ARS TOSCANA
agenzia regionale di sanità

Il ruolo di ARS Toscana nel monitoraggio della sicurezza dei vaccini COVID

Rosa Gini

Presentazione Rapporto sui Farmaci in Toscana 2021

Firenze, 15 dicembre 2021

Conflitto di interesse

L'ARS svolge numerosi studi di farmacoepidemiologia finanziati da organizzazioni pubbliche e private, aderenti al Codice di Condotta ENCePP

Il budget della PO di farmacoepidemiologia è parzialmente sostenuto da tali studi

ARS TOSCANA
agenzia regionale di sanità

Contenuti

- Una storia di successo
- Punti di forza di ARS

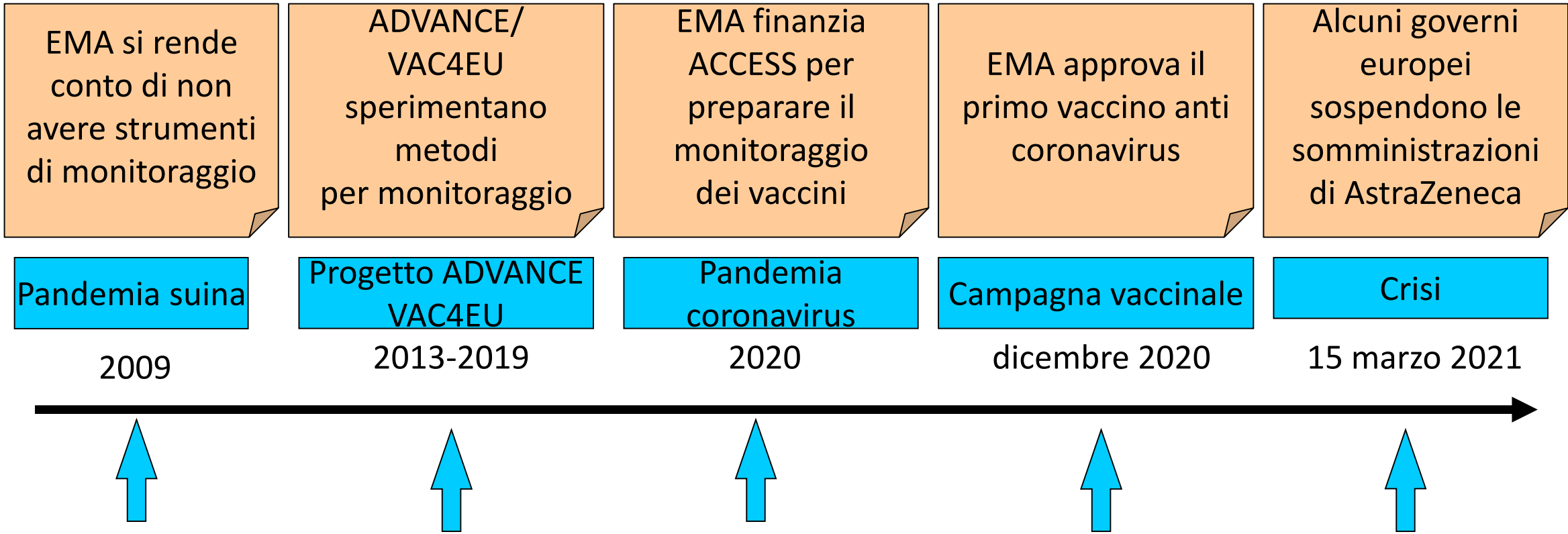
ARS TOSCANA
agenzia regionale di sanità

Contenuti

- **Una storia di successo**
- Punti di forza di ARS

ARS TOSCANA
agenzia regionale di sanità

Monitoraggio della sicurezza dei vaccini in EMA



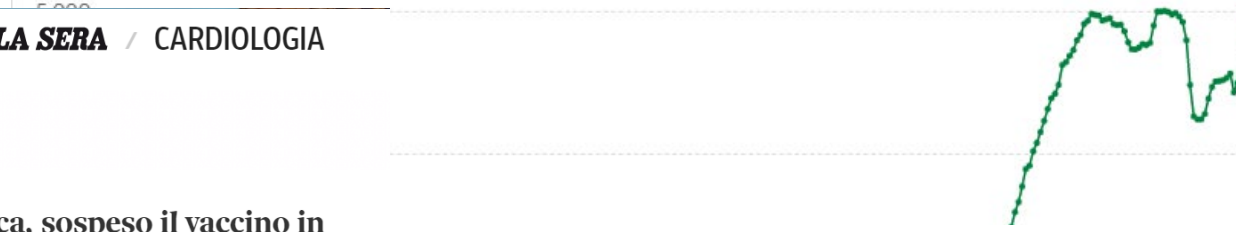
ARS TOSCANA
agenzia regionale di sanità

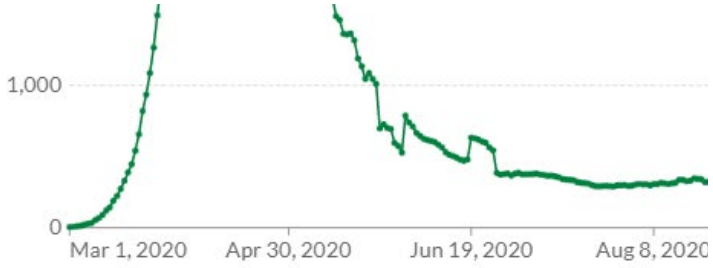
15 marzo

Daily new confirmed COVID-19 deaths

7-day rolling average. Due to limited testing and challenges in the attribution of the cause of death, confirmed deaths can be lower than the tru

LINEAR LOG





Source: Johns Hopkins University CSSE COVID-19 Data

CORRIERE DELLA SERA / CARDIOLOGIA

AstraZeneca, sospeso il vaccino in Italia, Germania, Francia, Spagna e Portogallo in via temporanea e precauzionale

L'Aifa ha sospeso la somministrazione del vaccino anti-Covid AstraZeneca, in linea con quanto deciso dalla Germania. Anche la Francia ha poi deciso di fermare le vaccinazioni con AstraZeneca. Giovedì arriverà un nuovo giudizio sul farmaco da parte dell'Ema

di Redazione Online

MENU TOP NEWS LA STAMPA

SPECIALE CORONAV

Coronavirus, tutti i Paesi che hanno bloccato il vaccino AstraZeneca: ragioni e dubbi

Le reazioni del vaccino anglosvedese spaventano anche se, va precisato, «sono stop precauzionali e temporanei». Ema:

MENU | CERCA la Repubblica ABBONATI GEDI SMILE | R | ACCEDI

Cronaca

CERCA

Vaccini, Palazzo Chigi: "Sospensione AstraZeneca per 4 giorni, 200mila dosi in meno, riassorbibili in due settimane"

Ordinanza del commissario Figliuolo: "Dosi residue a fine giornata a persone disponibili. Evitiamo gli sprechi". Se Ema darà l'ok Macron e Draghi d'accordo nel far ripartire speditamente le somministrazioni

Il ruolo d

Updated OE analyses pe
to the 16th March 2021

EMA performed an update
Eudravigilance up to the 1

Data sources used in th

Data provided by the ACC
from 2017-2020

- The databases
  - Coagu
    throm
  - Dissen
  - Cerebr
- Different data
  when several i
  literature), the

In addition a conservative
incidence rate estimate.

Cerebral Venous Sinus Thrombosis	IR per 100,000 Person years From ARS	EEA Expected 14d	EEA Observed 14d From EV	EEA OE 14d with 95% c.i.	EEA and UK Expected 14d	EEA and UK Observed 14d From EV	EEA and UK OE 14d with 95% c.i.
20-29	0.64	0.05	1	21.80 (0.28 - 121.32)	0.05	1	21.80 (0.28 - 121.32)
30-49	1.80	1.29	11	8.55 (4.26 - 15.31)	3.27	12	3.67 (1.89 - 6.41)
50-59	1.00	0.48	1	2.07 (0.03 - 11.53)	1.43	2	1.40 (0.16 - 5.06)
60-69	1.29	0.51	0	0.00 (0.00 - 7.23)	2.55	0	0.00 (0.00 - 1.44)
70-79	1.91	0.19	0	0.00 (0.00 - 19.37)	2.58	0	0.00 (0.00 - 1.42)
80+	1.55	0.12	0	0.00 (0.00 - 30.74)	0.71	0	0.00 (0.00 - 5.14)
Total		**2.63**	**13**	**4.94 (2.63 - 8.45)**	**10.58**	**15**	**1.42 (0.79 - 2.34)**

* *Based on cases retrieved using a search in Eudravigilance with the Preferred Terms, "cerebral venous thrombosis" and "cerebral venous sinus thrombosis"*

Embolic and thrombotic events	IR per 100,000 Person years From ARS	EEA Expected 14d	EEA Observed 14d From EV	EEA OE 14d with 95% c.i.
20-29	40.14	2.88	11	3.82 (1.91 - 6.84)
30-49	85.08	60.95	79	1.30 (1.03 - 1.62)
50-59	200.73	96.89	40	0.41 (0.29 - 0.56)
60-69	427.56	168.22	33	0.20 (0.14 - 0.28)
70-79	912.00	90.40	5	0.06 (0.02 - 0.13)
80+	2,055.95	158.30	8	0.05 (0.02 - 0.10)
Total		**577.64**	**182**	**0.32 (0.27 - 0.36)**

18 marzo

MENU | CERCA la Repubblica ABBONATI GEDI SMILE | ACCEDI

Ema, l'Agenzia europea del farmaco dice che AstraZeneca è sicuro ed efficace

MENU CERCA LA STAMPA IL QUOTIDIANO ABBONATI ACCEDI

Sei qui: Home > Cronaca

Ema: "AstraZeneca sicuro e efficace, 25 casi su 20 milioni di vaccinati". Domani alle 15 l'Italia riprende le vaccinazioni

Via libera dall'Agenzia europea del farmaco: «I benefici superano i rischi. Non si può escludere un legame con i rari casi tromboembolici. Indagheremo se ci sono rischi per chi assuma la pillola»

PAOLO FESTUCCIA

19 Marzo 2021 | Modificato il: 19 Marzo 2021 1 minuti di lettura

CORRIERE DELLA SERA / SALUTE

LA PANDEMIA

Vaccino AstraZeneca, la decisione dell'Ema: «È sicuro ed efficace». Draghi: «Da venerdì si riprende»

ARS TOSCANA
agenzia regionale di sanità

Il ruolo d

Updated OE analyses pe
to the 16th March 2021

EMA performed an update
Eudravigilance up to the 1

Data sources used in th

Data provided by the ACC
from 2017-2020

- The databases
  - Coagu
    throm
  - Dissen
  - Cerebr
- Different data
  when several i
  literature), the

In addition a conservative
incidence rate estimate.

Cerebral Venous Sinus Thrombosis	IR per 100,000 Person years From ARS	EEA Expected 14d	EEA Observed 14d From EV	EEA OE 14d with 95% c.i.	EEA and UK Expected 14d	EEA and UK Observed 14d From EV	EEA and UK OE 14d with 95% c.i.
20-29	0.64	0.05	1	21.80 (0.28 - 121.32)	0.05	1	21.80 (0.28 - 121.32)
30-49	1.80	1.29	11	8.55 (4.26 - 15.31)	3.27	12	3.67 (1.89 - 6.41)
50-59	1.00	0.48	1	2.07 (0.03 - 11.53)	1.43	2	1.40 (0.16 - 5.06)
60-69	1.29	0.51	0	0.00 (0.00 - 7.23)	2.55	0	0.00 (0.00 - 1.44)
70-79	1.91	0.19	0	0.00 (0.00 - 19.37)	2.58	0	0.00 (0.00 - 1.42)
80+	1.55	0.12	0	0.00 (0.00 - 30.74)	0.71	0	0.00 (0.00 - 5.14)
Total		**2.63**	**13**	**4.94 (2.63 - 8.45)**	**10.58**	**15**	**1.42 (0.79 - 2.34)**

* *Based on cases retrieved using a search in Eudravigilance with the Preferred Terms, "cerebral venous thrombosis" and "cerebral venous sinus thrombosis"*

Embolic and thrombotic events	IR per 100,000 Person years From ARS	EEA Expected 14d	EEA Observed 14d From EV	EEA OE 14d with 95% c.i.
20-29	40.14	2.88	11	3.82 (1.91 - 6.84)
30-49	85.08	60.95	79	1.30 (1.03 - 1.62)
50-59	200.73	96.89	40	0.41 (0.29 - 0.56)
60-69	427.56	168.22	33	0.20 (0.14 - 0.28)
70-79	912.00	90.40	5	0.06 (0.02 - 0.13)
80+	2,055.95	158.30	8	0.05 (0.02 - 0.10)
Total		**577.64**	**182**	**0.32 (0.27 - 0.36)**

8 aprile

MENU | CERCA

la Repubblica

ABBONATI | GEDI SMILE | R | ACCEDI

Cronaca

CERCA

AstraZeneca, ministero della Salute: raccomandato uso over 60. Seconda dose con lo stesso vaccino

adendo che è approvato per tutte le persone con più di 18 anni, ne raccomanda un uso
gli over-60. E aggiunge: "Basso il rischio di reazioni avverse di tipo tromboembolico a fronte della
la Covid-19". Aifa: "Al momento nessun segnale rischi trombosi vaccini mRNA"

CORRIERE DELLA SERA / POLITICA

LE RACCOMANDAZIONI

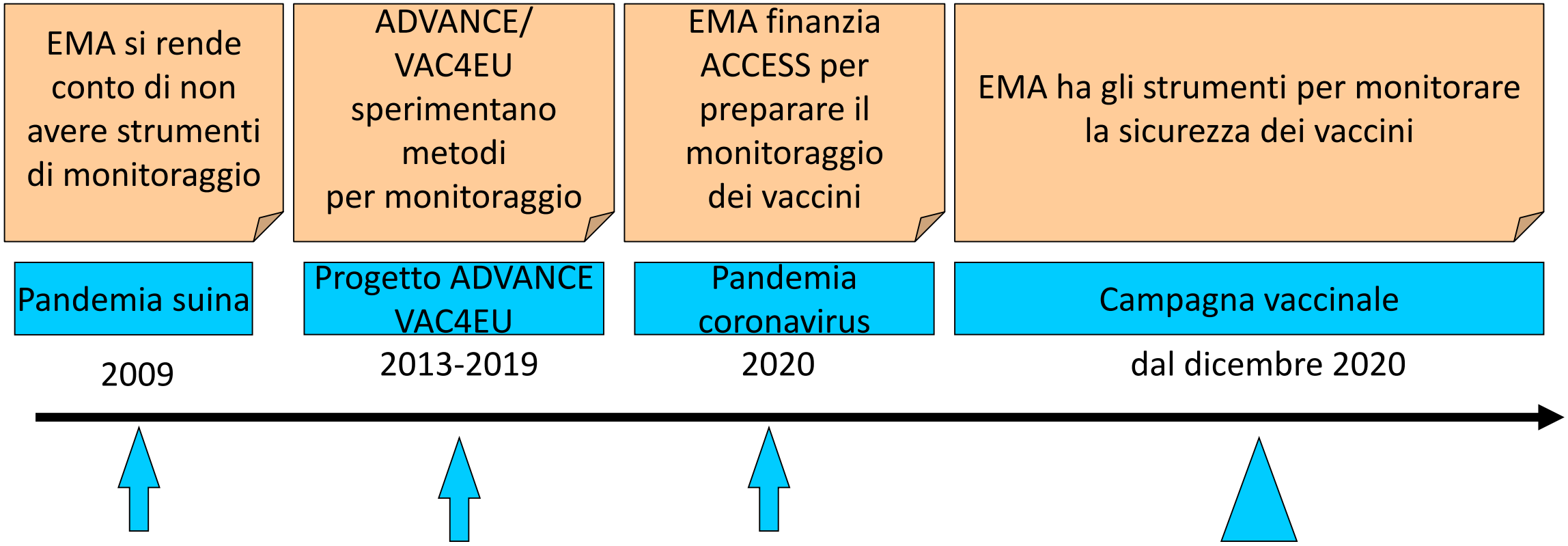
AstraZeneca, la circolare del ministero della Salute con nuovi limiti

Firmato dal direttore generale del ministero Gianni Rezza, il documento raccomanda «un uso preferenziale nelle persone con più di 60 anni». Ma il vaccino AstraZeneca è approvato a partire dai 18 anni

di Monica Guerzoni e Carlotta De Leo

ARS TOSCANA
agenzia regionale di sanità

Monitoraggio della sicurezza dei vaccini in EMA



ARS TOSCANA
agenzia regionale di sanità

Contenuti

- Una storia di successo
- **Punti di forza di ARS**

ARS TOSCANA
agenzia regionale di sanità

Coinvolgimento di ARS negli studi sui vaccini COVID

- Finanziati da EMA: ACCESS, ECVM, CVM
- Richiesti da EMA alle case produttrici: Pfizer, Moderna, AstraZeneca, Janssen
- Tutti gli studi si svolgono sotto l'ombrello di VAC4EU

ARS TOSCANA
agenzia regionale di sanità

Rigore metodologico

Vaccine 38 (2020) B56–B64

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Quantifying outcome misclassification in multi-database studies: The case study of pertussis in the ADVANCE project

Rosa Gini [a,*], Caitlin N. Dodd [b,c], Kaatje Bollaerts [d], Claudia Bartolini [a], Giuseppe Roberto [a], Consuelo Huerta-Alvarez [e], Elisa Martín-Merino [e], Talita Duarte-Salles [f], Gino Picelli [g], Lara Tramontan [g,h], Giorgia Danieli [g,h], Ana Correa [i], Chris McGee [i,j], Benedikt F.H. Becker [b], Charlotte Switzer [k,1], Sonja Gandhi-Banga [k], Jorgen Bauwens [l,m,n], Nicoline A.T. van der Maas [m,n], Gianfranco Spiteri [o], Emmanouela Sdona [o,2], Daniel Weibel [b], Miriam Sturkenboom [c,d,p]

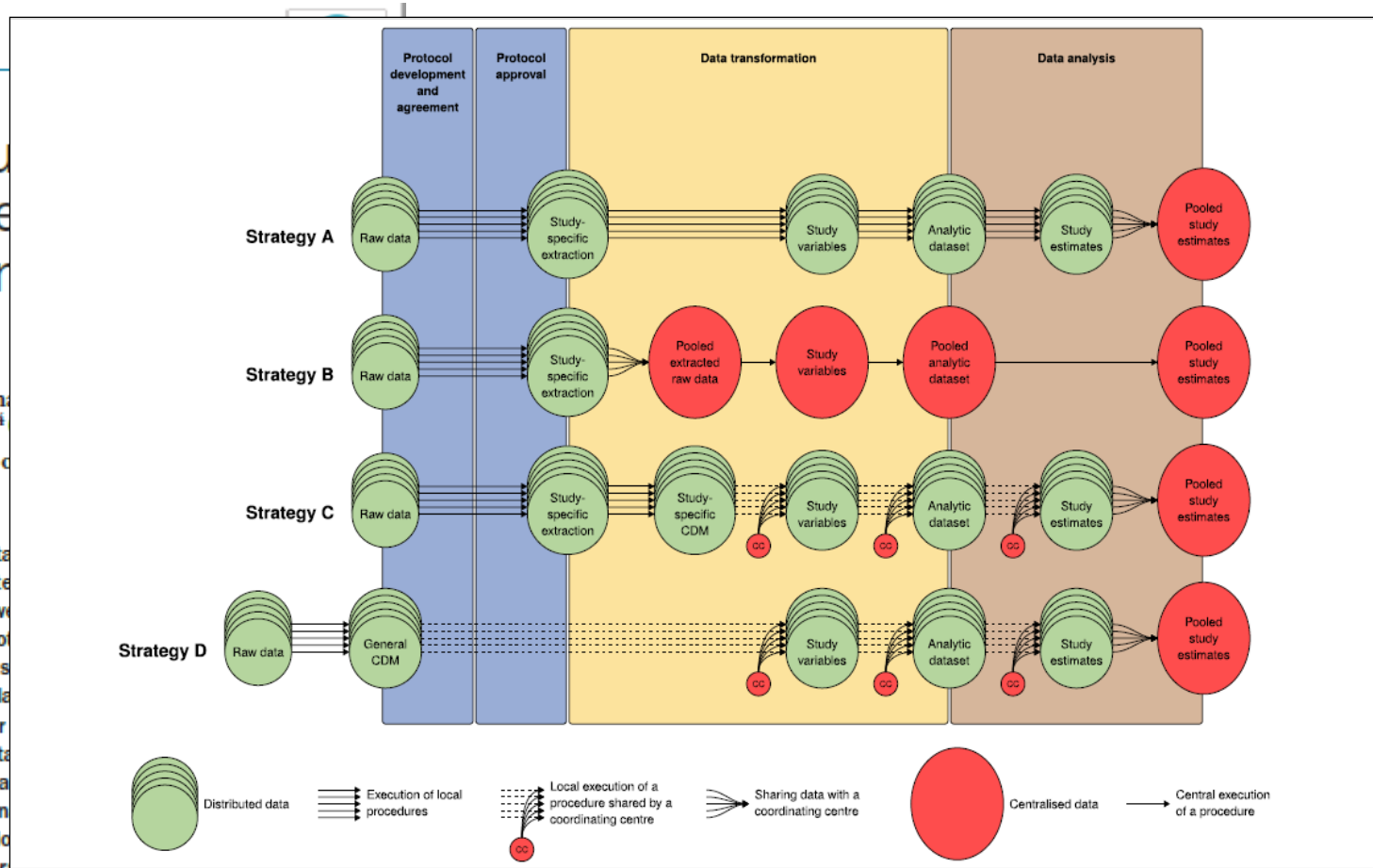
Capacità di analisi dei processi…

REVIEW

Different Strategies to Execute Mu… Studies for Medicines Surveillance… Real-World Setting: A Reflection on… European Model

Rona Gini[1,*], Miriam C. J. Sturkenboom[2], Janet Sultana[3], Alison Cave[4], Anna… Alexandra Pacurariu[4], Giuseppe Roberto[1], Tania Schink[7], Gianmario Candore[4]… Gianluca Trifirò[8] on behalf of the Working Group 3 of ENCePP (Inventory o… and methodological approaches for multisource studies)

Although postmarketing studies conducted in population-based databases often conta… in the order of millions, they can still be underpowered if outcomes or exposure of inte… is in subgroup effects. Combining several databases might provide the statistical powe… study (MDS) uses at least two healthcare databases, which are not linked with each ot… level, with analyses carried out in parallel across each database applying a common s… many MDSs have been performed in Europe in the past 10 years, there is a lack of cla… implications of the existing strategies to conduct them. In this review, we identify four… classified according to specific choices in the execution: *(A) local analyses*, where data… locally, with programs developed by each site; *(B) sharing of raw data*, where raw data… transferred without analysis to a central partner, where all the data are pooled and an… *data model with study-specific data*, where study-specific data are locally extracted, lo… model, and processed locally with centrally developed programs; and *(D) use of gener… all local data are extracted and loaded into a common data model, prior to and independent of any study protocol, and protocols are incorporated in centrally developed programs that run locally. We illustrate differences between strategies and analyze potential implications.



ARS TOSCANA
agenzia regionale di sanità

…e della natura dei dati europei

Check for updates

ARTICLE

From Inception to ConcePTION: Genesis of a Network to Support Better Monitoring and Communication of Medication Safety During Pregnancy and Breastfeeding

Nicolas H. Thurin[1,*,†], Romin Pajouheshnia[2,†], Giuseppe Roberto[3,†], Caitlin Dodd[4], Giulia Hyeraci[3], Claudia Bartolini[3], Olga Paoletti[3], Hedvig Nordeng[4], Helle Wallach-Kildemoes[4], Vera Ehrenstein[5], Elena Dudukina[5], Thomas MacDonald[6], Giorgia De Paoli[6], Maria Loane[7], Christine Damase-Michel[8], Anna-Belle Beau[8], Cécile Droz-Perroteau[1], Régis Lassalle[1], Jorieke Bergman[9], Karin Swart[10], Tania Schink[11], Clara Cavero-Carbonell[12], Laia Barrachina-Bonet[12], Ainhoa Gomez-Lumbreras[13], Maria Giner-Soriano[13], María Aragón[13], Amanda J. Neville[14], Aurora Puccini[15], Anna Pierini[16], Valentina Ientile[17], Gianluca Trifirò[18], Anke Rissmann[19], Maarit K. Leinonen[20], Visa Martikainen[20], Sue Jordan[21], Daniel Thayer[21], Ieuan Scanlon[21], Mary E. Georgiou[22], Marianne Cunnington[22], Morris Swertz[9], Miriam Sturkenboom[23] and Rosa Gini[3]

In 2019, the Innovative Medicines Initiative (IMI) funded the ConcePTION project—Building an ecosystem for better monitoring and communicating safety of medicines use in pregnancy and breastfeeding: validated and regulatory endorsed workflows for fast, optimised evidence generation—with the vision that there is a societal obligation to rapidly reduce uncertainty about the safety of medication use in pregnancy and breastfeeding. The present paper introduces the set of concepts used to describe the European data sources involved in the ConcePTION project and illustrates the ConcePTION Common Data Model (CDM), which serves as the keystone of the federated ConcePTION network. Based on data availability and content analysis of 21 European data sources, the ConcePTION CDM has been structured with six tables designed to capture data from routine healthcare, three tables for data from public health surveillance activities, three curated tables for derived data on population (e.g., observation time and mother-child linkage), plus four metadata tables. By its first anniversary, the ConcePTION CDM has enabled 13 data sources to run common scripts to contribute to major European projects, demonstrating its capacity to facilitate effective and transparent deployment of distributed analytics, and its potential to address questions about utilization, effectiveness, and safety of medicines in special populations, including during pregnancy and breastfeeding, and, more broadly, in the general population.

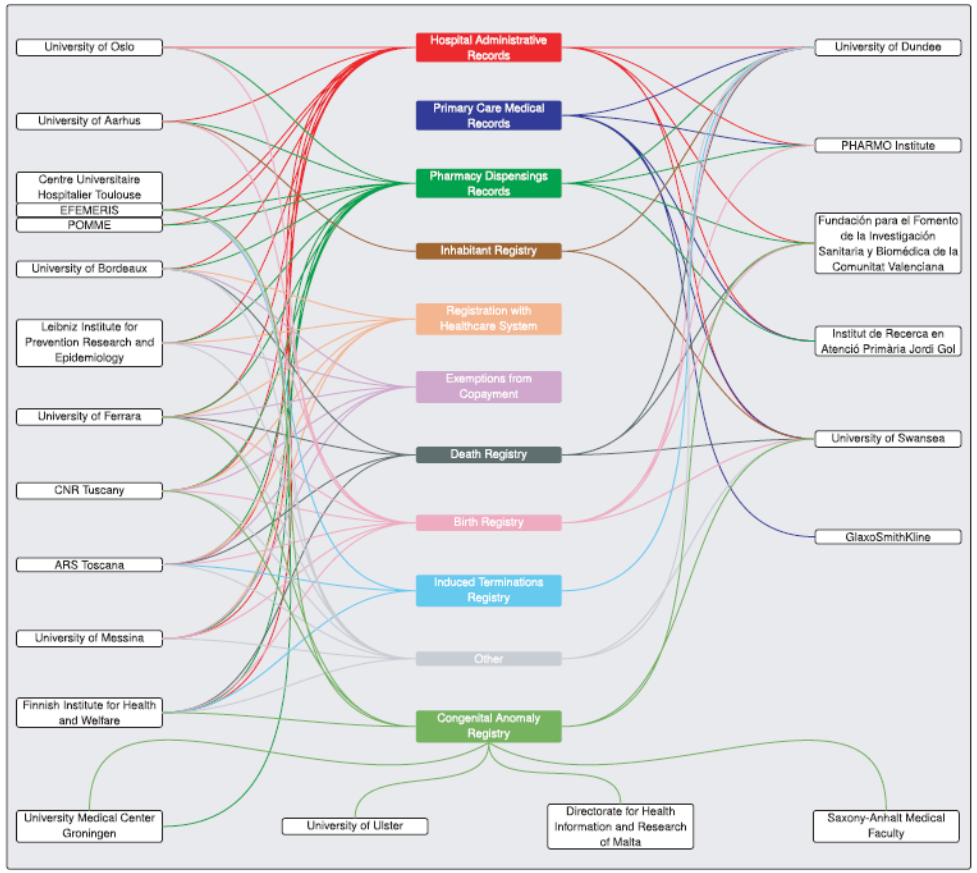


Figure 1 Data banks in each data source. Only data banks included in at least two data sources are represented, the others are summarized in "Other." The data banks are described in **Table 2**.

ARS TOSCANA
agenzia regionale di sanità

La capacità di fare rete

ARS TOSCANA
agenzia regionale di sanità

ENEPP

Journal Club

Vaccine 38 (2020) B76–B83

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

ELSEVIER

Vaccine

VAC4EU

ADVANCE: Towards near real-tir
benefits and risks using Europea

Kaatje Bollaerts [a,*], Tom de Smedt [a], Chris
Maria Alexandridou [a], Talita Duarte-Salles
Myint Tin Tin Htar [h], Lina Titievsky [i], Miri

[a] P95 Epidemiology and Pharmacovigilance, Koning Leopold III laan 1,
[b] Royal College of General Practitioners Research and Surveillance Cen
[c] Department of Clinical and Experimental Medicine, University of Sur
[d] Statens Serum Institut, Artillerivej 5, 2300 Copenhagen, Denmark
[e] ATS della Val Padana, Cremona, Italy
[f] Fundació Institut Universitari per a la recerca a l'Atenció Primària de
[g] Agenzia regionale di sanità della Toscana, Osservatorio di epidemiol
[h] Pfizer, 23-25 Avenue du Dr Lannelongue, 75014 Paris, France
[i] Pfizer, 219 East 42nd St, NY, NY 10017, USA
[j] Julius Global Health, University Medical Center Utrecht, Heidelberglaa
[k] VACCINE.GRID Foundation, Basel, Switzerland
[l] GSK, Av. Fleming 20, 1300 Wavre, Belgium

La qualità dei dati italiani…

Drug Safety
https://doi.org/10.1007/s40264-018-0732-5

REVIEW ARTICLE

The Role of European Healthcare Databases for Post-Marketing Drug Effectiveness, Safety and Value Evaluation: Where Does Italy Stand?

Gianluca Trifirò[1,20] · Rosa Gini[2] · Francesco Barone-Adesi[3] · Ettore Beghi[4] · Anna Cantarutti[5] · Annalisa Capuano[6] · Carla Carnovale[7] · Antonio Clavenna[8] · Mirosa Dellagiovanna[9] · Carmen Ferrajolo[6] · Matteo Franchi[5] · Ylenia Ingrasciotta[1] · Ursula Kirchmayer[10] · Francesco Lapi[11] · Roberto Leone[12] · Olivia Leoni[9] · Ersilia Lucenteforte[13] · Ugo Moretti[12] · Alessandro Mugelli[14] · Luigi Naldi[15] · Elisabetta Poluzzi[16] · Concita Rafaniello[6] · Federico Rea[5] · Janet Sultana[1] · Mauro Tettamanti[17] · Giuseppe Traversa[18] · Alfredo Vannacci[14] · Lorenzo Mantovani[19] · Giovanni Corrao[5]

ARS TOSCANA
agenzia regionale di sanità

…unita alla tempestività consentita dall’infrastruttura della regione Toscana

Ringraziamenti

[a] P95 Epidemiology and Pharmacovigilance, Koning Leopold III laan 1, 3001 Heverlee, Belgium
[b] Royal College of General Practitioners Research and Surveillance Centre, London, UK
[c] Department of Clinical and Experimental Medicine, University of Surrey, Guildford, UK
[d] Statens Serum Institut, Artillerivej 5, 2300 Copenhagen, Denmark
[e]
[f]
[g]
[h]
[i]
[j]
[k]
[l]

La Regione Toscana

[1]Agenzia regionale di sanità della Toscana, Florence, Italy; [2]Julius Global Health, Utrecht Medical Center University, Utrecht, The Netherlands; [3]Università di Messina, Messina, Italy; [4]European Medicines Agency, Amsterdam, The Netherlands; [5]Fondazione per la Ricerca Farmacologica Gianni Benzi Onlus, Valenzano, Italy; [6]Teddy European Network of Excellence for Paediatric Clinical Research, Pavia, Italy; [7]Leibniz Institute for Prevention Research and Epidemiology, Bremen, Germany; [8]Department of Biomedical and Dental Sciences and Morphofunctional Imaging, Università di Messina, Messina, Italy. *Correspondence: Rona Gini (rosa.gini@ars.toscana.it)

Received December 20, 2019; accepte

Tutti i colleghi dell'ARS Toscana
PO Farmacoepidemiologia
Giuseppe Roberto, Claudia Bartolini, Giulia Hyeraci, Olga Paoletti, Davide Messina, Giorgio Limoncella, Anna Girardi
P.O. Gestione dati sanitari
P. O. Soluzioni web
Risorse umane
Personale e segreterie
Tutti i colleghi ricercatori

[1]Bordeaux PharmacoEpi, INSERM CIC-P1401, Univ. Bordeaux, Bordeaux, France; [2]Utrecht Institute for Pharmaceutical Sciences, Utrecht Univ
Utrecht, The Netherlands; [3]Agenzia regionale di sanità della Toscana, Florence, Italy; [4]PharmacoEpidemiology and Drug Safety Research
Group, Department of Pharmacy, and PharmaTox Strategic Initiative, Faculty of Mathematics and Natural Sciences, University of Oslo, Oslo,
Norway; [5]Department of Clinical Epidemiology, Aarhus University, Aarhus, Denmark; [6]MEMO Research, School of Medicine, University of Dund
Dundee, UK; [7]Institute of Nursing and Health Research, Ulster University, Newtownabbey, UK; [8]INSERM, CERPOP: SPHERE, CIC 1436, Univers
Toulouse, Toulouse, France; [9]Department of Genetics, University of Groningen, University Medical Center Groningen, Groningen, The Netherla
[10]PHARMO Institute for Drug Outcomes Research, Utrecht, The Netherlands; [11]Leibniz Institute for Prevention Research and Epidemiology–BI
Bremen, Germany; [12]Fundació per al Foment de la Investigació Sanitaria i Biomédica de la Comunitat Valenciana (FISABIO), Valencia, Spain;
[13]Fundació Institut Universitari per a la recerca a l'Atenció Primària de Salut Jordi Gol i Gurina (IDIAPJGol), Universitat Autònoma de Barcelona
Bellaterra, Spain; [14]IMER Registry (Emilia Romagna Registry of Birth Defects), Center of Epidemiology for Clinical Research, University of Ferra
Ferrara, Italy; [15]Drug Policy Service, Emilia Romagna Region Health Authority, Bologna, Italy; [16]Epidemiology of Rare Diseases and Congenital
Anomalies Unit, National Research Council-Institute of Clinical Physiology (CNR-IFC), Pisa, Italy; [17]Department of Biomedical and Dental Scien
and Morpho-functional Imaging, University of Messina, Messina, Italy; [18]Department of Diagnostics and Public Health, University of Verona, V
Italy; [19]Malformation Monitoring Centre Saxony-Anhalt, Medical Faculty, Otto-von-Guericke-University, Magdeburg, Germany; [20]Finnish Institute
Health and Welfare, Helsinki, Finland; [21]Faculty of Health and Life Science, Swansea University, Swansea, UK; [22]Glaxosmithkline, Stevenage, U
[23]Department Datascience and Biostatistics, University Medical Center Utrecht, Utrecht, The Netherlands. *Correspondence: Nicolas H. Thurin
(nicolas.thurin@u-bordeaux.fr)

Service, Rome, Italy