COVID-19 Vaccine Effectiveness in Severe Acute Respiratory Infection (SARI) Cases

WHO Protocol overview

Capacity Building Session for Eastern Mediterranean Region
COVID-19 Vaccine Effectiveness Study
15 December 2021

Source
https://www.who.int/publications/i/item/WHO-EURO-2021-2481-42237-58308

epiconcept

Objectives

- **Primary objective:** To measure overall and **product-specific** COVID-19 VE against **laboratory-confirmed SARS-CoV-2** in **hospitalised SARI patients** eligible for COVID-19 vaccination.
- **Secondary objectives***: To measure VE against confirmed SARS-CoV-2
  - By age and sex groups
  - By Risk groups (e.g. specific conditions; pregnancy)
  - By number of doses
  - By time since vaccination (-->*duration of protection*)
  - Against SARS-CoV-2 genetic variants
  - Against More severe outcomes (e.g. oxygen therapy, ICU, in-hospital mortality)

If possible: To Identify potential factors that modify VE (e.g. flu vaccination, medications, specific exposures, etc.)

Study Design and Population

Study design

- Test-negative case-control

Study population

- SARI patients admitted for hospitalisation

Inclusion criteria	Exclusion criteria
• All or random subset of hospitalised patients meeting SARI case definition • Eligible for COVID-19 vaccination (part of target groups on date of admission)	• Contraindication for COVID-19 vaccine or swabbing • History of hospitalization within the 14 days prior to this admission

Proposed study period

- 6 months

WHO SARI Case Definition:
A hospitalized person (> 24 hrs) with acute respiratory infection, history of fever (or measured ≥ 38 C°) and cough, with symptom onset within last 10 days

Cases	Controls
SARI hospitalised patients testing **positive for SARS-CoV-2** admitted for at least 24h Onset within 10 days of admission *NB. It is essential to document date of symptom onset*	SARI hospitalised patients testing **negative for SARS-CoV-2** admitted for at least 24h Onset within 10 days of admission

Exposure and Outcome

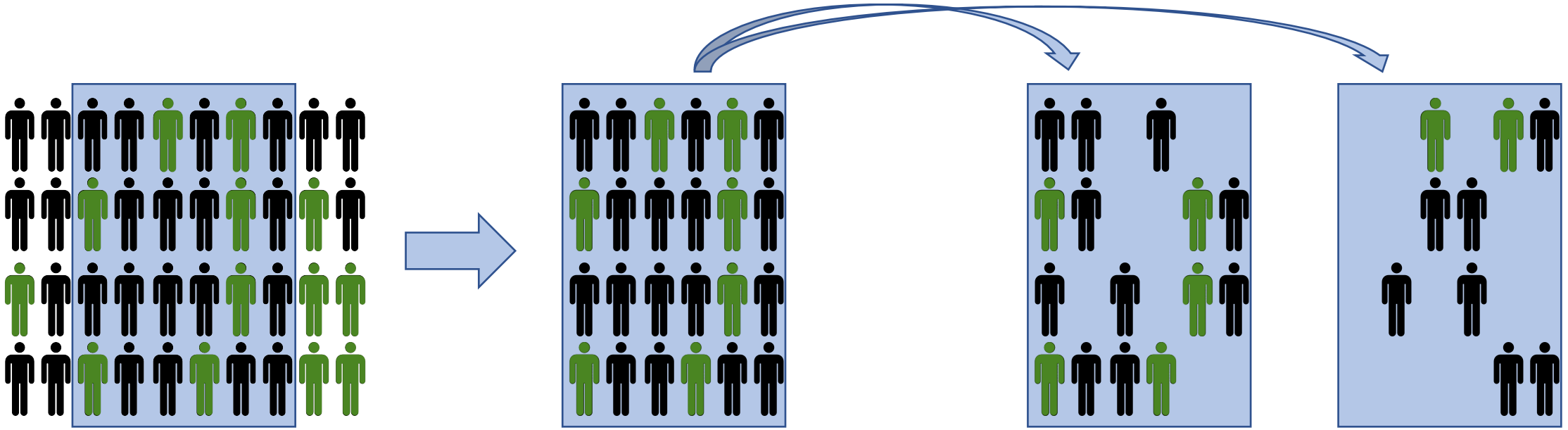
Exposure: vaccination

- Definition of *vaccinated* depends on the vaccine
- Number doses (fully v partially vaccinated)
- Date of vaccinations
- Brand
- Batch
- Highlights importance of good quality data collection and need to confirm vaccination data

Outcome

- SARS-CoV-2 **detection by RT-PCR** in patients of all ages, eligible for vaccination and hospitalised with SARI symptoms
- Type of genetic variant (*if possible*)
- Additional: markers of severity of disease during hospitalization

Test-negative case-control design



- Fitting eligibility criteria
- Providing consent

➢ Patients are swabbed (for SARS-CoV-2 RT-PCR testing)

➢ Info recorded on: vaccination history, comorbidities, prior hospitalization, occupation, etc.

VE (%) = (1 – OR) × 100

Adapted from: REVELAC-i network.
Original: Sullivan, Feng and Cowling, Expert Rev., Vaccines, 2014

Why use a TN case-control design?

Study Design	Advantages	Disadvantages
Cohort	Can more accurately define asymptomatic and symptomatic infections	Require a large sample size (1000s) and are expensive ($$$)
Traditional Case Control	Smaller sample size Less costly ($$)	Choosing control group comparable to cases in characteristics is difficult
Test-negative Design Case Control	Smaller sample size Less costly ($$) Reduces confounding by differences in health-care seeking behavior and by community variations in vaccine coverage between the 2 groups (as all participants from same community) Reduces likelihood of differential exposure misclassification Reduces likelihood of outcome misclassification Easier logistics, uses existing platforms (SARI surveillance)	Controls may still be different from cases Misclassification of case status, particularly if presenting late in course (severe>nonsevere) Other biases still need to be minimized In areas/times of high incidence, it may be difficult to recruit sufficient controls

"*Start small and build on convenient existing platforms*"

- TND CC considered most feasible and efficient design in most settings (including LMICs) as it is a **hospital-based** study using existing systems (e.g. no additional sample collection as routinely collected already)

TND-CC studies using SARI system

Building on existing surveillance infrastructure

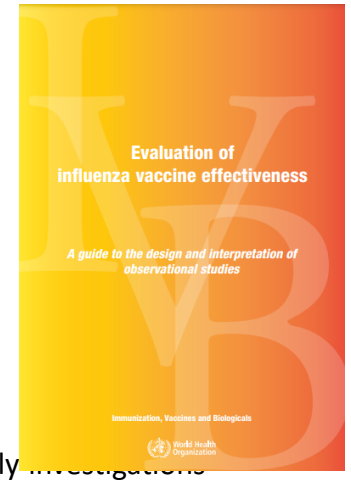
- SARI surveillance well established for influenza virological and disease surveillance:
- WHO recommends SARI surveillance systems include COVID-19 routine surveillance
  - Disease severity and risk factors
  - Virological monitoring (variants)
- Same platform can be utilised to collect data to measure **COVID-19 vaccine effectiveness**
- Builds system for other respiratory viruses (flu, RSV, etc.)

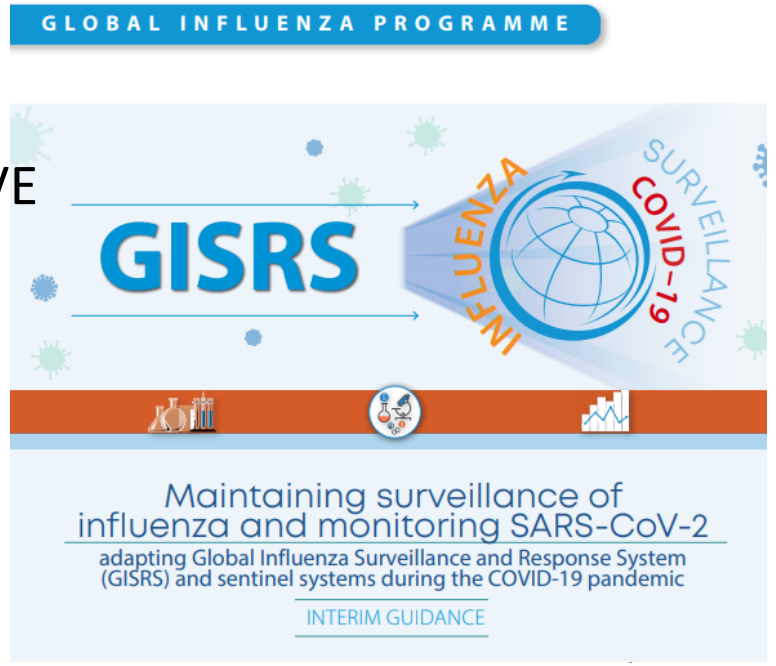
Sustainable system and process for regular vaccine evaluations

- 10 years of global experience using TND-CC for annual influenza VE
- Real-time monitoring of VE

Standardised UNITY VE protocols

- Enable pooling data for greater power
- Experience sharing and lessons learned
- Joining forces across sites and countries



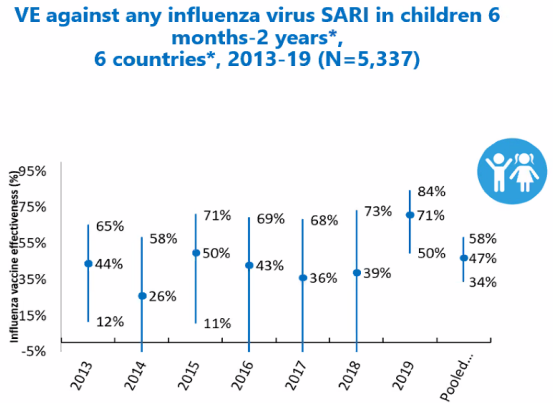


https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/early ...investigations

Implementation in other regions

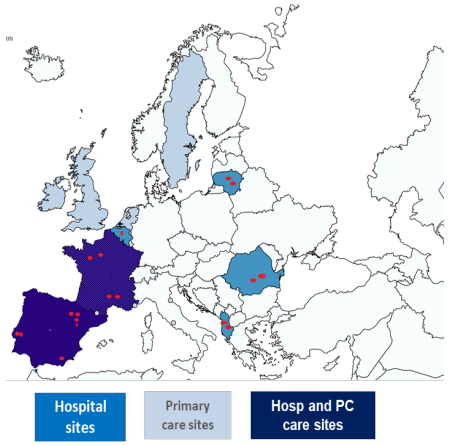
PAHO: REVELAC-i

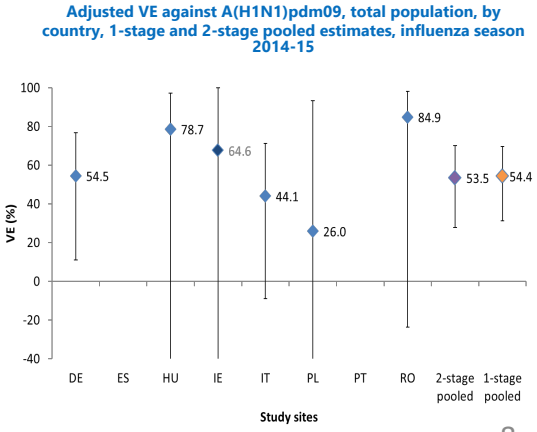
- Network for influenza vaccines evaluation in Latin America and Caribbean established in 2012
- 13 countries so far
- Network generates regional annual estimates of influenza VE in preventing influenza associated hospitalizations in children and elderly during influenza season
- COVID-19 VE ongoing since beginning of 2021
- Preliminary results available before the end of the year



EURO: I-MOVE

- Network for evaluating influenza vaccine effectiveness in Europe established in 2008
- Generates VE estimates against severe influenza
- 15 countries so far
- Multicentre COVID-19 VE study ongoing, data will be pooled across the region
- Preliminary results available (presented at the end of this workshop)

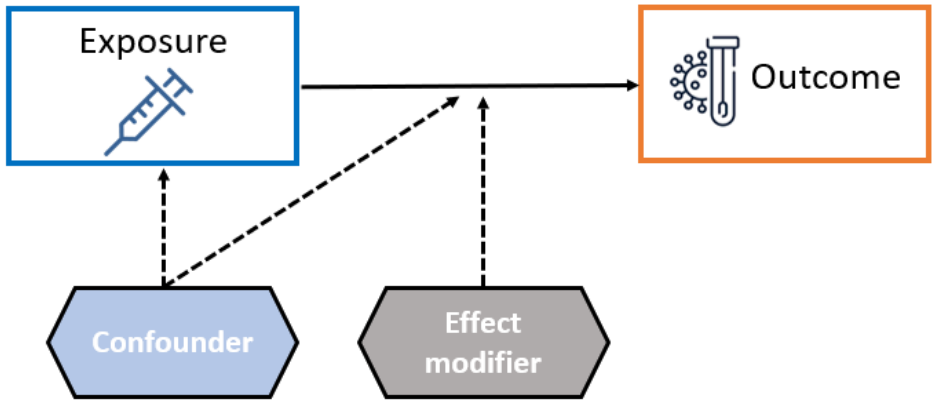




Effect modifiers and confounders

Essential variables to collect

- Demographic: age, sex, socio-economic status
- Health care worker status
- Chronic conditions and relevant medication
- Clinical information:
  - Length of stay
  - Oxygen use
  - ICU admission
  - Invasive ventilation
  - Death
  - Clinical signs of pneumonia (fever, cough, dyspnoea, fast breathing)
- Previous SARS-CoV-2 infection



Considerations

- Timing and progress of vaccination campaign in countries
- Existing SARI surveillance (influenza, COVID-19) experience in EMRO
- Commitment of actors (hospital staff and administration, laboratories)
- Testing capacities
  - RT-PCR COVID-19
  - For sequencing
- Hospital admission capacities
- Data collection from severely ill patients
- Documenting vaccination status
- Data management and sharing for pooled analyses
  - Common data entry system?
- Funding availability and options

Pooling data across countries

Why pool data?

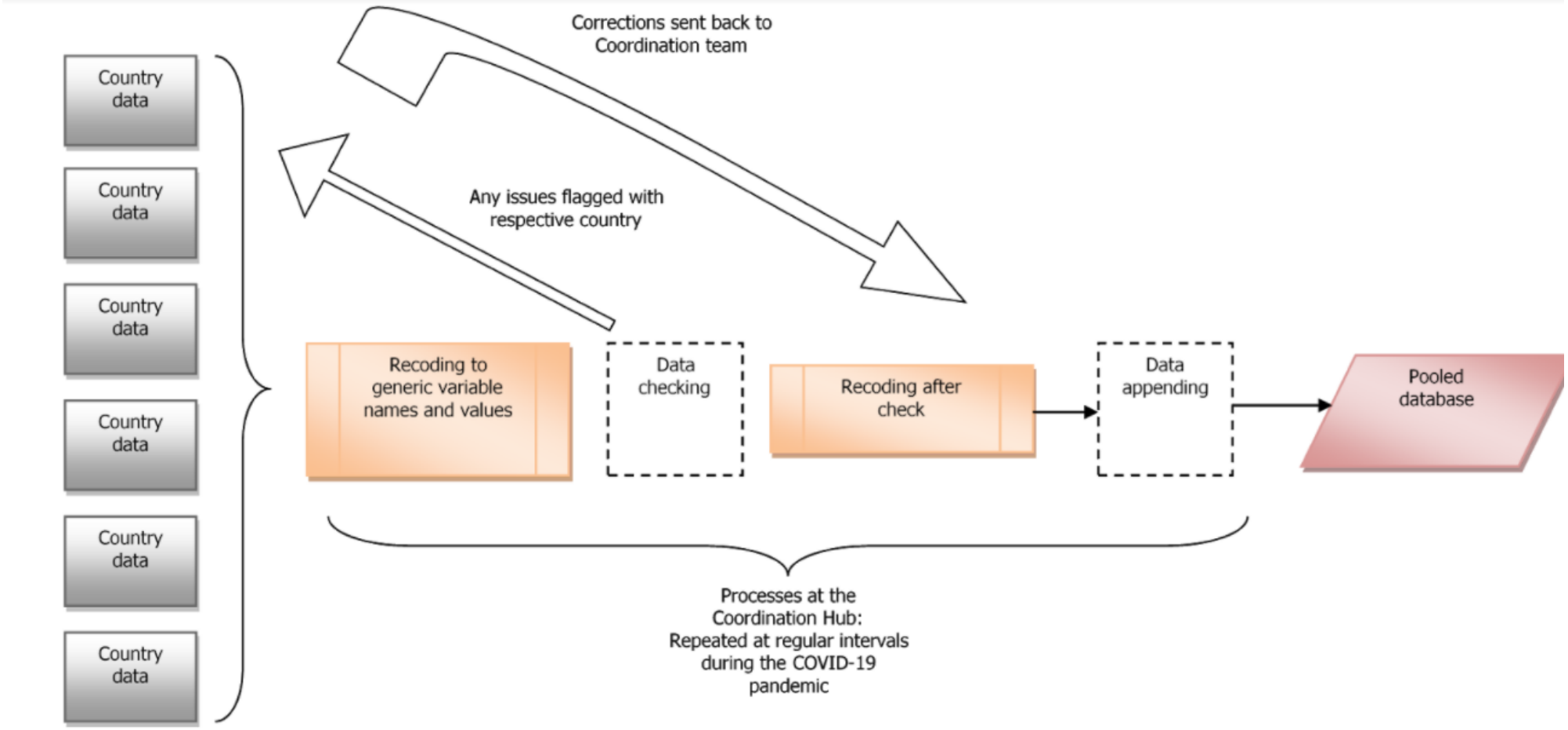
Challenges for COVID-19 vaccine effectiveness:

- Different vaccines by:
  - Country
  - age-group
  - risk group
  - time
- Different vaccine schedules/days between doses
- Variants
- Will sample size at study site level big enough?
- Pooling → larger sample size
  - Increase VE precision
  - Conduct sub-group analyses
  - Stratify by effect modifiers
  - Control for confounders

Pooling VE data: Network Collaboration

- Agreed WHO generic protocol
  - Plan of analysis
- Generic protocol adapted to each site
  - Site specific protocol
- Coordinating hub
  - Organises data management at central level
  - Develops data analysis scripts
  - Validates data for each site
  - Analyses pooled data
- Discuss interpretation of pooled analysis / results
- Key: constant exchange coordinating hub / study sites

EMRO COVID-19 - Pooled analysis data flow



Data management and sharing for pooled analyses
Common data entry system?