COVID-19 and Influenza VE Studies in the WHO European Region: Operational Challenges and Preliminary Results

Mark Katz
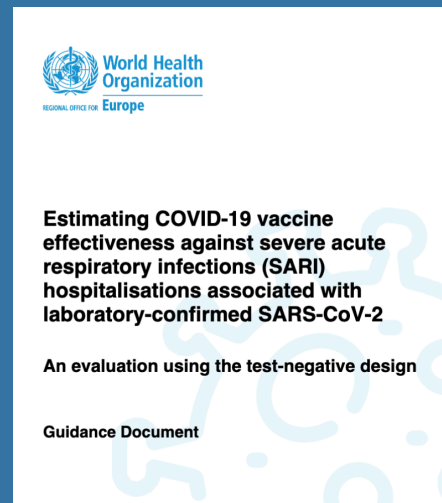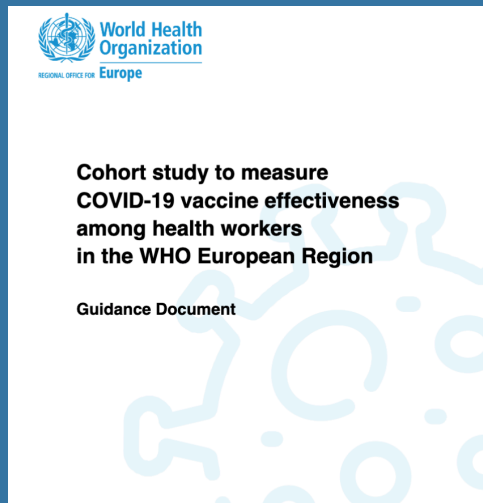
High Threat Pathogens Team, Health Emergencies

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Outline

- Background
- Covid VE studies in the eastern part of the WHO/Europe region
  - Healthcare worker (HCW) VE studies
    - Background
    - Results – general
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    - Background
    - Results
    - Challenges

Background

- In early 2021 WHO/Europe published two guidance documents
  - Evaluate COVID-19 and influenza vaccine effectiveness studies in HCWs
  - Enhance existing SARI surveillance systems so that they could be used to estimate COVID-19 and influenza VE

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Cohort study to measure COVID-19 vaccine effectiveness among health workers in the WHO European Region

Guidance Document

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Estimating COVID-19 vaccine effectiveness against severe acute respiratory infections (SARI) hospitalisations associated with laboratory-confirmed SARS-CoV-2

An evaluation using the test-negative design

Guidance Document

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HCW VE studies in eastern part of WHO/Europe region

- Three countries in the eastern part of the European region (Albania, Georgia, Azerbaijan) initiated HCW VE studies based on the guidance documents
- All studies started in early 2021 (Feb-April)
- Studies part of WHO Unity platform

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HCW VE studies - Methods (1)

- Prospective cohort study to evaluate VE against SARS-CoV-2 infection among hospital-based HCWs
  - Year 1: focus was Covid-19
  - Year 2: expanded to include influenza testing and vaccine monitoring

Methods (2)

- At a limited number of hospitals, all HCWs invited to participate in study

- At enrolment
  - Questionnaire: demographics, comorbidities, vaccine history, previous covid infection
    - Vaccine history and previous infections verified through national registry, database
  - Blood sample for serological testing for prior SARS-CoV-2 infection
  - Respiratory sample for SARS-CoV-2 testing by PCR*

*Albania only

Methods (3)

- Weekly symptom questionnaires

- Symptomatic patients
  - Respiratory swab collected, tested for SARS-CoV-2 by RT-PCR
    - (Year 2 – expanded to include influenza testing)

  - PCR-positive swabs from Albania, Azerbaijan sent to Charité Institute of Virology laboratory (Berlin, Germany) for whole genome sequencing
    - Georgia: sequencing at Lugar Center, Georgia

- Quarterly serology testing*
  - Anti-nucleocapsid antibody
  - Anti-spike antibody

*In Azerbaijan, serology collected every 6 months

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Methods (4) - Analysis

- Primary outcome:
  - Vaccine Effectiveness against symptomatic PCR-confirmed SARS-CoV-2 infection.
- As a secondary analysis
  - Vaccine effectiveness against a combined outcome
    - PCR-confirmed SARS-CoV-2 infection *or*
    - Seroconversion (a positive three-month or six-month anti-nucleocapsid antibody test in a participant who was previously seronegative)
  - Vaccine effectiveness against a combined outcome of PCR, Rapid Antigen Test and seroconversion
- VE estimated as (1 – hazard ratio)*100

HCW VE studies - Results

- Albania
  - Primary delta-predominant VE analysis (in clearance)
  - Omicron-predominant VE – preliminary analysis completed
- Azerbaijan
  - First interim analysis completed (manuscript in progress)
- Georgia
  - First interim analysis completed (manuscript in progress)

Results - Albania

- 19 February – 7 May 2021: 1504 participants from 3 hospitals enrolled
- Median age: 44 years (IQR 33-53)
- 79% female
- 47% nurses or midwives; 20% physicians
- At enrolment, 1054 (70%) HCWs had evidence of prior or current SARS-CoV-2 infection through PCR and/or serological assays

First Interim Analysis - Results

- Analysis Period: 19 February – 14 December, 2021
- VE of primary vaccine series

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HW VE studies - Challenges

- Testing Practices for hospital-based HCWs have changed
  - Through 2021, there was mandatory PCR testing for symptomatic hospital-based HCWs
  - From early 2022:
    - Increased rapid antigen testing, including home testing
    - Challenging to capture all symptomatic HCWs

- VE vs. infection, illness, but not severe disease
- Costly studies

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SARI VE studies - Background

- Early 2022: established a network of countries that monitor COVID-19 and influenza VE through existing SARI networks – **Euro-SAVE** (The European SARI Vaccine Effectiveness Network)

  - WHO SARI case definition
  - collect core data on enrolled patients
  - testing for COVID-19 and influenza by RT-PCR
  - genomic sequencing for influenza and SARS-CoV-2 in-country or at regional COVID-19 reference laboratories
  - country-level VE analyses and network-wide pooled analysis

Euro-SAVE current situation

- To date, six countries and areas, including Albania, Georgia, Kyrgyzstan, North Macedonia and Serbia, as well as Kosovo*, participate in the network

- Patient recruitment for SARI VE component began in the first country in November 2021

*All references to Kosovo should be understood to be in the context of the United Nations Security Council resolution 1244 1999

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Euro-SAVE, 2022

European Severe Acute Respiratory Infection Vaccine Effectiveness Network (Euro-SAVE), 2022

Euro-SAVE – Challenges

- Recruitment
  – Designated COVID-19 referral hospitals in some countries
  – Some are not part of original SARI surveillance system
    - All cases vs. all controls
  – Designated COVID-19 hospitals can change over time
    → Big implications for VE study; operationally challenging to switch hospitals mid-study

Euro-SAVE – Challenges

- Data management systems
  - In some countries, data management systems inadequate for enhanced VE
    - Data on SARI patients come from multiple sources
      - Hospital, lab(s), vaccine registry review
  - > New data platforms introduced

Euro-SAVE – Challenges

- Different data management systems
    - REDCap data management platform (3)
    - Kobo Toolbox (1)
    - Electronic Database Management System (1)
    - Internally developed national data management system (1)

  – different structures, variable names, coding

  → Recode country datasets into common format for pooled analysis

Euro-SAVE – Challenges

- Heterogeneity of sites: strength *and* limitation for pooled analysis
    - Different kinds of vaccines (7 vaccine products in use)
    - Variant circulation can differ
- → Challenge attaining power and combining diverse data

Euro-SAVE - Results

- First analysis with data from all six sites anticipated late 2022
- Aim to generate monthly VE estimates
    - Covid-19
    - Influenza

WHO/Europe VE studies – conclusions/future directions

- Existing SARI sentinel surveillance systems in WHO/Europe region provide excellent foundation for VE studies vs. severe disease

- HW VE studies have provided opportunity for relatively early VE estimates in region with limited data on VE, but challenging logistically, financially demanding

- Moving forward
  - Expand VE to include Covid and influenza 2022-2023
    - ?adequate influenza uptake for VE estimates
  - Pooling
    - HW VE studies: Interact network (US CDC)
    - Euro-SAVE: additional countries?

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