Risk Assessment of 32 Adverse Effects of Special Interest Following COVID-19 Vaccination in the French population

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INTRODUCTION

- Vaccines against COVID-19 have been administered to hundreds of millions of individuals globally
- Numerous studies have assessed their safety, frequently in response to alerts from health authorities
- Several safety signals identified in published case reports have yet to be systematically investigated

OBJECTIVE

- To assess the risk of 32 acute adverse events of special interest (AESI), prespecified by the European Medicines Agency[1], following COVID-19 vaccination in the French population

[1]European Medicines Agency. Consideration on core requirements for RMPs of COVID-19 vaccines. coreRMP19 guidance v3.1. EMA/PRAC/709308/2022. 2022

METHODS

DATA SOURCES

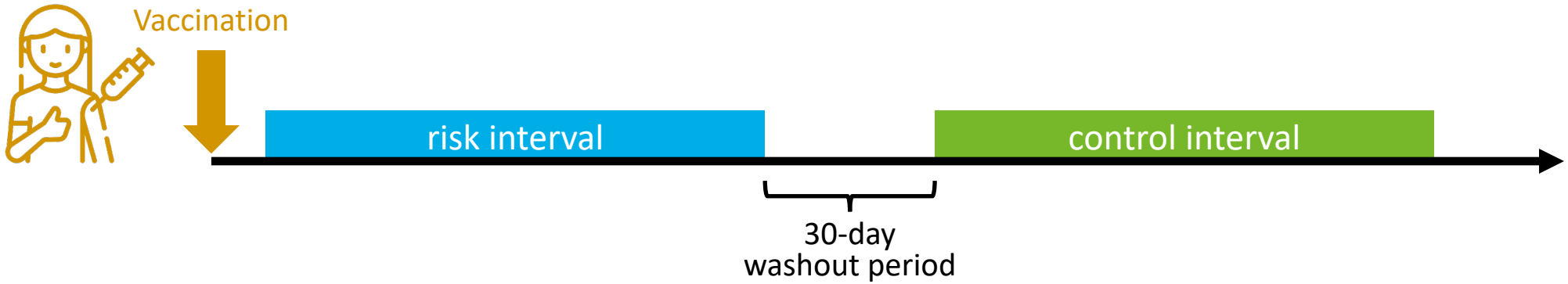
Extraction of patients with ≥1 AESI and ≥1 dose of COVID-19 vaccine in 2021 from

- **French National Healthcare Data System (SNDS)** *f ≤ 1.5/100 000*
  - 67 million individuals covered lifelong
  - National claims (drug dispensing, visits, procedures, etc.)
  - Hospital discharge summaries
  - Cause of death

- **10% SNDS sample** *f >1.5/100 000*

DESIGN

- **Self-controlled risk interval**



- AESI-specific intervals
- Risk interval = control interval, unique for a patient
- Incidence rate ratios (IRR) estimated using conditional Poisson regression
- $IRR = incidence\ rate_{\boldsymbol{risk}\ interval} / incidence\ rate_{\boldsymbol{control}\ interval}$

ANALYSES

- **Exposure**
  - All COVID-19 vaccines considered individually
  - Stratified by platform : mRNA, adenoviral vector
- **Outcomes**
  - 32 AESI across auto-immune, cardiovascular, hematological, metabolic or neurological outcomes, including death and COVID-19 positive test or hospitalization
  - Rare $f \leq 1.5/100\,000$ and non-rare $f > 1.5/100\,000$
- **Stratifications**
  - Age-classes, immunocompromised status, pregnancy status, etc.

RESULTS

VACCINATED POPULATION

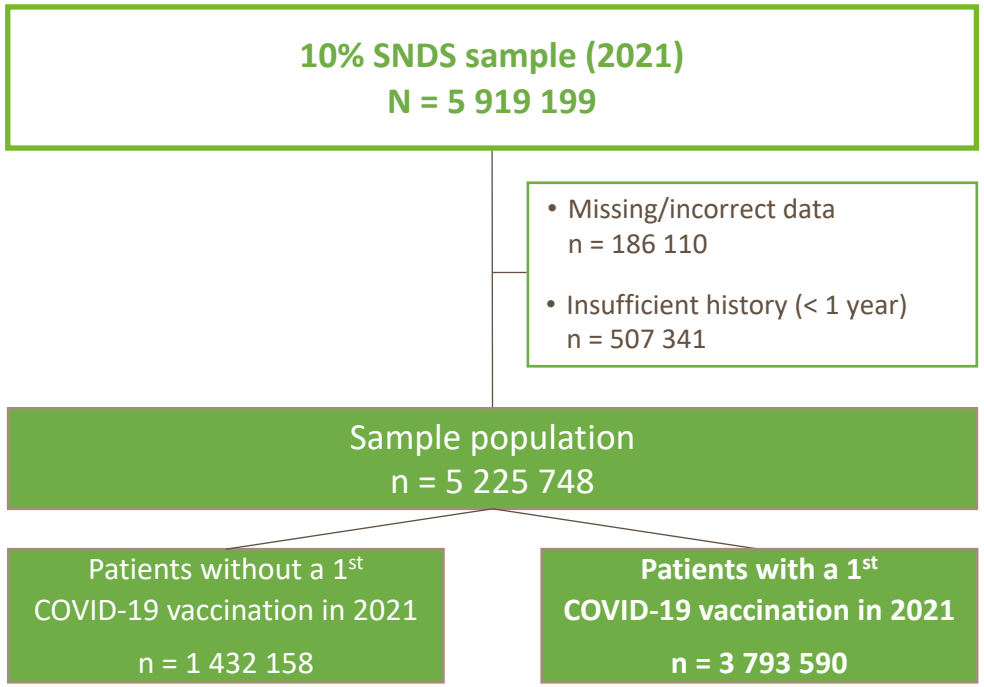


Figure 1. Identification and selection of the populations from the 10% SNDS sample

Table 1. Characteristics of the patients with a 1st COVID-19 vaccination in 2021, 10% SNDS sample

	Male n= 1 811 482	Female n= 1 982 108	Total n= 3 793 590
Sex, %	47.8	52.2	100.0
Age, median (years)	48.0	50.0	49.0
Number of comorbidities* %			
0	49.0	41.2	45.0
1	27.8	30.9	29.4
2	14.3	17.5	15.9
≥ 3	8.8	10.5	9.7
COVID-19 vaccine, % (2021)	100.0	100.0	100.0
mRNA BNT162b2	77.6	79.0	78.3
mRNA-1273	11.3	10.9	11.1
Adenoviral-vector ChAdOx1	9.0	8.2	8.6
Ad26.COV2.S	2.1	1.9	2.0

* During the 4-year pre-index period among the following comorbidities: cancer, chronic kidney disease, chronic liver disease, chronic respiratory disease, cardio/cerebrovascular disease, obesity, down syndrome, mental health disease, sickle cell disease, diabetes, immunodeficiency (including HIV)

ELEGIBLE POPULATIONS

ELEGIBLE POPULATIONS

FOR NON-RARE AESI

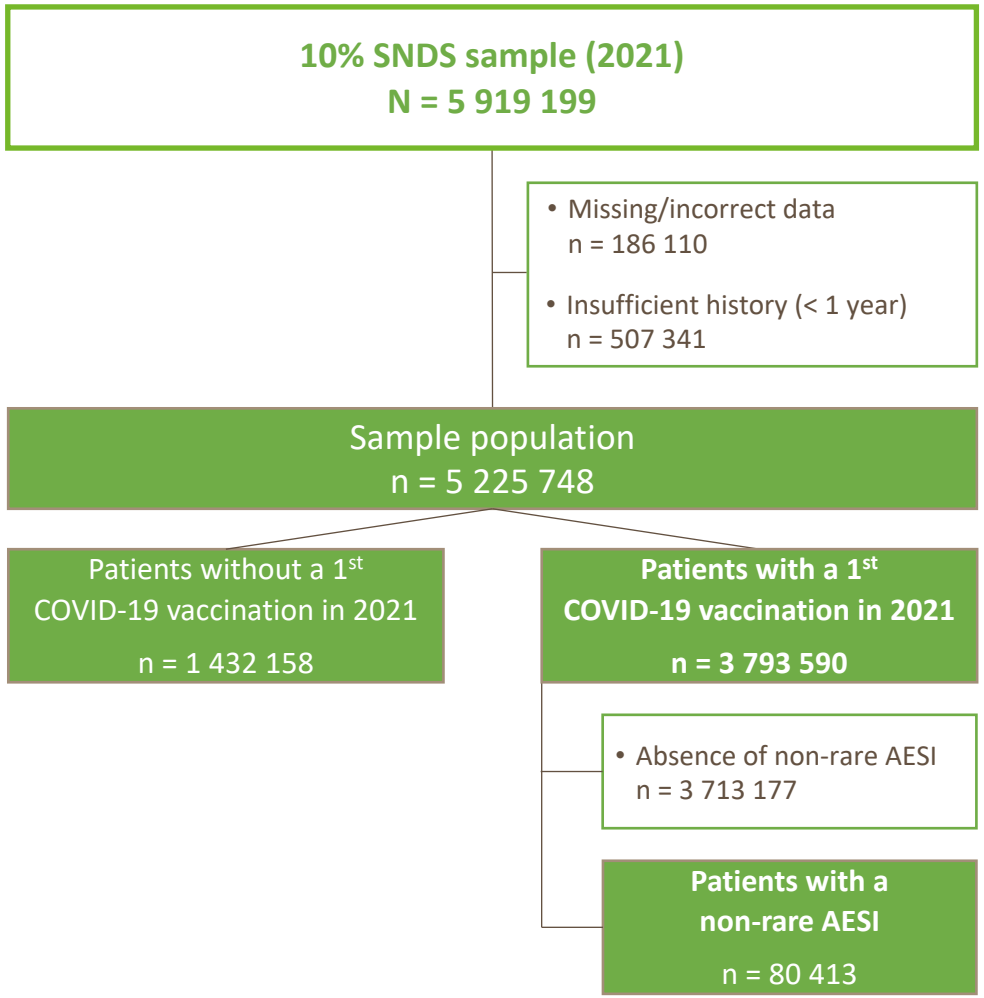


Figure 1. Identification and selection of the populations from the 10% SNDS sample

ELEGIBLE POPULATIONS

FOR NON-RARE AESI

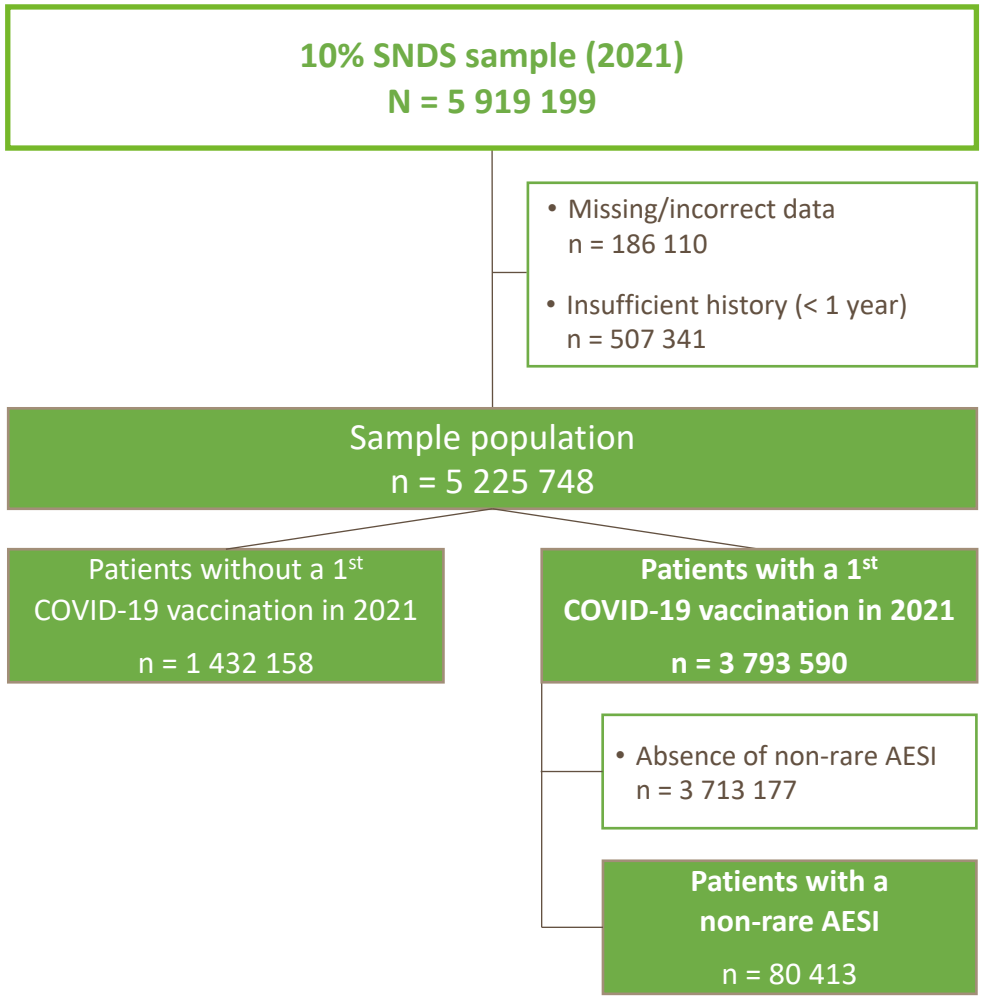


Figure 1. Identification and selection of the populations from the 10% SNDS sample

FOR RARE AESI

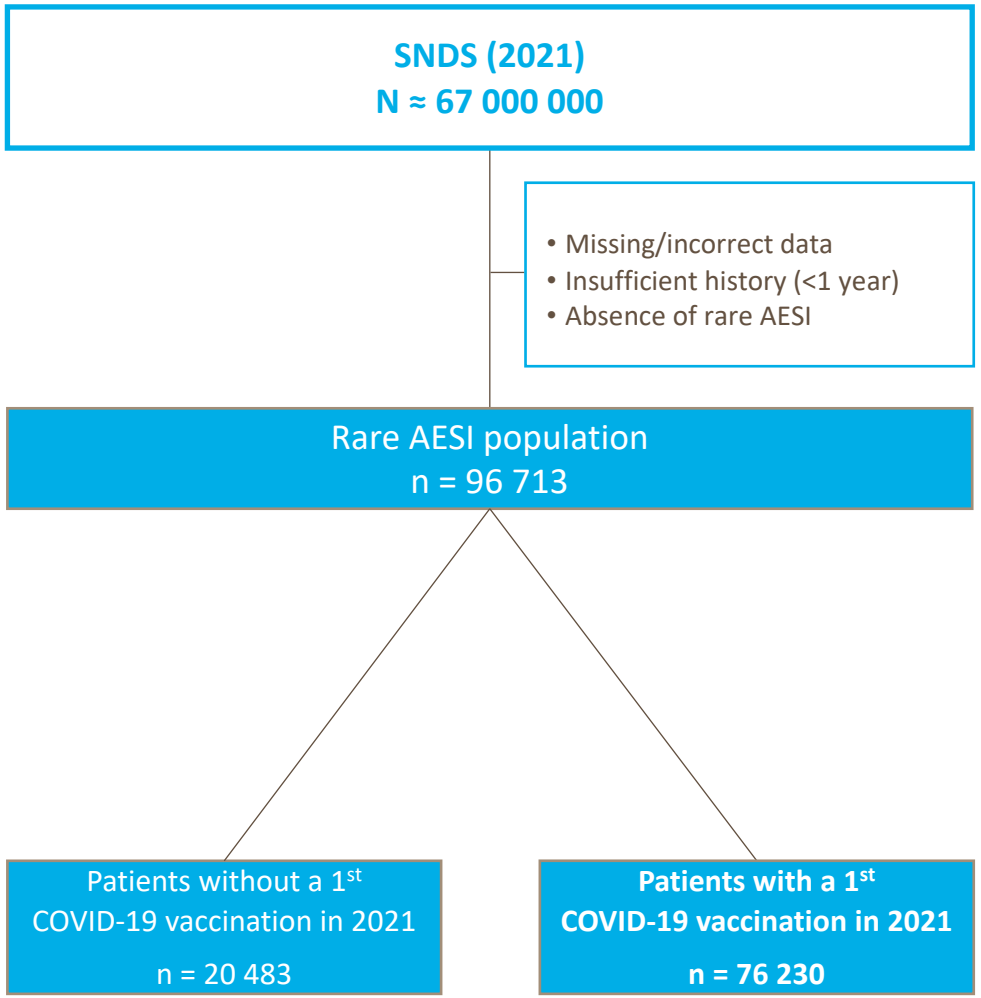


Figure 2. Identification and selection of the population with at least one rare AESI in the full SNDS database

AESI INCIDENCE RATE RATIO (IRR) FROM mRNA AND ADENOVIRAL-VECTOR COVID-19 VACCINES

Table 2.1. Incidence rate ratios (IRR) comparing the AESI incidence rates between risk and control intervals from the sample or the rare AESI populations, stratified by type of vaccine – Conditional Poisson regression models

	AESI type	mRNA vaccines IRR [95% CI]	Adenoviral-vector vaccines IRR [95% CI]
	Auto-immune diseases		
	Guillain-Barré Syndrome	0.94 [0.49 ; 1.83]	3.00 [0.61 ; 14.86]
	Acute disseminated encephalomyelitis	**10.00 [1.28 ; 78.12]**	1.00 [0.06 ; 15.99]
	Kawasaki disease	-	-
	Thrombocytopenia	1.12 [0.81 ; 1.54]	2.50 [0.49 ; 12.89]
	Cardiovascular system: Acute cardiovascular injury		
	Microangiopathy	**1.41 [1.01 ; 1.97]**	3.50 [0.73 ; 16.85]
	Heart failure	1.00 [0.92 ; 1.09]	0.96 [0.68 ; 1.34]
	Coronary artery disease (CAD)	1.11 [0.99 ; 1.26]	0.94 [0.64 ; 1.38]
	Arrhythmia	1.00 [0.92 ; 1.09]	1.22 [0.93 ; 1.60]
	Myocarditis or Pericarditis	**1.95 [1.41 ; 2.69]**	1.17 [0.39 ; 3.47]
	Myocarditis alone	**3.51 [3.02 ; 4.08]**	1.42 [0.68 ; 2.97]
	Circulatory system: Coagulation disorder		
	Disseminated intravascular coagulation (DIC)	**2.08 [1.07 ; 4.03]**	-
	VTE	1.13 [0.98 ; 1.32]	1.30 [0.76 ; 2.25]
	Thrombotic microangiopathy	1.20 [0.81 ; 1.77]	1.50 [0.25 ; 8.98]
	Hemorrhagic stroke	**1.32 [1.05 ; 1.66]**	1.40 [0.62 ; 3.15]
	Ischemic stroke	1.07 [0.96 ; 1.20]	1.00 [0.71 ; 1.41]
	Cerebral venous sinus thrombosis (CVST)	**1.87 [1.31 ; 2.67]**	**3.20 [1.17 ; 8.73]**
	Thrombotic thrombocytopenia syndrome	-	-
	Single Organ Cutaneous Vasculitis	1.20 [0.89 ; 1.61]	1.33 [0.56 ; 3.16]

Sample Population

AESIr Population

Table 2.2. Incidence rate ratios (IRR) comparing the AESI incidence rates between risk and control intervals from the sample or the rare AESI populations, stratified by type of vaccine – Conditional Poisson regression models

	AESI type	mRNA vaccines IRR [95% CI]	Adenoviral-vector vaccines IRR [95% CI]
	Nerves and central nervous system		
	Bells' palsy	1.00 [0.49 ; 2.05]	-
	Generalized convulsion	1.13 [0.89 ; 1.44]	0.69 [0.30 ; 1.62]
	Meningoencephalitis	1.16 [0.96 ; 1.40]	1.24 [0.65 ; 2.34]
	Transverse myelitis	0.83 [0.36 ; 1.93]	1.00 [0.06 ; 15.99]
	Skin and mucous membrane, bone and joints system		
	Erythema multiforme	2.50 [0.78 ; 7.97]	-
	Chilblain – like lesions	2.00 [0.50 ; 8.00]	-
	Rhabdomyolysis	1.34 [1.03 ; 1.74]	1.00 [0.48 ; 2.10]
	Severe Cutaneous Adverse Reactions (SCARs)	-	-
	Other system		
	Acute respiratory distress syndrome	1.19 [0.84 ; 1.70]	1.14 [0.41 ; 3.15]
	Acute pancreatitis	1.12 [0.90 ; 1.40]	2.14 [0.87 ; 5.26]
	Anosmia ageusia	0.92 [0.40 ; 2.08]	-
	Anaphylaxis	6.00 [0.72 ; 49.84]	-
	MISC-C	-	-
	Death		
	Death (any causes)	**0.10 [0.08 ; 0.12]**	**0.08 [0.04 ; 0.19]**
	Sudden death	0.75 [0.17 ; 3.35]	-
	COVID-19		
	Positive test or hospitalization	**1.11 [1.09 ; 1.12]**	**1.51 [1.40 ; 1.62]**

Sample Population

AESIr Population

CONCLUSION

- Analyses relying on a nationwide database of 67 million individuals
- Safety signals linked to COVID-19 vaccines warrant further investigation
- Design does not allow to draw strong conclusion at this stage since the SCRI design does not allow risk quantification
- Comparative cohort studies are ongoing to clarify signals and provide reliable risk quantification.

Thank you

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