ECDC Vaccine Effectiveness, Burden and Impact Studies (VEBIS) for COVID-19 and Influenza

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8th Joint WHO Regional Office for Europe & European Centre for Disease Prevention and Control Annual European Influenza and COVID-19 Surveillance Meeting 2022, 7 October 2022
Post marketing vaccine monitoring system – part of the approved ECDC’s legal mandate

“The Centre shall coordinate independent post-marketing effectiveness and safety monitoring studies collecting new information and/or using the relevant data collected by competent bodies. That work shall be conducted jointly with the European Medicines Agency and notably through a new vaccine monitoring platform”.

- 2010 BE Presidency H1N1 lessons learnt
- 2014 Council Conclusions
- 2015 Joint ECDC/EMA paper to SANTE and MBs
- 2017 Joint ECDC/EMA financial proposal as part of the EU MFF
- 2018 Council Recommendation
- 2019-2020 ECDC/EMA request for sustainable funding to SANTE
- 2020 SANTE adopts Health Union proposal with new Agencies’ mandates
- 2020 SANTE provides first funds for COVID-19 vaccine studies
**VEBIS* project**

VEBIS: Vaccine Effectiveness, Burden and Impact Studies

- For COVID and Influenza (since end of 2020)

Four multi-country studies with pooled analysis approach

In this first period vaccine effectiveness objectives have been prioritized

Hospital and primary care studies mainly based on long-standing influenza VE networks (I-MOVE; I-MOVE COVID-19)

VEBIS project implemented through an Open Call for tender awarded to Epiconcept

*Vaccine Effectiveness, Burden and Impact Studies for COVID-19 and Influenza*
## ECDC VEBIS studies

<table>
<thead>
<tr>
<th>Setting [no. of contract]</th>
<th>Type of study</th>
<th>Main outcome</th>
<th>Countries</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospitals</td>
<td>Test negative design</td>
<td>Severe disease; <strong>influenza</strong> and COVID-19</td>
<td>BE HR CZ FR DE EL IE HU LT LU NL MT PT ES RO</td>
</tr>
<tr>
<td>Health care workers cohort</td>
<td>Cohort study</td>
<td>Infection, COVID-19</td>
<td>HR IE IT PT ES LV EE PO EL</td>
</tr>
<tr>
<td>Electronic health care databases</td>
<td>Cohort study</td>
<td>Hospitalisation, COVID-19</td>
<td>DK, ES, NO, PT (BE, LU, NL)</td>
</tr>
<tr>
<td>Primary care</td>
<td>Test negative design</td>
<td>Moderate disease (~ARI/ILI), Influenza and COVID-19</td>
<td>HR FR DE HU IE NL ES PT RO SE</td>
</tr>
<tr>
<td>Long term care facilities</td>
<td>Cohort study (protocol only)</td>
<td>Symptomatic disease, COVID-19</td>
<td>Protocol only</td>
</tr>
<tr>
<td>Outbreaks</td>
<td>Cohort and case control (protocol only)</td>
<td>Symptomatic disease, COVID-19</td>
<td>Protocol only</td>
</tr>
</tbody>
</table>
Leveraging international protocols as well as creating and pilot new protocols
Leveraging SARI surveillance as part of the VEBIS studies

Support to SARI surveillance in 13 EU countries

And

In the 6 countries of the Western Balkan Region
**ECDC-IPA6 Action**

<table>
<thead>
<tr>
<th>ECDC-IPA6</th>
<th>Work stream 1</th>
<th>Work stream 2</th>
<th>Work stream 3</th>
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<tbody>
<tr>
<td><strong>Scope</strong></td>
<td>Preparatory measures for participation of IPA beneficiaries’ authorities in ECDC activities and systems</td>
<td>Advancement of One Health responses against AMR</td>
<td>Enhancing SARI surveillance to support the implementation of fit-for-purpose surveillance systems</td>
</tr>
<tr>
<td><strong>Beneficiaries</strong></td>
<td>Albania, Bosnia and Herzegovina, Kosovo, Montenegro, North Macedonia, Serbia, and Turkey</td>
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<tr>
<td><strong>Budget</strong></td>
<td>400,000 EUR</td>
<td>600,000 EUR</td>
<td>1,500,000 EUR</td>
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</table>

**Work Stream 1. Preparatory measures for the participation of the Western Balkans and Turkey in ECDC**
- Focus area 1.1 Strengthening surveillance and data sharing
- Focus area 1.2 Public health microbiology laboratory system capacities
- Focus area 1.3 Public health emergency preparedness and coordination

**Work Stream 2. Advancement of One-Health responses against AMR**
- Focus area 2.1 Gap analysis and country roadmaps on One-Health against AMR in WB
- Focus area 2.2 Support to the development of an electronic surveillance of AMR
- Focus area 2.3 Antibiotic awareness raising and securing political commitment

**Work Stream 3 Enhancing SARI surveillance and a follow-up on vaccine effectiveness**
Adopted and implemented national surveillance protocols ensuring their compliance with generic SARI protocol
SARI surveillance data routinely reported to ECDC according to pre-defined ECDC standards and EU-level requirements
Engage Western Balkans in ECDC VEBIS for infectious respiratory diseases (as a possible follow-up)
Pooled analysis within the studies and beyond
Acknowledgments

I-MOVE/VEBIS primary care sites:
- Croatia, IPH: V. Viskerina, S. Kurecic Filipovic, B. Kacic, I. Pem Novosel, G. Petrovic, M. Illic, I. Milinarić
- France, Sentinelles: A. Vilcu, M. Mahmadi-Moindze, T. Blanchon, A. Falchi; Institut Pasteur: V. Enouf, S. van der Werf
- Hungary, Semmelweis Institute: K. Horvath, B. Oroszi, A. Ferenczi, G. Turcsanyi
- Ireland, HSE-HPSC: L. Domengan, J. O'Donnell, A. McKenna; UCD-NVRL: C. Bennett, J. Connell
- The Netherlands, RIVM: M. de Lange, A. Meijer, F. Dijkstra, R. van Gageldonk; Nivel: M. Hooiwind
- Romania, Cantacuzino Institut: M. Lazar, A. Ivanciu, M. Mihai
- Spain, CNE & ISCTI: A. Larrauri, C. Mazagatos; CNM & ISCTI: F. Pozo, I. Casas
- Spain, ISPL, Navarra: J. Castilla, I. Casado Buesa, I. Martinez-Baz, C. Burgui
- Sweden: A. Wiman, A. Carnahan, N. Latorre-Margalef, L. Dillner

VEBIS hospital sites:

Study sites VEBIS hospital VE networks
- Belgium, Sciensano: BELSARINET
- Croatia, NIPH: G. Petrovic, Z. Lovric Makaric, I. Pem Novosel, P. Smoljo
- Czechia, PHI: H. Orliková
- Czechia, UH Brno: P. Husa, L. Součková
- Germany, RKI: S. Buda, R. Duerrwald, K. Tolksdorf
- Ireland, HPSC: L. Domengan, A. Cotter, N. Petty Saphon, M. Brady
- Hungary, Semmelweis Institute: B. Oroszi, KJ. Horvath
- Lithuania, Unl: G. Gefenaita, I. Jonikaite, M. Kuliese, A. Mickiene
- Netherlands, RIVM: FA. Niessen, MJ. Knol, PCJL. Bruijning-Verhagen
- Malta, HPDPD: J. Baruch, JP. Cauchi, M-L. Borg, A. Dzlugosie, T. Mellilo
- Romania, Cantacuzino: M. Lazar, I. Loghin, A. Marin, E. Duca
- Spain, ISPL, Navarra: J. Castilla, C. Burgui Alcaide, I. Casado Buesa
- Spain, National Centre for Epidemiology (CNE), ISCTII: A. Larrauri, C. Mazagatos Ateca
- Spain, National Centre for Microbiology (CNM), ISCTII: F. Pozo, V. Sandonis, I. Casas
- ECDC: A. Omokanye, S. Bacci, M. Kaczmarek, N. Nicolay
- Epiconcept: M. Maurel, M. Valenciano, A. Moren, A. Rose, V. Nancey, C. Laniec Delauney
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Study sites HCW study

- Croatia: Z Lovrić; G. Sarajlic; G Petrović
- Estonia: O Borissjuk; L Lohur; H Sepp; A Uusküla
- Greece: C. Mitsi; K. Tryfinopoulou; O. G Panagiotakopoulos
- Ireland (Galway): C. Fleming; (St. James): C. Bergin; (Beaumont): Beaumont: E. deBarra
- Italy (Catania): M Barchitta; A Agodi; (Rome): K De Gaetano Donati; S. Lamonica; R Murri; (Monza): P Bonfanti; V Orsini; M Rossi; A Spolti
- Latvia (Pauls Strandins): I Āboliņa, V Zvirbulis; (Children hospital): Dace Zavadska; (Riga East): Indra Zeltina
- Poland: K. Szuldrzynski
- Portugal: AJ. Fernandez; V da Silva Gaio; A Machado
- Spain (Barcelona): C Munoz-Almagro; M Cubells Pujal; A Martinez Berlanga; A Perez Arguello; F Scoler; L Sanchis Badenes; (Zaragoza): M Latorre; L. Clusa; A Milgaro; A Rezusta

ECDC: K Brolin

VEBIS Laboratory coordination: Raquel Guiomar, Francisco Pozo

VEBIS Consortium members from HPSC Ireland; INSA Portugal; ISCIIII, Spain; PHI Navarra;
Epiconcept: C Savulescu; A Prats; C. Lopez; R. Mulchandani; A Sentis; V Nancey; D. Bamba; K Voy; A Nardone
VEBIS hospital influenza and COVID-19 VE

15 study sites in 14 countries
Patients admitted to hospital for SARI
Test-negative design
All/systematic selection of SARI patients
Demographic, clinical, laboratory information
Samples tested for influenza and SARS-CoV-2
Influenza VE estimates
  o mid- and end-of-season (start: 2022/23 season)
COVID-19 VE estimates
  o ad hoc, as epidemiological situation warrants
  o so far, four to six times per year
HCW COVID-19 VE studies

20 hospitals in 9 countries

Prospective cohort study design

All HCWs invited (clinical & ancillary staff)

Demographic, clinical, community & in-hospital exposures, laboratory information

Weekly/biweekly molecular testing for SARS-CoV-2 and serology testing every 4-12 weeks

COVID-19 VE estimates
  - ad hoc, as epidemiological situation warrants
Primary care influenza and COVID-19 VE

11 study sites in 10 countries
Patients consulting physicians for ARI/ILI
Test-negative design
All/systematic selection of patients
Demographic, clinical, laboratory information
All samples tested for influenza and SARS-CoV-2
Influenza VE results:
  • Mid-season, end-of-season, real-time (2021-22)
COVID-19 VE results:
  • Ad hoc, as epidemiological situation warrants
VEBIS electronic health registries and COVID-19 VE

Seven sites to participate:
- 4 in 1st phase: Denmark, Navarra (Spain), Norway, Portugal
- 3 in 2nd phase: Belgium, Luxembourg, Netherlands

Cohorts study design

Linkage of EHR: administrative, vaccination registries, SARS-CoV-2 tests, hospitalisations, and healthcare databases

Multiple outcomes including hospitalisation, ICU admission, mortality

Exclusion of those with previous SARS-CoV-2 infection at enrolment and residents of long-term care facilities, and those outside target vaccination group

Monthly reporting of VE of primary and booster doses
- 8 week estimates
- 1 month lag in report
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Overview of ECDC funded VE studies

VE against **severe disease**; leveraging efforts of SARI surveillance at hospital level and other international protocols (I-MOVE-COVID-19 and WHO)
- COVID-19 and Influenza
- 14 countries (BE HR CZ FR DE EL IE LI LU MT PT ES LT RO)
- Test negative design, primary data collection
- Population of the study: individuals eligible for vaccination according to national vaccination programmes

VE against **moderate disease**; leveraging efforts of sentinel primary care surveillance and other international protocols (I-MOVE-COVID-19)
- COVID-19 and Influenza
- 10 countries (HR FR DE HU IE NL ES PT RO SE)
- Test negative design, primary data collection
- Population of the study: individuals eligible for vaccination according to national vaccination programmes

VE against **infection**, leveraging efforts of other international protocols (WHO)
- COVID-19
- 7 countries (active: HR IE IT PT ES LV) (ended: EE) (under discussion PO EL)
- Cohort study, primary data collection with repeated sampling (serology and oral fluid/NP sample)
- Population of the study: health care workers of hospitals (including adm staff in some setting)
- Ad hoc study: VE transmission VE in nosocomial setting (tbc)

VE **assessed through Health Care Databases**
- Population health databases
- COVID-19
- Pilot study: 4 countries (DK, NO, PT, ES) // VE against hospital admission in age +65 years; by age group and by time since booster vaccination /// 3 additional countries interested to join
- Retrospective cohort study
- Landscape report on available health databases across MS
Acknowledgements

Study participants
ECDC COVID-19 vaccine effectiveness hospital study participants:
• Belgium, Universitair Ziekenhuis Brussel: T Demuyser, L Seyler, E Van Nedervelde
• Belgium, Sciensano: C Barbezange, N Bossuyt, S Denayer, F Dufrasne, N Fischer, I Thomas, and
• Belgium Centre Hospitalier Universitaire Saint-Pierre: N Dauby
• Belgium Grand Hôpital de Charleroi: A Gillain, B Lissoir, X Holemans
• Belgium Jessa Ziekenhuis: K Magerman
• Belgium Algemeen Ziekenhuis Sint-Jan Brugge-Oostende: M Reyners
• Germany, RKI: S Buda, R Duerrwald, U Preuss, K Tolksdorf
• Greece, National Public Health Organization: M Amerali, S Michelaki, G Panagiotakopoulos
• Croatia, National Institute of Public Health: Z Lovrić Makarić, I Pem Novosel, G Petrović, P Smoljo
• Czechia, Public Health Institute: H Orliková
• Czechia, University Hospital Brno: P Husa, L Součková
• Ireland, Health Protection Surveillance Centre: L Domegan, R Duffy, J O'Donnell
• Luxembourg, Ministry of Health: N Aouali, F Berthet, G. Wirtz, G Fagherazzi, M Simon
• Malta, Health Promotion and Disease Prevention Directorate: J Baruch, M-L Borg, JP Cauchi, A Dziugyte, T Melillo
• The Netherlands, Centre for Infectious Disease Control, National Institute for Public Health and the Environment, Bilthoven: P Bruijning, M Knol, A Niessen
• Portugal, Instituto Nacional de Saúde Dr Ricardo Jorge: V Gaio, V Gomez, R Guiomar, I Kislaya, A Machado, B Nunes, A Rodrigues
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Epiconcept, Paris, France (hospital study): Jennifer Howard, Esther Kissling, Anthony Nardone, Angie Rose (hospital study)
ECDC: Sabrina Bacci, Nathalie Nicolay

ECDC Registry study:
• Spain, Instituto de Salud Carlos III : Susana Monge Corella, Amparo Larrauri
• Portugal, Instituto Nacional de Saúde: Irina Kislaya, Baltazar Nunes
• Navarra, Spain, Instituto de Salud Pública y Laboral de Navarra: Cristina Buguri, Itziar Casado, Jesús Castilla, Iván Martínez-Baz
• Denmark: Statens Serum Institut: Hanne-Dorthe Emborg, Katrin Finderup
• Norway, Norwegian Institute of Public Health: Jostein Starrfelt
Epiconcept, Paris, France: Alexis Sentis, Anthony Nardone
ECDC: Sabrina Bacci, Nathalie Nicolay