

Analysis of available data on possible SARS-CoV-2 reinfections from the SIDEP database

Data as of March 20, 2022

Key results

685,858 possible cases of reinfection identified between March 2, 2021 and March 20, 2022, of which 95.2% since December 6, 2021 (start of distribution of the Omicron variant in France)

50% of possible cases of reinfection were between 18 and 40 years old

88% of possible cases of reinfection for which a screening result was available and interpretable for the reinfection episode had a result suggestive of Omicron

5.4% of confirmed COVID-19 cases were possible reinfections in S11-2022

Description of available data on possible reinfections (SIDEP)

The possible cases of reinfection considered in this analysis are defined as **all people who presented at least two positive tests recorded in the SIDEP database (regardless of the type of test) carried out 60 days apart or more (for more information, see the case definition of a reinfection)**, with a collection date between January 1 , 2021 and March 20, 2022 inclusive. Indeed, a change concerning the identification of patients in the SIDEP database (pseudonym) occurred at the beginning of 2021 and did not make it possible to analyze the entire period from which the SIDEP data were available (from May 13, 2020).

Therefore, only people who were possibly reinfected on or after March 2, 2021 (January 1 , 2021 + 60 days) are identifiable in this analysis, and **any reinfection that occurred on or after January 1 , 2021 after a first episode in 2020 is not identifiable in the SIDEP database as part of this analysis.**

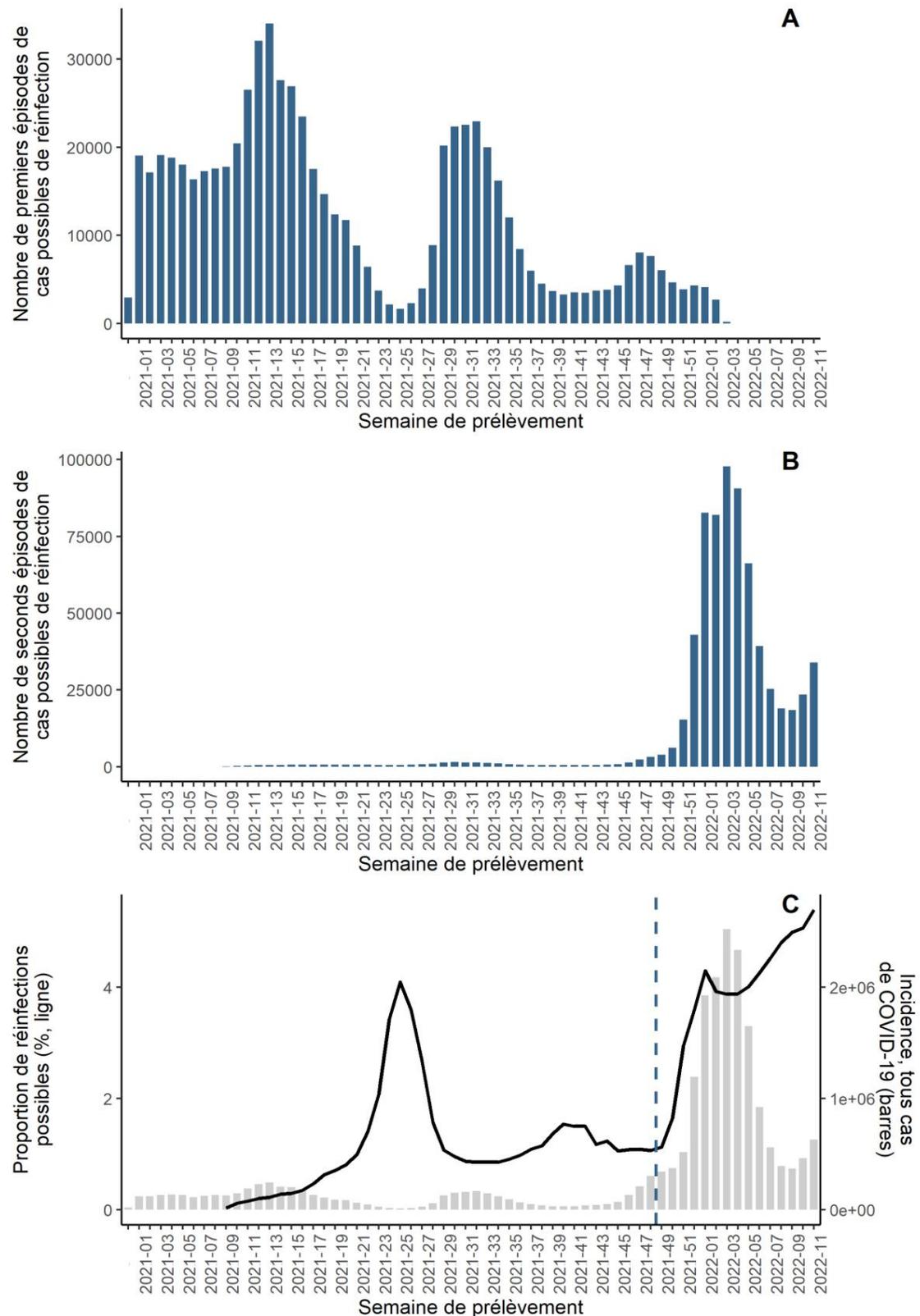
Numbers and temporal-spatial distribution of possible cases of reinfection

From March 2, 2021 to March 20, 2022, 685,858 possible cases of reinfection as defined above were identified in the SIDEP database. 99% of them (n=678,883) had two distinct episodes and 1% (6,975 people) had three or more episodes. In the rest of the document, the indicators relate only to people with 2 episodes of infection.

Figure 1 represents the date of the first and second episode for people who presented 2 distinct episodes. Most cases of reinfection had their first episode of infection during the 3rd and 4th waves of the epidemic (spring and summer 2021), and the vast majority of second episodes occurred during the 5th wave, with 95.2% (n=646,614) of episodes of possible reinfection occurring from December 6, 2021, i.e. approximately from the introduction and dissemination of the Omicron variant in France (Figure 1).

Figure 1. Temporal distribution of first (panel A) and second (panel B) infection episodes for possible reinfection cases that had two episodes, and proportion of possible reinfection cases reported to all COVID-19 cases (panel C), over the study period (daily data)

The vertical dotted blue line indicates December 6, 2021



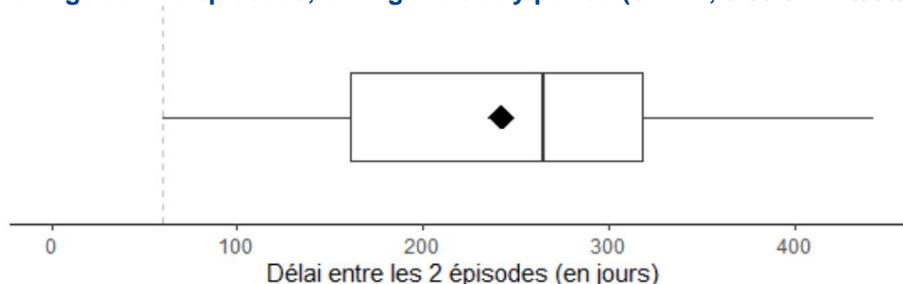
Source: SIDEP, Public Health France exploitation, from 01/01/21 to 03/20/22).

The scale of the ordinates is different between the different panels.

The time between the two episodes of infection was 242 days on average, with a median of 265 days and an interquartile range of 161 to 318 days (Figure 2).

Among the 678,883 cases with two episodes of infection, 8.4% had a delay between 60 and 89 days, 5% between 90 and 119 days, 18.6% between 120 and 179 days, 59.9% between 180 and 364 days and 8.1% of 365 days or more. It should be noted that **the share of possible cases of reinfection presenting a delay of between 60 and 89 days has decreased since the emergence of Omicron**, since it was 23.6% among the 42,281 possible cases of reinfection having had their 2nd episode before December 6, 2021, and that it is 7.4% among the 636,602 possible cases of reinfection having had their 2nd episode since this date.

Figure 2. Distribution of the time between the first and the second episode of infection, for possible cases of reinfection having had two episodes, during the study period (SIDEP, 01/01/21-20/03/22)



The time between the two episodes cannot be less than 60 days, by definition (vertical dotted line). The box represents the median (solid vertical line) as well as the 1st and 3rd quartiles, the diamond represents the mean, and the horizontal line represents the range of values observed for the time between the two episodes (minimum and maximum).

Proportion of reinfections among all confirmed cases of COVID-19

Possible cases of reinfection represented 3.3% of all confirmed cases of COVID-19 detected in the SIDEP database between March 2, 2021 and March 20, 2022. Over the entire period extending until December 5, 2021, this proportion was 0.8%. This proportion increased sharply from December 6, 2021, to 4.0% of all confirmed cases of COVID-19. **In week 11-2022, this proportion was 5.4%** (Figure 1C).

Regional distribution of possible cases of reinfection

Possible cases of reinfection have been detected in all French regions, with potentially significant differences between regions in terms of numbers and proportion of possible reinfections among all confirmed cases of COVID-19 during the study period (Table 1).

This proportion fluctuated between 2.6% in Brittany and 7% in Guyana.

Table 1. Regional numbers of possible cases of reinfection (having had two episodes) and relative share compared to all confirmed cases detected during the study period (March 2, 2021 - March 20, 2022), France

	Number of possible cases of reinfection	% of possible cases of reinfection out of all confirmed cases
Auvergne-Rhône-Alpes	81,283	3.7%
Burgundy-Franche-Comte	22,154	3.2%
Brittany	20,151	2.6%
Centre-Val-de-Loire	16,542	2.9%
Corsica	3,792	4.8%
Great East	51,163	3.5%
Guadeloupe	5,528	5.6%
Guyana	3,530	7.0%
Hauts-de-France	59,211	3.8%
Ile-de-France	155,992	5.0%
The meeting	7,269	2.7%
Martinique	4,615	4.5%
Mayotte	1,132	4.3%
Normandy	23,223	3.1%
New Aquitaine	46,344	3.0%
Occitania	64,406	4.1%
Pays de la Loire	26,506	2.8%
Provence-Alpes-Côte d'Azur	82,185	5.5%
Unknown region	3,857	
National level	678 883	3.3%

ÿSocio-demographic characteristics of possible cases of reinfection

The proportions of health professionals and people aged 18-40 were higher among possible cases of reinfection than among all confirmed cases of COVID-19 detected in SIDEP during the study period (6.2% versus 3.6% and 50.3% versus 37.7%, respectively). Conversely, the proportion of people aged over 60 was lower (4.1% versus 9.1% for those aged 61-80 and 1.5% versus 2.3% for those over 80) (Table 2).

Table 2. Sociodemographic characteristics of possible cases of reinfection and all confirmed cases detected in SIDEP (March 2, 2021 – March 20, 2022), France

	Possible cases of reinfection	Confirmed cases of COVID-19
Share of women	55.9%	53.6%
Proportion of healthcare professionals*	6.2%	3.6%
Breakdown by age group		
< 18 years	23.9%	26.6%
old 18-40 years	50.3%	37.7%
old 41-60 years	20.2%	24.3%
old 61-80 years	4.1%	9.1%
old > 80 years old	1.5%	2.3%

* Analysis carried out on people for whom information on the status of health professional was entered in the SIDEP database.

Presence/absence of symptoms during the 2 episodes

Among the cases for which information on the presence or absence of symptoms at the time of the positive test during the 2 episodes of COVID-19 was available in SIDEP, **52.7% of the possible cases of reinfection for which this information was available were symptomatic at the 2nd episode**, with all possible combinations of presence/absence of symptoms at the 2 episodes (Table 3). This proportion is similar to that of symptomatic people among all confirmed cases of COVID-19, during the study period (52.5%).

Table 3. Presence of symptoms when testing positive for 1st and 2nd episode of COVID-19, France (SIDEP)

1st episode	2nd episode	Percentage of possible cases of reinfection
Missing information for one or both episodes		15.3%
Asymptomatic	Asymptomatic	21.1%
Symptomatic	Symptomatic	25.3%
Asymptomatic	Symptomatic	19.5%
Symptomatic	Asymptomatic	18.8%

Analysis of screening results for possible cases of reinfection in mainland France

In mainland France, 53.5% of possible cases of reinfection (n= 350,912) had an interpretable screening result in the SIDEP database for the 1st or 2nd episode of COVID-19, 21.1% (n= 138 278) had an interpretable screening result for at least the 2nd episode, and 10.8% (n=70,711) had an interpretable screening result for both episodes of infection.

For this analysis, the different possible screening results in the SIDEP database are grouped into 5 categories (for more information on screening, see the page dedicated to [variant monitoring in France, including the technical document on screening dated 06/01/2022](#)) :

- Suspicion of Alpha variant: result "V1" or "A0B0C0" (only for the period 31/05/2021-08/29/2021);
- Result "V2" or "V3" (before 31/05/2021): suspicion of Beta or Gamma variant;
- "C1" result from 05/31/2021: suspicion of Delta variant;
- Result "A0C0" or "D1" only from 01/11/2021: suspicion of Omicron variant;
- Any other interpretable screening result: "Other" category.

Note that due to the nature of the screening data, each of the 5 categories may include several different variants. For example, several variants carrying the L452R mutation (screening result C1 in SIDEP) circulated in France, even if Delta was very largely in the majority from 05/31/2021. Similarly, VOI B.1.640 is currently screened A0C0 and can therefore be classified in the "suspicion of Omicron variant" category from 01/11/2021. These categories are therefore generated for information only and the results should be interpreted with caution.

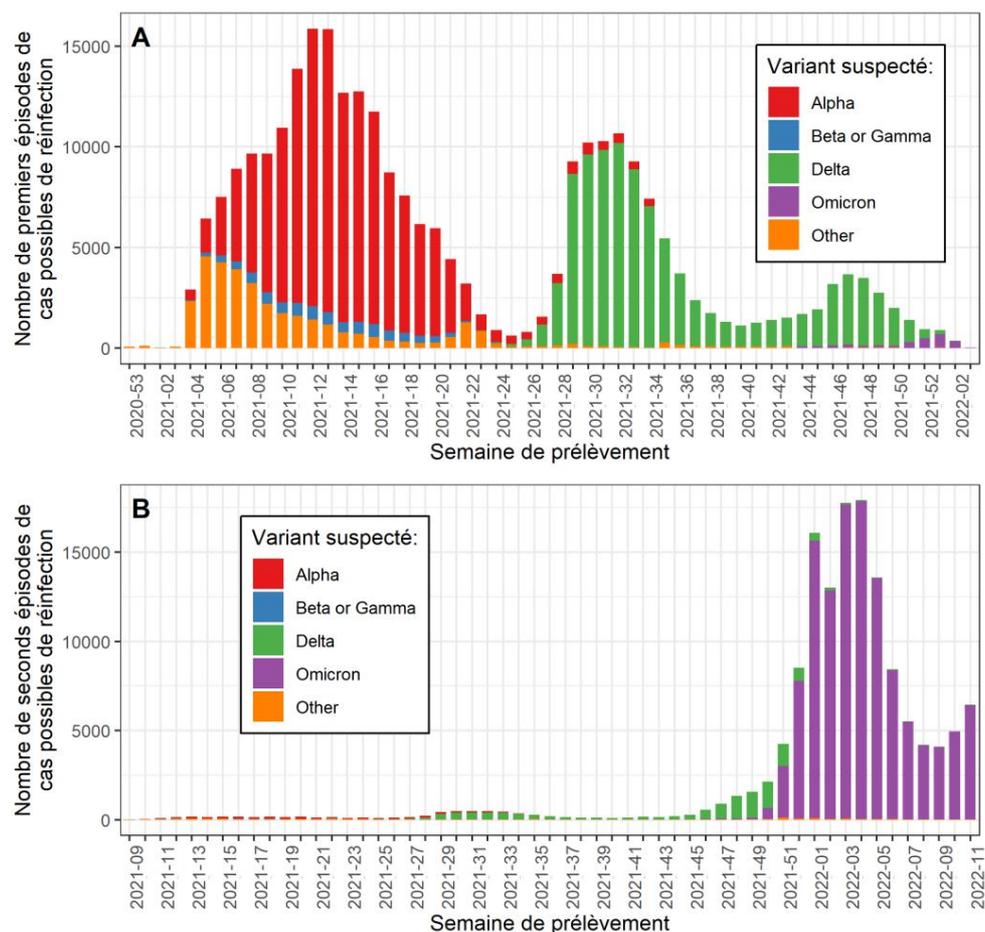
The majority of possible reinfections that occurred during the 3rd wave of spring 2021 are suspected to be due to the Alpha variant, while those that occurred during the 4th wave (summer 2021) are suspected to be due to the Delta variant. From week 51-2021, the majority of possible reinfections were suspected to be due to the Omicron variant (Figure 3).

Among the 70,711 possible cases of reinfection for which the information of the suspected variant was available for the first and the second episode, 42.6% of them presented a screening result compatible with a suspicion of Alpha variant during the 1st episode . and a suspected Omicron variant at the 2nd episode, and 34.0% of them presented a screening result compatible with a suspected Delta variant at the 1st episode and a suspected Omicron variant at the 2nd episode (Table 4) . Finally, 0.9% of

these cases had a screening result consistent with suspected Omicron variant (or B.1.640) during both episodes.

In total, over the entire study period, suspicion of the Omicron variant was found in 88.3% of the 138,278 possible cases of reinfection for which an interpretable screening result was available for the 2nd episode.

Figure 3. Temporal distribution of possible cases of reinfection with an interpretable screening result for at least one of the two episodes (panels A and B), metropolitan France (daily data)



Source: SIDEP, from 01/01/21 to 03/20/22

The ordinate scale is different between panels.

Table 4. Suspected variant in the first and second episodes of COVID-19 for possible cases of reinfection for which an interpretable screening result was available for the 2 episodes (n= 70,711), Metropolitan France

		Second episode				
		Alpha	Beta or Gamma	Delta	Omicron	Other
First episode	Alpha	0.9%	0.0%	3.2%	42.6%	0.5%
	Beta or Gamma	0.0%	0.0%	0.2%	2.8%	0.0%
	Delta	0.0%	0.0%	1.9%	34%	0.3%
	Omicron	0.0%		0.0%	0.9%	0.0%
	Other	0.1%		1.1%	11.1%	0.2%

Summary of the main results

The frequency of possible reinfections by SARS-CoV-2 has increased markedly since the introduction and distribution in France of the Omicron variant, at the beginning of December 2021. **After a short stabilization at the beginning of January 2022, the proportion of possible cases of reinfection reported to the Overall COVID-19 cases have been on the rise again since week 04-2022 and accounted for 5.4% of all confirmed COVID-19 cases in week 11** (Figure 1C).

It seems likely that the attenuation of the post-infectious or post-vaccination immune response within the French population plays a role in this marked increase in the frequency of possible cases of reinfection, in particular in people who have not had booster dose of the anti-COVID-19 vaccine.

It is also very likely that the very strong distribution in France of the Omicron variant, characterized by increased transmissibility and significant immune escape, amplifies this phenomenon. In addition, **the upward resumption of the circulation of SARS-CoV-2 observed for several weeks in France and the emergence of the Omicron BA.2 sub-lineage, which has dominated since week 09-2022, are two factors that may play a role in the current trend of increasing numbers of reinfections.**

Several recent studies have demonstrated the possibility of occurrence of re-infection with BA.2 following infection with BA.1, including within a very short period of time (less than 60 days)¹. Nevertheless, they agree on the fact that these are probably rare events. Reinfections occurring within less than 60 days are not identifiable in this analysis. However, it should be noted that the share of possible reinfections occurring within a short time (between 60 and 89 days) has decreased since the introduction of Omicron in France. In addition, the frequency of reinfections with a screening result suggestive of Omicron during the two episodes of infection remains very low (less than 1% of all possible reinfections with an interpretable screening result during the two episodes). **These two elements are currently not in favor of a significant frequency of reinfections by Omicron after a first episode due to Omicron, whatever the sub-lineage in question.**

Possible cases of reinfection have been detected in all French regions, at different frequencies depending on the region (minimum: 2.7% in Réunion, maximum: 7 in Guyana).

Several factors may contribute to these regional disparities (COVID-19 screening rate, vaccination coverage, circulation of different variants, etc.), and additional analyzes are needed to better characterize their respective impact on the risk of reinfection with SARS-CoV-2.

The proportion of healthcare professionals and young adults (18-40 years old) among possible cases of reinfection is always higher than among confirmed cases of COVID-19 detected in SIDEP during the study period. *On the other hand*, the share of people aged over 60 among possible reinfections is lower than that among confirmed cases of COVID-19. Several factors may explain this observation, in particular overexposure to SARS-CoV-2 infection due to professional activity and/or less adherence to barrier measures and social distancing, or vaccination coverage. lower among 18-40 year olds, compared to older populations where booster dose vaccination coverage is highest [[link to PE](#)].

The available data on the presence or absence of symptoms during the two episodes of COVID-19 indicate that **the majority of possible cases of reinfection were symptomatic at the time of their detection by a positive test for SARS-CoV-2, without significant difference. compared to confirmed cases of COVID-19.**

¹ Chemaitelly et al., 2022, MedRxiv (<https://doi.org/10.1101/2022.02.24.22271440>); Stegger et al., 2022, MedRxiv (<https://doi.org/10.1101/2022.02.19.22271112>); UKSHA, Weekly national Influenza and COVID-19 surveillance report Week 12 report (up to week 11 data) 24 March 2022 It should be taken into account that the time to reinfection is highly dependent on the dynamics of

² successive epidemic waves.

Limits of this data

While these data provide valuable information on possible reinfections by SARS-CoV-2, they have a number of limitations to be taken into account in the interpretation we make of them.

First of all, the analysis of the database could only be done from January 1, 2021, due to the evolution of the pseudonymization algorithm deployed in January 2021, preventing the identification of reinfections that occurred from January 1, 2021 after a 1st episode of COVID-19 during the year 2020. This leads to **an underestimation of the frequency of reinfections**.

Furthermore, the fact that it is not possible to collect clinical information (for example, absence of symptoms suggestive of COVID-19 between the 2 episodes), virological (viral load and sequencing) or epidemiological (concept of exposure at risk preceding the positive test) in SIDEP limits this analysis to possible cases of reinfection. The level of proof that these events really correspond to reinfections is therefore limited; a part, although probably limited, of the possible cases of reinfection could correspond to false positives in RT-PCR or antigenic test, or to prolonged detection of viral material in an immunocompromised person.

Because of the 60-day minimum time between episodes used in our reinfection case definition to identify possible cases, any reinfection that might occur within a shorter time is not accounted for in this analysis. Nevertheless, we do not have, at this stage, elements indicating that the occurrence of a reinfection by SARS-CoV-2 less than 60 days after a primary infection is a frequent phenomenon, nor that the fact of not taken into account in this analysis can have a significant impact on our interpretation of these data in terms of frequency or trend.

Finally, the absence of information on the clinical severity in SIDEP is lacking here to characterize more finely the impact that reinfections by SARS-CoV-2 have on the healthcare system.

Conclusion

Despite their limitations, the available data on possible cases of reinfection are a useful contribution to describing and characterizing the epidemiology of COVID-19, particularly in the event of the emergence of a new variant of SARS-CoV-2.

This work needs to be continued and supplemented, in particular by matching the SIDEP database with other national databases, in order to estimate the risk of reinfection by SARS-CoV-2 over time, depending on the different variants or vaccination status, or to estimate the risk of a serious form in the event of reinfection. Such work will make it possible, in particular in conjunction with the teams of modellers, to contribute to the assessment of the impact that COVID-19 could have in the months and years to come on the health of populations and the healthcare system.

<p>Cite this document: Analysis of available data on SARS-CoV-2 reinfections from the SIDEP database. The point on. March 31, 2022. Saint-Maurice: Public Health France, 9 p. Director of publication: Pr Geneviève Chêne. Legal deposit: March 31, 2022</p>
