from the knowledge that the test results are normal.[5]

Short term losses—False positive serum and ultrasound findings that lead to further investigation and hence anxiety.[5]

Long term gains—(1) Avoidance of the birth of a child with an open neural tube defect likely to survive for an indefinite period with poor quality of life;

TABLE I—*Assumptions used in calculating gains and losses with five screening options*

	Assumed value	Symbols used in calculations in table II
Population	100 000	a
No of pregnancies/100 000 screened:		
With abnormal serum α fetoprotein in option 1	5000	b
With abnormal serum α fetoprotein in options 2, 3, and 4	3000	c
With open spina bifida	205*	d
With open spina bifida and surviving beyond 24 h	133†	e
With anencephaly	295*	f
No/100 000 receiving:		
Diagnostic ultrasound in option 1	5000	g
Diagnostic ultrasound in option 2	3000	h
Diagnostic ultrasound in option 3	5000	i
Diagnostic ultrasound in option 4	3000	j
Diagnostic ultrasound in option 5	100 000	k
Amniocentesis in option 1	5000	l
Amniocentesis in option 2	3000	m
Amniocentesis in option 3	5000	n
Amniocentesis in option 4	3000	o
Amniocentesis in option 5	1000	p
Sensitivity of diagnostic ultrasonography in detecting anencephaly	100%‡	q
Sensitivity of diagnostic ultrasonography in detecting open spina bifida, options 1-4	80%‡	r
Sensitivity of diagnostic ultrasonography in detecting open spina bifida, option 5	60%‡	s
Single routine ultrasonography false positive rate, option 4	3%§	t
Diagnostic ultrasonography false positive rate, options 1-4	1%‖	u
Diagnostic ultrasonography false positive rate, option 5	3%‖	v
Spontaneous abortion rate after amniocentesis	1%¶	w
Morbidity rate after amniocentesis	1%**	x
False positive termination rate	0·02%**	y

Sources:
*South Wales Study.[3]
†Laurence and Tew.[9]
‡South Wales Study.[4]
§Conservative estimate, which must be no less than 0·03.
‖Published estimates vary widely[4 10-12]; the figure quoted is believed to be a conservative estimate for results likely to be achieved in day to day practice.
¶Medical Research Council amniocentesis study[13] and unpublished observation from South Wales Study.
**Unpublished observation from South Wales Study.

(2) avoidance of the stillbirth of an affected child or birth of a child dying shortly after birth.

Long term losses—(1) Death or morbidity of a normal fetus as a result of amniocentesis; (2) termination of pregnancy with a normal fetus as a result of diagnostic error; and (3) incorrect reassurance after a false negative screening test, with subsequent birth of an affected child.

To calculate the basic financial costs a systems analysis was applied, which identified a sequence of 25 processes in the screening programme. The revenue and capital costs of these were then identified. Time study diaries were used to calculate additional workload imposed by the various processes on existing or additional members of staff. All the financial information collected was then considered under the headings revenue (additional staff, consumables, terminations, publicity) and capital (equipment and buildings). All costs were based on 1980 prices and pay scales; we added 20% to pay scales to cover superannuation and National Insurance.

Results

Table II shows the non-financial gains and losses (and how these were calculated) for the various options, and table III shows the financial costs together with the main individual items of expenditure. Financial costs were considered only in terms of cost to the National Health Service. It was outside the scope of the present study to measure additional public or private financial costs arising from, for example, loss of earnings.

TABLE III—*Financial costs (in £1000/100 000 population, 1980 prices) of five options for screening for neural tube defects. (Assumed prevalence of open neural tube defects, including terminations, 5/1000)*

	Options				
	1	2	3	4	5
Revenue:					
Additional staff	371·6	330·1	357·4	390·8	399·9
Consumables	147·9	141·2	149·2	142·6	72·3
Terminations	59·5	56·3	61·1	59·5	63·9
Publicity	10·0	10·0	10·0	10·0	10·0
Capital (annuitised):*					
Equipment	65·7	65·7	65·7	79·9	79·0
Buildings	52·8	52·8	52·8	52·8	52·8
Total	707·5	656·1	696·2	735·6	677·9

*Assuming a seven year life for equipment, 50 years for buildings, and a 7% discount rate.[1]

Options 1 and 2 are similar strategies but require different levels of action (95th and 97th centiles). The overall cost of option 1 was slightly greater than option 2 but it was more sensitive in the detection of neural tube defects, especially potential handicapped survivors (table II). On the other hand, the loss of unaffected fetuses (deaths after amniocentesis and termination of normal fetuses) was 40% greater with option 1 than with option 2, and option 1 also had a greater potential for creating anxiety because of false positive results to serum α fetoprotein and diagnostic ultrasound tests.

Option 3, which added to option 2 detailed investigation for mothers with a close family history, gave a slight improvement in the detection rate of non-survivors (an additional 27 cases) but no improvement in the detection of potential survivors. Also, this option and option 1 gave higher risks of loss of unaffected fetuses (deaths after amniocentesis and terminations of normal fetuses) than did the other options.

Option 4 because it added routine ultrasound screening for all eligible women had a greater potential to produce anxiety than options 2, 3, or 5. The detection rate of potential survivors was the same as with options 2 and 3 but less than with options 1 and 5. It was also the most expensive option, costing 13% more than option 2. Costings were, however, based on the assumption that the total cost of ultrasound scanning was ascribed to the screening programme and did not take into account that routine scanning is already a de facto practice in many obstetric units.

For option 5 the basic costings were as firm as for the other options, but the other gains and losses were more tentative as this was the only option not based on hard practical data derived from field studies. Of particular importance was the "vigilance decrement"[6] that may result from the application of a procedure as a routine when the incidence of abnormalities is relatively low, as compared with a small selected high risk population. We assumed an overall diagnostic accuracy of 60% and a false positive rate of 3%, but these figures may have been optimistic for current day to day practice. There are other potential diagnostic benefits from detailed ultrasound screening, but the range of abnormalities that may be detected is dependent on the time and staff available, and this would require a separate study.

TABLE II—*Non-financial gains and losses of five screening options/100 000 screened with symbols indicating method of calculation in parentheses. (Assumed prevalence of open neural tube defects, including terminations, 5/1000)*

	Options				
	1	2	3	4	5
			Gains		
No of births with open neural tube defect surviving beyond 24 h avoided	66* (A)	55* (D)	55 (G)	55* (K)	72† (N)
No of births of non-survivors avoided	276* (B)	269* (E)	296* (H)	285* (L)	304† (P)
Total	342* (C)	324* (F)	351* (J)	340* (M)	376† (Q)
			Losses		
False positive tests:					
Postamniocentesis fetal deaths	50 (lw)	30 (mw)	50 (nw)	30 (ow)	10 (pw)
Postamniocentesis fetal morbidity	50 (lx)	30 (mx)	50 (nx)	30 (ox)	10 (yx)
Terminations of pregnancy with normal fetus	20 (ay)	20 (ay)	20 (ay)	20 (ay)	20 (ay)
False positive serum tests causing parental anxiety	4624 (b−(C+C/10))	2644 (c−(F+F/10))	2614 (c−(J+J/10))	2626 (c−(M+M/10))	0
False positive ultrasound examinations causing parental anxiety	50 (gu)	30 (hu)	50 (iu)	3030 (at+ju)	3000 (av)
False negative tests:					
Incorrect reassurance and subsequent birth of affected child	124 ((d+f)−(C+C/10))	144 ((d+f)−(F+F/10))	114 ((d+f)−(J+J/10))	126 ((d+f)−(M+M/10))	86 ((d+f)−(Q+Q/10))

*Actual number observed in South Wales Study projected to a population of 100 000. These figures take into account those pregnancies with open neural tube defects that, although detected, would not be terminated.
†Assumes that 90% of pregnancies with detected open neural tube defects likely to survive beyond 24 hours would be terminated.

Table IV shows the financial costs of avoiding the birth of a child with an open neural tube defect who is likely to survive for more than 24 hours after birth. Estimates are given for three different population prevalences of open neural tube defect and are based on an assumption that 65% of infants with open spina bifida will survive for more than 24 hours (table I). The range of costs was relatively small for a given prevalence, although option 5 was the cheapest and option 4 was the most expensive (25% more than option 1). A more important cost factor was the crucial influence of prevalence—every time it was halved the cost per abnormal birth avoided doubled.

TABLE IV—*Financial costs (£1000) of avoiding birth of a child with open neural tube defect surviving beyond 24 hours according to prevalence of condition (including terminations) in target population. (1980 prices)*

Option	Prevalence of open neural tube defect		
	5/1000	2·5/1000	1·25/1000
1	10·7	21·4	42·8
2	11·9	23·8	47·6
3	12·7	25·4	50·8
4	13·4	26·8	53·6
5	9·4	18·8	37·7

Discussion

In some established services policies other than the options discussed above have been adopted. For example, it is common practice to repeat tests after apparently abnormal serum results or to carry out repeat ultrasound scanning, thus reducing the number of cases requiring amniocentesis. On balance the overall costs vary little from the estimates that we have given for the various options, but the delay in termination of abnormal pregnancies is increased.

Ultrasound practices vary widely. Routine scanning may be undertaken by obstetricians of varying grades, specially trained midwives, radiologists, or radiographers, but the grade of operator makes little difference to the overall cost of screening. Although the workload is often absorbed in the overall services, we have made an allowance for the extra time used. It is common practice in some units to perform a routine scan in all pregnancies at the time of booking or at about 16 weeks' gestation. This has important clinical benefits such as early diagnosis of multiple pregnancy and gestational dating to provide an accurate baseline for future observations. If only half the additional cost of routine ultrasound scanning was ascribed to screening the overall cost for option 4 would be of the same order as options 1-3.

Other variables, particularly those relating to organisation and quality of services, are less easy to identify but may have a considerable influence on ultimate decisions concerning policy. For example, we based the losses from false positive results on our own experience, which may not be reflected in other areas and can only be determined by careful audit. The incidence of erroneous terminations quoted was based on false positive tests in our study, but this may be an underestimate as judged by later information. The study by the Royal College of Obstetricians and Gynaecologists on late abortions showed that, of all terminations of pregnancy resulting from the finding of a raised α fetoprotein concentration, 6·5% fetuses had no identified abnormality and in only 86% of the remainder was an open neural tube lesion identified.[7] If the national prevalence of open neural tube defects, including terminations during the study, is assumed to be two per 1000 it can be estimated that for one consultant obstetrician responsible for 800 deliveries annually even the high incidence of error quoted would represent only one erroneous termination in every three years. Thus a high incidence of error is easily missed without careful and accurate audit.

False positive results will inevitably create parental anxiety, which may or may not be dispelled by subsequent investigations indicating a normal fetus. Options 2, 3, and 5 each cause a similar level of anxiety, which is substantially lower than that caused by options 1 and 4. False negative tests resulting in incorrect reassurance and subsequent birth of an affected child are highest for option 2. The figure for option 3 is lower than for options 1 and 4, and the tentative figure for option 5 is lower still.

We calculated the financial costs of achieving a social gain, endeavouring to present the facts without judging them. Table IV shows the financial costs of avoiding a handicapped survivor, the main primary criterion on which many would base their policy decision. Longer term survival may be greatly influenced by neonatal management policies, especially in relation to surgical treatment, and in areas where the proportion of survivors is much lower the financial cost of detecting a fetus with open spina bifida that will survive will be correspondingly increased.

With respect to the development of a national or regional policy we think that the first question to be answered is not, "Which option should be adopted for a given prevalence?" but, "Are the costs of any of the options acceptable to the health authorities?" In the United Kingdom prevalences of neural tube defects (including terminations) of five per 1000 are now the exception rather than the rule, and prevalences of 1·25 to 2·5 per 1000 are the norm for much of the country. When the prevalence is 1·25 per 1000 the cost of avoiding the birth of a surviving infant with a neural tube defect may well be more than the National Health Service can afford. Expressed in terms of opportunities foregone, spending money to avoid the birth of one surviving child with an open neural tube defect might require the denial of the chance of improved quality and duration of life to five patients needing coronary bypass surgery or 2500 women who might otherwise undergo screening for cervical cancer, or the denial of an operation for hip replacement to 18 patients. Undiscounted excess lifetime costs to society incurred by a survivor with an open neural tube defect have been estimated at £118 000[8] and offered as justification for similar expenditure to avoid the event in the first place. There may well be, however, a substantial difference between what it might be worth to society to avoid the event on the one hand and what the National Health Service can afford on the other.

Although it is undesirable to deny any woman access to a test which she perceives to be beneficial, we think that further development of serum α fetoprotein screening should be discouraged in areas with a prevalence of neural tube defects below 2·5 per 1000 until some notion of maximum acceptable cost to the National Health Service has been agreed. It may, however, be that the non-financial gains and losses of screening for neural tube defects will be the biggest determinants of the acceptability or otherwise of this procedure. For example, in the most cost effective option (option 5) 30 normal fetuses may die and a subsequently unjustified suspicion of open neural tube defect will be raised against 3000 to avoid the birth of 376 babies with an open neural tube defect only 72 of whom will survive beyond 24 hours.

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