

Cost-effectiveness of neonatal IgE-screening for atopic allergy before 7 years of age

K. HJALTE¹, S. CRONER² and N.-I. MAX KJELLMAN²

¹The Swedish Institute for Health Economics, Lund, and ²Department of Pediatrics, University Hospital, Linköping, Sweden

Obvious atopic diseases developed in 18% of 1651 non-selected children before 7 years of age. More than 80% of newborns with high IgE concentrations in cord blood developed atopic diseases before this age. Although the sensitivity of the IgE test is rather low (40%), most cases (94%) of severe, long-lasting atopic disease show a high neonatal IgE concentration, and the specificity of the test is high (94%). Calculations of total costs of screening were made on the basis of family history alone compared with neonatal IgE-screening in two groups: (i) all newborn infants, or (ii) infants with a family history of atopic disease. The cost of preventive measures and treatment costs were included in the calculations. Results were compared with the cost of conventional treatment. Provided that preventive measures delay onset of symptoms in atopic-risk subjects (and assuming total patient compliance) then IgE-screening was cost-effective in both groups, which screening solely on a basis of family history was not. In Sweden there was a total saving of approx. 20 million SEK or 3 million US\$ per annum. Thus, IgE-screening of cord blood to select newborns for preventive measures is also economically worthwhile.

Key words: atopic disease; cord blood; cost-effectiveness; IgE; newborns.

Accepted for publication 14 September 1986

During the past decade, much interest has been focused on the means for predicting a subsequent atopic allergy (1, 2, 7, 8). We have shown that 82% of newborn infants with a cord blood IgE concentration > 0.9 kU/l develop some degree of atopic symptoms before 7 years of age in contrast to 30% of infants with a lower neonatal IgE concentration (8). Most children (94%) with severe, long-lasting symptoms of atopic disease were identified by an elevated cord blood IgE concentration.

Besides high sensitivity there are at least three prerequisites for neonatal screening for atopic allergy: (i) preventive measures should be available, (ii) screening and preventive measures should be acceptable to the child and the family, and (iii) screening should be cost-effective.

As there are studies which support recommendations of exclusive breast-feeding for 6

months and avoidance of smoking and pets in the infants' homes (3, 11), thus making screening for allergy risk meaningful, we decided to evaluate the cost-effectiveness of neonatal IgE-screening using Phadebas IgE PRIST® thereby applying economic aspects to our previous study group (8). We wanted to compare the costs of three different screening methods with that of a conventional method:

- I. IgE-screening of all newborn babies.
- II. IgE-screening solely of those with a positive family history.
- III. Prediction solely on the basis of family history.

The total costs of these screening programmes were compared with that of the conventional alternative, with no special preventive measures. A certain number of assumptions had to be made to provide a basis for comparison. The

monitoring period was the child's first 6 years. Information on costs was collected from various sources. The results imply that IgE screening of neonates is cost-effective.

MATERIAL AND METHODS

Children and follow-up

All infants ($n = 1884$) born in the community of Linköping during a 13-month period comprised the initial material. Cord blood was collected and serum frozen at -20°C pending analysis with Phadebas IgE PRIST®. The families were asked to fill in a questionnaire when the children had reached 18 months of age, as previously described (4). The cord blood IgE concentrations were compared with the family history, and the clinical diagnosis established at personal visits to the Pediatric Department of all children with a history suggesting atopic disease.

The same families were addressed again when their children had reached 3 and 6-7 of age. Doubtful answers in questionnaires were checked by telephone interviews and medical records were scrutinized. An accumulated and a current diagnosis of obvious, probable, or no

atopic disease was established in 1651 children as described in detail elsewhere (8). For the purpose of the present study, however, only obvious atopic disease (atopic eczema, bronchial asthma, allergic rhinitis, allergic urticaria and gastrointestinal allergy) was taken into account. Children with probable atopic disease were regarded as healthy.

No special recommendations concerning early feeding or allergen avoidance were given during the study.

An immediate family history of atopic disease i.e. in parents and/or siblings, was present in 31% of the children. A positive IgE-screening, i.e. a concentration in cord blood not less than 0.9 kU/l was found in 12.4% of the children.

Definitions

True positive (TP): positive test and showing atopic disease during the observation period, within 7 years of birth.

False positive (FP): positive test but healthy during the period.

False negative (FN): negative test but sick during the period.

True negative (TN): negative test and healthy during the period.

Table 1

Costs and probabilities for different groups defined by screening and conventional alternative. (For abbreviations see text)

Group	Probability	Cost components
1. True positive, TP	KIt_1	$s + h_1 + r_1 + b_1$
2. False positive, FP	$(1-KI) (1-t_2)$	$s + h_2 + r_2$
3. False negative, FN	$KI (1-t_1)$	$s + h_3 + b_3$
4. True negative, TN	$(1-KI) t_2$	$s + h_4$
5. Conventional atopic	KI	$h_5 + b_5$
6. Non-atopic, symptom-bearing	$(1-KI) w$	$h_6 + r_6$
7. Healthy	$(1-KI) (1-w)$	none

Table 2

Probabilities (%) used in evaluating the three screening programmes. (For abbreviations see text).

Screening programme	KI	TP	FP	FN	TN	t_1	t_2
I	18.2	7.3	5.3	10.9	76.5	40.0	93.5
II	28.6	11.4	4.6	17.2	66.8	40.0	93.5
III	18.2	9.0	22.4	9.2	59.4	72.6	28.6

Sensitivity of a test (t_1): conditional probability of a sick subject to have a positive test value.

Specificity of a test (t_2): conditional probability of a healthy subject to have a negative test value.

Accumulated incidence (KI): probability that a screened subject will contract atopic disease during the observation period.

The advantage of using the last three concepts above to express the probability of a child ending up in one of the *four screening groups* (TP, FP, FN and TN) is the freedom which they give us for isolating and calculating the effects of changes in KI, t_1 and t_2 (5, 14).

There are *three conventional groups* (no screening) formed after the possible development of symptoms and establishment of a diagnosis: 1) the children conventionally diagnosed as atopic within 6 years of birth can be expressed by the accumulated incidence, as above, 2) individuals who because of their symptoms have been examined but not considered atopic ("non-atopic"), and 3) children with no signs or symptoms of allergy ("healthy"). The distribution amongst the non-atopic and the healthy is estimated by a relationship (w) which assigns the share of non-atopics as the conditional probability of a child with symptoms being tested conventionally but who is not at present considered atopic.

The cost associated with each group can be divided into four main components: screening costs (s); prevention costs (r) consisting of all costs connected with the prevention and delaying of symptoms; treatment cost (b) defined in a broad sense; and finally the costs of conventional diagnosis (h) including various tests. Table 1 specifies the probability and actual costs associated with the seven defined groups.

It is now possible to compare the total costs of a certain screening programme with the total costs of alternative conventional detection. For each alternative, the expected costs for a newborn child will be calculated. The expected costs of a screening programme (S) will then be:

$$S = KI t_1 (s + h_1 + r_1 + G_1) + (1-KI) (1-t_2) (s + h_2 + r_2) + KI(1-t_1) (s + h_3 + b_3) + (1-KI) t_2 (s + h_4). \quad (\text{eq. } 1)$$

Similarly, the expected cost of the conventional method (K) is:

$$K = KI (h_3 + b_3) + (1-KI) w (h_6 + r_6). \quad (\text{eq. } 2)$$

The difference between S and K is the expected effect on total costs per child screened for the replacement of conventional detection by screening. Subtracting eq. 2 from eq. 1 yields:

$$S-K = KI [t_1 (s + h_1 + r_1 + b_1) + (1-t_1) (s + h_3 + b_3) - (h_3 + b_3)] + (1-KI) [(1-t_2) (s + h_2 + r_2) + t_2 (s + h_4) - w (h_6 + r_6)] \quad (\text{eq. } 3)$$

The expected change in total costs from screening a newborn child is the sum of two terms. The first term denotes the probability that a child will be atopic times the change in cost if this proves to be correct, while the second term denotes the probability that the child is healthy times the change in cost associated with a healthy child. If eq. 3 yields a negative value, screening is preferable to the conventional alternative and there is no need for a measure of benefit.

Screening based on the family history took only into account the history of parents and siblings (immediate family history).

The outcomes of the three different screening programmes are presented in Table 2.

Estimation of costs

Cost estimates have been made for the four different categories, and three general points must be made:

Firstly, the estimated cost for a child in an outcome group will be an average cost expressed as an expected value. Secondly, most of the costs (except the screening costs) will occur in different periods. Consequently, all costs have been discounted at a rate of 4%, but calculations at 0 and 10% have also been made. The presented cost figures are therefore present values. Thirdly, estimates of different cost components had to be made, with varying degrees of certainty, on the basis of available statistics.

In view of the above considerations cost estimates will only encompass monetary costs, independent of their distribution. Many of the private costs, e.g. medication and hygiene, can

be subsidized by the Swedish authorities. However, this has no bearing on the present study, which is confined to the social effectiveness of screening and not to the problem of who is paying what. The latter question, however, is of great importance for patient compliance. For the purpose of this study, we assumed complete compliance to preventive measures. Furthermore, all cost estimates end at 6 years of age and it is assumed that the accumulated incidence of atopic diseases at this age will be independent of whether preventive measures have been taken or not. Finally, all costs are estimated according to the price level prevailing at the beginning of 1985. Table 3 presents a summary of the cost components for the different outcome groups. A detailed description of all cost estimates will be found in Hjalte (6).

Screening costs comprise the cost of the screening test *per se* and the incremental cost associated with the sampling and testing. When a selected group of children are IgE-tested, the costs of selection must also be included (50 SEK). This selection cost is the only one incurred when screening of atopic allergy is made exclusively on the basis of family history.

Cost of prevention will depend on the recommendations made in the event of a positive screening test, and will consist of the cost of replacing deficiencies in breast-feeding and the cost of hygiene and avoiding allergens. Prolonged breast-feeding (6 months or more) has been shown effective in delaying the onset and reduc-

ing the severity of symptoms of allergic diseases (2, 3, 11). However, prolonged breast-feeding will not always be possible, and it is assumed that mothers will use replacement formulas containing no allergenic proteins, such as Nutramigen®. The incremental costs of such a replacement have been calculated. The costs of hygiene and avoidance of allergens have been estimated as both non-recurrent and recurrent, including incremental costs, e.g. cleaning, washing and special bed equipment.

The effect of these prevention measures has been assumed to delay the onset of atopic allergies by an average of 8 months and decrease existing treatment costs within the 6-year period by about 10%.

Costs of treatment will consist of the costs of hygiene and medication, and in-patient and out-patient care, and costs that reflect the value of production loss because parents must now and again stay at home to take care of their atopic children. Besides the non-recurrent hygiene costs at the age of onset, medication costs have also been estimated.

Some children, mainly those with asthma or eczema, will suffer so much from their disease that they will need periodic hospital care. Many atopic children will visit pediatric clinics each year as out-patients. The costs of in- and out-patient care will be substantial and are estimated to account for about a quarter of the total costs of all treatments. The main part (almost two thirds) of the treatment costs will represent

Table 3

Summary of cost estimates for the different outcome groups. All costs refer to an average child in each group. Present values in 1985 SEK. Rate of discount, 4%. Screening costs refer to the IgE-screening programme of all children

Outcome group	Screening costs (s)	Prevention costs (r)	Treatment costs (b)	Diagnosis costs (h)	Total costs
1. True positive	110	1723	15652	1174	18659
2. False positive	110	1621	-	469	2200
3. False negative	110	-	11037	1062	12209
4. True negative	110	-	-	212	322
5. Conventional atopic	-	-	14630	1174	15854
6. Non-atopic	-	971	-	1062	2033
7. Healthy	-	-	-	-	-

the value of production loss. Although most of the private loss will be covered by the Swedish social insurance system it will have great bearing on the social costs.

Some of the cost estimates are based on an interview study focusing on the costs involved with an atopic child in 41 families referred to a pediatric allergy department during 1985 (Lundkvist, Westergren & Malmesjö, in manuscript).

Cost of conventional diagnosis will include the costs involved in consultations with doctors, nurses and others in order to confirm the atopic disease and the specific allergens to which a child reacts. These costs will reflect the costs of visits and various tests, e.g. skin tests and RAST, and will be distributed between the time of onset and 6 years of age.

RESULTS

Table 4 presents the main results. The expected costs of both IgE-screening programmes will be lower than those of the conventional alternative. The second alternative, where the screened children were selected, accounts for the greatest cost reduction, whereas the screening programme based solely on family history will not lead to a reduction in costs. The importance of the selected discount rate of 4% has also been studied. In Table 4 the present values of the cost differences are also shown for the alternative discount rates of 0 and 10%. None of these discount rates will change the main results.

The cost-reducing effect of the IgE-screening programmes will be due to the preventive mea-

sures recommended (and assumed undertaken) to those outcome groups who have a positive test value. 10% reduction in treatment costs because of the delayed onset by an average of 8 months has also been calculated. The results in Table 5 show that the assumed delay of onset in itself is enough to make IgE-screening cost-effective. Even without delay of onset, the screening programme which includes all children will still be cost-effective, whereas the second IgE-screening alternative will not. Without the cost reduction effect and delay of onset none of the screening programmes will be cost-effective.

Some of the cost components were analysed separately in order to find the values required for the cost analysis to break-even. For example, the price of the screening test *per se* is of little importance for the main results and could be almost three times higher before the IgE-screening would become ineffective.

DISCUSSION

Atopic allergy is characterized by an inherited disposition towards IgE-mediated allergy and increased tissue hyperreactivity (10). A high concentration of IgE may be found before there are symptoms of atopic disease, thus providing a means of allergy screening in healthy children and even in newborns (1, 2, 3, 4, 7, 8). A perfect screening test for atopic allergy would identify all subjects who will contract atopic

Table 4

Difference in expected cost per child between the three screening programmes and the conventional alternative. Present values in 1985, SEK. Rates of discount 0.4 and 10%

Screening programme	Difference in cost		
	0%	4%	10%
I IgE, all	-253	-208	-154
II IgE plus family history	-326	-267	-196
III Family history only	161	163	165

Table 5

Effects on present values per child for screenings I and II under different combinations of the assumed delay of onset and cost reduction. Present value in 1985 SEK. Rate of discount, 4%

Combination of effects	Present value	
	I	II
Delay of onset and cost reduction	-208	-267
No delay of onset but cost reduction	-16	33
Delay of onset but no cost reduction	-94	-88
No delay of onset and no cost reduction	117	243

disease. Unfortunately, no known screening test is that perfect. However, in the present material IgE-screening was shown to be cost effective in spite of its limited sensitivity (40%). We have, however, had some difficulties in finding relevant information on costs and have encountered various difficulties. As an example, treatment costs will differ considerably in relation to a shift in the time of onset, severity, duration and kind of allergic disease among the children. These costs are obviously difficult to calculate. Further investigations on this point are needed.

For the purpose of this study treatment costs had to be estimated, to some extent based on selected interviews. Likewise, the delay of onset of symptoms had to be estimated from available sources.

Fundamental to the whole concept of allergy screening in newborn infants is that preventive measures are effective. A thorough review of the literature shows that studies which are truly prospective and conscientiously evaluated (preferably performed blinded by an independent allergist) also show a reduction in atopic disease through extensive prevention programmes, including breast-feeding exclusively until the age of 6 months (11). However, there are also good studies which do not show this effect. This may depend upon an unintentional intake of non-human proteins being included in the breast milk. Preliminary results of an ongoing study of the effect of maternal diet during lactation shows a significant reduction at 9 months of age in the diet group compared to randomized control group (Hattevig et al, to be published).

Many recent studies have included environmental measures such as pet-free homes, and no animal products in bedding (11). To our knowledge the preventive effect of such measures has not been evaluated separately but it has been shown that early pet contact increased the risk for subsequent sensitization (12).

In this study, we had to assume 100% compliance to the recommendations. We know that occasional small doses of allergen are especially good sensitizers and less than 100% compliance regarding exclusive breast-feeding might jeopardize the whole idea of prevention. Naturally,

a lower compliance can explain the lack of effect of preventive measures in some of the large-scale studies (11).

A prerequisite for the cost-effectiveness of preventive measures is the ability to identify special risk groups where the probability of contracting atopic diseases is high. Only these groups would be recommended for special prevention. The cost for this prediction method is the cost of the screening test and might be regarded as high in a situation where all children are screened on a routine basis at the time of birth. On the other hand, this study shows that to focus only on this cost would be highly misleading in the long-term. In fact, if undertaken in Sweden, preventive measures will lower the expected total costs for atopic allergies before 6 years of age by about 20 million SEK (about 3 million US\$) per year. IgE-screening of atopic allergies in newborn children is an example where most of the cost-reduction effect will be of a private character. It is also true that the prevention costs, considered as an investment, will be private and financed by the parents of the atopic children. However, the direct screening costs will add to the public health care bill. Nevertheless, this increase should be more than compensated for by the reduction in expected future health care costs.

Screening would be justified on the basis of costs reduction alone. On the other hand, non-monetary costs incurred by a screening programme (e.g. anxiety and lack of understanding from relatives and friends) may sometimes be considerable thus reducing the value of prevention. It has, however, not been possible to consider such costs in this study. The savings are heavily dependent on total patient compliance.

It is not possible to compare the results of this cost-effectiveness study because no other studies of the economic value of screening of atopic allergy seem to exist. Allergy-related cost studies refer mainly to estimates of total costs primarily for asthma (9, 13, 15). The results of these other studies, however, are not entirely applicable to the evaluation of screening programmes.

REFERENCES

1. Busquet, J., Ménardo, J.-L., Viala, J.-L. & Michel, F.-B.: Predictive value of cord serum IgE determination on the development of "early-onset" atopy. *Ann Allergy* 51, 291-295, 1983.
2. Businco, L., Marchetti, F., Pellegrini, G., & Perlini, R.: Predictive value of cord blood IgE levels in "at risk" newborn babies and influence of type of feeding. *Clin. Allergy* 13, 503-508, 1983.
3. Chandra, R. K., Puri, S. & Cheema, P. S.: Predictive value of cord blood IgE in the development of atopic disease and role of breast-feeding in its prevention. *Clin. Allergy* 15, 517-522, 1985.
4. Croner, S., Kjellman, N.-I. M., Eriksson, B. & Roth, A.: IgE Screening in 1701 infants and the development of atopic disease during infancy. *Arch. Dis. Child* 57, 364-368, 1982.
5. Gravell, H. S. E., Simpson, P. R. & Chamberlain, J.: Breast cancer screening and health service cost. *J. Health Econ.* 1, 185-207, 1982.
6. Hjalte, K.: Efficiency of neonatal screening of atopic allergy (in Swedish). IHE Report 1985:10, Lund. The Swedish Institute for Health Economics, 1985.
8. Kjellman, N.-I. M. & Croner, S.: Cord blood IgE determination for allergy prediction - a follow-up to seven years of age in 1651 children. *Ann. Allergy* 54, 31-34, 1984.
9. Marion, R. J., Creer, T. L. & Reynolds, R. V. C.: Direct and indirect cost associated with the management of childhood asthma. *Ann. Allergy* 54, 31-34, 1985.
10. Nelson, H. S.: The atopic diseases. *Ann. Allergy* 55, 441-447, 1985.
11. Saarinen, U. M.: Prophylaxis for atopic disease. *Clin. Rev. Allergy* 2, 151-167, 1984.
12. Suoniemi, I. L., Björkstén, F. & Haahtela, T.: Dependence of immediate hypersensitivity in the adolescent period on factors encountered in infancy. *Allergy* 36, 263-268, 1981.
13. Thompson, S.: Astmasjukdomens samhällsekonomiska kostnader. IHE Report 1981:8, Lund. The Swedish Institute for Health Economics, 1981.
14. Weinstein, M. C., Fineberg, H. V., Elstein, A. S. et al.: Clinical decision analysis. W. B. Saunders, Philadelphia, 1980.
15. Young, P.: Asthma and allergies: An optimistic future. Washington D.C. U.S. Department of Health and Human Services. NIH Publication No. 80-388, March 1980.

Address:

Max Kjellman, M.D.
 Department of Pediatrics
 University Hospital
 S-581 85 Linköping
 Sweden

This document is a scanned copy of a printed document. No warranty is given about the accuracy of the copy. Users should refer to the original published version of the material.