



HAL
open science

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

Nicolas Romain-Scelle, Christelle Elias, Philippe Vanhems

► To cite this version:

Nicolas Romain-Scelle, Christelle Elias, Philippe Vanhems. COVID-19 vaccine is correlated with favourable epidemiological indicators in the Auvergne-Rhône-Alpes region (France): An ecological study. *Vaccine*, 2022, 40 (5), pp.695-700. 10.1016/j.vaccine.2021.12.036 . hal-04352853

HAL Id: hal-04352853

<https://hal.science/hal-04352853>

Submitted on 22 Jul 2024

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution - NonCommercial 4.0 International License

1 **COVID-19 vaccine is correlated with favourable epidemiological indicators in the**
2 **Auvergne-Rhône-Alpes region (France): an ecological study.**

3 Nicolas Romain-Scelle^a, Christelle Elias^{a,b}, Philippe Vanhems^{a,b,c}

4 ^aService Hygiène, Epidémiologie et Prévention, Centre Hospitalier Edouard Herriot, Hospices
5 Civils de Lyon, Lyon, France.

6 ^bÉquipe Santé Publique, Epidémiologie et Eco-évolution des Maladies Infectieuses CIRI-
7 Centre International de Recherche en Infectiologie, Université de Lyon, Université Claude
8 Bernard Lyon 1, Inserm, U1111, CNRS, UMR5308, ENS Lyon, Lyon, France.

9 ^cINSERM, F-CRIN, Lyon Centre of Innovative Clinical Research Network in Vaccinology (I-
10 REIVAC), CIC 1417, Paris, France.

11 Corresponding author: Philippe.vanhems@chu-lyon.fr

12

13 **Funding**

14 This research did not receive any specific grant from funding agencies in the public, commercial, or
15 not-for-profit sectors.

16 **Data availability**

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

- 20 • Infection data: [https://www.data.gouv.fr/fr/datasets/donnees-relatives-aux-resultats-des-](https://www.data.gouv.fr/fr/datasets/donnees-relatives-aux-resultats-des-tests-virologiques-covid-19/)
21 [tests-virologiques-covid-19/](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”
- 22 • Vaccination data: [https://www.data.gouv.fr/fr/datasets/donnees-relatives-aux-personnes-](https://www.data.gouv.fr/fr/datasets/donnees-relatives-aux-personnes-vaccinees-contre-la-covid-19-1/)
23 [vaccinees-contre-la-covid-19-1/](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
24 “vacsi-reg-YYYY-MM-AA-HHhmm.csv”
- 25 • Reproduction number and hospitalisation data:
26 [https://www.data.gouv.fr/fr/datasets/synthese-des-indicateurs-de-suivi-de-lepidemie-covid-](https://www.data.gouv.fr/fr/datasets/synthese-des-indicateurs-de-suivi-de-lepidemie-covid-19/)
27 [19/](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”

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

29 **Acknowledgements**

30 We thank the following organisations for access to national data: Santé publique France
31 (www.santepubliquefrance.fr), Paris University Hospital (AP-HP, www.aphp.fr), French Health
32 Insurance (Assurance Maladie, <https://assurance-maladie.ameli.fr/>), Health General Direction at the
33 Solidarity and Health Ministry (DGS, <https://solidarites-sante.gouv.fr/>)).

34 **Keywords:**

35 COVID-19

36 SARS-CoV-2

37 Vaccine impact

38 Ecological study

39 Open data

40 **Abstract (141 words)**

41 COVID-19 vaccination has proven to be effective in preventing severe cases, reducing viral load, and
42 transmissibility. The aim of this study was to evaluate the impact of vaccination 11 months after
43 implementation on epidemiological indicators and the effective reproduction number in one French
44 region. We plotted four indicators with vaccination coverage as the explaining variable and estimated
45 the impact of vaccination using the reduction rates in infections and hospital admissions. A reduction
46 of 98% in COVID-19-related hospitalisation 11 months after the vaccine campaign began in January
47 2021 has been reported while vaccine coverage increased over time. Those results do not make it
48 possible to postulate a causal relationship but do support the effect of vaccination against multiple
49 variants of concern. Non-pharmaceutical measures remain necessary to attain complete epidemic
50 control. Open epidemiological data should be considered to monitor vaccine effectiveness wherever
51 possible.

52 **Introduction**

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

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

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

76 **Methods**

77 This study was conducted in the Auvergne-Rhône-Alpes French administrative region
78 (estimated population in 2020: 8,032,377 inhabitants, capital: Lyon), between January 1 and
79 November 15, 2021. The study region is highlighted in Fig. 3. We collected the following weekly
80 publicly available epidemiological indicators for all 12 administrative subdivisions (French
81 departments) of the region: SARS-CoV-2 new infection rate (/100,000 person-week), rate of hospital
82 admissions for COVID-19 (/100,000 person-week), proportion of testing positivity for SARS-CoV-2
83 carriage (/100 persons tested), and vaccine coverage (partial and complete, /100 inhabitants). Partial
84 and complete vaccine coverage are respectively defined as incomplete (lacking one dose) and
85 complete vaccination (excluding boosters) with respect of previous COVID-19 and altered immune
86 response at an individual level according to the French national guidelines from the French “Haute
87 Autorité de Santé”. We do not take into account for booster injections, as we do not have sufficient
88 cases and data to provide any meaningful results. Infection data (incidence rate, positivity rate) are
89 collected from the national testing information system, hospital admission data from the victim
90 information system, and vaccination data from the national vaccination information system. We also
91 collected the estimated R_e , computed weekly from infection data following the method described in
92 Cori et al. (12), only available for the entire region. Every dataset used in the analysis was colligated
93 by the national public health agency (Santé publique France), and mandated to be available through
94 the French government open-data platform (11). The information systems collected personal data in
95 compliance with French law and regulations (13–15).

96 We plotted pandemic-related indicators (Y axis) as a function of vaccine coverage (X axis) for
97 each day all indicators were estimated. To provide a meaningful visualisation of the lockdown and
98 curfews periods on the figures, regional vaccine coverage observed at the beginning and end of each
99 relevant period was used. The impact of vaccination was calculated using the formula cited by
100 Hanquet et al. (16): $IMPACT = \frac{IR_{pre-vaccine} - IR_{post-vaccine}}{IR_{pre-vaccine}} = 1 - IRR^1$, with the incidence rate on
101 December 15, 2020 as a pre-vaccine reference. This impact estimation was calculated for the region
102 and all of its 12 subdivisions on November 15, 2021. To account for the delay between vaccine
103 injection and effective immunization, all vaccine-related indicators were joined with the
104 epidemiologic indicators using a 14-day lag. The R software (17) with ggplot2 (18) and mgcv (19)

¹ With IR : incidence rate ; IRR : incidence rate ratio

105 packages was used. Penalized cubic regression spline was used to produce tendency lines and their
106 respective confidence interval (with α risk = 0.05).

107 **Results – Discussion**

108 A total of 3240 repeated measurements of incidence rate, % of positive testing, hospital
109 admissions and 90 measurements of R_e according to partial or complete vaccine coverage are plotted
110 in Figs. 1 and 2 respectively. The national control measures active during the study period were a first
111 curfew (Dec 15 to April 2, 2021, orange), one lockdown (April 3 to May 2, 2021, red), and a second
112 curfew (May 3 to June 20, 2021, orange). During both curfews, public movement was restricted from
113 the evening until morning, with the starting hour varying between 6 and 8 PM. The lockdown mainly
114 reintroduced limited movement to a short perimeter around one's house at all times, and suspension
115 of on-site work if not necessary. In Fig. 1, panels a-d show a decrease in viral diffusion within the
116 general population until May 3, 2021, end of the second curfew. Infection rate trends past this date
117 do not appear associated with vaccine coverage for the number of infection cases, although the
118 dispersion seems to decrease at a high level of vaccine coverage. Panels e and f indicate a similar
119 trend among hospital admissions until the end of the first curfew. Compared to the indicators
120 monitoring viral circulation within the general population, hospital admissions appear less correlated
121 to viral circulation as vaccine coverage increases, with dispersion noticeably lower as vaccine
122 coverage is high. Fig. 2 graphically links the underlying effective reproduction rate of SARS-CoV-2 in
123 the French population and vaccine coverage. This figure suggests no impact of vaccine coverage on
124 the increase in viral circulation within the general population: the reproduction rate is observed
125 above 1 at various levels of vaccine coverage within the study region. Table 1 provides a numerical
126 description of the impact of COVID-19 vaccines in the 12 administrative subdivisions of our study
127 region, showing a strong decrease in the incidence rates of hospital admissions with an estimated
128 impact of 0.98 in the region. This result is homogeneous across the region, with a minimum of 0.72 in
129 one department regarding hospital admissions. The estimated impact of vaccination upon both viral
130 circulation indicators is considerably more mitigated, with a regional mean estimated at 0.21, and
131 departmental estimates ranging between -0.55 and 0.59.

132 This study presented an overview of the relationship between epidemiological indicators and
133 vaccine coverage in one French region over 11 months. Accounting for the lockdown and curfews
134 during the study period, those results suggest an impact of vaccination on hospital admissions and to
135 a lesser degree on the proportion of individuals testing positive. Of course, the ecological nature of
136 this study prevents us from drawing further conclusions since we could not account for all of the
137 factors involved in the natural evolution of the current pandemic such as mask-use or other non-

138 pharmaceutical preventive measures. The lack of individual-level data prevents us from proposing a
139 causal link between the studied indicators although such proposals have already been published.
140 However, ecological results remain a useful tool to comfort findings from clinical studies and
141 analytical epidemiological studies, especially considering the challenges to confirm a causal effect of
142 vaccine against an active, recent, and partially understood pandemic.

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

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

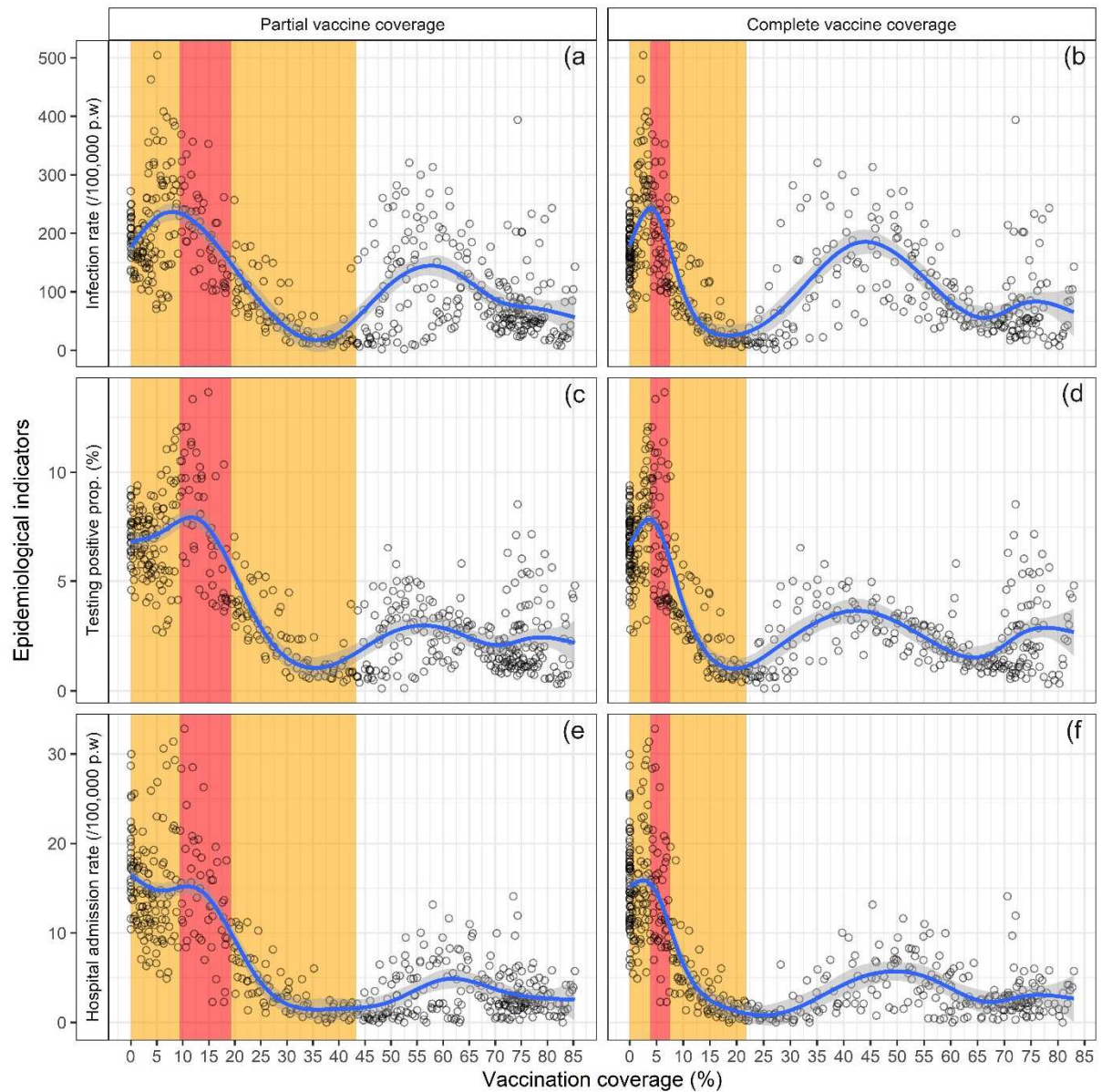
157 The present analysis was conducted between January 1 and November 15, 2021, a time-
158 period marked by two emerging variants of concern. The alpha variant reached 45.7% of prevalence
159 among infection cases mid-February, peaked at 89% mid-April and was pushed back to 50% by June
160 21 as Delta reached 43.1% a week later, and over 90% by July 19 (20). Those results are coherent
161 with previous literature regarding vaccine efficacy on severe cases and infection and considering the
162 genetic variability of SARS-CoV-2 during the study period, support the effect of vaccination against
163 multiple variants of concern. The Auvergne-Rhone-Alpes region may not be representative of the
164 country, but epidemiological studies performed in this area included a total population of more than
165 8 million inhabitants and could generate results that could be compared with other areas in France
166 or other countries in Europe with neighbouring demographic indicators such as Switzerland or
167 Austria.

168 In conclusion, these results support an encouraging control of COVID-19 in France since the
169 implementation of vaccinations. Variant emergence, appropriate individual preventive measures,

170 non-pharmaceutical interventions and vaccines constitute the major determinants of the future
171 spread of SARS-CoV-2 in France.

172

174 **Fig. 1: SARS-CoV-2 Incidence infection rate, SARS-CoV-2 test positive proportion and hospital**
 175 **admission rate by reported COVID-19 vaccination coverage, Auvergne Rhône-Alpes region, France,**
 176 **January 1, 2021-November 15, 2021**

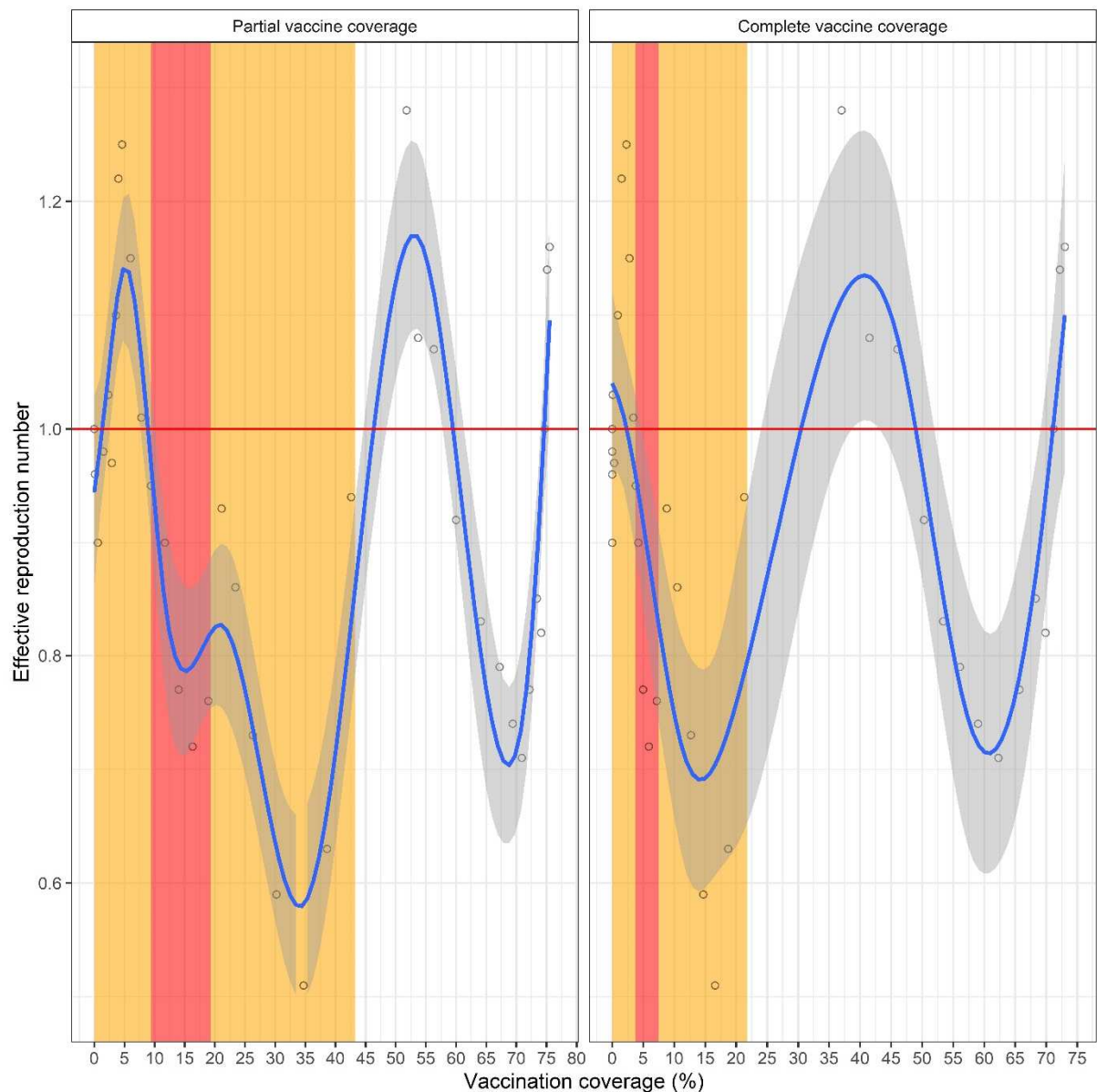


177

178 Each point in this figure represents one measure of one epidemiological indicator as a function of
 179 vaccine coverage in one of the 12 administrative subsets of the Auvergne-Rhône-Alpes region.
 180 Vaccine coverage was matched to the indicator measured with a 14-day lag to consider the time to
 181 acquire immunization. The grey area around the tendency line represents the 95% confidence
 182 interval. The orange area represents the curfew period, the red area the lockdown period.

183 p-w: person-week

184 **Fig. 2: Reproduction number with respect to level of COVID-19 vaccination coverage, Auvergne**
 185 **Rhône-Alpes region, France, January 1, 2021- November 11, 2021**



186

187 Each point in this figure represents one measure of the effective reproduction number as a function
 188 of vaccine coverage in the Auvergne-Rhône-Alpes region. Vaccine coverage was matched to the
 189 indicator measured with a 14-day lag to consider the time to acquire immunization. The grey area
 190 around the tendency line represents the 95% confidence interval. The orange area represents the
 191 curfew period, the red area the lockdown period. The horizontal red line represents the stability
 192 value 1.0 for the effective reproduction number. The R_e calculations were based on the method by
 193 Cori et al.(12).

194

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

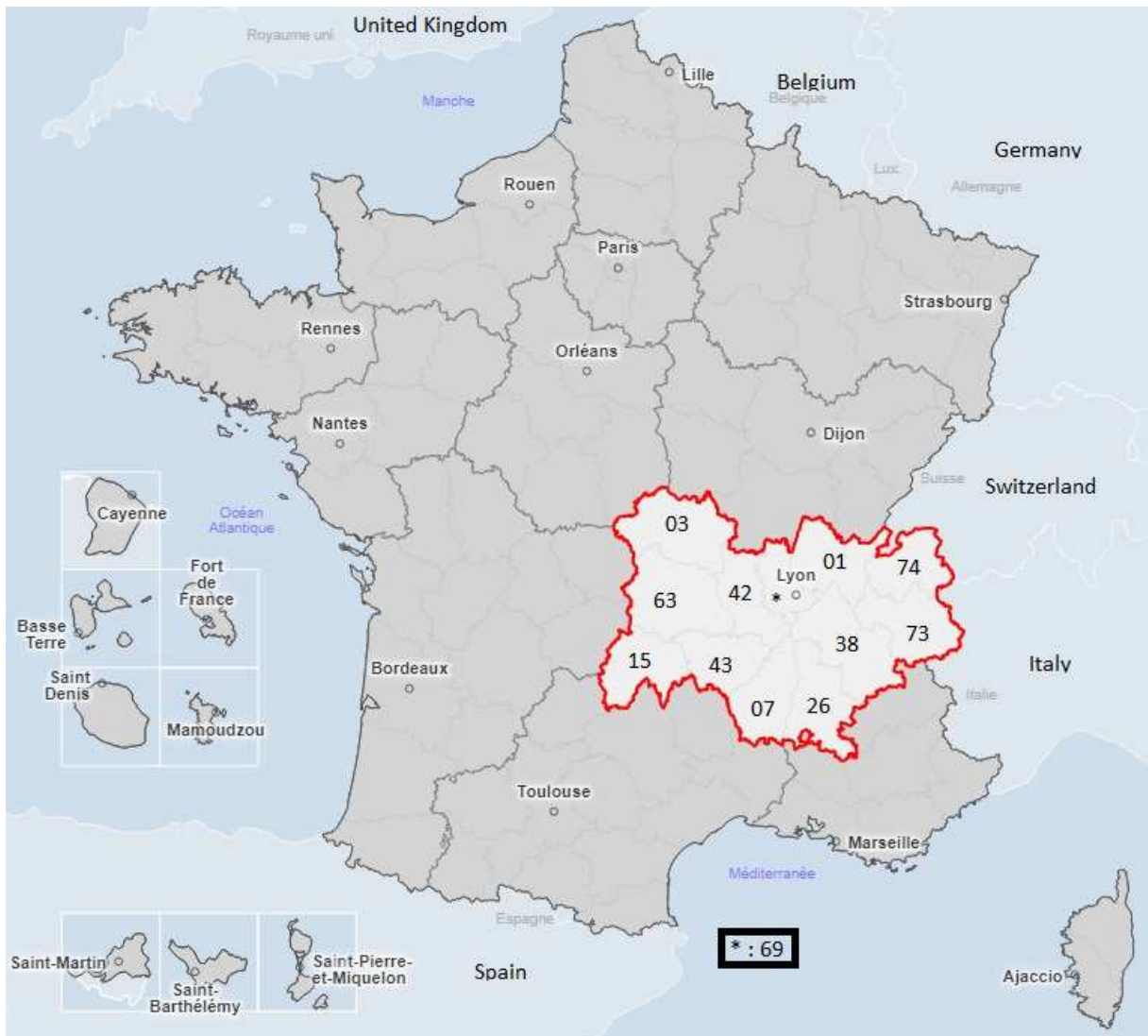
Department	01	03	07	15	26	38	42	43	63	69	73	74	Region
Population (thousands)	657	331	327	143	521	1,265	765	227	660	1,876	433	828	8,032
Infection incidence rate on December 15, 2020 (reference period)	161	207	187	148	174	211	164	133	132	185	160	188	178
Hospital admission incidence rate on December 15, 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

197 **The incidence rate unit is /100,000 person-week**

198 *Interpretation: a 98% reduction in hospital admission rate was observed between December 15,
 199 2020 and November 15, 2021 across the region

200 *The included departments are named as follows: Ain (01), Allier (03), Ardèche (07), Cantal (15),*
 201 *Drôme (26), Isère (38), Loire (42), Haute-Loire (43), Puy-de-Dôme (63), Rhône (69), Savoie (73), Haute-*
 202 *Savoie (74).*

203 **Figure 3: Auvergne-Rhône-Alpes and its administrative subdivisions (departments) among all**
 204 **French administrative regions (continental and overseas)**



205
 206 *Source : GEODES – Santé publique France / 2020 – IGN-Admin Express – IGN-Insee. Obtained from*
 207 *<https://geodes.santepubliquefrance.fr>.*

208 *The included departments are named as follows: Ain (01), Allier (03), Ardèche (07), Cantal (15),*
 209 *Drôme (26), Isère (38), Loire (42), Haute-Loire (43), Puy-de-Dôme (63), Rhône (69), Savoie (73), Haute-*
 210 *Savoie (74).*

211

212 **Declaration of competing interests**

213 PV has received grants from Merck Sharp & Dohme and Anios, and consulting fees from Astellas
214 Pharma, Sanofi and Pfizer. These organisations were not involved in the analysis or writing of this
215 manuscript. The authors declare that they have no known competing financial interests or personal
216 relationships that could have appeared to influence the work reported in this paper.

217 **References**

- 218 1. Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, et al. Safety and Efficacy of
219 the BNT162b2 mRNA Covid-19 Vaccine. *N Engl J Med*. 2020 Dec 31;383(27):2603–15.
- 220 2. Baden LR, El Sahly HM, Essink B, Kotloff K, Frey S, Novak R, et al. Efficacy and Safety of the
221 mRNA-1273 SARS-CoV-2 Vaccine. *N Engl J Med*. 2021 Feb 4;384(5):403–16.
- 222 3. Jacobson KB, Pinsky BA, Montez Rath ME, Wang H, Miller JA, Skhiri M, et al. Post-vaccination
223 SARS-CoV-2 infections and incidence of presumptive B.1.427/B.1.429 variant among healthcare
224 personnel at a northern California academic medical center. *Clin Infect Dis* [Internet]. 2021 Jun
225 17 [cited 2021 Jun 29];(ciab554). Available from: <https://doi.org/10.1093/cid/ciab554>
- 226 4. Levine-Tiefenbrun M, Yelin I, Katz R, Herzel E, Golan Z, Schreiber L, et al. Decreased SARS-CoV-2
227 viral load following vaccination. *medRxiv*. 2021 Feb 8;2021.02.06.21251283.
- 228 5. Milman O, Yelin I, Aharony N, Katz R, Herzel E, Ben-Tov A, et al. Community-level evidence for
229 SARS-CoV-2 vaccine protection of unvaccinated individuals. *Nat Med*. 2021 Jun 10;1–3.
- 230 6. Impact of Vaccination on Household Transmission of SARS-COV-2 in England [Internet]. Alliance
231 for Pandemic Preparedness. 2021 [cited 2021 Jun 29]. Available from:
232 [https://depts.washington.edu/pandemicalliance/2021/04/29/impact-of-vaccination-on-](https://depts.washington.edu/pandemicalliance/2021/04/29/impact-of-vaccination-on-household-transmission-of-sars-cov-2-in-england/)
233 [household-transmission-of-sars-cov-2-in-england/](https://depts.washington.edu/pandemicalliance/2021/04/29/impact-of-vaccination-on-household-transmission-of-sars-cov-2-in-england/)
- 234 7. Salje H, Kiem CT, Lefrancq N, Courtejoie N, Bosetti P, Paireau J, et al. Estimating the burden of
235 SARS-CoV-2 in France. *Science*. 2020 Jul 10;369(6500):208–11.
- 236 8. Kwok KO, Lai F, Wei WI, Wong SYS, Tang JWT. Herd immunity – estimating the level required to
237 halt the COVID-19 epidemics in affected countries. *J Infect*. 2020 Jun 1;80(6):e32–3.
- 238 9. Pouwels KB, Pritchard E, Matthews PC, Stoesser N, Eyre DW, Vihta K-D, et al. Impact of Delta on
239 viral burden and vaccine effectiveness against new SARS-CoV-2 infections in the UK [Internet].
240 2021 Aug [cited 2021 Dec 2] p. 2021.08.18.21262237. Available from:
241 <https://www.medrxiv.org/content/10.1101/2021.08.18.21262237v1>
- 242 10. Tang P, Hasan MR, Chemaitelly H, Yassine HM, Benslimane FM, Al Khatib HA, et al. BNT162b2
243 and mRNA-1273 COVID-19 vaccine effectiveness against the SARS-CoV-2 Delta variant in Qatar.
244 *Nat Med*. 2021 Nov 2;1–8.
- 245 11. Santé publique France - data.gouv.fr [Internet]. [cited 2021 Jun 29]. Available from:
246 <https://www.data.gouv.fr/fr/organizations/sante-publique-france/>
- 247 12. Cori A, Ferguson NM, Fraser C, Cauchemez S. A New Framework and Software to Estimate Time-
248 Varying Reproduction Numbers During Epidemics. *Am J Epidemiol*. 2013 Nov 1;178(9):1505–12.

- 249 13. Décret n° 2020-551 du 12 mai 2020 relatif aux systèmes d'information mentionnés à l'article 11
250 de la loi n° 2020-546 du 11 mai 2020 prorogeant l'état d'urgence sanitaire et complétant ses
251 dispositions [Internet]. May 13, 2020. Available from:
252 <https://www.legifrance.gouv.fr/loda/id/JORFTEXT000041869923/>
- 253 14. Décret n° 2020-1690 du 25 décembre 2020 autorisant la création d'un traitement de données à
254 caractère personnel relatif aux vaccinations contre la covid-19 [Internet]. 2020-1690 Dec 26,
255 2020. Available from: <https://www.legifrance.gouv.fr/jorf/id/JORFTEXT000042739429>
- 256 15. Article R3131-10-1 - Code de la santé publique - Légifrance [Internet]. Code de la Santé Publique
257 Mar 10, 2018. Available from:
258 https://www.legifrance.gouv.fr/codes/article_lc/LEGIARTI000036698009
- 259 16. Hanquet G, Valenciano M, Simondon F, Moren A. Vaccine effects and impact of vaccination
260 programmes in post-licensure studies. *Vaccine*. 2013 Nov 19;31(48):5634–42.
- 261 17. {R Core Team}. R: A Language and Environment for Statistical Computing [Internet]. Vienna,
262 Austria: R Foundation for Statistical Computing; 2021. Available from: [https://www.R-](https://www.R-project.org/)
263 [project.org/](https://www.R-project.org/)
- 264 18. Wickham H. *ggplot2: Elegant Graphics for Data Analysis* [Internet]. Springer-Verlag New York;
265 2016. Available from: <https://ggplot2.tidyverse.org>
- 266 19. Wood SN. *Generalized Additive Models: An Introduction with R*. 2nd ed. Chapman and Hall/CRC
267 Press; 2017.
- 268 20. Coronavirus : chiffres clés et évolution de la COVID-19 en France et dans le Monde [Internet].
269 [cited 2021 Nov 30]. Available from: [https://www.santepubliquefrance.fr/dossiers/coronavirus-](https://www.santepubliquefrance.fr/dossiers/coronavirus-covid-19/coronavirus-chiffres-cles-et-evolution-de-la-covid-19-en-france-et-dans-le-monde)
270 [covid-19/coronavirus-chiffres-cles-et-evolution-de-la-covid-19-en-france-et-dans-le-monde](https://www.santepubliquefrance.fr/dossiers/coronavirus-covid-19/coronavirus-chiffres-cles-et-evolution-de-la-covid-19-en-france-et-dans-le-monde)
- 271