

Appendix. Supplementary materials

Appendix 1 • Milestones of the French sanitary crisis and its management

Context

24/01/2020	First confirmed Covid-19 case in France
14/02/2020	First Covid-19 death in France

Lockdowns

17/03/2020	10/05/2020	First lockdown
11/05/2020	01/06/2020	First phase of lifting of lockdown restrictions (gradual reopening according to local health situations)
02/06/2020	21/06/2020	Second phase of lifting of lockdown restrictions
17/10/2020	29/10/2020	Curfew in Île-de-France and in eight metropolitan areas between 9 p.m. and 6 a.m.
30/10/2020	14/12/2020	Second lockdown
15/12/2020	15/01/2021	Curfew between 8 p.m. and 6 a.m. throughout metropolitan France
16/01/2021	02/04/2021	Curfew between 6 p.m. and 6 a.m. throughout metropolitan France
03/04/2021	02/05/2021	Third lockdown
03/05/2021	29/06/2021	Gradual lifting of the lockdown restrictions, end of travel restrictions
03/05/2021	18/05/2021	<i>Curfew between 7 p.m. and 6 a.m.</i>
19/05/2021	08/06/2021	<i>Curfew between 9 p.m. and 6 a.m.</i>
09/06/2021	29/06/2021	<i>Curfew between 11 p.m. and 6 a.m.</i>

Schools closures

16/03/2020	10/05/2020	Closure of all nurseries and schools
11/05/2020	02/06/2020	Gradual reopening of schools
05/04/2021	25/04/2021	Closure of schools
26/04/2021	02/05/2021	Closure of colleges and high schools

Activity restrictions

29/02/2020	Prohibition of public gatherings of more than 5,000 people; in the most affected municipalities, all collective gatherings are prohibited, schools are closed and it is recommended to limit travel
14/03/2020	Closure of so-called “non-essential” businesses and establishments open to the public (restaurants, bars, cinemas, nightclubs, etc.)
17/03/2020	Ban on leaving the house, except for certain reasons requiring a daily covid travel certificate
17/03/2020	Closure of the external European Union borders
11/05/2020	Wearing a face mask is mandatory in public transport
01/07/2020	Gradual reopening of borders
20/07/2020	Wearing a face mask is mandatory in closed public places
27/08/2020	Wearing a face mask is mandatory in all closed places
30/10/2020	Ban on leaving the house, except for certain reasons requiring a daily covid travel certificate
30/10/2020	Closure of so-called “non-essential” businesses and establishments open to the public (restaurants, cafes, cinemas, nightclubs, etc.)
28/11/2020	Reopening of shops (except bars, restaurants and sports halls)

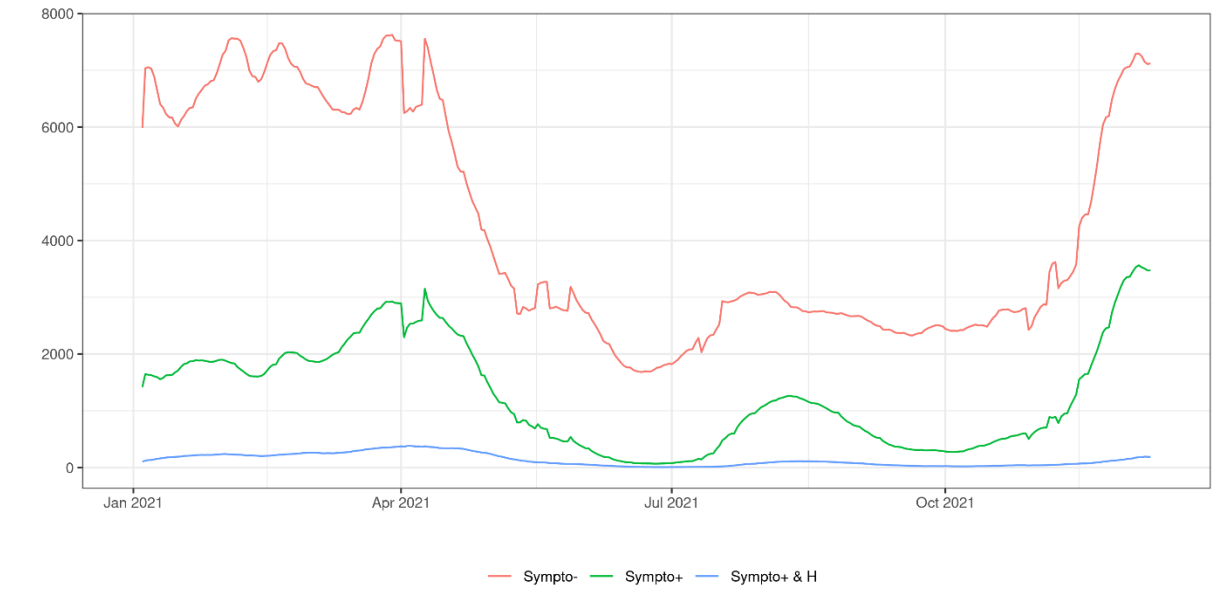
31/01/2021	Closure of the external European Union borders
03/04/2021	Limitation of travel to a radius of 10 kilometres
03/04/2021	Closure of so-called "non-essential" businesses
19/05/2021	Reopening of terraces (in cafes, bars and restaurants), shops and cultural and sports venues (with restrictions)
09/06/2021	Reopening of cafes, bars and restaurants, easing of restrictions
09/06/2021	Reopening of borders, subject to conditions depending on the country
Tests, vaccination, health pass	
27/01/2020	Development of a screening test (Pasteur)
06/04/2020	Beginning of screening of vulnerable people
12/05/2020	SI-DEP centralizes test results in a national database
28/05/2020	Test reimbursed by the French health insurance on prescription
25/07/2020	Test reimbursed by the French health insurance without medical prescription
17/10/2020	Deployment of rapid antigenic tests
27/12/2020	Beginning of the vaccination campaign (residents and staff of accommodation establishments for the elderly)
02/01/2021	Opening of vaccination to health workers, caregivers and firefighters caregivers aged 50 or over
18/01/2021	Opening of vaccination to persons aged 75 or over, then gradually to younger ages
06/02/2021	Opening of vaccination to health workers, caregivers and firefighters
19/02/2021	Opening of vaccination to persons aged 50 to 64 with comorbidities
02/03/2021	Opening of vaccination to persons aged 65 to 74 with comorbidities
27/03/2021	Opening of vaccination to persons aged 70 or over
12/04/2021	Opening of vaccination to persons aged 55 or over
01/05/2021	Opening of vaccination to all adults with comorbidities
10/05/2021	Opening of vaccination to persons aged 50 or over
31/05/2021	Opening of vaccination to all adults without condition
09/06/2021	Health pass is mandatory for public gatherings of more than 1,000 people
15/06/2021	Opening of vaccination to 12-17 years old
21/07/2021	Extension of the use of the health pass to public gatherings off more than 50 people
09/08/2021	Extension of the use of the health pass to all places of sociability without size criteria, to interregional public transport, etc.
01/09/2021	Opening of booster dose to persons aged 65 or over, elderly home residents, persons with comorbidities six months after the initial complete vaccination
15/09/2021	Mandatory vaccination for health workers and certain professions dealing with people
15/10/2021	End of reimbursement of tests by the French health Insurance, except on prescription and for vaccinated persons and minors
27/11/2021	Opening of booster dose to all eligible adults and eligibility for the booster vaccination is lowered to five months after the initial complete vaccination
28/12/2021	Eligibility for the booster vaccination is lowered to three months after the initial complete vaccination

Appendix 2 • Description of the study population

Table 1. • Descriptive characteristics of the sample, data collected from January 1st to December 12, 2021.

	Symptomatic negatives	Symptomatic positives	Hospitalized
Number of persons	N=1,475,037	N=437,694	N=45,802
Characteristic			
Sex — no. (%)			
Female	848,818 (57.5)	226,306 (51.7)	18,592 (40.6)
Male	626,208 (42.5)	211,387 (48.3)	27,210 (59.4)
Missing data	11 (<0.1)	1 (<0.1)	0
Age — no. (%)			
50-64 yr	815,682 (55.3)	276,597 (63.2)	14,323 (31.3)
65-74 yr	348,718 (23.6)	95,273 (21.8)	11,733 (25.6)
75-84 yr	174,709 (11.8)	39,127 (8.9)	9,690 (21.2)
≥ 85 yr	135,928 (9.2)	26,697 (6.1)	10,056 (22.0)
Comorbidity — no. (%)			
No	289,793 (19.6)	162,870 (37.2)	12,051 (26.3)
Yes	1,185,244 (80.4)	274,824 (62.8)	33,751 (73.7)
One dose — no. (%)			
No	812,653 (55.1)	291,036 (66.5)	36,345 (79.4)
Yes	662,384 (44.9)	146,658 (33.5)	9457 (20.6)
One dose type — no. (%)			
Comirnaty (Pfizer/BioNTech)	471,622 (71.2)	100,159 (68.3)	6,597 (69.8)
Spikevax (Moderna)	55,554 (8.4)	8,314 (5.7)	605 (6.4)
Vaxzevria (AstraZeneca)	121,270 (18.3)	32,864 (22.4)	1,865 (19.7)
Janssen	13,938 (2.1)	5,321 (3.6)	390 (4.1)
Two doses — no. (%)			
No	970,735 (65.8)	330,638 (75.5)	41,262 (90.1)
Yes	504,302 (34.2)	107,056 (24.5)	4,540 (9.9)
Two doses type— no. (%)			
Comirnaty (Pfizer/BioNTech)	390,933 (77.5)	78,262 (73.1)	3,373 (74.3)
Spikevax (Moderna)	47,118 (9.3)	6,116 (5.7)	278 (6.1)
Vaxzevria (AstraZeneca)	66,251 (13.1)	22,678 (21.2)	889 (19.6)

Figure 6 • Daily counts of controls, symptomatic and hospitalized cases (averaged over the last 7 days), data collected from January 1st to December 12, 2021



Abbreviations: Sympto+ (cases): symptomatic individuals with a laboratory confirmed SARS-CoV-2 infection (cases); Sympto+ & H (hospitalized cases): symptomatic individuals with a laboratory confirmed SARS-CoV-2 infection and hospital admission for Covid-19. Sympto- (controls): individuals with symptoms non-related to SARS-CoV-2 infection.

Appendix 3 •

Table 2. • Covid-19 vaccine effectiveness (in %) against symptomatic infections and hospitalizations among persons aged 50 years or over, according to the time elapsed since the receipt of each vaccine dose, data collected from January 1st to December 12, 2021.

Age	50 years or over		50 years and older With Comorbidity	
Vaccination status	VE(S+)	VE(H+)	VE(S+)	VE(H+)
D1: 0-14	-20.8 (-23.3--18.3)	15 (11.1-18.8)	-5.5 (-8.5--2.4)	28 (24.2-31.7)
D1: 15-21	26.2 (23.9-28.4)	59.9 (56.8-62.9)	28.5 (25.5-31.6)	61.6 (58.4-64.9)
D1: 22-28	44.5 (42.5-46.6)	76 (73.7-78.3)	44.6 (41.9-47.3)	76.3 (73.8-78.9)
D2: 0-7	50.4 (47.4-53.4)	76.7 (73-80.4)	57.6 (54.0-61.2)	80 (76.5-83.5)
D2: 8-14	70 (68.1-71.8)	84.5 (82.1-87.0)	71 (68.6-73.5)	85.6 (83-88.2)
D2: 15-30	82.4 (81.5-83.2)	90.9 (89.6-92.2)	82.9 (81.7-84.1)	91 (89.5-92.4)
D2: 1M-2M	76.7 (76-77.4)	94.1 (93.4-94.8)	78.4 (77.4-79.3)	94.5 (93.9-95.2)
D2: 2M-3M	70.5 (69.7-71.4)	93.5 (92.8-94.2)	69.9 (68.5-71.2)	93.2 (92.4-94)
D2: 3M-4M	65.7 (64.8-66.7)	92.7 (92.0-93.4)	66 (64.6-67.4)	92.5 (91.6-93.3)
D2: 4M-5M	56.2 (55.2-57.3)	91.7 (91.0-92.4)	56.2 (54.5-57.9)	91.4 (90.6-92.2)
D2: 5M-6M	53.7 (52.6-54.8)	92.2 (91.6-92.8)	49.6 (47.8-51.5)	91.2 (90.4-91.9)
D2: > 6M	53.1 (51.9-54.3)	89.8 (89.1-90.6)	47 (44.9-49.0)	88.1 (87.0-89.1)
DR: 1-7	56.6 (54.3-59)	91.3 (89.7-93.0)	51.7 (47.9-55.5)	90.2 (88.1-92.2)
DR > 7	91.9 (91.6-92.3)	98.7 (98.5-99.0)	90.5 (89.9-91.1)	98.4 (98.2-98.7)

Table 3. • Covid-19 vaccine effectiveness (in %) by age group against symptomatic infections and hospitalizations among persons aged 50 years or over, according to the time elapsed since the receipt of each vaccine dose, data collected from January 1st to December 12, 2021.

Age	50-64 yr		65-74 yr		75-85 yr		≥ 85 yr	
Vaccination status	VE(S+)	VE(H+)	VE(S+)	VE(H+)	VE(S+)	VE(H+)	VE(S+)	VE(H+)
D1: 0-14	-17.2 (-20.4--14)	13.3 (5.8-20.8)	-23.7 (-29.2--18.2)	6.5 (-2.1-15.2)	-29.9 (-37.7--22)	-4.9 (-15.5-5.6)	-20.5 (-28.8--12.2)	2.0 (-8.4-12.4)
D1: 15-21	33.0 (30.1-35.9)	72.2 (67.2-77.3)	25.2 (20.4-30)	56.7 (50.1-63.2)	15.9 (9-22.9)	46.0 (37.8-54.2)	15.9 (7.5-24.3)	39.1 (29.3-49)
D1: 22-28	47.0 (44.3-49.8)	83.0 (78.8-87.1)	45.8 (41.6-50)	80.6 (76.3-84.9)	42.9 (37.4-48.5)	68.6 (62.6-74.6)	23.4 (14.6-32.2)	52.3 (43.2-61.5)
D2: 0-7	51.0 (46.9-55.2)	82.5 (75.4-89.5)	56.6 (50.7-62.6)	86.6 (81.1-92.2)	49.3 (41.5-57.1)	73.0 (64.8-81.2)	55.6 (47.1-64.2)	60.7 (49-72.5)
D2: 8-14	71.4 (69.0-73.8)	80.2 (74.1-86.2)	73.5 (69.8-77.3)	82.7 (76.9-88.5)	67.4 (62.2-72.5)	82.3 (76.6-88)	68.4 (62.8-74)	85.0 (80-90.1)
D2: 15-30	81.1 (79.9-82.2)	91.8 (89.4-94.2)	83.8 (81.9-85.6)	89.1 (85.9-92.3)	86.4 (84.4-88.5)	92.6 (90.2-94.9)	84.7 (82.2-87.2)	89.8 (86.7-92.8)
D2: 1M-2M	75.9 (75.0-76.8)	95.4 (94.4-96.5)	75.6 (74-77.2)	94.0 (92.6-95.4)	82.5 (80.8-84.3)	93.8 (92.3-95.3)	82.3 (80.2-84.4)	92.0 (90.2-93.8)
D2: 2M-3M	71.4 (70.4-72.4)	95.5 (94.5-96.5)	70.1 (68.3-71.9)	92.6 (91.2-94.1)	71.7 (68.7-74.6)	90.1 (87.8-92.5)	75.9 (72.7-79.1)	90.7 (88.4-93.1)
D2: 3M-4M	68.4 (67.4-69.5)	94.6 (93.6-95.7)	62.8 (60.7-64.9)	92.4 (91-93.8)	63.4 (59.9-66.8)	88.4 (86.1-90.8)	60.9 (56-65.8)	82.7 (78.9-86.6)
D2: 4M-5M	60.3 (59.1-61.6)	94.7 (93.7-95.7)	57.1 (54.9-59.3)	91.0 (89.5-92.5)	52.3 (48.2-56.3)	87 (84.6-89.4)	38.2 (31-45.4)	72.1 (66.6-77.5)
D2: 5M-6M	59.3 (58.1-60.6)	95.5 (94.7-96.3)	52.5 (50.2-54.9)	92.4 (91.2-93.5)	44.1 (39.7-48.5)	82.6 (79.9-85.4)	30.4 (23-37.8)	73.2 (68.3-78.1)
D2: > 6M	58.6 (57.2-60)	94 (92.9-95.2)	52.8 (50.2-55.4)	90.0 (88.3-91.6)	36.9 (32-41.8)	82.2 (79.5-85)	27.4 (20-34.8)	69.8 (64.8-74.8)
DR: 1-7	64.8 (62-67.6)	95.7 (93.1-98.3)	53.4 (49-57.9)	93.1 (90.4-95.8)	38.3 (28.9-47.6)	85.8 (80.7-91)	37.3 (21.5-53)	62.8 (47.9-77.8)
DR > 7	93.0 (92.3-93.6)	98.8 (98.0-99.6)	92.5 (91.8-93.1)	99.0 (98.7-99.4)	89.9 (88.8-90.9)	98.2 (97.7-98.7)	89.0 (87.5-90.5)	97.3 (96.5-98.1)

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Table 4. • Covid-19 vaccine effectiveness (in %) by variant of concern against symptomatic infections and hospitalizations among persons aged 50 years or over, according to the time elapsed since the receipt of each vaccine dose, data collected from January 1st to December 12, 2021.

Variant	Original Strain		Alpha		Beta/Gamma		Delta	
Vaccination status	VE(S+)	VE(H+)	VE(S+)	VE(H+)	VE(S+)	VE(H+)	VE(S+)	VE(H+)
D1: 0-14	-32.6 (-43.5--21.7)	1.7 (-16.7-20.1)	-23.9 (-27.6--20.2)	4.8 (-1.3-10.8)	-20.1 (-33.7--6.4)	2.2 (-20.4-24.7)	4.5 (-0.2-9.2)	16.7 (6.0-27.4)
D1: 15-21	24.0 (14.3-33.6)	61.3 (48.2-74.4)	26.5 (23.2-29.8)	56.6 (51.9-61.3)	4.6 (-11.2-20.4)	40.8 (19.3-62.4)	38.9 (34.6-43.2)	63.3 (55.4-71.3)
D1: 22-28	49.4 (41.7-57.1)	69.6 (57.4-81.8)	43.8 (40.8-46.8)	75.7 (72.3-79.2)	30.6 (17.3-43.8)	55.8 (36.8-74.7)	51.3 (47.4-55.2)	79.9 (73.9-85.8)
D2: 0-7	64.6 (51.6-77.6)	80.8 (62.5-99.2)	58.4 (53.9-62.9)	79.4 (74.2-84.7)	28.3 (3.7-52.9)	50.7 (17.3-84.1)	48.4 (43.7-53.2)	79.3 (72.7-85.9)
D2: 8-14	82.3 (75.5-89.2)	93.6 (86.8-100.4)	75.6 (72.7-78.6)	87.9 (84.3-91.4)	57.7 (42.0-73.4)	79.2 (59.1-99.3)	69.4 (66.9-72.0)	80.6 (75.8-85.3)
D2: 15-30	91.9 (88.3-95.5)	95.8 (91.6-100)	91.3 (90.1-92.5)	93.7 (91.8-95.6)	84.2 (78.2-90.3)	98.2 (95.7-100.8)	78.6 (77.4-79.9)	89.3 (87.2-91.4)
D2: 1M-2M	84.5 (78.5-90.6)	97.2 (93.1-101.3)	87.0 (85.8-88.3)	95.2 (94-96.4)	68.0 (59.1-76.9)	90.6 (83.3-97.8)	74.0 (73.1-74.8)	94.1 (93.3-95.0)
D2: 2M-3M	88.7 (78.9-98.5)	93.3 (78.7-107.9)	84.0 (81.8-86.2)	96.9 (95.4-98.3)	61.2 (45.7-76.8)	96.7 (90.1-103.3)	68.6 (67.6-69.5)	92.7 (91.9-93.6)
D2: 3M-4M							64.6 (63.6-65.5)	92.2 (91.4-93)
D2: 4M-5M							56.3 (55.2-57.4)	91.5 (90.7-92.2)
D2: 5M-6M							53.8 (52.7-54.9)	92 (91.4-92.6)
D2: > 6M							52.4 (51.1-53.7)	89.5 (88.7-90.3)
DR: 1-7							55.9 (53.5-58.3)	90.9 (89.1-92.7)
DR > 7							91.9 (91.5-92.3)	98.7 (98.5-99.0)

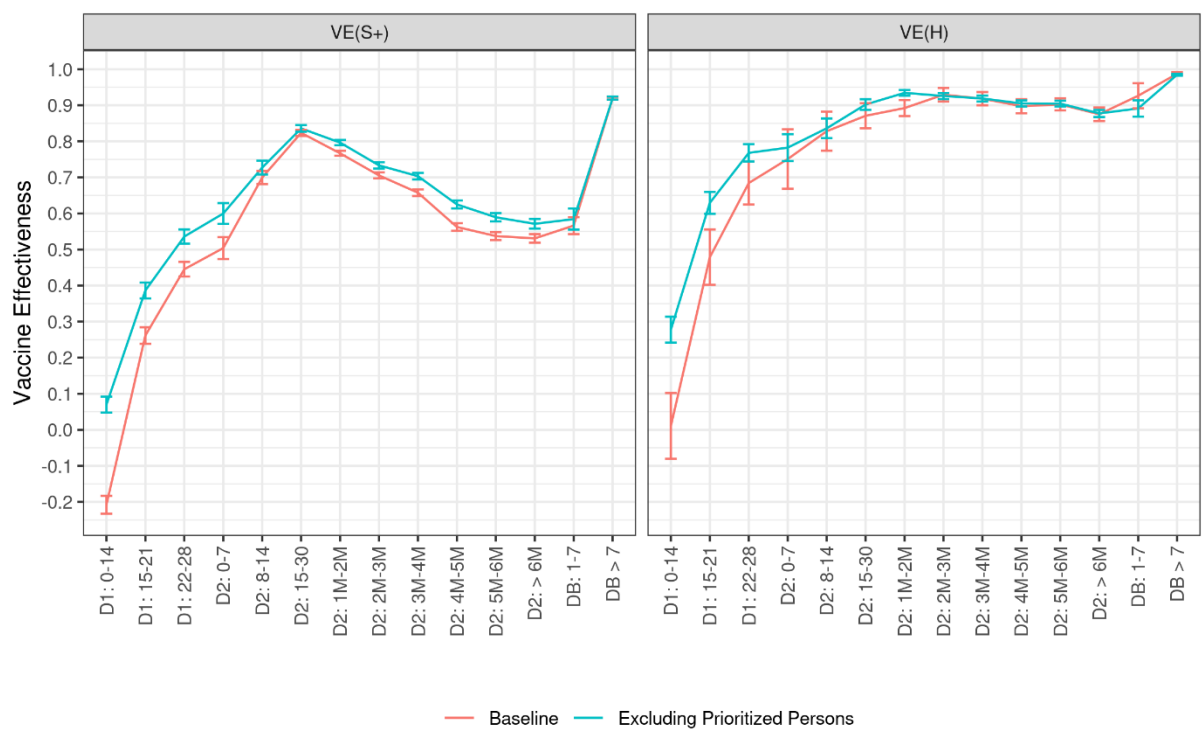
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Delta variant cases are approximated by cases from July 7 to December 12, 2021.

Appendix 4 • Downward bias due to targeting vulnerable individuals

Presence of comorbidities is derived either from prior knowledge from the health insurance on the person status or because a physician recommended to prioritize a non-eligible (at-the-time) individual during the vaccination campaign. Thus, the latter is rare for unvaccinated persons. An alternative specification excludes from the sample persons who are classified as comorbid on a physician recommendation in order to benefit from the vaccine in priority. In this alternative specification, the odd ratio in the early period post first dose indicates a decreased risk [OR: 0.93 (CI 95% 91-95)] instead of the increase risk observed in the baseline specification. The comparison of our estimates to this alternative may inform on the extent of the downward bias due to targeting individuals on unobserved factors. The downward bias in the vaccine effectiveness against symptomatic diseases is very limited in the first month following the second dose, but could reach six percentage points after four months. In contrast, vaccine effectiveness against hospitalization are very similar in both alternatives.

Figure 9 • Covid-19 vaccine effectiveness against symptomatic infections and hospitalizations among persons aged 50 years or over, according to the time elapsed since the receipt of each vaccine dose, data collected from January 1st to December 12, 2021, when excluding persons prioritized by a physician for vaccine administration.



Appendix 5 • Matching characteristics

45 Among persons aged 50 years or over hospitalized for Covid-19 (data source: SI-VIC), 72% have a linked positive RT-PCR test, collected from fifteen days before admission to the end of their stay (source: SI-DEP) over our analysis period. Among persons aged 50 years or over hospitalized for Covid-19 (data source: SI-VIC), 73% have a match in the VAC-SI register, which covers nearly all French residents and allows to recover the vaccination status. Among persons aged 50 years reporting symptoms in the last seven days before a RT-PCR test (data source: SI-DEP), 84 % have a match in the VAC-SI register, thus a known vaccination status.