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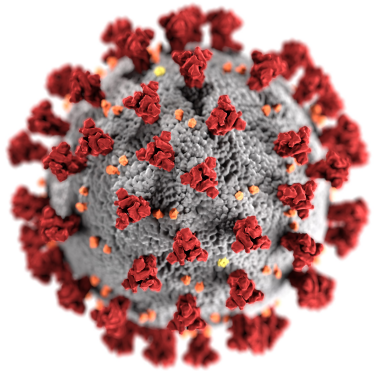
vACCine covid-19  monitoring readinESS

Miriam Sturkenboom,
University Medical Center Utrecht
On behalf of all the contributing organizations in the EU PE&PV network and participants

Organizations participating in ACCESS project

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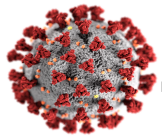
vACCine covid-19  monitoring readinESS

VAC4EU
VAccine monitoring Collaboration for Europe

Lareb
Nederlands Bijwerkingen Centrum
Netherlands Pharmacovigilance Centre

National Institute for Public Health and the Environment
Ministry of Health, Welfare and Sport

sciensano

agencia española de medicamentos y productos sanitarios

PHARMO

Universiteit Utrecht

BIPS Leibniz Institute for Prevention Research and Epidemiology - BIPS

Tampere University

AARHUS UNIVERSITY

RTI (h)(s) Health Solutions

Fundación para el Fomento de la Investigación Sanitaria y Biomédica de la Comunitat Valenciana

Bordeaux PharmacoEpi BPE

IDIAP Jordi Gol

PEDIANET

ARS TOSCANA
agenzia regionale di sanità

UiO : University of Oslo

UMC Utrecht

Led through the EU PE&PV network & leadership University Utrecht

Expectations

EUROPEAN MEDICINES AGENCY

- Infrastructure in place before Covid-19 vaccines are introduced on the market with adequate demonstration of feasibility
- Data collection at vaccine brand name level (+batch number if possible), age categories, gender, relevant special populations
- System to be used if needed by different stakeholders for the monitoring of the coverage, safety and effectiveness – governance allowing data sharing with:
  - vaccine manufacturers, as appropriate in accordance with risk management plan
  - regulators, public health authorities, others
- Transparency is key for public confidence into ability for monitoring and minimising risks
  - EMA to organise consultation of VM and consumers' and health care professionals' associations on main deliverables (timing and scope to be agreed)
- Regular interactions with monitoring committee incl. regulators and ECDC
- Possibility of international collaboration

Classified as internal/staff & contractors by the European Medicines Agency

What does ACCESS for EMA?

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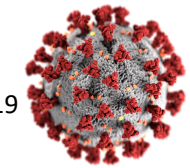
vACCine covid-19  monitoring readinESS

- Identified list of Adverse Events of Special Interest & definitions & codes (delivered in August)
- **Writing protocols/plans** for
  - Background rate calculation of AESI using electronic health care data
  - Post-introduction (primary data collection & use of EHR
    - **Safety assessment**: prospective from patients (apps), retrospective based on EHR databases or hospital based monitoring
    - **Effectiveness assessment**: prospective: test negative design, retrospective using EHR data
    - **Coverage monitoring**
    - **Integration of benefit/risk**

- Deliver background rates for AESI in 7 countries
- Feasibility assessment of organizations & governance for implementation

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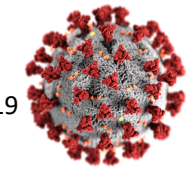
vACCine covid-19  monitoring readinESS

AESI LIST & BGR

AESI list

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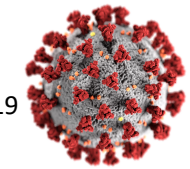
vACCine covid-19  monitoring readinESS

- 38 events
- Based on SPEAC/BC list as starting point*
- We added Narcolepsy and maternal/neonatal outcomes
- Event definition forms & codes (ICD-9/10, READ, ICPC) and algorithms drafts created see https://vac4eu.org/covid-19-vaccine-monitoring/)

Many COVID-related events (e.g. enhanced disease)

* https://brightoncollaboration.us/priority-list-aesi-covid/

Background rates of AESI: Data Sources

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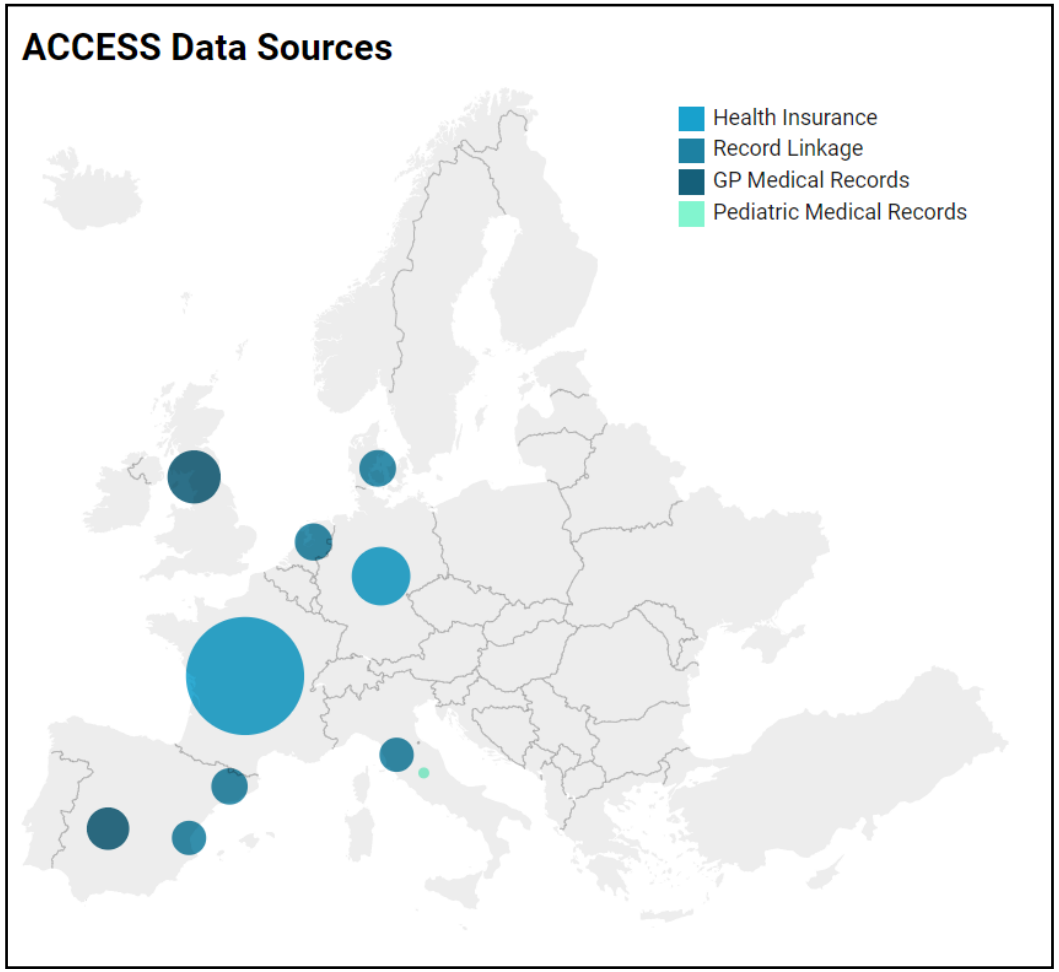

Number of individual data sources: 10
Total active population: 133.8 M

Provenance data

General Practice encounters: 7/10
Hospital encounters: 8/10
Medical birth registries: 7/10

What will be delivered?

- Full protocol available in EUPAS37273
- Rates

***Task leadership**: UMC Utrecht, Caitlin Dodd, Corinne Willame, participation of many data access providers: BIFAP, ARS Tuscany, Pedianet, IDIAP Jordi Gol, FISABIO, Aarhus, University Utrecht (CPRD), UMCU (PHARMO), BIPS, Bordeaux BPE*

Methods used

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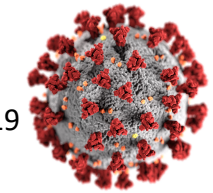
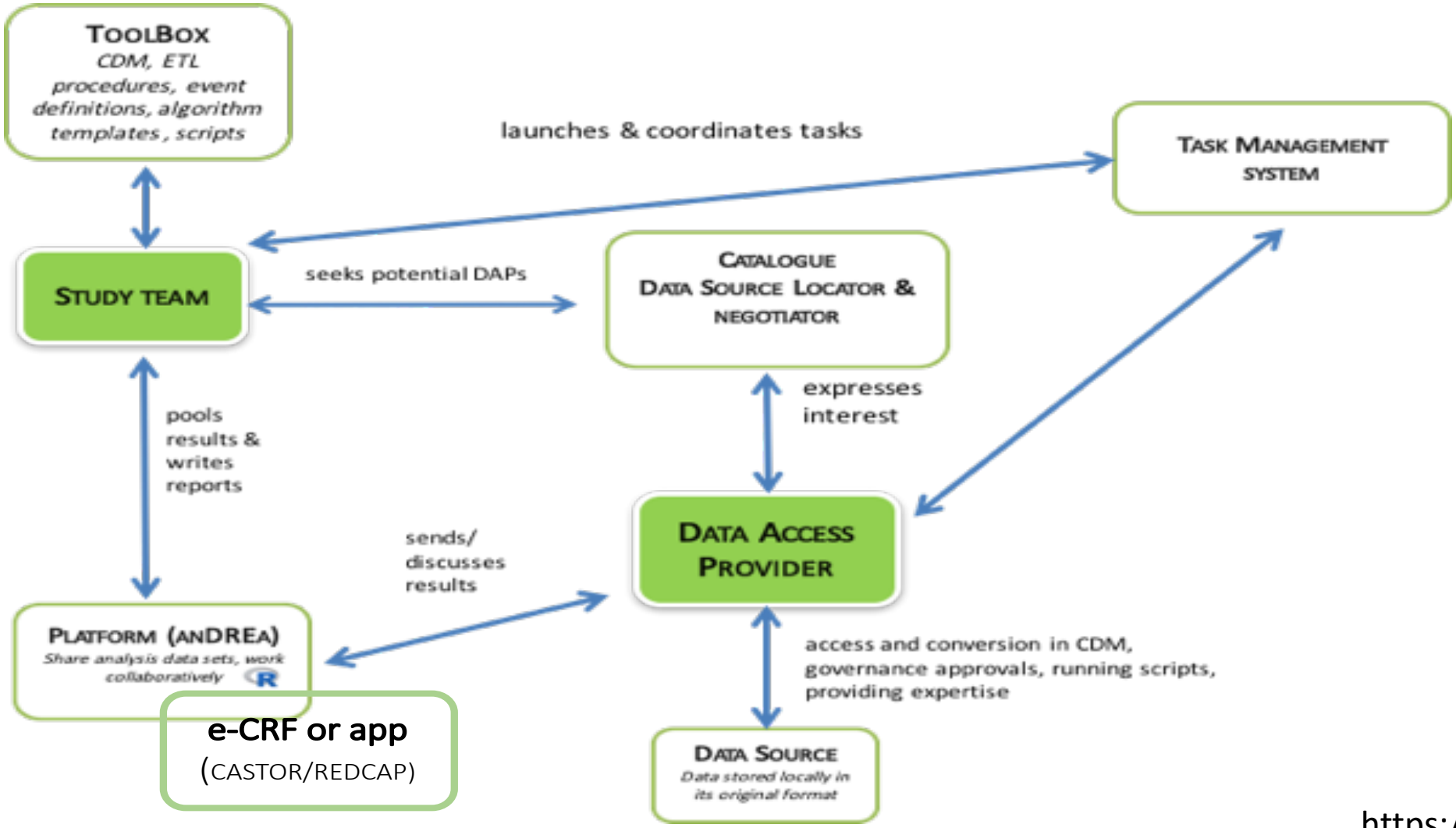
vACCine covid-19  monitoring readinESS

- Common protocol, common data model and common analytics
  - **Common data model**: ConcePTION CDM https://www.imi-conception.eu/wp-content/uploads/2020/10/ConcePTION-D7.5-Report-on-existing-common-data-models-and-proposals-for-ConcePTION.pdf
    - CDM allows for syntactic harmonization, semantic harmonization per study
    - CDM used for EMA tendered research (Retinoids/valproate, ACCESS, CONSIGN)
  - **Common analytics**: R-functions and tooling (created by ARS Tuscany, UMCU, UU, U. Swansea)
    - Quality checks (level 1-3) (developed in ConcePTION)
    - Modular (re-usable) functions for data transformation and application of study design

Using VAC4EU infrastructure



https://vac4eu.org

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Protocols for

COVID-19 VACCINE SAFETY STUDIES

Note: protocols not yet endorsed by EMA

Four types of safety protocols

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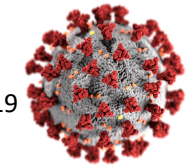

Signal detection

- **Prospective cohort event monitoring through apps (led by LAREB)**

Rapid assessment of signals

- **Ecological studies or SCRI using EHR data (led by UMCU)**

Evaluation of safety signals

- **Retrospective hospital case based studies for signal evaluation (led by RTI)**
  - Case crossover
  - SCRI
  - Case coverage
- **Retrospective safety evaluation studies based on electronic health records (**led by UMCU)
  - Cohort
  - Case control
  - SCRI/SCCS/CC

Note: protocols not yet endorsed by EMA

Decision framework signal evaluation

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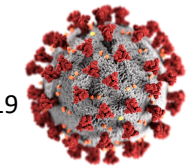

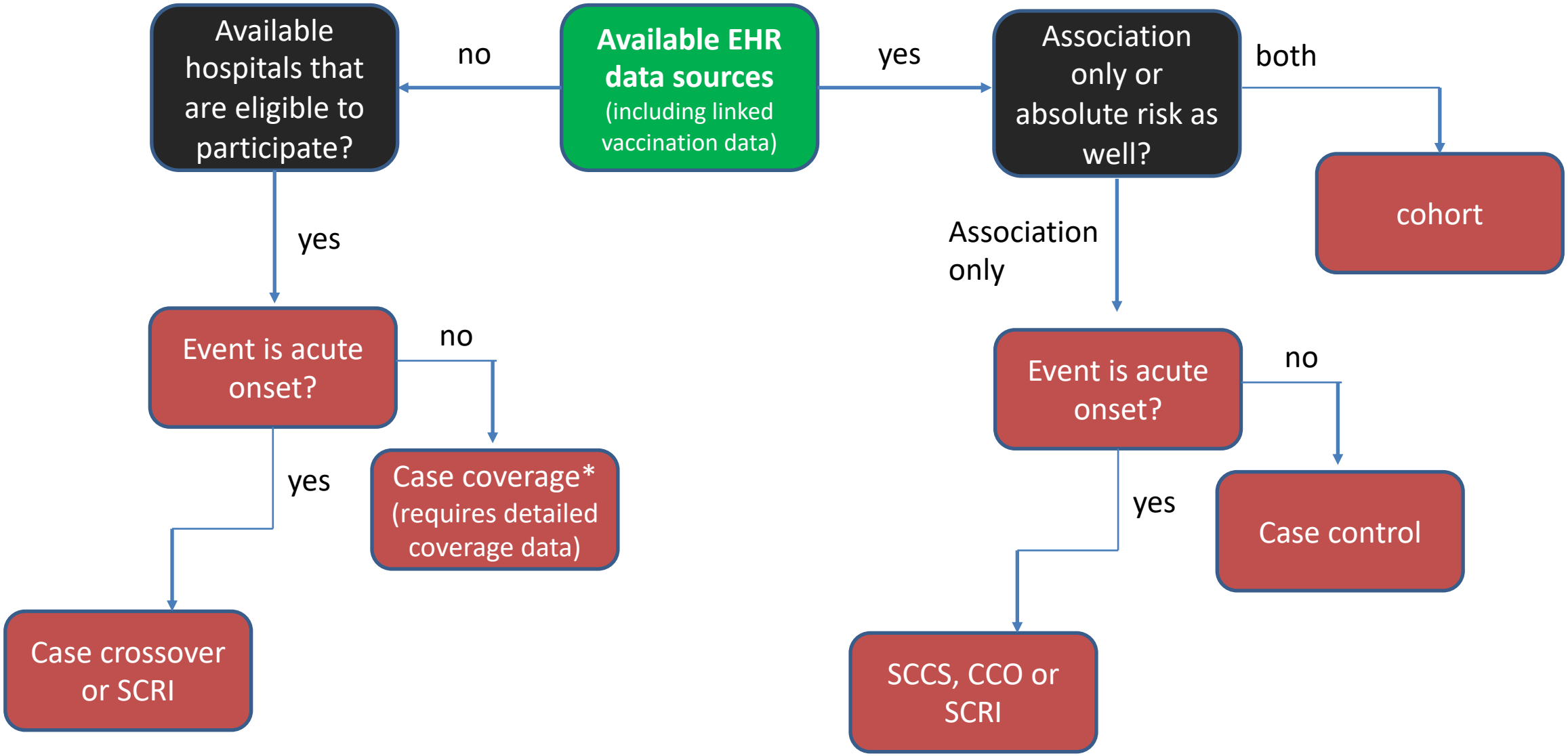

Note: not yet endorsed by EMA

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Protocols

COVID-19 VACCINE EFFECTIVENESS

Note: protocols not yet endorsed by EMA

Monitoring effectiveness of COVID-19 vaccines using health care databases (RTI-HS)

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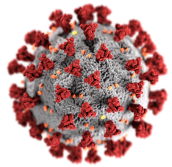

Design	Retrospective cohort study • Includes feasibility assessment • Includes variations in study design, methodological considerations	
Data sources	Health care databases which include information about vaccination status, hospitalisations, and comorbidities	
Study population	Should match the indicated and recommended population for the vaccine	
Events	• Hospitalization for COVID-19 • COVID-19 intensive care unit admission • Mortality due to COVID--19	• All-cause mortality • Hospitalizations for respiratory infections
Exposure assessment	**Exposure:** Vaccination with a specific COVID-19 vaccine **Comparator:** Unvaccinated; receipt of non-COVID-10 vaccine; other COVID-19 vaccine	
Timing	After accumulation and availability of data • Feasibility assessment, including negative control • Site-specific analyses • Pooling	

Effectiveness using test-negative design (FISABIO)

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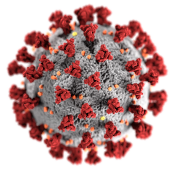

MONITORING VACCINE EFFECTIVENESS USING A TEST-NEGATIVE DESIGN

TIMING

1. Data collection
2. Mid-season data sharing
3. Quality check
4. End-season data sharing
5. Analysis
6. Reporting VE estimates

DATA SOURCES

Prospective data collection

SETTING

Hospitals

EXPOSURE ASSESSMENT

Vaccination registries
Medical records
Vaccination cards

OUTCOME

Laboratory-confirmed SARS-CoV-2

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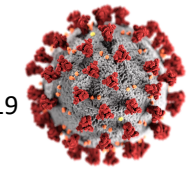
vACCine covid-19  monitoring readinESS

CAPACITY ASSESSMENT IN EUROPE

Note: not yet endorsed by EMA

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Capacity assessment in Europe: interim data from ACCESS (not cleaned and not approved by EMA)

Organizations who indicated they are willing to participate in studies

	BE	CZ	CR	DK	FI	FR	DE	IR	IT	LA	NL	NO	PT	RO	SL	ES	SE	UK	Total
Responses per country	**3**	**14**	**1**	**1**	**3**	**3**	**2**	**3**	**6**	**1**	**2**	**1**	**20**	**1**	**1**	**7**	**3**	**2**	**74**

Approach:
ENCePP centers & PRAC members (through EMA),
all ECDC advisory members (personally) & snowballing

Detailed capacity assessment is being collected at the moment

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Countries indicating to be interested in participating in COVID-19 vaccine monitoring (interim data)

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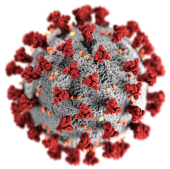


GOVERNANCE TO IMPLEMENT THE STUDIES

VAccine monitoring Collaboration for Europe

https://vac4eu.org

What is VAC4EU?

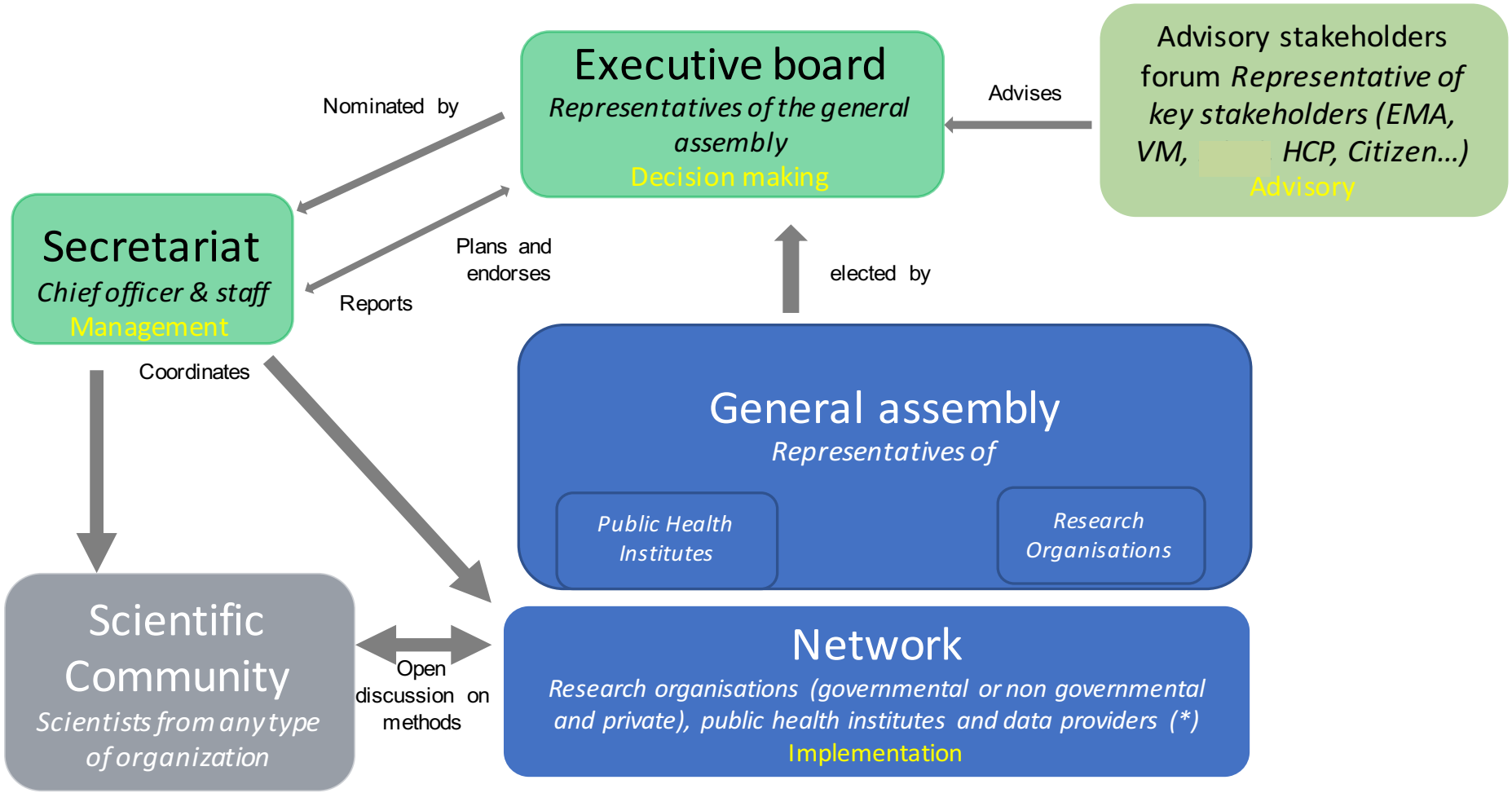
VAC4EU
VAccine monitoring Collaboration for Europe

- VAC4EU was established for this as a result of the design, testing and governance discussions in the IMI-ADVANCE project*
- VAC4EU is a member-based, international non-for profit association with headquarters in Belgium, it runs on membership fees, donations and study overheads
- VAC4EU aims to facilitate member organizations to collaborate and conduct studies according to transparent VAC4EU processes, ENcePP or ADVANCE code of conduct, and available IT infrastructures
- VAC4EU also aims to facilitate an open scientific community for discussions between stakeholders (organizing webinars and working groups)

- Kurz X, Bauchau V, Mahy P, et al. The ADVANCE Code of Conduct for collaborative vaccine studies. Vaccine. 2017;35(15):1844-1855.
- Sturkenboom M, Bahri P, Chiucchiuini A, et al. Why we need more collaboration in Europe to enhance post-marketing surveillance of vaccines [published online ahead of print, 2019 Oct 31]. Vaccine. 2019;S0264-410X(19)31002-3. doi:10.1016/j.vaccine.2019.07.081
- Torcel-Pagnon L, Bauchau V, Mahy P, et al. Guidance for the governance of public-private collaborations in vaccine post-marketing settings in Europe. Vaccine. 2019;37(25):3278-3289. doi:10.1016/j.vaccine.2019.04.073

Governance of the entity

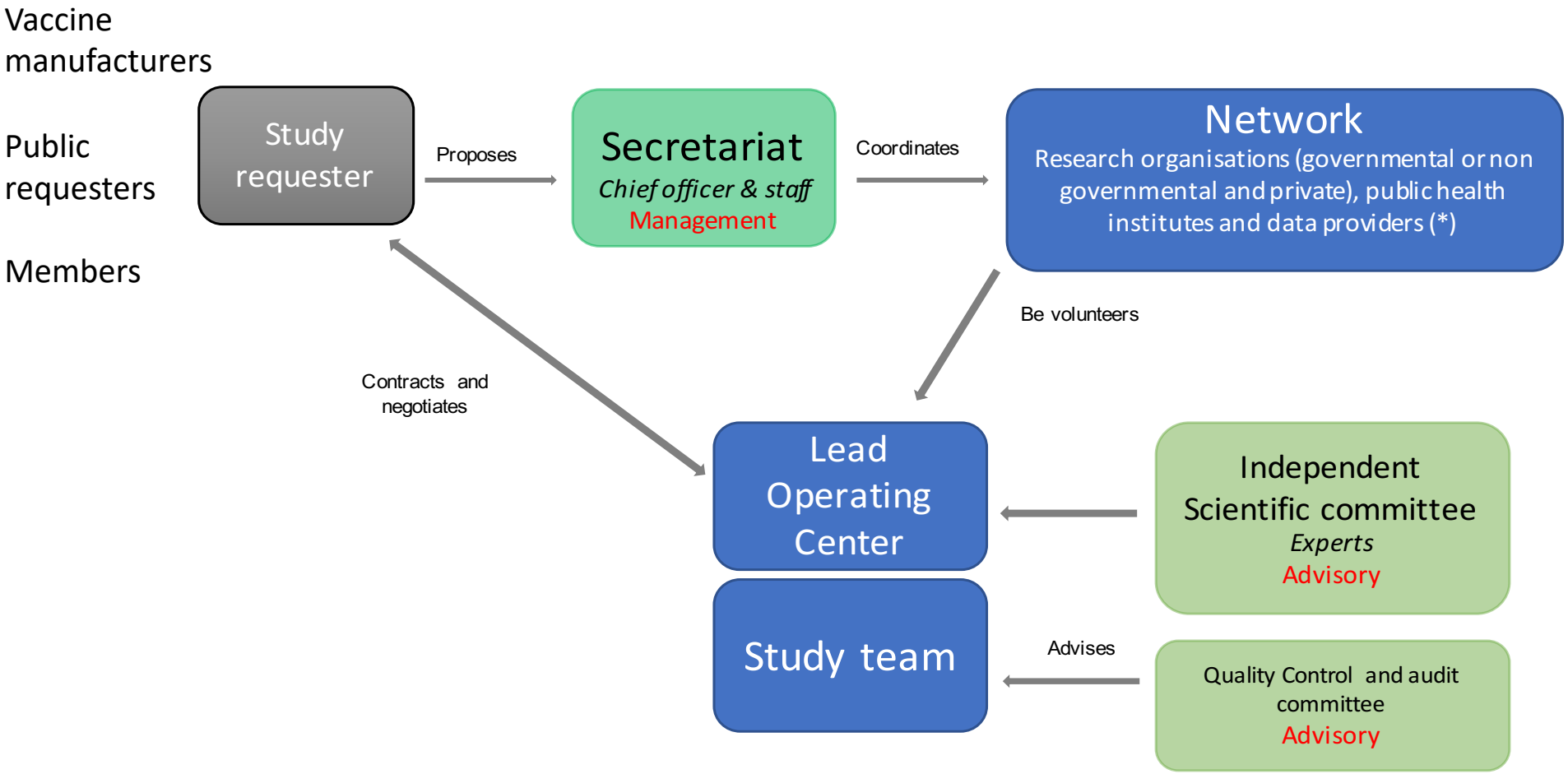
VAccine monitoring Collaboration for Europe



*publicly listed organizations not allowed

Governance of studies through VAC4EU

VAccine monitoring Collaboration for Europe



(*) under the condition of being qualified and able to provide either access to relevant data and/or relevant expertise to the post-marketing monitoring of vaccines (exposure, coverage, risks, benefits). Publicly listed organizations are not allowed

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Committed members

sciensano

REGIONE LAZIO

Bordeaux PharmacoEpi BPE

National Institute for Public Health and the Environment
Ministry of Health, Welfare and Sport

ARS TOSCANA
agenzia regionale di sanità

netherlands pharmacovigilance centrelareb

UMC Utrecht

Penta

UNIVERSITÀ di VERONA

Fundación para el Fomento de la Investigación Sanitaria y Biomédica de la Comunitat Valenciana

PEDIANET

RTI (h)(s) Health Solutions

BIPS Leibniz Institute for Prevention Research and Epidemiology - BIPS

UiO : University of Oslo

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Organizations that expressed interest to become member

If you want to stay in touch or become a member

https://vac4eu.org