Assessing and Communicating Adverse Events Following Immunization (AEFIs)

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Outline

- AEFI – Key Definitions
- Causality Assessment
- Communicating AEFI
- Country Experience

Adverse Event Following Immunization (AEFI)

Definition (CIOMS/WHO)

Any untoward medical occurrence

which follows immunization and which **does not necessarily have a causal relationship** with the use of vaccine

The adverse event may be

any unfavourable or unintended sign, an abnormal laboratory finding , a symptom or a disease

Definition and application of terms for vaccine pharmacovigilance. Report of CIOMS/WHO Working Group on Vaccine Pharmacovigilance. Geneva, Council for International Organizations of Medical Sciences, 2012. See: http://www.who.int/vaccine_safety/initiative/tools/CIOMS_report_WG_vaccine.pdf (accessed 2 January 2018).

CIOMS/WHO Cause-specific Definitions of AEFIs

1. Vaccine product-related reaction	• One or more of the inherent properties of the vaccine product
2. Vaccine quality defect-related reaction	• One or more quality defects of the vaccine product, including the administration device, as provided by the manufacturer
3. Immunization error-related reaction	• Inappropriate vaccine handling, prescribing or administration and that thus, by its nature, is **preventable**
4. Immunization anxiety-related reaction	• Anxiety about the immunization
5. Coincidental event	• Something other than the vaccine product, immunization error or immunization anxiety

Case selection for detailed investigation and causality assessment of AEFI:

- **Serious AEFI**
- **Clusters & events above expected rate/ severity**
- **Evaluation of suspected Signals**
- **Other AEFI***

As decided by reviewing team / committee

✓If **immunization error is suspected**

✓Significant events of **unexplained cause** within 30 days of vaccination

✓Events causing significant **parental or community concern** (e.g. HHE, febrile seizures)

Serious AEFI

- Death
- Hospitalization or prolongation of existing hospitalization
  (e.g., encephalopathy, seizures, aseptic meningitis)
- Persistent or significant disability or incapacity *(e.g., paralysis)*
- Congenital anomaly/birth defect
- Life-threatening

'Serious' is not synonymous with 'severe' (i.e., intensity or severity of the event)

Source: report of CIOMS/WHO Working Group on Vaccine Pharmacovigilance, 2012

Outline

- AEFI – Key Definitions
- **Causality Assessment**
- Communicating AEFI
- Country Experience

Causality and Causality assessment

Causality*

- Is the relationship between two events (the cause and the effect), where the second event is a consequence of the first

Causality Assessment

- Determining if such a relationship exists and if so to what extent

*A direct cause is a factor in absence of which the effect would not occur (necessary cause).

*Sometimes, there are multiple factors that can precipitate or function as co-factors for the effect (event) to occur.

Prerequisites for assessing causality for an AEFI case

- The AEFI case investigation should have been completed
- All details of the case should be available at the time of assessment
- There must be a "**valid diagnosis**"
  - *The valid diagnosis refers to the extent to which the unfavorable or unintended sign, abnormal laboratory finding, symptom or disease is defined.*

- Case report form,
- Case Investigation Form,
- Completed clinical Case record,
- Lab report,
- Autopsy report, Details of field investigations,
- Blank causality Assessment worksheets

WORKSHEET FOR AEFI CAUSALITY ASSESSMENT (WHO)

Worksheet for AEFI causality assessment

Jan 2018

Patient ID/ Name : DoB/ Age: Sex: Male/ Female

Step 1 (Eligibility)

Name one of the vaccines administered before this event	What is the Valid Diagnosis?	Does the diagnosis meet a case definition?

Create your question on causality here

Has the _____ vaccine / vaccination caused _____(The event for review in step 2 - valid diagnosis)

Is this case eligible for causality assessment? Yes/ No; If, "Yes", proceed to step 2

Step 2 (Event Checklist) ✓ (check) all boxes that apply

I. Is there strong evidence for other causes?	Y	N	UK	NA	Remarks
1. In this patient, does the medical history, clinical examination and/ or investigations, **confirm** another cause for the event?	□	□	□	□	
II. Is there a known causal association with the vaccine or vaccination?					
Vaccine product					
1. Is there evidence in published peer reviewed literature that this vaccine may cause such an event if administered correctly?	□	□	□	□	
2. Is there a biological plausibility that this vaccine could cause such an event?	□	□	□	□	
3. In this patient, did a specific test demonstrate the causal role of the vaccine ?	□	□	□	□	
Vaccine quality					
4. Could the vaccine given to this patient have a quality defect or is substandard or falsified?	□	□	□	□	
Immunization error					
5. In this patient, was there an error in prescribing or non-adherence to recommendations for use of the vaccine (e.g. use beyond the expiry date, wrong recipient etc.)?	□	□	□	□	
6. In this patient, was the vaccine (or diluent) administered in an unsterile manner?	□	□	□	□	
7. In this patient, was the vaccine's physical condition (e.g. colour, turbidity, presence of foreign substances etc.) abnormal when administered?	□	□	□	□	
8. When this patient was vaccinated, was there an error in vaccine constitution/preparation by the vaccinator (e.g. wrong product, wrong diluent, improper mixing, improper syringe filling etc.)?	□	□	□	□	
9. In this patient, was there an error in vaccine handling (e.g. a break in the cold chain during transport, storage and/or immunization session etc.)?	□	□	□	□	
10. In this patient, was the vaccine administered incorrectly (e.g. wrong dose, site or route of administration; wrong needle size etc.)?	□	□	□	□	
Immunization anxiety (Immunization Triggered Stress Response - ITSR)					
11. In this patient, could this event be a stress response triggered by immunization (e.g. acute stress response, vasovagal reaction, hyperventilation or anxiety)?	□	□	□	□	
II (time). If "yes" to any question in II, was the event within the time window of increased risk?					
12. In this patient, did the event occur within a plausible time window after vaccine administration?	□	□	□	□	
III. Is there strong evidence against a causal association?					
1. Is there a body of published evidence (systematic reviews, GACVS reviews, Cochrane reviews etc.) **against** a causal association between the vaccine and the event?	□	□	□	□	
IV. Other qualifying factors for classification					
1. In this patient, did such an event occur in the past after administration of a similar vaccine?	□	□	□	□	
2. In this patient did such an event occur in the past independent of vaccination?	□	□	□	□	
3. Could the current event have occurred in this patient without vaccination (background rate)?	□	□	□	□	
4. Did this patient have an illness, pre-existing condition or risk factor that could have contributed to the event?	□	□	□	□	
5. Was this patient taking any medication prior to the vaccination?	□	□	□	□	
6. Was this patient exposed to a potential factor (other than vaccine) prior to the event (e.g. allergen, drug, herbal product etc.)?	□	□	□	□	

Y: Yes N: No UK: Unknown NA: Not applicable or Not available

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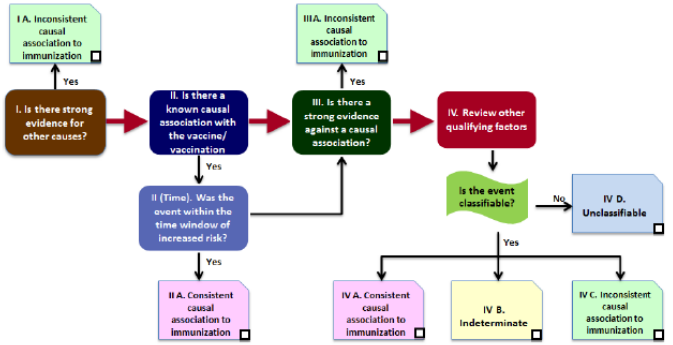
Page 1

Step 3 (Algorithm) review all steps and ✓ all the appropriate boxes



Notes for Step 3:

Step 4 (Classification) ✓ all boxes that apply

Adequate information available

A. Consistent with causal association to immunization

- A1. Vaccine product-related reaction (As per published literature)
- A2. Vaccine quality defect-related reaction
- A3. Immunization error-related reaction
- A4. Immunization anxiety-related reaction (ITSR**)

B. Indeterminate

- B1. *Temporal relationship is consistent but there is insufficient definitive evidence for vaccine causing event (may be new vaccine-linked event)
- B2. Reviewing factors result in conflicting trends of consistency and inconsistency with causal association to immunization

C. Inconsistent with causal association to immunization

- C. Coincidental: Underlying or emerging condition(s), or conditions caused by exposure to something other than vaccine

Adequate information not available

- Unclassifiable

Specify the additional information required for classification :

*B1: This is a potential signal and maybe considered for investigation
** Immunization Triggered Stress Response

Summarize the classification logic in the order of priority:

With available evidence, we could conclude that the classification is _____because:

With available evidence, we could **NOT** classify the case because:_____

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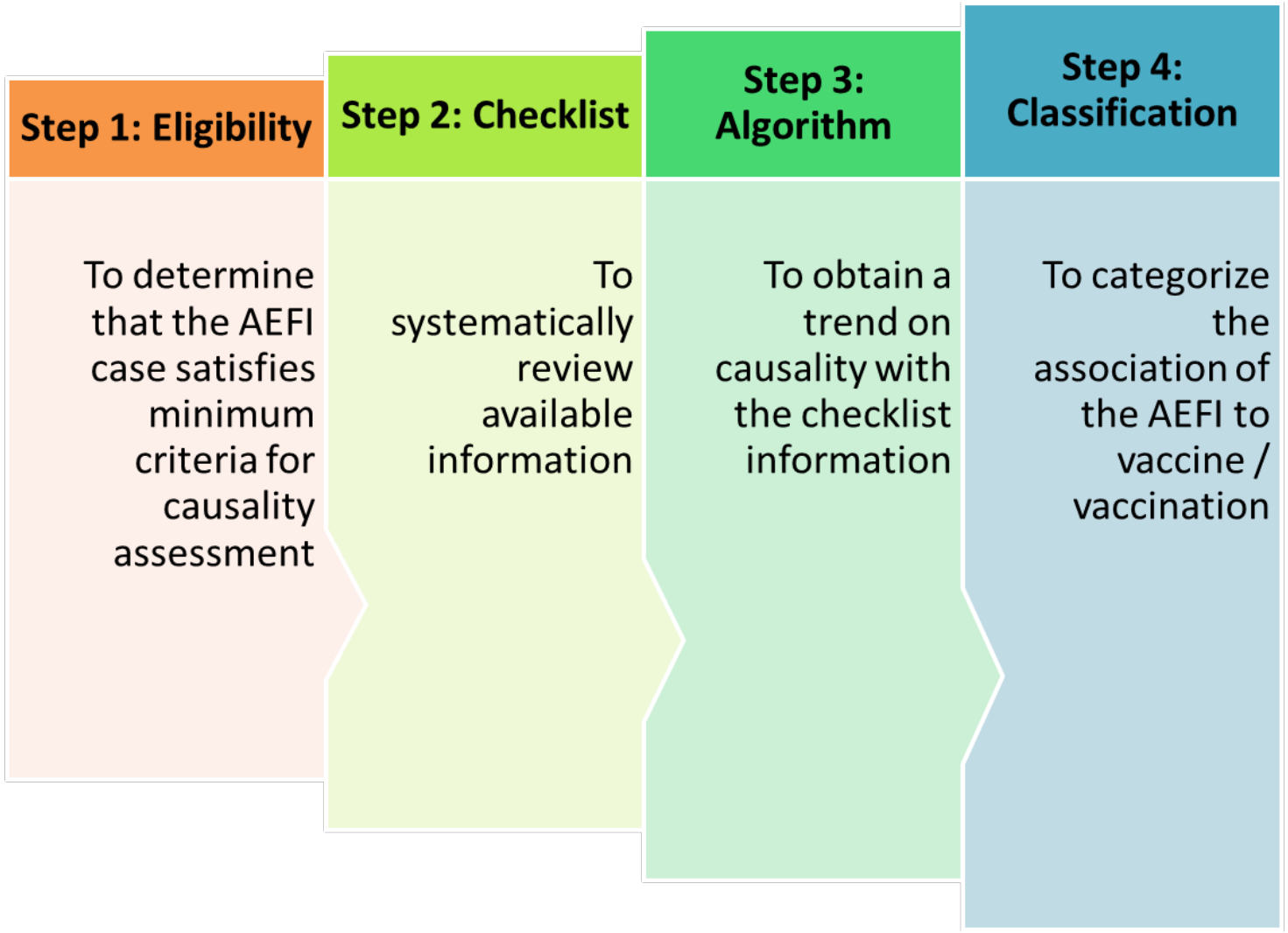
Page 2

Causality Assessment Steps



Step 1: Eligibility

AEFI case

- Ensure AEFI investigation is completed and all details of the case is available
- Retain case details in a retrievable database

Identify vaccine(s)

- Identify one vaccine (implicated) administered before this event

Valid Diagnosis

- Select the unfavorable or unintended sign, abnormal laboratory finding, symptom or disease you want to check causality.

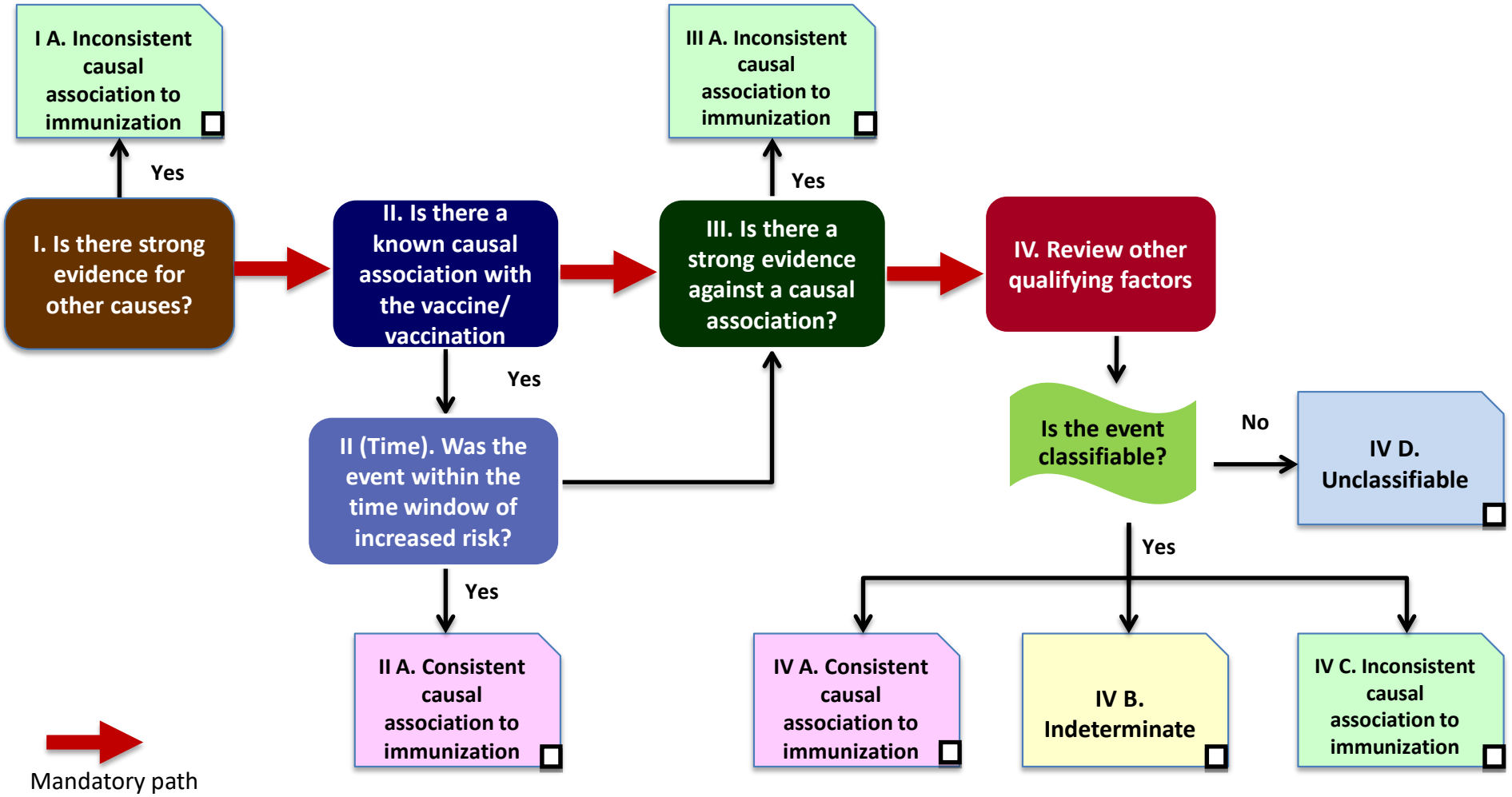
Case definition

- Brighton Collaboration definition, Standard literature definition, National definition or other approved definition

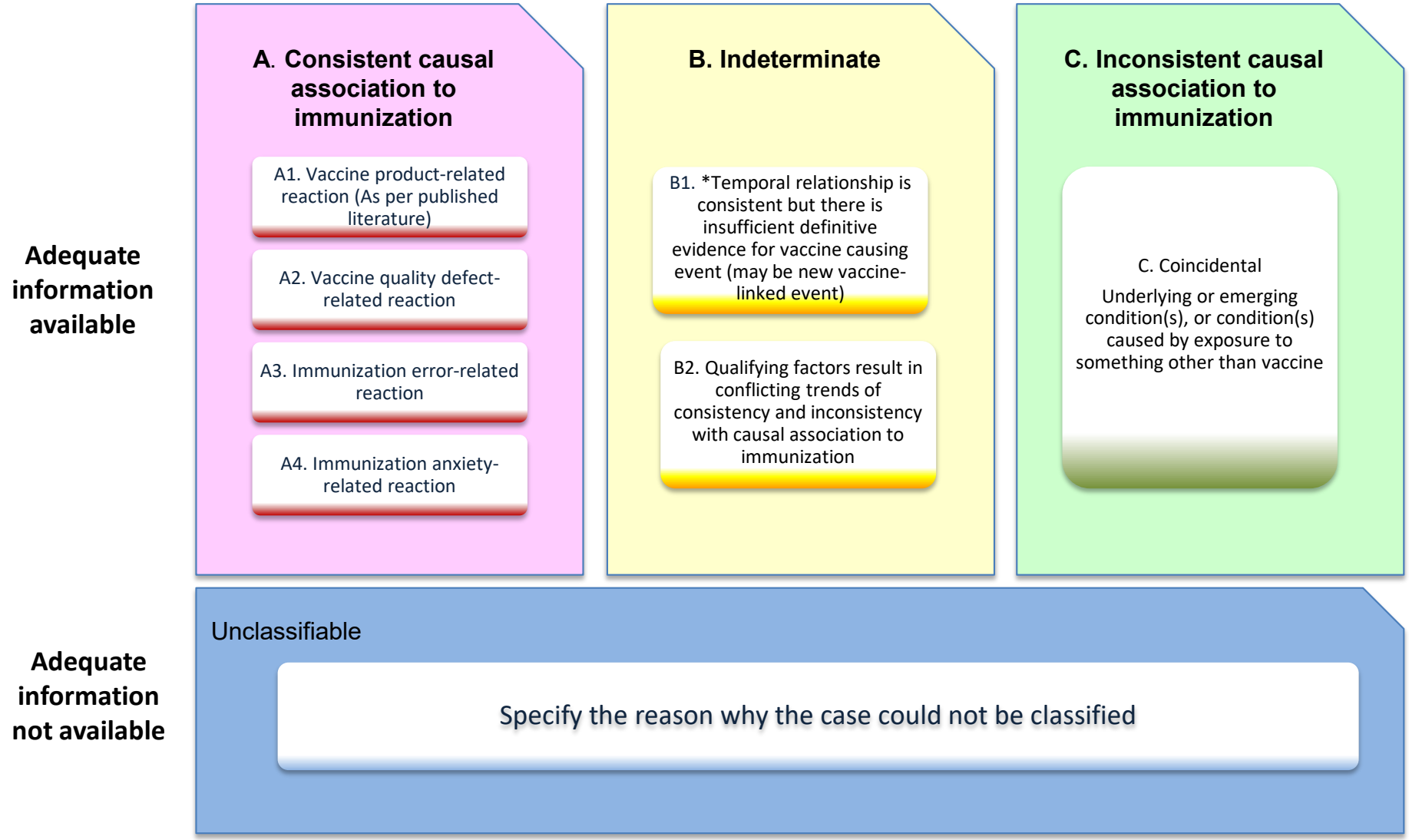
Step 2: Checklist

	Y	N	UK	NA
I. Is there strong evidence for other causes?	☐	☐	☐	☐
II. Is there a known causal association with the Vaccine / Vaccination • Vaccine product (Relationship with vaccine ingredients) • Vaccine quality • Immunization error • Immunization anxiety	☐	☐	☐	☐
II (Time). Was the event within the time window of increased risk?	☐	☐	☐	☐
III. Is there a strong evidence against a causal association?	☐	☐	☐	☐
IV. Other Qualifying Factors	☐	☐	☐	☐

Step 3 Algorithm (summary)



Step 4: Classification

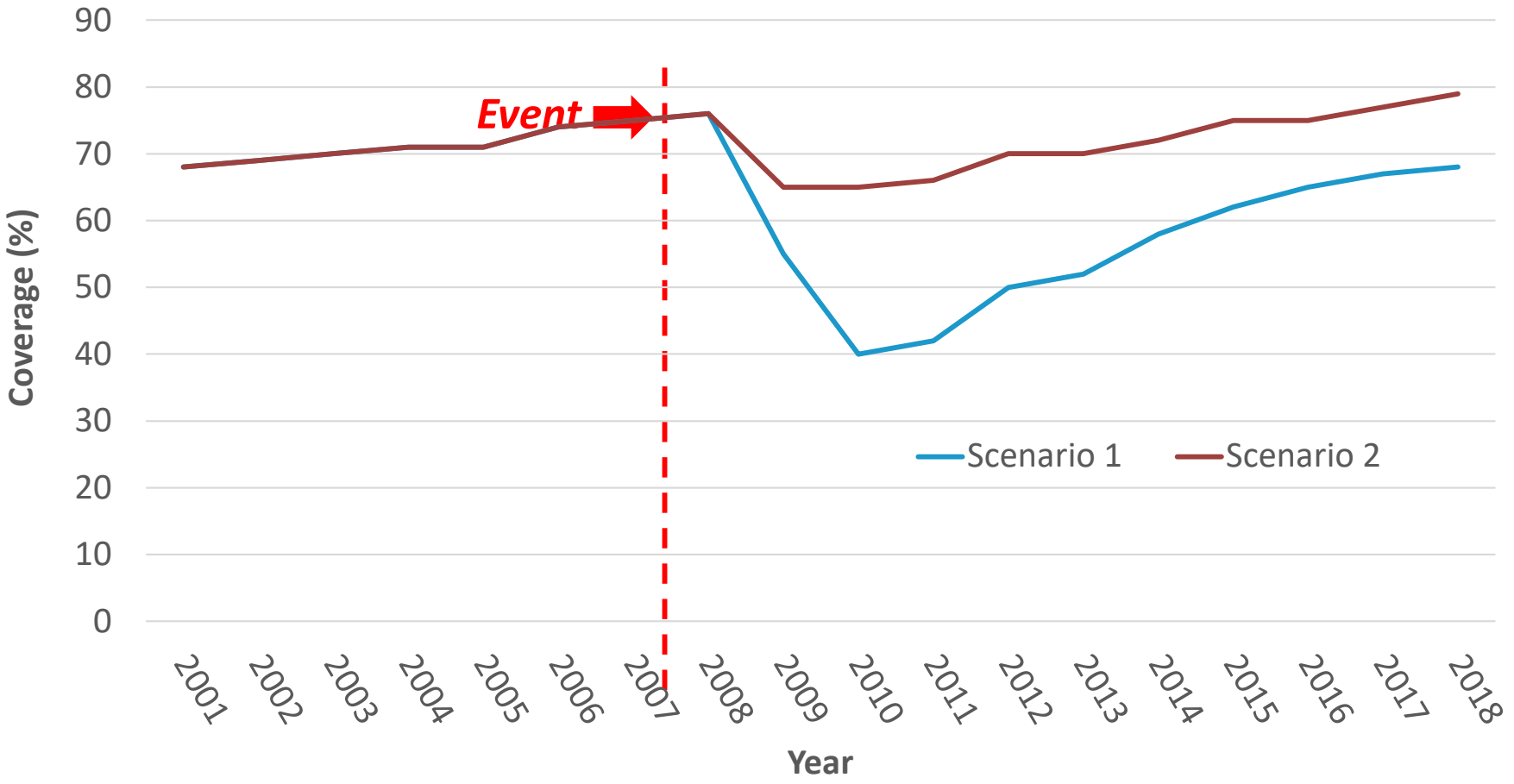


*B1 : Potential signal and maybe considered for investigation

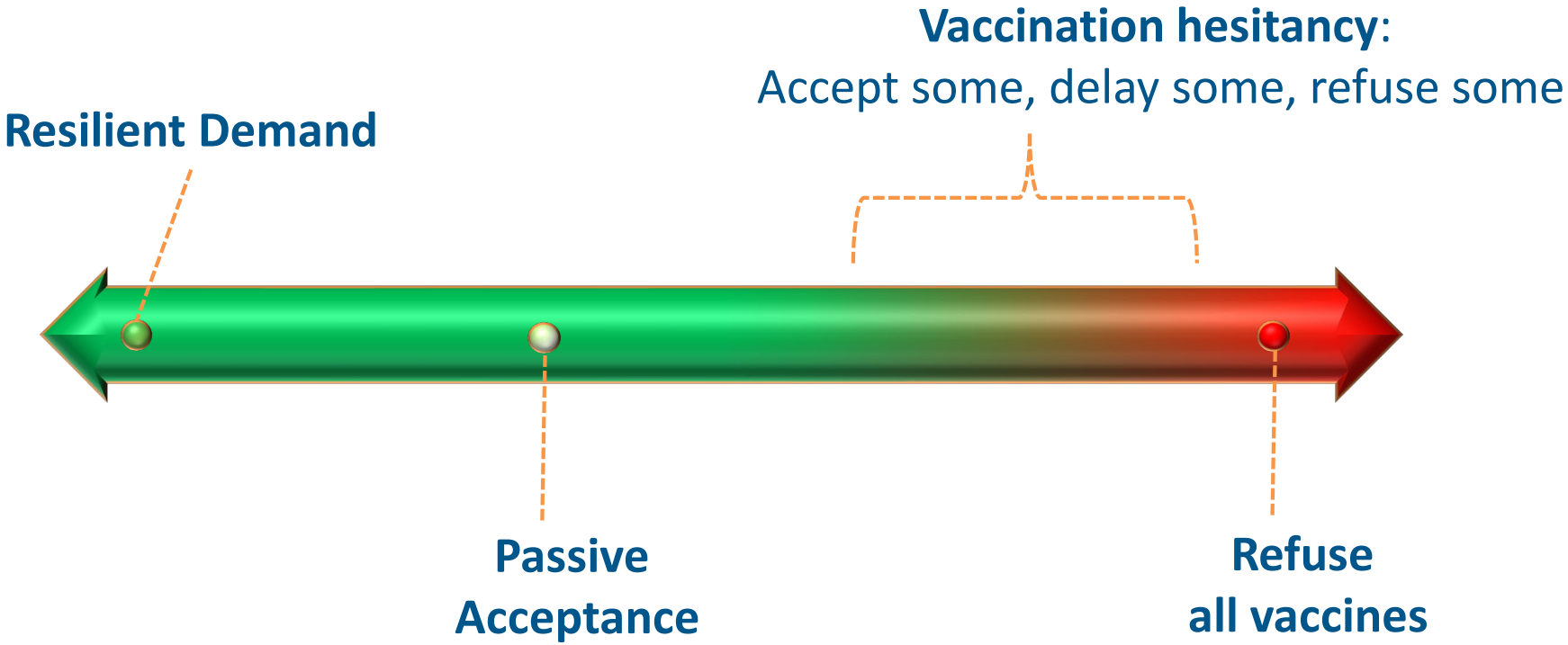
Outline

- AEFI – Definition
- Causality Assessment
- **Communicating AEFI**
- Country Experience

How can an AEFI impact a programme?



Building and Sustaining Demand



Proactive Risk Management

- **Coordinate closely between AEFI response and communications**
- **Prepare and plan** for the inevitable serious AEFI/event
  - Ensure an up-to-date risk communications plan is in place
- **Build resiliency** across all components of the programme
  - Ensure communities understand that vaccines are safe and effective and prevent against deadly diseases

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- **Country Experience**

Japanese Encephalitis Campaign 2017

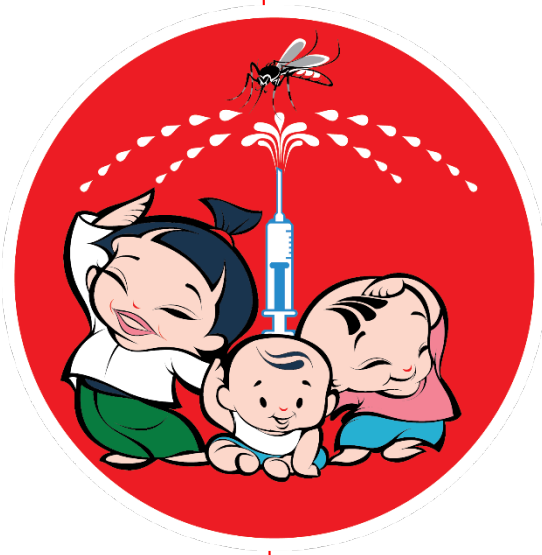
- Nationwide Campaign
- Total Target (9 month to 15 years) = 13.6 millions (26 % of the total population)

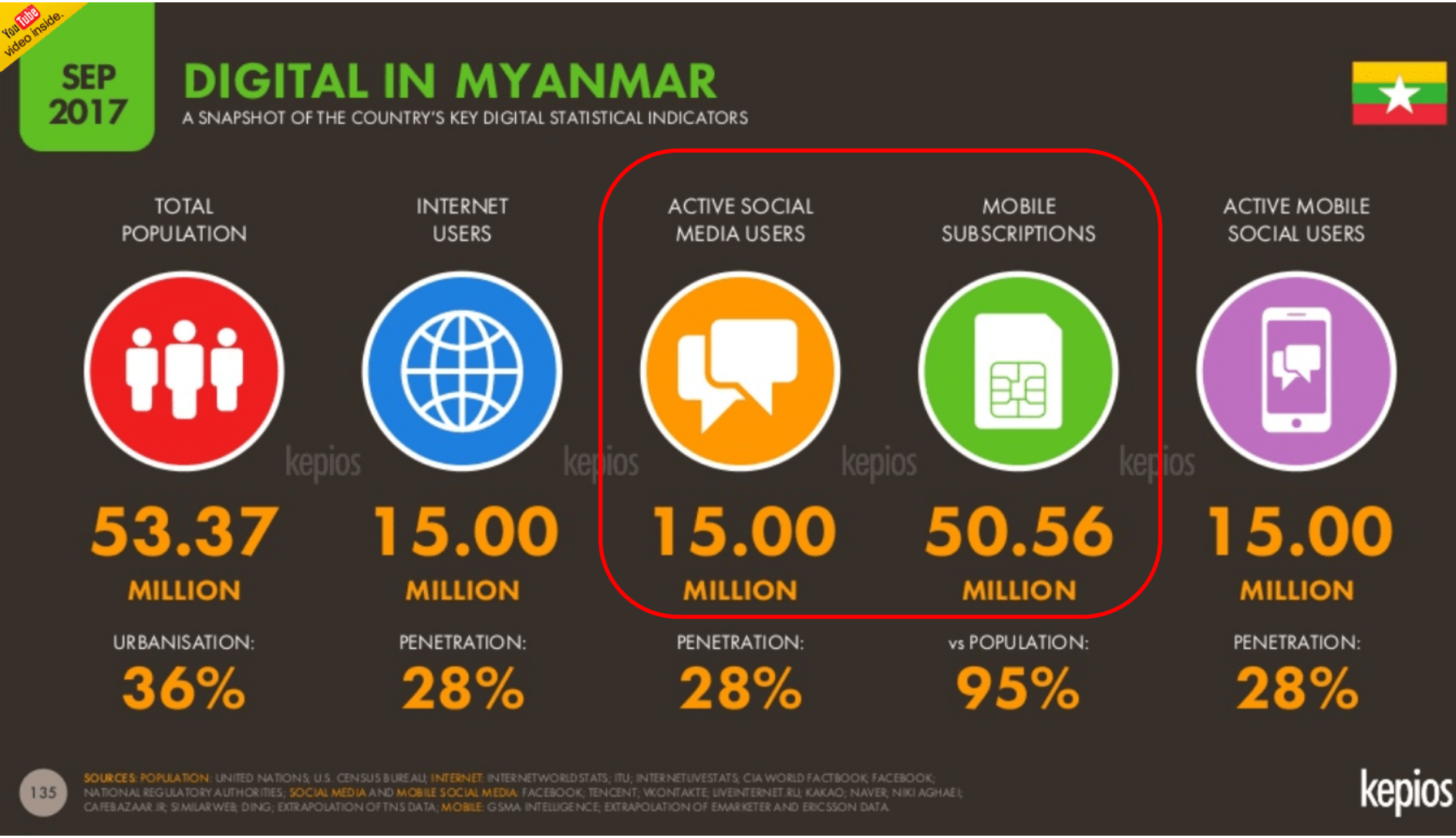
TWO PHASES

✓ School phase vaccination -
  - ✓ Target- 8.7 million
  - ✓ 15 - 23 Nov 2017

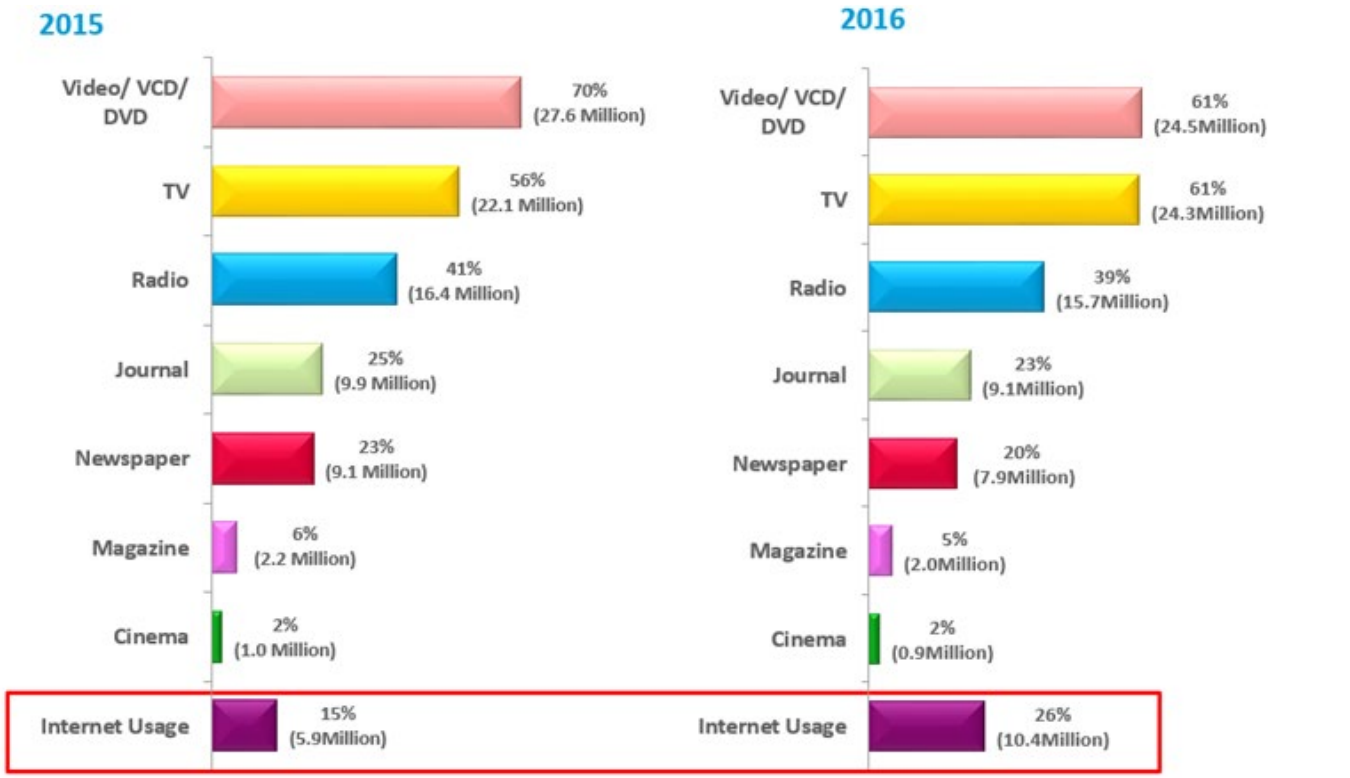
✓ Community phase vaccination –
  - ✓ Target- 4.9 million
  - ✓ 11 - 20 Dec 2017

- In hard to reach areas, only one phase for children of all age group
- WHO prequalified live attenuated JE Vaccine (SA 14-14-2) was used




YouTube video inside.
SEP 2017
DIGITAL IN MYANMAR
A SNAPSHOT OF THE COUNTRY'S KEY DIGITAL STATISTICAL INDICATORS
TOTAL POPULATION
53.37 MILLION
URBANISATION: 36%
INTERNET USERS
15.00 MILLION
PENETRATION: 28%
ACTIVE SOCIAL MEDIA USERS
15.00 MILLION
PENETRATION: 28%
MOBILE SUBSCRIPTIONS
50.56 MILLION
vs POPULATION: 95%
ACTIVE MOBILE SOCIAL USERS
15.00 MILLION
PENETRATION: 28%
kepios
135
SOURCES: POPULATION: UNITED NATIONS; U.S. CENSUS BUREAU; INTERNET: INTERNETWORLDSTATS; ITU; INTERNETLIVESTATS; CIA WORLD FACTBOOK; FACEBOOK; NATIONAL REGULATORY AUTHORITIES; SOCIAL MEDIA AND MOBILE SOCIAL MEDIA: FACEBOOK; TENCENT; VKONTAKTE; LIVEINTERNET.RU; KAKAO; NAVER; NIKI AGHAEI; CAFEBAZAAR.IR; SIMILARWEB; DING; EXTRAPOLATION OF TNS DATA; MOBILE: GSMA INTELLIGENCE; EXTRAPOLATION OF EMARKETER AND ERICSSON DATA.

Media Landscape in Myanmar

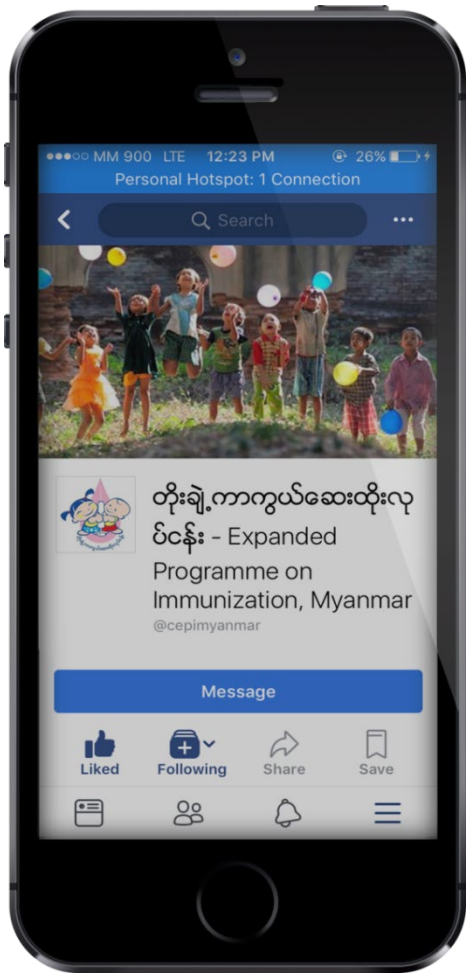


Base: 10+ Total Myanmar population 2015 = 39.7 Million Base: 10+ Total Myanmar population 2016 = 40.0 Million

Source: 2016 Consumer & Media View 8

Communication Channels used in JE Campaign (2017)

Print Media	Posters, Pamphlets, Advocacy Folder with fact sheets, Invitation cards
Broadcast Media	TV & Radio (TV spots, Radiospots, Songs, PSA, Interview, Documentary, Interviews, Music Videos, Jingles, Chyron/Crawler)
Media Engagement	
Transit Media	Billboard, Street banners, Bus/Taxi/Trishaw
Electronic Media	SMS reminders (minus two weeks till the campaign), Hotline
Local Media	Miking, Community events & meetings
IPC	Face-to-face health educations by BHS and volunteers, house-to-house visits
Social Media	www.facebook.com/cepimyanmar (Official Facebook Page for cEPI established one month before the campaign)



During Campaign

- One serious AEFI case – reported resulting in death on second day of the campaign (phase 1) which created a level of concern by the media and general public
- JE was a viral topic across Facebook and Soundbite

How we deal with the case

- Real time consultation - could be done for case management
- The field investigation was done by the AEFI committee and experts to get the valid diagnosis
- Ministry of Health and Sports could release the press statement and communicated with public within 48 hours through MoHS website and EPI fb page
  - messages and comments were responded promptly
  - the outrage of the community has been managed

Total Reported AEFI cases

- Total reported AEFI cases = 16,641 (0.13% of total vaccinees)
  - Minor cases= 15,950 (0.127%)
  - Total Serious AEFI cases = 705 (0.005%) – majority (about – vaccine reactions, immunization anxiety related reactions, others – co-incidental
- There were total **14 deaths** (10 in school phase and 4 in community phase)

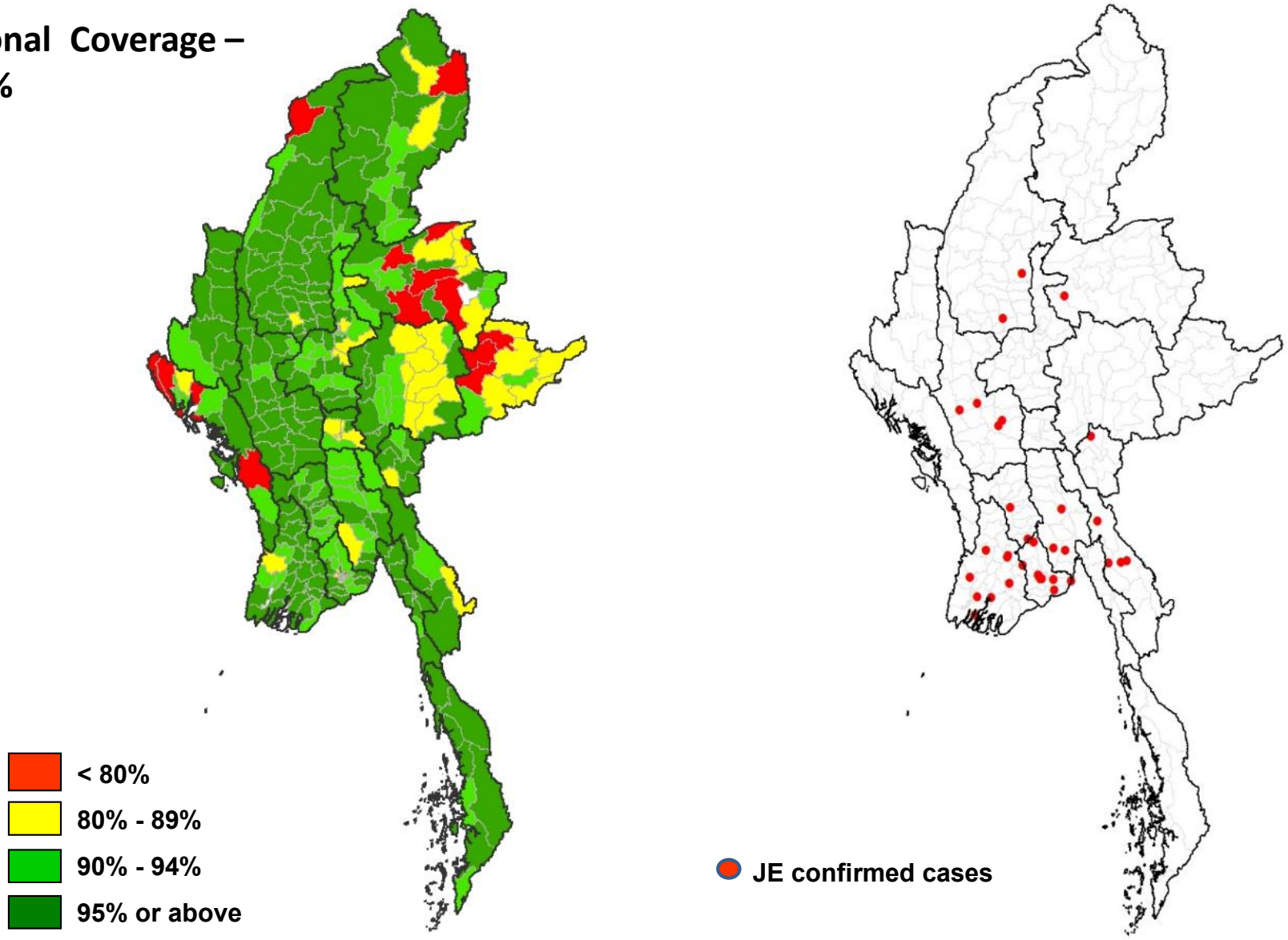
Causality Assessment

Comprehensive review of clinical, pathological and epidemiological findings of each expired case was done for **causality assessment by the experts of the national AEFI committee** with the technical support of **SEARO and WHO HQ** and all cases were classified as

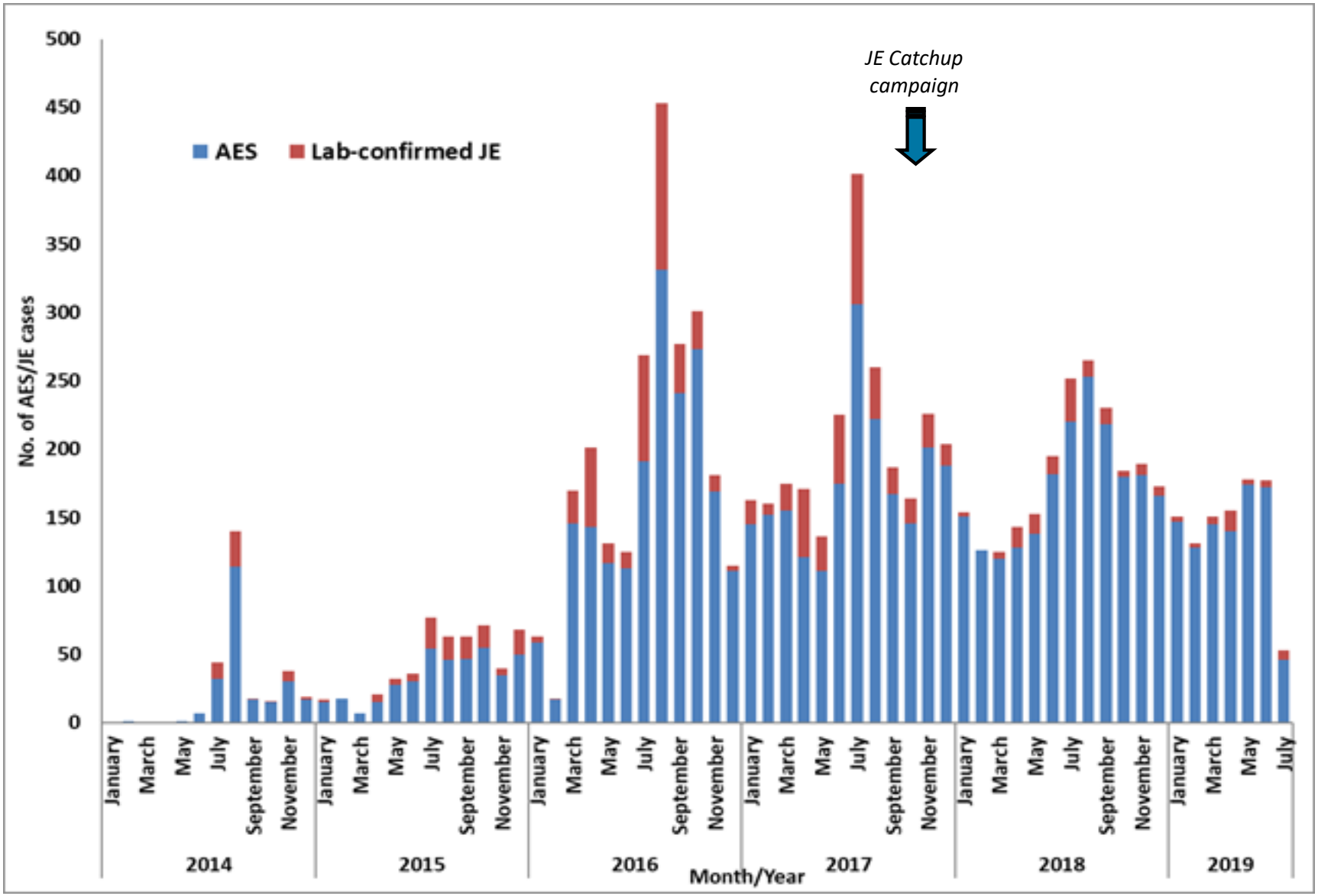
- **Co-Incidental Causes** and not related with JE vaccine
- The Ministry released the press statements with the updated information on serious AEFI cases through MoHS website and on EPI fb page
- Press Conference – conducted after each phase of campaign

Coverage of JE Campaign Vs Distribution of JE Cases in 2018

National Coverage – 92.5%



JE incidence: lab confirmed and reported AES cases by months 2014-2019*



*Data as of 31 August 2019

Key Strategies used in communication

1. Media Briefing
2. Two-way communication with parents
   - Radio
   - Social Media
   - Hotline
3. Public Opinion Monitoring

Acknowledgements

- Dr Madhava Ram Balakrishnan, WHO HQ
- Diane Summers, Demand Team Lead, UNICEF NYHQ
- EPI, WHO and Unicef colleagues (Myanmar)

THANK YOU!

Kyay Zu Tin Par Tal

During JE Campaign

Total number of AEFI cases reported	No =16,641 Rate = 122/100,000 Vacinee
Total number of serious cases reported	705 (JRF)
Number of AEFI cases investigated	705
Number of AEFI cases which were reviewed and analyzed by AEFI committee	14

Source: WHO/UNICEF Joint Reporting form 2016-2017 and Annual EPI reporting form 2016-2017

Serious AEFI reporting During JE Campaign

Year	# of district reporting/ total # of districts	Total AEFI cases			Vaccine reaction		Programme errors		Coincidental		Others	
		Reported	Investigated	hospitalized	total	death	total	death	total	death	total	death
2017	120/330	705	705	704	488	0	0	0	225 (14)	(14)	0	0

Source of data: AERF reports