

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

Data as of April 28, 2022

## Key results

**961,550** possible cases of reinfection identified between March 2, 2021 and April 24, 2022, of which 96.7% since December 6, 2021 (beginning of the distribution of the Omicron variant in France)

**48%** of possible cases of reinfection were between 18 and 40 years old

**93%** of possible cases of reinfection for which a screening result was available and interpretable had a result suggestive of infection with the Omicron variant during the second episode

**6.9%** of all confirmed COVID-19 cases were possible reinfections, weekdays 2022-H16

## 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 (RT-PCR or Antigenic 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 April 24, 2022 inclusive. Indeed, a change concerning the identification of patients (pseudonym) in the SIDEP database 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 from March 2, 2021 (1st January 2021 + 60 days) are identifiable in this analysis, and **any reinfection that occurred from January 1 , 2021 after a first episode in 2020 is not identifiable in the SIDEP database for this analysis.**

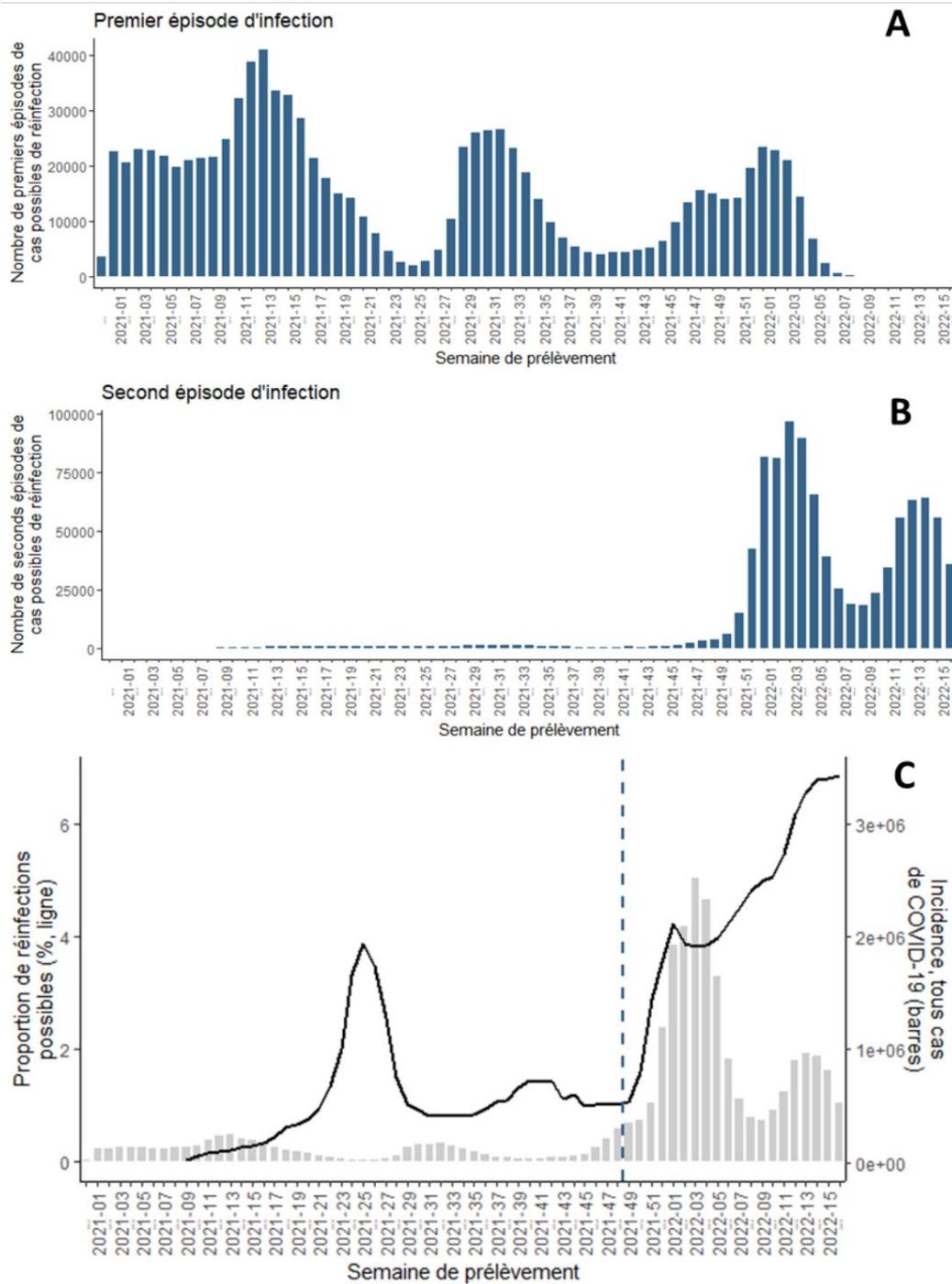
## Numbers and temporal-spatial distribution of possible cases of reinfection

From March 2, 2021 to April 24, 2022, 961,550 possible cases of reinfection as defined above were identified in the SIDEP database. 99% of them (n=948,103) had two distinct episodes and 1% (13,447 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. The vast majority of second episodes occurred during the 5th wave, with 96.7% (n=917,186) 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. Time distribution of first (panel A) and second (panel B) infection episodes for possible cases of reinfection having had two episodes, and proportion of possible cases of reinfection reported to all COVID-19 cases (panel C), during the study period (daily data)**

The vertical dotted blue line indicates December 6, 2021.



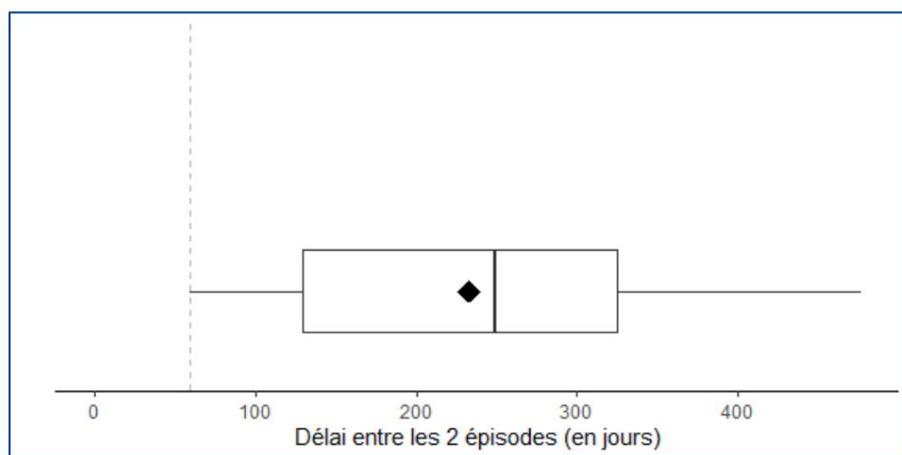
Source: SIDEP, Public Health France exploitation, from 01/01/21 to 04/24/22

Note that the ordinate scale is different between the three graphs.

**The mean time between the two episodes of infection was 233 days (i.e. just over 7 months), with a median of 249 days and an interquartile range of 130 to 325 days (Figure 2).**

Among the 948,103 cases with two episodes of infection, 13.6% had a delay between 60 and 89 days, 9.2% between 90 and 119 days, 15.7% between 120 and 179 days, 49.4% between 180 and 364 days and 12.1% 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 40,566 possible cases of reinfection having had their 2nd episode before December 20, 2021, and that it is 13.1% among the 907,537 possible cases of reinfection having had their 2nd episode since this date. Dec. 20 is the approximate date **Omicron became the majority among reinfections, according to screening data.**

**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**



Source: SIDEP, 01/01/21-24/04/22

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 first and third 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 3.8% of all confirmed cases of COVID-19 detected in the SIDEP database between March 2, 2021 and April 24, 2022. Over the entire period extending until December 5, 2021, this proportion was 0.7%. This proportion increased sharply from December 6, 2021, to 4.5% of all confirmed cases of COVID-19. **Weekdays 2022-S16, this proportion was 6.9%** (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 2.5% in Brittany and 4.8% 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 - April 24 2022), France

	Number of possible cases of reinfection	% of possible cases of reinfection out of all confirmed cases
Auvergne-Rhône-Alpes	113,359	3.2%
Burgundy-Franche-Comte	32,352	3.0%
Brittany	30,490	2.5%
Centre-Val-de-Loire	24,460	2.7%
Corsica	5,783	4.1%
Great East	72,334	3.2%
Guadeloupe	6,986	4.5%
Guyana	3,833	4.8%
Hauts-de-France	83,746	3.3%
Ile-de-France	216,470	4.0%
The meeting	11,869	2.8%
Martinique	5,398	3.5%
Mayotte	1,184	3.3%
Normandy	35,613	2.9%
New Aquitaine	61,272	2.7%
Occitania	89,586	3.6%
Pays de la Loire	37,264	2.5%
Provence-Alpes-Côte d'Azur	10,8737	4.5%
Unknown region	7	
National level	948 103	3.4%

## 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 (6.0% versus 3.7% and 47.8% versus 36.4%, respectively). Conversely, the proportion of people aged over 60 was lower (4.7% versus 10.8% for those aged 61-80 and 1.7% versus 2.8% 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-April 24, 2022), France

	Possible cases of reinfection	Confirmed cases of COVID-19
Share of women	56.7% 6.0%	54.1%
Proportion of healthcare professionals*		3.7%
Breakdown by age group		
< 18 years	24.6%	24.9%
old 18-40 years	47.8%	36.4%
old 41-60 years	21.1%	25.2%
old 61-80 years	4.7%	10.8%
old > 80 years old	1.7%	2.8%

\* Analysis carried out on the people for whom the information on the status of health professional was provided 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, **55.5% 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 (54.7%).

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		15.1%
Asymptomatic	Asymptomatic	20.1%
Symptomatic	Symptomatic	26.8%
Asymptomatic	Symptomatic	20.5%
Symptomatic	Asymptomatic	17.5%

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

In mainland France, 52.7% of possible cases of reinfection (n= 482,910) had an interpretable screening result in the SIDEP database for the 1st or 2nd episode of COVID-19, 23.1% (n= 212 194) had an interpretable screening result for at least the 2nd episode, and 11.5% (n= 105,323) 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.

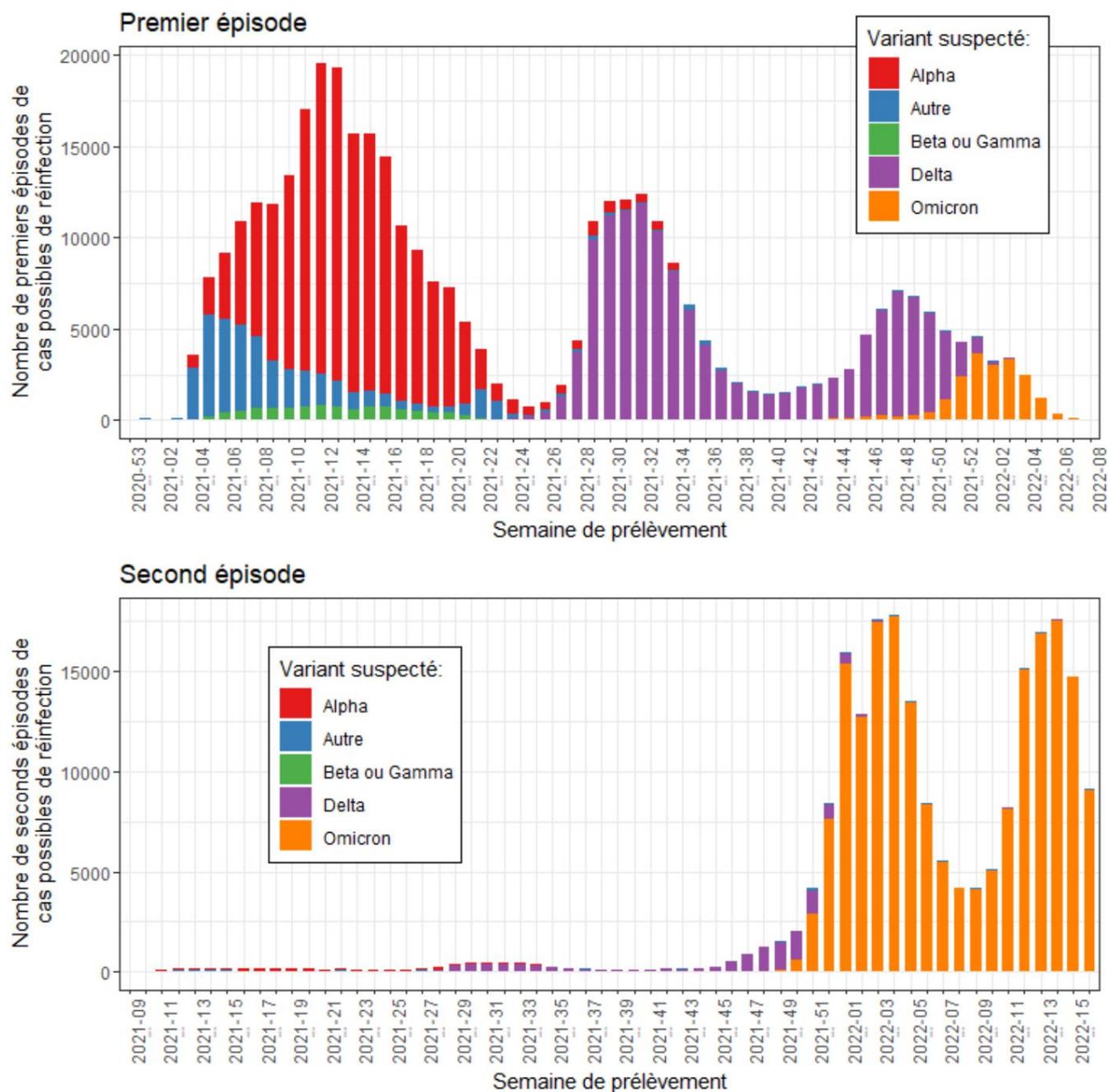
The majority of possible reinfections that occurred during the 3rd wave of spring 2021 are suspected to be due to the Alpha variant, while those that occurred during the 4th wave (summer 2021) are suspected to be due to the Delta variant. As of week 2021-W51, the majority of possible reinfections were suspected to be due to the Omicron variant (Figure 3).

Among the 105,323 possible cases of reinfection for which the information of the suspected variant was available for the first and the second episode, 39.5% of them presented a screening result compatible with a suspicion of Alpha variant during the 1st episode . and a suspicion of Omicron variant during the

2nd episode, and 35.8% of them presented a screening result compatible with a suspicion of Delta variant during the 1st episode and a suspicion of Omicron variant during the 2nd episode (Table 4). Finally, 6.7% of these cases had a screening result compatible with a suspicion of Omicron variant (or B.1.640) during both episodes.

In total, **over the entire study period, suspicion of the Omicron variant was found in 92.6% of the 212,194 possible cases of reinfection** for which an interpretable screening result was available for the 2nd episode, whereas the Omicron variant was only detected on national territory from December 2021.

**Figure 3. Temporal distribution of possible reinfection cases with an interpretable screening result for the first and second episode. Metropolitan France (daily data)**



Source: SIDEP, from 01/01/21 to 04/24/22

Note that the ordinate scale is different between the 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= 105,323), Metropolitan France**

		Second episode				
		Alpha	Beta or Gamma	Delta	Omicron	Other
First episode	Alpha	0.6%	0.0% 0.0%	2.1%	39.5%	0.4%
	Beta or Gamma	0.0%	0.0% 0.0%	0.2%	2.5%	0.0%
	Delta	0.0%	0.0%	1.2%	35.8%	0.2%
	Omicron	0.0%		0.0%	6.7%	0.0%
	Other	0.1%		0.7%	10.0%	0.2%

## Analysis of data on possible reinfections by SARS-CoV-2 on the basis of a minimum delay of 30 days versus 60 days between the two episodes of Covid-19

For all the analyzes presented above, two positive diagnoses of SARS-CoV-2 are considered possible reinfections only if they are separated by at least 60 days. The description of cases of early reinfection in the literature has led to questioning this threshold. We present below an analysis of the impact of lowering it to 30 days.

From January 31, 2021 to March 27, 2022, 848,715 possible cases of reinfection with a minimum time to reinfection of 30 days were identified in the SIDEP database. Of these, 98% (832,391 people) had two episodes of infection, and 2% (16,324 people) had 3 or more episodes of infection at least 30 days apart.

By only retaining for the analysis people who had presented two distinct episodes of infections, nearly 13% of them presented a delay between the two episodes of between 30 and 59 days. No increase in their frequency has been observed during the study period, in particular since the introduction and dissemination of the Omicron variant in France. Moreover, these possible reinfections occurring within a period ranging from 30 to 59 days show marked differences with respect to those occurring at least 60 days apart.

Table 5 presents the distribution by age group of possible cases of reinfection occurring within a period of between 30 and 59 days versus those occurring within a period greater than or equal to 60 days. We observe that the proportion of people aged over 60 is significantly higher among possible reinfections occurring within a short period of time (30-59 days) compared to those occurring 60 days or more after a first episode (19% versus 5.4%). On the other hand, the proportion of people aged 18 to 40 is lower in possible early reinfections compared to others (34.3% versus 49.5%).

Furthermore, it was shown through these data that the proportion of women among the cases of reinfection was comparable in the two delay groups, that that of health professionals was slightly lower among possible reinfections with a delay of between 30 and 59 days compared to the others (4% versus 6%), and that that of people residing in nursing homes was significantly higher (2% versus 0.7%).

Table 5. Distribution of possible cases of reinfection by age group and according to the time between the two episodes, period from 01/31/2021 to 03/27/2022

The two episodes, period from 31/01/2021 to 27/03/2022 Time between the two episodes of infection	All possible cases of reinfection (n=832,391)		Possible reinfections occurring within 30-59 days (n=107,568)		Possible reinfections occurring within 60 days or more (n=724,823)	
	Number	Percentage	Number	Percentage	Number	Percentage
< 18 years old	207,974	25%	28,972	26.9%	179,002	24.7%
18 -40 years old	395,888	47.6%	36,931	34.3%	358,957	49.5%
41 – 60 years	167 658	20.1%	21,094	19.6%	146,564	20.2%
61 – 80 years	41 801	5%	12,595	11.7%	29,206	4%
> 80 years	18,132	2.2%	7,719	7.2%	10,413	1.4%
Unknown age	938	0.1%	257	0.2%	681	0.1%

It has been shown that age is associated with a prolonged duration of detection of the viral genome after a primary infection and that it is moreover likely that regular screening campaigns in communities of elderly people favor these prolonged detections. Thus, these observations suggest that the specificity of the case definition of a possible reinfection would decrease markedly by shortening the delay from 60 to 30 days, with a higher proportion of "false-positives", i.e. cases prolonged virus detection and not actual reinfection with SARS-CoV-2.

This analysis also showed that the frequency of possible reinfections with a result suggestive of infection by Omicron at both episodes is higher than that of the other identical combinations of screening results, regardless of the delay. This illustrates well the immune escape capacities of this variant compared to the wild strain of SARS-CoV-2 or other variants, and is consistent with several recent studies which have shown that reinfections with SARS-CoV-2 can occur very soon after a first episode of COVID-19, in particular by Omicron.

Nevertheless, the occurrence of a reinfection very shortly after a first episode of COVID-19 seems to remain a rare phenomenon, and the proportion of these early reinfections is a minority among all reinfections. It therefore seems very likely that by keeping the timeframe at 60 days, the underestimation of the true number of SARS-CoV-2 reinfections is minor.

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## 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 steadily increased since week 2022-W04 and accounted for 6.9% of all confirmed COVID-19 cases in week 2022-W16** (Figure 1C).

It is very likely that the very strong distribution in France of the Omicron variant, characterized by increased transmissibility and significant immune escape, plays a significant role in this increase in the frequency of possible cases of reinfection. It also seems more likely that the decrease in post-infectious or post-vaccination immune protection over time in the French population amplifies this phenomenon. **In addition, the upward resumption of SARS-CoV-2 circulation observed from week 2022-S09 to week 2022-S14 and the emergence of the Omicron BA.2 sub-lineage, which is more transmissible than BA. 1 and majority since week 2022-W09, are two factors that may play a role in the current trend of increasing numbers of reinfections.**

Several recent studies have highlighted the possibility of occurrence of reinfection with BA.2 following

BA.1 infection, including within a very short period (less than 60 days)<sup>1</sup>. Nevertheless, these studies agree on the fact that these are probably rare events. The analysis of possible reinfections occurring between 30 and 59 days shows that it is difficult to take them into account due to lack of specificity of the signal. It should be noted that the proportion of possible reinfections occurring within a short period of time (between 60 and 89 days) has decreased since the introduction of Omicron in France<sup>2</sup>. The frequency of reinfections with a screening result suggestive of Omicron during the two episodes of infection remains in the minority but is clearly increasing (6.7% of all possible reinfections with an interpretable screening result during the two episodes) showing a probable effect of the strong circulation of BA.2 between the weeks 2022-S09 to 2022-S14.

### **Possible cases of reinfection have been detected in all French regions, at different frequencies depending on the region** (minimum: 2.5% in Brittany, maximum: 4.8% 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, including overexposure to SARS-CoV-2 infection due to professional activity and/or less adherence to barrier measures and social distancing, lower vaccination coverage among 18-40 year olds compared to older populations where booster dose vaccination coverage is highest, or even the impact of all-cause mortality among older people, which de facto reduces the probability of noticing a reinfection.

The available data on the presence or absence of symptoms during the two episodes of COVID-19 indicate that **55% 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.**

## **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 after a 1st episode of COVID-19 during the year 2020.

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.

Finally, data on vaccination status were not available for this analysis and the absence of information on clinical severity in SIDEp is lacking here to characterize more finely the impact that reinfections with SARS-CoV-2 have had on the healthcare system.

<sup>1</sup> 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

<sup>2</sup> successive epidemic waves.

## 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.

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