The cost-effectiveness of screening the US blood supply for West Nile virus

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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
Six strategies for the screening of blood supplies for West Nile virus using nucleic acid amplification testing were examined. The screening strategies took minipool (pools of 6 to 16 donations) versus individual donation testing into consideration, as well as the geographic and seasonal nature of West Nile virus activity.

Strategy 1 was no screening
Strategy 2 was national minipool testing for half of the year (1/2 minipool).
Strategy 3 was national minipool testing over the entire year (1 minipool).
Strategy 4 was individual donation testing for one third of the year in one quarter of the country, with minipool testing for the rest of the country and the remainder of the year (1/12 individual donation + 11/12 minipool).
Strategy 5 was individual donation testing for the entire year in one quarter of the country, with minipool testing for the rest of the country (1/4 individual donation + 3/4 minipool).
Strategy 6 was individual donation testing for one third of the year in the entire country, with minipool testing for the remainder of the year (1/3 individual donation + 2/3 minipool).
Strategy 7 was national individual donation testing over the entire year (1 individual donation).

Type of intervention
Screening.

Economic study type
Cost-utility analysis.

Study population
The study population was a hypothetical cohort of donated blood, including components such as erythrocytes, platelets and fresh-frozen plasma.

Setting
The setting was a blood bank. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness data were derived from studies published between 1993 and 2005. No dates for resource consumption were explicitly reported. The price year was 2003.
Source of effectiveness data
The effectiveness evidence was derived from a synthesis of completed studies and authors’ assumptions.

Modelling
A Markov cohort simulation model was constructed to assess the costs and benefits associated with the 6 screening strategies in comparison with no screening. Each patient in the cohort received one unit of whole blood or an equivalent amount of component (erythrocytes, platelets, or fresh-frozen plasma) from a single donor. The core structure of the model was reported. In particular, regardless of the type of screening (or no screening strategy), patients could receive infected or non-infected blood units. In case of no transmission, patients could survive or die due to the transfusion. In case of disease transmission, patients (both those who were and were not immunocompromised) could develop either asymptomatic infection (and then survive or die depending on post-transfusion mortality) or symptomatic infection. The latter could be characterised by either fever (and then patients could survive or die due to post-transfusion mortality) or neuroinvasive disease (and patients could survive, develop neurologic sequelae, or die due to post-transfusion mortality). A lifetime horizon was used.

Outcomes assessed in the review
The outcomes estimated from the literature were:

- the death rates,
- the probabilities of West Nile virus in donated blood,
- the accuracy of the screening test,
- the probability of recovery after neuroinvasive disease, and
- the quality of life (QoL) associated with neuroinvasive West Nile virus infection.

Study designs and other criteria for inclusion in the review
It was unclear whether a systematic review of the literature was undertaken to identify primary studies. Much of the data came from the US Centers for Disease Control and Prevention (CDC) and from a study of West Nile virus infection. Since QoL estimates were not available for persons who required a blood transfusion or for the health states in people with West Nile virus infection, weights based on data presented in the catalogue of preference scores from the US Cost Effectiveness Registry were used. Few details of the other primary studies were reported.

Sources searched to identify primary studies
Not stated.

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

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

Number of primary studies included
Eleven primary studies provided the clinical evidence used in the model.
Methods of combining primary studies
A narrative approach appears to have been used to combine the primary estimates.

Investigation of differences between primary studies
Not stated.

Results of the review
The donation to blood component adjustment factor was 1.45 (range: 1 - 1.9).

The probability of West Nile virus transmission in a donated blood unit was 1,000/13.6 million donations.

The probability of West Nile virus in a donated blood product tested by minipool nucleic acid testing was 10% (range: 6 - 14).

The probability of West Nile virus in a donated blood product tested by individual-donation nucleic acid testing was 1% (range: 0.6 - 2.5).

The age at transfusion was 60 years.

The probability of post-transfusion mortality was 31.5% (range: 21 - 43) during the first year after transfusion, 14% (range: 10 - 18) during the second year after transfusion, and 10% after the second year after transfusion.

The probability of symptomatic West Nile virus infection was 0.20.

The probability of neuroinvasive West Nile virus infection was 0.01.

The increased risk for death after transfusion for persons aged 55 years or older who develop neuroinvasive disease was 0.127.

The percentage of components transfused to persons with immunocompromise was 25% (range: 10 - 40).

The probability of recovery after neuroinvasive disease was 0.227.

The average QoL preference weight for persons with neuroinvasive West Nile virus infection was 0.75.

Methods used to derive estimates of effectiveness
The authors made some assumptions that were used in the decision model.

Estimates of effectiveness and key assumptions
The probability of symptomatic West Nile virus infection for immunocompromised persons was 0.40.

The increased risk for death after transfusion for persons aged 55 years or older who develop neuroinvasive disease and have underlying immunocompromise was 0.254.

The average QoL preference weight for persons receiving a transfusion was 0.90.

Measure of benefits used in the economic analysis
The summary benefit measure used was the quality-adjusted life-years (QALYs). These were estimated by combining survival data with QoL estimates. All data were derived from the literature or were based on authors' assumptions. An annual discount rate of 3% was applied.
Direct costs
A societal perspective was adopted in the analysis. The direct costs included were for minipool and individual-
donation nucleic acid testing (reagent, labour and facility), outpatient management for symptomatic West Nile virus,
transportation and miscellaneous services for symptomatic West Nile virus, rehabilitation for neuroinvasive West Nile
virus infection, and inpatient services for West Nile virus infection. The unit costs and the quantities of resources used
were generally not presented separately, although the unit costs associated with each test were reported. The source of
the resource use data was unclear, although treatment patterns might have been based on authors’ opinions. The costs
came from multiple sources such as published studies and personal communications. All costs were updated to 2003
values using the medical care component of the Consumer Price Index. Discounting was relevant, owing to the long
timeframe of the analysis, and an annual rate of 3% was applied.

Statistical analysis of costs
The costs were treated deterministically in the base-case, but probabilistic distributions were assigned in the sensitivity
analysis.

Indirect Costs
The indirect costs (i.e. productivity losses associated with both recovering from symptomatic West Nile virus infection
and mortality of a 60-year-old person) were included in the economic evaluation because a societal perspective was
adopted. The unit costs were not presented separately from the quantities of resources used. The costs were estimated
on the basis of published data. As in the analysis of the direct costs, the price year was 2003 and an annual discount
rate of 3% was applied.

Currency
US dollars ($).

Sensitivity analysis
Univariate sensitivity analyses were carried out on key model inputs using published ranges of values. A probabilistic
sensitivity analysis was also performed. In general, triangular distributions were used for both the costs and
probabilities of events.

Estimated benefits used in the economic analysis
The lifetime QALYs per patient associated with no screening were 3.85. The extra QALYs gained over no screening
were 0.0000155 with strategy 2, 0.0000155 with strategy 3, 0.0000156 with strategy 4, 0.0000158 with strategy 5,
0.000016 with strategy 6 and 0.000017 with strategy 7.

Cost results
The lifetime costs per patient associated with no screening were $0.19.

The extra costs over no screening were $3.84 with strategy 2, $6.77 with strategy 3, $7.36 with strategy 4, $8.75 with
strategy 5, $9.98 with strategy 6 and $13.84 with strategy 7.

Synthesis of costs and benefits
Incremental cost-utility ratios (additional cost per QALY gained) were calculated to combine the costs and benefits of
the alternative screening strategies.

In comparison with no screening, the additional cost per QALY gained was $272,000 with strategy 2, $483,000 with
strategy 3, $520,000 with strategy 4, $609,000 with strategy 5, $688,000 with strategy 6 and $897,000 with strategy 7.
In comparison with the next less effective strategy, the additional cost per QALY gained was $272,000 with strategy 2, $31,900,000 with strategy 4, $6,237,000 with strategy 5, $11,028,000 with strategy 6 and $4,330,000 with strategy 7. Strategy 3 was dominated by strategy 2, which was less costly but equally effective.

The univariate sensitivity analysis showed that the most important influences on the cost-effectiveness of screening donated blood for West Nile virus were the prevalence of West Nile virus-positive donations and the cost of minipool and individual donation testing. If the residual risk for West Nile virus infection increases to 1,000 per 1 million components under the no screening strategy, any screening strategy would be highly cost-effective. If the residual risk with no screening decreases to less than 25 per 1 million components, the cost per QALY of any strategy would exceed $1 million.

The probabilistic sensitivity analysis was used to generate acceptability curves. These suggested that it is highly unlikely that the additional cost per QALY gained of any screening strategy would be lower than $150,000.

Authors' conclusions
The strategy of minipool testing for half of the year was the most cost-effective option for West Nile virus screening in donated blood. However, the eradication of West Nile virus from blood supplies was an inefficient use of societal resources since it did not compare favourably with the cost-effectiveness of other health care interventions. On the other hand, testing for West Nile virus was more cost-effective than nucleic acid testing for the human immunodeficiency virus and hepatitis C virus.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparators was clear. One of the strategy (strategy 4: 1/12 individual donation + 11/12 minipool) reflected standard care in the authors' setting. Reasons for the selection of the other comparators were clearly stated. The basic comparator was no screening, which appears to have been appropriate. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness data were estimated from published studies. It was not stated whether a systematic review of the literature was undertaken to identify primary studies, which appear to have been included selectively. Most of the evidence came from CDC sources, although there was limited information on the studies used to estimate clinical inputs. Further, the authors made some assumptions because of the lack of published evidence or uncertainty in some data. The issue of variability in the data was addressed in the probabilistic sensitivity analysis.

Validity of estimate of measure of benefit
The benefit measure used in the analysis was appropriate as QALYs capture the impact of the interventions on the most relevant dimensions of care (i.e. survival and QoL). In addition, QALYs are comparable with the benefits of other health care interventions. Discounting was applied and the impact of alternative discount rates was assessed in the sensitivity analysis. The source of the utility weights was stated. The utility associated with a person requiring a transfusion was based on an assumption since there was a lack of data.

Validity of estimate of costs
The selection of a societal perspective was appropriate and all the relevant categories of costs were considered. Indirect costs, which incorporated not only absenteeism from work due to recovering from disease but also the value of a death, were also included. A detailed breakdown of the cost items was not provided and the costs, in general, were presented as macro-categories. Resource use data were not given, which limits the possibility of replicating the cost analysis in other settings. Most of the costs came from published studies, but limited information on these studies was provided. The use of probabilistic sensitivity analyses enhances the robustness of the cost estimates used in the model. The price year was reported, which aids reflation exercises in other time periods.
Other issues
The authors did not compare their findings with those from other studies. They also did not explicitly address the issue of the generalisability of the study results to other settings. However, extensive sensitivity analyses were carried out, which enhance in part the external validity of the study. The authors noted some limitations of their analysis. First, outcomes of West Nile virus infection from the general population were used. Second, there was some uncertainty in the cost for West Nile virus minipool and individual donation testing, as well in the cost of illness. Third, the analysis assumed that epidemic activity of West Nile virus was seasonally and geographically focused.

Implications of the study
The study results did not support the implementation of screening programmes for the detection of West Nile virus in donated blood.

Source of funding
Supported by an unrestricted grant from Blood Systems Foundation.

Bibliographic details

PubMedID
16204161

Other publications of related interest


Indexing Status
Subject indexing assigned by NLM

MeSH
Blood Transfusion /economics /standards; Blood-Borne Pathogens /isolation & purification; Computer Simulation; Cost-Benefit Analysis; Decision Trees; Humans; Markov Chains; Middle Aged; Nucleic Acid Amplification Techniques; Prevalence; Quality-Adjusted Life Years; United States /epidemiology; West Nile Fever /epidemiology /transmission; West Nile virus /isolation & purification

AccessionNumber
22005008381

Date bibliographic record published
31/05/2006

Date abstract record published
31/05/2006