Cost-effectiveness analysis of universal childhood hepatitis A vaccination in Brazil: regional analyses according to the endemic context

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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.

CRD summary
The objective was to assess the cost-effectiveness of a universal childhood hepatitis A vaccination programme in Brazil. The authors concluded that a universal childhood vaccination programme could be a dominant (cost reducing and outcome improving) strategy in all regions of Brazil. The study was based on valid methodology but more details surrounding the choice of evidence may have been useful. The authors conclusions seem reasonable.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
To assess the cost-effectiveness of a universal childhood hepatitis A vaccination programme in Brazil.

Interventions
Two strategies were compared: universal childhood hepatitis A vaccination programme in the second year of life and the current strategy (vaccination of high risk persons). Universal vaccination comprised two vaccine doses administered six months apart in the second year of life. High risk individuals included patients at risk of serious illness such as those with chronic liver disease, coagulopathy, haemoglobinopathy, cystic fibrosis, persons aged 13 years or less with HIV infection, carriers of hepatitis B and C virus, immunocompromised hosts and candidates for donor and transplant organs.

Location/setting
Brazil/outpatient/in-patient

Methods
Analytical approach:
An age- and time-dependent dynamic model was developed to estimate incidence of hepatitis A over a 30-year period. The model accounted for the herd effects of a universal immunisation programme. The analysis was run separately for low endemicity areas (North, Northeast and Midwest macro-regions, referred to as the North model) and high endemicity areas (South and Southeast regions, referred to as the South model). A decision model was used to estimate health services utilisation and costs of the two strategies. The authors stated that the analysis was conducted from health system and societal perspectives.

Effectiveness data:
Various sources were used to derive estimates for prevalence of hepatitis A, age-specific proportions of icteric cases, vaccine coverage, wastage rates and herd effects. These included primary data collection, Nation Health Information Systems, literature and authors’ assumptions. Endemicity estimates for hepatitis A were based on data from a nationwide population survey of seroprevalence of hepatitis conducted across the 27 Brazilian state capitals. The authors stated that the base case assumed effective coverage of 85% (94% vaccine efficacy and 90% vaccination coverage) and wastage rate of 5%. Waning immunity was not considered. The model incorporated a variable force of infection accounting for herd effects of a universal immunisation programme. The current vaccine strategy was assumed to have no effects on transmission of hepatitis A due to its low coverage.

Monetary benefit and utility valuations:
Measure of benefit:
The benefit was measured in terms of cases averted, deaths averted and life-years saved. Future benefits were discounted at 5%.

Cost data:
Two perspectives were presented. The analysis conducted from the health system perspective included direct medical costs such as medical visits, diagnostics tests, medications and hospitalisations (including liver transplantation and follow-up post-transplantation). The analysis conducted from the societal perspective incorporated family transportation costs and indirect costs (lost productivity) and all direct medical costs. Lost productivity was considered for the patient or caregivers (assumed to be the mother) for children aged under 15 years. Lost productivity was calculated by multiplying the estimated number of working days lost by the national average wage for women. Costs were derived from various sources such as the Brazilian Medical Association, Brazilian National Immunization Program (2008), Hospitalization Information System registers, a national household survey, National Agency of Transplantation, State of Sao Paulo System for Transplantation, Notifiable Diseases Information System, authors' assumptions and expert opinion. Costs were reported in 2008 Brazilian Real (R$). Future costs were discounted at 5%.

Analysis of uncertainty:
Due to uncertainty around baseline parameter values, univariate and bivariate sensitivity analysis on key parameters, such as the frequency of icteric cases, rates of hospitalisation, liver transplantation, vaccine price and outpatient care costs. A reduction of 1% a year in the incidence of hepatitis A due to improvement in sanitary conditions was considered in the sensitivity analyses.

Results
World Health Organisation (WHO) criteria for DALYs (disability-adjusted life-years) averted related to country GDP (gross domestic product) was used as a threshold for cost-effectiveness. Results were presented in full in the paper; only life-years gained outcomes and societal costs are presented here.

For the North model (low endemicity), compared to standard care, universal vaccination resulted in 14,263 life-years gained (67% reduction in life-years lost). From a societal perspective standard care disease treatment cost was R$7,994,666,912 and universal vaccination disease treatment cost was R$4,146,691,719 (48% reduction). The intervention cost (cost of vaccine plus administration, accounting for wastage and coverage) for the current strategy was R$13,449,071 and the universal vaccination intervention cost was R$1,563,205,826.

For the South model (high endemicity) universal vaccination resulted in 26,153 life-years gained (62% reduction in life years lost). The current vaccination strategy disease treatment cost was R$13,863,427,939 and universal vaccination disease treatment cost was R$7,082,620,447 (49% reduction). The intervention cost was R$62,496,666 for current practice and R$1,512,334,409 for universal vaccination.

Universal vaccination was the dominant strategy (more effective and less expensive than the current vaccination strategy) for the base case analysis under both perspectives and for all regions of Brazil.

The intervention remained dominant for all of the bivariate sensitivity analyses and for most of the univariate sensitivity analyses. The results were most sensitive to changes in the percentage of symptomatic infection, vaccine price and outpatient costs. The results in the South model were more robust than the North and national models.

Authors’ conclusions
The authors concluded that a universal childhood vaccination programme could be a dominant (cost reducing and outcome improving) strategy in all regions of Brazil.

CRD commentary
Interventions:
The intervention seemed appropriate and the most appropriate comparator (current practice) was incorporated. Some discussion around the move to a one-dose strategy in the future was discussed but alternative vaccinations were not.
Effectiveness/benefits:  
The effectiveness estimates and sources used to derive them were reported clearly. The sources were specific to the Brazilian context but the authors did not justify their choice of sources or describe the methods used to identify them. A systematic literature review was reported but whether the best available evidence was used was unclear. The basic characteristics of the primary data sources (such as study population, design, follow-up) were not reported so it was hard to assess the validity of the clinical inputs.

Costs:  
Costs and sources used to derive them were clearly reported and specific to the Brazilian context. Costs included in each analyses were appropriate for the perspectives. Overall costs for disease treatment and intervention were not reported for the health system perspective. The authors stated that health care utilisation and costs of adverse events following hepatitis A vaccination were not considered as they were expected to be rare and mild and the associated costs were considered to be insignificant. Costs were discounted at an annual rate of 5%, which appeared appropriate for this setting but may have implications for the generalisability of the study.

Analysis and results:  
The mathematical SIRV (susceptible, infected/infectious, recovered and vaccinated individuals) model and the decision analytic model were reported in detail along with the parameter estimation methods. The analysis did not deal with DALYs so it was unclear whether the WHO willingness to pay threshold was appropriate. This was used due to a lack of a Brazilian threshold of cost-effectiveness. For the sensitivity analyses, the range of values over which parameters were altered was reported clearly but no justification for the choice of ranges was given. In many cases the chosen ranges altered parameter values in one direction only (which is not good practice). Only univariate and limited bivariate sensitivity analysis was conducted; probabilistic sensitivity analysis in which all model parameters were varied simultaneously according to assigned probability distributions would have more accurately reflected the effect of parameter uncertainty on the results. Nevertheless the results appear to be robust with universal vaccination remaining dominant or cost-effective over most values.

The authors highlighted that a limitation of their study was that introduction of a new vaccine in the programme would require a preliminary assessment of the cold chain capacity and the required adjustments and investments, which was not considered in their analyses.

Concluding remarks:  
The study was based on valid methodology but more details surrounding the choice of evidence may have been useful. The authors conclusions seem reasonable.

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