

Vaccine effectiveness studies to guide immunization policy



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Technical Consultation Meeting for the EM Regional COVID-19 Vaccine Effectiveness Studies

12–13 November 2023 | Cairo, Egypt



World Health Organization

REGIONAL OFFICE FOR THE **Eastern Mediterranean**

Outline

- **Vaccine effectiveness from immunization perspectives**
- **Programmatic criteria for VE**
- **Coordination with NITAG in VE studies**
- **Recommendation to guide immunization policy**
- **Summary**



“Vaccine effectiveness is the foundation of immunization policy”

WHO advise on overall global policies and strategies, ranging from vaccines and technology, research and development, to delivery of immunization and its linkages with other health interventions.





"Immunization policy is a balancing act between vaccine effectiveness, safety, cost, and the burden of disease"

Overall, vaccine effectiveness and immunization policy are essential for protecting public health from vaccine-preventable diseases. By monitoring vaccine effectiveness and updating immunization policies as needed, we can help to ensure that everyone has the best possible protection against these diseases.



Measures of vaccine performance

Different level-Different measures

Immunogenicity - individuals

- Capacity of the vaccine to induce antibody production

Vaccine efficacy - individuals

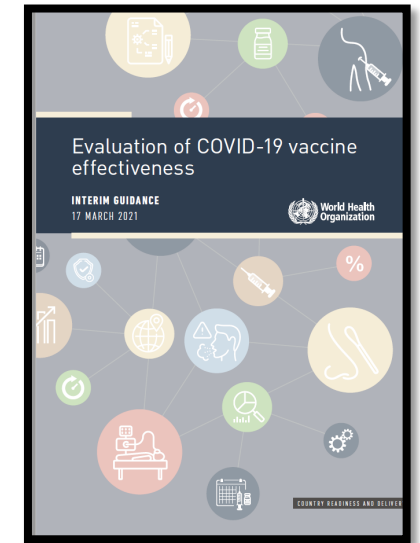
- Reduced risk of infection or disease among vaccinated individuals resulting from vaccination in carefully controlled circumstances; estimated from randomized clinical trials

Vaccine effectiveness - individuals

- Reduced risk of infection or disease among vaccinated individuals attributed to vaccination in real-world conditions; estimated from observational (non-randomized) studies

Vaccine impact - population

- Reduction in incidence of infection or disease in a population where some members are vaccinated
 - Vaccine coverage (direct effects in vaccinated, indirect effects due to herd protection)
 - Can also pertain to other measures besides disease (health systems' functioning and capacity and economic indicators)



Objectives of post-introduction Covid-19 vaccine effectiveness evaluations

1. Evaluate real-world performance of vaccines

- Cold chain (e.g., ultra-cold storage), timing and completeness of dosing schedule
- General population (e.g., persons excluded from trials)
- Different circulating virus variants

2. Address gaps in evidence of vaccine efficacy from clinical trials

- Outcomes of interest (e.g. severe disease, death, infection, transmission)
- Subpopulations at risk (e.g. the very old, persons living with HIV)
- Duration of protection from vaccines
- Effect of new variants or antigenic drift
- Effectiveness of vaccines co-administered with routine vaccines

3. Provide input into models that estimate impact

4. Provide post-authorization confirmation of effectiveness for conditionally approved products

Suggested criteria to undertake vaccine effectiveness evaluations from immunization perspectives

- Clear public health rationale
- Experienced epidemiologic team
- Dedicated staffing
- Identified sites of enrolment
- Availability of reliable diagnostic tests in the study population
- Ability to ascertain accurately vaccination status
- Data collection, management and analytic capacity in place
- Ability to enroll enough participants
- Data dissemination plan in place
- Funding secured to conduct rigorous evaluation
- Functional ethical review committee to review protocol expeditiously

**Proposed stake
holders' areas of
coordination for
vaccine effectiveness
studies**



A clear benefit to public health;



Experienced epidemiological team and dedicated staff



Identification of study sites with strong capacity and enough diagnostic tests



Ability to enroll enough participants



Data collection, management and analytic capacity in place and proper data dissemination



Ethical review follow up and rigorous evaluation

Existing platforms that can be used for vaccine effectiveness evaluations

- Surveillance systems for severe acute respiratory infections (SARI), influenza-like illness (ILI), other syndromic disease surveillance in sentinel hospitals
- Health worker surveillance
- Administrative databases
- Well-defined outbreaks

Designs for vaccine effectiveness studies

Most feasible

- ✓ Test negative (case control study)

In a clinical center, possible case-patients are considered for inclusions

- Those confirmed are case-patients
- Those negative are control-subjects

- ✓ Cohort

Health Care workers in different health facilities

- Followed up for symptoms and/or disease

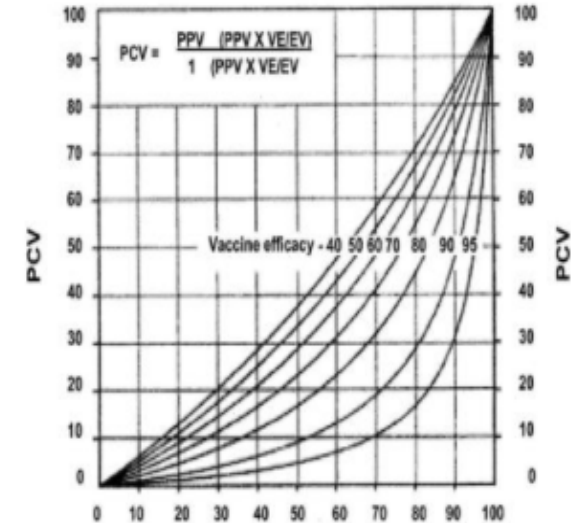
OTHERS

- ? Screening method

- Estimating vaccine effectiveness on the basis of coverage and proportion of vaccinated among cases

- Other types of case control studies

- PCV: Proportion of cases vaccinated
- PPV: Proportion of the population vaccinated
- VE: Vaccine efficacy



Orenstein WA et al. Field evaluation of vaccine efficacy. Bull World Health Organ 1985; 63:1055-68

Nomogram to estimate vaccine effectiveness using the quick screening methods in the field

Vaccine effectiveness studies only make sense when there are enough people vaccinated (Above 30%)

Programmatic criteria to establish the need of a vaccine effectiveness study

Guidance to immunization policy: vaccine effectiveness studies are done where needed

- Sufficient vaccination coverage attained in at least one group in the country (Necessary)
- Specific initiatives to reach and document high coverage in specific target groups (e.g., health care workers (HCWs), elderly or people with co-morbidities)
- Vaccine impact not at the level expected
- Large population size
- Vaccine products used:
 - Multiple vaccines
 - Vaccines poorly documented from a VE point of view

Outcomes to consider for policy guidance

Case identification “laboratory confirmed, preferably PCR”; Vaccination status documented

I-BASIC

- ✓ Symptomatic disease
- ✓ Severe disease (Hospitalization, admission to ICU)

II- ADVANCED (More difficult)

- ? Death
- ? Infection
- ? Transmission

Real-world evidence provides important insights into vaccine effectiveness



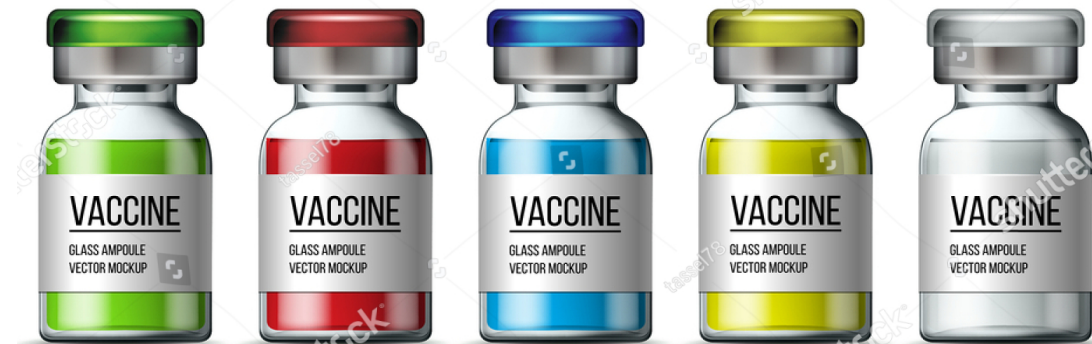
With the emergence of the delta variant of SARS-CoV-2, effectiveness decreased against disease but not against severe disease and deaths

Importance of working with national immunization programme and NITAGs in vaccine effectiveness studies

Studies needs to be linked to vaccination strategies

- Type of vaccine(s) administered
- Enough vaccination roll out
- Geographical spread of vaccination
- Following the National Deployment and Vaccine use Plan (NDVP) framework
 - Proportion of population covered
 - Prioritized group
 - Targeted approach
 - Special population (Refugees, IDPs...)

<https://www.who.int/tools/covid-19-vaccine-introduction-toolkit#Evaluation%20of%20COVID-19%20vaccine%20introduction>



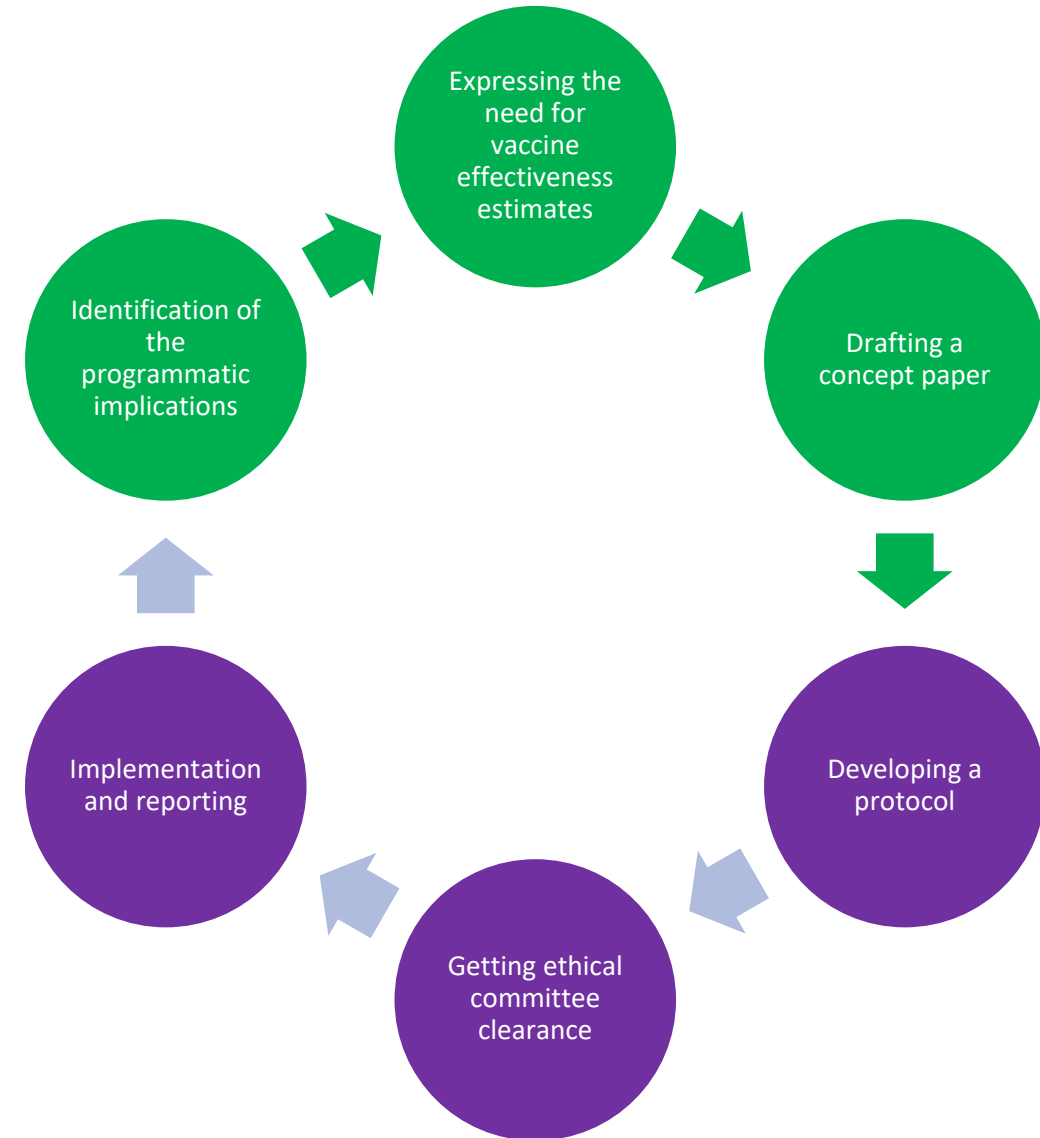
Collaboration between national immunization programmes, The technical advisory group and research institutions on vaccine effectiveness studies

Role of the national immunization programme

- "Why?": Expressing the need for the information to understand a situation (e.g., persistence of transmission)
- "So what?": The implication of the vaccine and thus further decision for further improvement

Role of academic / research partners to implement studies of ensured quality

- "What?": Suitable study addressing the research question according to the vaccine strategy adopted
- "How?": Capacity building to ensure highest research quality for a reliable estimate



Steps of Evidence to Recommendations (EtR) to guide immunization policy makers

Step 1

The Question

- Policy question from the MoH
- Focused policy question from the NITAG (PICO - population, intervention, comparison & outcome)

Step 2

The criteria

- Decide the type of evidence necessary for your context
- Prioritize the evidence you want to collect
 - ✓ Critical
 - ✓ Important
 - ✓ Less important

Step 3

The evidence

- Gather, analyze evidence
- Assess quality
- Synthesize evidence in the EtR framework
- Prepare documents

Step 4

The recommendation

- Discuss draft recommendation
- Vote on recommendation

These 4 steps are broken down into 7 modules dispensed over 3 days in an EtR workshop



MoH: Ministry of Health
PICO: Population, Intervention, Comparison and Outcome
NITAG: National Immunization Technical Advisory Group

Starts and ends here - the EtR framework

PICO Question	Step 1			
Background				
DOMAIN Step 2	CRITERIA	JUDGEMENTS	EVIDENCE	ADDITIONAL INFORMATION
1. Problem	Is the problem of public health importance?		Step 3	
2. Benefits & harms of the options	Are desirable anticipated effects large? Are undesirable anticipated effects small? Balance between benefits and harms. What is the quality of evidence for critical outcomes?			
3. Values & preferences	Does the target population feel the desirable effects are large relative to the undesirable effects?			
4. Resource use	Are the resources required small? What is the cost-effectiveness?			
5. Equity	What would be the impact on health inequities?			
6. Acceptability	Which option is acceptable to key stakeholders? To the target population?			
7. Feasibility	Is the intervention feasible to implement?			
Balance of consequences				
Type of recommendation				
Recommendation (text)	Step 4			
Implementation considerations				
Monitoring and evaluation				
Research priorities				

Generic categories of evidence and elements for each criteria to elucidate the domain: Domain 2: Benefits and harms of the options

Element	Categories of evidence
2.1 Vaccine characteristics	<ul style="list-style-type: none"> • Vaccine presentation • Formulation • Dosage • Route of administration • Administration schedule • Possibility of co-administration with other vaccines and drugs • Flexibility of vaccination schedule • Cold chain and logistic requirements
2.2 Safety	<ul style="list-style-type: none"> • Type, consequences and frequency of short and long-term adverse events following vaccination • Risk groups or risk factors for adverse events • Contraindications or precautions
2.3 Efficacy & effectiveness	<ul style="list-style-type: none"> • Vaccine efficacy/effectiveness and types of protection afforded • Critical determinants of the immune response associated with protection • Duration of protection and waning of immunity in general and risk groups • Interference regarding protection or immunity with other vaccines
2.4 Vaccine indirect effects	<ul style="list-style-type: none"> • Herd immunity/protection • Potential negative population impact of emergence of non-vaccine serotypes

Summary

- ❖ Vaccine effectiveness is one of the measures to understand how well vaccine work. It's a key piece of the puzzle to measure impact
- ❖ COVID-19 illustrated the importance of differentiating outcomes of vaccine effectiveness studies
- ❖ Effectiveness can be examined with a range of methods, from quick screening methods to formal studies
- ❖ Working on vaccine effectiveness includes some programmatic aspects and some operational research aspects
- ❖ NITAGs are important bodies to engage in establishing the need for a vaccine effectiveness study and making use of the results
- ❖ Vaccine effectiveness is a corner stone in guiding immunization policy to introduce, continue or change any vaccine

THANK YOU



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Refresher on study designs in epidemiology

	Ill	Non ill	Total
Exposed	a	b	a+b
Non exposed	c	d	c+d
Total	a+c	b+d	a+b+c+d

Cohort study

Compares exposed and unexposed in terms of disease

Case control study

	Cases	Controls	Total
Exposed	a	b	-
Non exposed	c	d	-
Total	a+c	b+d	-

Compares cases and controls in terms of exposures