Vaccine 72 (2026) 128057

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

COVID-19 vaccination: Does knowledge of higher immunity influence first and second COVID-19 booster uptake? A study carried out in a university population

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ARTICLE INFO

Keywords:
Immunity
first and second COVID-19 booster uptake
prevention
public health

ABSTRACT

Background: Knowledge of prior immunity may influence individuals' decisions about continuing their vaccination schedule. Based on a previous study, we hypothesise that participants who believe they have higher immunity due to knowledge of previous infection(s) or a higher level of neutralising antibodies will be less likely to get a boost, namely a first and a second COVID-19 booster vaccine.
Methods: This research is part of a longitudinal study carried out among students and staff of the University of Liège (ULiège), Belgium, between April 2021 and December 2022, whose objectives included studying vaccine hesitancy to COVID-19. For the analyses, two dependent variables were considered: the first and the second COVID-19 booster vaccine (yes/no). Binary logistic regressions were performed to explore the relationship between these variables and sociodemographic characteristics, health literacy, past COVID-19 vaccination intentions, knowledge of SARS-CoV-2 infection and anti SARS-CoV-2 neutralizing antibody levels.
Results: The sample included 822 participants. Globally, 88.8% of participants received the first booster vaccine compared to 21.8% for the second booster vaccine. Lower past COVID-19 vaccine intention, knowledge of previous SARS-CoV-2 infection and higher neutralizing antibody levels were associated with a lower first COVID-19 booster uptake. Lower age, lower past COVID-19 vaccine intention and knowledge of higher neutralizing antibody levels were associated with a lower second COVID-19 booster uptake.
Conclusions: The results show that COVID-19 vaccination decreases with time. Our initial hypothesis is partially confirmed, with an influence of knowledge of previous SARS-CoV-2 infection and neutralizing antibodies on the first booster vaccine uptake and an influence of knowledge of neutralizing antibodies on the second booster vaccine. A long-term, personalized and transparent educational approach, centred on knowledge of prior immunity for the individual and current scientific knowledge/uncertainties about vaccine and infection-related protection, appears to be necessary to enable individuals to make a more informed decision about vaccination.

1. Introduction

Since the development of COVID-19 vaccines and official marketing approval for the first vaccine in Europe at the end of December 2020 [1], vaccination campaigns have been launched to recommend primary vaccination. Due to the decrease of immunity and so vaccine protection over time [2–4] including limited protection against variants [5], booster vaccines were recommended. Several studies have highlighted the benefits of booster vaccines in protecting individuals against infection and severe COVID-19-related outcomes namely severe disease,

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https://doi.org/10.1016/j.vaccine.2025.128057
Received 28 January 2025; Received in revised form 13 November 2025; Accepted 27 November 2025
Available online 12 December 2025

hospitalisation and death [6–11]. Data on vaccination coverage around the world at the end of December 2023 showed that 56.0% of people had received a complete primary vaccination and 28.0 % had received a COVID-19 booster vaccine [12]. In Belgium, after the vaccination of priority groups (healthcare workers, elderly people, people at risk, etc.), COVID-19 primary vaccination for the general population (in this study the general population refers to the population aged 18 to 64) started on May-June 2021 with mainly two types of vaccines namely mRNA vaccines (PfizerBioNTech and Moderna in two doses), and viral vector vaccines (AstraZeneca in two doses and Johnson & Johnson in a single dose). Booster vaccinations with mRNA vaccines started on December 2021 for the first booster and on September 2022 for the second booster vaccine with notably bivalent vaccine for the general population. However, it is important to note that booster doses, or even more frequent booster doses, have been recommended for select populations at different stages of the COVID-19 vaccination campaign [13]. According to Sciensano, 76.9% of Belgian people were primary vaccinated, 61.0% received a first booster vaccine, and 32.8% received a second booster vaccine at the end of December 2022 [14].

From a public health perspective, and in order to better support individuals in their vaccination decisions, it is important to understand the factors that influence their choice, including whether or not to continue with their vaccination schedule. Several studies highlighted the reasons for a drop in vaccination by identifying the factors of a lower booster uptake such as (e.g.) lower age, lower level of education, most serious side effects after second dose of primary vaccination, higher complacency, higher conspiracy-based beliefs, lower compliance with official vaccination recommendations [15–19]. However, most studies have not examined the influence of knowledge of prior immunity (such as a previous COVID-19 infection and/or the presence of neutralising antibodies) on COVID-19 booster vaccinations or have sometimes produced controversial results [19,20]. In addition, most of these studies have been carried out on the general population [20]. Studying the factors influencing vaccine uptake in specific groups such as the academic population is crucial if interventions tailored to the needs of this population are to be designed and developed, such as recommended in da Silva Sousa 2025 [21]. In Belgium, a study carried out at the University of Liege among 1030 participants showed that a higher past COVID-19 primo-vaccination intention was associated with a maintenance of non-intention regarding first COVID-19 booster vaccine. In addition, this study showed that knowledge of previous SARS-CoV-2 infection and of a higher neutralizing antibody level was associated with a change between positive intention to non-vaccination [22].

Based on the study mentioned above, we observed that knowledge of prior immunity can influence vaccination against COVID-19, probably because individuals believe they are protected against the virus. So, we wanted to continue our research and, in this study, we sought to understand whether knowledge of higher immunity had an influence on COVID-19 booster vaccinations among an academic population. We hypothesized that participants who believe they have higher immunity due to knowledge of previous infection(s) or a higher level of neutralizing antibodies will be less likely to get a boost, namely a first and a second COVID-19 booster vaccine.

2. Materials and methods

2.1. Context

This research is part of a longitudinal study carried out among students and staff of the University of Liège (ULiège), Belgium, between April 2021 and December 2022, with the aim of studying SARS-CoV-2 infections, immune responses to SARS-CoV-2 infections and vaccines, and vaccine hesitancy (SARSSURV-ULiège study). The inclusion criteria were as follows: participants had to be between 18 and 67 years of age (67 being the legal retirement age in Belgium) and to give their participation consent via an online form. Any member of staff whose contract came to an end before 31 December 2021 and students (first year of Bachelor and diploma year) enrolled in the 2020-2021 academic year were excluded as the participants could not have been followed over a longer period of time [23]. To address this issue of vaccine hesitancy, several studies have been carried out [22,24,25] using the SARSSURV database, each with more specific objectives.

The SARSSURV study, conducted among staff and students at the University of Liège, made it possible to study knowledge of anti-SARS-CoV-2 immunity and to monitor the vaccination status of participants (see 2.3. Studied parameters and data collection). In this study, the opportunity provided by the SARSSURV study was used to assess the impact of knowledge of anti-SARS-CoV-2 immunity on COVID-19 vaccination monitoring.

2.2. Study population

The population of ULiège comprises 5,633 staff and 28,064 students. All members of the university who met the study criteria received a personalised invitation to participate in the SARSSURV study, i.e. 3,576 staff and 25,378 students. This was a voluntary sampling method. A total of 1706 participants were included in SARSSURV study and after checking the inclusion criteria, 3 were not included. During the SARSSURV study, 849 participants were lost during follow-up, not allowing monitoring of their vaccination schedule. Thus, 854 participants were still enrolled in the SARSSURV study at the end of the study (December 2022). Among these, 4 participants had inconsistent data regarding COVID-19 primary vaccination and 26 were not COVID-19 primary vaccinated (24 not vaccinated and 2 not vaccinated during the recommended time-period[2]). So, 824 participants were fully vaccinated during the primary vaccination period. After that, 2 participants were COVID-19 boosted outside the recommended time-period[3]. Finally, 822 participants were boosted or not during the booster vaccination period and were included in this present study (Figure 1).

2.3. Studied parameters and data collection

The data were collected from several sources at various times during the SARSSURV study. First, the sociodemographic characteristics, health literacy, SARS-CoV-2 infection and eventually primary vaccination were collected using the self-administered questionnaires distributed via an online platform during the study registration period, starting on 1 April 2021 (before the launch of the primary vaccination campaign for general population in Belgium).

Next, throughout the SARSSURV study, the participants were invited to provide (via a dedicated secure online platform or by calling/emailing a member of the research team) information regarding any change in their vaccination status or a SARS-CoV-2 infection, as soon as possible, in order to keep the database up-to-date. Following any new infection or vaccination, a nurse from the research team scheduled a blood draw at two weeks and then at every three months.

Finally, intentions regarding a first and a second COVID-19 booster vaccine were collected using a self-administered questionnaire that was distributed via an online platform. Regarding first COVID-19 booster vaccine intention, data were collected between 13 October 2021 and 26 December 2021 (before the launch of the first booster campaign for general population in Belgium).

Regarding second COVID-19 booster vaccine intention, data were collected between 12 July 2022 and 22 September 2022 (before the

[2] The end of the recommended time-period for primary vaccination extends until before the start of the campaign for the first booster dose for the general population.

[3] The end of the recommended time-period for the first booster dose extends until before the start of the campaign for the second booster dose for the general population.

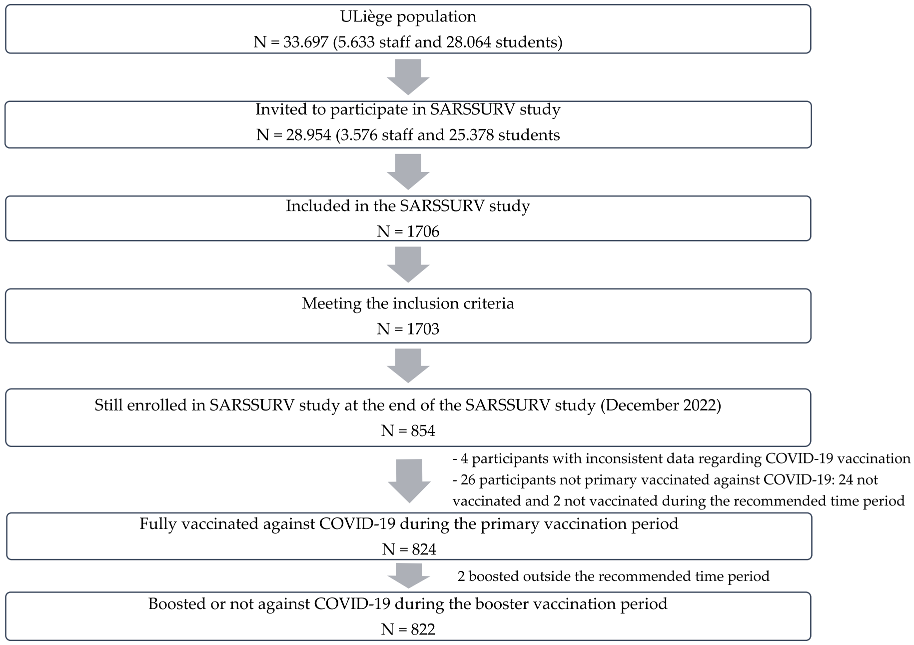

Fig 1. Flowchart of study participants

launch of the second booster campaign for general population in Belgium).

2.3.1. *Dependent variables*

2.3.1.1. First and second COVID-19 booster vaccine. Participants reported any change in their vaccination status and the date of the vaccination. If participants reported a date for booster vaccine, they were considered boosted, namely a first booster vaccine and/or a second booster vaccine. Otherwise, they were considered not boosted.

2.3.2. *Independent variables*

2.3.2.1. Knowledge of anti-SARS-CoV-2 immunity. The knowledge of anti-SARS-CoV-2 immunity was measured via two parameters in this study:

- *Knowledge of personal SARS-CoV-2 infection*: The SARS-CoV-2 infection history included SARS-CoV-2 infections (yes/no), confirmed by a saliva-based self-test performed as part of the SARSSURV study [23] or by a test carried out outside of the study and reported by a research team participant (PCR saliva test, PCR nasopharyngeal test, self-test).
- *Knowledge of neutralizing antibodies*: The level of the neutralizing antibodies against COVID-19 was collected using the most recent blood sample, which was scheduled 15 days after a positive SARS-CoV-2 infection or a COVID-19 vaccination and then every three months as follow-up. A member of the research team communicated the results to each participant via phone or letter. The neutralising antibody result was communicated to participants in addition to its categorisation corresponding to the reference thresholds ($< 1/20$: Insufficient level of neutralising antibodies; $\geq 1/20$ and $< 1/320$: Normal level of neutralising antibodies; $\geq 1/320$: High level of neutralising antibodies). The current uncertainties and ongoing studies concerning the effectiveness of protection against infection by different variants, and the duration of protection over time were also communicated to participants to inform them of the limited current knowledge and the need to implement the recommended preventive measures. Virus neutralization test (VNT) was carried out with SARS-CoV-2 strain BetaCov/Belgium/SartTilman/2020/1 in 96-well plates containing Vero E6 cells (ATCC CRL-1586). Six dilutions of each heat-inactivated serum were used (1:10 to 1:320—corresponding to final testing dilutions 1:20 to 1:640). In each VNT, a positive control serum from the Belgian National Reference Centre (Sciensano) was used. Sera were mixed vol/vol with 100 $TCID_{50}$/reaction of SARS-CoV-2 virus and incubated at 37°C for 1 hour. Then, the serum plus virus mixture was transferred to the cells in suspension in triplicate. The VNT relies on cytopathic effect (CPE) observation under light microscopy at day 5 post-infection. Dilutions of serum associated with CPE were considered as negative, while the absence of CPE indicated a complete neutralization of SARS-CoV-2 inoculum (positive). Virus neutralization titer was reported as the highest dilution of serum that neutralized CPE in 50% of the wells.

2.3.3. *Other independent variables*

2.3.3.1. Sociodemographic Characteristics. The sociodemographic characteristics included the institutional status (response scale: student or staff member), gender (response scale: male or female) and age (response scale: open ended response in years).

2.3.3.2. Health Literacy. The single item literacy screener (SILS), slightly adapted for this study, was used in order to assess the health literacy of ULiège staff members and students [26]. “When you read instructions, pamphlets, or other written material from your doctor or pharmacy, how often do you need help to understand the messages?” (response scale: Likert scale ranging from 0 (never) to 100 (always)).

2.3.3.3. Intention regarding first and second COVID-19 booster vaccine. The participants’ intentions to be boosted against COVID-19 were collected using the following two questions:

- One question for first COVID-19 booster vaccine intention: “What is your current intention regarding accepting a booster dose when

offered? (October-December 2021) (response scale: Likert scale ranging from 0 (no intention) to 100 (total intention))";
- One question for second COVID-19 booster vaccine intention: "On a scale of 0 to 100, what would be your intention to accept a new dose of vaccine?" (response scale: Likert scale ranging from 0 (no intention) to 100 (total intention))" (July-September 2022).

2.4. Data analysis

Two dependent variables were considered for the analyses, namely the first COVID-19 booster vaccine (yes/no) and the second COVID-19 booster vaccine (yes/no).

For participants vaccinated, the SARS-CoV-2 infection(s) between the previous COVID-19 vaccine and the new COVID-19 vaccine, namely between the primary vaccination and the first booster vaccine or between the first booster vaccine and the second booster vaccine were grouped into a single variable (presence or absence of infection). If participants were not boosted (first booster dose or second booster dose), the absence or presence of infection(s) was considered until the launch of the vaccination campaign for the next vaccine.

The histograms, quantile-quantile plots, and the Shapiro–Wilk tests were used to evaluate the normality of the distribution of the quantitative variables. Appropriate descriptive statistics were performed, with the frequency and percentage (%) for the qualitative variables and median (P50) and the interquartile ranges (IQR, P25–P75) for skewed distributed quantitative variables. Comparison between staff and students was made with $\chi 2$ test for qualitative variables.

The univariate binary logistical regressions were performed to explore the relationship between, respectively, the first COVID-19 booster vaccine or the second COVID-19 booster vaccine and the various factors. Significant variables ($p<0.05$) in univariate analyses were included in the multivariate model. The significance level was set at $p < 0.05$. The statistical analyses were performed by institutional status, i.e. staff and students. The analyses were carried out using R statistical software version 4.1.0. The data are stored for as long as necessary in order to achieve the study's objectives. The statistical analyses were performed on the observed data only; the missing data were not imputed.

2.5. Ethical and Legal Aspects

The study was approved by the University Hospital of Liège Ethics Committee (reference number 2021/96, dated 26 March 2021). Written informed consent online was obtained from each participant before enrolment in the SARSSURV study. After the enrolment in the SARSSURV study, a unique identification code (ID) was attributed to each participant [23]. The data were handled in a confidential manner by the SARSSURV team and anonymized prior to any analysis. The compliance with data protection regulations were approved by the official University of Liège data protection officer.

3. Results

3.1. Characteristics of the study sample

As shown in Table 1, of the 822 participants included in this study, 76.4% were staff members and 62.2% were female. The median age of participants was 41.0 (IQR, 28.0-50.0) years (45.0 (38.0-53.0) years for staff and 23.0 (20.0-27.0) years for students). Participants reported a median health literacy score of 7.0 (0-19.0) (7.0 (0-15.8) for staff and 9.0 (0-20.0) for students) on a Likert scale ranging from 0 (never) to 100 (always).

The median intention regarding COVID-19 vaccine was 100 (85.0-100) (100 (90.0-100) for staff and 95.0 (71.5-100) for students) for the first booster vaccine and 80.0 (50.0-100) (80.0 (50.0-100) for staff and 75.5 (51.8-95.0) for students) for the second booster vaccine. Regarding SARS-CoV-2 infection, 16.6% of participants (16.4% of staff and 17.0% of students) had a SARS-CoV-2 infection before first booster vaccine and 54.0% (57.2% of staff and 42.7% of students) before second booster vaccine. Neutralizing antibodies before first booster vaccine were categorized as insufficient for 12.8% of participants (14.5% of staff and 5.9% of students), normal for 65.1% of participants (64.3% of staff and 68.4% of students) and high 22.2% of participants (21.3% of staff and 25.7% of students). Before second booster vaccine, 0.4% of participants (0.5 of staff and 0% of students) had an insufficient level of neutralizing antibodies, 26.5% (27.3% of staff and 23.6% of students) a normal level and 73.1% (72.2% of staff and 76.4 of students) a high level. Due to lower distribution of the variable in the insufficient category, particularly among students and before second booster vaccine, only the normal and high categories were considered for univariate and multivariate analyses.

Table 1
Characteristics of 822 participants included in the study

	All		Staff		Students	
Variable	**N**	**N (%)**	**N**	**N (%)**	**N**	**N (%)**
Institutional status	822					
Staff		628 (76.4)				
Student		194 (23.6)				
Gender	822		628		194	
Female		511 (62.2)		382 (60.8)		129 (66.5)
Male		311 (37.8)		246 (39.2)		65 (33.5)
Age (years)*	822	41.0 (28.0-50.0)	628	45.0 (38.0-53.0)	194	23.0 (20.0-27.0)
Health literacy*	813	7.0 (0.0-19.0)	626	7.0 (0-15.8)	187	9.0 (0-20.0)
First COVID-19 booster vaccine intention*	703	100 (85.0-100)	535	100 (90.0-100)	168	95.0 (71.5-100)
Second COVID-19 booster vaccine intention*	604	80.0 (50.0-100)	484	80.0 (50.0-100)	120	75.5 (51.8-95.0)
SARS-CoV-2 infection (before first booster vaccine)	822		628		194	
Yes		136 (16.6)		103 (16.4)		33 (17.0)
No		686 (83.5)		525 (83.6)		161 (83.0)
SARS-CoV-2 infection (before second booster vaccine)	730		566		164	
Yes		394 (54.0)		324 (57.2)		70 (42.7)
No		336 (46.0)		242 (42.8)		94 (57.3)
Neutralizing antibodies (before first booster vaccine)	745		593		152	
Insufficient		95 (12.8)		86 (14.5)		9 (5.9)
Normal		485 (65.1)		381 (64.3)		104 (68.4)
High		165 (22.2)		126 (21.3)		39 (25.7)
Neutralizing antibodies (before second booster vaccine)	726		565		161	
Insufficient		3 (0.4)		3 (0.5)		0 (0)
Normal		192 (26.5)		154 (27.3)		38 (23.6)
High		531 (73.1)		408 (72.2)		123 (76.4)

*P50 (P25-P75)
Legend: N, number

3.2. First and second COVID-19 booster uptake

First and second COVID-19 booster uptake are shown in Table 2. Regarding first booster vaccine, 88.8% of participants (90.1% of staff and 84.5% of students) were boosted. Regarding second booster vaccine, 21.8% of participants (25.8% of staff and 7.9% of students) were boosted. The percentage of boosted participants (first and second booster) is significantly higher among staff members.

3.3. Factors influencing first COVID-19 booster uptake

Results of univariate and multivariate analyses of factors influencing first COVID-19 booster uptake among staff members and students are presented in Table 3.

Among staff, univariate analyses showed that gender, age, first COVID-19 booster vaccine intention, knowledge of SARS-CoV-2 infection and neutralizing antibody level were significantly associated with first COVID-19 booster uptake. Regarding multivariate analysis, first COVID-19 booster vaccine intention, knowledge of SARS-CoV-2 infection and neutralizing antibody level were significantly associated with first COVID-19 booster uptake. The higher the first COVID-19 booster vaccine intention, the less likely participants were not to be boosted. Participants who knew they had been infected or who knew they had higher level of neutralising antibodies were less likely to receive a booster dose than participants who had not been infected or who had normal levels of neutralising antibodies. The model is written as:

$$\log(\pi/1-\pi) = 0.83 + 0.68\ \text{Gender} - 0.03\ \text{Age} - 0.05\ \text{First COVID} - 19\ \text{booster vaccine intention} + 3.18\ \text{SARS} - \text{CoV} - 2\ \text{infection (before first booster vaccine)} + 1.50\ \text{Neutralizing antibodies (before first booster vaccine)}$$

Among students, univariate analysis showed that first COVID-19 booster vaccine intention, knowledge of SARS-CoV-2 infection and neutralizing antibody level were significantly associated with first COVID-19 booster uptake. Regarding multivariate analysis, the same factors as the staff members were significantly associated with first COVID-19 booster uptake. The model is written as:

$$\log(\pi/1-\pi) = -1.01 - 0.02\ \text{First COVID} - 19\ \text{booster vaccine intention} + 2.68\ \text{SARS} - \text{CoV} - 2\ \text{infection (before first booster vaccine)} + 1.47\ \text{Neutralizing antibodies (before first booster vaccine)}$$

Table 2
First and second COVID-19 booster uptake of 822 participants included in the study

	All		Staff		Students		
Variable	N	N (%)	N	N (%)	N	N (%)	P
First COVID-19 booster vaccine	822		628		194		**0.03**
Yes		730 (88.8)		566 (90.1)		164 (84.5)	
No		92 (11.2)		62 (9.9)		30 (15.5)	
Second COVID-19 booster vaccine	730		566		164		**<0.0001**
Yes		159 (21.8)		146 (25.8)		13 (7.9)	
No		571 (78.2)		420 (74.2)		151 (92.1)	

Legend: N, number; P, p-value; *, significant p-value < 0.05

3.4. Factors influencing second COVID-19 booster uptake

Results of univariate and multivariate analyses of factors influencing second COVID-19 booster uptake among staff members and students are presented in Table 4.

Among staff, univariate analyses showed that gender, age, second COVID-19 booster vaccine intention, knowledge of SARS-CoV-2 infection and neutralizing antibody level were significantly associated with second COVID-19 booster uptake. Regarding multivariate analysis, age, second COVID-19 booster vaccine intention and knowledge of neutralizing antibody level were significantly associated with second COVID-19 booster uptake. The higher the age and the second COVID-19 booster vaccine intention, the less likely participants were not to be boosted. Participants who knew they had higher level of neutralising antibodies were more likely not to be boosted than participants who had a normal neutralizing antibody level. The model is written as:

$$\log(\pi/1-\pi) = 7.34 + 0.28\,Gender - 0.10\,Age - 0.03\,Second\,COVID - 19\,booster\,vaccine\,intention + 0.23\,SARS - CoV - 2\,infection\,(before\,second\,booster\,vaccine) + 0.79\,Neutralizing\,antibodies\,(before\,second\,booster\,vaccine)$$

Among students, univariate analyses showed that only second COVID-19 booster vaccine intention was significantly associated with second COVID-19 booster uptake. The higher the second COVID-19 booster vaccine intention, the less likely participants were not to be boosted.

4. Discussion

4.1. First and second COVID-19 booster uptake

The results of our study showed that COVID-19 vaccination decreases with doses, with 88.8% of participants who had the first booster vaccine compared to 21.8% for the second booster vaccine. There are several possible explanations for this such as a return to normal life after the first booster dose due to a decrease in cases and less concern than when the omicron variant first appeared, as expressed by people aged 18 and over living in the US [27]; a decrease in precautionary measures [13] and, more generally, vaccine fatigue [28,29]. This decrease in the percentage was also observed in the national data [14]. This decrease in vaccination over time suggests that support should be provided throughout vaccination campaigns because repeated doses are necessary to obtain longer-lasting immunity [30].

In addition, our results highlighted a significant difference in percentages between staff and student with a higher percentage of staff than students (90.1% and 84.5% respectively for the first booster), particularly for the second booster (25.8% and 7.9% respectively). There are several possible explanations for this: (1) the younger population, less affected by severe forms of COVID-19, may have initially intended to get vaccinated for the sake of collective protection by reducing virus transmission. However, advances in scientific knowledge have shown that transmission is still possible despite vaccination [30,31], which may have influenced the decision of younger adults to receive the first and second booster doses; (2) younger participants are unsure if they are concerned by this second booster dose because they have not received an official invitation [13].

Influence of knowledge of anti-SARS-CoV-2 immunity on first and second COVID-19 booster uptake

The results of this present study showed that our initial hypothesis "participants who believe they have higher immunity due to knowledge of previous infection(s) or a higher level of neutralizing antibodies will be less likely to get a boost, namely a first and a second COVID-19 booster vaccine" is partially confirmed:

Table 3
Results of univariate and multivariate binary logistic regressions of factors influencing first COVID-19 booster uptake among staff members and students

	Staff					Students				
	Univariate			Multivariate (n = 429)		Univariate			Multivariate (n = 123)	
Variable	n	No vs Yes OR (95%CI)	P	No vs Yes OR (95%CI)	P	n	No vs Yes OR (95%CI)	P	No vs Yes OR (95%CI)	P
Gender	628		**0.0088**		0.18	194		0.38		
Female (vs male)		2.16 (1.21-4.08)		1.97 (0.74-5.69)			1.46 (0.63-3.70)			
Age (years)	628	0.96 (0.94-0.98)	**0.0016**	0.97 (0.93-1.02)	0.20	194	1.00 (0.94-1.05)	0.99		
Health literacy	626	1.01 (0.99-1.02)	0.34			187	1.01 (0.99-1.03)	0.39		
First COVID-19 booster vaccine intention	535	0.95 (0.94-0.96)	**<0.0001**	0.95 (0.93-0.97)	**<0.0001**	168	0.98 (0.97-0.99)	**0.0019**	0.98 (0.96-0.99)	**0.0048**
SARS-CoV-2 infection (before first booster vaccine)	628		**<0.0001**		**<0.0001**	194		**<0.0001**		**<0.0001**
Yes (vs. No)		31.85 (16.93-63.49)		24.06 (8.98-75.08)			18.51 (7.54-48.28)		14.60 (4.53-53.40)	
Neutralizing antibodies (before first booster vaccine)	507		**<0.0001**		**0.0019**	143		**<0.0001**		**0.0126**
High (vs. Normal)		9.19 (5.15-16.95)		4.50 (1.73-12.29)			8.06 (3.32-20.63)		4.36 (1.38-14.43)	

Legend: n, number; OR, odds ratio; P, p-value; *, significant p-value < 0.05

Table 4
Results of univariate and multivariate binary logistic regressions of factors influencing second COVID-19 booster uptake among staff members and students

	Staff					Students				
	Univariate			Multivariate (n = 480)		Univariate			Multivariate (n = /)	
Variable	n	No vs Yes OR (95%CI)	P	No vs Yes OR (95%CI)	P	n	No vs Yes OR (95%CI)	P	No vs Yes OR (95% CI)	P
Gender	566		**0.0091**	1.33 (0.82-2.15)	0.25	164		0.75		
Female (vs male)		1.66 (1.13-2.43)					0.82 (0.21-2.65)			
Age (years)	566	0.90 (0.88-0.92)	**<0.0001**	0.91 (0.88-0.93)	**<0.0001**	164	0.96 (0.90-1.03)	0.25		
Health literacy	565	1.00 (0.99-1.01)	0.88			158	1.01 (0.98-1.05)	0.71		
Second COVID-19 booster vaccine intention	484	0.97 (0.96-0.97)	**<0.0001**	0.97 (0.96-0.98)	**<0.0001**	120	0.96 (0.91-0.99)	**0.01**		
SARS-CoV-2 infection (before second booster vaccine)	566		**0.0406**		0.35	164		0.75		
Yes (vs. No)		1.49 (1.02-2.17)		1.26 (0.77-2.06)			1.21 (0.39-4.16)			
Neutralizing antibodies (before second booster vaccine)	562		**<0.0001**		**0.0026**	161		0.96		
High (vs. Normal)		2.40 (1.60-3.59)		2.21 (1.32-3.71)			0.97 (0.21-3.37)			

Legend: n, number; OR, odds ratio; P, p-value; *, significant p-value < 0.05

1) The influence of participants' knowledge of previous SARS-CoV-2 infection on first COVID-19 booster uptake: Our study showed that having ever had SARS-CoV-2 infection was a predictor of the first booster vaccine refusal among staff and students, this factor become statistically not significant regarding the second booster. A significant negative effect of SARS-CoV-2 infection(s) on first COVID-19 booster uptake was also demonstrated in other studies; among Norwegian adults [32], in an academic population in Belgium [22] and in a general population in Belgium [33]. There are several possible explanations for this. First, worries about symptoms experienced following infection have decreased due to mainly mild to moderate forms [34–36]. A second explanation is the potentially limited scientific knowledge about the need for vaccination following infection while several studies have highlighted the benefits of hybrid immunity [11,37–39].

2) The influence of participants' knowledge of neutralizing antibody level on first and second COVID-19 booster uptake: Staff members and students with higher antibody level were less likely to be boosted (first booster). This negative effect was also observed in other studies on first booster vaccine intention [40] and on change between intention and final decision regarding COVID-19 booster vaccination. In other words, knowledge of higher neutralizing antibody levels was predictor of COVID-19 booster dose refusal among staff and students who initially intended to get boosted [22]. A possible explanation is that belief about vaccines protection while many studies have highlighted the decrease of immunity and so vaccine protection over time [2–4] including limited protection against variants [5]. However, our results showed that this factor become less significant among staff and insignificant among students

regarding the second booster vaccine perhaps because of a small number of boosted participants among students.

These results showed that knowledge of neutralizing antibodies appear to have a greater impact than knowledge of prior SARS-CoV-2 infection on the vaccination decision over time among staff, may be due to an objectible trace of immunity.

The results suggest the importance of a personalized and transparent educational approach, also recommended by da Silva Sousa 2025 [21], centred on knowledge of prior immunity for the individual and current scientific knowledge/ uncertainties about vaccine and infection-related protection, to enable individuals to make an informed decision about vaccination.

4.2. Others factors that influence first and second COVID-19 booster uptake

In addition to influence of immunity on first and second COVID-19 booster uptake, we observed a positive significant effect of first or second COVID-19 booster intention on first (among staff and students) or second (only among students) COVID-19 booster uptake. This association was also demonstrated in a previous study on first booster uptake [41]. Regarding second booster dose, our study showed that higher age was positively associated with higher COVID-19 booster uptake among staff members, consistent with results from another study in general population in Belgium mentioned above [33]. A possible explanation is that individuals with a higher age are more afraid of the disease. These results highlight the importance of increasing awareness of vaccination among younger individuals.

4.3. Research prospects

This present study includes limited parameters namely some parameters analyzed in the previous study on factors influencing change between first COVID-19 booster intention and uptake carried out at the University of Liege in Belgium. In terms of future research prospects, it would be interesting to include other factors such as individual perception or other sociodemographic characteristics in order to analyze if they have an influence on booster vaccines as recommended by Vermeiren et al. regarding the general population in Belgium [33].

4.4. Strengths of the study

The main strength of the study is the well documented population studied. Indeed, university populations, namely students and staff members, offer data from a closed population, which in turn allows action on the factors that influence the first and the second COVID-19 booster uptake in a specific population.

4.5. Limits of the study

First, the results may not be representative of the university population and cannot be generalized to the Belgian population at large because it looked at a volunteer sample from a highly educated university population with high health literacy and past intention to get a first COVID-19 booster vaccine and did so, the sample is very small for students. Second, there was a social-desirability bias that may have influenced the results (particularly for the following parameters: first / second COVID-19 booster vaccine intention and first / second COVID-19 booster vaccine uptake), although the questionnaires were administered to participants via an online platform in order to minimize such a bias. Third, the dates considered for the end of the vaccination campaign relating to the different doses can be discussed depending on the age of the individuals, their profession, and the presence of possible comorbidities. Fourth, the data concerning changes in the vaccination status were self-reported by the participants and were not verified. Lastly, participants with recent vaccination or recent infection may have been vaccinated after the end of the study due to sufficiently high antibody levels.

5. Conclusions

The results show that COVID-19 vaccination decreases with time, particularly among students. Our initial hypothesis is partially confirmed: knowledge of previous SARS-CoV-2 infection and higher neutralizing antibodies were predictors of a lower first COVID-19 booster uptake whereas only knowledge of higher neutralizing antibodies was associated with a lower second COVID-19 booster uptake. Other variables namely lower past COVID-19 vaccine intention and lower age (only regarding second booster) were also associated with lower COVID-19 boosters uptake. In the event of future pandemics, these results suggest the importance of more regular monitoring of vaccination behaviour and the factors that may influence it, for example through a vaccination barometer. They also highlight the importance of a more focused / personalised and transparent educational approach, implemented by primary healthcare professionals and centred, for example, on knowledge of prior immunity for the individual and current scientific knowledge/uncertainties about vaccine and infection-related protection to enable individuals to make an informed decision about vaccination.

Availability of data and materials

Due to compliance with data protection regulations and ethical restrictions, data are available from the Ethics Committee of the Faculty of Medicine of the University of Liège (ethique@chu.ulg.ac.be) for researchers who meet the criteria for access to confidential data.

CRediT authorship contribution statement

Marine Paridans: Writing – review & editing, Writing – original draft, Visualization, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Nicolas Gillain:** Writing – review & editing, Software, Investigation. **Eddy Husson:** Writing – review & editing, Software. **Gilles Darcis:** Writing – review & editing. **Claude Saegerman:** Writing – review & editing. **Laurent Gillet:** Writing – review & editing. **Fabrice Bureau:** Writing – review & editing. **Anne-Françoise Donneau:** Writing – review & editing, Formal analysis. **Michèle Guillaume:** Writing – review & editing, Validation, Supervision, Methodology, Conceptualization. **Benoit Pétré:** Writing – review & editing, Validation, Supervision, Methodology, Conceptualization.

Consent for publication

Not Applicable

Ethics approval and consent to participate

The study was approved by the University Hospital of Liège Ethics Committee (reference number 2021/96, dated 26 March 2021). Written informed consent online was obtained from each participant before enrolment in the SARSSURV study. After the enrolment in the SARSSURV study, a unique identification code (ID) was attributed to each participant [19]. The data were handled in a confidential manner by the SARSSURV team and anonymized prior to any analysis. The compliance with data protection regulations were approved by the official University of Liège data protection officer.

Funding

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

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.

Acknowledgements

We would like to thank all of the students and staff, and the staff from the Public Health Department and the University of Liège laboratory, who gave their time to take part in this study.

Data availability

Data will be made available on request.

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