Cost-effectiveness of oseltamivir treatment for children with uncomplicated seasonal influenza
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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
This study examined the cost-effectiveness of oseltamivir for seasonal influenza in children who had not been vaccinated against it, focusing on drug resistance. The authors concluded that empiric treatment was likely to be cost-effective, especially for children aged one to 11 years, but this was highly dependent on the prevalence of oseltamivir resistance in the circulating influenza virus strains. Key issues, such as the children's age and treatment resistance, were considered. The conclusions appear to be robust.

Type of economic evaluation
Cost-utility analysis

Study objective
This study examined the cost-effectiveness of oseltamivir as a treatment for seasonal influenza in children who had not been vaccinated against it, focusing on resistance to oseltamivir.

Interventions
Three strategies were considered: no antiviral treatment; rapid diagnostic testing, with oseltamivir for those with positive results; and oseltamivir for all patients (five-day course).

Location/setting
USA/primary care.

Methods
Analytical approach:
The analysis was based on a decision model, with a one-year time horizon. Five age cohorts were considered: 12 to 23 months, two years, three to four years, five to 11 years, and 12 to 17 years. The authors stated that the perspective included health care costs and parent time costs.

Effectiveness data:
The efficacy of oseltamivir was from clinical trials, while other estimates were from surveillance databases. Expert opinion was used where there was no published evidence. The rate of resistance to oseltamivir was a key input and was based on data from the 2008 to 2009 influenza season in the USA.

Monetary benefit and utility valuations:
The utility values were from primary data, published literature, and expert opinion.

Measure of benefit:
Quality-adjusted life-years (QALYs) were the summary benefit measure.

Cost data:
The health care costs included drugs, out-patient visits, rapid influenza diagnostic tests, medications, emergency department visits, and hospitalisations. Parent time included their child's influenza illness, treatment, and adverse events. The drug costs were based on average wholesale prices. Other costs were from Medicare, a cost database, and published studies. All costs were in US $ and the price year was 2008.
Analysis of uncertainty:
One-way sensitivity analyses were carried out on all the model inputs. The ranges of values were from published sources or expert opinion. A scenario analysis considered a cohort of children who were vaccinated against seasonal influenza. A probabilistic analysis was carried out using probability distributions for all the model inputs.

Results
In all age groups, the cheapest and least effective strategy was no treatment, followed by testing, then empiric treatment. For example, in the cohort aged 12 to 23 months, the expected costs were $103 with no therapy, $130 with testing, and $149 with empiric treatment. The QALYs were 0.9941 with no therapy, 0.9949 with testing, and 0.9952 with empiric treatment.

With testing over no treatment, the incremental cost per QALY gained was $36,100 in children aged 12 to 23 months, $25,900 in two-year-olds, $40,000 in three- to four-year-olds, $40,300 in five- to 11-year-olds, and $71,200 in 12- to 17-year-olds. With empiric treatment over testing, the incremental cost per QALY gained was $54,100 in children aged 12 to 23 months, $29,200 in two-year-olds, $66,500 in three- to four-year-olds, $42,700 in five- to 11-year-olds, and $110,400 in 12- to 17-year-olds.

The rate of circulating influenza viruses that were resistant to oseltamivir was an influential input: the higher this rate, the less favourable the cost-effectiveness ratio for oseltamivir, especially when used without testing. Other influential inputs were the rate of influenza in children who sought medical attention for an influenzalike illness, the risk of otitis media after oseltamivir, and the sensitivity of testing. Less favourable cost-effectiveness estimates were observed in the vaccinated cohort.

In the three- to four-year-old cohort, at a societal willingness-to-pay threshold of $100,000 per QALY, the percentage of simulations that were cost-effective was 49 for empiric treatment, 34 for testing, and 17 for no intervention.

Authors’ conclusions
The authors concluded that empiric treatment with oseltamivir was likely to be cost-effective, especially for children aged one to 11 years, but this was highly dependent on the prevalence of oseltamivir resistance in the circulating influenza virus strains.

CRD commentary
Interventions:
The three comparators were appropriately selected and appear to be generalisable to other settings. The authors stated that these were the recommended options in the USA. Zanamivir was not included because it could not be used for as wide an age group of children as oseltamivir, and it was not suitable for children with certain conditions.

Effectiveness/benefits:
The clinical inputs were from sources that were selected without a literature review. The efficacy of oseltamivir was from a clinical trial that should have had good internal validity, but was not described. Other inputs came from US sources to reflect the setting. Little information was given on this published evidence, making an objective assessment of its validity impossible, but all clinical parameters were varied in the sensitivity analysis. QALYs were an appropriate benefit measure because of the impact of influenza on quality of life, but the methods used to obtain the utility weights were not provided.

Costs:
A broad perspective was adopted and included a wide range of costs. The unit costs and resource quantities were extensively reported in an online appendix. Typical and appropriate US sources were used to estimate these costs. Reflation exercises will be possible as the price year was reported. Variations in the economic inputs were assessed in the sensitivity analyses.

Analysis and results:
The results were clearly reported for all age cohorts. An incremental approach was used to combine the costs and benefits of the three strategies. Discounting was not required as the time horizon was one year. Deterministic and probabilistic analyses were performed to assess uncertainty and the results were clearly illustrated. The authors stated...
that some of the benefits of oseltamivir, such as a reduced risk of pneumonia and any indirect effects, might have been excluded and their inclusion might have favoured empiric treatment. Comparisons were made with other studies, which generally found better results for oseltamivir as drug resistance was not considered. The transferability of the results was not discussed, but the findings might be relevant to settings with similar costs and epidemiology.

Concluding remarks:
The cost-effectiveness framework was conventional and key issues, such as the children's age and treatment resistance, were considered. The authors' conclusions appear to be robust.

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