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Short communication

# COVID-19 vaccine is correlated with favourable epidemiological indicators in the Auvergne-Rhône-Alpes region (France): An ecological study

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ABSTRACT

COVID-19 vaccination has proven to be effective in preventing severe cases, reducing viral load, and transmissibility. The aim of this study was to evaluate the impact of vaccination 11 months after implementation on epidemiological indicators and the effective reproduction number in one French region. We plotted four indicators with vaccination coverage as the explaining variable and estimated the impact of vaccination using the reduction rates in infections and hospital admissions. A reduction of 98% in COVID-19-related hospitalisation 11 months after the vaccine campaign began in January 2021 has been reported while vaccine coverage increased over time. Those results do not make it possible to postulate a causal relationship but do support the effect of vaccination against multiple variants of concern. Non-pharmaceutical measures remain necessary to attain complete epidemic control. Open epidemiological data should be considered to monitor vaccine effectiveness wherever possible.

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## 1. Introduction

COVID-19 vaccination started in France in January 2021 in the context of an elevated incidence rate of new SARS-CoV-2 infection cases, estimated at 180/100,000 the first calendar week of 2021. Elderly individuals in long-term care facilities constituted the first target population for the vaccine with a progressive extension of target populations between January, 1st and May, 12th. On that date, vaccination was open to the general population 18 years and older without prioritisation based on active comorbidities.

Clinical studies have now demonstrated the benefit of the vaccines beyond protection against the development of severe cases of COVID-19 with an efficacy between 60% and 85% [1,2], a reduction in viral load among asymptomatic carriers [3,4] and therefore, a reduction in transmissibility [5,6].Vaccine coverage requirements to reach herd immunity in the general population have also been estimated to be approximately 70% [7,8]. Although previously cited estimations were found against strains not yet showing mutations of concern, efficacy of currently available vaccines against the delta variant was found to be comparable regarding hospital admissions and lower (with varying estimates) regarding infection [9,10]. Additional and convergent results from various locations based on various study designs are needed to confirm the positive impact of the vaccines on the pandemic since health determinants differ from one country to another. The monitoring of the COVID-19 pandemic in France is built on reactive information systems for fast and adapted public health response. Standardised data collection from validated sources by the national public health agency (Santé publique France) enable analysis in real time of epidemiological indicators including national vaccine coverage in various French regions [11].

The objective was to report a graphical ecological analysis to correlate the increase in vaccination use by time with the epidemiological indicators of viral circulation in the Auvergne-Rhône-Alpes region, including the effective reproduction number ($R_e$) until November 15, 2021.

## 2. Methods

This study was conducted in the Auvergne-Rhône-Alpes French administrative region (estimated population in 2020: 8,032,377 inhabitants, capital: Lyon), between January 1 and November 15, 2021. The study region is highlighted in Fig. 3. We collected the

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following weekly publicly available epidemiological indicators for all 12 administrative subdivisions (French departments) of the region: SARS-CoV-2 new infection rate (/100,000 person-week), rate of hospital admissions for COVID-19 (/100,000 person-week), proportion of testing positivity for SARS-CoV-2 carriage (/100 persons tested), and vaccine coverage (partial and complete, /100 inhabitants). Partial and complete vaccine coverage are respectively defined as incomplete (lacking one dose) and complete vaccination (excluding boosters) with respect of previous COVID-19 and altered immune response at an individual level according to the French national guidelines from the French "Haute Autorité de Santé". We do not take into account for booster injections, as we do not have sufficient cases and data to provide any meaningful results. Infection data (incidence rate, positivity rate) are collected from the national testing information system, hospital admission data from the victim information system, and vaccination data from the national vaccination information system. We also collected the estimated $R_e$, computed weekly from infection data following the method described in Cori et al. [12], only available for the entire region. Every dataset used in the analysis was colligated by the national public health agency (Santé publique France), and mandated to be available through the French government open-data platform [11]. The information systems collected personal data in compliance with French law and regulations [13–15].

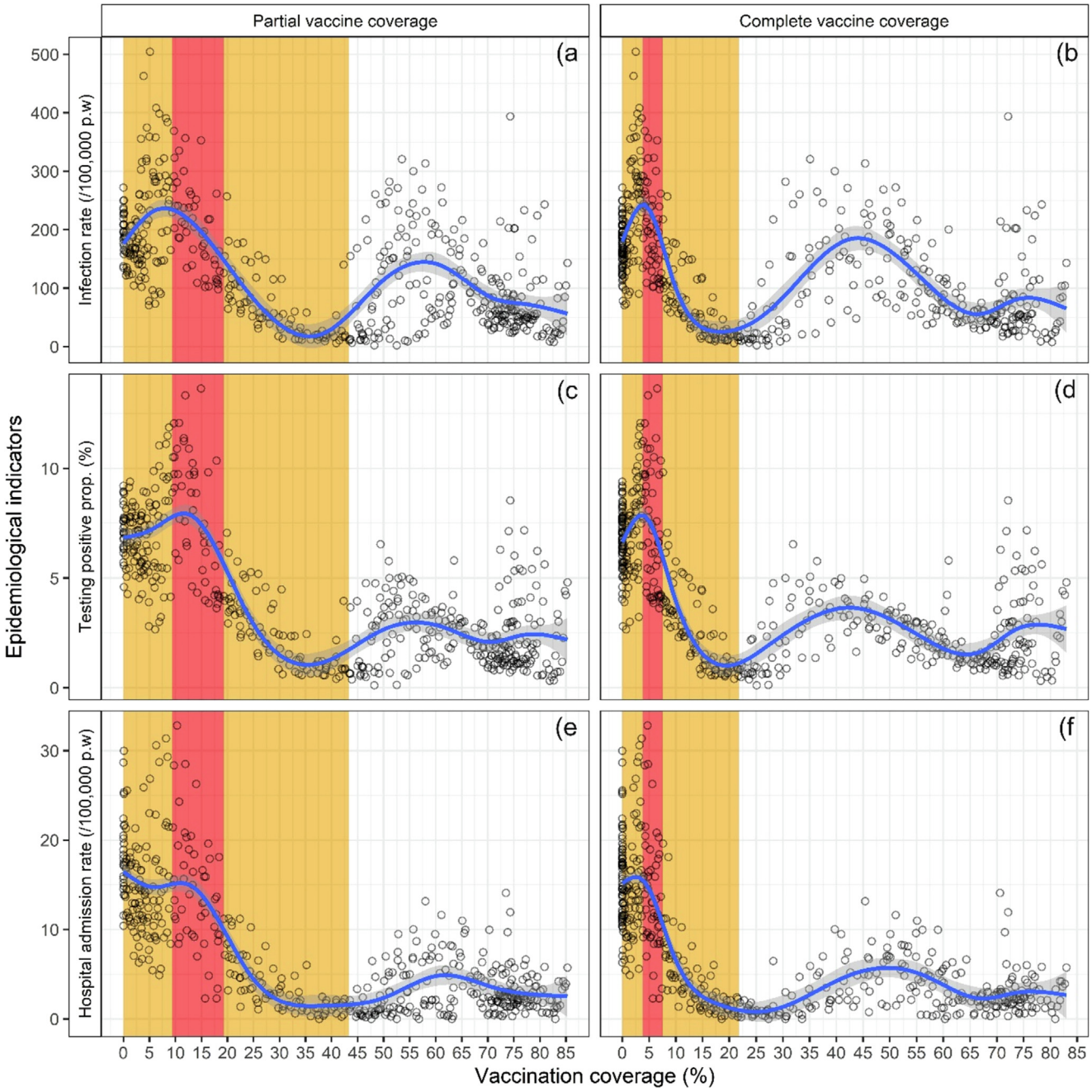


**Fig. 1. SARS-CoV-2 Incidence infection rate, SARS-CoV-2 test positive proportion and hospital admission rate by reported COVID-19 vaccination coverage, Auvergne Rhône-Alpes region, France, January 1, 2021-November 15, 2021.** Each point in this figure represents one measure of one epidemiological indicator as a function of vaccine coverage in one of the 12 administrative subsets of the Auvergne-Rhône-Alpes region. Vaccine coverage was matched to the indicator measured with a 14-day lag to consider the time to acquire immunization. The grey area around the tendency line represents the 95% confidence interval. The orange area represents the curfew period, the red area the lockdown period. p-w: person-week.

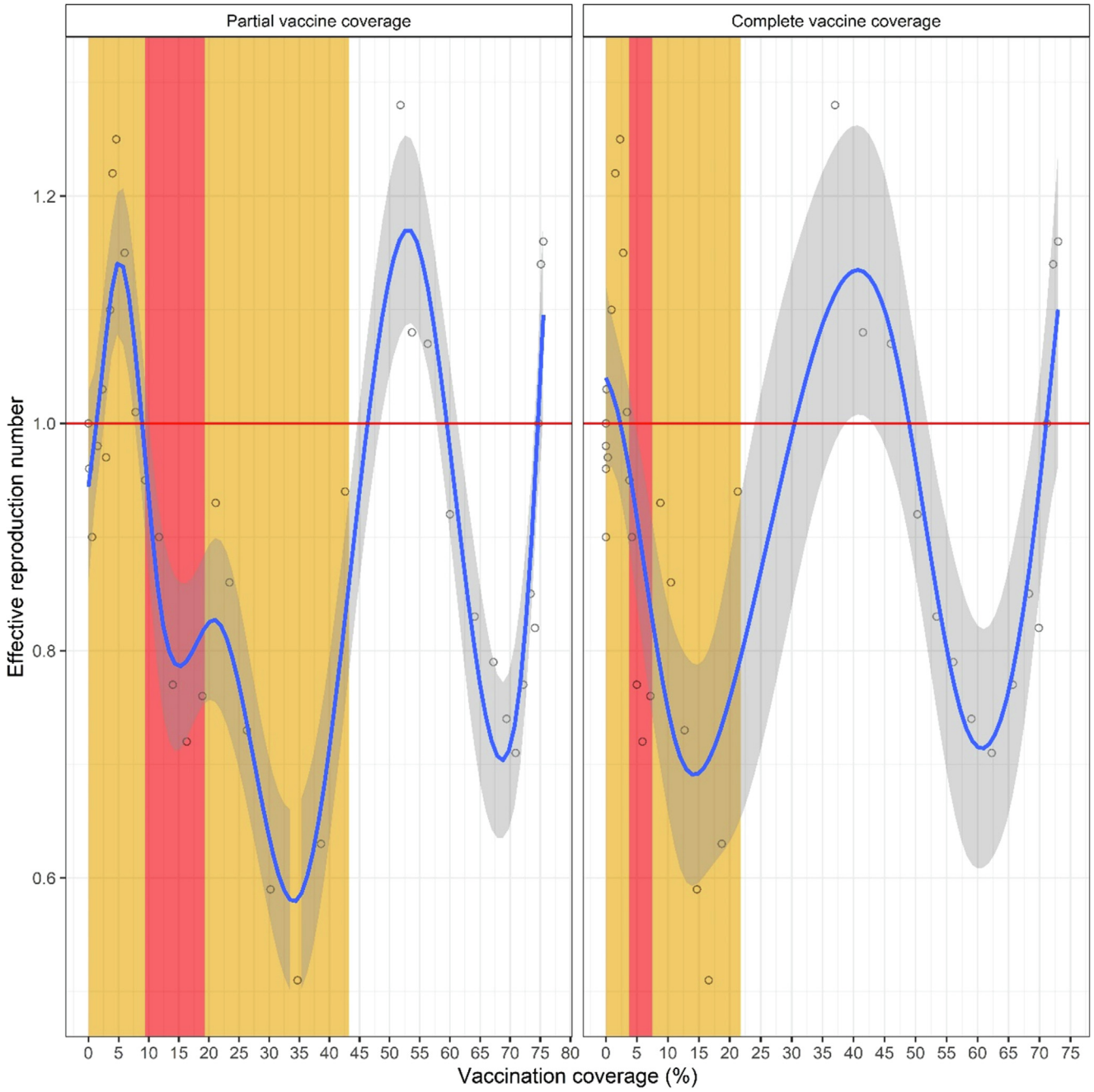


**Fig. 2. Reproduction number with respect to level of COVID-19 vaccination coverage, Auvergne Rhône-Alpes region, France, January 1, 2021- November 11, 2021.** Each point in this figure represents one measure of the effective reproduction number as a function of vaccine coverage in the Auvergne-Rhône-Alpes region. Vaccine coverage was matched to the indicator measured with a 14-day lag to consider the time to acquire immunization. The grey area around the tendency line represents the 95% confidence interval. The orange area represents the curfew period, the red area the lockdown period. The horizontal red line represents the stability value 1.0 for the effective reproduction number. The $R_e$ calculations were based on the method by Cori et al.(12).

We plotted pandemic-related indicators (Y axis) as a function of vaccine coverage (X axis) for each day all indicators were estimated. To provide a meaningful visualisation of the lockdown and curfews periods on the figures, regional vaccine coverage observed at the beginning and end of each relevant period was used. The impact of vaccination was calculated using the formula cited by Hanquet et al. [16]: $IMPACT = \frac{IR_{pre-vaccine} - IR_{post-vaccine}}{IR_{pre-vaccine}} = 1 - IRR$,[1] with the incidence rate on December 15, 2020 as a pre-vaccine reference. This impact estimation was calculated for the region and all of its 12 subdivisions on November 15, 2021. To account for the delay between vaccine injection and effective immunization, all vaccine-related indicators were joined with the epidemiologic indicators using a 14-day lag. The R software [17] with ggplot2 [18] and mgcv [19] packages was used. Penalized cubic regression spline was used to produce tendency lines and their respective confidence interval (with $\alpha$ risk = 0.05).

## 3. Results – Discussion

A total of 3240 repeated measurements of incidence rate, % of positive testing, hospital admissions and 90 measurements of $R_e$

[1] With IR : incidence rate ; IRR : incidence rate ratio.

according to partial or complete vaccine coverage are plotted in Figs. 1 and 2 respectively. The national control measures active during the study period were a first curfew (Dec 15 to April 2, 2021, orange), one lockdown (April 3 to May 2, 2021, red), and a second curfew (May 3 to June 20, 2021, orange). During both curfews, public movement was restricted from the evening until morning, with the starting hour varying between 6 and 8 PM. The lockdown mainly reintroduced limited movement to a short perimeter around one's house at all times, and suspension of on-site work if not necessary. In Fig. 1, panels a-d show a decrease in viral diffusion within the general population until May 3, 2021, end of the second curfew. Infection rate trends past this date do not appear associated with vaccine coverage for the number of infection cases, although the dispersion seems to decrease at a high level of vaccine coverage. Panels e and f indicate a similar trend among hospital admissions until the end of the first curfew. Compared to the indicators monitoring viral circulation within the general population, hospital admissions appear less correlated to viral circulation as vaccine coverage increases, with dispersion noticeably lower as vaccine coverage is high. Fig. 2 graphically links the underlying effective reproduction rate of SARS-CoV-2 in the French population and vaccine coverage. This figure suggests no impact of vaccine coverage on the increase in viral circulation within the general population: the reproduction rate is observed above 1 at various levels of vaccine coverage within the study region. Table 1 provides a numerical description of the impact of COVID-19 vaccines in the 12 administrative subdivisions of our study region, showing a strong decrease in the incidence rates of hospital admissions with an estimated impact of 0.98 in the region. This result is homogeneous across the region, with a minimum of 0.72 in one department regarding hospital admissions. The estimated impact of vaccination upon both viral circulation indicators is considerably more mitigated, with a regional mean estimated at 0.21, and departmental estimates ranging between −0.55 and 0.59.

This study presented an overview of the relationship between epidemiological indicators and vaccine coverage in one French region over 11 months. Accounting for the lockdown and curfews during the study period, those results suggest an impact of vaccina-

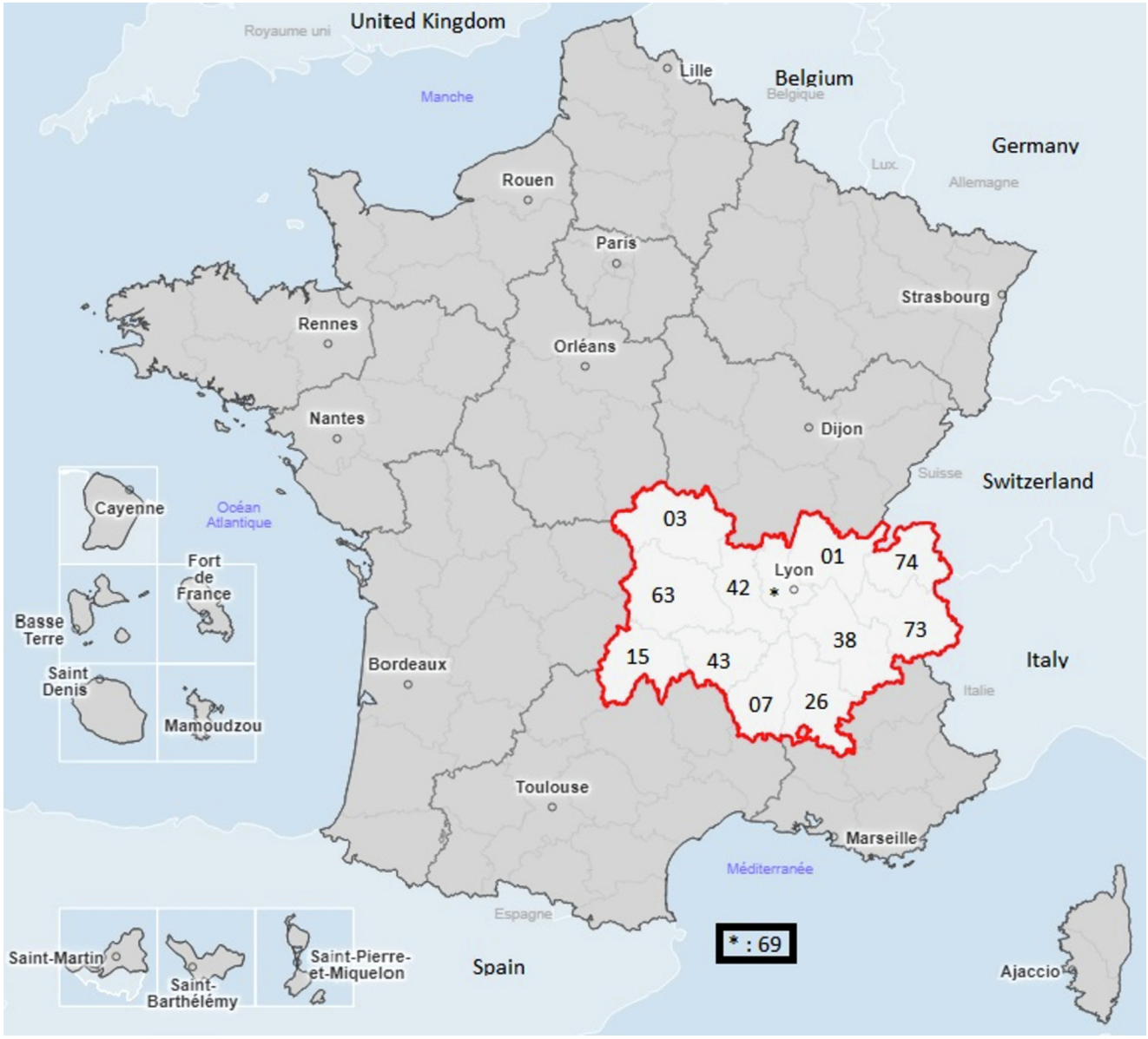


**Fig. 3. Auvergne-Rhône-Alpes and its administrative subdivisions (departments) among all French administrative regions (continental and overseas).** *Source : GEODES – Santé publique France / 2020 – IGN-Admin Express – IGN-Insee. Obtained from https://geodes.santepubliquefrance.fr.. The included departments are named as follows: Ain (01), Allier (03), Ardèche (07), Cantal (15), Drôme (26), Isère (38), Loire (42), Haute-Loire (43), Puy-de-Dôme (63), Rhône (69), Savoie (73), Haute-Savoie (74).*

**Table 1**
Estimations of vaccine impact between December 15, 2020 and November 15, 2021 in the Auvergne-Rhône-Alpes region and its 12 departments.

| Department | 01 | 03 | 07 | 15 | 26 | 38 | 42 | 43 | 63 | 69 | 73 | 74 | Region |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Population (thousands) | 657 | 331 | 327 | 143 | 521 | 1,265 | 765 | 227 | 660 | 1,876 | 433 | 828 | 8,032 |
| Infection incidence rate on December 15, 2020 (reference period) | 161 | 207 | 187 | 148 | 174 | 211 | 164 | 133 | 132 | 185 | 160 | 188 | 178 |
| Hospital admission incidence rate on December 15, 2020 (reference period) | 8.2 | 32.0 | 14.1 | 11.9 | 15.0 | 21.2 | 9.5 | 22.9 | 11.1 | 17.5 | 24.3 | 16.7 | 16.7 |
| Infection incidence rate on November 15, 2021 | 131 | 103 | 242 | 86 | 114 | 128 | 129 | 101 | 86 | 135 | 149 | 104 | 131 |
| Hospital admission incidence rate on November 15, 2021 | 0.30 | 4.83 | 6.42 | 2.80 | 3.27 | 3.64 | 3.40 | 1.76 | 2.42 | 3.46 | 4.85 | 2.78 | 0.30 |
| Partial vaccine coverage (%) on November 15, 2021 | 64 | 85 | 74 | 84 | 79 | 73 | 80 | 75 | 76 | 81 | 77 | 75 | 64 |
| Complete vaccine coverage (%) on November 15, 2021 | 61 | 83 | 72 | 82 | 77 | 71 | 77 | 74 | 75 | 79 | 76 | 74 | 61 |
| Impact on infection incidence rate on November 15, 2021 | 0.21 | 0.31 | −0.55 | −0.03 | 0.29 | 0.28 | 0.23 | 0.26 | 0.21 | 0.16 | 0.23 | 0.59 | 0.21 |
| Impact on hospital admissions on November 15, 2021 | 0.98 | 0.87 | 0.72 | 0.83 | 0.82 | 0.86 | 0.82 | 0.93 | 0.81 | 0.86 | 0.83 | 0.88 | 0.98 |

The incidence rate unit is /100,000 person-week
*Interpretation: a 98% reduction in hospital admission rate was observed between December 15, 2020 and November 15, 2021 across the region
*The included departments are named as follows: Ain (01), Allier (03), Ardèche (07), Cantal (15), Drôme (26), Isère (38), Loire (42), Haute-Loire (43), Puy-de-Dôme (63), Rhône (69), Savoie (73), Haute-Savoie (74).*

tion on hospital admissions and to a lesser degree on the proportion of individuals testing positive. Of course, the ecological nature of this study prevents us from drawing further conclusions since we could not account for all of the factors involved in the natural evolution of the current pandemic such as mask-use or other non-pharmaceutical preventive measures. The lack of individual-level data prevents us from proposing a causal link between the studied indicators although such proposals have already been published. However, ecological results remain a useful tool to comfort findings from clinical studies and analytical epidemiological studies, especially considering the challenges to confirm a causal effect of vaccine against an active, recent, and partially understood pandemic.

The results regarding hospital admissions must be assessed with respect to the varying advancement of the vaccination campaign among ages: as old age is a determinant risk factor for severe COVID-19, the impact of vaccination is likely associated with an effective coverage among the elderly. By June 1, 2021, within the study region, complete vaccination coverage reached above 75% for individuals aged 75 or more and 58% between 70 and 74, with all other age groups below 37%. By November 15, 2021, final date of the study period, complete coverage reached 75% at minimum (among individuals aged 20 to 25). This signals a differential impact of vaccination in the first semester of 2021 with a likely stronger effect on hospital admissions than during the second semester.

We took advantage of multiple reliable and exhaustive data collection systems to diffuse encouraging trends regarding vaccination effects on the pandemic mitigation effort. Owing to the public effort to make these datasets open to the general public in France and abroad, this class of analysis can be easily replicated in one or multiple nations and to a degree included in the general surveillance of vaccine effectiveness.

The present analysis was conducted between January 1 and November 15, 2021, a time-period marked by two emerging variants of concern. The alpha variant reached 45.7% of prevalence among infection cases mid-Febuary, peaked at 89% mid-April and was pushed back to 50% by June 21 as Delta reached 43.1% a week later, and over 90% by July 19 [20]. Those results are coherent with previous literature regarding vaccine efficacy on severe cases and infection and considering the genetic variability of SARS-CoV-2 during the study period, support the effect of vaccination against multiple variants of concern. The Auvergne-Rhone-Alpes region may not be representative of the country, but epidemiological studies performed in this area included a total population of more than 8 million inhabitants and could generate results that could be compared with other areas in France or other countries in Europe with neighbouring demographic indicators such as Switzerland or Austria.

In conclusion, these results support an encouraging control of COVID-19 in France since the implementation of vaccinations. Variant emergence, appropriate individual preventive measures, non-pharmaceutical interventions and vaccines constitute the major determinants of the future spread of SARS-CoV-2 in France.

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## Data availability

The open-data repository of all epidemiological data publicly available used in this analysis is available at https://www.data.gouv.fr/fr/organizations/sante-publique-france/. The specific datasets used are available at the following URLs:

- Infection data: https://www.data.gouv.fr/fr/datasets/donnees-relatives-aux-resultats-des-tests-virologiques-covid-19/, file named "sp-pos-quot-dep-YYYY-MM-AA-HHhmm.csv"
- Vaccination data: https://www.data.gouv.fr/fr/datasets/donnees-relatives-aux-personnes-vaccinees-contre-la-covid-19–1/, files named "vacsi-dep-YYYY-MM-AA-HHhmm.csv" and "vacsi-reg-YYYY-MM-AA-HHhmm.csv"
- Reproduction number and hospitalisation data: https://www.data.gouv.fr/fr/datasets/synthese-des-indicateurs-de-suivi-de-lepidemie-covid-19/, file named "table-indicateurs-open-data-dep- YYYY-MM-AA-HHhmm.csv"

All specific datasets used in this analysis and the scripts are available on demand.

## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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