The cost-effectiveness of antenatal varicella screening with post-partum vaccination of susceptibles

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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
Two antenatal varicella screening strategies with potential postpartum vaccination of susceptible individuals were examined. One strategy was an initial verbal screen followed by a serological screen for those with a negative or uncertain history (V+S screen), while the other was a universal serological screening (SER screen).

The V+S screen involved verbally screening first-time pregnant women and serotesting those with negative or uncertain histories, followed by postpartum vaccination of seronegative women.

The SER screen involved the serologic screening of first-time pregnant women, regardless of history, and postpartum vaccination of those with negative serology.

Type of intervention
Screening.

Economic study type
Cost-effectiveness analysis and cost-utility analysis.

Study population
The study population comprised a hypothetical cohort of first-time pregnant women aged 15 to 44 years. Two different cohorts of UK- and Bangladesh-born women were considered.

Setting
The setting was primary care. The economic study was carried out in the UK.

Dates to which data relate
Most of the effectiveness data and some resource use data were derived from studies published between 1952 and 2004. No dates for other resource use data were explicitly reported. The costs were estimated using 2002/03 prices.

Source of effectiveness data
The effectiveness evidence was derived from a synthesis of published studies.

Modelling
A decision tree was constructed to assess the costs and benefits of the three strategies examined in the study. Limited information on the characteristics of the tree was reported. The time horizon of the model appears to have been lifetime. The authors stated that the model took the hypothesis that infection acquired during pregnancy is associated with the same risk of congenital varicella syndrome (CVS) or neonatal disease, regardless of previous prophylaxis, into
Outcomes assessed in the review
The outcomes assessed from the literature were:

data on force of infection in both parous and non-parous women;
seroprevalence data;
the sensitivity and specificity of both verbal screening and serologic testing;
vaccine efficacy;
VZIG efficacy;
primary care consultations for woman with varicella;
the probabilities of hospitalisation in both non-pregnant women and pregnant women;
the length of stay in hospital;
the probabilities of severe disease given vaccination and given VZIG;
the probability of death following hospitalisation;
the probability of CVS in the first trimester; and
the probability of neonatal varicella following infection around term.

Study designs and other criteria for inclusion in the review
It appears that the primary studies have been identified selectively rather than by a systematic review of the literature. Serological data came from an unpublished study, while other data came from the Office of National Statistics, test manufacturers, and the Hospitalisation Episode Statistics database.

Sources searched to identify primary studies
Not reported.

Criteria used to ensure the validity of primary studies
Not reported.

Methods used to judge relevance and validity, and for extracting data
Not reported.

Number of primary studies included
Eleven sources of clinical data were used.

Methods of combining primary studies
Not relevant.
Investigation of differences between primary studies
Not reported.

Results of the review
The force of infection was 0.15 in parous women and 0.07 in non-parous women.

The rate of seroprevalence was 0.95.

The secondary attack rate was 0.61.

The sensitivity of verbal screening was 0.90 and the specificity was 0.50.

The sensitivity of serologic testing was 0.97 and the specificity was 1.

Vaccine efficacy was 0.75.

VZIG efficacy was 0.56.

The average number of primary care consultations for woman with varicella was 1.14.

The probability of hospitalisation was 0.01 in non-pregnant women and 0.03 in pregnant women.

The length of stay in hospital was 2.7 days for both pregnant and non-pregnant women.

The probability of severe disease given vaccination was 0.03.

The probability of severe disease given VZIG was 0.

The probability of death following hospitalisation was 0.002.

The probability of CVS in the first trimester was 0.012.

The probability of neonatal varicella following infection around term was 0.624.

Measure of benefits used in the economic analysis
The summary benefit measure used was the expected number of cases of varicella in pregnancy. This was estimated from the decision model. Other model outputs were also reported. These included varicella cases, varicella-related deaths, children born with CVS, and neonatal varicella cases. The benefits were discounted at an annual rate of 3.5%.

Direct costs
The analysis of the costs was carried out from the perspective of the NHS. It included the costs of general practitioner (GP) consultations, nurse consultations, serologic tests, vaccination, VZIG, primary care drugs, inpatient drugs, inpatient stay (infectious diseases), anomaly scans, acyclovir treatment for neonates with varicella, inpatient stay for neonatal varicella, and the treatment of CVS. The unit costs were presented for all items, but quantities of resources used were reported only for some costs. Further, the costs associated with CVS were presented as a macro-category and a detailed breakdown of the cost categories was not reported. The resource use data appear to have been derived from authors' opinions and some published sources. The costs came from typical NHS sources (the British National Formulary and Personal Social Services Research Unit), the Royal London Hospital, GP practices in London, and a published study. The base-case analysis assumed that the verbal screen was cost-free. Discounting was relevant, as the costs were incurred during a long timeframe, and an annual discount rate of 3.5% was applied. The costs used in the model were estimated at 2002/03 rates, and costs established in previous years were inflated to 2002/03 values using the Hospital and Community Health Services Pay and Prices Index.
Statistical analysis of costs
Statistical analyses of the costs were not performed.

Indirect Costs
The indirect costs were not considered.

Currency
UK pounds sterling ( ).

Sensitivity analysis
A univariate sensitivity analysis was carried out by varying clinical and economic model inputs. The ranges were mostly obtained from published sources. Alternative scenarios, including the use of a different serological test, were also considered.

Estimated benefits used in the economic analysis
The current burden of varicella was estimated. The model predicted:

- an incidence of 262 varicella cases per 100,000 person-years (239 in UK-born women and 598 in Bangladesh-born women), with 10 cases occurring during pregnancy (9.1 in UK-born women and 22.8 in Bangladesh-born women),
- 0.004 varicella-related deaths (0.003 in UK-born women and 0.01 in Bangladesh-born women),
- 0.06 children born with CVS (0.1 in UK-born women and 0.1 in Bangladesh-born women), and
- 0.16 cases of neonatal varicella (0.1 in UK-born women and 0.4 in Bangladesh-born women).

The overall number of varicella cases in pregnancy per 100,000 women screened was:

- 98 (81 in UK-born women and 272 in Bangladesh-born women) with the current strategy,
- 31 (25 in UK-born women and 85 in Bangladesh-born women) with the SER screen, and
- 77 (63 in UK-born women and 213 in Bangladesh-born women) with the V+S screen.

Cost results
The current economic burden of disease was obtained from the decision model. It amounted to 69,074 for total varicella costs, 9,748 for adult varicella infection costs, 25,204 for CVS costs, 742 for neonatal varicella costs, and 27,425 for VZIG costs (including administration) per 100,000 person-years.

The total costs per 100,000 persons screened were 728,363 with the current strategy, 1,770,404 with the SER screen, and 570,293 with the V+S screen.

The total costs in UK-born women were 643,485 with the current strategy, 1,711,629 with the SER screen, and 495,252 with the V+S screen.

The total costs in Bangladesh-born women were 1,581,166 with the current strategy, 2,360,934 with the SER screen, and 1,324,257 with the V+S screen.

Synthesis of costs and benefits
Incremental cost-effectiveness ratios were calculated to combine the costs and benefits of the alternative strategies.
V+S screening dominated the current strategy, which turned out to be more costly and less effective in reducing varicella cases during pregnancy.

The incremental cost per additional varicella infection in pregnancy averted with serological screening over verbal then serological screening was 15,441 (19,205 and 4,176 for UK and Bangladeshi women, respectively).

For serological screening to be considered cost-effective using the widely accepted threshold of 30,000 per quality-adjusted life-year (QALY) gained in a cost-utility analysis, a varicella infection during pregnancy would need to produce an average QALY loss of 0.51 (0.64 and 0.14 for UK and Bangladesh-born women, respectively).

When the analysis was restricted to women aged younger than 30 years, for Bangladesh-born women the cost per additional case in pregnancy avoided with routine serological screening over verbal screening ranged from 604 for women aged 20 - 24 years to 2,082 for those aged 25 - 29. Moreover, such a programme would be deemed cost-effective for QALY losses of 0.02 to 0.07 per case in pregnancy (for women aged 20 to 24 years and 25 to 29, respectively), which might be considered a realistic scenario. For UK-born women younger than 30 years, the QALY losses associated with varicella in pregnancy would have to be far higher at 0.26 to 0.43 per case, thus screening might not be cost-effective.

The sensitivity analysis showed that the results for Bangladesh-born women were sensitive to the force of infection and also the specificity and sensitivity of verbal screening. In particular, with a considerably lower force of infection or specificity and sensitivity than that assumed in the model, the V+S screen strategy was no longer cost-saving. In the subgroup of UK-born women, the base-case results were sensitive to the proportion of pregnant women seeking medical advice following exposure to varicella. The lower the proportion of women seeking advice, the more cost-saving the current strategy became. Changes in other variables or alternative scenarios did not alter the conclusions of the base-case analysis.

Authors' conclusions
Both screening and vaccination strategies prevented varicella cases in pregnant women in comparison with the current strategy in the UK. Specifically, verbal screening followed by serological screening could be cost-saving to the National Health Service (NHS) for both UK- and Bangladesh-born women. Universal serological screening was more costly but more effective than verbal screening, and it could be cost-effective to universally screen younger immigrant mothers.

CRD COMMENTARY - Selection of comparators
The choice of the comparator was appropriate since the current standard of care was compared with two alternative strategies for pregnant women at risk of varicella. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness evidence was derived from selectively identified studies. A systematic review of the literature does not appear to have been performed. There was limited information on the studies used to estimate the clinical inputs. The methods used to extract and combine the primary estimates were not described, and the issue of heterogeneity across the primary studies was not addressed. The issue of variability in the data was addressed in the sensitivity and scenario analyses. The authors noted that a limitation of the analysis was the lack of data on fertility rates by parity.

Validity of estimate of measure of benefit
The summary benefit measure was specific to the disease considered in the study. It is not comparable with the benefits of other health care interventions. QALYs could not be calculated directly because of the lack of published data associated with utility values for varicella in pregnancy. However, the minimum changes in QALY required for the interventions to be cost-effective were presented. Discounting was applied, as UK guidelines recommend.
Validity of estimate of costs
The analysis of the costs was consistent with the perspectives adopted in the study. The unit costs were presented separately from the quantities of resources for only some items, and this might limit the possibility of replicating the analysis in other settings. Some costs were presented as macro-categories. The authors investigated the issue of variability in the cost estimates in the sensitivity analysis. However, statistical analyses of the costs were not performed. The authors reported the price year, which will simplify reflation exercises in other settings.

Other issues
The authors did not make extensive comparisons of their findings with those from other studies. The issue of the generalisability of the study results to other settings was implicitly addressed in the sensitivity analyses, where alternative estimates for costs and probability rates were considered. The study referred to pregnant women and this was reflected in the conclusions of the analysis. A positive aspect of the study was the sub-group analysis by country of birth and age. More details of the decision model used to obtain the costs and benefits of each strategy would have been useful in assessing the appropriateness of some assumptions.

Implications of the study
The study results suggested that the verbal screening of all first-time pregnant women followed by serological screening of those with a negative or uncertain history could prevent cases in pregnancy and be cost-saving from the perspective of the NHS. Routine serological screening could be cost-effective for younger mothers who were born in countries where varicella infection in childhood is less common.

Source of funding
None stated.

Bibliographic details

PubMedID
16236401

DOI
10.1016/j.vaccine.2005.09.028

Other publications of related interest


Indexing Status
Subject indexing assigned by NLM

MeSH
Adolescent; Adult; Age Factors; Antibodies, Viral /blood; Bangladesh /epidemiology /ethnology; Chickenpox /diagnosis /immunology /prevention & control; Chickenpox Vaccine /administration & dosage; Cohort Studies; Cost-Benefit