One-year results from the vaccination campaign against COVID-19 infection in 47 million individuals with severe mental disorders and other chronic diseases

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Abstract
Severe mental disorders have been associated with increased COVID-19 mortality. The aim of this study was to evaluate the results of the vaccination campaign against COVID-19 after 1 year using exhaustive population-based data. In this nationwide population-based study, we used data from the French national medico-administrative database (SNDS) and the COVID Vaccine teleservice from January 4, 2021 (date of activation of the teleservice) to January 30th, 2022. As of January 30th, 2022, the rate of first injection in France was 80.2% (54 million people) and the rate of booster vaccination was 78.3% (52.7 million people). Except for opioid use disorder, all individuals with chronic illnesses or risk factors for poor COVID-19 outcome (e.g., smoking and obesity) had higher rates of vaccination than the general population (from 83.4 to 94.5% vs. 78.3%). However, the four diseases ranking last for both initial and booster vaccinations were mental disorders: alcohol use disorders (86 and 84.3%), neurodevelopmental psychiatric disorders (85.3 and 83.7%), schizophrenia-spectrum disorder (85 and 83.4%) and opioid use disorders (72.9 and 69.4%). Except for opioid disorders, all patients with mental disorders had higher rates of vaccination compared to the general population. However, these rates were lower than other chronic diseases at risk of severe COVID-19 outcomes. Vaccination campaigns must redouble their efforts to improve vaccination penetration in patients with mental disorders.

Keywords Mental health · Psychiatry · Schizophrenia · Mood disorders · Depressive disorders · COVID-19

Introduction
Adequate vaccination coverage against COVID-19 is an important step to fight against this pandemic. The vaccine campaign began in Europe in February 2021. The EU advises prioritizing vaccination for people at risk for severe COVID-19, but leaves it to member states to decide which medical conditions get prioritized. Early after the first wave of the pandemic, analysis of population-based data found increased risk of COVID-19 infection and mortality in individuals with severe psychiatric disorders [1]. This finding was replicated in multiple countries across the world by investigators reporting a constant increase in risk of COVID-19 mortality in patients with psychiatric disorders. We synthesized these data in a recent meta-analysis [2]. Among all patients with mental disorders who were studied, those with severe mental disorders (schizophrenia and bipolar disorders) were at the highest risk of COVID-19 mortality. Soon after this publication, the Center for Disease Control and Prevention (CDC) updated its list of conditions associated with severe COVID-19, including severe mental disorders.

However, vaccination strategies have often overlooked these patients. Despite the scientific evidence for increased risk, patients with severe psychiatric disorders were listed in the priority groups for vaccination against COVID-19 in only 8 of 20 European countries (Belgium, Denmark, France, Germany, Malta, the Netherlands, Spain and the UK). Only four of them (Denmark, Germany, the Netherlands, and the
(UK) had some form of higher vaccination priority for outpatients with severe mental illness. Some other countries listed institutionalized patients or patients with disabilities, possibly including patients with severe mental disorders.

Several studies have shown that patients with psychiatric disorders had paradoxically lower vaccination rates and higher vaccination hesitancy compared to the rest of the population [3].

The aim of this study was to evaluate the results of this vaccination campaign after 1 year using exhaustive population-based data.

Methods

Data sources and population

In this nationwide population-based study, we used data from the French national medico-administrative database (SNDS) and the COVID Vaccine teleservice from January 4, 2021 (date of activation of the teleservice) to January 30th, 2022. The SNDS covers approximately 99% of the population for which medical data are systematically collected. A mapping of chronic diseases according to a validated algorithm developed by the French National Health Insurance is available [4]. This information system centralizes individual COVID-19 vaccination data to ensure traceability for pharmacovigilance and vaccination campaign management purposes. The vaccination data were matched to the SNDS in order to provide vaccination rates according to diagnoses of chronic medical and psychiatric diseases.

Indicators’ definition

The first injection rate is the number of patients who received at least one first injection of vaccine. The initial completed vaccination rate is the percentage of patients whose vaccination was considered completed, defined as: two vaccine injections (general case), a single vaccine injection with COVID-19 infection (before or after the first injection), a single injection with Janssen vaccine, or three vaccine injections for immunocompromised patients.

Mental disorders were defined by the International Classification of Disease codes and the use of some treatments when specific of a disorder. The algorithms that define the disease groups use some of the following elements:

- codes from the 10th International Classification of Diseases (ICD-10),
- drugs that are quasi-specific to certain diseases,
- ICD-10 codes for hospitalization diagnoses (principal diagnosis, related diagnosis, and associated diagnosis).

The following groups of mental disorders were defined: alcohol use disorders (F10*), opioid use disorders (F11*), schizophrenia-spectrum disorders [F20* to F29*] or chronic antipsychotic treatment (ATC code N05A except for N05AN01 and N05AL06), anxiety and mood disorders ([F30* to F48*] or chronic antidepressant or mood regulator treatment (N06A, N05AN01, N03AG01, N03AG02), neurodevelopmental psychiatric disorders (F80*–F89*). The identification of a condition in year n may use data from up to 5 years (years n to n–4). The diseases are mostly non-exclusive as the same individual may be affected by several conditions. For example, a person being treated for cancer and a psychiatric condition will fall into both groups of conditions. The details for group definitions are available at https://www.epi-phare.fr/. The detailed method to define the schizophrenia-spectrum disorders or chronic antipsychotic treatment group is available on the French Assurance website and detailed in Appendix [5]. The chronic antipsychotic treatment was included to identify outpatients followed up in the private sector.

Ethical considerations

Since the data were anonymized, no informed consent was required.

Results

As of January 30th, 2022, the rate of first injection in France was 80.2% (54 million people) and the rate of booster vaccination was 78.3% (52.7 million people). The results for severe mental disorders and other chronic diseases are presented in Table 1 and geographical disparities in Fig. 1. Except for opioid use disorder, all individuals with chronic illnesses or risk factors for poor COVID-19 outcome (e.g., smoking and obesity) had higher rates of vaccination than the general population (from 83.4 to 94.5% vs. 78.3%). However, the four diseases ranking last for both initial and booster vaccinations were mental disorders: alcohol use disorders (86 and 84.3%), neurodevelopmental psychiatric disorders (85.3 and 83.7%), schizophrenia-spectrum disorder (85 and 83.4%) and opioid use disorders (72.9 and 69.4%).

Discussion

Our results confirm preliminary results suggesting that patients with substance use disorders have lower rates than the rest of the population [3, 6], especially for opioid use disorders. The COVID-19 pandemic collided with the opioid epidemic and longstanding health inequities to exacerbate the disproportionate harms experienced by persons
| Disease                                      | N    | First injection rate (%) | Rate of completed initial vaccination schedule (%) |
|----------------------------------------------|------|--------------------------|--------------------------------------------------|
| Lung transplantation                          | 1,170| 95.1                     | 94.5                                             |
| Prostate cancer under surveillance            | 288,720| 94.0                     | 93.6                                             |
| Liver transplantation                         | 4,330| 94.0                     | 93.5                                             |
| Hypolipidemic treatments                      | 6,601,480| 93.7                     | 93.2                                             |
| Prostate cancer in active treatment           | 181,110| 93.3                     | 92.8                                             |
| Lung cancer under surveillance                | 47,780| 93.0                     | 92.4                                             |
| Colorectal cancer under surveillance          | 202,270| 92.3                     | 91.6                                             |
| Female breast cancer under surveillance       | 460,660| 92.2                     | 91.6                                             |
| Chronic dialysis                              | 40,950| 92.1                     | 91.2                                             |
| Coronary artery disease                       | 1,871,650| 91.8                     | 91.1                                             |
| Antihypertensive treatments                   | 11,755,580| 91.8                     | 91.1                                             |
| Renal transplantation                         | 40,190| 91.7                     | 91.0                                             |
| Female breast cancer in active treatment      | 201,680| 91.5                     | 90.9                                             |
| Other cancers in active treatment phase       | 642,510| 91.6                     | 90.9                                             |
| Other cancers under surveillance              | 857,760| 91.5                     | 90.9                                             |
| Heart transplants                             | 1,420 | 91.7                     | 90.8                                             |
| Colorectal cancer in active treatment         | 109,820| 91.3                     | 90.7                                             |
| Lung cancer in active treatment               | 56,450| 91.3                     | 90.7                                             |
| Cystic fibrosis                               | 5,660 | 91.4                     | 90.5                                             |
| Valvular disease                              | 574,860| 91.2                     | 90.3                                             |
| Cardiac rhythm or conduction disorders        | 2,068,860| 91.1                     | 90.2                                             |
| Obliterative arteriopathy of the lower limb   | 585,130| 90.9                     | 90.1                                             |
| Hereditary metabolic diseases or amyloidosis  | 95,620| 90.8                     | 90.1                                             |
| Parkinson’s disease                           | 232,670| 91.0                     | 90.1                                             |
| Rheumatoid arthritis and related diseases     | 276,600| 90.6                     | 89.8                                             |
| Anxiety and mood disorders or chronic antidepressant or mood regulator treatment | 4,173,770| 90.7                     | 89.8                                             |
| Diabetes                                     | 3,739,430| 90.1                     | 89.4                                             |
| Mental retardiation                           | 101,940| 90.4                     | 89.4                                             |
| Trisomy 21                                    | 24,140| 90.0                     | 89.4                                             |
| Chronic respiratory diseases (excluding cystic fibrosis) | 2,893,540| 89.6                     | 88.7                                             |
| Ankylosing spondylitis and related diseases   | 222,000| 89.4                     | 88.6                                             |
| Psoriasis                                    | 290,690| 89.4                     | 88.5                                             |
| Pulmonary embolism                            | 142,280| 89.2                     | 88.2                                             |
| Chronic inflammatory bowel diseases           | 269,010| 88.7                     | 87.9                                             |
| Obesity (hospital stay)                       | 860,340| 88.7                     | 87.8                                             |
| Stroke                                       | 796,830| 88.7                     | 87.7                                             |
| Heart failure                                 | 592,190| 88.4                     | 87.3                                             |
| Hemophilia or severe hemostasis disorders     | 46,800| 88.0                     | 87.2                                             |
| Myopathy or myasthenia                       | 41,810| 87.7                     | 86.8                                             |
| Dementia (including Alzheimer’s disease)      | 481,470| 88.0                     | 86.7                                             |
| Smoking                                      | 2,656,380| 87.9                     | 86.7                                             |
| Liver disease                                 | 363,010| 87.7                     | 86.5                                             |
| HIV infection                                 | 145,490| 87.3                     | 86.1                                             |
| Epilepsy                                     | 269,340| 86.3                     | 85.0                                             |
| Multiple sclerosis                            | 113,900| 86.0                     | 84.8                                             |
| Paraplegia                                    | 83,250| 85.9                     | 84.7                                             |
| Alcohol use disorders                         | 697,180| 86.0                     | 84.3                                             |
| Neurodevelopmental psychiatric disorders      | 55,340| 85.3                     | 83.7                                             |
with opioid use disorder [7]. High doses of opioids might exacerbate the respiratory depression found in COVID-19 patients and their chronic use can trigger opioid tolerance [8]. The higher doses used during the pandemic might result in greater adverse effects and increased risk of COVID-19 infection and mortality [9–11]. Opioid use disorders have, therefore, been targeted as a population at a particular risk of COVID-19 mortality. However, the patients were reported to have high rates of vaccination hesitancy and lower adherence to CDC guidelines [12], which is confirmed in our results.

Contrary to Israel [13], individuals with schizophrenia-spectrum disorders have higher rates of initial vaccination and booster vaccination compared to those without schizophrenia-spectrum disorders in France. This high rate of vaccination may be explained by the prioritization for vaccination of patients with mental disorders following the publication of the mortality data of these individuals in France [1]. People with schizophrenia who are not included in the healthcare system (e.g., homeless people) may not be captured in the present results, which may lead to a (small) overestimation of the prevalence of vaccination in this population [14, 15].

Limitations

Distribution by disease is not possible for patients not matched to the SNDS (approximately 1% of the population).

Conclusion

Except for opioid disorders, all the patients with mental disorders had higher rates of vaccination compared to the general population. However, these rates were lower than other chronic diseases at risk of severe COVID-19 outcomes. Vaccination campaigns must redouble their efforts to improve vaccination penetration in patients with mental disorders.

| Disease                                           | N   | First injection rate (%) | Rate of completed initial vaccination schedule (%) |
|---------------------------------------------------|-----|--------------------------|-----------------------------------------------|
| Psychotic disorders or chronic antipsychotic treatment | 728,440 | 85.0                     | 83.4                                           |
| Opioid use disorder                                | 206,550 | 72.9                     | 69.4                                           |

Fig. 1 Geographical disparities

Table 1 (continued)
Appendix: Definition of the schizophrenia-spectrum disorder or chronic antipsychotic treatment group

Individual with a long-term condition in year n with ICD-10 codes of schizophrenia, schizotypal disorder, persistent delusional disorder, acute and transient psychotic disorder, induced delusional disorder, schizoaffective disorder, other non-organic psychotic disorders, non-organic psychosis without specification, and/or individuals hospitalized for these same reasons—in a non-psychiatric health establishment (Medicine, surgery, obstetrics (main or related diagnosis) and/or Follow-up and rehabilitation care (main disease manifestation, etiological affection)) and/or psychiatric facility (main or associated diagnosis)—during years n to n – 1, and/or individuals hospitalized for these same reasons in a non-psychiatric health establishment (Medicine, surgery, obstetrics, (main, related or associated diagnosis, or main or related diagnosis of one of the Medical Unit Summaries)) and/or Follow-up and rehabilitation care (main disease manifestation, etiological affection or associated diagnosis)), etiological condition or associated diagnosis) and/or psychiatric care (main or associated diagnosis)—during years n to n – 4 OR having received at least 3 deliveries of neuroleptics during year n (on different dates), i.e., a drug with an ATC code (Anatomical Therapeutic Chemical Classification) beginning with N05A, with the exception of Lithium-based specialties (used as a mood stabilizer) and Neuriplège® (muscle relaxant).

Data sharing The data are available on request to the corresponding author.

Declarations

Conflict of interest The authors report no conflicts of interest and no drug manufacture was involved at any stage of this manuscript.

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