Pharmacovigilance of Covid-19 vaccines – part 2
–
How the CDC is lying to you

Surya ARBY

12/28/2021

Monitoring tools

Passive reporting

- VAERS – USA ; Eudravigilance – EU ; standard everywhere
- Under reporting
- Poor quality of reports (missing / incorrect data)
- Cannot establish causality (in nearly most cases, there are exceptions : rechallenge in multi dose schedules)
- Signal detection / hypothesis generating
- Defective by design ; mostly useless for us

Advanced surveillance / true safety investigations

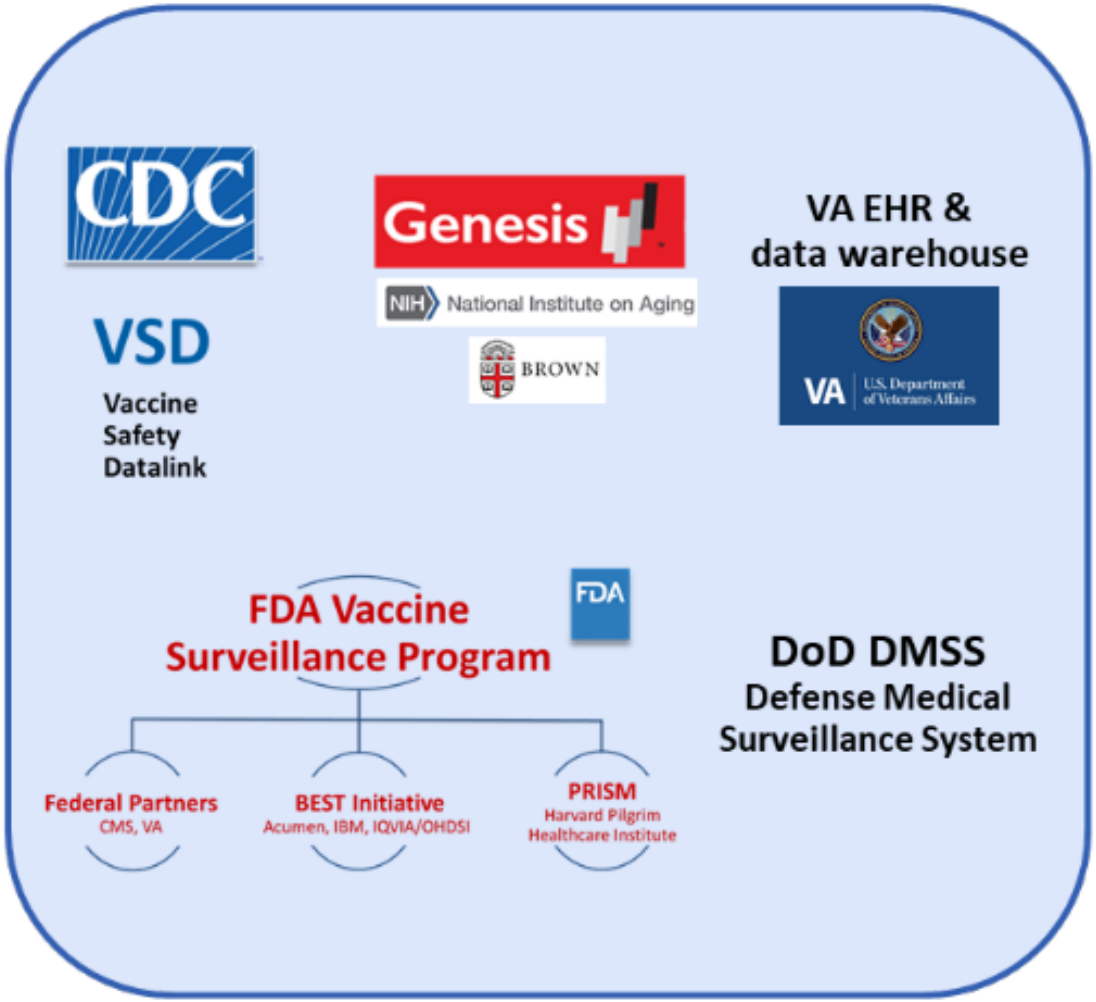
- Observed-to-expected
- Cohorts (vax vs. unvaxxed ; no randomization)
- Case-controls / self controlled studies

➔ Large Linked Databases (LLDB) → Electronic health Records + administrative claims

➔ Unlike passive reporting, those tools provide « true » epidemiological data

➔ Works only on a predefined set of AESI, you only find what you look for

USA : the big picture



Surveillance / investigations

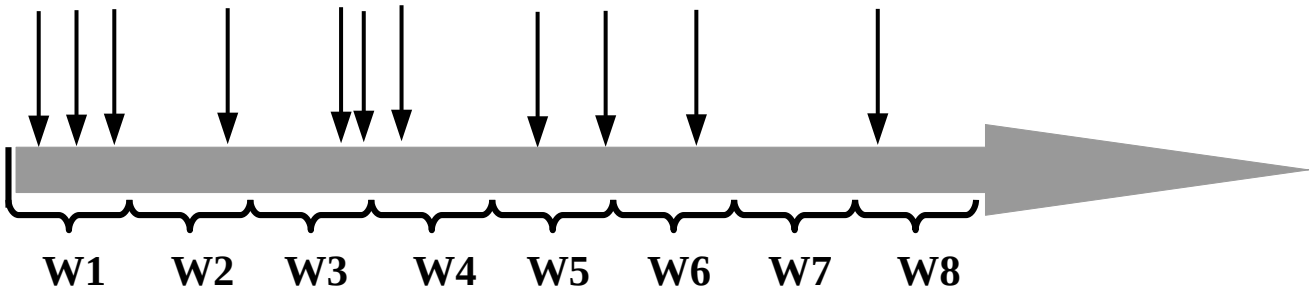
- **CDC / VSD** : analyses run every week ; data lag is 2 weeks ; max 6 weeks
- **CMS (Medicare)** : analyses run every week ; data lag is 4 to 6 weeks → **triggered an alert on the 12th July 2021**
- **Veterans aministration**
- **Best/PRISM Claims DB** : Optum / CVS Health / HealthCore
- Other sources ? Blue Health Intelligence (BHI)

Self controlled studies ?

Self-controlled Studies

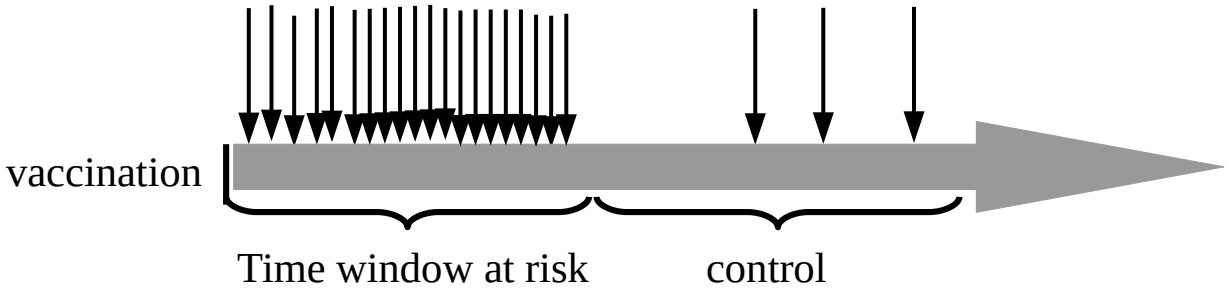
- No need to get unvaccinated
- Keeps only cases (SCCS) or vaccinated cases ! (SCRI)
- Individuals compared to themselves : « when » instead of « who » (vax or unvax)
- Starts from the exposure and looks for the AESI (future)

Adverse event of specific interest (AESI)

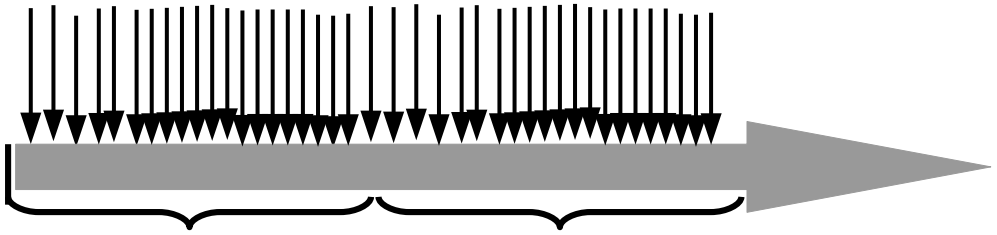


vaccination

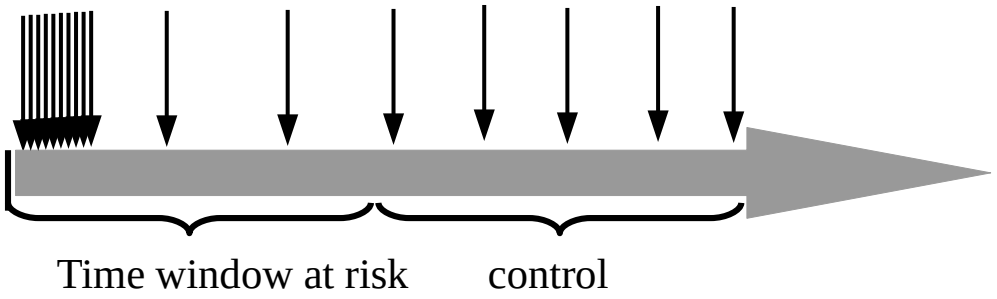
Self-controlled Studies



Self-controlled Studies



Self-controlled Studies



Self-controlled Studies

- SCRI doesn’t work with long / insidious onset
- Works very well for acute / well defined events (easy to code)
- No reverse causation with SCRI, all events occur after the exposure ! (unidirectional design)
- Case Crossover : starts from the AESI and looks back in the past for the exposure

CDC’s VSD #1342

Rapid Cycle Analysis (RCA) to monitor the safety of COVID-19 vaccines in near real-time within the Vaccine Safety Datalink; Nicola Klein, James Donahue, Eric Weintraub

- **vaccinated concurrent comparator**
- unvaccinated concurrent comparators
- **Self-controls**

*For each 2-dose vaccine used in the VSD population, we will conduct separate analyses for each of three types of **21-day risk interval** [...] Similarly, we will conduct separate analyses for each of these types of **42-day risk intervals**, as secondary analyses.*

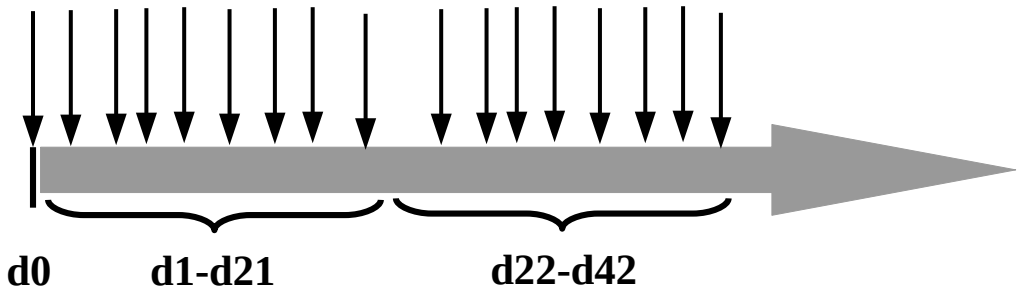
Guillain-Barré Syndrome following any mRNA COVID-19 Vaccine: Chart Review Summary (as of July 3, 2021)

- 40 GBS cases identified within 1-98 days following any mRNA vaccine
  - After quick review ruled out 16/39 (1 pending), 23/39 proceeded to full review.
  - 21/23 with completed full review and adjudication (2 pending).

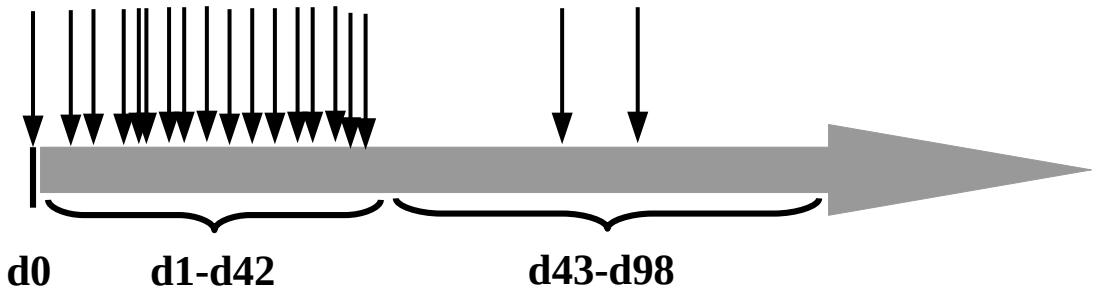
- **Adjudication confirmed 19/21 as GBS following any mRNA vaccine**
  - 1 case post-vaccination day 0
  - **8 cases post-vaccination days 1-21**
  - 8 cases post-vaccination days 22-42
  - 2 case post-vaccination days 43-98

Guillain-Barré Syndrome (GBS) after Janssen COVID-19 vaccine: Vaccine Safety Datalink (VSD); Dr. N Klein; ACIP Presentation Slides: July 22, 2021 Meeting

CDC's VSD #1342

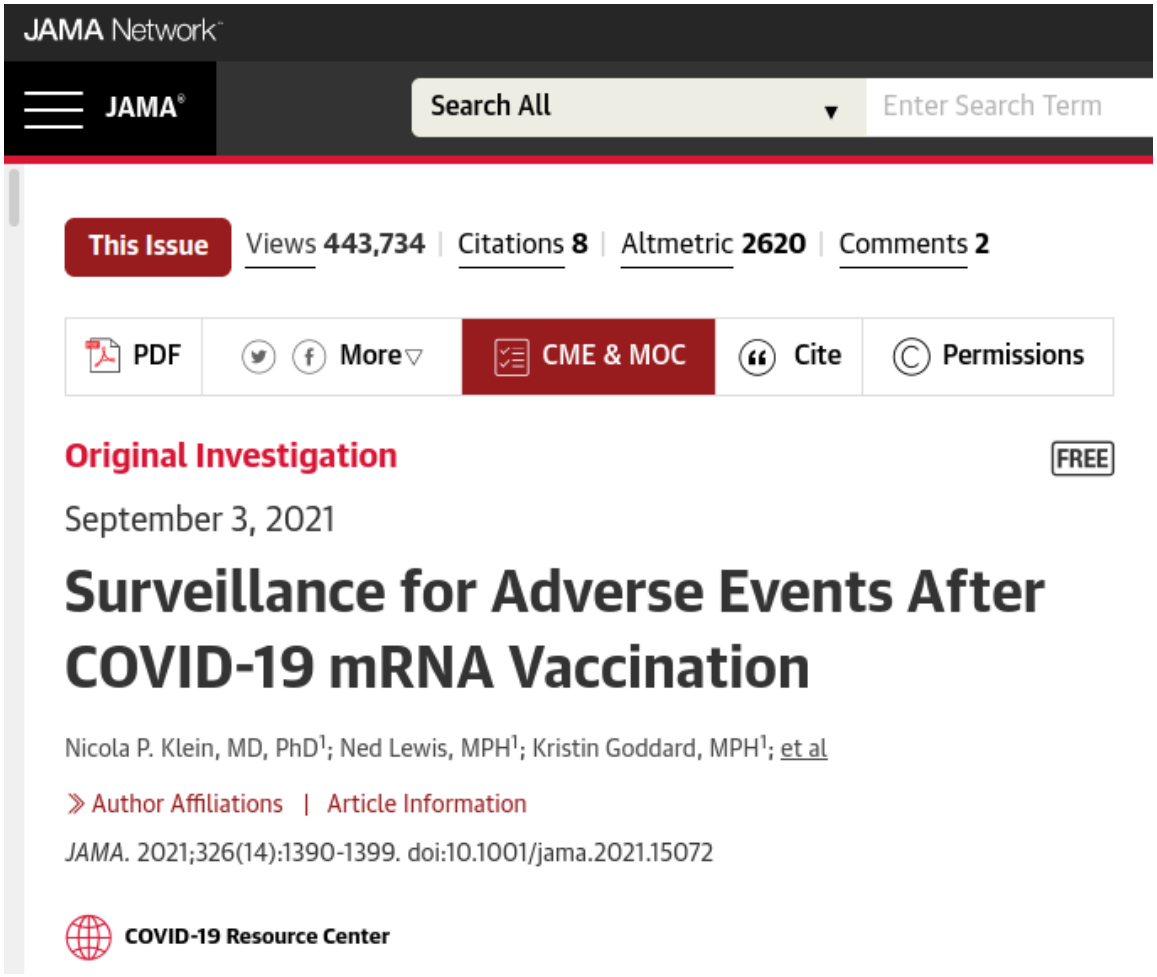


8 cases through day 1-21 (risk) ; 8 cases through day 22-42 (control) ;
→ no risk



16 cases through day 1-42 (risk) ; 2 cases through day 43-98 (control) ;
→ **unadjusted RR = 10.6.**

CDC's VSD #1342



Klein NP, Lewis N, Goddard K, et al. Surveillance for Adverse Events After COVID-19 mRNA Vaccination. JAMA. 2021;326(14):1390–1399. doi:10.1001/jama.2021.15072

CDC's VSD #1342

Findings In this interim analysis of surveillance data from 6.2 million persons who received 11.8 million doses of an mRNA vaccine, **event rates for 23 serious health outcomes were not significantly higher for individuals 1 to 21 days after vaccination compared with similar individuals at 22 to 42 days after vaccination**.

The surveillance protocol, **including planned analyses not presented here**, is available at [...]

→ They only show the results for the time window at-risk set to 21 days, never for the 42 days, my comment sent to the JAMA requesting the extra analyses has been rejected within 15 minutes after submission.

Comments (1)

Guillain-Barré Syndrome after COVID-19 Vaccination in the Vaccine Safety Datalink

Kayla E. Hanson, Kristin Goddard, Ned Lewis, Bruce Fireman, Tanya R. Myers, Nandini Bakshi, Eric Weintraub, James G. Donahue, Jennifer C. Nelson, Stan Xu, Jason M. Glanz, Joshua T.B. Williams, Jonathan D. Alpern, Nicola P. Klein

doi: https://doi.org/10.1101/2021.12.03.21266419

Guillain-Barré Syndrome after COVID-19 Vaccination in the Vaccine Safety Datalink;
Kayla E. Hanson, Kristin Goddard, Ned Lewis, Bruce Fireman, Tanya R. Myers, Nandini Bakshi, Eric Weintraub, James G. Donahue, Jennifer C. Nelson, Stan Xu, Jason M. Glanz, Joshua T.B. Williams, Jonathan D. Alpern, Nicola P. Klein: medRxiv 2021.12.03.21266419; doi: https://doi.org/10.1101/2021.12.03.21266419

CDC's VSD #1342

the adjusted RR in the 1-21 vs. 22-42 days following mRNA vaccines was **0.56** (95% CI: 0.21-1.48). [...]

The 1-21 day risk interval allowed for timelier analyses and avoids bias introduced from the short interval between doses for mRNA vaccines. However, a 1-42 day risk interval was also used, since this interval is often used in vaccine safety studies of GBS and other outcomes.

→ Results for the 42 days time-window are shown for Janssen / JJ but never for the mRNA Products.

CDC's VSD #1342

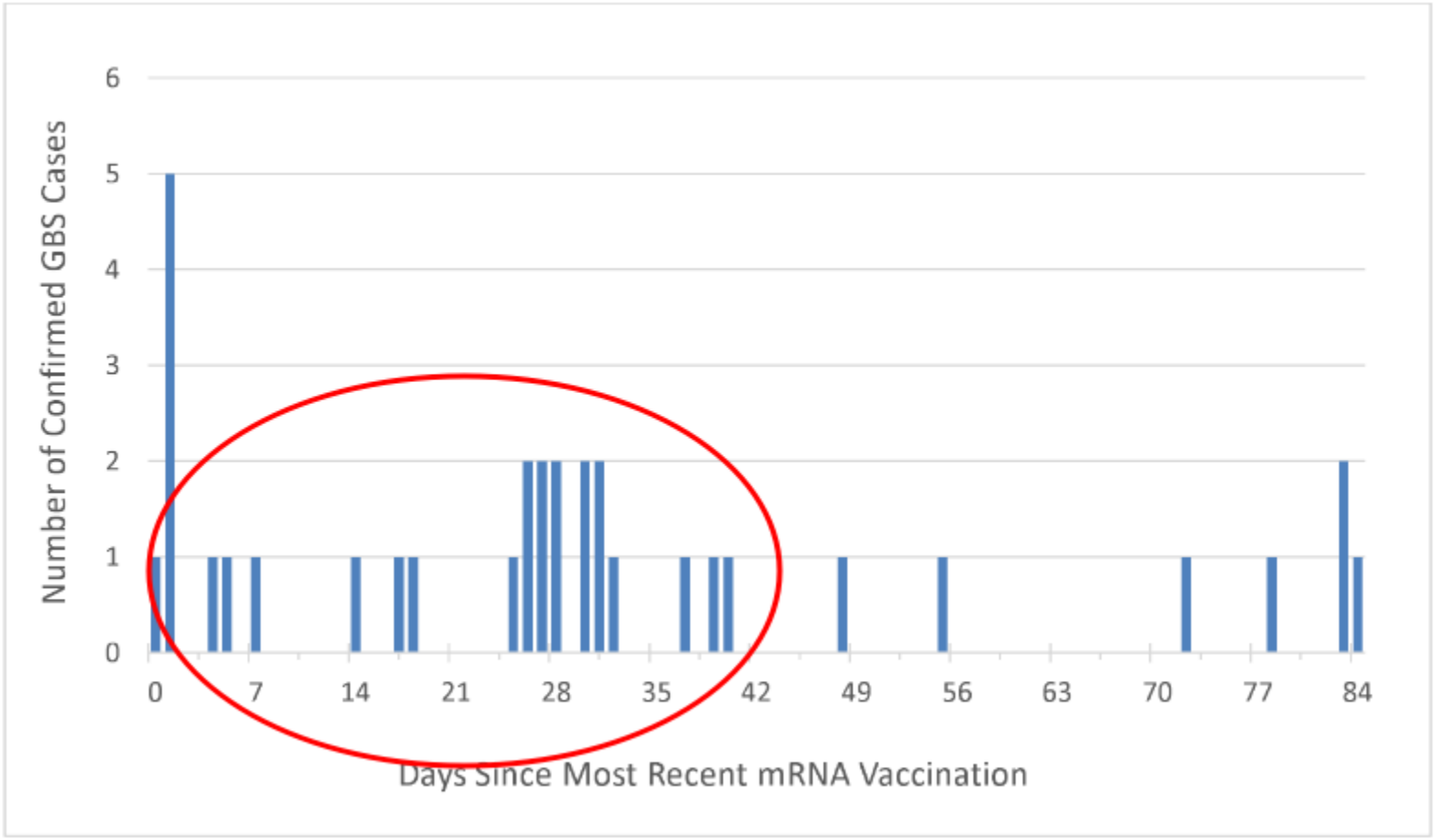
During the **1-84 days** after first and second doses of mRNA vaccines, 71 potential cases of GBS were identified: 70 (99%) were reviewed and adjudicated (1 pending), and **34 (49%) were confirmed.**

Eleven cases (32%) had symptom onset in the 1-21 days after vaccination and 15 cases (44%) had symptom onset in the 22-42 days after vaccination.

→ So we have 11+15=26 cases in the 1-42 window-at-risk, 8 in the 43-84 control window.
Unadjusted RR = 3,25

CDC's VSD #1342

B. mRNA Vaccination



FDA’s Sentinel

- https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/initial-results-near-real-time-safety-monitoring-covid-19-vaccines-persons-aged-65-years-and-older
- July 12, 2021
- *One of these methods, called near real-time surveillance, detected* ***four potential AEIs in the Medicare healthcare claims*** *database of persons aged 65 years and older who had received the* ***Pfizer/BioNTech*** *COVID-19 vaccine. The four potential AEI are* ***pulmonary embolism, acute myocardial infarction, immune thrombocytopenia, and disseminated intravascular coagulation****. The screening methods have not identified these AEI after vaccination in persons 65 years and older who received the two other authorized COVID-19 vaccines.*

FDA's Sentinel

- FDA/CBER/OBE
- « near real-time surveillance » = observed-to-expected based on background rates computed from 2017 to 2020
- SCCS on CV events (July 2021) : 1-28 days for AMI, PE, DIC ; 1-42 days for Immune Thrombocytopenia (ITP)
- Routine : cohort + SCCS

The end