JAPANESE ENCEPHALITIS (JE) VACCINE FOR CHILDREN 9 MOS TO 59 MOS OLD (RECLASSIFIED aHTA)

Health Technology Assessment Philippines

OVERVIEW AND CONTEXT

Background

Nominated HT	Japanese Encephalitis (JE) Vaccine	
	Live, attenuated, recombinant JE vaccine *Originally nominated HT*	Inactivated JE vaccine*
Applied dosing regimen	**Primary:** 0.5 mL as single dose. **Booster dose:** May be given 5 years after the primary dose, in patients at continued risk.	**Primary:** 2 doses given 4 weeks apart. (<3 years is 0.25 ml, and 0.5 ml for those aged ≥3 years) *WHO 2015*
Drug/ Therapeutic class	Prophylactic vaccines	
Mode of administration	Injected Subcutaneously (SC)	Injected Intramuscularly (IM)
Nominator	Department of Health – Disease Prevention and Control Bureau (DOH-DPCB)	
Date of submission	11 May 2022	29 May 2024
FDA CPR Status	Initial	Monitored Release

** The inactivated JE vaccine was not initially included in the assessment but was later included upon the availability of the MR-CPR for the inactivated JE vaccine.*

Rationale of the Assessment

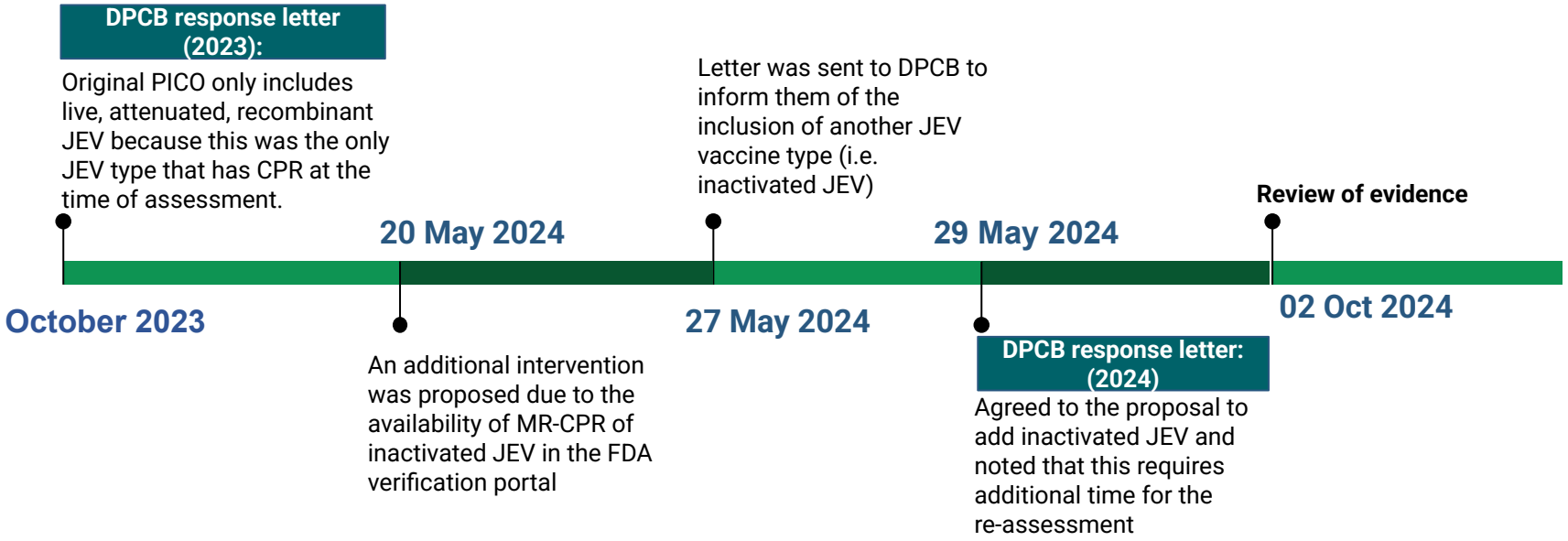
Topic Nominator: DOH - DPCB

Rationale:

JEV is in the DOH Omnibus Health Guidelines for Children but not included in any of the following:

- National Immunization Program
- Primary Care Benefit Package of the PhilHealth
- Philippine National Formulary

Overview and context



Relevant Document:

- **Final TP List 2022** - including JE vaccine in the prioritized list
- **Dossier**

Policy Question

Should ***live, attenuated, recombinant AND/OR inactivated Japanese Encephalitis vaccine*** for the ***prevention of Japanese Encephalitis*** among ***children 9 to 59 months old*** be included in the Philippine National Formulary and National Immunization Program?

Final RQ (PICO Format)

Population	Children aged 9 to 59 months old
Intervention	• Live, attenuated, recombinant Japanese Encephalitis vaccine • Inactivated Japanese Encephalitis vaccine
Comparator	No vaccination
Outcome	**<u>Vaccine efficacy/ effectiveness</u>** • Japanese encephalitis • Clinical meningitis • Encephalitis **<u>Immunogenicity</u>** • Seroprotective titers **<u>Safety</u>** • Adverse events • Vaccine-related/ vaccine-associated neurologic adverse events • Serious adverse events

BACKGROUND

Japanese Encephalitis

- from a **flavivirus** related to dengue, yellow fever and West Nile viruses
- exists in a transmission cycle between mosquitoes, pigs and/or water birds (enzootic cycle)
- **transmitted to humans through bites from infected mosquitoes** of the *Culex* species (mainly *Culex tritaeniorhynchus*)
- **main cause of viral encephalitis** in many countries of Asia

Reference: WHO, 2019

Japanese Encephalitis

- Incubation Period: ~5-15 days
- Symptoms:
  - Initial symptoms: fever, headache, and vomiting
  - Mental status changes, neurologic symptoms, weakness, and movement disorders
  - Seizures are common, especially among children.
- **<1% develop neurological illness**
- **Among patients who develop encephalitis (infection of the brain), 20% – 30% die.**
  - **30%-50% of survivors continue to have neurologic, cognitive, or psychiatric symptoms.**

Reference: US CDC, 2022

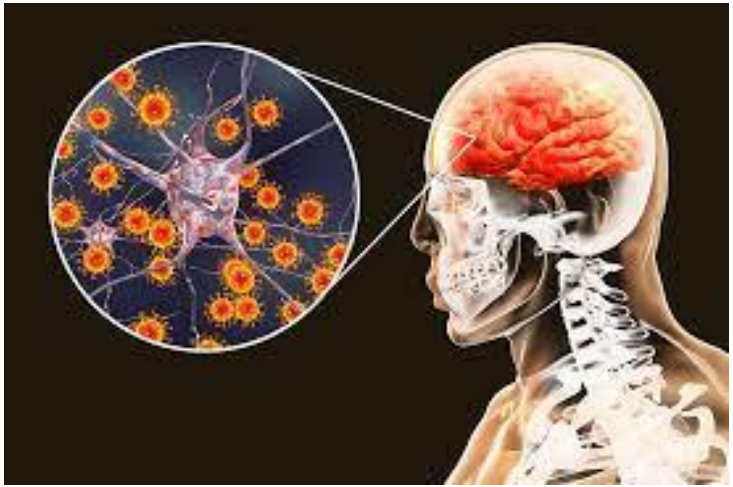
Available JE Vaccine Types and Platforms (WHO, 2015)

JEV Types	Platforms	Remarks
Inactivated	Mouse-brain culture	• Most inactivated mouse brain-derived products have been discontinued. In a few countries there is continued production for domestic supply, although in general these are being phased out.
WHO Pre-qualified **Inactivated**	**Vero-cell culture**	• Primary immunization requires 2 intramuscular doses administered 4 weeks apart. • The dose for those aged <3 years is 0.25 ml, and 0.5 ml for those aged ≥3 years.
Live, attenuated, recombinant	**Vero-cell culture**	• Primary immunization is with **1 dose** given subcutaneously at 9 months of age or older. • A booster dose is recommended 12–24 months later for those <18 years of age.
Live attenuated	Primary hamster kidney	• Primary immunization consists of 1 dose (0.5ml) given subcutaneously from 8 months of age or older.

WHO SAGE Position Paper.PDF

Japanese Encephalitis

- **No specific treatments** have been found to benefit patients with JE. **Treatment is symptomatic.**
  - Rest, fluids, and over-the-counter pain medications may relieve some symptoms.
  - Hospitalization for supportive care and close observation is generally required.
- **Vaccines are available to prevent JE**



Reference: US CDC, 2022

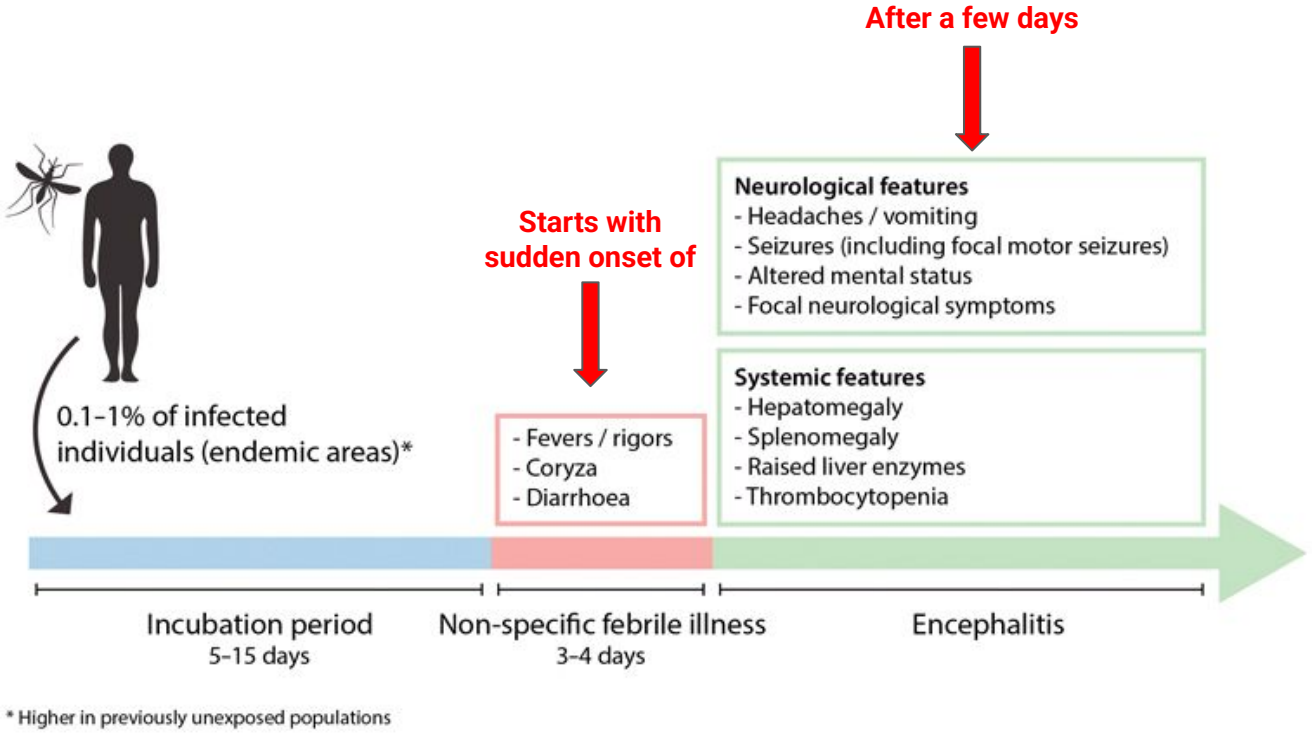
Spectrum and Progression of Disease: Japanese Encephalitis

- **Most JE infections are mild** (fever and headache) or without apparent symptoms
- Approximately **1 in 250** infections results in **severe clinical illness**
  - *Severe disease is characterized by rapid onset of high fever, headache, neck stiffness, disorientation, coma, seizures, spastic paralysis and ultimately death*

(WHO, 2024)

- Average length of hospital stay: 2 to 3 weeks
- 37.9 to 45.4% had moderate to severe neurologic deficits on discharge

(Lopez et al., 2021)



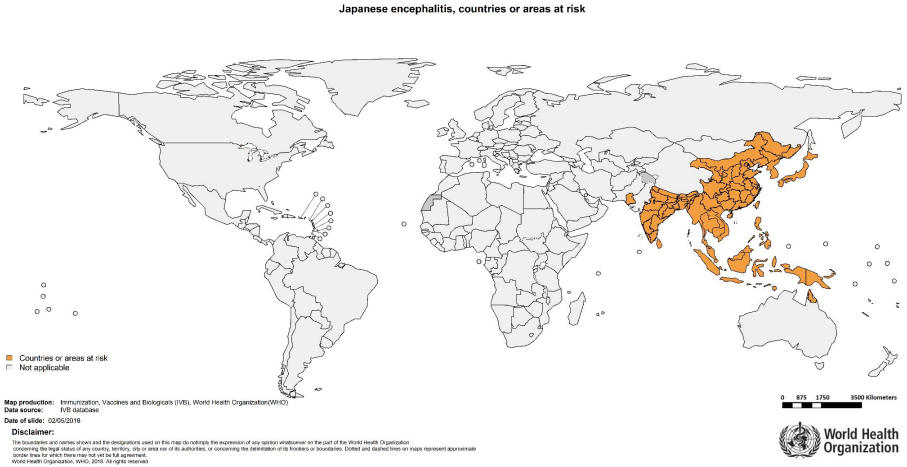
JE Vaccine Types available in the Philippines

JE Type	FDA registration	Mechanism of action
Live, attenuated, recombinant, vero cell JEV	*Initial* Indication: • 9 months of age and over: single dose of reconstituted live, attenuated, recombinant, vero cell JEV 0.5 mL injection should be administered for primary immunization	• The virus replicates locally and elicits neutralising antibodies and cell-mediated immune responses that are specific to the JE virus *(Product Insert)* • This also contain weakened pathogens, but their attenuation or modification involves recombinant DNA technology.
Inactivated, vero cell JEV	*Monitored Release* Indication: • 2 doses (0.25 mL) for children ≥ 1 to < 3 y/o • 2 doses (0.5 mL) for children ≥ 3 to ≤ 49 yo	• A vero-cell based purified inactivated vaccine acts by inducing antibodies that neutralize live JEV *(Product Insert)*

CI: RESPONSIVENESS TO DISEASE MAGNITUDE AND SEVERITY

Japanese Encephalitis: Global Burden

- JE is endemic in **24 countries in the WHO** *Southeast Asia and Western Pacific* regions
- Annual Cases: 68,000 (1.8 per 100,000)
  - Estimated 56,847 cases in 2019
- Annual Deaths: 13,600 to 20,400
  - Estimated 20,642 deaths in 2019
- JE primarily affects **children**. Overall annual incidence in endemic countries:
  - **0-14 years old: ~5.4 per 100,000**
  - ≥15 years old: ~0.6 per 100,000



Reference: Moore et al, 2021, WHO, 2019, WHO, 2015

24 JE-endemic Countries [WHO, 2015]

1	Australia	7	North Korea	13	Myanmar	19	Russia
2	Bangladesh	8	India	14	Nepal	20	Singapore
3	Bhutan	9	Indonesia	15	Pakistan	21	Sri lanka
4	Brunei	10	Japan	16	Papua New Guinea	22	Thailand
5	Cambodia	11	Laos	17	Philippines	23	Timor leste
6	China	12	Malaysia	18	South Korea	24	Vietnam

Recommendation from the Omnibus Health Guidelines (OHG), 2023

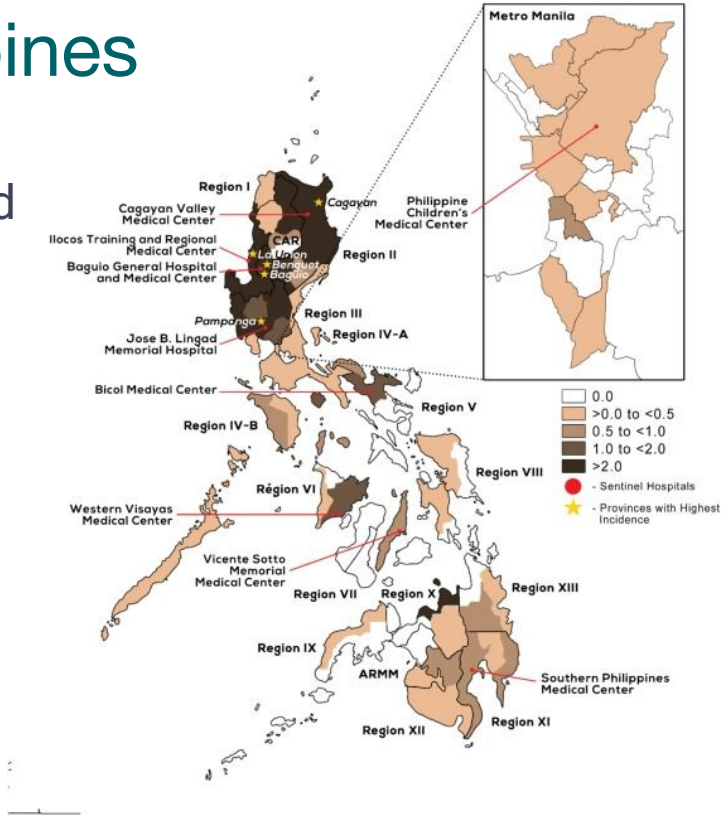
Eligible Population Group or Condition	Recommended Vaccine	Strength of Recommendation (if available) and Reference Guideline
Vaccines that may be given in areas with high burden of high risk of a particular disease	6 - 9 years old: Typhoid Conjugate Vaccine	Weak[6]
	2 - 9 years old: Typhoid Polysaccharide Vaccine	Weak[6]
	≤ 18 years old: Japanese Encephalitis Vaccine^	Weak[6]

^ High risk areas for Japanese Encephalitis:Luzon - Nueva Ecija, Tarlac, Metro Manila, Bulacan, Laguna, Mindoro Pampanga; Visayas - Camarines Norte, Camarines Sur, Northern Samar, Iloilo, Negros Oriental; Mindanao - North Cotabato

Japanese Encephalitis: Philippines

- Nationwide incidence of laboratory-confirmed JE: **0.7/100,000 in <15 years old**
  - Region 2: 3.1/100,000 in <15 years old
  - Region 1: 2.6/100,000 in <15 years old
  - CAR: 2.6/100,000 in <15 years old
  - Region 3: 2.1/100,000 in <15 years old

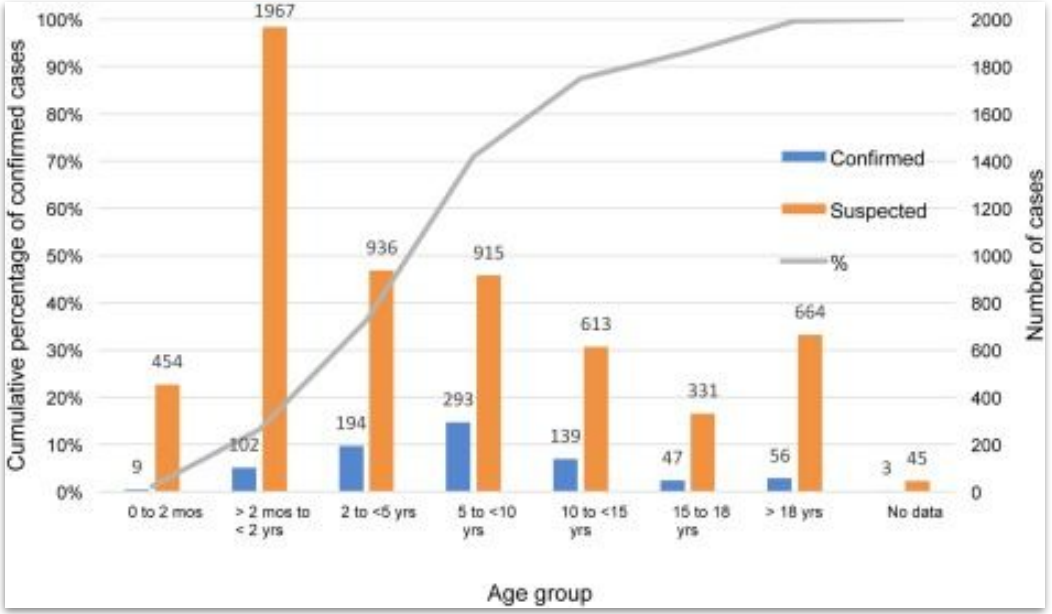
Reference: [Lopez et al, 2021]



Japanese Encephalitis: Philippines

- Findings from the study showed that there were 843 laboratory-confirmed JE cases from January 2014 to December 2017. Of these:
  - 737/843 (87.4%) confirmed cases among children aged <15 years
  - 296/843 (35.1%) confirmed cases among children aged >2 months to <5 years
- Reference: Lopez et al, 2021

January 2014 to December 2017



The highest number of confirmed JE cases is observed in the 5 to <10 years age group, followed by the 2 to <5 years age group. Cases decline with age, with fewest in those >18 years.

JE Surveillance in the PH in 2021 [1 of 5]

Acute Meningitis-Encephalitis Syndrome (AMES) Surveillance:

- Integrated surveillance system of both **japanese encephalitis** and **bacterial meningitis**.
- Collects epidemiological data useful in making evidence-based decisions.
- AMES is used as a **surrogate for JE cases** in surveillance.

General Description of JE Surveillance in 2021 [2 of 5]

Test used	Panbio JE/Dengue IgM Combo Enzyme-linked Immunosorbent Assay (ELISA)
Specimens	Serum and cerebrospinal fluid (CSF)
Positive Result	Presence of JE virus-specific IgM antibody
Sentinel sites	*See photo to the right*
Case definition	*See next slide*
Reference	PIDSR (2021), DOH (2022)

Annex A: List of Selected Hospital Sentinel Surveillance (HSS) Pilot Sites (as of December 7, 2021)

Region	iHOMIS user	Ownership	Non-iHOMIS user	Ownership
CAR	Baguio General Hospital and Medical Center	DOH	St. Louis University Hospital of the Sacred Heart	Private
II	Region II Trauma and Medical Center	DOH	Cagayan Valley Medical Center	DOH
			Southern Isabela Medical Center	DOH
V	Bicol Medical Center	DOH	Universidad de Sta. Isabel De Naga Inc.	Private
	Bicol Regional Training and Teaching Hospital	DOH		
VI	Western Visayas Medical Center	DOH	Corazon Locsin Montelibano Memorial Regional Hospital	DOH
X	Northern Mindanao Medical Center	DOH	Maria Reyna-xavier University Hospital Inc.	Private
XI	None	-	Southern Philippines Medical Center	DOH
			Davao Regional Medical Center	DOH
			Davao Doctors Hospitals	Private
			Brokenshire Integrated Health Ministries, Inc.	Private
			San Pedro Hospital of Davao City Inc.	Private
XII	Cotabato Regional And Medical Center	DOH	St. Elizabeth Hospital Inc	Private
	South Cotabato Provincial Hospital	DOH		
NCR	San Lazaro Hospital	DOH	None	-
	National Children's Hospital	DOH		
	Dr. Jose N. Rodriguez Memorial Hospital	DOH		

General Description of JE Surveillance in 2021 [3 of 5]

Case definition used by PIDSR in their 2021 surveillance	
Severe case	Having **at least three of the four symptoms: disorientation, fever, neck stiffness, and seizures**
Mild case	**Cases which do not meet the criteria for severe cases.**
Hospital admissions	Hospital admissions were defined through the case having a valid admission date entry, and outpatient cases were defined as having invalid admission dates (i.e. NULL values).
Acute encephalitis syndrome (AES)	*A case of AES is defined as a person of any age with acute-onset fever and at least one of the following:* • Change in mental status (e.g. confusion, disorientation, coma, or inability to talk) • New-onset seizures (excluding simple febrile seizures)
Probable JE	An AES case that occurs in close geographical and temporal relationship to a laboratory-confirmed case of JE, in the context of an outbreak.

Results of JE Surveillance in 2021 [4 of 5]

LABORATORY RESULTS OF REPORTED CASES

Out of the 2,736 reported cases, 433 (16%) specimens have been tested. There were 112 (88%) positive for *Japanese encephalitis* (JE) on ELISA. Seven (6%) from the 112 confirmed JE were also tested for other disease like dengue (*Table 5.1.2*).

Table 5.1.2. Laboratory Results of Acute Meningitis-Encephalitis Syndrome Cases Philippines, 2021

AMES Cases		%
TOTAL	**2,736**	**100**
1. Number of cases tested*	**433**	16%
Positive	**128**	30%
Haemophilus Influenza	1	1%
*Japanese encephalitis**	112	88%
Streptococcus pneumoniae	9	7%
Neisseria Meningitis	1	1%
Other organism (Dengue)*	**12**	3%
Pending	**39**	9%
Negative	**266**	61%
2. Not tested	**2,303**	84%

**Multiple responses*

2021 PIDSR Annual Report

- 2,736 reported AMES cases
- 433 specimens tested
- 112/433 JE confirmed cases

Results of JE Surveillance in 2021 [5 of 5]

Table 5.1.3. Laboratory Confirmed Japanese Encephalitis Cases, Deaths, and Case Fatality Rates (CFR) by Region, Philippines, 2020 vs 2021

Region	2020			2021			% Change in Cases	
	Cases	Deaths	CFR	Cases	Deaths	CFR		
PHILIPPINES	126	0	0%	112	4	4%	↓	11%
I*	14	0	0%	27	0	0%	↑	93%
II*	65	0	0%	26	0	0%	↓	60%
III*	24	0	0%	8	1	13%	↓	67%
CALABARZON	0	0	-	0	0	-	→	0%
MIMAROPA	0	0	-	1	0	0%	↑	100%
V*	10	0	0%	20	1	5%	↑	100%
VI*	1	0	0%	14	0	0%	↑	1300%
VII*	3	0	0%	0	0	-	↓	100%
VIII	0	0	-	2	0	0%	↑	200%
IX	0	0	-	0	0	-	→	0%
X	0	0	-	0	0	-	→	0%
XI*	1	0	0%	1	0	0%	→	0%
XII	0	0	-	1	0	0%	↑	100%
BARMM	0	0	-	0	0	-	→	0%
CAR*	8	0	0%	7	1	14%	↓	13%
Caraga	0	0	-	2	0	0%	↑	200%
NCR*	0	0	-	3	1	33%	↑	300%

*Region with AMES Sentinel sites

2021 PIDSR Annual Report

- 112 laboratory-confirmed JE cases of the 433 specimens tested
- Highest cases in **Region I and II.**
- 60% males
- Median: 7 years old
- 4 confirmed JE deaths

Reference: PIDSR AR 2021

JE surveillance in the more recent years: Philippines [1 of 2]

	2020		2021		2022		2023		2024	
	Mild	Severe	Mild	Severe	Mild	Severe	Mild	Severe	Mild	Severe
	Due to the lack of data fields in PIDSR-IS, severe cases are defined as having at least three of the four symptoms: disorientation, fever, neck stiffness, and seizures. Mild cases are cases which do not meet the criteria for severe cases.									
Number of laboratory-confirmed JE cases disaggregated by disease severity	**109**	**16**	**98**	**14**	**117**	**6**	**80**	**43**	**17**	**8**
Number of hospital admissions among laboratory-confirmed JE cases disaggregated by disease severity							**79**			
Number of laboratory-confirmed JE cases treated in the outpatient setting	**0**		**0**		**0**		**1**		**0**	

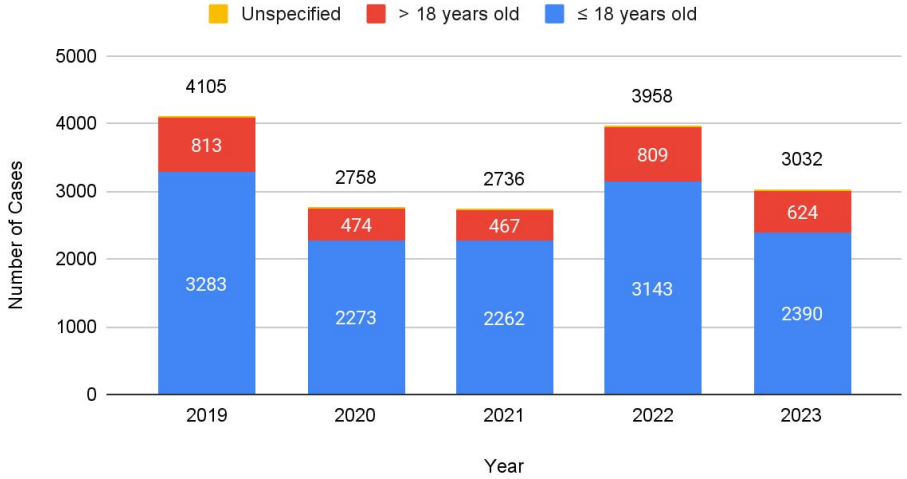
Key findings:

- **Mild JE cases consistently and significantly outnumbered severe JE cases** in the Philippines between 2020 and 2024. **Notably, almost all *(one patient was treated in the outpatient setting)* confirmed JE cases were hospitalized, regardless of severity.**
- Outpatient management of JE was exceptionally rare, with only one case recorded in 2023
- A significant decline in the number of cases was observed in 2024, probably due to still ongoing processing of 2024 data, since the highest number of JE cases is usually seen during the months of July to October (Lopez et al., 2021).

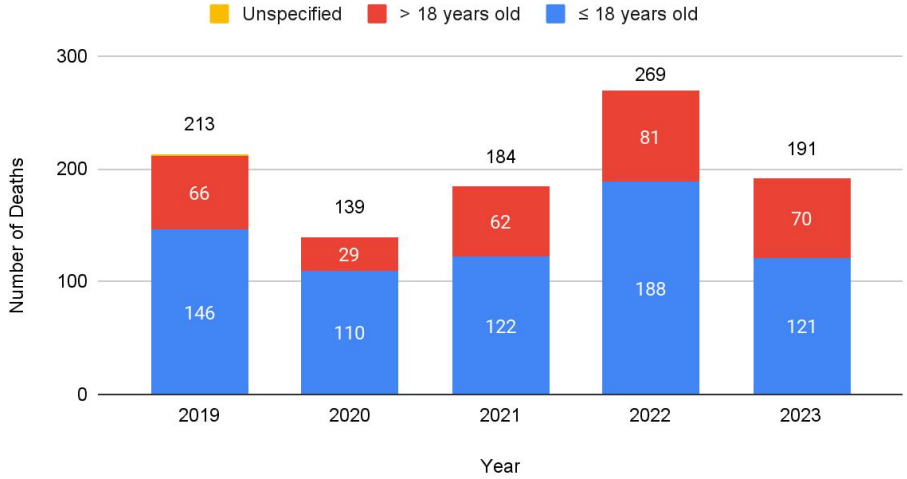
JE surveillance in the more recent years: Philippines [2 of 2]

Acute Meningitis and Encephalitis Syndrome (AMES) Suspected Cases (2019 to 2023):

Age Disaggregated Cases



Age Disaggregated Deaths



*2023 data (until September 16, 2023 only)

Reference: [EB] 2019-2023_Cases-Deaths-Age

AMES (combined JE and bacterial meningitis) cases and mortality are consistently and significantly higher in the ≤18 age group than the >18 age group from 2019 to 2023

C1: Responsiveness to Disease Magnitude and Severity

Summary

Global Burden

- JE primarily affects children, with an annual incidence of 5.4/100,000 among children <15 years old.

JE in the Philippines

- JE incidence in the Philippines is 0.7/100,000 among children <15 years old.
- 87.4% of the confirmed cases are children aged <15 years.
- 35.1% of confirmed cases were among children aged >2 months to <5 years.
- In 2021, there were 112 confirmed JE cases with age ranging from less than one (1) month to 64 years old with a median age of seven (7) years old. Four (4) confirmed deaths due to JE were reported.
- From 2020 to 2024, majority of recorded JE cases were mild. Still, almost all (one patient was treated in the outpatient setting) confirmed JE cases were hospitalized, regardless of severity.
- In 2022 and 2023, the Philippines reported an increase in confirmed Japanese Encephalitis (JE) cases, with 123 cases recorded in both years. However, a significant decline was observed in 2024, with only 25 confirmed JE cases reported *Note: This is probably due to incomplete processing of 2024 surveillance data.*
- The average length of hospital stay is two to three weeks (ranging from 16 to 22 days).

C1: RESPONSIVENESS TO DISEASE MAGNITUDE AND SEVERITY

RQ1.1 **What is the magnitude and severity of Japanese encephalitis in children aged 9 to 59 months old as a public health problem?**

Japanese encephalitis (JE) is the main cause of viral encephalitis and is endemic in 24 countries across the WHO South-East Asia and Western Pacific regions (WHO, 2015). JE primarily affects children, with an annual global incidence of 5.4 per 100,000 among children under 15 years old.

In 2021, the Philippines reported 112 laboratory-confirmed JE cases and four (4) confirmed JE-related deaths, with Regions I and II having the highest case counts (PIDSR, 2021). In 2022 and 2023, the Philippines reported an increase in confirmed JE cases, with 123 cases recorded in both years. However, a significant decline was observed in 2024, with only 25 confirmed JE cases reported probably due to incomplete processing of data in the late months of 2024. Notably, the proportion of hospitalized patients from 2020-2024 was similar to the number of laboratory-confirmed cases, suggesting that only probable JE cases requiring hospital admission were tested for the disease. Additionally, the data on hospitalized cases included cases from mild to severe indicating that even mild cases are admitted. The average length of hospital stay is two to three weeks (ranging from 16 to 22 days) according to Lopez et al (2021).
According to the OHG 2023 of the DOH, the following are declared as areas with high risk for JE:

- Luzon - Nueva Ecija, Tarlac, Metro Manila, Bulacan, Laguna, Mindoro, Pampanga, Camarines Norte, Camarines Sur;
- Visayas - Northern Samar, Iloilo, Negros Oriental;
- Mindanao - North Cotabato

Meanwhile, in terms of AMES (combined JE and bacterial meningitis), both cases and mortality were consistently and significantly higher in the <18 age group from 2019 to 2023. The local incidence of JE among children under 15 years old is 0.7 per 100,000, with 35.1% of confirmed cases among children aged >2 months to <5 years (Lopez et al, 2021).

Compared to dengue infection which reported 350,696 cases in 2024, JE has a low incidence (i.e. 24 confirmed cases in 2024). Despite this, JE has a case fatality rate of 20-30% and a severe disease sequelae, with 30-50% of survivors having permanent neurologic, cognitive, or psychiatric symptoms (US CDC, 2022). Locally, 3.6% (4/112) deaths was recorded in 2021.

C2.I: WHO AND DOH RECOMMENDATIONS

Japanese Encephalitis Vaccine (Live and Inactivated) for children aged 9 to 59 months old

Is there a DOH-approved/ local society CPG recommending this HT?	**YES** but no vaccine type specified **OHG (2023)**: Vaccines that may be given to children ≤ 18 years old in areas with high burden of high risk of a particular disease *(weak recommendation, very low certainty of evidence)* *High risk areas for JE:* *Luzon - Nueva Ecija, Tarlac, Metro Manila, Bulacan, Laguna, Mindoro, Pampanga, Camarines Norte, Camarines Sur; Visayas - Northern Samar, Iloilo, Negros Oriental; Mindanao - North Cotabato* Reference of OHG: **PHEX 2021**: *"Vaccines that may be given to children ≤18 years old from high risk-areas* of a particular disease (Weak recommendation, Very low certainty of evidence)"* - *Although no specific vaccine was mentioned in the recommendation, live attenuated recombinant JEV (IMOJEV) was the only locally available JE vaccine, as cited by PHEX in Table 2.* - *"**Benefits outweigh the risk of harm and evidence shows that vaccination prevents encephalitis,** but some panelists believe more high-quality evidence are needed on burden of disease, cost-effectiveness, equity, acceptability and feasibility to make a strong recommendation."*
Is there a local society certifying the HT as standard of care?	**PIDSP (2025): JE live* attenuated vaccine** Children aged 9 months to 17 years to receive two (2) doses - first dose (primary) followed by a 2nd dose (booster)**, 12 months minimum interval **Used PHEX (2021) as a basis for its childhood immunization schedule in 2025. Further, live JEV (IMOJEV) was the only locally available JE vaccine with FDA authorization during the PHEX review.* ***According to PIDSP, their recent recommendation for live JEV was based on the manufacturer's recommendation. Upon validation with IMOJEV, the approved FDA indication for live JE is one (1) primary dose followed by a booster dose given preferably 1 year after the first vaccination.*

Details of the Pilot implementation in 2019

DM 2019-0018 & DM 2019-0018-A: *"Operational Guide for the Introduction of Japanese Encephalitis Vaccine in the Philippine National Immunization Program*

Description of the Pilot Implementation	
Year Implemented	2019
Target age group	Children 9 months to 59 months old
Pilot regions	Regions I, II, III, CAR
JEV type used • **Manufacturer** • **No. of doses**	Live attenuated JE vaccine (SA 14-14-2) • Manufacturer: Chengdu Institute of Biological Products Co., Ltd. • 1 dose
Immunization campaign	Community-based (combination of fixed site or modified fixed site)

Results of the Pilot Implementation	
• % Coverage	**Overall Coverage in 4 pilot regions:** 340,747 (16%) **CAR:** 107,887 (62%) **Region II:** 40,136 (11%) **Region III:** 192,744 (16%)

JE Cases Pre- and Post-Pilot Immunization

Pilot Regions	2018		2019*			2020			2021		
	Cases	Deaths	Cases	Deaths	%	Cases	Deaths	%	Cases	Deaths	%
Region I	39	0	49	5	↑ 26%	14	0	↓ 71%	27	0	↑ 93%
Region II	49	2	25	0	↓ 49%	65	0	↑ 160%	26	0	↓ 60%
Region III	70	2	19	0	↓ 73%	24	0	↑ 26%	8	1	↓ 67%
CAR	20	0	10	0	↓ 50%	8	0	↓ 20%	7	1	↓ 13%

*Year of pilot vaccination campaign
% Change in Cases from Previous Year

Key Notes:

- **Region 2** has the **lowest coverage (11% only)** during the pilot campaign
  - The increase in cases in 2020 may be attributed to insufficient vaccine coverage
- **CAR** has the **highest coverage (62%)** during the pilot campaign
  - The decrease in JEV cases reflects the probable impact of effective vaccination efforts

Japanese Encephalitis Vaccine (Live and Inactivated) for children aged 9 to 59 months old

Is the HT in the WHO EML?

YES - EML Reference: SAGE Position Paper, 2015; WHO Information Sheet (2016)

Live, attenuated, recombinant vaccines (vero-cell derived)

- A live, attenuated, recombinant (chimeric) JE vaccine was licensed in Australia in 2010 and since then licensed and used in a growing number of Asian countries
- Primary immunization is with **1 dose** given subcutaneously at 9 months of age or older.
- A booster dose is recommended 12–24 months later for those <18 years of age.

Live attenuated, primary hamster kidney cell-derived

- Primary immunization consists of **1 dose** (0.5ml) given subcutaneously from 8 months of age or older.

Inactivated vero-cell vaccines:

- Primary immunization requires **2 intramuscular doses** administered 4 weeks apart.
- The dose for those aged <3 years is 0.25 ml, and 0.5 ml for those aged ≥3 years.

SAGE Position Paper, 2015 - BASIS FOR RECOMMENDATION

General recommendation	**JE vaccination should be integrated into national immunization schedules in all areas where JE is recognized as a public health priority despite low JE-confirmed cases**
Section	**Summary of justification**
Immunogenicity/ effectiveness [Seroprotection rate]	**[Live, attenuated, recombinant]** ● 9–18 months: **99.3%** ● 12–24 months: **100%** ● 12–18 months: **95.0%** ● 36–42 months: **89.7%** **[Inactivated]** ● 1–2 years old: **95.7%** (one month following the second dose) ● 2 months to 18 years old: **≥99%**
Safety	According to the WHO Global Advisory Committee on Vaccine Safety (GACVS) review, all JE vaccine types – including inactivated Vero cell, live attenuated, live, attenuated, recombinant – have demonstrated **acceptable safety profiles.**
Cost-effectiveness	One dose of live attenuated JE vaccine was very **cost-effective by WHO criteria**, or cost-saving. The cost per case averted ranged from US$1,200 (live attenuated vaccine introduced into routine schedule in China) (Ding et al., 2003) to US$21,928 (inactivated mouse brain-derived vaccine introduced through mass campaigns followed by routine use in India*) (Suraratdecha et al., 2006). The cost per DALY averted ranged from US$22 (live attenuated vaccine introduced into the routine programme in Cambodia*) (Touch et al., 2010) to US$1,247 (inactivated mouse brain-derived vaccine introduced through mass campaigns followed by routine use in India*) (Suraratdecha et al., 2006). **Cambodia and India are lower-middle income countries*

2023 WHO Model List of Essential Medicines

Recommendations for certain regions	
Japanese encephalitis vaccine	
tick-borne encephalitis vaccine	
yellow fever vaccine	

PH FDA Verification Portal

	Product Information	Registration Number	Generic Name	Brand Name	Dosage Strength	Dosage Form	Pharmacologic Category	Manufacturer	Country of Origin	Application Type	Issuance Date	Expiry Date
View		BR-1000	Japanese Encephalitis Virus (Live, Attenuated)	Imojev	Formulation: After reconstitution, one dose (0.5 mL) contains 4.0-5.8 log Plaque Forming Units (PFU) live, attenuated, recombinant Japanese Encephalitis Virus.	Powder for Suspension for Injection (SC)	-	Government Pharmaceutical Organization - Merieux Biological Products Co., Ltd.	Thailand	Initial (Variation)	13 July 2022	13 July 2027
View		BR-923	Japanese Encephalitis Vaccine (Live, Attenuated)	Imojev	Formulation: After reconstitution, one dose (0.5 mL) contains 4.0-5.8 log Plaque Forming Units (PFU) live, attenuated, recombinant Japanese Encephalitis Virus.	Powder for Suspension for Injection (SC)	-	Government Pharmaceutical Organization - Merieux Biological Products Co., Ltd.	Thailand	Initial (Variation)	13 July 2022	13 July 2027
View		BR-1465	Japanese Encephalitis Vaccine (Inactivated, Adsorbed)	Jeev	6 mcg/0.5 mL	Suspension for Injection (IM)	Vaccines	Biological E. Limited	India	Monitored Release (MR) [Reapplication]	08 February 2024	08 February 2029

WHO Prequalified JE Vaccines

Date of Prequalification	Vaccine Type	Commercial Name	Presentation	No. of doses	Manufacturer	Responsible NRA
03/08/2016	Japanese Encephalitis Vaccine (Inactivated) (3µg Pediatric)	JEEV® (3µg)	Vial	1	Biological E. Limited	Central Drugs Standard Control Organization
02/10/2018	Japanese Encephalitis Vaccine (Inactivated) (3µg Pediatric)	JEEV® (3µg)	Vial	5	Biological E. Limited	Central Drugs Standard Control Organization
12/07/2013	Japanese Encephalitis Vaccine (Inactivated) 6µg	JEEV® (6µg)	Vial	1	Biological E. Limited	Central Drugs Standard Control Organization
02/10/2018	Japanese Encephalitis Vaccine (Inactivated) 6µg	JEEV® (6µg)	Vial	5	Biological E. Limited	Central Drugs Standard Control Organization
18/09/2014	Japanese Encephalitis Vaccine (live, attenuated)	IMOJEV MD	Two vial set (active + excipient)	4	GPO-MBP Co., Ltd.	Thai Food and Drug Administration

C2.2: COUNTRY GUIDELINES

Review of Guidelines

26

Total Guidelines Scoped

*(**25** JE-endemic countries/areas;*
***1** JEV guideline from WHO SAGE)*

17 of 26

guidelines positively recommend Japanese Encephalitis vaccine use

9 of 26

Bangladesh, Bhutan, Brunei, North Korea, Pakistan, Papua New Guinea, Russia, Singapore, Timor Leste

countries/areas have no recommendations for Japanese Encephalitis vaccine use

Review of Guidelines

24

Total Country NIP Scoped

(Philippines, Australia, Bangladesh, Bhutan, Brunei, Myanmar, Cambodia, China, India, Indonesia, Japan, Laos, Malaysia, Nepal, North Korea, Pakistan, Papua New Guinea, Russia, Singapore, South Korea, Sri Lanka, Thailand, Timor Leste, Vietnam)

13 of 24

countries include Japanese Encephalitis vaccine in their NIP

(Myanmar, Cambodia, China, India, Indonesia, Japan, Laos, Malaysia, Nepal, South Korea, Sri Lanka, Thailand, Vietnam)

11 of 24

Countries **DO NOT include Japanese Encephalitis vaccine in their NIP**

(Australia, Bangladesh, Bhutan, Brunei, North Korea, Pakistan, Papua New Guinea, Philippines, Russia, Singapore, Timor Leste)

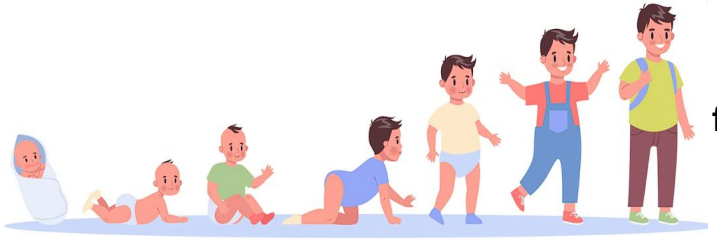
Japanese encephalitis Reported cases by JE-endemic countries that includes JEV in their NIP

Country	Incidence rate (2023) per 1,000,000	Country	Incidence rate (2023) per 1,000,000
Myanmar	0.4	Malaysia	0.4
Cambodia	0.1	Nepal	3.5
China	0.1	South Korea	0.2
India	0.9	Sri Lanka	0.3
Indonesia	0	Thailand	0
Japan	None reported	Vietnam	1.4
Laos	2.6		

Source: WHO 2023

Review of Guidelines: AGE GROUPS

Of the **17** countries and guidelines that positively recommend or include Japanese Encephalitis vaccine in their NIP:



17 of **17** Recommend **for Pedia <18 years old**

5 of **17** Recommends for **adults**

Review of Guidelines: AGE GROUPS

Guidelines	Pedia	Adult	Guidelines	Pedia	Adult
WHO			Myanmar		
Philippines*			Nepal		
Australia*			North Korea		
Bangladesh			Pakistan		
Bhutan			Papua New Guinea		
Brunei			South Korea		
Cambodia			Russia		
China			Singapore		
India			Sri Lanka		
Indonesia			Taiwan		
Japan			Thailand		
Laos			Timor-Leste		
Malaysia			Vietnam		

- For the guidelines that recommend JE vaccine in the NIP for pediatric population, **the age of starting vaccination vary depending on the JE vaccine type** (e.g., live or inactivated JEV)
  See next slide for starting age of vaccination
- The target age of vaccination in the Philippines are children from **9 to 59 months of age**

With positive recommendations for JEV from guidelines or societies but not included in the NIP

Red - countries that do not include JEV in their NIP

Review of Guidelines: Starting Age of Vaccination

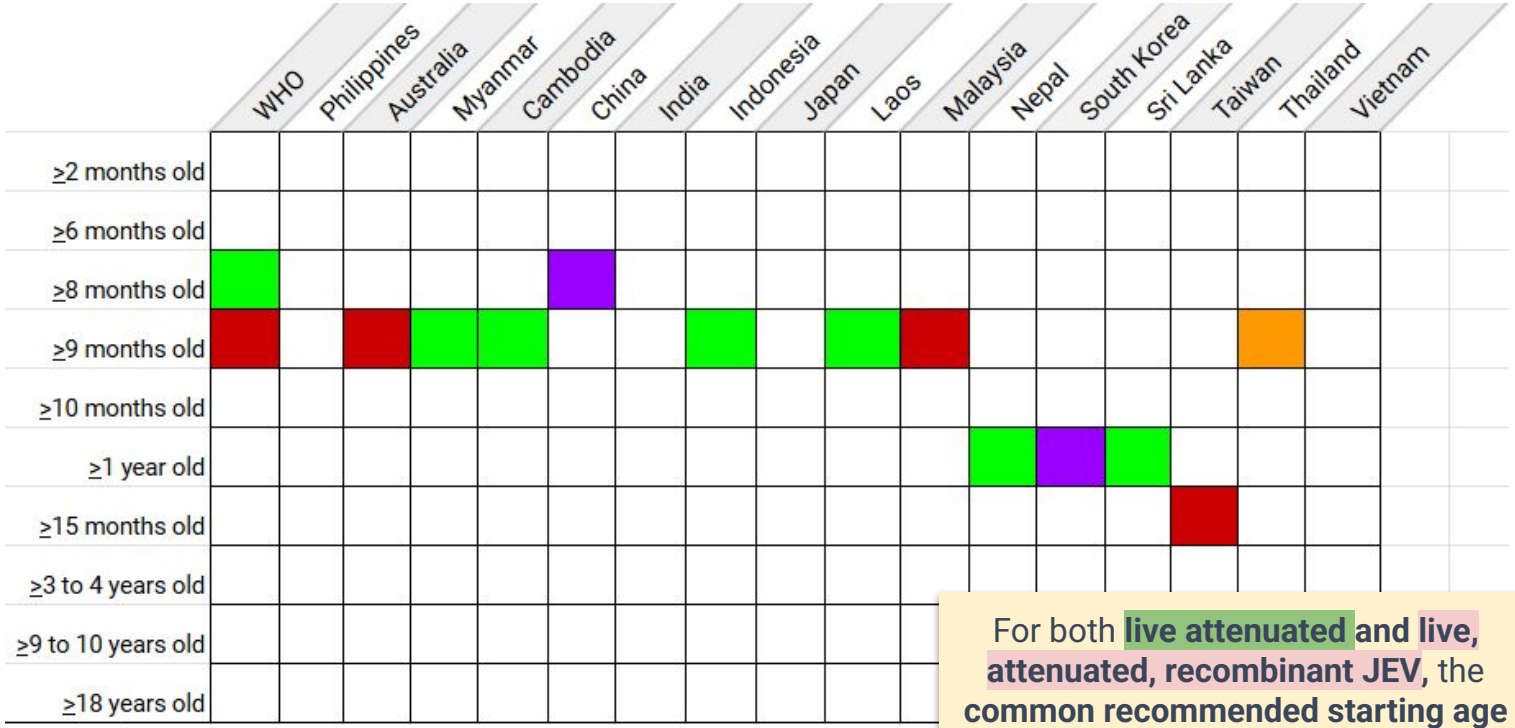
	WHO	Philippines	Australia	Myanmar	Cambodia	China	India	Indonesia	Japan	Laos	Malaysia	Nepal	South Korea	Sri Lanka	Taiwan	Thailand	Vietnam
≥2 months old																	
≥6 months old																	
≥8 months old																	
≥9 months old																	
≥10 months old																	
≥1 year old																	
≥15 months old																	
≥3 to 4 years old																	
≥9 to 10 years old																	
≥18 years old																	

Legend

- Live Attenuated Vaccine
- Inactivated Vaccine
- Live, attenuated, recombinant Vaccine
- Both Live and Inactivated Vaccine
- Both Live attenuated and live, attenuated, recombinant
- No specified type

Japanese Encephalitis Vaccine

Review of Guidelines: Starting Age of Vaccination



For both **live attenuated and live, attenuated, recombinant JEV**, the **common recommended starting age of vaccination ranges between 8 months to 1 year,** with more than half of the guidelines (8 of 13) recommending JEV at 9 mos.

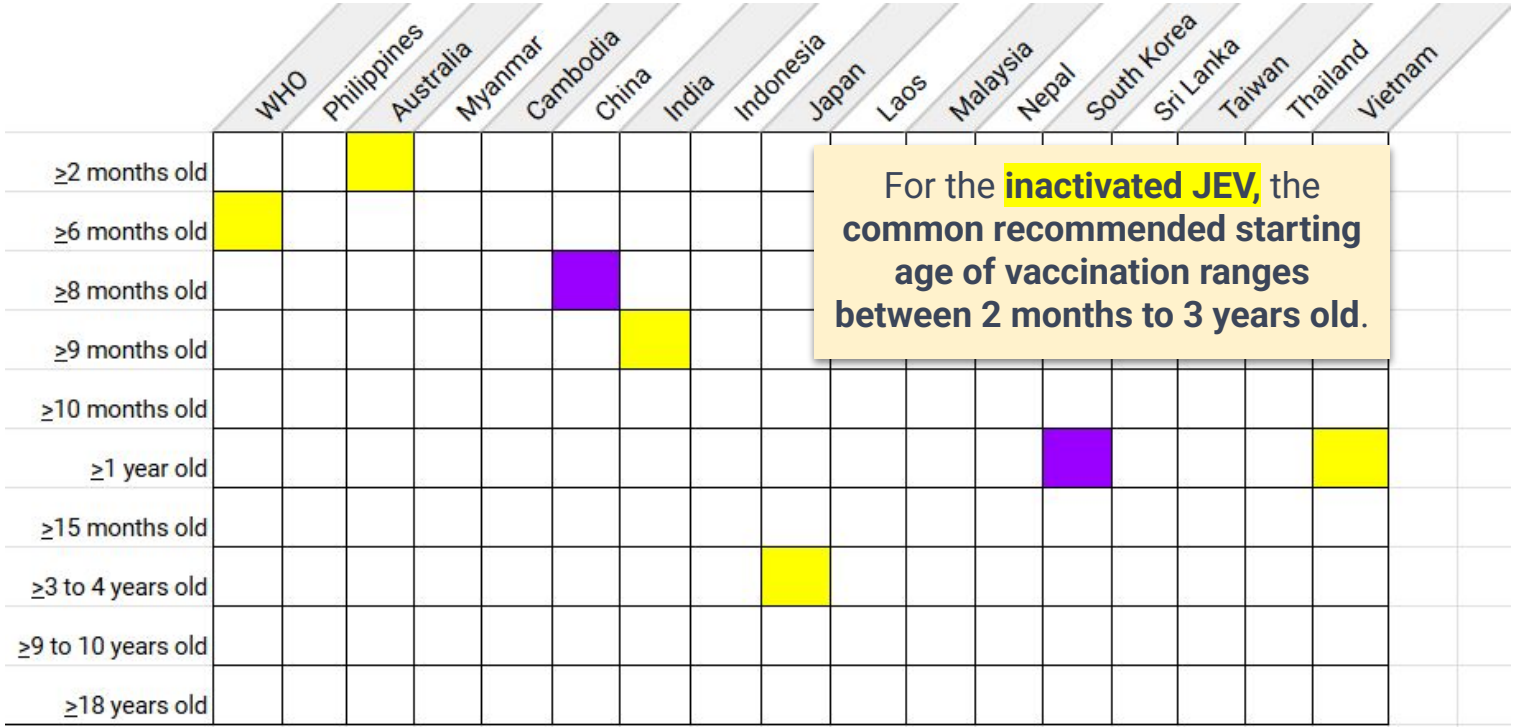
Legend

- Live Attenuated Vaccine
- Inactivated Vaccine
- Live, attenuated, recombinant Vaccine
- Both Live and Inactivated Vaccine
- Both Live attenuated and live, attenuated, recombinant
- No specified type

Vaccine

DOST PHILIPPINES

Review of Guidelines: Starting Age of Vaccination



For the **inactivated JEV,** the **common recommended starting age of vaccination ranges between 2 months to 3 years old.**

Legend

- Live Attenuated Vaccine
- Inactivated Vaccine
- Live, attenuated, recombinant Vaccine
- Both Live and Inactivated Vaccine
- Both Live attenuated and live, attenuated, recombinant
- No specified type

Review of Guidelines: JEV Vaccine Type

As of 17 December 2024, both the live, attenuated, recombinant and inactivated JE vaccines are authorized by the FDA

Of the 17 guidelines that recommend JE Vaccine				
Live Attenuated JE Vaccine only (n=6)	**Live, attenuated, recombinant JE Vaccine only (n=2)**	**Inactivated JE Vaccine only (n=3)**	**Both Live (Attenuated OR Attenuated, Recombinant) and Inactivated JE Vaccine (n=5)**	**Not specified (n=1)**
Cambodia Indonesia Laos Myanmar Nepal Sri Lanka	Malaysia Taiwan	India Japan Vietnam	WHO Australia China South Korea Thailand	Philippines

Review of Guidelines: Dosing Schedule

Of the **13** countries and guidelines that positively recommend **live (attenuated or live, attenuated, recombinant) JEV**

6 of **13**
Recommend **1 Dose of JE Vaccine only**

3 of **13**
Recommend **Primary Vaccination with Booster Dose**

4 of **13**
Recommend **2 Doses of JE Vaccine**

No Guidelines
Recommend **3 Doses of JE Vaccine**

Review of Guidelines: Dosing Schedule

Of the **8** countries and guidelines that positively recommend **Inactivated JEV**

No Guidelines

Recommend **1 Dose of JE Vaccine**

3 of **8**

Recommend **2 Doses of JE Vaccine**

4 of **8**

Recommend for **Primary Vaccination with Booster Dose**

1 of **8**

Recommend for **3 Doses of JE Vaccine**

Review of Guidelines: Dosing Schedule

Of the 13 guidelines that recommend LIVE (attenuated or attenuated, recombinant) JE Vaccine				
1 Dose JE Vaccine (n=6)	**2 Dose JE Vaccine (n=4)**	**3 Dose JE Vaccine (n=0)**	**Primary Vaccination (1 dose) with Booster Vaccine (n=3)**	**No Specified type of vax (n=1)**
WHO Cambodia Laos Myanmar Nepal Sri Lanka	China South Korea Taiwan Thailand	None	Australia Indonesia Malaysia	Philippines

Review of Guidelines: Dosing Schedule

Of the 8 guidelines that recommend INACTIVATED JE Vaccine				
1 Dose JE Vaccine (n=0)	**2 Dose JE Vaccine (n=3)**	**3 Dose JE Vaccine (n=1)**	**Primary Vaccination with Booster Vaccine (n=4)**	**No Specified type of vax (n=1)**
	WHO Australia India	Vietnam	China *(4 primary dose)* Japan *(2 primary dose)* South Korea *(3 primary dose)* Thailand *(2 primary dose)*	Philippines

C2: CLINICAL EFFICACY, EFFECTIVENESS, SAFETY (REVIEW OF GUIDELINES)

RQ2.1: What are the recommendations and guidelines of HTA agencies and ministries of health on the use of japanese encephalitis vaccine?

According to WHO SAGE Position Paper (2015), which recommended that use of both live, attenuated, recombinant and inactivated JE vaccine, the seroprotection rate at one month after the primary series of a **live, attenuated, recombinant JE vaccine ranged from 89.7% to 100% among children aged 9 months to 42 months,** while for **inactivated JE vaccine,** the seroprotection rates at one month after the primary series ranged from **95.7% to 99% among children aged 2 months to 18 years.** In terms of safety, the post-marketing data 12 months following market introduction of JE vaccines in Europe, USA, and Australia **did not show any safety signals of concern**. Further, a review by WHO Global Advisory Committee on Vaccine Safety (GACVS) concluded that **all JE vaccine types, including inactivated and live, attenuated, recombinant, have demonstrated acceptable safety profiles.**

Upon review of WHO SAGE (2015) and 24 country guidelines where JE is noted to be endemic, JEV is positively recommended by the WHO and 16 countries. JEV is also included in the national immunization programs in 13 of 24 JE-endemic countries (i.e., Myanmar, Cambodia, China, India, Indonesia, Japan, Laos, Malaysia, Nepal, South Korea, Sri Lanka, Thailand, Vietnam). However, the Philippines and 10 other countries (i.e. Australia, Bangladesh, Bhutan, Brunei, North Korea, Pakistan, Papua New Guinea, Russia, Singapore, Timor Leste) do not have JEV in their NIP.

In the Philippines, a pilot implementation was conducted in 2019 for children 9 months to 59 months old in Regions I, II, III, CAR. One dose of the live attenuated JE vaccine (*manufactured by Chengdu Institute of Biological Products Co., Ltd,*) was administered in communities. The overall vaccination coverage of the pilot implementation in the four regions was only 16%.

Among the guidelines that recommend JE vaccines:

- WHO and 16 countries recommend JEV for the pediatric population aged <18 years old. Along with WHO, four countries recommend JEV for adults as well.
- In terms of JE vaccine type, six (6) countries recommend live attenuated JE vaccine only, two (2) countries recommend live, attenuated, recombinant JE vaccine only, three (3) countries recommend inactivated JE vaccine only, while WHO and four (4) countries recommend both live (attenuated or recombinant) and inactivated JE vaccine. To note, **the Philippine DOH OHG 2023 did not specify the recommended JE vaccine type; however, FDA-registered live, attenuated, recombinant and inactivated JE vaccines are both available in the market. To note, the DOH OHG 2023 recommends JE vaccination for high risk areas only.**
- In terms of number of doses:
    - Of the 13 guidelines recommending **live (attenuated or attenuated, recombinant) JEV**, a **1-dose primary schedule** is recommended by almost half of the guidelines (6 of 13).
    - Of the 8 guidelines recommending **inactivated JEV**, a **primary series (*ranging from 2 to 4 doses)* with booster/s** is recommended by half of the guidelines (4 of 8).

C3: COSTING ANALYSIS

Overview of Results: Cost of vaccination per vaccinee

JE Vaccine	Cost per dose	Doses required	Cost of vaccination per vaccinee*
live, attenuated, recombinant JEV (0.5 ml) *Note: Recommended dose for ages **9 mos and above***	[Redacted, confidential information]	One-dose	**₱1,914.91**
Inactivated JEV (0.25ml) *Note: Recommended dose for ages 9 mos to **< 3 yo***	[Redacted, confidential information]	Two-dose	**₱1,869.05**
Inactivated JEV (0.5 ml) *Note: Recommended dose for ages **3 yo and above***	[Redacted, confidential information]	Two-dose	**₱3,729.27**

**Source of cost data:*

- *Live, attenuated, recombinant: Company submission*
- *Inactivated JEV: Company submission*

Overview of Results: Total Budget Impact

Cost Component Subtotal	Costs (Php)	
	Live, attenuated, recombinant	Inactivated
Target Population *Assumption: 100% of the population* are yet to be vaccinated*	3,916,064	3,916,064
Vaccines and Vaccine Consumables Cost	₱7,050,581,832.05	₱10,155,743,096.65
Logistics Cost	₱448,335,545.54	₱134,803,777.06
Service Delivery Cost	₱0.00	₱0.00
TOTAL BUDGET IMPACT	**₱7,498,917,377.59**	**₱10,290,546,873.71**

**Children 9 months to less than 5 years old in the identified high risk areas*

Costing Inputs Remarks and Assumptions [1 of 7]

<table>
<tr><th rowspan="3">Cost Component</th><th colspan="3">Remarks/Assumptions</th></tr>
<tr><th rowspan="2">Live, attenuated, recombinant</th><th colspan="2">Inactivated</th></tr>
<tr><th>0.25 ml (9 mos to less < 3 y/o)</th><th>0.5 ml (3 to < 5 y/o)</th></tr>
<tr><td rowspan="2">Vaccine Costs</td><td rowspan="2">• 1 dose, 0.5 mL per vial [Redacted, confidential information]
• Primary immunization: 1 dose (0.5ml) for 9 mos of age or older (SAGE, 2015)</td><td colspan="2">1 vial contains 0.5 mL of vaccine, [Redacted, confidential information]</td></tr>
<tr><td>• 1 vial, 2 doses (0.25 mL per dose)
• Primary immunization: 2 doses, 0.25 mL per dose, ages < 3 y/o (SAGE, 2015)</td><td>• 2 vials, 0.5 mL per dose
• Primary immunization: 2 doses, 0.5 mL per dose, ages 3 yo and above (SAGE, 2015)</td></tr>
</table>

Costing Inputs Remarks and Assumptions [2 of 7]

Cost Component	Remarks/Assumptions		
	Live, attenuated, recombinant	Inactivated	
		0.25 ml (9 mos to less < 3 y/o)	0.5 ml (3 to < 5 y/o)
Population	Less than 5 years old	9 mos to less than 3 years old	3 to 5 years old
	TOTAL POPULATION OF CHILDREN LESS THAN 5 IN THE PHILIPPINES		
	11,118,639 *DPCB 2024 Projected children <5 years of age in 2024*	6,583,692 *Proportion of < 3 years old computed based on PSA 2020 population and DPCB 2024 projection*	4,534,948 *Proportion of 3 years old to < 5 years old computed based on PSA 2020 population and DPCB 2024 projection*
	NO DATA: TOTAL POPULATION OF CHILDREN LESS THAN 5 IN THE IDENTIFIED HIGH RISK AREAS; SEE NEXT SLIDE FOR HTAD ESTIMATION		

Costing Inputs Remarks and Assumptions [3 of 7]

Cost Component	Remarks/Assumptions		
	Live, attenuated, recombinant	Inactivated	
		0.25 ml (9 mos to less < 3 y/o)	0.5 ml (3 to < 5 y/o)
Population **High Risk Areas:** *Nueva Ecija; Tarlac; Metro Manila; Bulacan; Laguna; Mindoro; Pampanga; Camarines Norte; Camarines Sur; Northern Samar; Iloilo; Negros Oriental; North Cotabato)*	**HTAD Projection based on the 2020 PSA data** 2024 TOTAL POPULATION OF CHILDREN LESS THAN 5 IN THE **IDENTIFIED HIGH RISK AREAS** **Assuming all children shall be vacinnated**		
	? *No response from DPCB*	? *No response from DPCB*	? *No response from DPCB*

Available information		Proposed calculations
A. 2020 **Total** Population (nationwide) A.1. number of <3 yo Population A.2. number of 3 to <5 yo Population	→	D. Proportion of <3 yo and 3 to <5yo to the total population (2020) = [A.1 or A.2] / A
B. 2020 **Total** population in each **high risk area**		E. Total number of <3 yo and 3 to <5yo children in high risk areas (2020) = D*B
C. PH 2020-2021 **Growth Rate**		F. **Total number of <3 yo and 3 to <5yo children in high risk areas (2024) = $E*(1+C)^n$** ***[END GOAL]*** *n=how many years projected from the past*

Costing Inputs Remarks and Assumptions [4 of 7]

Cost Component	Remarks/Assumptions		
	Live, attenuated. recombinant	Inactivated	
		0.25 ml (9 mos to less < 3 y/o)	0.5 ml (3 to < 5 y/o)
Population **High Risk Areas:** *Nueva Ecija; Tarlac; Metro Manila; Bulacan; Laguna; Mindoro; Pampanga; Camarines Norte; Camarines Sur; Northern Samar; Iloilo; Negros Oriental; North Cotabato)* *Assumption: 100% of the population is yet to be vaccinated*	**Less than 5 years old**	**9 mos to less than 3 years old**	**3 to 5 years old**
	HTAD Projection based on the 2020 PSA data 2024 TOTAL POPULATION OF CHILDREN LESS THAN 5 IN THE **IDENTIFIED HIGH RISK AREAS**		
	3,916,064 *PSA 2020-based Projection of children <5 years of age in high risk areas in 2024*	**2,318,823** *PSA 2020-based Projection of children < 3 years old in high risk areas in 2024*	**1,597,240** *PSA 2020-based Projection of children 3 years old to < 5 years old in high risk areas in 2024*

Available information	Generated values	Proposed calculations
A. 2020 **Total** Population (nationwide) A.1. number of <3 yo Population A.2. number of 3 to <5 yo Population	A: 109,033,245 A.1.: 6,554,582 A.2.: 4,514,897	D. Proportion of <3 yo and 3 to <5yo to the total population (2020) = **[A.1 or A.2]/ A** **Proportion <3 yo Population: 0.06011544461** **Proportion 3 to <5 yo Population: 0.04140844382**
B. 2020 **Total** population in each **high risk area**	B: *See next slide*	E. Total number of <3 yo and 3 to <5yo children in high risk areas (2020) = **D*B** **number of <3 yo Population: 2,185,662** **number of 3 to <5 yo Population: 1,505,488**
C. PH 2020-2021 Growth Rate	C: 1.49%	F. **Total number of <3 yo and 3 to <5yo children in high risk areas (2024) = $E*(1+C)^4$** ***[END GOAL, see values above]***

Costing Inputs Remarks and Assumptions [5 of 7]

High-risk areas:	Based on 2020 census [TOTAL]
Nueva Ecija	2,310,134
Tarlac	1,503,456
Metro Manila	13,484,462
Bulacan	3,708,890
Laguna	3,382,193
Mindoro	1,433,693
Pampanga	2,437,709
Camarines Norte	629,699
Camarines Sur	2,068,244
Northern Samar	639,186
Iloilo	2,051,899
Negros Oriental	1,432,990
North Cotabato	1,275,185
TOTAL	36,357,740

Costing Inputs Remarks and Assumptions [6 of 7]

<table>
<tr><th rowspan="3">Costing Parameter</th><th colspan="3">Remarks/Assumptions</th></tr>
<tr><th rowspan="2">Live, attenuated, recombinant</th><th colspan="2">Inactivated</th></tr>
<tr><th>0.25 ml (9 mos to less < 3 y/o)</th><th>0.5 ml (3 to < 5 y/o)</th></tr>
<tr><td>Vaccine Consumables Cost</td><td colspan="3">Includes cost for auto-disable (AD) syringes and safety boxes</td></tr>
<tr><td colspan="2">• No cost for syringe since 1 syringe and 2 needles already included in package.
• Unit cost of safety box: ₱40.7 (each safety box contains 100 syringes) (DOH, 2024)</td><td colspan="2">• Unit cost of syringe: ₱2.48
• 10.00% wastage for AD syringe
• Unit cost of safety box: ₱40.7 (each safety box contains 100 syringes)
Reference: (DOH, 2024)</td></tr>
<tr><td>Logistics Costs
(Vaccine Consumables)</td><td colspan="3">General assumptions for transportation
• 29.65% of vaccines are transported by land and sea (Luzon areas)
• 70.35% of vaccines are transported by air (Visayas/ Mindanao areas)
• Rate of transport by land and sea is Php 3,400 per cbm
• Average rate of transport by air is Php 189/kg
AD Syringe
• Size: 0.089 cbm per box of syringe (average) containing 2,433 syringe (ave)
• Weight: 12.81kg (average) containing 2,433 syringe (average)
Safety collector box
• Size: 0.016 cbm per box of safety collector box (ave) containing 25 safety collector boxes
• Weight: 6.45 kg (average) containing 25 safety collector boxes</td></tr>
</table>

Costing Inputs Remarks and Assumptions [7 of 7]

Costing Parameter	Remarks/Assumptions		
	Live, attenuated, recombinant	Inactivated	
		0.25 ml (9 mos to less < 3 y/o)	0.5 ml (3 to < 5 y/o)
Logistics Costs *(Vaccine)*	• Carton dimension: 5.4 x 2.8 x 13.6 cm	• Carton dimensions: 14.5 x 10.8 x 4.5 cm *Box of 48 vials (1 dose each)*	
	Transportation • Biothermal packaging dimension: 62 x 42 x 43 cm with 1.00% wastage • 29.65% of vaccines are transported by land and sea (Luzon areas) • 70.35% of vaccines are transported by air (Visayas/ Mindanao areas) • Rate of transport by land and sea is Php 3,150 per cbm • Average rate of transport by air is Php 636.43/kg • Valuation cost is 0.5% of the total value of vaccine transported by land and sea • Valuation cost is 1% of the total value of vaccine transported by air		
	Storage • Rate of storage at Php 28.00 per liter per month • Storage of primary vaccines is assumed to last only for 3 days but we assume 1 month to account for staggered delivery.		
Service Delivery Cost	None since for routine implementation		

Results: Cost per vaccinee

JE Vaccine	Cost per dose	Doses required	Cost of vaccination per vaccinee*
Live, attenuated, recombinant JEV (0.5 ml) *Note: Recommended dose for ages **9 mos and above***	[Redacted, confidential information]	One-dose	**₱1,914.91**
Inactivated JEV (0.25ml) *Note: Recommended dose for ages 9 months to **< 3 yo***	[Redacted, confidential information]	Two-dose	**₱1,869.05**
Inactivated JEV (0.5 ml) *Note: Recommended dose for ages **3 yo and above***	[Redacted, confidential information]	Two-dose	**₱3,729.27**

**Considering other costs (e.g. consumables and logistic costs)*

Results: Total Budget Impact

TOTAL POPULATION OF CHILDREN 9 MOS TO LESS THAN 5 Y/O IN THE IDENTIFIED HIGH RISK AREAS

Cost Component Subtotal	Costs (Php)	
	Live, attenuated, recombinant	Inactivated
Target Population	3,916,064	3,916,064
Vaccines and Vaccine Consumables Cost	₱7,050,581,832.05	₱10,155,743,096.65
Logistics Cost	₱448,335,545.54	₱134,803,777.06
Service Delivery Cost	₱0.00	₱0.00
TOTAL BUDGET IMPACT	**₱7,498,917,377.59** <	**₱10,290,546,873.71**

Assumption: 100% of the population are yet to be vaccinated

Total Budget Impact [PH vs HIGH-RISK AREA IN PH]

Cost	Costs (Php)	
	Live, attenuated, recombinant	Inactivated
TOTAL POPULATION OF CHILDREN LESS THAN 5 IN THE PHILIPPINES	₱21,291,172,564.20 [₱21.29 B]	₱29,217,268,478.83 [₱29.22 B]
TOTAL POPULATION OF CHILDREN LESS THAN 5 IN THE IDENTIFIED HIGH RISK AREAS	₱7,498,917,377.59 **[₱7.50 B]**	₱10,290,546,873.71 **[₱10.29 B]**

Key Findings

TOTAL POPULATION OF CHILDREN 9 MOS TO LESS THAN 5 Y/O IN THE IDENTIFIED HIGH RISK AREAS

Cost Component Subtotal (Php)	Live, attenuated, recombinant	Inactivated	
		0.25 ml (9 mos to less < 3 y/o)	0.5 ml (3 to < 5 y/o)
Cost of Vaccines			
Vaccine Consumables			
Logistics Cost			
Service Delivery Cost			
TOTAL BUDGET IMPACT	**₱7.50 B**	₱4.33 B	₱5.96 B
		< ₱10.29 B	
Cost of vaccination per vaccinee	**₱1,914.91**	**₱1,869.05**	**₱3,729.27**

Key findings: The vaccine strategy with the lowest vaccination cost per vaccinee is live, attenuated, recombinant.

The annual budget impact to the government is ₱7.50B for live, attenuated, recombinant and ₱10.29B for inactivated JE.

Budget Impact of JEV Implementation

TOTAL POPULATION OF CHILDREN 9 MOS TO LESS THAN 5 Y/O IN THE IDENTIFIED HIGH RISK AREAS

JE Vaccine	Total cost of JEV for all target vaccinees* for 2024 (children <5 years of age)	NIP Budget for 2025	% cost of JEV from total NIP budget
Live, attenuated, recombinant JEV (0.5 ml)	₱7.50 B	₱7.96 B	Estimated to consume **94.25% of the 2025 NIP Budget**
Inactivated JEV (0.25, 0.5 ml)	₱10.29 B		**129.33% Exceeds 2025 NIP Budget**

**assuming all children less than 5 years old are to be vaccinated*

PhilHealth Case Rates for treating JE vs Possible cost to be averted by using JE vaccine

	PREVENTION: Cost of vaccine per vaccinee		TREATMENT: Possible cost to be averted using JE vaccine (supportive tx only)
Live attenuated recombinant vaccine	**₱1,914.91**		Case rate for JE: **₱41,145** Case rate for unspecified viral encephalitis, viral encephalomyelitis, or viral meningoencephalitis: **₱41,145** Estimated cases from 2020-2024= **588 JE-confirmed cases** **588*₱41,145 = ₱24.2 M** **Estimated cost = ₱24.2 M*** **based on historical data of JEV cases from 2020-2024*
Inactivated vaccine [9 months to < 3 yo]	**₱1,869.05**	<	
Inactivated vaccine [3 yo to < 5 yo] ***Note:*** *No antiviral drugs available for JE*	**₱3,729.27**		

The introduction of JE vaccination may avert the high cost of treatment for JE, its complications, as well as productivity loss from caregivers.

C3: Costing

RQ3: **What is the cost implication of adding JEV in the NIP? What is the total cost of vaccination per vaccinee?**

The comparative cost analysis showed that the vaccination cost per patient for **live, attenuated, recombinant JEV was Php 1,914.91** for children 9 months and older. Meanwhile, for **inactivated JEV, the vaccination cost per patient is Php 1,869.05 for children less than 3 years old and Php 3,729.27 for children 3 years old and above**.

Meanwhile, assuming all children less than 5 years old are to be vaccinated, financing the Japanese encephalitis vaccination program in **high risk areas for children aged 9 to 59 months** will incur **Php 7.50 billion for live, attenuated, recombinant JEV and Php 10.29 billion for inactivated JEV. The live, attenuated, recombinant JEV is estimated to consume 94.25% of the National Immunization Program (NIP) 2025 Budget while the inactivated JEV will exceed the 2025 NIP budget of Php 7.96 billion.**

Meanwhile, each case of Japanese encephalitis is estimated to cost the healthcare system Php 41,145.00, based on PhilHealth case rate for JE, and unspecified viral encephalitis, viral encephalomyelitis, or viral meningoencephalitis. To note, this is the cost per case and does not factor in the number of children who may be prevented from acquiring JE. The number of cases that were diagnosed with JE from 2020-2024 were 588 cases (across all severities) and can incur a total cost of Php 24,193,260.00.

While the budget impact of JE vaccine is deemed high, its introduction will avert the cost of treatment for Japanese encephalitis, its complications, as well as productivity loss from caregivers. This underscores the need for increased funding for the NIP with a move to introduce and cover JEV.

OVERALL RECOMMENDATION

Summary of Evidences and Judgment

RQ	Direction of Judgment
C1: What is the **magnitude and severity** of Japanese Encephalitis as a public health problem?	• Significant burden in high risk areas • Has a case fatality rate of 20-30% and a severe disease sequelae, with 30-50% of survivors having permanent neurologic, cognitive, or psychiatric symptoms
C2.1 What are the **recommendations and guidelines** of **DOH and WHO** on the use of JEV for children 9 months to 59 months?	• JEV in general is recommended in the Omnibus Health Guidelines (2023) and was recommended in the PHEX (2021). • Both JEV vaccine types (live, attenuated, recombinant and inactivated) are included in the WHO EML and in the WHO SAGE Position Paper (2015).
C2.2: What are the **recommendations and guidelines** of ministries of health on the use of JEV for children 9 months to 59 months?	In terms of vaccination age group, most guidelines (17/26) positively recommend JEV for pediatric population • Live attenuated JEV alone is the top recommended regimen (6/17), followed by both live (attenuated or attenuated, recombinant) and inactivated JEV (5/17). • Two (2/17) recommended live, attenuated, recombinant alone while three (3/17) countries recommended inactivated JEV alone.

Summary of Evidences and Judgment

RQ	Direction of Judgment
C3.1: What is the **cost implication** of adding JEV in the NIP? What is the total cost of vaccination per vaccinee?	• **Live attenuated recombinant JEV had the least cost per vaccinee** • Vaccination cost per patient: - ₱1,914.91 for live, attenuated, recombinant - ₱1,864.81 and ₱3,720.78 for inactivated JEV for children under 3 years old and > 3 yo to < 5 yo, respectively. • Each case of Japanese encephalitis is estimated to cost the healthcare system Php 41,145.00, based on PhilHealth case rate for JE, and unspecified viral encephalitis, viral encephalomyelitis, or viral meningoencephalitis. This is the cost per case and does not factor in the number of children who may be prevented from acquiring JE. The number of cases that were diagnosed with JE from 2020-2024 were 588 cases (across all severities) and can incur a total cost of Php 24,193,260.00.
C3.2: What is the **budget impact** of adding JEV in the NIP?	• The annual budget impact to the government is ₱7.50B for live, attenuated, recombinant and ₱10.29B for inactivated JEV. • **The live, attenuated, recombinant JEV is estimated to consume 94.25% of the National Immunization Program (NIP) 2025 Budget while the inactivated JEV will exceed the 2025 NIP budget of Php 7.96 billion.**

THANK YOU!