About this guide:

Japanese encephalitis (JE), a viral infection of the brain, is transmitted to humans by mosquitoes. It begins like the flu and can progress to a brain infection, killing up to 30 percent of its victims and leaving up to half of its survivors with permanent brain damage such as memory loss, impaired cognition, paralysis, seizures, the inability to speak, and other mental disorders. Providing lifelong care for survivors is a significant financial strain on families and on government health care systems. There is no treatment to cure JE. Vaccination is the only reliable way to prevent infection.

This guide is designed to help country decision-makers understand the evidence around JE vaccine introduction, the potential benefits, how to incorporate JE vaccines into their country’s immunization program, and how to monitor and evaluate the vaccines after introduction. It consists of six modules, including:

1. Does my country need JE vaccine?
2. Is JE vaccination cost effective?
3. Which JE vaccine should my country use?
4. How should my country introduce JE vaccine?
5. Can my country afford a JE vaccination program?
6. Is my country’s JE vaccination program working?

The modules are intended to help address some of the common challenges countries often face and provide practical tools needed to make informed decisions about JE vaccine introduction, expansion, and sustainability.

Additionally, because the risk of JE varies from year-to-year, country-to-country, and even district-to-district, this guide may also serve as a model for other vaccines and diseases that are unevenly distributed and, as a result, not generally seen as universal childhood immunizations (e.g., dengue, typhoid, or cholera).
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**MODULE 1: JE BURDEN**

**MODULE 2: COST-EFFECTIVENESS**

**MODULE 3: VACCINE PRODUCTS**

**MODULE 4: INTRODUCTION STRATEGY**

**MODULE 5: COSTING ANALYSIS**

**MODULE 6: MONITORING & EVALUATION**

**ABOUT THIS GUIDE**
DOES MY COUNTRY NEED JE VACCINE?

Module 1
Human immunization is the only effective method for JE prevention.

In all areas where JE is recognized as a public health priority, WHO recommends implementing a one-time JE vaccination campaign in at-risk populations followed by incorporation of JE vaccine into routine immunization.

Absence of the highest-quality JE surveillance system should not delay introduction or expansion of JE vaccine.

If your country is not able to collect high-quality data on confirmed JE cases, WHO recommends that you still consider vaccination where there is a suitable environment for JE virus transmission.
Does my country need JE vaccine?

To determine whether your country should introduce JE vaccine, it is important to assess whether JE poses a significant public health burden. While the best way to understand the burden in your country is through laboratory-based disease surveillance, it is not the only way. As noted by WHO, countries without a strong surveillance system in place but with evidence of JE disease occurrence should not wait to introduce JE vaccine. This module will describe different ways to determine if your country needs JE vaccine.

Monitoring JE disease burden through routine disease surveillance

Globally, an estimated 70,000 JE cases occur in the JE-endemic region of Asia (Figure 1) each year, but for many reasons, this is likely an underestimate. JE surveillance is difficult because most JE infections do not cause symptoms. When illness does develop, it can be a simple febrile illness, meningitis, myelitis, or encephalitis. Encephalitis, the most severe and most commonly reported type of JE virus infection, cannot be clinically distinguished from other causes of acute encephalitis syndrome (AES).

WHO recommends that countries monitor year-to-year fluctuation in disease incidence using JE-specific laboratory testing of cerebrospinal fluid or serum from persons with AES. However, these tests require special diagnostic equipment and reagents and well-trained laboratory professionals. As a result, testing may not be available in poor, rural JE-endemic areas. Because access to laboratory testing may be limited, disease surveillance systems that do not require every case to be tested are often used.
What is sentinel surveillance?
Sentinel surveillance uses a limited number of carefully selected hospitals (“sentinel hospitals”) to collect high-quality data on a disease. This data is reported and collected by a central system to signal trends, identify outbreaks, and monitor the burden of a disease. Sentinel surveillance can account for different diagnostic capacities at hospitals and can be combined with laboratory confirmation and syndromic surveillance.

SENTINEL HOSPITAL SURVEILLANCE
Because encephalitis is a severe illness, most affected patients are cared for in hospitals. WHO therefore recommends that all JE-endemic countries carry out at least sentinel hospital surveillance with laboratory confirmation of JE.

SYNDROMIC AES SURVEILLANCE
Syndromic AES surveillance identifies persons with AES according to the clinical case definition, which is a person of any age, at any time of year with the acute onset of fever and a change in mental status (including symptoms such as confusion, disorientation, coma, or inability to talk) and/or new onset of seizures (excluding simple febrile seizures). While JE is the leading cause of viral AES, it is not the only cause. Many countries have syndromic surveillance for all AES cases, which includes cases due to JE virus and those due to other infectious and non-infectious causes. Some or all of these AES cases may then be selected for laboratory testing to identify the proportion of AES cases due to JE.

Although the proportion of AES cases due to JE may vary widely by location and year based on ecological conditions, studies have shown that AES incidence correlates well with JE incidence. Because AES surveillance can be used to approximate JE burden even without confirmatory JE testing, it has been used to show the impact of JE vaccination. In Thailand, for example, officials successfully used AES with limited laboratory testing to show the impact of vaccination on reducing JE morbidity (Figure 2).

In addition, AES surveillance is a sustainable solution to rapidly identify encephalitis outbreaks. During epidemiologic investigations of these AES outbreaks, it may be found that such outbreaks are due to JE or to some other preventable cause. As a result, WHO states that AES surveillance is important for understanding all causes of encephalitis.

**FIGURE 2. MORBIDITY RATES OF ENCEPHALITIS AND JAPANESE ENCEPHALITIS, THAILAND 1980-2000**

![Graph showing morbidity rates](image)

Officials in Thailand estimated JE morbidity rate using a combination of reported incidence and serology data. Estimated JE morbidity rates have been following similar declining patterns of encephalitis.
Assessing JE disease burden with limited data

In countries without AES or JE surveillance but where the ecology, geography, and agricultural practices are similar to those in an adjacent JE-endemic country or region, you can determine the likelihood that JE virus transmission is occurring by conducting seroprevalence studies or investigating AES outbreaks.

In a stable population where ecological conditions support annual JE transmission, these studies can identify areas that likely have annual JE virus transmission to humans. When combined with other demographic information such as age, occupation, or time spent in the village, seroprevalence studies can identify at-risk populations who may benefit from vaccination.

During epidemiologic investigations of AES outbreaks, public health authorities respond to an AES outbreak to discover its etiology. If JE is identified as the cause, it is likely that some AES cases prior to the outbreak were due to JE because the ecological conditions that support virus transmission to humans remain relatively constant from year to year. In such cases, JE-specific disease surveillance should be established.

For help in developing a plan to assess JE disease burden in your country, contact the appropriate WHO regional office: South-East Asia Regional Office or Western Pacific Regional Office.

JE does not occur evenly across a country; some areas are at greater risk than others. Using surveillance data to map the geographic distribution and incidence (number of cases per 100,000 persons) in your country is an important step in tracking mosquito-borne diseases, since distribution and incidence may change over time. Mapping can help track disease changes in different regions and identify at-risk populations. With an estimate of JE burden and a map of the geographic distribution of JE cases, your country can identify priority areas for intervention.

Once you better understand the JE burden in your country, you will need to decide on a control strategy. WHO, Gavi, and JE experts maintain that human immunization is the only effective JE prevention method and that JE vaccine should be integrated into routine childhood immunization schedules wherever JE is recognized as a public health priority.

There is little evidence to support sustained reduction of the JE disease burden from interventions such as vector control, bed nets, swine immunization, or animal sequestration. WHO specifically recommends that these other interventions should not divert efforts or resources from childhood JE vaccination.
However, there is clear evidence that, when high vaccine coverage is achieved and sustained, JE vaccines greatly reduce the number of human JE cases. Because humans are dead-end hosts, human vaccination does not reduce natural zoonotic transmission. As a result, non-immune persons living in JE-endemic areas are always at risk for JE virus infection.

If your country was not able to conduct JE surveillance or found a low number of confirmed JE cases, WHO recommends that JE vaccination should still be considered where there is a suitable environment for JE virus transmission. This includes the presence of animal reservoirs such as pigs and wading birds, suitable mosquito vectors, ecological conditions supportive of JE virus transmission, and proximity to other countries or regions with a known JE burden.

Overall, countries should prioritize JE immunization where disease burden exists, while simultaneously strengthening surveillance systems to ensure strong data are available to support future decisions.

References
7 Igarashi A. Control of Japanese encephalitis in Japan: Immunization of humans and animals and vector control. Current Topics in Microbiology and Immunology, 2002,267:139–152.

Cover and inside cover photos: PATH/Aaron Joel Santos; back: PATH/Julie Jacobson
Based on the above global recommendations and evidence, the best way to determine if your country needs JE vaccine can be summarized through these steps:

1. **Collect JE disease surveillance data.** This can be done by implementing AES or sentinel hospital surveillance programs and by developing a way for some or all AES cases to undergo JE-specific laboratory testing. If a full surveillance program is not feasible, you can use existing data, carry out limited surveillance, conduct short-term surveillance during an AES or JE outbreak, conduct special studies, or use data from neighboring countries. Talk to your WHO regional office for guidance on the best JE surveillance methods for your country.

2. **Analyze the burden of JE in your country.** If available, create a map using data from surveillance or special studies to gain understanding of how JE is distributed geographically and among the population. Mapping will remain an important tool to help determine where you can make improvements after an immunization program is in place. However, countries without a strong JE surveillance system in place but with evidence that JE disease is occurring should not wait to consider JE vaccine introduction.

3. **Make a decision about JE vaccination.** WHO recommends integrating JE vaccine into national immunization schedules in all areas where surveillance shows JE to be a public health priority. Even if a low JE burden is found, WHO recommends consideration of a JE vaccination program where there is a suitable environment for JE virus transmission.

WHO also advises that cost-effectiveness analyses specific to the country or region may be informative for decisions about JE vaccine introduction. For more information on cost-effectiveness, see *Module 2: Is JE vaccination cost-effective?*
IS JE VACCINATION COST-EFFECTIVE?

Module 2
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.\(^1,2\) This module will review those analyses.

Understanding costs and benefits of JE vaccination

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.\(^2\)

Existing cost-effectiveness data

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

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, 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


Cover and back photos: PATH/Lesley Reed; inside cover: PATH/Lisa Mueller; back inside cover: PATH/Aaron Joel Santos
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.
 WHICH JE VACCINE SHOULD MY COUNTY USE?

Module 3
Three JE vaccines have been prequalified by WHO as safe, effective, and acceptable for procurement by United Nations agencies.

Vaccination programs using any of the WHO-prequalified JE vaccines would provide lifesaving protection from JE for your country’s children.

Each vaccine has different dosing and administration requirements, which can impact costs and vaccine introduction logistics. The number of required doses is an important cost driver of vaccination programs.

Live vaccines that provide significant protection and potentially life-long immunity after a single-dose primary injection have some advantages over inactivated vaccines, including lower operational costs for delivery. WHO-prequalified inactivated vaccines, however, may have higher efficacy.
Which JE vaccine should my country use?

After confirming the JE disease burden and considering cost-effectiveness of JE vaccination in your country, you will need to decide which vaccine to use. Three JE vaccines are WHO-prequalified as high-quality, safe, effective, and available for procurement by United Nations (UN) agencies. This module provides information on the safety, immunogenicity, effectiveness, and dosage requirements of these vaccines.

WHO-prequalified JE vaccines

WHO prequalification is a process that uses a transparent, scientifically sound assessment to help ensure that medical commodities such as vaccines for high-burden diseases meet global standards of quality, safety, and efficacy in order to optimize use of health resources and improve health outcomes. As of mid-2016, three JE vaccines have been prequalified (Table 1). WHO has reviewed the manufacturing process and clinical testing and prequalified these vaccines as high-quality, safe, and immunogenic. As with all WHO-prequalified vaccines, they are available for procurement by UN agencies.

<table>
<thead>
<tr>
<th>IMAGE</th>
<th>TRADE NAMES (abbreviation)</th>
<th>VACCINE TYPE</th>
<th>MANUFACTURER</th>
<th>DOSES (WHO rec.)</th>
<th>COUNTRIES WHERE VACCINE IS LICENSED*</th>
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</thead>
<tbody>
<tr>
<td><img src="CD.JEVAX%C2%AE" alt="Image of CD.JEVAX®" /> and RS.JEV® (CD-JEV)</td>
<td>Live attenuated; uses SA 14-14-2 strain</td>
<td>Chengdu Institute of Biological Products (China)</td>
<td>1</td>
<td>Cambodia, China, India, Laos, Malaysia, Myanmar, Nepal, South Korea, Sri Lanka, Thailand, Vietnam</td>
<td></td>
</tr>
<tr>
<td><img src="IMOJEV%C2%AE" alt="Image of IMOJEV®" /> and ChimeriVax-JE™ (JE-CV)</td>
<td>Live recombinant; uses genes from SA 14-14-2 and yellow fever</td>
<td>GPO-MBP Co., Ltd. (Thailand)</td>
<td>1</td>
<td>Australia, Brunei, Hong Kong, Malaysia, Myanmar, Philippines, Singapore, Thailand</td>
<td></td>
</tr>
<tr>
<td><img src="JEEV%C2%AE" alt="Image of JEEV® (JEEV)" /></td>
<td>Inactivated, Vero cell-derived, uses SA 14-14-2</td>
<td>Biological E (India)</td>
<td>2</td>
<td>India</td>
<td></td>
</tr>
</tbody>
</table>

*Licensure as of June 2016. Subject to change.

Non-prequalified JE vaccines

In addition to the three WHO-prequalified JE vaccines, more than ten other JE vaccines are made. All are inactivated and derived from either infected mouse brains or cell cultures. Although mouse brain-derived vaccines are effective, in 2006, WHO recommended mouse brain-derived vaccines be replaced by newer JE vaccines. This was due to safety concerns as well as the variability of manufacturing, higher price, and need for repeated doses and boosters, which often
make mouse brain-derived vaccines unaffordable in many JE-endemic countries. Except for JEEV (Table 1), these inactivated, cell culture-derived JE vaccines have not been WHO-prequalified as of mid-2016 and often have limited or no international distribution. Because non-prequalified vaccines are not eligible for UN procurement, they will not be discussed further in this module.

All WHO-prequalified JE vaccines are considered safe, have very few serious adverse events following immunization (AEFIs) attributed to them, and are considered safer than older, mouse brain-derived vaccines. WHO’s 2015 position paper on JE vaccines states that all three prequalified vaccines have acceptable safety profiles.1

Due to its long history and widespread use in China and India, CD-JEV has the largest safety database of the three prequalified vaccines.2 In a 2014 review of population-based AEFI surveillance in Guangdong Province, China, only 36 serious AEFIs were reported among 23.3 million infants vaccinated with CD-JEV.3 According to a 2016 AEFI review in India, of the over 145 million children under 15 who have been immunized with CD JEV in 20 Indian states between 2006 and mid-2016, only 53 AEFI deaths were reported and none of them were caused due to the vaccine.4 While passive surveillance systems often result in underreporting of AEFIs, WHO has reviewed both population-based and clinical trial safety data for CD-JEV on multiple occasions and has confirmed the vaccine’s acceptable safety profile.1

Due to limited widespread use, the other prequalified JE vaccines have less safety data. While population-based AEFI studies of JE-CV have not been performed, clinical trials in children and adults suggest that it has a safety profile similar to CD-JEV and superior to the mouse brain-derived vaccines.5,6 JEEV’s safety has only been studied in a few clinical trials in India. However, JEEV is made using the same vaccine strain and cell line and inactivated in the same way as the non-prequalified JE vaccine IXIARO® as part of a technology transfer. Because IXIARO® has been studied extensively in clinical trials and population-based AEFI surveillance,7 WHO extends IXIARO’s® safety profile to JEEV due to the quality of the data and the degree of similarity between IXIARO® and JEEV.

WHO states that more safety data are needed for prequalified JE vaccines.8 In particular, CD-JEV could benefit from more safety data about its use in adults, JE-CV from population-based AEFI surveillance studies, and JEEV from safety data following co-administration with measles vaccine. Safety data from pregnant women or immunocompromised persons would be useful for all of these vaccines.
 module 3  •  WHICH JE VACCINE SHOULD MY COUNTRY USE?

FIND OUT MORE

What is vaccine immunogenicity?
Vaccine immunogenicity is a vaccine’s ability to elicit a protective immune response to a disease-causing organism (pathogen). After vaccination, the immune system becomes prepared to fight the pathogen contained in the vaccine by creating proteins called antibodies. If the pathogen is encountered again, these antibodies will bind to it, preventing it from attacking cells while also triggering other immune cells to destroy the pathogen. A vaccine is considered to be immunogenic if the concentration of pathogen-specific antibodies in a person’s blood rises to a protective level after vaccination.

JE vaccine immunogenicity and effectiveness

All three WHO-prequalified JE vaccines have been found to be highly immunogenic in clinical trials in both JE-endemic and non-endemic settings. Across clinical trials for these vaccines, 80 to 100 percent of those vaccinated developed antibody concentrations that are considered protective against JE disease.3,9

Vaccine effectiveness studies, which differ from immunogenicity studies by looking at the ability of the vaccine to protect against disease in real-world settings, have only been completed for CD-JEV in JE-endemic areas. In JE-endemic parts of Nepal, among persons vaccinated during CD-JEV campaigns when they were

<table>
<thead>
<tr>
<th>JEV VACCINE</th>
<th>DOSES IN PRIMARY SERIES</th>
<th>AGE RANGE</th>
<th>DOSAGE</th>
<th>BOOSTER</th>
<th>ADMINISTRATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD-JEV</td>
<td>1</td>
<td>≥8 months</td>
<td>0.5 ml</td>
<td>No</td>
<td>Subcutaneous</td>
</tr>
<tr>
<td>JE-CV</td>
<td>1</td>
<td>≥9 months</td>
<td>0.5 ml</td>
<td>No</td>
<td>Subcutaneous</td>
</tr>
<tr>
<td>JEEV</td>
<td>2 (4 weeks apart)</td>
<td>1–49 years</td>
<td>12-35 months: 3μg 3–49 years: 6μg</td>
<td>No*</td>
<td>Intramuscular</td>
</tr>
</tbody>
</table>

*a India’s national regulatory authority has not approved an indication for a booster dose of JEEV for adults or children. However, Valneva recommends a booster of Ixiaro® 12 months after primary immunization for adults residing in JE-endemic areas. Similar recommendations will likely be made for JEEV. Additionally, a Phase III trial of Ixiaro® in children showed a pronounced booster response when a dose was delivered 12 months following the primary series.10
1 to 15 years old, effectiveness was 98.5 percent one year after immunization\textsuperscript{11} and 96.2 percent after five years.\textsuperscript{12}

**JE vaccine dosing requirements**

When considering JE vaccine introduction, it is important to consider the recommended dosing regimen, the number of doses in a primary series, and whether a booster dose is required (Table 2). Vaccines that require multiple doses in the primary series or need booster doses will incur greater costs due to the purchase of more vaccine and greater operational costs of vaccinating the same person on multiple occasions.

Because of the programmatic costs to administer multiple doses, a vaccine requiring only one dose without a booster shot may be more cost-effective for some countries. For more information on the cost-effectiveness of JE vaccines, please see Module 2: Is JE vaccination cost-effective?

**References**


RECOMMENDATIONS • Module 3

As this module shows, all three of the currently WHO-prequalified JE vaccines are safe and immunogenic. Vaccination programs using any of the WHO-prequalified JE vaccines should provide protection from JE for your country’s children with very little risk of AEFIs. Your country’s choice of vaccine may be based on a variety of cultural, political, and economic factors unique to your country, but when choosing a JE vaccine, it is helpful to:

1. **Prioritize WHO-prequalified vaccines.** The WHO prequalification process works with national regulatory authorities to ensure that vaccines are manufactured in high-quality conditions and are safe, immunogenic, and effective. WHO-prequalified vaccines are eligible for procurement by UNICEF and other United Nations agencies that purchase vaccines for low- and middle-income countries and development partners such as Gavi, the Vaccine Alliance.

2. **Consider dosing schedules and administration requirements.** These requirements can have major implications on the immunization supply chain, logistics of delivery, and cost. All of these items can affect the overall cost-effectiveness of vaccination. Additionally, countries should consider how JE vaccination schedules would fit into existing childhood immunization schedules to optimize delivery of multiple childhood vaccines.

3. **Inquire about vaccine cost and availability.** Vaccine costs vary widely from country to country based on supply and demand and distribution agreements. As a result, it is not possible to compare these costs at a global level. Reach out to your WHO regional office, UNICEF, in-country vaccine suppliers, or vaccine manufacturers for more information about specific JE vaccine costs and availability for your country.

Your country’s choice of vaccine will have far-reaching implications for introduction. For guidance on how to develop a JE vaccine introduction plan, see *Module 4: How should my country introduce JE vaccines?*
Navigating vaccine introduction
a guide for decision-makers

JAPANESE ENCEPHALITIS (JE)

HOW SHOULD MY COUNTRY INTRODUCE JE VACCINES?

Module 4
WHO recommends that JE-endemic countries conduct a one-time JE vaccination campaign in the primary target population and then incorporate JE vaccine into the national immunization program (NIP) as routine immunization.

Routine immunization with any of the three WHO-prequalified JE vaccines can be done within existing NIP vaccination schedules without requiring additional visits.

Determining and ordering the right number of vaccine doses and injection supplies is critical to prevent stockouts and wastage.

Assessing and updating cold chain equipment and personnel, immunization cards, and data recording and reporting forms must be completed for all target areas and age groups before introducing JE vaccine.

Health worker training is key to ensure proper administration, safety, and dissemination of accurate information about JE vaccination.

Advocacy, communications, and social mobilization activities improve the reach and impact of JE vaccination programs by building demand and acceptance of JE vaccine from parents, community leaders, and policymakers.

KEY TAKEAWAYS • Module 4
How should my country introduce JE vaccines?

After your country decides which JE vaccine to introduce, the next step is to determine how JE vaccine will be integrated into your national immunization program (NIP). NIP managers need to develop a detailed vaccine introduction plan detailing all the activities and steps required for a successful and sustainable introduction. This module is based on WHO recommendations in Principles and Considerations for Adding a Vaccine to a National Immunization Program. It provides guidance on strategies, logistic preparation, and other things that should be considered for JE vaccine introduction.

Determining a target population for campaigns

In JE-endemic settings, WHO recommends a one-time “catch-up” campaign in the primary target population followed by incorporation of JE vaccine into the NIP as part of routine immunization. To conduct such campaigns, countries must specify the age groups and geographic locations that make up the target population which will impact the campaign strategy. Vaccination can occur nationally or only in selected areas within the country and can be school-based or community-based. Additionally, campaigns can be phased, adding new areas over time, or started simultaneously in all areas.

The age and location of a target population should be based on the burden of JE in your country (see Module 1: Does my country need JE vaccine?). However, there are sometimes other considerations. For example, in Nepal, even though the highest JE rate is still in children less than 15 years old, the Nepal Ministry of Health and Population noted increasing JE rates in persons older than 15 years in some regions. To address this, Nepal conducted campaigns in new districts and allowed limited vaccination of adults (Figure 1).

Choosing a schedule and immunization strategy for JE vaccination in the NIP

When shifting from campaigns to routine immunization, your country will need to define the optimal JE vaccination schedule. Because routine JE immunization aims to secure early, lifelong protection, WHO recommends JE vaccination to start no earlier than the youngest age recommended by each vaccine manufacturer:

- 6 months of age for the inactivated Vero cell-derived JEEV vaccine;
- 8 months of age for the live attenuated CD-JEV vaccine; and
- 9 months of age for the live recombinant JE-CV vaccine.

FIGURE 1. NEPAL DISTRICTS COVERED IN JE VACCINATION CAMPAIGNS, 2006–2011

Ages targeted in campaigns
- Whole population above 1 year
- 1-15 years
Because many childhood vaccines are administered between 6 and 12 months of age, there are several already-planned clinic visits during which the three WHO-prequalified JE vaccines can be added without requiring an additional visit. No concerns over safety or immunogenicity have been identified for co-administration of any of the WHO-prequalified JE vaccines with other childhood vaccines.¹

While simultaneous national rollouts will have faster public health impact, some countries choose to introduce in a phased or regional manner due to limited resources, logistical concerns, or disease burden data. In 2005, a large JE outbreak in India’s eastern Uttar Pradesh led to a regional introduction of JE vaccines in 11 high-risk districts that has expanded to more states and districts as endemic JE is recognized in new areas.

By this point in the planning process, your country has already chosen which JE vaccine to introduce (see Module 3: Which JE vaccine should my country introduce?). An additional decision is to select the specific presentation and formulation for that vaccine. In some cases, only one presentation and formulation may be available.

All of the WHO-prequalified JE vaccines come in vials. The WHO-prequalified presentation for JEEV is a one-dose vial only; for JE-CV, a four-dose vial only; and for CD-JEV, either a one- or five-dose vial. CD-JEV and JE-CV come in a two-vial set with the live virus in a lyophilized powder in one vial and the diluent to reconstitute the vaccine in the second vial. JEEV comes in a ready-to-use liquid formulation in one vial.

The price per dose should not be the only factor in decision-making. Different presentations and formulations may have different qualities that impact cost and public health benefit. Multi-dose vaccine vials are less expensive to purchase and take up less storage space than single-dose vials but can result in greater wastage. Lyophilized vaccines that must be reconstituted before use, such as CD-JEV and JE-CV, require additional steps before administration. WHO recommends selecting presentations and formulations based on safety, ease of use, vaccine wastage rates, and cold chain requirements.³

Once your country determines which formulation and presentation to use, the next step will be procurement of vaccine and related supplies. A country may assume full ownership and responsibility for procurement. Alternatively, a country may delegate vaccine procurement to agencies such as UNICEF Supply.
Division. This was the primary method used by Laos and Cambodia to introduce JE vaccine in 2015 and 2016, respectively. A third option would be to collaborate with other countries to build a pooled procurement mechanism.² When planning for procurement, be mindful of the national regulatory approval processes and timelines, both in your country and the country of manufacture.

No matter which procurement method is chosen, accurately forecasting the needed number of vaccine doses and injection supplies is critical to prevent stockouts and wastage which can compromise the quality of your country’s JE vaccination program. Additionally, to ensure matched quantities of vaccine and injection supplies and reduce costs and errors in procurement, WHO recommends procuring product bundles. For help in conducting multi-year forecasts of vaccine and injection supply needs, see the WHO Vaccine Forecasting Tool.⁵

Your country’s NIPs will also need to estimate, assess, and prepare JE vaccine storage and transportation requirements and current capacity. Requirements for JE vaccines should include cold storage, vaccine transport equipment and personnel, dry storage for syringes and safety boxes, and waste management equipment. The WHO Logistics Forecasting Tool can help NIPs determine the requirements per child.⁶

To assess your country’s current cold and dry storage capacity, WHO recommends that NIPs conduct an up-to-date inventory of all equipment and personnel involved in the storage and transport of vaccines and related supplies at all levels of the system.² Various tools are available to inventory supply chain capacity, including the Cold Chain Equipment Manager⁷ and the Effective Vaccine Management assessment.⁸

By comparing the inventory of storage capacity with the estimated additional needs for JE vaccine introduction, your country can identify gaps in storage and transport capacity that should be addressed before introduction.

Training health workers, supervisors, and NIP staff about JE and the new vaccine is important to ensure proper administration and safety as well as dissemination of accurate information. Because two of three WHO-prequalified JE vaccines are reconstituted before administration, their use may present a challenge for health workers. For specific health worker training resources on JE vaccines, see WHO and PATH’s CD-JEV Japanese Encephalitis Vaccine Introduction Training Modules for Health Care Workers.⁹
Advocating for & communicating about JE vaccines

A coordinated set of advocacy, communications, and social mobilization activities is a key element of JE vaccine introduction. These are critical to building vaccine demand and acceptance among families, community leaders, and policymakers. During a JE campaign in the Maharajganj district of Uttar Pradesh, India, interviews with caregivers of immunized children revealed that many learned about the campaign from the NIP’s information, education, and communications (IEC) materials and activities (Figure 2).

In JE-related communication, your country should emphasize that vaccination is the only effective way to prevent JE. Additionally, if your country has used other JE vaccines in the past, IEC materials should explain why a new vaccine is being introduced and provide guidance for previously vaccinated children or adults. Sensitization meetings with community leaders, medical practitioners, and the media may be a good way to spread these messages.

Developing a New Vaccine Introduction Plan

The final step in planning JE vaccine introduction is to summarize the strategies and components described in this module into a New Vaccine Introduction (NVI) Plan. The plan should build on broader plans, strategies, and activities, such as the National Immunization Plan, National Health Plan, or Comprehensive Multi-Year Plan. It should include required updates to information systems, such as child immunization or health cards and forms used to record and report vaccinations. Additionally, countries should develop detailed microplans that translate goals and activities from the national strategic plan into ones more relevant for provincial- and district-level campaigns. For help developing and managing your country’s plan, see WHO’s NVI Checklist and NVI Activity List and Timeline.

References


Cover photo: PATH/ Aaron Joel Santos; inside cover: PATH/Satvir Malhotra; back inside cover: PATH/Rocky Prajapati.
Developing a strategy and detailed plan for the successful and sustainable introduction of JE vaccines into your country’s NIP requires many steps and considerations. Fortunately, WHO provides a range of recommendations, guides, tools, and templates to help countries through this process. In order to make evidence-based decisions about the most effective way to introduce JE vaccines, it is recommended to:

1. **Determine a target population for campaigns based on surveillance data, safety, and logistics.** High-quality JE surveillance data specific to your country is not necessary to conduct campaigns.

2. **Choose a schedule and immunization strategy for JE vaccination in the NIP.** Schedules should be chosen based on potential impact, safety, and simplicity.

3. **Select the vaccine presentation and formulation.** Presentation and formulation should be chosen based on safety, ease of use, vaccine wastage rates, and cold chain requirements.

4. **Procure JE vaccine and injection supplies based on supply forecasting.** For assistance in conducting multi-year forecasts of vaccine and injection supply needs, see the WHO Vaccine Forecasting Tool.

5. **Determine vaccine management, cold chain, logistics, and data recording and reporting needs for JE vaccines.** Your country should compare needs with capacity using tools such as the WHO Logistics Forecasting Tool and Cold Chain Equipment Manager. Based on these assessments, additional equipment or cold room expansion may be needed.

6. **Train health personnel on JE vaccines.** Health workers, medical officers, supply chain and logistics managers, and other health personnel need to be properly trained to ensure safe and effective vaccination.

7. **Develop an advocacy and communications plan for JE vaccines.** Your country should be sure to emphasize that vaccination is the only effective way to prevent JE.

8. **Summarize your country’s JE vaccine introduction strategies and plans in a New Vaccine Introduction Plan.** Additionally, your country should translate national goals and activities into detailed microplans for provincial- and district-level campaigns. For help in developing and managing your country’s plan, see the WHO NVI Checklist and NVI Activity List and Timeline.
CAN MY COUNTRY AFFORD A JE VACCINATION PROGRAM?

Module 5
Determining the costs and requirements to finance a new JE vaccination program is the final, essential step in deciding to introduce JE vaccine into a national immunization program.

Before introduction, countries should analyze and update comprehensive multi-year plans, budgets, and financing plans to include JE vaccines.

The World Health Organization (WHO) provides several useful and standardized tools for performing vaccine introduction costing analyses, which focus on affordability and sustainability.

Affordability focuses on a country’s ability to cover up-front costs, whereas financial sustainability looks at the long-term financial impact of adding new vaccines on the immunization budget. Both are important for all countries to consider.
Can my country afford a JE vaccination program?

After developing a plan for JE vaccine introduction, the final steps in decision-making are to analyze the affordability and sustainability of JE vaccination and determine how your country will finance the plan. WHO recommends that decision-makers carefully evaluate the potential short- and long-term financial impacts of adding new vaccines to the national immunization program (NIP) budget. This module provides an overview of how to estimate JE vaccine introduction costs, assess affordability and long-term financial sustainability, and update relevant budgets and policies.

Conducting a costing analysis

While you likely considered the cost-effectiveness and return on investment of a JE vaccination program (see Module 2: Is JE vaccination cost-effective?), JE vaccine introduction usually depends on being able to make an initial investment. By conducting a costing analysis, you can determine the costs of adding JE vaccine to the NIP and its effect on the budget over time. Costs are specifically based on your country’s chosen vaccine and integration plan (see Module 3: Which JE vaccine should my country introduce? and Module 4: How should my country introduce JE vaccines?). If the costing analysis reveals suboptimal sustainability, your country should revise its integration plan and reanalyze, leading to a revision cycle of planning and budgeting that can improve long-term sustainability (Figure 1).

Several standardized tools, such as WHO’s electronic costing tool for comprehensive multi-year plans (cMYPs) for immunization, are available to help countries estimate costs.

FIGURE 1. DESIGN OF THE cMYP COSTING TOOL.

Source: WHO 2014.

Estimating the costs of JE vaccination

The first step in a costing analysis is to estimate the costs associated with introducing JE vaccine. The WHO cMYP costing tool includes common cost inputs needed to successfully deliver vaccine and make necessary program changes as your country
outlined in its JE vaccine introduction plan (see Module 4: How should my country introduce JE vaccines?). Your country’s JE vaccine introduction plan may include components such as additional health workers or immunization sessions, new delivery strategies, cold chain improvements, and expansion of disease surveillance and program monitoring that may be required to ensure JE vaccination coverage remains high (Figure 2). These costs must also be taken into account in the costing estimate.

While vaccine cost is generally the first and most frequently discussed budget item, a costing analysis that takes into account all costs of JE vaccine introduction may identify other components that can significantly increase the cost of introduction. In Myanmar, for example, a costing analysis of a JE vaccine introduction plan that included a catch-up campaign followed by routine immunization found that operational costs were larger than the cost of purchasing and shipping the vaccine. Similarly, an analysis conducted for a JE vaccination campaign in Bali, Indonesia, also found that operational costs significantly exceeded the cost of the vaccine.

Gavi support covers a portion of the vaccine and operational costs per child in the target population for vaccination campaigns. In addition, Gavi-eligible countries receive a one-time vaccine introduction grant to cover the operational costs of transition to

FIGURE 2. COSTS TO INCLUDE WHEN ESTIMATING FUNDING NEEDS FOR JE VACCINE INTRODUCTION

Source: WHO 2014.
Assessing affordability and sustainability of JE vaccination

Once you have estimated the costs of your country’s JE vaccination plan, the next step in a costing analysis is to determine its affordability and sustainability according to established standards. Affordability focuses on the ability of the health system to cover the initial introduction costs, while financial sustainability looks at the long-term impact of adding a new vaccine to the NIP budget.2

A new vaccine is considered affordable if it can be introduced and absorbed into the NIP budget without significantly affecting available resources for other vaccines or public health priorities.2 Using standard indicators, the affordability of introducing JE vaccines should be compared to other public health interventions or programs to get a better sense of their relative impact on the budget. If the program-specific costs with a new vaccine represent a substantial share of the total government health budget or expenditures in a particular year, the program may be pushing the limits of affordability, requiring significant efforts to mobilize resources and sustain the new vaccine in the coming years.

To analyze financial sustainability, the cost of introducing JE vaccine should be compared with current and future financing. Any gap between costs and available funds for a certain year (referred to as the annual funding gap) should be estimated for the next several years.2,3 The WHO cMYP costing tool calculates the funding gap based on current and projected financing and breaks it down by program components, such as vaccines, personnel, and transport.1 The funding gap can change significantly, however, based on timing of the introduction. For example, one analysis conducted for Myanmar suggested that delaying introduction of JE vaccines by five years could increase costs by up to 115 percent due to various factors, including increases in the price of the vaccine and a growing target population.1 Additionally, it can be useful to perform a more comprehensive budget impact analysis that includes the benefits of JE vaccination (e.g., averted health care costs), which offset some of the costs of vaccine introduction.

Long-term financial sustainability of a JE vaccination program should be a major consideration before introduction. If the use of JE vaccine is suspended due to a lack of funding, it can have serious implications for disease control and health outcomes.2 Additionally, if funds are diverted from other health programs to pay for the new
vaccine, it can potentially affect other important programs. Careful planning is needed to ensure that other important health programs and services are not adversely affected. To ensure financial sustainability of JE vaccines, countries can increase the reliability of funding, improve program efficiency to minimize the additional resources needed, and/or mobilize additional resources. Additional resources can come from expansion of the health budget, leveraging of existing resources, or external donations or loans. For example, to help cover initial introduction costs and improve long-term sustainability of its JE vaccination program, Nepal leveraged resources that were established and used in its polio program as well as applied for a loan from the World Bank. After Gavi funding for JE vaccination became available, Nepal used Gavi funding to expand JE vaccination to additional districts in 2016.8

If the decision to introduce JE vaccine is made and the program’s affordability and sustainability are evaluated positively, the national budget, cMYP, and NIP budget and financing plan need to be updated to include all costs associated with JE vaccine introduction as outlined in the costing analysis. Updating the cMYP to include JE vaccine presents an opportunity to identify weak areas of the immunization program and health system that may impede successful introduction or progress of the overall immunization program and to make plans to strengthen these areas. Additionally, all plans and budgets need to specify the sources of the funding and whether new resources mobilization strategies will be needed.

Countries applying for Gavi support for JE vaccination campaigns need to provide a cMYP that includes JE as well as a New Vaccine Introduction Plan (see Module 4: How should my country introduce JE vaccines?). If the current cMYP does not yet include JE vaccination, countries must submit a timeline for updating the cMYP.3

References

Cover photo, inside cover: PATH/Rocky Pranjapat; back inside cover: PATH/Julie Jacobson
Developing a comprehensive, sustainable plan to finance the introduction and maintenance of a JE vaccination program is the final, key step in deciding and preparing to introduce vaccine. To determine how your country can finance JE vaccination, it is recommended to:

1. **Estimate the comprehensive costs associated with adding JE vaccines to your country’s NIP and assess affordability and long-term sustainability.** Expenses include not only the cost of the vaccine but all programmatic costs involved with training, planning, and delivery. These costs should be compared with the cost savings that will result from fewer JE cases once the vaccination program is in place as well as with your country’s current budgets. WHO provides several standardized tools that can help account for all program costs associated with the introduction.

2. **Modify plans for integrating JE vaccines into the EPI as needed to improve sustainability.** If an initial costing analysis reveals that introduction of JE vaccine would not be affordable or sustainable, the integration plan should be revisited and modified to optimize program efficiency and minimize resources needed. Once you have a revised plan, the costing analysis should be reconducted. This cyclic process should be repeated until your country has a viable JE vaccine integration plan that is both affordable and sustainable.

3. **Analyze and update comprehensive multi-year plans, budgets, and financing plans for JE vaccines.** Budgets and plans should be developed and modified based on the results of affordability and sustainability analyses. All budgets should indicate the sources of the funding, and new resource mobilization strategies may be required. WHO provides templates, checklists, and other tools to help countries develop their own customized budgets and plans.
Navigating vaccine introduction
a guide for decision-makers

JAPANESE ENCEPHALITIS (JE)

IS MY COUNTRY'S JE VACCINATION PROGRAM WORKING?

Module 6
• The success of a JE vaccination program can be measured by the number of children vaccinated, the overall proportion of eligible children vaccinated, and the subsequent reduction of JE and acute encephalitis syndrome (AES) cases.

• Monitoring and evaluating the success of a vaccination program is a process that should begin with monitoring before vaccination starts.

• Because JE is only one cause of encephalitis, other causes of AES will still be present after JE vaccine is introduced.

• Monitoring and evaluation are important to assess and communicate the health benefits, cost-effectiveness, and efficiency of your country’s JE immunization program.
Is my country’s JE vaccination program working?

After your country has introduced JE vaccine, it is important to monitor and evaluate the progress and success of introduction. Monitoring is the systematic and continuous process of collecting and examining data, procedures, and practices. Once this information is collected, evaluation is performed to measure progress, identify problems, develop solutions, and guide policies and interventions. For JE vaccine programs, it is important to focus on the number and proportion of vaccine-eligible children actually immunized, the reduction of JE and AES cases, and a population-based estimate of adverse events following immunization. Through monitoring and evaluation, immunization program managers can improve the quality, safety, and benefits of your country’s JE immunization program, maximize program efficiency and cost-effectiveness, and provide evidence of success to policymakers, donors, and the public.2

Monitoring coverage of JE vaccine

One primary method to evaluate JE immunization programs is to measure vaccination coverage.2 Because JE burden is greatest among children, this requires tracking the total number of vaccine-eligible children in an area intended for vaccination (target population) as well as the number of children actually vaccinated by age, by gender, and by location. These data are used to determine the vaccine coverage by age, by gender, and by location. Coverage is often measured using administrative data from immunization registries, vaccination cards, and tally sheets collected at the local level and aggregated regionally and nationally to estimate the actual proportion immunized.3 In situations where higher-quality vaccine coverage data are critically needed, population-based immunization coverage surveys should be used.

When possible, JE vaccine coverage data should always be reviewed in conjunction with JE disease surveillance data. In Uttar Pradesh, India, following a 2011 introduction campaign, JE surveillance data showed a less-than-expected decline in JE incidence. However, a cross-sectional coverage survey showed that only half of the eligible children had received one dose of JE vaccine.4 Because the survey included questions about vaccine acceptance and vaccine administration, it was possible to identify factors that contributed to low community acceptance resulting in low vaccine coverage and lower vaccine impact than expected. Information from population-based coverage surveys such as this, which can include questions about community knowledge, attitudes, and practices in addition to coverage, not only result in accurate measures of vaccine coverage but also inform program improvements and future JE vaccination campaigns.

Comparing coverage with other vaccines in your country’s Expanded Programme on Immunization (EPI) can identify potential problems with the introduction, such as low community acceptance, local vaccine stockouts, and other program issues needing corrective action.2 By examining and comparing coverage rates of all EPI vaccines before and after JE vaccine is introduced, your country can identify trends, problems, and opportunities for improvement.5
Conducting JE surveillance before and after vaccine introduction is the best way to measure the impact of JE vaccination programs on disease incidence, morbidity, and mortality. A country’s ability to measure JE vaccine impact generally depends on having an existing JE disease surveillance system with capacity for laboratory testing (see Module 1: Does my country need JE vaccine?). While some disease surveillance is necessary to measure impact, the absence of robust or perfect national surveillance does not have to impede measuring JE vaccine’s impact in countries with limited resources. For example, your country could use secondary sources of information such as retrospective medical record reviews.

Additionally, countries can use AES surveillance as a proxy for JE surveillance. WHO recommends that AES surveillance is important to identify all preventable causes of encephalitis and, in the absence of JE laboratory testing, may show JE vaccine impact with some limitations. In Nepal, following the 2006-2009 JE vaccination campaigns, JE incidence was 72 percent lower than before the campaigns began. Additionally, AES incidence was 58 percent lower than before the campaigns began (Figure 1). AES is a commonly reported disease syndrome, so the number of AES cases prevented was three times the number of laboratory-confirmed JE cases prevented. This finding strongly suggests that the JE burden was significantly underreported prior to JE vaccine introduction and that many AES cases were actually JE cases. However, a drop in AES incidence may not always be seen following JE vaccine introduction because a significant proportion of AES cases may be due to agents other than JE virus.

Monitoring the impact of JE vaccination on JE incidence has numerous benefits. Evidence of the overall impact of a JE vaccination program may be critical to maintaining long-term political and financial support for the program. This may be especially true in low-income countries where, once external donor support ends, the country must cover vaccine procurement costs on its own. Disease surveillance can be used to monitor overall performance of the immunization program and identify program weaknesses. Evidence of ongoing JE after vaccine introduction may reveal new or pre-existing weaknesses in vaccine delivery systems, such as compromises in the cold chain or programmatic challenges that reduce coverage (e.g., inadequate microplanning or monitoring of campaigns). Finally, tracking changes in disease epidemiology can identify new at-risk groups, help anticipate future needs, and detect JE outbreaks.

The costs of supporting JE and/or AES surveillance should be considered in the overall costs of the immunization program or another appropriate budget (See Module 5: Can my country...
Monitoring JE vaccine safety

All WHO-prequalified JE vaccines are considered safe when the vaccine is shipped, stored, handled, and administered in a specified manner (see Module 3: Which JE vaccine should my country use?). These requirements should be thoroughly covered during logistics preparations and health worker training and supervision (see Module 4: How should my country introduce JE vaccines?). However, it is important for all countries to monitor vaccine safety, including detecting and investigating adverse events following immunization (AEFIs). In addition, safety is assessed during prequalification by reviewing data from clinical trials. Because these trials may not be large enough to capture rare AEFIs, ongoing monitoring of vaccine safety in a much larger population can be very valuable.

AEFIs may cause public concern. Early identification of AEFIs by the government and subsequent investigations may allow detection of problems with shipping, storing, handling, or administering the vaccine—mistakes that can be corrected through further health worker training and supervision.2,14 Such transparency may inspire confidence in the JE vaccination program as well as other vaccination programs. In contrast, failure to identify such problems may result in suspicion of the national immunization program, reduce public confidence, and lead to low uptake of JE vaccine and other important vaccines.

afford JE vaccination?). Once surveillance begins, the system and methods to find suspected JE cases, laboratory diagnostics, and other analyses should remain consistent. Otherwise, changes in surveillance methods could confuse the analysis of the impact of the vaccination program on JE incidence.
WHO recommends that all countries conduct post-introduction evaluations (PIEs) 6 to 12 months following new vaccine introductions and has prepared a PIE tool for country use. PIEs use surveillance and monitoring data to provide a comprehensive assessment of the vaccine introduction’s impact on the country’s immunization program and to rapidly identify problems needing correction. The PIE may improve the overall quality of the JE vaccination program and may also provide valuable lessons for future new vaccine introductions. Additionally, evidence of the impact and success of the program can be shared with donors, policymakers, and the public to further strengthen support for JE immunization.

References

Cover photo: PATH/Rocky Prajapati; inside cover: courtesy Bill & Melinda Gates Foundation; back inside cover: PATH/Vu Minh Huong
Planning and decision-making for JE vaccination will continue long after introduction. In order to ensure support for and success of your country’s JE immunization program, it is important to:

1. Assess the reach of the program through coverage monitoring. Because the public health impact of JE disease is greatest among children, coverage data should focus on the number of children covered. By considering coverage and JE incidence together, you may identify potential programmatic or epidemiologic issues that necessitate adjustments.

2. Evaluate the public health impact of the program through JE or AES disease monitoring. While laboratory JE diagnostic testing provides the most accurate assessment of JE immunization program impact, AES monitoring may be useful if JE is not specifically monitored. Apart from evaluating the program’s health impact, disease monitoring can provide information about potential changes in JE epidemiology and detect JE outbreaks.

3. Monitor the safety of JE vaccine through post-introduction safety monitoring. While all WHO-prequalified vaccines have acceptable safety profiles, post-introduction safety surveillance helps identify rare adverse events and potential handling and administration errors.

4. Use observations from monitoring and surveillance to evaluate and make any needed adjustments. Conducting post-introduction evaluations of JE immunization programs can lead to improvements in the implementation of JE vaccination, strengthen the overall immunization program, and provide valuable lessons for future vaccine introductions. Evidence of the success, cost-effectiveness, and public health impact of the program helps maintain political and financial support as well as the public’s confidence in vaccine programs.
FOR MORE INFORMATION OR QUESTIONS
about introducing JE vaccine in your country,
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