Cost-effectiveness of antenatal screening for neonatal alloimmune thrombocytopenia


Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
The study examined three strategies of antenatal screening for neonatal alloimmune thrombocytopenia (NAIT) based on different levels of risk.

With the first strategy (level 1), human platelet antigen (HPA) 1a, negative women were tested for anti-HPA 1a antibodies around weeks 22 and 34 of gestation. All pregnant women with anti-HPA 1a antibodies were subjected to two ultrasonographic examinations and blood flow velocity measurements of the foetus between 28 and 36 weeks' gestation.

With the second strategy (level 2), only HPA 1a negative women with anti-HPA 1a antibody levels higher than 100 arbitrary units (AU)/mL at weeks 22 or 34 of gestation were offered follow-up as in the previous strategy.

With the third strategy (level 3), only women who carried both the HPA 1bb and HLA DRB3*0101 genotypes were tested for anti-HPA 1a antibodies in weeks 22 and 34, and all immunised women were subsequently followed-up.

Mothers at risk were offered an intervention that consisted of Caesarean section 2 to 4 weeks prior to term, with compatible platelets available for immediate transfusion in case the newborn was thrombocytopenic.

All these strategies were compared with no antenatal screening for NAIT.

Type of intervention
Screening.

Economic study type
Cost-utility analysis.

Study population
The study population comprised a hypothetical cohort of pregnant women.

Setting
The setting was secondary care. The economic study was carried out in Norway.

Dates to which data relate
The clinical data came from studies published between 2001 and 2006. Some data on resource use and costs were derived from studies published between 1999 and 2006. The price year was 2005.

Source of effectiveness data
The clinical data used in the model were:
the probabilities of HPA 1a negative platelet type among pregnant women, immunisation against HPA 1a antigen and severe NAIT in newborns,

the risk of neurological sequelae and death among those with severe NAIT,

drop-outs due to abortion,

women lost from the programme because of acute vaginal delivery,

life expectancy for children with or without sequelae.

Modelling
A decision analytic model was constructed to simulate the natural history of disease and subsequent patient management with the alternative strategies in a hypothetical cohort of 100,000 pregnant women. The structure of the decision tree pathways was extensively illustrated. The decision tree was identical for the three strategies. The possible events were immunisation against HPA 1a and the birth of children with or without NAIT. The terminal branches of the tree represented three possible health states. Specifically, healthy, disabled with intracranial haemorrhage (ICH), or dead. A lifetime time horizon was applied.

Sources searched to identify primary studies
Most of the clinical data were derived from a large study reporting the results of the screening and intervention programme implemented in three of the five health regions in Norway, covering 60% of the Norwegian population. Life expectancy in Norway was derived from national statistics, while life expectancy in babies borne with sequelae came from a published study. The risk for neurological sequelae and deaths among those with severe NAIT was based on data from a large review of the literature that explored the morbidity and mortality of reported cases of NAIT-related ICH. Some data were based on unpublished results from the aforementioned large Norwegian screening study.

Methods used to judge relevance and validity, and for extracting data
The Norwegian observational study was deliberately selected on the grounds that it was the most representative and valid study available on the epidemiology of disease and the impact of screening for the authors' context. The methods used to derive the other data were unclear. However, some data came from a study that was based on a large review of the literature. Original estimates were not combined as each study provided a single value.

Measure of benefits used in the economic analysis
The summary benefit measure was the quality-adjusted life-years (QALYs). These were estimated using the decision model. The utility weights used to calculate QALYs were derived from the Cost Effectiveness Analysis Registry, details of which were not given. The QALYs were discounted at an annual rate of 4%. The number of prevented NAIT-related deaths and sequelae was also reported as a further model output.

Direct costs
The cost/resource boundary of the analysis was that of the health care system. The cost categories included in the analysis were those associated with HPA 1 typing, HLA DRB3*0101 typing, anti-HPA 1a antibody detection, anti-HPA 1a antibody quantification, ultrasonographic examination and blood flow velocity measurements in the foetus (two examinations during pregnancy), delivery-related costs, treatment of severe NAIT, and the lifetime medical costs for a disabled child. The unit costs and the quantities of resources used were presented separately only for some categories of costs, other costs being reported as macro-categories. Screening and intervention costs were estimated using customary charges for laboratory tests and diagnosis-related group (DRG) cost lists for in-hospital care. Delivery-related costs were obtained from a published study. The costs of NAIT-related complications were derived from a European study whilst, in view of the lack of Norwegian estimates, lifetime medical costs for survivors came from a published study conducted in the USA. The long-term costs were discounted at an annual rate of 4%. The price year was 2005.
Statistical analysis of costs
No statistical analysis of the costs or quantities was performed.

Indirect Costs
Productivity costs were not considered.

Currency
The costs were initially measured in Norwegian kroner (NOK) and then converted to euros (EUR). The conversion rate was EUR 1 = NOK 8.11.

Sensitivity analysis
A univariate sensitivity analysis was undertaken to investigate the robustness of the cost-utility ratios to variations in the clinical and economic inputs of the model. The estimates were varied across published ranges. A probabilistic Monte Carlo simulation with 10,000 iterations was also performed by assigning probabilistic distributions to the model inputs. Details of these probabilistic distributions were given.

Estimated benefits used in the economic analysis
Compared with no screening, screening strategies (regardless of the level of risk selected) prevented approximately 80% of NAIT-related deaths and sequelae.

The discounted number of QALYs gained from screening 100,000 pregnant women ranged from 210 to 230 (770 to 830 undiscounted), depending on the screening strategy implemented (the result for the individual strategies were not reported).

Cost results
The total costs of a screening and intervention programme for 100,000 women were approximately EUR 910,000 for level 1 screening, EUR 620,000 for level 2 screening and EUR 850,000 for level 3 screening.

The estimated total cost (accounting for avoided complications) for 100,000 pregnancies was EUR 3.52 million with no screening, EUR 1.85 million with screening at level 1, EUR 1.72 million at level 2, and EUR 1.76 million at level 3.

Synthesis of costs and benefits
An incremental analysis was carried out to combine the costs and benefits of the alternative strategies.

The incremental analysis showed that all screening programmes were dominant over no screening, which was both less effective and more expensive. This result was mainly due to the reductions in the occurrence of cerebral sequelae and its associated cost-savings.

The sensitivity analysis showed that the three screening strategies were similar in terms of the costs and QALYs. The probabilistic sensitivity analysis revealed that, at a societal willingness-to-pay of between EUR 10,000 and EUR 100,000, strategy 3 had the greatest probability of being cost-effective. Strategy 2 was preferred at lower thresholds. Using the recommended threshold value of EUR 53,000 per QALY in Norway, the probability that screening was cost-effective approached 100% for all strategies.

The deterministic sensitivity analysis suggested that screening was cost-saving over no screening as long as HPA 1 typing cost less than EUR 20 per test. Overall, the results of the analysis were robust to the variations considered in the sensitivity analysis.
Authors' conclusions

The antenatal screening programme for neonatal alloimmune thrombocytopenia (NAIT) was found to be cost-effective in comparison with no screening. However, the net costs and benefits of the three strategies were fairly similar, and the study did not give clear guidance as to which one would be preferable.

CRD COMMENTARY - Selection of comparators

The rationale for the choice of the comparators was clear in that all possible strategies of screening for NAIT were considered, including the current screening strategy implemented in Norway. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness

The sources of the clinical data were given. No systematic search for data was reported, but a justification for the selection of some sources was given. National data were used for most estimates, which was appropriate. However, limited information on the design and characteristics of some primary studies was given, which limits the possibility of assessing their validity.

Validity of estimate of measure of benefit

The benefit measure (QALYs) was modelled. The source of the utility values and quality of life estimates were reported whereas details of the methodology used to elicit these values were not. The benefits were discounted as recommended by international guidelines, but undiscounted results were also reported. Other model outputs were also given.

Validity of estimate of costs

The categories of costs included in the analysis were consistent with the perspective adopted in the study. Productivity costs were not included because of a lack of reliable data. A breakdown of cost items for screening costs was given, but the unit costs and quantities of resources used were not presented separately for some costs that were reported as macro-categories. The sources of the costs were given. Statistical analyses of the costs were not performed, but the impact of variations in some cost items was considered and a probabilistic sensitivity analysis was conducted by assigning appropriate distributions to cost items. Discounting was performed. The price year was reported, which will facilitate deflation exercises in other time periods.

Other issues

The authors stated that their results differed from those found in other published studies and discussed potential explanations for these discrepancies. The issue of generalisability of the study results to other settings was extensively addressed in the sensitivity analysis. The authors noted some limitations of their analysis, such as the lack of published prospective data on ICH, the use of uncertain long-term costs for children with severe neurological sequelae, and the exclusion of any negative consequence of screening (e.g. anxiety of pregnant women).

Implications of the study

The authors stated that their findings might support health authorities considering a national screening programme for NAIT.

Source of funding

None stated.

Bibliographic details

Other publications of related interest

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Indexing Status

Subject indexing assigned by NLM

MeSH

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