Navigating vaccine introduction: a guide for decision-makers

JAPANESE ENCEPHALITIS (JE)

Module 2

IS JE VACCINATION COST-EFFECTIVE?
Cost-effectiveness analysis is a useful way to compare the costs and benefits of introducing and maintaining JE vaccination with those of not introducing the vaccine. It is an important tool for decision-makers considering JE vaccination programs. While no cost-effectiveness data are yet available for two of the three WHO-prequalified vaccines, all analyses to-date of the WHO-prequalified CD-JEV vaccine have found JE vaccination to be cost-effective, highly cost-effective, or even cost-saving, despite wide variation in modeled incidence rates and dosing schedules. If your country has a JE burden, it is likely that JE vaccination will be cost-effective, comparable to other vaccines in childhood immunization schedules. Because of the wealth of existing data, it is not necessary for every country to conduct their own cost-effectiveness analysis. Instead, you can look at existing studies from countries with a JE burden and characteristics comparable to your own.
Is JE vaccination cost-effective?

After determining whether your country has a JE burden, the next step to consider is whether JE vaccine introduction is a cost-effective public health intervention. Cost-effectiveness analysis (CEA) is a useful tool to compare the costs and health effects of alternative courses of action, such as introducing and maintaining JE vaccination versus no vaccination, or introducing JE vaccine under various vaccination strategies. CEA can provide important evidence for decision-makers to consider. Several CEAs have been conducted for JE vaccines in a variety of countries, and in countries and regions with a JE disease burden, JE vaccination has been found to be a highly cost-effective public health intervention comparable to other childhood vaccinations. This module will review those analyses.

Several variables should be included when considering the cost-effectiveness of JE vaccine. What is the national or subnational JE incidence? What age groups are affected? How effective is the vaccine? How much does the vaccine cost to purchase and deliver? How frequent and serious are the adverse events following immunization? These variables and their potential impact on the cost-effectiveness of JE vaccination programs are outlined in Table 1.

For JE, many variables are relatively similar across endemic countries (i.e., at-risk age groups, disease severity and complications, case fatality ratio). These variables contribute to the high cost of JE, which is deadly, expensive to treat, and often causes permanent neurologic damage in young children. However, the total cost-effectiveness can vary based on the total burden of JE in your country, the effectiveness and duration of immunity of the specific vaccine chosen, the cost of acquiring the vaccine, immunization system readiness, and the cost of vaccinating children. Because JE risk is not evenly distributed across a country or population, JE incidence can be highly variable. Additionally, because JE surveillance and laboratory testing have been historically poor, the burden of disease is often unknown or imprecise, making CEAs difficult to perform.

While costs can vary greatly depending on vaccine type and dosing schedule used, all three of the currently WHO-prequalified JE vaccines (live attenuated CD-JEV; live recombinant JE-CV; and inactivated Vero cell-based JEEV) represent a significant reduction in JE vaccine cost compared to the older, inactivated mouse brain-derived (mbd) vaccines.²

All of the existing cost-effectiveness analyses for currently WHO-prequalified JE vaccines, which have all been for the live-attenuated CD-JEV vaccine, have found JE vaccination programs to be cost-effective.¹ The studies found consistent cost-effectiveness, or even cost savings, across a wide variation of modeled incidence rates, dosing schedules, and country environments, including the

Understanding costs and benefits of JE vaccination

What is cost-effectiveness analysis?

To determine the best use of limited resources, decision-makers use health economic evaluations to compare the costs and consequences of alternative courses of action. CEA is one type of health economic evaluation. CEAs estimate the ratio of the difference in costs over the difference in health effects between two proposed interventions to compare the cost-effectiveness of a new intervention (intervention 1) with another intervention, which could be the current practice (intervention 2). This ratio is known as the incremental cost-effectiveness ratio (ICER), and can be expressed as:

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\text{ICER} = \frac{(C_1 - C_2)}{(E_1 - E_2)}
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Where:
- \(C\) = Cost of intervention
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Existing cost-effectiveness data

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How is cost-effectiveness measured?

One common cost-effectiveness measure is the cost per disability-adjusted life-year (DALY) averted. A DALY is one lost year of life for one person due to early death and/or various levels of illness or disability that add up to one lost year of healthy life over time. By measuring DALYs averted by a health intervention, we account for prevented disability as well as death.

Interventions with a cost per DALY averted that is between one and three times the per-capita GDP are considered cost-effective by WHO. Most childhood vaccines in national immunization programs range from US$7 to $438 per DALY averted.

For example, the International Vaccine Institute’s 2007 model of JE vaccination in Bali, Indonesia, suggests that vaccination with CD-JEV would be cost-effective at a wide range of incidence rates. At a JE incidence rate of 6 cases per 100,000 people, the cost per averted DALY was US$31. Even at an incidence rate as low as 3 cases per 100,000 people, the cost per DALY averted is $112. When the incidence rate rises to 9 cases per 100,000 people, the cost per DALY averted drops to $4 (Figure 1). At JE incidence rates of 3 to 9 cases per 100,000 people, the cost per DALY averted is US$3 to US$31.

### TABLE 1. VARIABLES AND THEIR IMPACT ON COST-EFFECTIVENESS (CE) OF JE VACCINATION

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
<th>Effect on CE of vaccination</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease incidence</td>
<td>Varies by country and within countries.</td>
<td>Higher incidence, more CE</td>
</tr>
<tr>
<td>Infection-to-illness ratio</td>
<td>Varies; between 100:1 and 500:1.</td>
<td>Lower ratio, more CE</td>
</tr>
<tr>
<td>Vaccine cost</td>
<td>Varies by vaccine type.</td>
<td>Lower cost, more CE</td>
</tr>
<tr>
<td>Operational costs of vaccinating children</td>
<td>Varies by country and vaccination strategy.</td>
<td>Lower operational costs, more CE</td>
</tr>
<tr>
<td>Case fatality ratio (CFR)</td>
<td>Relatively constant across countries.</td>
<td>Higher CFR, more CE</td>
</tr>
<tr>
<td>Number of doses to achieve immunity</td>
<td>Varies by vaccine type.</td>
<td>Fewer doses, more CE</td>
</tr>
<tr>
<td>Vaccine effectiveness (VE)</td>
<td>Varies; data for mouse brain-derived &amp; CD-JEVAX vaccines only.</td>
<td>Higher VE, more CE</td>
</tr>
<tr>
<td>Duration of vaccine-induced immunity</td>
<td>Varies by vaccine type.</td>
<td>Long duration (e.g., live vaccines), more CE</td>
</tr>
<tr>
<td>Cost of treating long-term neurologic deficit in survivors</td>
<td>Varies by country, ~30% of survivors neuro-impaired.</td>
<td>Higher cost, more CE</td>
</tr>
<tr>
<td>Cost of treating acute encephalitis</td>
<td>Varies by country, but generally expensive. In Nepal, family outlay is 5-10 times the monthly income.</td>
<td>Higher cost, more CE</td>
</tr>
<tr>
<td>At-risk age group</td>
<td>Rates constant within age brackets across countries. Higher incidence in persons &lt;15-years-old.</td>
<td>Younger age, more CE</td>
</tr>
<tr>
<td>Adverse events following immunization (AEFI)</td>
<td>Varies by vaccine type.</td>
<td>Fewer AEFI or fewer serious AEFI, more CE</td>
</tr>
</tbody>
</table>

follows: Shanghai, China; Andhra Pradesh, India; Bali, Indonesia; Cambodia; and Guizhou Province, China.

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cases per 100,000, the costs per averted DALYs for JE vaccination in Bali are considered highly cost-effective and comparable to the cost-effectiveness of other childhood vaccines.9

Cost-effectiveness analyses have also been completed for different JE vaccine types. Generally, although the older, inactivated mouse brain-derived vaccine is considered cost-effective, it is troubled by safety and other issues and shown to be considerably less cost-effective than CD-JEV.2 The other WHO-prequalified JE vaccines, the live recombinant JE-CV and the inactivated JEEV, have not yet been evaluated for cost-effectiveness.

One analysis conducted in Shanghai, China (2003) directly compared the cost-effectiveness of two vaccine types in the same country.7 By modeling three hypothetical birth cohorts—one with no vaccination, one with inactivated vaccine, and one with CD-JEV—and following them for 30 years, the analysis found that while both vaccines would be cost-effective and cost-saving, CD-JEV resulted in a higher number of lives saved and significantly higher cost savings than the alternative due to its higher vaccine efficacy and fewer required doses.

While there are no CE data for JEEV or JE-CV, all of the cost-effectiveness analyses on JE vaccination with WHO-prequalified CD-JEV vaccine conducted to date show that JE vaccination is cost-effective in JE-endemic countries. With the availability of newer JE vaccines at low public-sector prices, cost-effectiveness and access to JE vaccines throughout Asia has greatly improved.

Additionally, in 2014, Gavi, the Vaccine Alliance began offering support for JE vaccination campaigns for children up to 15 years of age in Gavi-eligible, JE-endemic countries. This support includes the cost of vaccine, operational costs to perform
vaccination campaigns, and an additional grant to help the country transition to routine JE immunization. In 2016, the Gavi Board also approved cofinancing for JE vaccine used in routine immunization in Gavi-eligible countries that have not yet introduced into routine with domestic resources. Countries would be required to cofinance a portion of the costs in the year of introduction, depending on the phase of the Gavi transition process that they are in. This Gavi support will reduce the cost of vaccine for those countries’ programs.

References

If your country has even a small-to-moderate JE burden, evidence shows that JE vaccination will likely be cost-effective. Based on global recommendations and evidence, the best ways to assess the cost-effectiveness of JE vaccination in your country are to:

1. **Explore existing analyses.** When evaluating whether to introduce JE vaccination programs, it is useful to explore the CEAs described above or any others that may have been conducted in your country or in countries of similar economic status and JE burden.

2. **Compare data inputs to your country’s data.** If an existing analysis uses a similar or lower JE incidence rate to your country and the analysis shows cost-effectiveness or cost savings, it is likely that an analysis in your country would have similar results.

3. **Optionally, conduct a CEA for your country.** This may be a good alternative if no comparable CEA studies exist. However, these analyses usually require data that may be difficult to obtain, and they are not necessary for every country to conduct due to the wealth of evidence and tools already in existence.

4. **Reach out for more information.** For more information on cost-effectiveness analyses for JE vaccination, reach out to your regional WHO office.