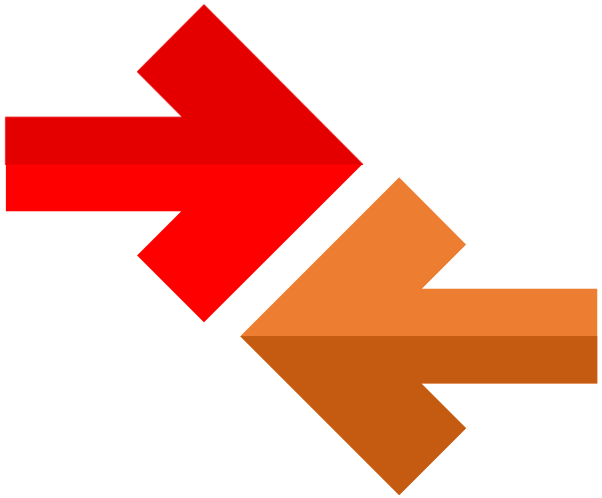
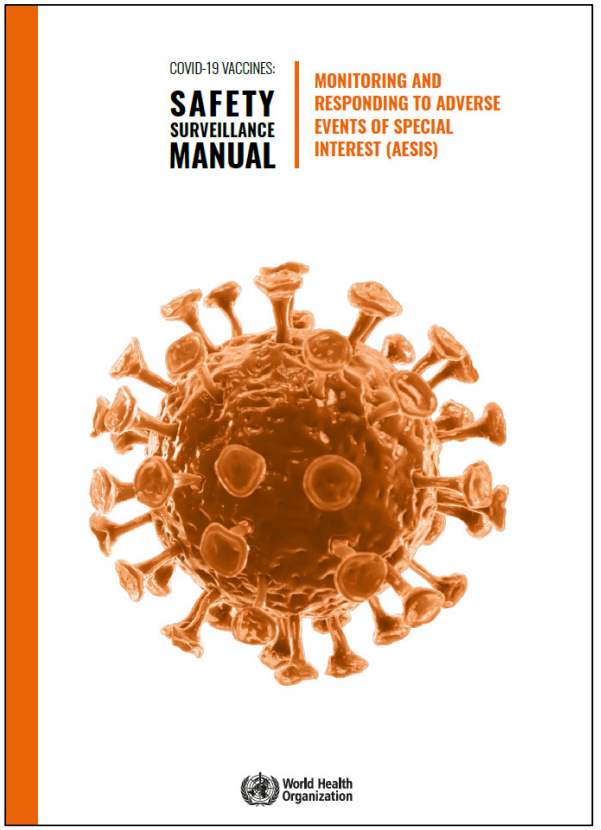
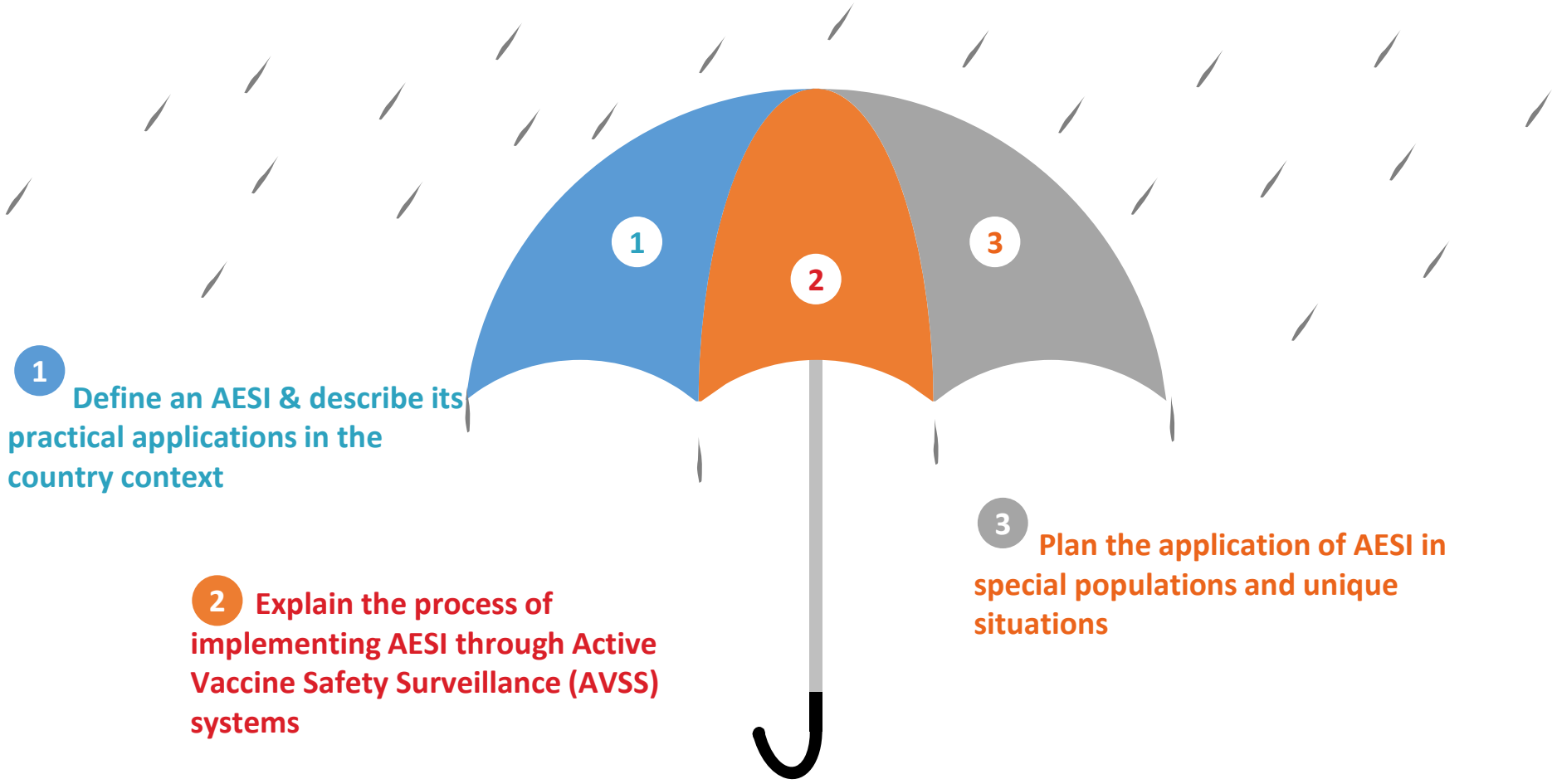
Monitoring and responding to AESI





Learning objectives: The learner should be able to



1 **Define an AESI & describe its practical applications in the country context**

2 **Explain the process of implementing AESI through Active Vaccine Safety Surveillance (AVSS) systems**

3 **Plan the application of AESI in special populations and unique situations**

Presentation structure

Define and understand the difference between AEFI and AESI

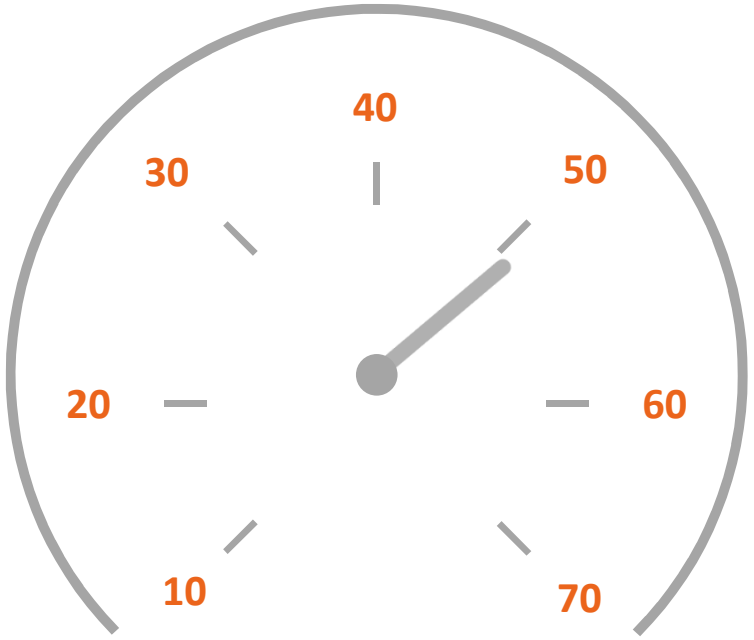
Apply the concept of Active vaccine safety surveillance (AVSS) to AESI

AESI in special situations

Implement AESI in the field level

Definition: Adverse events of special interest (AESI)

- An AESI is a pre-specified medically-significant event that has the potential to be causally associated with a vaccine product that needs to be carefully monitored and confirmed by further special studies



AESIs identified through active vaccine safety surveillance (AVSS) systems if there is

proven association with immunization that is true for most, if not all, vaccines

proven association with a known vaccine platform or adjuvant that is being used in any COVID-19 vaccine.

theoretical concern based on immunopathogenesis of COVID-19 disease

theoretical concern related to viral replication during COVID-19 infection

theoretical concern because it has been demonstrated in an animal model with one or more candidate vaccine platforms.

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Differences between AEFIs and AESIs and practical implications

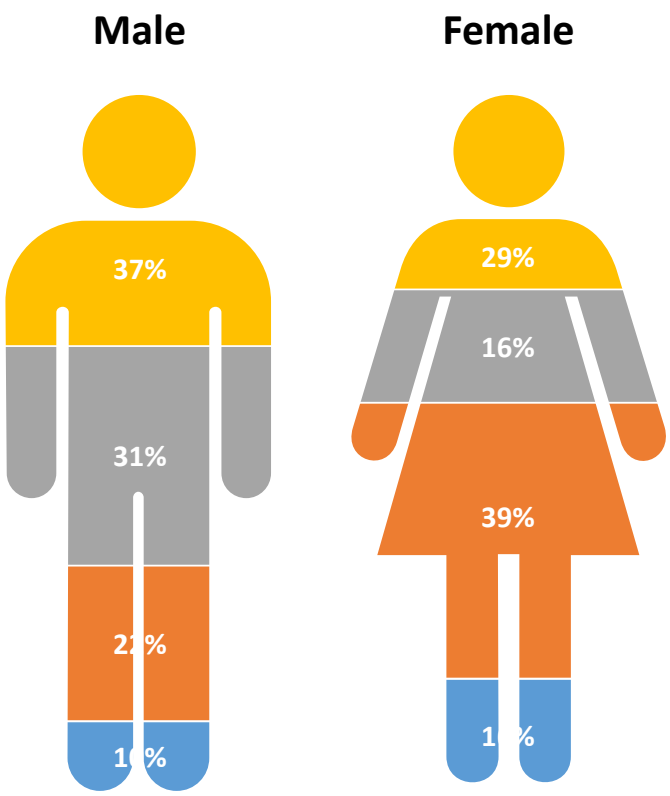
	AEFI	AESI in the context of COVID-19
What	Any untoward medical occurrence that follows immunization, and that does not necessarily have a causal relationship with the usage of the vaccine. The adverse event may be any unfavourable or unintended sign, abnormal laboratory finding, symptom or disease	A pre-specified event that has the potential to be causally associated with a vaccine product that needs to be carefully monitored and confirmed by further special studies
Purpose of collecting information	To identify all events after vaccination – determine if serious, investigate (serious) and do causality assessment.	To identify pre-specified specific events by a set criterion and determine if the event is associated with COVID-19 vaccination.
Identification method	Identified via spontaneous reporting by vaccine recipients or their parents, or health care workers or other persons who first notice the event.	Identified via an active surveillance system in sentinel sites or electronic health record (EHR-based cohort studies, CC, SCCS, rapid assessment e.g. VSD, VAC4EU, GVDN) by a health care worker or other staff in the system

Differences between AEFIs and AESIs and practical implications

	AEFI	AESI in the context of COVID-19
Case definitions	Important	Critical
Type of reporting	All events that follow immunization and are notified to the health care system.	All events identified through active surveillance that fit the case definition, irrespective of immunization status
Training	All frontline immunization staff in health care facilities (public and private); and other relevant staff for reporting, investigation, data analysis, and causality assessment	Immunization staff and other health care workers in sentinel sites and predefined active surveillance systems, NIP/EPI mangers, NRA, research staff, national AEFI committee
Users	Health care workers, NIP/EPI managers, NRA, surveillance and information managers, epidemiologists, surveillance and information managers, vaccine safety partners including the community	Sentinel site staff, NIP/EPI managers, NRA, epidemiologists, national AEFI committees, study teams

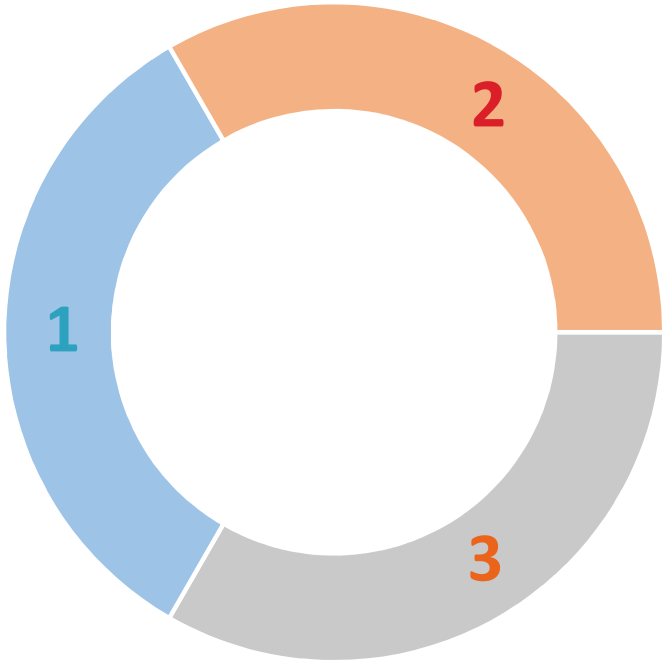
Active vaccine safety surveillance (AVSS)

Active vaccine safety surveillance (AVSS) systems aim to collect complete, accurate information about adverse events following immunization (AEFIs) and their risk factors in a defined population via a continuous organized process



Benefits of active vaccine safety surveillance

1. AVSS systems can be used for signal detection



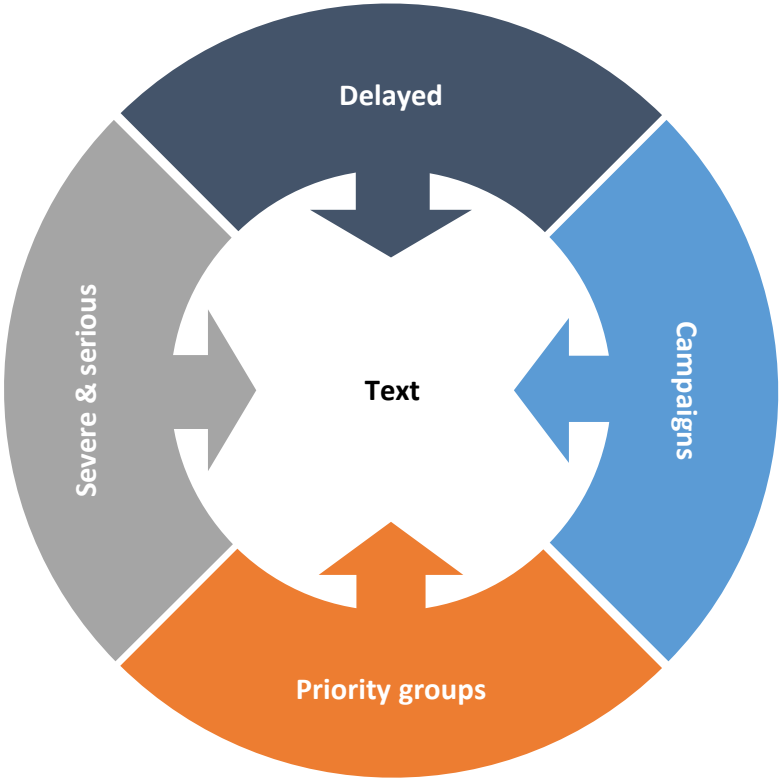
2. Determine the rate of an event in a defined population

3. Determine the relative risk of the event

- the chance of the event occurring in those who were vaccinated with the specific vaccine, compared with those who were not
- the change in the event rate over time

Types of AESIs identified with AVSS systems

- Delayed AESIs
- Severe and serious AESIs



- AESIs in priority target groups
- Surveillance of AESIs during mass COVID-19 immunization campaigns

Key considerations - Implementing AVSS systems for COVID-19 vaccine-related AESIs

Complementary to existing passive surveillance systems

When significant knowledge gaps cannot be addressed through passive surveillance

Have sufficient funding and robust governance systems

Have systems in place to share collected data widely and transparently

When it is important to define the risk and risk factors in the population immunized with COVID-19 vaccines

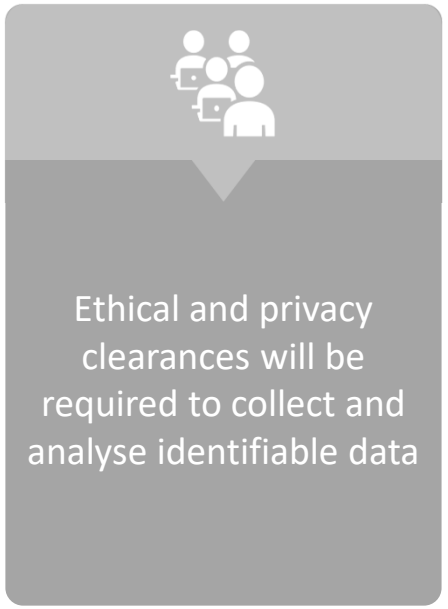
Use harmonized protocols wherever possible

Operate independently without conflicts of interests.

World Health Organization

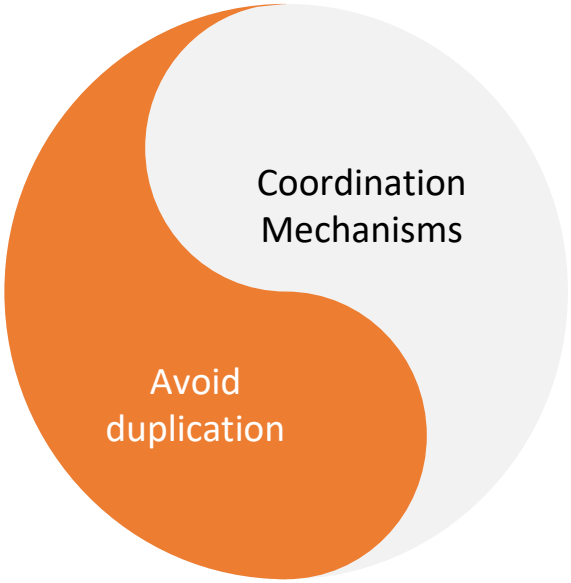
MRB

AVSS: Resources, governance and ethical considerations



Co-ordination of AVSS systems

Coordination will avoid duplication of effort and increase the size of the population under surveillance, thus enabling the assessment of very rare events and making comparisons



Implemented though global coordination of AVSS systems, as well as regional or national coordination, through the proposed or existing governance and research structures

Core and complete data sets to be collected for the AVSS system

		Vaccination data	Health events or outcomes	Demographic data
Complete data set	Core data set	Vaccine brand name	Adverse event(s)	Age at onset
		Lot number	Date of onset of symptoms	Gender
		Date of vaccination	Serious	Medical conditions
		Dose number	Outcome	Medication
		Site of vaccination	–	–
		Place of vaccination	Place of care	–
		Vaccine antigens	–	–
		Concomitant vaccines	–	–
		Route administration	–	–

Key resources available and being developed for COVID-19 vaccine listed AESIs

Description	Purpose	Setting to use
Brighton case definitions	To provide a standard case definition so safety data are comparable	See https://brightoncollaboration.us/covid-19/ for latest list and definitions
AESI confirmation and Interpretation forms	Detailed data form to facilitate standardized data collection and interpretation focused on the Brighton criteria to assess LOC.	case investigation and assessment — AEFI signal / cluster investigation — outcome validation for analytic and epidemiological studies
Tabular checklist and algorithm to determine certainty	Abbreviated tabular form to summarize available case data and assign LOC	same as above but where data have been collected and data abstraction is not needed
Automated tool to determine LOC for cases	To replace the previous Brighton online ABC tool	— training for LOC determination — causality assessment where first step is to determine LOC — any setting where LOC needs to be assessed

Key resources available and being developed for COVID-19 vaccine listed AESIs

Description	Purpose	Setting to use
Background rates and risk factors of AESI	To provide summarized data on incidence of event as coincidental events by age, gender and geography	— epidemiologic studies where expected versus observed are compared — public reassurance in terms of 'expected' coincidental events
ICD and MedDRA codes	To assist in identifying or coding events from or for health care or pharmacovigilance databases	— AEFI MedDRA coding — coded database searches
Template protocols	Assess background rates, conduct active surveillance	

Important Links

https://docs.google.com/spreadsheets/d/1QgF35nYcsaFN3DZTOtV_lP0TYqQzsDMUQBAd5M9brrM/edit#gid=1666959512

https://brightoncollaboration.us/

https://brightoncollaboration.us/covid-19/

World Health Organization

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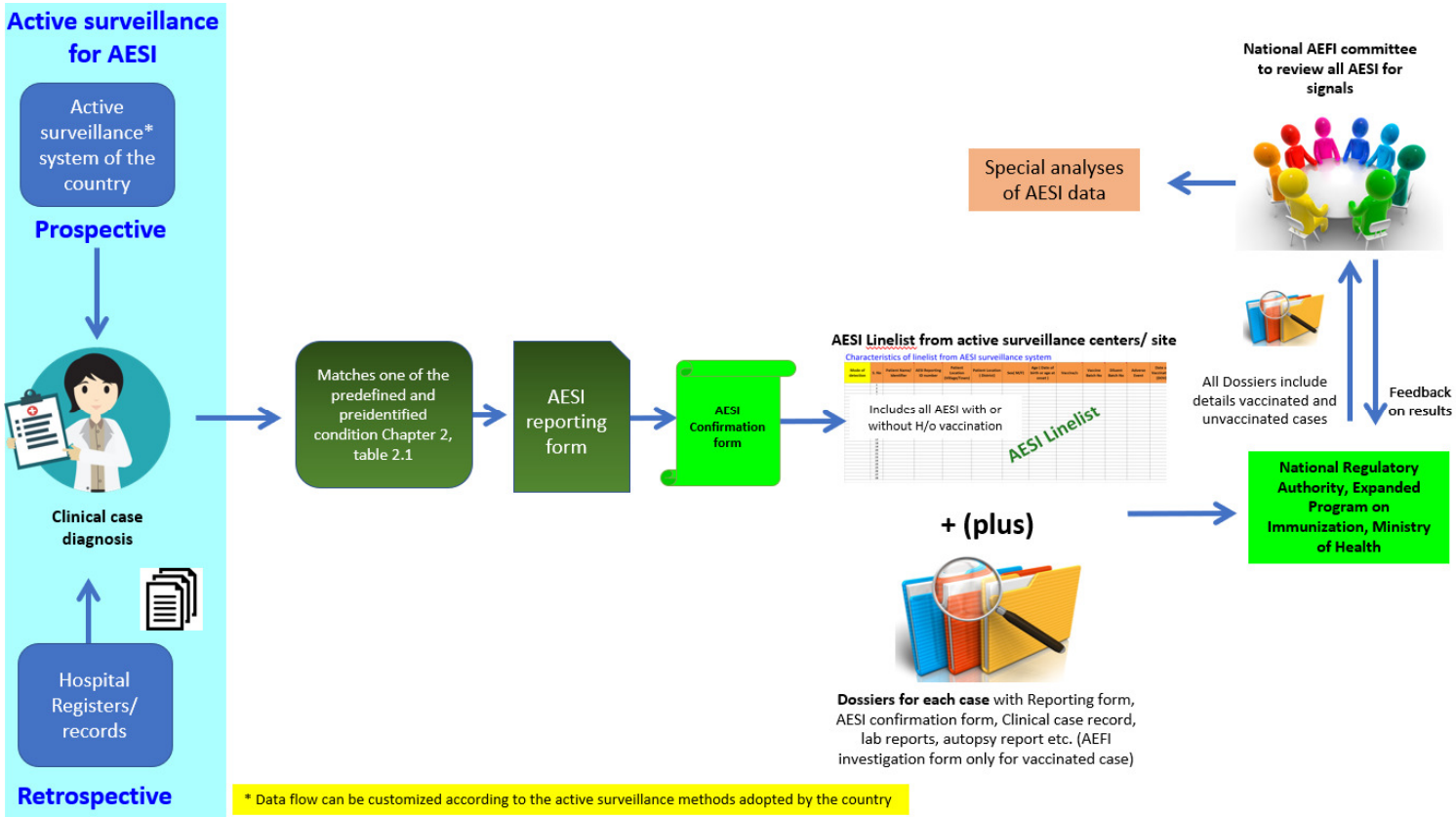
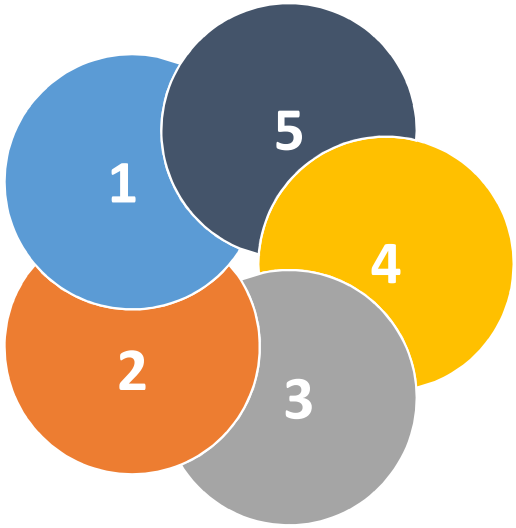
In-country reporting and processing of AESIs



World Health Organization

MRB

Detecting & processing AESIs though AVSS



Through cohort event monitoring (CEM), sentinel surveillance (SS) and data linkage (DL) using case definitions

Specific electronic AVSS tools (e.g. m-health (MH) and e-health (EH))

Vaccine exposure information should be obtained

Use AESI reporting form AESI confirmation form for the specific, AESI, detailed clinical records and results of additional tests must be collated & AESI linelist

Dossiers for each AESI should be submitted to the national level (NRA/NIP/ EPI/MoH) in compliance with the country protocol and shared with specially trained national AEFI committee.

Initial causality assessment of Covid19 vaccinated AESI

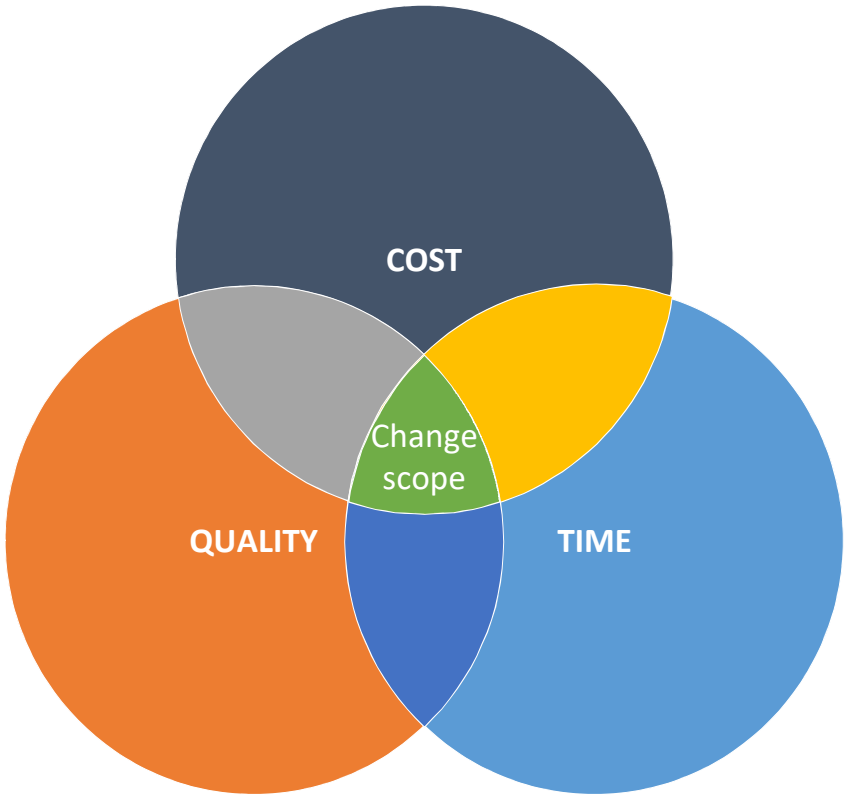
After confirming the absence of programmatic errors, Immunization stress related responses or coincidental events, Covid19 vaccinated AESI cases will have to be categorised by the committee as

"'B1 -Indeterminate' because the temporal relationship is consistent but there is insufficient definitive evidence for vaccine causing the event (it may be a new vaccine-linked event)"

Data analyses for AESI cases from AVSS

The causality assessment committee trained to review population-based scientific data needs to compare the incidence of the AESI among the COVID-19 vaccinated and unvaccinated individuals within a specific population and identification of signals for further characterization

The committee should review the national, regional and global epidemiological data to determine if there is a pattern in the profile of reports received e.g., clusters of similar events in space, time and vaccine administered



Reconciling AESI data

Information about AESIs can be obtained from a passive AEFI surveillance system (spontaneous reporting) or from an AVSS system.

The data from both systems cannot be collated (merged) because the data collection methods are different, and they represent different cohorts of individuals and should, therefore be analysed separately.

Prioritizing preparedness for AESI

1 **At the time of vaccine authorization, countries need to review the RMP and discuss the risks and benefits with their respective in-country national immunization technical advisory groups (NITAGS) or regional immunization technical advisory groups (RITAGS).**

2 **They need to determine if they have the capacity to implement active surveillance for AESIs**

3 **Then they should set priorities for which AESIs are most relevant to a given setting and adopt a system most suitable**

Summary of tools recommended for AESI

Description	Purpose	Status for COVID-19
Detailed case definitions for AESI	To determine if clinical details comply with standard case definition by an expert	Available for some conditions and under development for others
Simplified case definitions for AESI	To determine if clinical details comply with standard case definition by a frontline health care provider	To be developed (some available)
AESI reporting form	To collect information for all AESI cases that have been notified in a standard common format for linelisting	Separate AESI reporting form developed for COVID-19
AESI linelist	To collate the AESI details from AESI reporting forms	Separate AESI linelist format developed for COVID-19

Summary of tools recommended for AESI

Description	Purpose	Status for COVID-19
AESI confirmation form	To collect confirmation information when AESI cases are identified. Separate form for eachcondition	To be developed
Investigation form for AESI cases that have history of COVID-19 vaccination	To collect detailed information when serious AEFI cases are investigated	Adapted to include COVID-19 specific questions
Causality assessment for AESI cases that have history of COVID-19 vaccination	To determine case classification of all AESI cases that have a history of COVID-19 vaccination reported from the passive surveillance system	Retain current method used for AEFI unchanged
Detailed analysis format of AESI as per protocol	Will depend on study protocol	Will depend on study protocol

AESI for pregnant women, neonates and immunocompromised individuals

The full impact of COVID-19 disease on pregnancy outcomes for mother and foetus as well as for new-borns is still unclear

It is not yet clear whether vaccination will be recommended for pregnant or immunocompromised individuals. As a general rule, live vaccines are contraindicated for both

It will be essential to plan to follow pregnancy outcomes with, for example, a registry of all such occurrences for any adverse outcomes to the mother, foetus or new-born

Sudden unexpected death as an AESI

Sudden death has not yet been added to the AESI list. However, it will be essential to be prepared to enable rapid response

A thorough field investigation should be conducted and autopsy performed according to the protocol for suspected COVID-19 cause of death. https://pubmed.ncbi.nlm.nih.gov/32653819/

Knowing regional and age-specific background incidence of sudden deaths as well as relevant risk factors will be essential for causality assessment.

Appropriate communication at all stages of investigation, causality assessment and its outcomes will be critical.

Key points to remember

01

AVSS should be implemented complementary to the country's passive surveillance (spontaneous reporting) system

02

AVSS for AESI can be implemented through Cohort event monitoring, sentinel site surveillance or data linkage

03

AESI should be prioritized and shortlisted for AVSS

04

Specific protocols and tools will need to be adopted by the country based on the local situation

References

- CIOMS. Guide to active vaccine safety surveillance. Available from: https://cioms.ch/publications/product/cioms-guideto-active-vaccine-safety-surveillance/
- Data linkage https://www.cdc.gov/vaccinesafety/ensuringsafety/monitoring/vsd/index.html
- Global Advisory Committee on Vaccine Safety, 27-28 May 2020 https://www.who.int/vaccine_safety/committee/reports/May_2020/en/
- Safety Platform for Emergency vACcines (SPEAC). https://brightoncollaboration.us/speac/