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Cumulative incidence of SARS-CoV-2 infection within the homeless population: insights from a citywide longitudinal study

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ABSTRACT

Objectives The aim of this study was to determine the risk factors associated with SARS-CoV-2 infection in a cohort of homeless people using survival analysis. Seroprevalence in the homeless community was also compared to that of the general population.

Design Cohort Study

Setting Data were collected across two testing sessions, 3 months apart, during which each participant was tested for anti-SARS-CoV-2 antibodies and completed a face-to-face surveys.

Participants All homeless adults sleeping rough, in slums or squats, in emergency shelters or transitional accommodation in Marseille were eligible.

Primary outcome measures Occurrence of a seroconversion event defined as a biologically confirmed SARS-CoV-2 infection. Local data from a national seroprevalence survey were used for comparison between homeless people and the general population.

Results A total of 1249 people were included. SARS-CoV-2 seroprevalence increased from 6.0% [4.7-7.3] during the first session to 18.9% [16.0-21.7] during the second one, compared to 3.0% [1.9-4.2] and 6.5% [4.5-8.7] in the general population. Factors significantly associated with an increased risk of COVID-19 infection were: having stayed in emergency shelters (1.93 [1.18 – 3.15]), being an isolated parent (1.64 [1.07-2.52]) and having contact with more than 5-15 people per day (1.84 [1.27 – 2.67]). By contrast, smoking (0.46 (0.32 – 0.65)), having financial resources (0.70 (0.51 – 0.97)) and psychiatric or addictive comorbidities (0.52 (0.32 – 0.85)) were associated with a lower risk.

Conclusion We confirm that homeless people have higher infection rates than the general population, with increased risk in emergency shelters. There is growing evidence that, in addition to usual preventive measures, public policies should pay attention to adapt the type of accommodation and overall approach of precariousness.

Data availability statement

The datasets generated and analyzed during the current study are not publicly available due to special authorization to transfer databases given by the CNIL. Upon prior authorization by the CNIL, the dataset would be available from the corresponding author upon reasonable request. Additionally, the study protocol is available upon request. All data requests should be addressed to the corresponding author.

Strengths and limitations of this study

- Description of risk factors of SARS-CoV-2 infection in a large study population with high-quality and statistically robust methodology.
- First surveillance data from a cohort of homeless people providing an incidence rate of seroconversion and comparing seroprevalence with the general population at two different time points.
- Studies showed high prevalence of SARs-CoV-2 among homeless people in shelters, but no longitudinal studies confirmed these findings, put them into perspective, or considered homeless populations beyond shelters.
- Quantification of the excess risk associated with staying in emergency shelters and among the most economically vulnerable
- Characteristics of study participants upon inclusion and at the end of follow-up were also different, roofless and younger populations were most frequently lost to follow-up because of a higher mobility.

Keywords

Homeless population, COVID-19, cohort study, seroprevalence, prevalence, SARS-CoV-2

INTRODUCTION

The crisis generated by the COVID-19 pandemic suddenly widened the gap in access to healthcare, especially for vulnerable populations [1]. Before the pandemic, homelessness was already associated with higher health inequalities compared to the general population [2].

Public policies had to devise new strategies to limit the impact of the evolving pandemic on healthcare systems and societies. For example, the French Government imposed 2 stringent lockdowns in 2020. These restrictions were accompanied in most cities by a sheltering program for homeless people, with allocation of extra emergency shelters, transitional accommodations and requisitioned hotels [3]. In parallel however, there was a rise of precariousness in France, with an increase in the number of homeless people [4,5]. Studies show that homeless people are at high risk of developing SARS-CoV-2 infection due to physical proximity, crowded emergency shelters and unsafe or unhygienic living conditions [6,7]. In this context, data on the spread of the SARS-CoV-2 virus and immunity among the homeless are essential to inform policy stakeholders and to contain epidemic dynamics.

In France, in May 2020, a nationwide study in the general population estimated that seroprevalence ranged from 3.5% (South East of France) to 10.8% (North East of France) [8], emphasizing the need for regionally specific data. This seroprevalence reflected the regional heterogeneity at the beginning of the pandemic. A high prevalence rate of SARS-CoV-2 infection was reported in people living in homeless shelters [7,9,10], which also showed a high rate of severe COVID-19 symptoms, potentially due to a lack of access to the health care and a high prevalence of comorbidities such as lung or heart diseases [11–13]. To our knowledge, there is no representative data of an entire homeless population to describe the dynamics of the prevalence of SARS-CoV-2 infection over time.

The aim of this study was to determine the risk factors associated with SARS-CoV-2 infection in a cohort of homeless people using survival analysis. Seroprevalence in the homeless community was also compared to that of the general population.

METHODS

Study Design

The present study was a descriptive and prospective cohort. Study design, participants and sampling were described in a previous study [14].

Study Area and Population

The study area was the city of Marseille, the second largest city in France with 889,029 inhabitants, suffering from a high level of poverty [15].

Eligible population

Data from the local orientation system for emergency and transitional accommodation (SIAO) and the NGO Doctors of the World estimated that in 2020, at the beginning of the COVID-19 outbreak, there were 2,322 homeless adults living in emergency, transitional shelters or hostels and 619 to 817 living in squats or slums (Supplementary Table 1). No point-in-time census was available for people living on the streets in Marseille.

Inclusion criteria

In order to focus on the homeless people the furthest from housing, we decided to select those characterized by the greatest residential instability: people sleeping rough, in squats or slums, in stabilization shelters, in emergency shelters or hostels, respectively corresponding to the following categories of the European typology of homelessness (ETHOS): ETHOS 1, 2, 3 and 8 [16].

Participant selection

In the absence of a point-in-time count, random sampling was impossible. We set a 2-month inclusion period, during which we systematically offered all homeless people aged over 18 to participate in the study. Recruitment of participants was also facilitated by the "Accés aux Soins des Sans Abris (ASSAb) network" of assistance to homeless people: 18 homeless outreach teams working in streets, hotels, squats or slums, 5 emergency shelters and 10 transitional accommodations.

Investigations

Two specific sessions of serological testing were conducted in order to assess seroprevalence. The first session lasted from June 5 to August 5, 2020, and the second from September 11 to December 18, 2020. At each session, each participant was tested using a rapid diagnostic serological test, and completed a face-to-face survey investigating: socio-demographic characteristics; comorbidities; past and current medical history of COVID-19; difficulties in access to care, water, food or hygiene supplies; compliance with the preventive measures (social

distancing, wearing a face mask, and hand washing). Questions were asked by trained local interviewers in the participants' native language to improve comprehension and to minimize the information bias.

Community Engagement and Medical Care

Community awareness interventions were conducted during the two testing sessions, to secure the commitment and participation of a majority of homeless people. Community engagement started by meetings with the community leaders or mediators but also the healthcare workers and the members of local institutions or NGOs implicated in health for homeless people with the help of a local network (ASSAB) in charge of coordination with these different stakeholders. Interviewers were sensitized to the study objectives, interventions and expected role of the community. A mobile team including an infectious disease specialist, a nurse and a community mediator followed the positive cases.

Field Biological Analysis

We used the rapid serological test "Biosynex COVID-19 BSS®", that detects immunoglobulin M (IgM) and G (IgG) in 10 minutes with high specificity and sensitivity (>95% and 90% respectively) [17].

Data Analysis

Descriptive analyses of sociodemographic characteristics were performed using numbers and percentage for categorical data, or medians and interquartile range (IQR) for quantitative data. The seroprevalence of COVID-19 infection was investigated between February 1, 2020 and December 18, 2020. All the participants were considered to have a negative serology on February 1, 2020 before the first cases were detected in early March 2020 in Marseille. In the event of seroconversion, infection was reported as confirmed at the time of serological testing, with the possibility of overestimating the number of person-days before infection. This methodological choice was made in relation to the different predictive variables also collected at the time of the serological test. To assess seroprevalence rate according to presence or absence of symptoms, bootstrap resampling approach with a set of 1,000 samples was used to create 95% confidence intervals (CI) based on IgM/IgG sensitivity and specificity and their 95%CI. Kaplan-Meier methods along with the log rank test were used to establish statistical differences in seroprevalence rates between types of ETHOS accommodation [16]. A Cox model was performed using both baseline covariates and time-dependent covariates. Time-dependent covariates were the following: type of ETHOS accommodation (i.e. street, emergency shelters, hotels, transitional shelter or squat/slum), type of accommodation (private or shared room/area), number of contacts per day, having financial resources and having work. We fitted a multivariate Cox model by considering as eligible variables those that were significant in a univariate analysis at the 10% level, and considering all pairwise interactions. The covariate "number of contacts per day" was forced into the model as it was considered to be a relevant variable. Then, we used the Stepwise selection function in R, which starts with an empty model and adds/removes predictors according to AIC criteria. Unadjusted and adjusted Hazard ratios (HR) and 95 % CI were given.

All of the statistical analyses were carried out using R software, and differences with p values of <0.05 were considered statistically significant.

Seroprevalence data of our study were compared with data from a representative sample of the general population living in Marseille, which were derived from a national seroprevalence survey (EpiCov) [18]. Results of seroprevalence in the general population were obtained from home self-samples of dried blood spots, in order to detect IgG antibodies (Euroimmun ELISA-S) [18].

All the confirmed cases of COVID-19 by positive SARS-CoV-2 PCR in Marseille registered from January 1 to December 31, 2020, by the French national monitoring department (SI-DEP) from *Santé Publique France* [19], were used to describe the local incidence rate of COVID-19 infection in cases per person-weeks.

Patients and public involvement: Public were involved in conduct (questionnaire were conducted by peer workers) and dissemination plans of this research (the results were presented to the public via photo and sound exhibitions and radio broadcasts in Marseille city).

RESULTS

During the first session from June 5 to August 5, 2020, 1241 people were included. Median age was 38 years [IQR 22], 70.40% were men (n=874) with 98 (8.1%) of participants living rough, 358 (29.5%) in emergency shelters, 197 (16.2%) in hostels, 196 (16.2%) in transitional shelters, and 363 (29.9%) in squats and slums (Table 1). Around half of the participants, 52.2% (n=648/1241), had confirmed or possible risk factors for severe COVID-19 disease, including cancer, obesity, cardiac or pulmonary disease and severe renal insufficiency. In addition, half of the participants (52.0%, n=645) reported active tobacco consumption. A total of 58.1% (n=721) of the participants tested during the first session were also tested at the second session.

Table 1: Population characteristics (n=1241)

Baseline characteristics		n (%) or median [IQR]
Gender		
	Men	874 (70.4%)
	Women	367 (29.6%)
Age, median, years		38 [22]
Age <= 65 years		1179 (95.0%)
French Nationality		222 (18.4%)
Country of Birth		
	France	234 (18.9%)
	Europe	416 (33.5%)
	Africa	282 (22.7%)
	Other	279 (22.5%)
	Missing	30 (2.4%)
Educational attainment		
	None	560 (45.1%)
	Lower secondary	445 (35.9%)
	Upper secondary or vocational	122 (9.8%)
	Missing	114 (9.2%)
Household status		
	Isolated adult	660 (53.2%)
	Isolated parent	129 (10.4%)
	Family	411 (33.1%)
	Missing	41 (3.3%)
Health insurance		
	No	345 (27.8%)
	Yes	826 (66.6%)
	Missing	70 (5.6%)
Financial resources		
	No	448 (36.1%)
	Yes	730 (58.8%)
	Missing	63 (5.1%)
Working situation [a]		
	No	949 (76.5%)
	Yes	229 (18.5%)
	Missing	63 (5.1%)
Total length of homelessness		
	<= 5 years	775 (62.4%)
	> 5 years	393 (31.7%)
	Missing data	73 (5.9%)
Typology ETHOS*		
	ETHOS 1: street	98 (8.1%)
	ETHOS 2: emergency shelters	358 (29.5%)
	ETHOS2: hotels	197 (16.2%)
	ETHOS 3: transitional shelters	196 (16.2%)
	ETHOS 8: squats, slums	363 (29.9%)
Type of accommodation		
	Private room or area	524 (42.2%)
	Shared room or area	648 (52.2%)
	Missing data	69 (5.6%)
Number of contacts per day		
	<= 5	714 (58.0%)
	5 to 15	410 (33.3%)
	>15	107 (8.7%)
Tobacco consumption		
	No	480 (38.7%)
	Yes	645 (52.0%)
	Missing	116 (9.3%)
Comorbidity		
Psychiatric or addictive comorbidities		295 (23.8%)
Obesity		72 (6.5%)
Diabetes		91 (8.1%)
Chronic Respiratory Pathology		99 (9.2%)
Cardiovascular Pathology		152 (14.1%)
Chronic renal failure with dialysis		23 (2.1%)
Cancer		24 (2.2%)

SD: Standard Deviation; IQR: Inter Quartile Range.
a: declared or undeclared employment.
*ETHOS: European Typology on Homelessness and Housing Exclusion [16]

Figure 1 aims to contextualize the study's test sessions within SARS-CoV-2 epidemics in Marseille, and shows the official incidence of COVID-19 in the city in 2020 as well as lockdown dates [19].

A total of 74/1241 of participants had positive serology in the first campaign, with 2.5% of positive IgM tests, 5.2% positive IgG tests and 1.7% positive IgM and IgG tests. In the second campaign, 136/721 of participants had positive serology with 8.1% of positive IgM tests, 17.5% positive IgG tests and 6.8% positive IgM and IgG tests.
Seroprevalence was 6.0% (IQR 4.7-7.3) (n=1241) in the first campaign and 18.9% (IQR 16.0-21.7) (n=721) in the second campaign, and had significantly increased (p<0.005) (Figure 2). In comparison, seroprevalence in the general population in Marseille was 3.0% [1.9-4.2] in May to June and 6.5% (CI95% 4.5-8.7) in November to December 2020 and had significantly increased (p<0.005) (Figure 2).

Factors Associated with SARS-CoV-2 Infection
A total of 180 participants presented a SARS-CoV-2 seroconversion defined by a positive serology result for SARS-CoV-2 (IgM or IgG). Average time of infection from February 1, 2020 was 230 days (IQR 162-277). Figure 3 shows the Kaplan Meier curves according to the participant's type of accommodation. Homeless people living in emergency shelters and hotels had a significantly higher risk of SARS-CoV-2 infection compared to their counterparts over the study follow-up period (p<0.001).

Table 2 shows univariate and multivariate analysis of the factors associated with the SARS-CoV-2 seroprevalence. Univariate analysis identified an association between positive serological results and participants coming from Africa (2.51 (1.45 – 4.33)) or those applying physical distancing (1.61 (1.14 – 2.27)). These two variables were not retained in the final model. Difficult access to hygiene products was also associated with lower seroprevalence in univariate analysis (0.72 (0.52 – 0.96)) but not in multivariate analysis. Being an isolated parent (1.64 (1.07 – 2.52)), spending more than 33% (1.70 (1.11 – 2.62)) or 66% (1.93 (1.18 – 3.15)) of time living in an emergency shelter during follow-up, and having between 5 to 15 daily contacts (1.84 (1.27 – 2.67)), were associated with SARS-CoV-2 infection in multivariate analysis. By contrast, having financial resources (1.64 (1.07 – 2.52)), being a smoker at the time of the survey (0.46 (0.32 – 0.65)) and having psychiatric or addictive comorbidities (0.52 (0.32 – 0.85)) were associated with a lower risk of SARS-CoV-2 seroprevalence. Figure 4 summarizes the Cox multivariable regression analysis. Other potential risk factors, such as educational attainment, gender, age, total length of homelessness in the life of participants, wearing a mask, hand washing, difficult access to water or not having health insurance were not associated with SARS-CoV-2 prevalence.

Table 2: Univariate and multivariable analysis of the seroprevalence of SARS-CoV-2 infection between February and December 2020 in homeless people living in Marseille

Results

		Univariate analysis		Multivariate analysis [£]
		HR (CI95%)	p-value	Adjusted HR (CI95%)
Gender				
	Men	ref		
	Women	0.97 (0.70 - 1.34)	0.900	
Age, years				
	<=65	Ref		
	>65	1.66 (0.99 – 2.77)	0.050	
Country of Birth				
	France	ref		
	Europe	1.45 (0.83 – 2.55)	0.193	
	Africa	2.51 (1.45 – 4.33)	**0.001[£]**	
	Other	2.80 (1.63 – 4.79)	<0.001	
Educational attainment				
	None	ref		
	Lower secondary	1.32 (0.96 – 1.82)	0.090	
	Upper secondary or vocational	1.14 (0.63 – 2.05)	0.670	
Household status				
	Isolated adult	ref		ref
	Isolated parent	1.78 (1.18 – 2.67)	**0.006**	**1.64 (1.07 – 2.52)**
	Family	0.78 (0.55 – 1.11)	0.168	0.78 (0.50 – 1.20)
Health insurance				
	No	Ref		
	Yes	0.96 (0.69 – 1.34)	0.800	
Having financial resources				
	No	Ref		Ref

	Yes	0.64 (0.47 – 0.86)	**0.003**	**0.70 (0.51 – 0.97)**
Having work				
	No	Ref		
	Yes	0.71 (0.45 – 1.12)	0.110	
Total length of homelessness				
<= 5 years		ref		
> 5 years		0.95 (0.69 – 1.30)	0.700	
Percent of time spent in emergency shelters*				
	<33%	Ref		ref
	33 to 66%	1.68 (1.15 – 2.46)	**0.007**	**1.70 (1.11 – 2.62)**
	>66%	2.45 (1.59 – 3.76)	**<0.001**	**1.93 (1.18 – 3.15)**
Number of daily contacts				
	<=5 per day	Ref		Ref
	>5 to <=15 per day	1.21 (0.88 – 1.65)	0.100£	**1.84 (1.27 – 2.67)**
	>15 per day	0.68 (0.33 – 1.40)	0.200	1.45 (0.69 – 3.04)
Wearing mask				
	No, somewhat no	Ref		
	Yes, somewhat yes	1.23 (0.85 – 1.78)	0.300	
Physical distancing				
	No, somewhat no	Ref		
	Yes, somewhat yes	1.61 (1.14 – 2.27)	**0.007£**	
Hand washing				
	No, somewhat no	ref		
	Yes, somewhat yes	1.43 (0.99 – 2.06)	0.060	
Difficult access to hygiene products				
	No, never, rarely	Ref		ref
	Yes, always, often	0.72 (0.52 – 0.96)	**0.040**	0.75 (0.50 – 1.12)
Difficult access to water				
	No, never, rarely	Ref		
	Yes, always, often	0.76 (0.54 – 1.09)	0.100	
Difficult access to food				
	No, never, rarely	Ref		
	Yes, always, often	0.83 (0.62 – 1.12)	0.200	
Smoking status				
	Non smoker	Ref		ref
	Smoker	0.39 (0.28 – 0.53)	**<0.001**	**0.46 (0.32 – 0.65)**
Psychiatric or addictive comorbidity				
	No	Ref		ref
	Yes	0.46 (0.30 – 0.69)	**<0.001**	**0.52 (0.32 – 0.85)**

$: total of participants in the analysis: 1241; missing values exist for some of the independent variables; for example smoking status (n=116), educational attainment (n=114), health insurance (n=70), self-reported financial resources (n=63) or household status (n=41).
*: Percentage was calculated on the basis of each participant's exposed time until the event or until the end of the follow-up in the absence of an event.
£: We fitted a multivariable model containing all variables that were significant in a univariate analysis at the 10% level. We used the Stepwise selection function in R (a mix between forward and backward selection), which starts with an empty model and adds predictors according to AIC criteria. Accordingly, "Country of birth" and "physical distancing" were considered in the multivariate model and removed. In addition, "number of contacts" was forced into the model as a relevant variable.

Symptomatology of participants with positive SARS-CoV-2 serological status

Among participants with SARS-CoV-2 infection (positive IgM or IgG or both, n=180), 67.6% reported no symptoms (Table 3). Among participants with symptomatic SARS-CoV-2 infections, the most common symptoms were fever, cough, headache and fatigue. Even if participants with a positive serological status reported Covid-19 syndrome (fever, cough, anosmia, headache notably) significantly more often than participants without serological immunity (Table 3), the frequency of symptoms reported did not appear to be strictly specific to SARS-CoV-2 infection.

Table 3: Symptoms according to serological status (n=1241)

	Negative serological status n (%)	**CI95% $**	**Positive serological status n (%)**	**CI95%$**	**P-value**
Individuals missing symptom data (n=303)	302 (24.3%)		1 (0.1%)		
Individuals with symptom data	759 (75.7%)		179 (99.9%)		

(n=938)					
Asymptomatic patient	656 (86.4%)	(84.7 – 91.4)	121 (67.6%)	(65.8 – 71.5)	<0.001
Participants with symptoms	103 (13.6%)	(11.7 – 14.3)	58 (32.4%)	(30.6 – 34.1)	
Fever	42 (4.0%)	(2.1 – 4.1)	36 (18.0%)	(16.1 – 18.9)	<0.001
Cough	38 (3.7%)	(1.8 – 3.8)	28 (14.0%)	(12.1 – 14.6)	<0.001
Dyspnea	16 (1.5%)	(0.0 – 1.5)	8 (4.0%)	(2.1 – 4.1)	0.040
Headache	41 (3.9%)	(2.0 – 4.0)	36 (18.0%)	(16.2 – 18.9)	<0.001
Anosmia	15 (1.4%)	(0.0 – 1.4)	21 (10.5%)	(8.6 – 10.9)	<0.001
Rhinitis	39 (3.7%)	(1.8 – 3.8)	21 (10.5%)	(8.6 – 10.9)	<0.001
Fatigue	35 (3.4%)	(1.5 – 3.5)	38 (19.0%)	(17.1 – 20.0)	<0.001
Diarrhoea	15 (1.4%)	(0.0 – 1.4)	15 (7.5%)	(5.6 – 7.8)	<0.001
Joint pain	15 (1.4%)	(0.0 – 1.4)	19 (9.5%)	(7.6 – 10.0)	<0.001
Odynophagia	22 (2.1%)	(0.0 – 2.1)	14 (7.0%)	(5.1 – 7.3)	<0.001
Chills	21 (2.0%)	(0.0 – 2.0)	17 (8.5%)	(6.6 – 8.8)	<0.001
Mottling	1 (0.1%)	(0.0 – 0.1)	0 (0%)	(0.0 – 0.1)	0.999
Skin rash	1 (0.1%)	(0.0 – 0.1)	3 (1.5%)	(0.0 – 1.5)	0.014
Conjunctivitis	9 (0.8%)	(0.0 – 0.7)	8 (4.0%)	(2.1 – 4.1)	0.002
Other	5 (0.5%)	(0.0 – 0.4)	2 (1.0%)	(0.0 – 0.9)	0.316

CI95%: confidence interval at 95%
$: an exact test of a simple null hypothesis about the probability of success in a Bernoulli experiment was performed, with confidence level for the returned confidence interval.

DISCUSSION

The present study is the first to describe the dynamics of SARS-CoV-2 seroprevalence among a large cohort of 1241 homeless people living in Marseille, France. Analysis of data from homeless participants with positive serology results over time, revealed a high prevalence of asymptomatic infection and significant associations between positive serology and the lack of financial resources, being an isolated parent, having between 5 and 15 daily contacts, and the time spent in emergency shelters. Repeated seroprevalence studies enabled to estimate the cumulative incidence of SARS-CoV-2 infection in both asymptomatic and symptomatic people, offering valuable data to inform public health policy-makers [7,20]. In the general population, asymptomatic individuals represent up to 68% of SARS-CoV-2 infections [7,21] and contribute to the rapid spread of the disease [1]. In our study, the estimated prevalence of SARS-CoV-2 increased from 6.01% [4.68-7.34] in June to August to 18.86 % [16.00-21.72] in September to December and remained higher than in the general population. Indeed, a cross-sectional study evaluating the seroprevalence of SARS-CoV-2 antibodies across the general population in Marseille in May and November, 2020, found 3.0% [1.9-4.2] and 6.5% (CI95% 4.5 – 8.7), respectively. The increasing gap in seroprevalence between the general population and the homeless population may be due to a potential breakdown of protective measures for people in the most precarious situations [5]. The available data on homeless people comes from cross-sectional studies, that mainly found high seroprevalence [7,9,10]. However, the testing approach was different and concerned a population selected from one type of accommodation (mainly emergency shelters) and results also depend on the intensity of the local epidemic at the time of the survey. A lower infection rate with increasing age was reported in several population-based serological studies, which is not consistent with our findings [22,23]. We observed no differences, in univariate analysis, in estimated seropositivity for older participants or for participants who had comorbidities. These results suggest that aged homeless people at risk of severe COVID-19 disease may be infected by SARS CoV-2 at the same rate as other adults. The pandemic has played an important role in amplifying health inequalities that already existed [24,25]. Increasing evidence has emerged, highlighting that COVID-19 mortality is higher for those who are socioeconomically deprived. We reported in our findings, in addition to the poorest condition of homelessness, that not having financial resources during the pandemic crisis was also a risk factor of SARS-CoV-2 seroprevalence. The link between socioeconomic status and development of infectious disease is well documented, and the main mechanisms reported to be associated with higher occurrence rates of communicable diseases included poor housing, lack of education, nutritional deficiencies, poor work conditions and hygiene [26].

African homeless immigrants had higher SARS-CoV-2 prevalence rates in our study compared to other nationalities. These findings were consistent with French, English or US studies which reported higher seroprevalence rates and mortality in black ethnic groups [8,27,28]. The homeless are a heterogeneous population. Even if homeless people already face disparity in health outcomes in the current COVID-19 pandemic, African immigrants are a subgroup at even more risk. Thus, it could be important to generate accessible health information and preventive measures for this subgroup, adapted to their literacy and specific needs.

Our study reported lower SARS-CoV-2 infection rates in participants with mental disorders or substance abuse. This is surprising since substance use disorders have frequently been reported to increase the risk of infectious diseases and mental illness to impact awareness of vulnerability to infection and help-seeking when symptoms of COVID-19 develop [29,30]. Since social contacts are the way in which the infection is spread, this lower seroprevalence could be interpreted as a sign of exclusion of these particularly stigmatized people [31]. It should also be noted that in Marseille there are specific healthcare mobile teams for people suffering from mental disorders and substance abuse [32]. This type of specific program has previously reported positive results in pandemic context [33].

In line with the findings of other studies, we observed a considerable proportion of positive subjects (67.6%) with asymptomatic infection [21,34,35]. Some symptoms (fever, cough, headache or fatigue notably) were significantly associated with positive SARS-CoV-2 serology and should be repeated to people during interventions on prevention and information.

As previously described, smoking prevalence was lower in seropositive SARS-CoV-2 participants in our study [36]. Even if prevalence was lower, smoking was associated with an increased risk of hospitalization and morbidity [37]. In our study, a substantial proportion of participants reported alcohol and tobacco consumption. In homeless populations a large proportion of deaths are therefore substance-attributable [38].

Our study reinforces the negative role of overcrowded types of accommodation for homeless people, which increase SARS-CoV-2 transmission. In the USA and France, emergency shelters and their high population density appear to increase the risk of infection [7,10]. Shelters should be considered as high-risk environments and stays there should be limited to the minimum. Providing adequate housing with individual bathroom facilities could be the most effective strategy for mitigating SARS-CoV-2 transmission in homeless communities, as was reported in a modeling study and by field healthcare workers [39,40]. Our findings also show an association with a high prevalence in shelters and hostels, which highlights the limits of individual preventive measures in transitional collective accommodations. These studies illustrate a good compliance with preventive measures, notably in collective accommodations, but these are clearly insufficient to limit the spread of infection. Homeless people in the pandemic must face concurrent risks: the risk of SARS-CoV-2 infection in shelters and collective accommodation, and the risk of the lack of access to food, water or hygiene products in more insecure housing conditions [41].

Throughout the course of the pandemic, healthcare and housing programs for homeless people have been modified. However, our results suggest that overcrowded and large emergency shelters or transitional accommodation including hostels increase the risk of SARS-CoV-2 transmission which pleads to adapt social and public health infrastructures towards good quality, smaller and semi-private accommodation. Holistic action (food, hygiene and financial support, health insurance, specific vaccination program…) must also be taken to ensure that the needs of these individuals are met sufficiently for them to be able to limit viral spread, survive this pandemic and be well enough equipped to endure the following economic crisis.

In addition, our findings highlight two other risk factors linked to socioeconomic inequalities: the lack of financial resource and being an isolated parent. Furthermore, people with low financial resources or single parents with one child are potentially more likely to seek outside support which may increase the risk of viral exposure, as it was previously described for people who have to work outside [42].

Strengths and limitations

Our study has number of strengths. Although studies have shown an increased risk of SARS-CoV-2 infection in homeless people, this is the first surveillance data from a cohort providing an incidence rate of seroconversion and comparing seroprevalence with the general population at two different time points. Our study described risk factors of SARS-CoV-2 infection in a large study population with high-quality and statistically robust methodology. Our findings quantify the excess risk associated with staying in emergency shelters. We also found evidence of SARS-CoV-2 infection among the most economically vulnerable (lack of financial resources, isolated parent) highlighting the need for a comprehensive and proactive approach including financial aid, food, water, adequate housing, mobile healthcare and social assistance for this vulnerable population.

Our study has also some limitations. Although it is representative of different homelessness categories (living in the street, slum, squat, emergency shelter or transitional accommodation), the sample was not randomly enrolled and therefore our findings may not reflect true seroprevalence, as a potential selection bias cannot be excluded. Characteristics of study participants upon inclusion and at the end of follow-up were also different, roofless and younger populations were most frequently lost to follow-up because of a higher mobility. We may also underestimate seroprevalence and false negative results cannot be excluded [43,44]. Finally, the serological tests between the general population and the homeless population were not exactly the same. This may account for some of the observed differences in seroprevalence rates between the two populations.

Policy implications and further research

There is growing evidence that, in addition to usual preventive measures, public policies should pay attention to adapt the type of accommodation and overall approach of precariousness. The findings of this study can guide European and other governments' disease control planning; to find optimal solutions to house people in less crowded accommodations, prioritizing individual rather than collective settings and a global approach, thus restricting transmission. To complete these results, future studies in this vulnerable population should assess the morbidity and mortality associated with SARS-CoV-2.

CONCLUSIONS

The longitudinal cohort of homeless people in Marseille revealed an increase in the seroprevalence of SARS-CoV-2 infection. This was higher than that observed in the general population and reflects precarious living conditions and inadequate types of accommodation for this vulnerable population.

Data availability statement

The datasets generated and analyzed during the current study are not publicly available due to special authorization to transfer databases given by the CNIL. Upon prior authorization by the CNIL, the dataset would be available from the corresponding author upon reasonable request. Additionally, the study protocol is available upon request. All data requests should be addressed to the corresponding author.

Ethics statements

Patient consent for publication

Not applicable

Ethical Approval

All participants provided a written informed consent. The COVIDHomeless study was designed and carried out in compliance with the Declaration of Helsinki and with legal and regulatory provisions. It was approved by the French ethics committee of Ile-de-France VI on May 28, 2020 (CPP IDF VI - number 44-20; ID: 2020-AO1398-31). The database was anonymized and declared to the French data protection commission (*Commission Nationale de l'Informatique et des Libertés*, CNIL, n°2018172v0).

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Contributors: First draft of the manuscript: EmM, SL, ElM, AT. Contributed to writing the manuscript: EmM, SL, ElM, AA, JL, LN, TB, MM, SNW, JW and AT. EM, TB and MM collected the data and samples. EmM, LN, MM performed biological analysis. Data analysis: EmM, SL, AA, AT. Study design: EmM, SL, TB, AT. All authors contributed to subsequent drafts and have reviewed and agreed with the content of the final manuscript.

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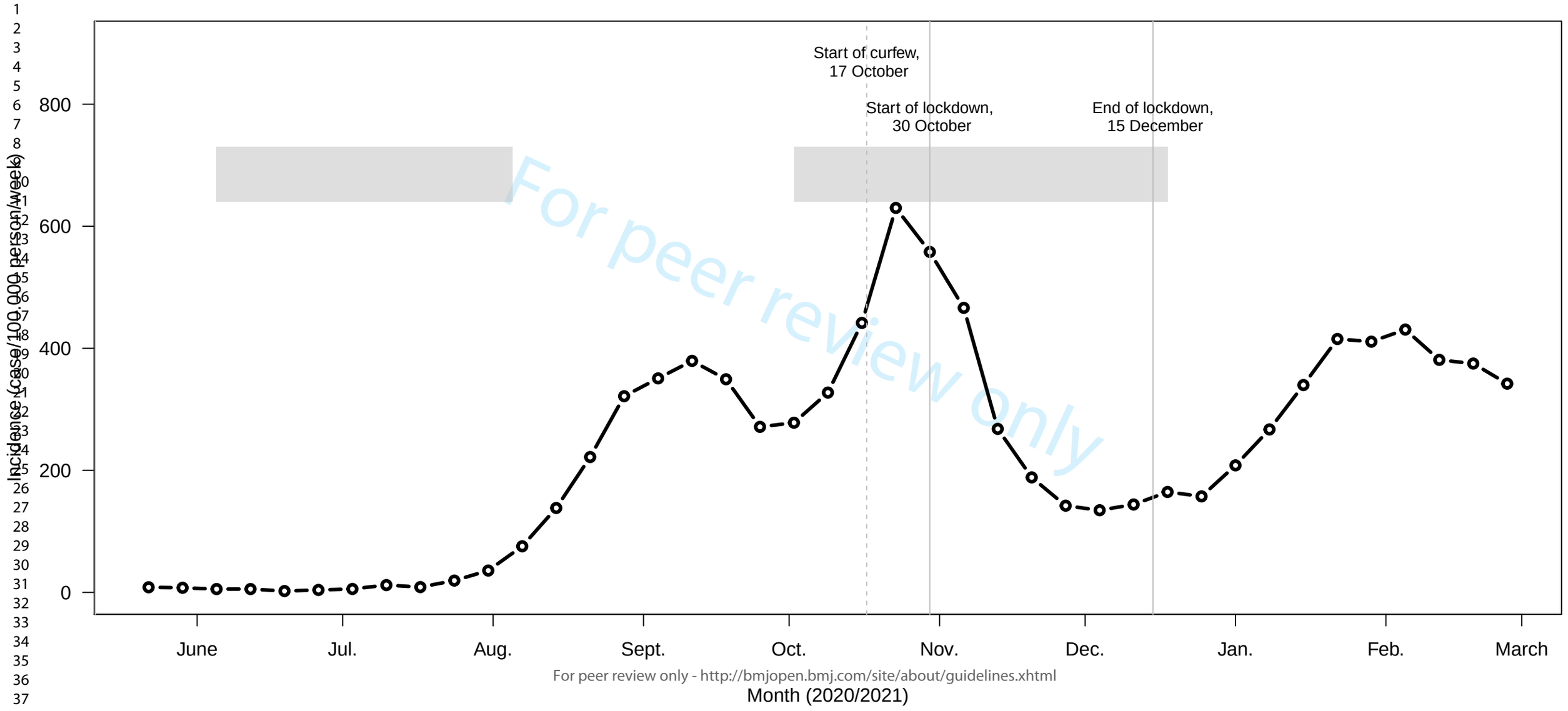
Figure legend

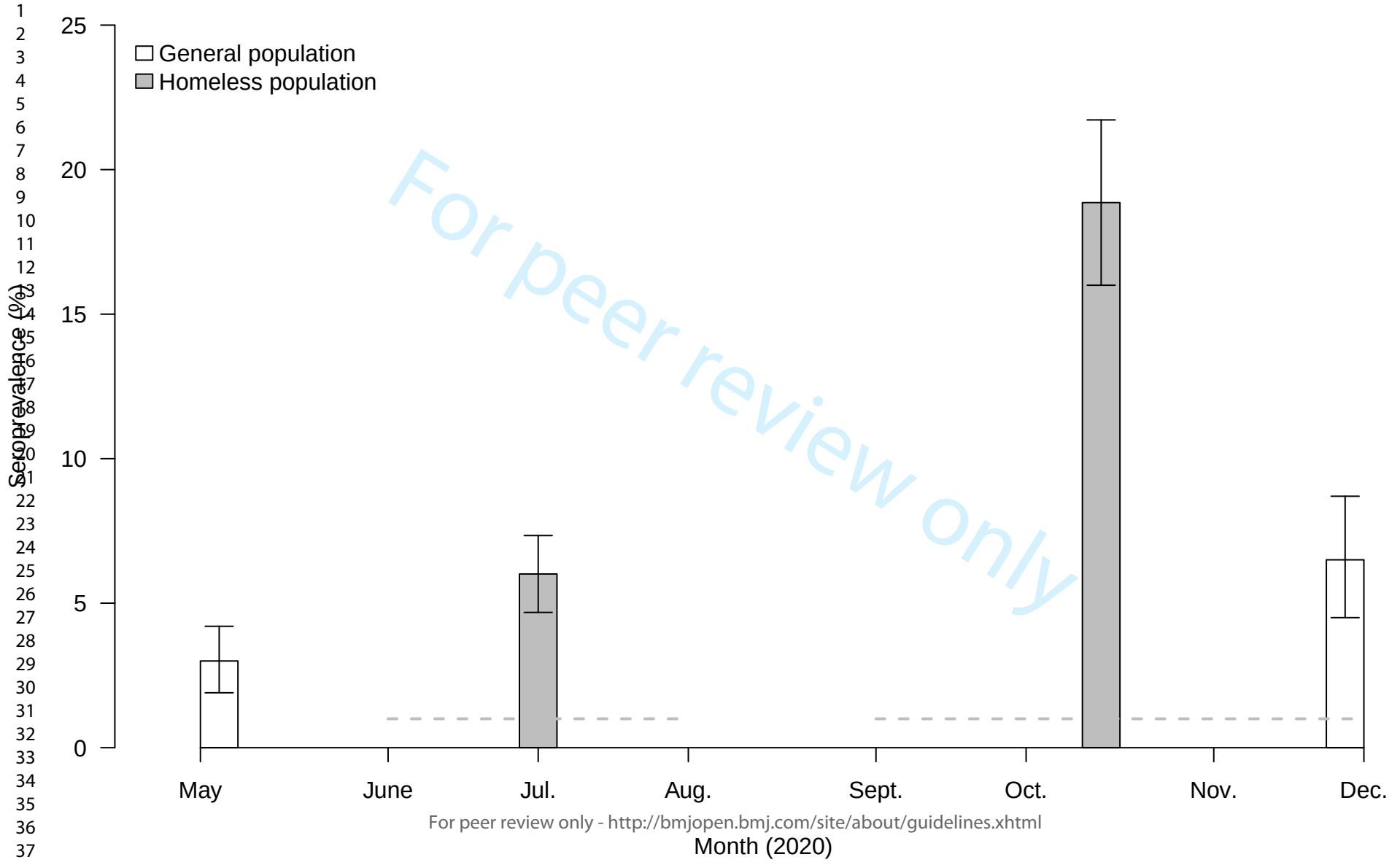
Figure 1: SARS-CoV-2 epidemics in Marseille, with data provided by the French national monitoring platform (SI-DEP) from *Santé Publique France* [19]
In gray the two campaigns with serological testing and questionnaires.

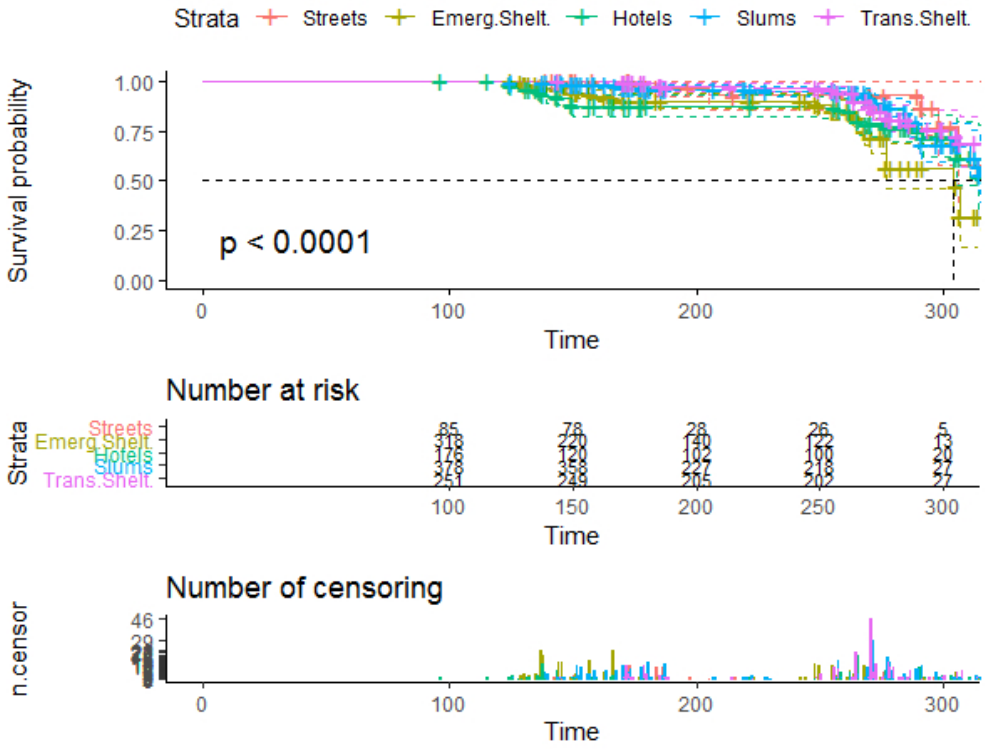
Figure 2: Seroprevalence rates during the two serological testing campaigns[$] in homeless people cohorts and results for the general population from the EpiCov study in Marseille
*General population seroprevalence rate data come from the EpiCov study in Marseille. $: Bootstrap resampling approach with a set of 1,000 samples was used to create confidence intervals, accounting for variability in the sensitivity and specificity of the serological assay.

Figure 3: Risk of SARS-CoV-2 infection by type of housing for homeless participants estimated by the Kaplan-Meier method, including 95% CI. Censoring and number of participants at risk at different time points are indicated.
Street: people living rough (ETHOS1); Emerg.Shelt.: people living in emergency shelters (ETHOS2); Hostel: people living in hostels (ETHOS3); Slums: people living in slums or squats (ETHOS8); Trans.Shelt.: people living in transitional accommodation for the homeless (ETHOS4)

Figure 4: Cox multivariable logistic regression analysis of risk factors of SARS-CoV-2 seroprevalence in homeless people in Marseille
Having_Comorb_PsyAddic: Psychiatric or addictive comorbidities







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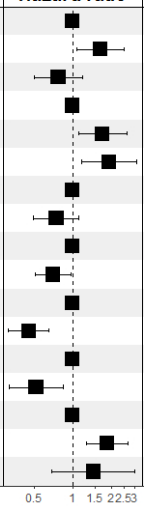
157x124mm (96 x 96 DPI)

Variable		N	Hazard ratio	p
Household_status	Isolated adults	589	Reference	
	Isolated parent	121	1.64 (1.07, 2.52)	0.024
	Family	338	0.78 (0.50, 1.20)	0.255
Percent_time_shelter	<=33	764	Reference	
	33 to 66	139	1.70 (1.11, 2.62)	0.016
	>=66	145	1.93 (1.18, 3.15)	0.009
Difficulty_access_hygiene_products	No,never,rarely	685	Reference	
	Yes,always,often	363	0.75 (0.50, 1.12)	0.160
Having_FinancialResources	No	459	Reference	
	Yes	589	0.70 (0.51, 0.97)	0.033
Tobacco	Non smoker	452	Reference	
	Smoker	596	0.46 (0.32, 0.65)	<0.001
Having_Comorb_PsyAddic	No	784	Reference	
	Yes	264	0.52 (0.32, 0.85)	0.009
Number_Daily_contact	<=5	634	Reference	
	5-15	319	1.84 (1.27, 2.67)	0.001
	>15	95	1.45 (0.69, 3.04)	0.331



Cox multivariable logistic regression analysis of risk factors of SARS-CoV-2 seroprevalence in homeless people in Marseille

Having_Comorb_PsyAddic: Psychiatric or addictive comorbidities

274x147mm (96 x 96 DPI)

Supplementary Table 1: Representativeness of the sample

Type of accommodation	Estimation of the target population*	Source	Number of effectively enrolled people
Squats or slums (Ethos 8)	619 to 817	NGO (MDM - Doctors of the World) – April 2020	363
Emergency shelters (Ethos 2)	795	Official administrative data (SIAO) – April 2020	358
Collective transitional shelters (Ethos 3)	634	Official administrative data (SIAO) – April 2020	196
Hostels mobilized during the covid crisis (Ethos 2)	893	Official administrative data (Service+) – July 2020	197
Street (Ethos 1)	?	No usable source of data	98

* *Adult homeless population living in the city of Marseille*. MDM (Médecins du Monde): Doctors of the World NGO; SIAO (Services intégrés de l'accueil et de l'orientation): Integrated reception and guidance services

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	3
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3-4
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	3
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*4*
Bias	9	Describe any efforts to address potential sources of bias	3-4
Study size	10	Explain how the study size was arrived at	3-4 and supl. file
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	3-4
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	4
		(*b*) Describe any methods used to examine subgroups and interactions	4
		(*c*) Explain how missing data were addressed	4
		(*d*) If applicable, explain how loss to follow-up was addressed	4
		(*e*) Describe any sensitivity analyses	4
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	3-4 and supl. file
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	5
		(b) Indicate number of participants with missing data for each variable of interest	5
		(c) Summarise follow-up time (eg, average and total amount)	5
Outcome data	15*	Report numbers of outcome events or summary measures over time	5
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	5-7
		(*b*) Report category boundaries when continuous variables were categorized	5-7
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	5-7
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	5
Discussion			
Key results	18	Summarise key results with reference to study objectives	8-9
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9
Generalisability	21	Discuss the generalisability (external validity) of the study results	9
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	12

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Cumulative incidence of SARS-CoV-2 infection within the homeless population: insights from a citywide longitudinal study

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Cumulative incidence of SARS-CoV-2 infection within the homeless population: insights from a citywide longitudinal study

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ABSTRACT

Objectives The aim of this study was to determine the risk factors associated with SARS-CoV-2 infection in a cohort of homeless people using survival analysis. Seroprevalence in the homeless community was also compared to that of the general population.
Design Cohort Study
Setting Data were collected across two testing sessions, 3 months apart, during which each participant was tested for anti-SARS-CoV-2 antibodies and completed a face-to-face surveys.
Participants All homeless adults sleeping rough, in slums or squats, in emergency shelters or transitional accommodation in Marseille were eligible.
Primary outcome measures Occurrence of a seroconversion event defined as a biologically confirmed SARS-CoV-2 infection. Local data from a national seroprevalence survey were used for comparison between homeless people and the general population.
Results A total of 1249 people were included. SARS-CoV-2 seroprevalence increased from 6.0% [4.7-7.3] during the first session to 18.9% [16.0-21.7] during the second one, compared to 3.0% [1.9-4.2] and 6.5% [4.5-8.7] in the general population. Factors significantly associated with an increased risk of COVID-19 infection were: having stayed in emergency shelters (1.93 [1.18 – 3.15]), being an isolated parent (1.64 [1.07-2.52]) and having contact with more than 5-15 people per day (1.84 [1.27 – 2.67]). By contrast, smoking (0.46 (0.32 – 0.65)), having financial resources (0.70 (0.51 – 0.97)) and psychiatric or addictive comorbidities (0.52 (0.32 – 0.85)) were associated with a lower risk.
Conclusion We confirm that homeless people have higher infection rates than the general population, with increased risk in emergency shelters. There is growing evidence that, in addition to usual preventive measures, public policies should pay attention to adapt the type of accommodation and overall approach of precariousness.

Data availability statement
The datasets generated and analyzed during the current study are not publicly available due to special authorization to transfer databases given by the CNIL. Upon prior authorization by the CNIL, the dataset would be available from the corresponding author upon reasonable request. Additionally, the study protocol is available upon request. All data requests should be addressed to the corresponding author.

Strengths and limitations of this study

- Description of risk factors of SARS-CoV-2 infection in a large study population with high-quality and statistically robust methodology.
- First surveillance data from a cohort of homeless people providing an incidence rate of seroconversion and comparing seroprevalence with the general population at two different time points.
- Large number of people lost to follow-up and difficulties in following a cohort of homeless people who are highly mobile
- Sensitivity of detection by repeated serological tests.

Keywords
Homeless population, COVID-19, cohort study, seroprevalence, prevalence, SARS-CoV-2

INTRODUCTION

The crisis generated by the COVID-19 pandemic suddenly widened the gap in access to healthcare, especially for vulnerable populations [1]. Before the pandemic, homelessness was already associated with higher health inequalities compared to the general population [2].

Public policies had to devise new strategies to limit the impact of the evolving pandemic on healthcare systems and societies. For example, the French Government imposed 2 stringent lockdowns in 2020. These restrictions were accompanied in most cities by a sheltering program for homeless people, with allocation of extra emergency shelters, transitional accommodations and requisitioned hotels [3]. In parallel however, there was a rise of precariousness in France, with an increase in the number of homeless people [4,5]. Studies show that homeless people are at high risk of developing SARS-CoV-2 infection and reinfection due to physical proximity, crowded emergency shelters and unsafe or unhygienic living conditions[6–8]. In this context, data on the spread of the SARS-CoV-2 virus and immunity among the homeless are essential to inform policy stakeholders and to contain epidemic dynamics.

In France, in May 2020, a nationwide study in the general population estimated that seroprevalence ranged from 3.5% (South East of France) to 10.8% (North East of France) [9], emphasizing the need for regionally specific data. This seroprevalence reflected the regional heterogeneity at the beginning of the pandemic. A high prevalence rate of SARS-CoV-2 infection was reported in people living in homeless shelters [7,10,11], which also showed a high rate of severe COVID-19 symptoms, potentially due to a lack of access to the health care and a high prevalence of comorbidities such as lung or heart diseases [12–14]. To our knowledge, there is no representative data of an entire homeless population to describe the dynamics of the prevalence of SARS-CoV-2 infection over time.

The aim of this study was to determine the risk factors associated with SARS-CoV-2 infection in a cohort of homeless people using survival analysis. Seroprevalence in the homeless community was also compared to that of the general population.

METHODS

Study Design

The present study was a descriptive and prospective cohort. Study design, participants and sampling were described in a previous study [15]. Each participant receives individualized follow-up and repeated testing at the inclusion and 3 month later. There was no resampling.

Study Area and Population

The study area was the city of Marseille, the second largest city in France with 889,029 inhabitants, suffering from a high level of poverty [16].

Eligible population

Data from the local orientation system for emergency and transitional accommodation (SIAO) and the NGO Doctors of the World estimated that in 2020, at the beginning of the COVID-19 outbreak, there were 2,322 homeless adults living in emergency, transitional shelters or hostels and 619 to 817 living in squats or slums (Supplementary file 1). No point-in-time census was available for people living on the streets in Marseille.

Inclusion criteria

In order to focus on the homeless people the furthest from housing, we decided to select those characterized by the greatest residential instability: people sleeping rough, in squats or slums, in stabilization shelters, in emergency shelters or hostels, respectively corresponding to the following categories of the European typology of homelessness (ETHOS): ETHOS 1, 2, 3 and 8 [17].

Participant selection

In the absence of a point-in-time count, random sampling was impossible. We set a 2-month inclusion period, during which we systematically offered all homeless people aged over 18 to participate in the study. Recruitment of participants was also facilitated by the "Accés aux Soins des Sans Abris (ASSAb) network" of assistance to homeless people: 18 homeless outreach teams working in streets, hotels, squats or slums, 5 emergency shelters and 10 transitional accommodations.

Investigations

Two specific sessions of serological testing were conducted in order to assess seroprevalence. The first session lasted from June 5 to August 5, 2020, and the second from September 11 to December 18, 2020. At each session, each participant was tested using a rapid diagnostic serological test, and completed a face-to-face survey investigating: socio-demographic characteristics; comorbidities; past and current medical history of COVID-19; difficulties in access to care, water, food or hygiene supplies; compliance with the preventive measures (social

distancing, wearing a face mask, and hand washing). Questions were asked by trained local interviewers in the participants' native language to improve comprehension and to minimize the information bias.

Community Engagement and Medical Care

Community awareness interventions were conducted during the two testing sessions, to secure the commitment and participation of a majority of homeless people. Community engagement started by meetings with the community leaders or mediators but also the healthcare workers and the members of local institutions or NGOs implicated in health for homeless people with the help of a local network (ASSAB) in charge of coordination with these different stakeholders. Interviewers were sensitized to the study objectives, interventions and expected role of the community. A mobile team including an infectious disease specialist, a nurse and a community mediator followed the positive cases.

Patients and public involvement: Public were involved in conduct (questionnaire were conducted by peer workers) and dissemination plans of this research (the results were presented to the public via photo and sound exhibitions and radio broadcasts in Marseille city).

Field Biological Analysis

We used the rapid serological test "Biosynex COVID-19 BSS®", that detects immunoglobulin M (IgM) and G (IgG) in 10 minutes with high specificity and sensitivity (>95% and 90% respectively) [18].

Data Analysis

Descriptive analyses of sociodemographic characteristics were performed using numbers and percentage for categorical data, or medians and interquartile range (IQR) for quantitative data. The seroprevalence of COVID-19 infection was investigated between February 1, 2020 and December 18, 2020. All the participants were considered to have a negative serology on February 1, 2020 before the first cases were detected in early March 2020 in Marseille. In the event of seroconversion, infection was reported as confirmed at the time of serological testing, with the possibility of overestimating the number of person-days before infection and regardless of the results of subsequent serological tests. This methodological choice was made in relation to the different predictive variables also collected at the time of the serological test. To assess seroprevalence rate according to presence or absence of symptoms, bootstrap resampling approach with a set of 1,000 samples was used to create 95% confidence intervals (CI) based on IgM/IgG sensitivity and specificity and their 95%CI. Kaplan-Meier methods along with the log rank test were used to establish statistical differences in seroprevalence rates between types of ETHOS accommodation [17]. A survival analysis was carried out to address the spread of COVID 19 among the targeted population. The time (in months) was defined as follows: the starting date was the date of February 01 2020, date at which none positive cases were registered in Marseille, that is a when all participants could be considered to have a COVID19-negative status. The event was a positive SARS-CoV-2 status, whatever a positive SARS-CoV-2 PCR or a positive serological test informed the diagnosis. His or her status was considered positive regardless of the results of subsequent serological tests. For those with a PCR test achieved, the date of the event corresponded to the PCR date, corrected with the date of the first symptoms when reported. For positive participant with a rapid serological test, the reported date of the first symptoms was considered. For participant with a positive serological test but with no history of symptoms, we considered the date of the testing strategy performed by the research team. No additional corrections were made in absence of any informative data. Participants tested negative at the first testing wave but being lost to follow up at the second testing wave were censored at the date of the last collection data. The cut-off date was December 18 2020, precisely 11.2 months after the starting date. A Cox model was performed using both baseline covariates and time-dependent covariates. Time-dependent covariates were the following: type of ETHOS accommodation (i.e. street, emergency shelters, hotels, transitional shelter or squat/slum), type of accommodation (private or shared room/area), number of contacts per day, having financial resources and having work. We fitted a multivariate Cox model by considering as eligible variables those that were significant in a univariate analysis at the 5% level, and considering all pairwise interactions. The covariate "number of contacts per day" was forced into the model as it was considered to be a relevant variable. We tested the assumption of proportional hazards using Schoenfeld residuals. Then, we used the Stepwise selection function in R, which starts with an empty model and adds/removes predictors according to AIC criteria. Unadjusted and adjusted Hazard ratios (HR) and 95 % CI were given.

All of the statistical analyses were carried out using R software, and differences with p values of <0.05 were considered statistically significant.

Seroprevalence data of our study were compared with data from a representative sample of the general population living in Marseille, which were derived from a national seroprevalence survey (EpiCov) [19]. Results of

seroprevalence in the general population were obtained from home self-samples of dried blood spots, in order to detect IgG antibodies (Euroimmun ELISA-S) [19].
All the confirmed cases of COVID-19 by positive SARS-CoV-2 PCR in Marseille registered from January 1 to December 31, 2020, by the French national monitoring department (SI-DEP) from *Santé Publique France* [20], were used to describe the local incidence rate of COVID-19 infection in cases per person-weeks.

RESULTS

During the first session from June 5 to August 5, 2020, 1241 people were included. Median age was 38 years [IQR 22], 70.40% were men (n=874) with 98 (8.1%) of participants living rough, 358 (29.5%) in emergency shelters, 197 (16.2%) in hostels, 196 (16.2%) in transitional shelters, and 363 (29.9%) in squats and slums (Table 1). Approximately 37% of eligible ETHOS 2,3 and 8 participants were included in the study (Supplementary file 1). Around half of the participants, 52.2% (n=648/1241), had confirmed or possible risk factors for severe COVID-19 disease, including cancer, obesity, cardiac or pulmonary disease and severe renal insufficiency. In addition, half of the participants (52.0%, n=645) reported active tobacco consumption. A total of 58.1% (n=721) of the participants tested during the first session were also tested at the second session.

Table 1: Population characteristics (n=1241)

Baseline characteristics	**n (%) or median [IQR]**
Gender	
Men	874 (70.4%)
Women	367 (29.6%)
Age, median, years	38 [22]
Age <= 65 years	1179 (95.0%)
French Nationality	222 (18.4%)
Country of Birth	
France	234 (18.9%)
Europe	416 (33.5%)
Africa	282 (22.7%)
Other	279 (22.5%)
Missing	30 (2.4%)
Educational attainment	
None	560 (45.1%)
Lower secondary	445 (35.9%)
Upper secondary or vocational	122 (9.8%)
Missing	114 (9.2%)
Household status	
Isolated adult	660 (53.2%)
Isolated parent	129 (10.4%)
Family	411 (33.1%)
Missing	41 (3.3%)
Health insurance	
No	345 (27.8%)
Yes	826 (66.6%)
Missing	70 (5.6%)
Financial resources	
No	448 (36.1%)
Yes	730 (58.8%)
Missing	63 (5.1%)
Working situation [a]	
No	949 (76.5%)
Yes	229 (18.5%)
Missing	63 (5.1%)
Total length of homelessness	
<= 5 years	775 (62.4%)
> 5 years	393 (31.7%)
Missing data	73 (5.9%)
Typology ETHOS*	
ETHOS 1: street	98 (8.1%)
ETHOS 2: emergency shelters	358 (29.5%)
ETHOS2: hotels	197 (16.2%)
ETHOS 3: transitional shelters	196 (16.2%)
ETHOS 8: squats, slums	363 (29.9%)
Type of accommodation	
Private room or area	524 (42.2%)
Shared room or area	648 (52.2%)
Missing data	69 (5.6%)
Number of contacts per day	
<= 5	714 (58.0%)

5 to 15	410 (33.3%)
>15	107 (8.7%)
Tobacco consumption	
No	480 (38.7%)
Yes	645 (52.0%)
Missing	116 (9.3%)
Comorbidity	
Psychiatric or addictive comorbidities	295 (23.8%)
Obesity	72 (6.5%)
Diabetes	91 (8.1%)
Chronic Respiratory Pathology	99 (9.2%)
Cardiovascular Pathology	152 (14.1%)
Chronic renal failure with dialysis	23 (2.1%)
Cancer	24 (2.2%)

SD: Standard Deviation; IQR: Inter Quartile Range.
a: declared or undeclared employment.
*ETHOS: European Typology on Homelessness and Housing Exclusion [17]

A total of 74/1241 of participants had positive serology in the first campaign, with 2.5% of positive IgM tests, 5.2% positive IgG tests and 1.7% positive IgM and IgG tests. In the second campaign, 136/721 of participants had positive serology with 8.1% of positive IgM tests, 17.5% positive IgG tests and 6.8% positive IgM and IgG tests. Of the 74 participants with positive serology at the start of the study, 43 were able to be followed up and have a new serology 3 months later. A total of 69.8% (n=30) still had positive serology. Thus, in 30.2% of cases (n=13) there was a rapid negativation of serology.
Seroprevalence was 6.0% (IQR 4.7-7.3) (n=1241) in the first campaign and 18.9% (IQR 16.0-21.7) (n=721) in the second campaign, and had significantly increased (p<0.005) (Figure 1. In comparison, seroprevalence in the general population in Marseille (EpiCoV-Marseille) was 3.0% [1.9-4.2] in May to June and 6.5% (CI95% 4.5-8.7) in November to December 2020 and had significantly increased (p<0.005) (Figure1).

Factors Associated with SARS-CoV-2 Infection
A total of 180 participants presented a SARS-CoV-2 seroconversion defined by a positive serology result for SARS-CoV-2 (IgM or IgG). At inclusion (n=74/1241) or as part of the cohort follow-up (n=136/721). Average time of infection from February 1, 2020 was 230 days (IQR 162-277). Figure 2 shows the Kaplan Meier curves according to the participant's type of accommodation. Homeless people living in emergency shelters and hotels had a significantly higher risk of SARS-CoV-2 infection compared to their counterparts over the study follow-up period (p<0.001).

Table 2 shows univariate and multivariate analysis of the factors associated with the SARS-CoV-2 seroprevalence. Univariate analysis identified an association between positive serological results and participants coming from Africa (2.51 (1.45 – 4.33)) or those applying physical distancing (1.61 (1.14 – 2.27)). These two variables were not retained in the final model. Difficult access to hygiene products was also associated with lower seroprevalence in univariate analysis (0.72 (0.52 – 0.96)) but not in multivariate analysis. Being an isolated parent (1.64 (1.07 – 2.52)), spending more than 33% (1.70 (1.11 – 2.62)) or 66% (1.93 (1.18 – 3.15)) of time living in an emergency shelter during follow-up, and having between 5 to 15 daily contacts (1.84 (1.27 – 2.67)), were associated with SARS-CoV-2 infection in multivariate analysis. By contrast, having financial resources (1.64 (1.07 – 2.52)), being a smoker at the time of the survey (0.46 (0.32 – 0.65)) and having psychiatric or addictive comorbidities (0.52 (0.32 – 0.85)) were associated with a lower risk of SARS-CoV-2 seroprevalence. Figure 3 summarizes the Cox multivariable regression analysis. Other potential risk factors, such as educational attainment, gender, age, total length of homelessness in the life of participants, wearing a mask, hand washing, difficult access to water or not having health insurance were not associated with SARS-CoV-2 prevalence.

Table 2: Univariate and multivariable analysis of the seroprevalence of SARS-CoV-2 infection (n=180/1241) between February and December 2020 in homeless people living in Marseille

Results

		Univariate analysis		Multivariate analysis [£]
		HR (CI95%)	p-value	Adjusted HR (CI95%)
Gender				
	Men	ref		
	Women	0.97 (0.70 - 1.34)	0.900	
Age, years				

	<=65	Ref		
	>65	1.66 (0.99 – 2.77)	0.050	
Country of Birth				
	France	ref		
	Europe	1.45 (0.83 – 2.55)	0.193	
	Africa	2.51 (1.45 – 4.33)	**0.001£**	
	Other	2.80 (1.63 – 4.79)	<0.001	
Educational attainment				
	None	ref		
	Lower secondary	1.32 (0.96 – 1.82)	0.090	
	Upper secondary or vocational	1.14 (0.63 – 2.05)	0.670	
Household status				
	Isolated adult	ref		ref
	Isolated parent	1.78 (1.18 – 2.67)	**0.006**	**1.64 (1.07 – 2.52)**
	Family	0.78 (0.55 – 1.11)	0.168	0.78 (0.50 – 1.20)
Health insurance				
	No	Ref		
	Yes	0.96 (0.69 – 1.34)	0.800	
Having financial resources				
	No	Ref		Ref
	Yes	0.64 (0.47 – 0.86)	**0.003**	**0.70 (0.51 – 0.97)**
Having work				
	No	Ref		
	Yes	0.71 (0.45 – 1.12)	0.110	
Total length of homelessness				
	<= 5 years	ref		
	> 5 years	0.95 (0.69 – 1.30)	0.700	
Percent of time spent in emergency shelters*				
	<33%	Ref		ref
	33 to 66%	1.68 (1.15 – 2.46)	**0.007**	**1.70 (1.11 – 2.62)**
	>66%	2.45 (1.59 – 3.76)	**<0.001**	**1.93 (1.18 – 3.15)**
Number of daily contacts				
	<=5 per day	Ref		Ref
	>5 to <=15 per day	1.21 (0.88 – 1.65)	0.100£	**1.84 (1.27 – 2.67)**
	>15 per day	0.68 (0.33 – 1.40)	0.200	1.45 (0.69 – 3.04)
Wearing mask				
	No, somewhat no	Ref		
	Yes, somewhat yes	1.23 (0.85 – 1.78)	0.300	
Physical distancing				
	No, somewhat no	Ref		
	Yes, somewhat yes	1.61 (1.14 – 2.27)	**0.007£**	
Hand washing				
	No, somewhat no	ref		
	Yes, somewhat yes	1.43 (0.99 – 2.06)	0.060	
Difficult access to hygiene products				
	No, never, rarely	Ref		ref
	Yes, always, often	0.72 (0.52 – 0.96)	**0.040**	0.75 (0.50 – 1.12)
Difficult access to water				
	No, never, rarely	Ref		
	Yes, always, often	0.76 (0.54 – 1.09)	0.100	
Difficult access to food				
	No, never, rarely	Ref		
	Yes, always, often	0.83 (0.62 – 1.12)	0.200	
Smoking status				
	Non smoker	Ref		ref
	Smoker	0.39 (0.28 – 0.53)	**<0.001**	**0.46 (0.32 – 0.65)**
Psychiatric or addictive comorbidity				
	No	Ref		ref
	Yes	0.46 (0.30 – 0.69)	**<0.001**	**0.52 (0.32 – 0.85)**

$: total of participants in the analysis: 1241; missing values exist for some of the independent variables; for example smoking status (n=116), educational attainment (n=114), health insurance (n=70), self-reported financial resources (n=63) or household status (n=41).

*: Percentage was calculated on the basis of each participant's exposed time until the event or until the end of the follow-up in the absence of an event.

£: We fitted a multivariable model containing all variables that were significant in a univariate analysis at the 10% level. We used the Stepwise selection function in R (a mix between forward and backward selection), which starts with an empty model and adds predictors according to AIC criteria. Accordingly, "Country of birth" and "physical distancing" were considered in the multivariate model and removed. In addition, "number of contacts" was forced into the model as a relevant variable.

Symptomatology of participants with positive SARS-CoV-2 serological status

Among participants with SARS-CoV-2 infection (positive IgM or IgG or both, n=180), 67.6% reported no symptoms (Table 3). Among participants with symptomatic SARS-CoV-2 infections, the most common symptoms were fever, cough, headache and fatigue. Even if participants with a positive serological status reported Covid-19 syndrome (fever, cough, anosmia, headache notably) significantly more often than participants without serological immunity (Table 3), the frequency of symptoms reported did not appear to be strictly specific to SARS-CoV-2 infection.

Table 3: Symptoms reported in the last 3 months prior the serological test according to serological status (n=1241)

	Negative serological status n (%)	CI95% $	Positive serological status n (%)	CI95%$	P-value
Individuals missing symptom data (n=303)	302 (24.3%)		1 (0.1%)		
Individuals with symptom data (n=938)	759 (75.7%)		179 (99.9%)		
Asymptomatic patient	656 (86.4%)	(84.7 – 91.4)	121 (67.6%)	(65.8 – 71.5)	<0.001
Participants with symptoms	103 (13.6%)	(11.7 – 14.3)	58 (32.4%)	(30.6 – 34.1)	
Fever	42 (4.0%)	(2.1 – 4.1)	36 (18.0%)	(16.1 – 18.9)	<0.001
Cough	38 (3.7%)	(1.8 – 3.8)	28 (14.0%)	(12.1 – 14.6)	<0.001
Dyspnea	16 (1.5%)	(0.0 – 1.5)	8 (4.0%)	(2.1 – 4.1)	0.040
Headache	41 (3.9%)	(2.0 – 4.0)	36 (18.0%)	(16.2 – 18.9)	<0.001
Anosmia	15 (1.4%)	(0.0 – 1.4)	21 (10.5%)	(8.6 – 10.9)	<0.001
Rhinitis	39 (3.7%)	(1.8 – 3.8)	21 (10.5%)	(8.6 – 10.9)	<0.001
Fatigue	35 (3.4%)	(1.5 – 3.5)	38 (19.0%)	(17.1 – 20.0)	<0.001
Diarrhoea	15 (1.4%)	(0.0 – 1.4)	15 (7.5%)	(5.6 – 7.8)	<0.001
Joint pain	15 (1.4%)	(0.0 – 1.4)	19 (9.5%)	(7.6 – 10.0)	<0.001
Odynophagia	22 (2.1%)	(0.0 – 2.1)	14 (7.0%)	(5.1 – 7.3)	<0.001
Chills	21 (2.0%)	(0.0 – 2.0)	17 (8.5%)	(6.6 – 8.8)	<0.001
Mottling	1 (0.1%)	(0.0 – 0.1)	0 (0%)	(0.0 – 0.1)	0.999
Skin rash	1 (0.1%)	(0.0 – 0.1)	3 (1.5%)	(0.0 – 1.5)	0.014
Conjunctivitis	9 (0.8%)	(0.0 – 0.7)	8 (4.0%)	(2.1 – 4.1)	0.002
Other	5 (0.5%)	(0.0 – 0.4)	2 (1.0%)	(0.0 – 0.9)	0.316

CI95%: confidence interval at 95%

$: an exact test of a simple null hypothesis about the probability of success in a Bernoulli experiment was performed, with confidence level for the returned confidence interval.

DISCUSSION

The present study is the first to describe the dynamics of SARS-CoV-2 seroprevalence among a large cohort of 1241 homeless people living in Marseille, France. Analysis of data from homeless participants with positive serology results over time, revealed a high prevalence of asymptomatic infection and significant associations between positive serology and the lack of financial resources, being an isolated parent, having between 5 and 15 daily contacts, and the time spent in emergency shelters. Repeated seroprevalence studies enabled to estimate the cumulative incidence of SARS-CoV-2 infection in both asymptomatic and symptomatic people, offering valuable data to inform public health policy-makers [7,21]. In the general population, asymptomatic individuals represent up to 68% of SARS-CoV-2 infections [7,22] and contribute to the rapid spread of the disease [1]. In our study, the estimated prevalence of SARS-CoV-2 increased from 6.01% [4.68-7.34] in June to August to 18.86 % [16.00-21.72] in September to December and remained higher than in the general population. Indeed, a cross-sectional study evaluating the seroprevalence of SARS-CoV-2 antibodies across the general population in Marseille in May and November, 2020, found 3.0% [1.9-4.2] and 6.5% (CI95% 4.5 – 8.7), respectively. The increasing gap in seroprevalence between the general population and the homeless population may be due to a potential breakdown of protective measures for people in the most precarious situations [5]. The available data on homeless people comes from cross-sectional studies, that mainly found high seroprevalence [7,10,11]. However, the testing approach was different and concerned a population selected from one type of accommodation (mainly emergency shelters) and results also depend on the intensity of the local epidemic at the time of the survey. A lower infection rate with increasing age was reported in several population-based serological studies, which is not consistent with

our findings [23,24]. We observed no differences, in univariate analysis, in estimated seropositivity for older participants or for participants who had comorbidities. These results suggest that aged homeless people at risk of severe COVID-19 disease may be infected by SARS CoV-2 at the same rate as other adults. The pandemic has played an important role in amplifying health inequalities that already existed [25,26]. Increasing evidence has emerged, highlighting that COVID-19 mortality is higher for those who are socioeconomically deprived. We reported in our findings, in addition to the poorest condition of homelessness, that not having financial resources during the pandemic crisis was also a risk factor of SARS-CoV-2 seroprevalence. The link between socioeconomic status and development of infectious disease is well documented, and the main mechanisms reported to be associated with higher occurrence rates of communicable diseases included poor housing, lack of education, nutritional deficiencies, poor work conditions and hygiene [27].

African homeless immigrants had higher SARS-CoV-2 prevalence rates in our study compared to other nationalities. This is despite the fact that North and Sub-Saharan Africans are grouped together for analysis in our study. These findings were consistent with French, English or US studies which reported higher seroprevalence rates and mortality in black ethnic groups [9,28,29]. The homeless are a heterogeneous population. Even if homeless people already face disparity in health outcomes in the current COVID-19 pandemic, African immigrants are a subgroup at even more risk. Thus, it could be important to generate accessible health information and preventive measures for this subgroup, adapted to their literacy and specific needs.

Our study reported lower SARS-CoV-2 infection rates in participants with mental disorders or substance abuse. This is surprising since substance use disorders have frequently been reported to increase the risk of infectious diseases and mental illness to impact awareness of vulnerability to infection and help-seeking when symptoms of COVID-19 develop [30,31]. Since social contacts are the way in which the infection is spread, this lower seroprevalence could be interpreted as a sign of exclusion of these particularly stigmatized people [32]. It should also be noted that in Marseille there are specific healthcare mobile teams for people suffering from mental disorders and substance abuse [33]. This type of specific program has previously reported positive results in pandemic context [34].

In line with the findings of other studies, we observed a considerable proportion of positive subjects (67.6%) with asymptomatic infection [22,35,36]. Some symptoms (fever, cough, headache or fatigue notably) were significantly associated with positive SARS-CoV-2 serology and should be repeated to people during interventions on prevention and information.

As previously described, smoking prevalence was lower in seropositive SARS-CoV-2 participants in our study [37]. Even if prevalence was lower, smoking was associated with an increased risk of hospitalization and morbidity [38]. In our study, a substantial proportion of participants reported alcohol and tobacco consumption. In homeless populations a large proportion of deaths are therefore substance-attributable [39].

Our study reinforces the negative role of overcrowded types of accommodation for homeless people, which increase SARS-CoV-2 transmission. In the USA and France, emergency shelters and their high population density appear to increase the risk of infection [7,11]. Indeed, the emergency shelters are short term shelters that can accommodate several hundred people in Marseille with common sanitary facilities [40]. Collective transitional shelters are longer term, smaller facilities offering more consistent social work. The first French lockdown was ordered on March 17, 2020, as emergency shelters are already full in normal times, hotels were required. In these hotels, people did not have kitchen facilities and often found themselves in high-density grouping areas, especially at meal times or in the few outdoor spaces available [40]. Shelters should be considered as high-risk environments and stays there should be limited to the minimum. Providing adequate housing with individual bathroom facilities could be the most effective strategy for mitigating SARS-CoV-2 transmission in homeless communities, as was reported in a modeling study and by field healthcare workers [41,42]. Our findings also show an association with a high prevalence in shelters and hostels, which highlights the limits of individual preventive measures in transitional collective accommodations. These studies illustrate a good compliance with preventive measures, notably in collective accommodations, but these are clearly insufficient to limit the spread of infection. Homeless people in the pandemic must face concurrent risks: the risk of SARS-CoV-2 infection in shelters and collective accommodation, and the risk of the lack of access to food, water or hygiene products in more insecure housing conditions [43].

Throughout the course of the pandemic, healthcare and housing programs for homeless people have been modified. However, our results suggest that overcrowded and large emergency shelters or transitional accommodation including hostels increase the risk of SARS-CoV-2 transmission which pleads to adapt social and public health infrastructures towards good quality, smaller and semi-private accommodation. Holistic action (food, hygiene and financial support, health insurance, specific vaccination program…) must also be taken to ensure that the needs of these individuals are met sufficiently for them to be able to limit viral spread, survive this pandemic and be well enough equipped to endure the following economic crisis.

In addition, our findings highlight two other risk factors linked to socioeconomic inequalities: the lack of financial resource and being an isolated parent. Furthermore, people with low financial resources or single parents with one

child are potentially more likely to seek outside support which may increase the risk of viral exposure, as it was previously described for people who have to work outside [44].

Strengths and limitations

Our study has number of strengths. Although studies have shown an increased risk of SARS-CoV-2 infection in homeless people, this is the first surveillance data from a cohort providing an incidence rate of seroconversion and comparing seroprevalence with the general population at two different time points. Our study described risk factors of SARS-CoV-2 infection in a large study population with high-quality and statistically robust methodology. Our findings quantify the excess risk associated with staying in emergency shelters. We also found evidence of SARS-CoV-2 infection among the most economically vulnerable (lack of financial resources, isolated parent) highlighting the need for a comprehensive and proactive approach including financial aid, food, water, adequate housing, mobile healthcare and social assistance for this vulnerable population.

Our study has also some limitations. Although it is representative of different homelessness categories (living in the street, slum, squat, emergency shelter or transitional accommodation), the sample was not randomly enrolled and therefore our findings may not reflect true seroprevalence, as a potential selection bias cannot be excluded. Characteristics of study participants upon inclusion and at the end of follow-up were also different, roofless and younger populations were most frequently lost to follow-up because of a higher mobility. We may also underestimate seroprevalence and false negative results cannot be excluded [45,46]. Finally, the serological tests between the general population and the homeless population were not exactly the same. This may account for some of the observed differences in seroprevalence rates between the two populations.

Policy implications and further research

There is growing evidence that, in addition to usual preventive measures, public policies should pay attention to adapt the type of accommodation and overall approach of precariousness. The findings of this study can guide European and other governments' disease control planning; to find optimal solutions to house people in less crowded accommodations, prioritizing individual rather than collective settings and a global approach, thus restricting transmission. To complete these results, future studies in this vulnerable population should assess the morbidity and mortality associated with SARS-CoV-2.

CONCLUSIONS

The longitudinal cohort of homeless people in Marseille revealed an increase in the seroprevalence of SARS-CoV-2 infection. This was higher than that observed in the general population and reflects precarious living conditions and inadequate types of accommodation for this vulnerable population.

Contributorship statement: First draft of the manuscript: EmM, SL, ElM, AT. Contributed to writing the manuscript: EmM, SL, ElM, AA, JL, LN, TB, MM, SNW, JW and AT. EM, TB and MM collected the data and samples. EmM, LN, MM performed biological analysis. Data analysis: EmM, SL, AA, AT. Study design: EmM, SL, TB, AT. All authors contributed to subsequent drafts and have reviewed and agreed with the content of the final manuscript.

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Data sharing statement

The datasets generated and analyzed during the current study are not publicly available due to special authorization to transfer databases given by the CNIL. Upon prior authorization by the CNIL, the dataset would be available from the corresponding author upon reasonable request. Additionally, the study protocol is available upon request. All data requests should be addressed to the corresponding author.

Ethics statements

Patient consent for publication

Not applicable

Ethical Approval

All participants provided a written informed consent. The COVIDHomeless study was designed and carried out in compliance with the Declaration of Helsinki and with legal and regulatory provisions. It was approved by the ethics committee on May 28, 2020 (CPP IDF VI - number 44-20; ID: 2020-AO1398-31). The database was anonymized and declared to the French data protection commission (*Commission Nationale de l'Informatique et des Libertés*, CNIL, n°2018172v0).

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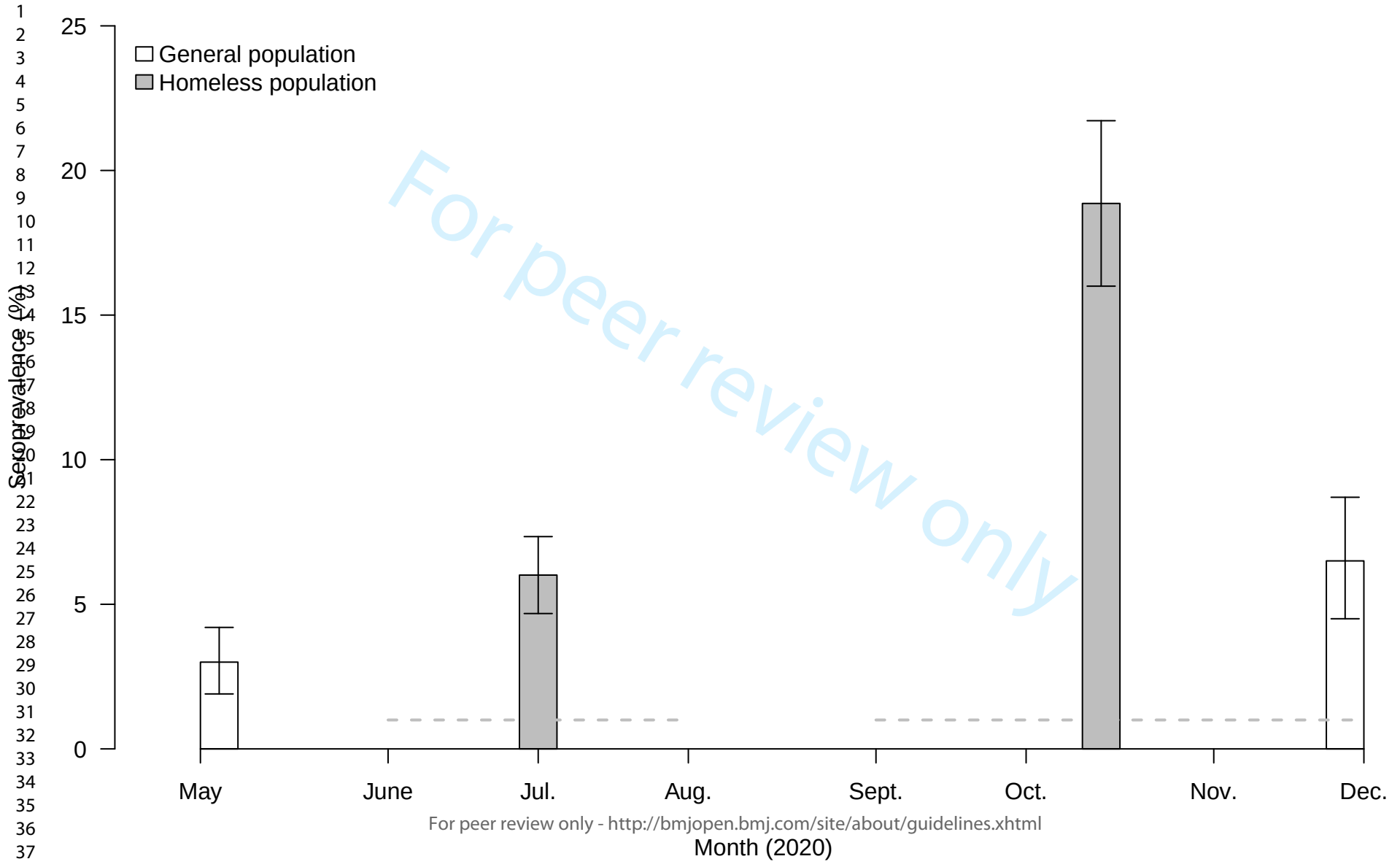
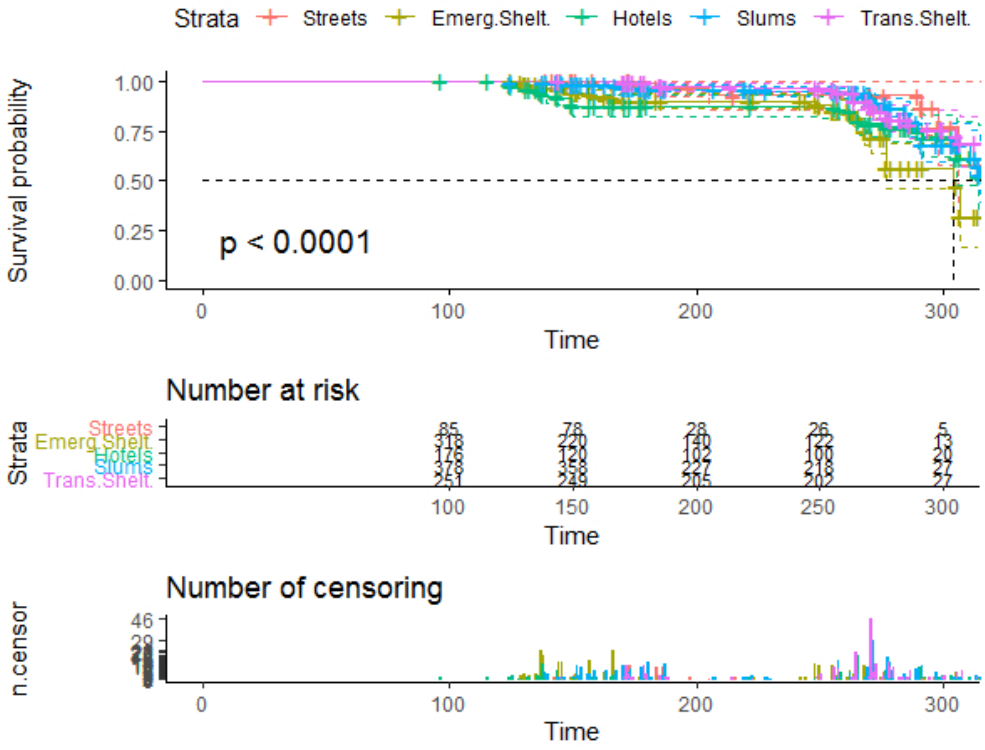
Figures and their legends

***Figure* 1: Seroprevalence rates during the two serological testing campaigns[$] in homeless people cohorts and results for the general population from the EpiCov study in Marseille**
*General population seroprevalence rate data come from the EpiCov study in Marseille. $: Bootstrap resampling approach with a set of 1,000 samples was used to create confidence intervals, accounting for variability in the sensitivity and specificity of the serological assay.

***Figure* 2: Risk of SARS-CoV-2 infection by type of housing for homeless participants estimated by the Kaplan-Meier method, including 95% CI. Censoring and number of participants at risk at different time points are indicated.**
Street: people living rough (ETHOS1); Emerg.Shelt.: people living in emergency shelters (ETHOS2); Hostel: people living in hostels (ETHOS3); Slums: people living in slums or squats (ETHOS8); Trans.Shelt.: people living in transitional accommodation for the homeless (ETHOS4)

***Figure* 3: Cox multivariable logistic regression analysis of risk factors of SARS-CoV-2 seroprevalence in homeless people in Marseille.**
Having_Comorb_PsyAddic: Psychiatric or addictive comorbidities

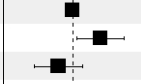




Risk of SARS-CoV-2 infection by type of housing for homeless participants estimated by the Kaplan-Meier method, including 95% CI. Censoring and number of participants at risk at different time points are indicated.Street: people living rough (ETHOS1); Emerg.Shelt.: people living in emergency shelters (ETHOS2); Hostel: people living in hostels (ETHOS3); Slums: people living in slums or squats (ETHOS8); Trans.Shelt.: people living in transitional accommodation for the homeless (ETHOS4)

157x124mm (96 x 96 DPI)

Variable		N	Hazard ratio	p
Household_status	Isolated adults	589	Reference	
	Isolated parent	121	1.64 (1.07, 2.52)	0.024
	Family	338	0.78 (0.50, 1.20)	0.255
Percent_time_shelter	<=33	764	Reference	
	33 to 66	139	1.70 (1.11, 2.62)	0.016
	>=66	145	1.93 (1.18, 3.15)	0.009
Difficulty_access_hygiene_products	No,never,rarely	685	Reference	
	Yes,always,often	363	0.75 (0.50, 1.12)	0.160
Having_FinancialResources	No	459	Reference	
	Yes	589	0.70 (0.51, 0.97)	0.033
Tobacco	Non smoker	452	Reference	
	Smoker	596	0.46 (0.32, 0.65)	<0.001
Having_Comorb_PsyAddic	No	784	Reference	
	Yes	264	0.52 (0.32, 0.85)	0.009
Number_Daily_contact	<=5	634	Reference	
	5-15	319	1.84 (1.27, 2.67)	0.001
	>15	95	1.45 (0.69, 3.04)	0.331



Cox multivariable logistic regression analysis of risk factors of SARS-CoV-2 seroprevalence in homeless people in MarseilleHaving_Comorb_PsyAddic: Psychiatric or addictive comorbidities

274x147mm (96 x 96 DPI)

Supplementary Table 1: Representativeness of the sample

Type of accommodation	Estimation of the target population*	Source	Number of effectively enrolled people
Squats or slums (Ethos 8)	619 to 817	NGO (MDM - Doctors of the World) – April 2020	363
Emergency shelters (Ethos 2)	795	Official administrative data (SIAO) – April 2020	358
Collective transitional shelters (Ethos 3)	634	Official administrative data (SIAO) – April 2020	196
Hostels mobilized during the covid crisis (Ethos 2)	893	Official administrative data (Service+) – July 2020	197
Street (Ethos 1)	455	First census of homeless people living in streets – January 2022 - No usable source of data in 2020	98

* *Adult homeless population living in the city of Marseille*. MDM (Médecins du Monde): Doctors of the World NGO; SIAO (Services intégrés de l'accueil et de l'orientation): Integrated reception and guidance services

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	3
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3-4
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	3
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*4*
Bias	9	Describe any efforts to address potential sources of bias	3-4
Study size	10	Explain how the study size was arrived at	3-4 and supl. file
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	3-4
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	4
		(*b*) Describe any methods used to examine subgroups and interactions	4
		(*c*) Explain how missing data were addressed	4
		(*d*) If applicable, explain how loss to follow-up was addressed	4
		(*e*) Describe any sensitivity analyses	4
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	3-4 and supl. file
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	5
		(b) Indicate number of participants with missing data for each variable of interest	5
		(c) Summarise follow-up time (eg, average and total amount)	5
Outcome data	15*	Report numbers of outcome events or summary measures over time	5
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	5-7
		(*b*) Report category boundaries when continuous variables were categorized	5-7
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	5-7
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	5
Discussion			
Key results	18	Summarise key results with reference to study objectives	8-9
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9
Generalisability	21	Discuss the generalisability (external validity) of the study results	9
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	12

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Cumulative incidence of SARS-CoV-2 infection within the homeless population: insights from a citywide longitudinal study

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Cumulative incidence of SARS-CoV-2 infection within the homeless population: insights from a citywide longitudinal study

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Word count: 3184

ABSTRACT

Objectives The aim of this study was to determine the risk factors associated with SARS-CoV-2 infection in a cohort of homeless people using survival analysis. Seroprevalence in the homeless community was also compared to that of the general population.
Design Cohort Study
Setting Data were collected across two testing sessions, 3 months apart, during which each participant was tested for anti-SARS-CoV-2 antibodies and completed a face-to-face surveys.
Participants All homeless adults sleeping rough, in slums or squats, in emergency shelters or transitional accommodation in Marseille were eligible.
Primary outcome measures Occurrence of a seroconversion event defined as a biologically confirmed SARS-CoV-2 infection. Local data from a national seroprevalence survey were used for comparison between homeless people and the general population.
Results A total of 1249 people were included. SARS-CoV-2 seroprevalence increased from 6.0% [4.7-7.3] during the first session to 18.9% [16.0-21.7] during the second one, compared to 3.0% [1.9-4.2] and 6.5% [4.5-8.7] in the general population. Factors significantly associated with an increased risk of COVID-19 infection were: having stayed in emergency shelters (1.93 [1.18 – 3.15]), being an isolated parent (1.64 [1.07-2.52]) and having contact with more than 5-15 people per day (1.84 [1.27 – 2.67]). By contrast, smoking (0.46 (0.32 – 0.65)), having financial resources (0.70 (0.51 – 0.97)) and psychiatric or addictive comorbidities (0.52 (0.32 – 0.85)) were associated with a lower risk.
Conclusion We confirm that homeless people have higher infection rates than the general population, with increased risk in emergency shelters. There is growing evidence that, in addition to usual preventive measures, public policies should pay attention to adapt the type of accommodation and overall approach of precariousness.

Data availability statement
The datasets generated and analyzed during the current study are not publicly available due to special authorization to transfer databases given by the CNIL. Upon prior authorization by the CNIL, the dataset would be available from the corresponding author upon reasonable request. Additionally, the study protocol is available upon request. All data requests should be addressed to the corresponding author.

Strengths and limitations of this study

- Description of risk factors of SARS-CoV-2 infection in a large study population with high-quality and statistically robust methodology.
- First surveillance data from a cohort of homeless people providing an incidence rate of seroconversion and comparing seroprevalence with the general population at two different time points.
- Large number of people lost to follow-up and difficulties in following a cohort of homeless people who are highly mobile
- Sensitivity of detection by repeated serological tests.

Keywords
Homeless population, COVID-19, cohort study, seroprevalence, prevalence, SARS-CoV-2

INTRODUCTION

The crisis generated by the COVID-19 pandemic suddenly widened the gap in access to healthcare, especially for vulnerable populations [1]. Before the pandemic, homelessness was already associated with higher health inequalities compared to the general population [2].

Public policies had to devise new strategies to limit the impact of the evolving pandemic on healthcare systems and societies. For example, the French Government imposed 2 stringent lockdowns in 2020. These restrictions were accompanied in most cities by a sheltering program for homeless people, with allocation of extra emergency shelters, transitional accommodations and requisitioned hotels [3]. In parallel however, there was a rise of precariousness in France, with an increase in the number of homeless people [4,5]. Studies show that homeless people are at high risk of developing SARS-CoV-2 infection and reinfection due to physical proximity, crowded emergency shelters and unsafe or unhygienic living conditions[6–8]. In this context, data on the spread of the SARS-CoV-2 virus and immunity among the homeless are essential to inform policy stakeholders and to contain epidemic dynamics.

In France, in May 2020, a nationwide study in the general population estimated that seroprevalence ranged from 3.5% (South East of France) to 10.8% (North East of France) [9], emphasizing the need for regionally specific data. This seroprevalence reflected the regional heterogeneity at the beginning of the pandemic. A high prevalence rate of SARS-CoV-2 infection was reported in people living in homeless shelters [7,10,11], which also showed a high rate of severe COVID-19 symptoms, potentially due to a lack of access to the health care and a high prevalence of comorbidities such as lung or heart diseases [12–14]. To our knowledge, there is no representative data of an entire homeless population to describe the dynamics of the prevalence of SARS-CoV-2 infection over time.

The aim of this study was to determine the risk factors associated with SARS-CoV-2 infection in a cohort of homeless people using survival analysis. Seroprevalence in the homeless community was also compared to that of the general population.

METHODS

Study Design

The present study was a descriptive and prospective cohort. Study design, participants and sampling were described in a previous study [15]. Each participant receives individualized follow-up and repeated testing at the inclusion and 3 month later. There was no resampling.

Study Area and Population

The study area was the city of Marseille, the second largest city in France with 889,029 inhabitants, suffering from a high level of poverty [16].

Eligible population

Data from the local orientation system for emergency and transitional accommodation (SIAO) and the NGO Doctors of the World estimated that in 2020, at the beginning of the COVID-19 outbreak, there were 2,322 homeless adults living in emergency, transitional shelters or hostels and 619 to 817 living in squats or slums (Supplementary File 1). No point-in-time census was available for people living on the streets in Marseille.

Inclusion criteria

In order to focus on the homeless people the furthest from housing, we decided to select those characterized by the greatest residential instability: people sleeping rough, in squats or slums, in stabilization shelters, in emergency shelters or hostels, respectively corresponding to the following categories of the European typology of homelessness (ETHOS): ETHOS 1, 2, 3 and 8 [17].

Participant selection

In the absence of a point-in-time count, random sampling was impossible. We set a 2-month inclusion period, during which we systematically offered all homeless people aged over 18 to participate in the study. Recruitment of participants was also facilitated by the "Accés aux Soins des Sans Abris (ASSAb) network" of assistance to homeless people: 18 homeless outreach teams working in streets, hotels, squats or slums, 5 emergency shelters and 10 transitional accommodations.

Investigations

Two specific sessions of serological testing were conducted in order to assess seroprevalence. The first session lasted from June 5 to August 5, 2020, and the second from September 11 to December 18, 2020. At each session, each participant was tested using a rapid diagnostic serological test, and completed a face-to-face survey investigating: socio-demographic characteristics; comorbidities; past and current medical history of COVID-19; difficulties in access to care, water, food or hygiene supplies; compliance with the preventive measures (social

distancing, wearing a face mask, and hand washing). Questions were asked by trained local interviewers in the participants' native language to improve comprehension and to minimize the information bias.

Community Engagement and Medical Care

Community awareness interventions were conducted during the two testing sessions, to secure the commitment and participation of a majority of homeless people. Community engagement started by meetings with the community leaders or mediators but also the healthcare workers and the members of local institutions or NGOs implicated in health for homeless people with the help of a local network (ASSAB) in charge of coordination with these different stakeholders. Interviewers were sensitized to the study objectives, interventions and expected role of the community. A mobile team including an infectious disease specialist, a nurse and a community mediator followed the positive cases.

Field Biological Analysis

We used the rapid serological test "Biosynex COVID-19 BSS®", that detects immunoglobulin M (IgM) and G (IgG) in 10 minutes with high specificity and sensitivity (>95% and 90% respectively) [18].

Data Analysis

Descriptive analyses of sociodemographic characteristics were performed using numbers and percentage for categorical data, or medians and interquartile range (IQR) for quantitative data. The seroprevalence of COVID-19 infection was investigated between February 1, 2020 and December 18, 2020. All the participants were considered to have a negative serology on February 1, 2020 before the first cases were detected in early March 2020 in Marseille. In the event of seroconversion, infection was reported as confirmed at the time of serological testing, with the possibility of overestimating the number of person-days before infection and regardless of the results of subsequent serological tests. This methodological choice was made in relation to the different predictive variables also collected at the time of the serological test. To assess seroprevalence rate according to presence or absence of symptoms, bootstrap resampling approach with a set of 1,000 samples was used to create 95% confidence intervals (CI) based on IgM/IgG sensitivity and specificity and their 95%CI. Kaplan-Meier methods along with the log rank test were used to establish statistical differences in seroprevalence rates between types of ETHOS accommodation [17]. A survival analysis was carried out to address the spread of COVID 19 among the targeted population. The time (in months) was defined as follows: the starting date was the date of February 01 2020, date at which none positive cases were registered in Marseille, that is when all participants could be considered to have a COVID19-negative status. The event was a positive SARS-CoV-2 status, whatever a positive SARS-CoV-2 PCR or a positive serological test informed the diagnosis. His or her status was considered positive regardless of the results of subsequent serological tests. For those with a PCR test achieved, the date of the event corresponded to the PCR date, corrected with the date of the first symptoms when reported. For positive participant with a rapid serological test, the reported date of the first symptoms was considered. For participant with a positive serological test but with no history of symptoms, we considered the date of the testing strategy performed by the research team. In order to take into account in the analysis, in regards to the mobility of the participants, in terms of the place of residence and the possibility of changes in socio-demographic characteristics, we took the data at the time of the positive test for SARS CoV2 participants and at the time of the last test for negative patients throughout the follow-up. No additional corrections were made in absence of any informative data. Participants tested negative at the first testing wave but being lost to follow up at the second testing wave were censored at the date of the last collection data. The cut-off date was December 18 2020, precisely 11.2 months after the starting date. A Cox model was performed using both baseline covariates and time-dependent covariates. Time-dependent covariates were the following: type of ETHOS accommodation (i.e. street, emergency shelters, hotels, transitional shelter or squat/slum), type of accommodation (private or shared room/area), number of contacts per day, having financial resources and having work. We fitted a multivariate Cox model by considering as eligible variables those that were significant in a univariate analysis at the 5% level, and considering all pairwise interactions. The covariate "number of contacts per day" was forced into the model as it was considered to be a relevant variable. We tested the assumption of proportional hazards using Schoenfeld residuals. Then, we used the Stepwise selection function in R, which starts with an empty model and adds/removes predictors according to AIC criteria. Unadjusted and adjusted Hazard ratios (HR) and 95 % CI were given.

All of the statistical analyses were carried out using R software, and differences with p values of <0.05 were considered statistically significant.

Seroprevalence data of our study were compared with data from a representative sample of the general population living in Marseille, which were derived from a national seroprevalence survey (EpiCov) [19]. Results of seroprevalence in the general population were obtained from home self-samples of dried blood spots, in order to detect IgG antibodies (Euroimmun ELISA-S) [19].

All the confirmed cases of COVID-19 by positive SARS-CoV-2 PCR in Marseille registered from January 1 to December 31, 2020, by the French national monitoring department (SI-DEP) from *Santé Publique France* [20], were used to describe the local incidence rate of COVID-19 infection in cases per person-weeks.

Patients and public involvement: Public were involved in conduct (questionnaire were conducted by peer workers) and dissemination plans of this research (the results were presented to the public via photo and sound exhibitions and radio broadcasts in Marseille city).

RESULTS

During the first session from June 5 to August 5, 2020, 1241 people were included. Median age was 38 years [IQR 22], 70.40% were men (n=874) with 98 (8.1%) of participants living rough, 358 (29.5%) in emergency shelters, 197 (16.2%) in hostels, 196 (16.2%) in transitional shelters, and 363 (29.9%) in squats and slums (Table 1). A total of 30% of the participants in the cohort changed their place of residence during follow-up. Approximately 37% of eligible ETHOS 2, 3 and 8 participants were included in the study (Supplementary File 1). Around half of the participants, 52.2% (n=648/1241), had confirmed or possible risk factors for severe COVID-19 disease, including cancer, obesity, cardiac or pulmonary disease and severe renal insufficiency. In addition, half of the participants (52.0%, n=645) reported active tobacco consumption. A total of 58.1% (n=721) of the participants tested during the first session were also tested at the second session.

Table 1: Population characteristics (n=1241)	
Baseline characteristics	**n (%) or median [IQR]**
Gender	
Men	874 (70.4%)
Women	367 (29.6%)
Age, median, years	38 [22]
Age <= 65 years	1179 (95.0%)
French Nationality	222 (18.4%)
Country of Birth	
France	234 (18.9%)
Europe	416 (33.5%)
Africa	282 (22.7%)
Other	279 (22.5%)
Missing	30 (2.4%)
Educational attainment	
None	560 (45.1%)
Lower secondary	445 (35.9%)
Upper secondary or vocational	122 (9.8%)
Missing	114 (9.2%)
Household status	
Isolated adult	660 (53.2%)
Isolated parent	129 (10.4%)
Family	411 (33.1%)
Missing	41 (3.3%)
Health insurance	
No	345 (27.8%)
Yes	826 (66.6%)
Missing	70 (5.6%)
Financial resources	
No	448 (36.1%)
Yes	730 (58.8%)
Missing	63 (5.1%)
Working situation [a]	
No	949 (76.5%)
Yes	229 (18.5%)
Missing	63 (5.1%)
Total length of homelessness	
<= 5 years	775 (62.4%)
> 5 years	393 (31.7%)
Missing data	73 (5.9%)
Typology ETHOS*	
ETHOS 1: street	98 (8.1%)

ETHOS 2: emergency shelters	358 (29.5%)
ETHOS2: hotels	197 (16.2%)
ETHOS 3: transitional shelters	196 (16.2%)
ETHOS 8: squats, slums	363 (29.9%)
Type of accommodation	
Private room or area	524 (42.2%)
Shared room or area	648 (52.2%)
Missing data	69 (5.6%)
Number of contacts per day	
<= 5	714 (58.0%)
5 to 15	410 (33.3%)
>15	107 (8.7%)
Tobacco consumption	
No	480 (38.7%)
Yes	645 (52.0%)
Missing	116 (9.3%)
Comorbidity	
Psychiatric or addictive comorbidities	295 (23.8%)
Obesity	72 (6.5%)
Diabetes	91 (8.1%)
Chronic Respiratory Pathology	99 (9.2%)
Cardiovascular Pathology	152 (14.1%)
Chronic renal failure with dialysis	23 (2.1%)
Cancer	24 (2.2%)

SD: Standard Deviation; IQR: Inter Quartile Range.
a: declared or undeclared employment.
*ETHOS: European Typology on Homelessness and Housing Exclusion [17]

A total of 74/1241 of participants had positive serology in the first campaign, with 2.5% of positive IgM tests, 5.2% positive IgG tests and 1.7% positive IgM and IgG tests. In the second campaign, 136/721 of participants had positive serology with 8.1% of positive IgM tests, 17.5% positive IgG tests and 6.8% positive IgM and IgG tests. Of the 74 participants with positive serology at the start of the study, 43 were able to be followed up and have a new serology 3 months later. A total of 69.8% (n=30) still had positive serology. Thus, in 30.2% of cases (n=13) there was a rapid negativation of serology.
Seroprevalence was 6.0% (IQR 4.7-7.3) (n=1241) in the first campaign and 18.9% (IQR 16.0-21.7) (n=721) in the second campaign, and had significantly increased (p<0.005) (Figure 1. In comparison, seroprevalence in the general population in Marseille (EpiCoV-Marseille) was 3.0% [1.9-4.2] in May to June and 6.5% (CI95% 4.5-8.7) in November to December 2020 and had significantly increased (p<0.005) (Figure1).

Factors Associated with SARS-CoV-2 Infection
A total of 180 participants presented a SARS-CoV-2 seroconversion defined by a positive serology result for SARS-CoV-2 (IgM or IgG). At inclusion (n=74/1241) or as part of the cohort follow-up (n=136/721). Average time of infection from February 1, 2020 was 230 days (IQR 162-277). Figure 2 shows the Kaplan Meier curves according to the participant's type of accommodation. Homeless people living in emergency shelters and hotels had a significantly higher risk of SARS-CoV-2 infection compared to their counterparts over the study follow-up period (p<0.001).

Table 2 shows univariate and multivariate analysis of the factors associated with the SARS-CoV-2 seroprevalence. Univariate analysis identified an association between positive serological results and participants coming from Africa (2.51 (1.45 – 4.33)) or those applying physical distancing (1.61 (1.14 – 2.27)). These two variables were not retained in the final model. Difficult access to hygiene products was also associated with lower seroprevalence in univariate analysis (0.72 (0.52 – 0.96)) but not in multivariate analysis. Being an isolated parent (1.64 (1.07 – 2.52)), spending more than 33% (1.70 (1.11 – 2.62)) or 66% (1.93 (1.18 – 3.15)) of time living in an emergency shelter during follow-up, and having between 5 to 15 daily contacts (1.84 (1.27 – 2.67)), were associated with SARS-CoV-2 infection in multivariate analysis. By contrast, having financial resources (1.64 (1.07 – 2.52)), being a smoker at the time of the survey (0.46 (0.32 – 0.65)) and having psychiatric or addictive comorbidities (0.52 (0.32 – 0.85)) were associated with a lower risk of SARS-CoV-2 seroprevalence. Figure 3 summarizes the Cox multivariable regression analysis. Model remains unchanged even by adjusting on age and sex (Supplementary file 2).

Other potential risk factors, such as educational attainment, gender, age, total length of homelessness in the life of participants, wearing a mask, hand washing, difficult access to water or not having health insurance were not associated with SARS-CoV-2 prevalence.

Table 2: Univariate and multivariable analysis of the seroprevalence of SARS-CoV-2 infection (n=180/1241) between February and December 2020 in homeless people living in Marseille

Results	**Univariate analysis**		**Multivariate analysis [£]**
	HR (CI95%)	p-value	Adjusted HR (CI95%)
Gender			
Men	ref		
Women	0.97 (0.70 - 1.34)	0.900	
Age, years			
<=65	Ref		
>65	1.66 (0.99 – 2.77)	0.050	
Country of Birth			
France	ref		
Europe	1.45 (0.83 – 2.55)	0.193	
Africa	2.51 (1.45 – 4.33)	**0.001[£]**	
Other	2.80 (1.63 – 4.79)	<0.001	
Educational attainment			
None	ref		
Lower secondary	1.32 (0.96 – 1.82)	0.090	
Upper secondary or vocational	1.14 (0.63 – 2.05)	0.670	
Household status			
Isolated adult	ref		ref
Isolated parent	1.78 (1.18 – 2.67)	**0.006**	**1.64 (1.07 – 2.52)**
Family	0.78 (0.55 – 1.11)	0.168	0.78 (0.50 – 1.20)
Health insurance			
No	Ref		
Yes	0.96 (0.69 – 1.34)	0.800	
Having financial resources			
No	Ref		Ref
Yes	0.64 (0.47 – 0.86)	**0.003**	**0.70 (0.51 – 0.97)**
Having work			
No	Ref		
Yes	0.71 (0.45 – 1.12)	0.110	
Total length of homelessness			
<= 5 years	ref		
> 5 years	0.95 (0.69 – 1.30)	0.700	
Percent of time spent in emergency shelters*			
<33%	Ref		ref
33 to 66%	1.68 (1.15 – 2.46)	**0.007**	**1.70 (1.11 – 2.62)**
>66%	2.45 (1.59 – 3.76)	**<0.001**	**1.93 (1.18 – 3.15)**
Number of daily contacts			
<=5 per day	Ref		Ref
>5 to <=15 per day	1.21 (0.88 – 1.65)	0.100[£]	**1.84 (1.27 – 2.67)**
>15 per day	0.68 (0.33 – 1.40)	0.200	1.45 (0.69 – 3.04)
Wearing mask			
No, somewhat no	Ref		
Yes, somewhat yes	1.23 (0.85 – 1.78)	0.300	
Physical distancing			
No, somewhat no	Ref		
Yes, somewhat yes	1.61 (1.14 – 2.27)	**0.007[£]**	
Hand washing			
No, somewhat no	ref		
Yes, somewhat yes	1.43 (0.99 – 2.06)	0.060	
Difficult access to hygiene products			
No, never, rarely	Ref		ref
Yes, always, often	0.72 (0.52 – 0.96)	**0.040**	0.75 (0.50 – 1.12)
Difficult access to water			
No, never, rarely	Ref		
Yes, always, often	0.76 (0.54 – 1.09)	0.100	
Difficult access to food			
No, never, rarely	Ref		

Yes, always, often	0.83 (0.62 – 1.12)	0.200	
Smoking status			
Non smoker	Ref		ref
Smoker	0.39 (0.28 – 0.53)	**<0.001**	**0.46 (0.32 – 0.65)**
Psychiatric or addictive comorbidity			
No	Ref		ref
Yes	0.46 (0.30 – 0.69)	**<0.001**	**0.52 (0.32 – 0.85)**

$: total of participants in the analysis: 1241; missing values exist for some of the independent variables; for example smoking status (n=116), educational attainment (n=114), health insurance (n=70), self-reported financial resources (n=63) or household status (n=41).
*: Percentage was calculated on the basis of each participant's exposed time until the event or until the end of the follow-up in the absence of an event.
£: We fitted a multivariable model containing all variables that were significant in a univariate analysis at the 10% level. We used the Stepwise selection function in R (a mix between forward and backward selection), which starts with an empty model and adds predictors according to AIC criteria. Accordingly, "Country of birth" and "physical distancing" were considered in the multivariate model and removed. In addition, "number of contacts" was forced into the model as a relevant variable.

Symptomatology of participants with positive SARS-CoV-2 serological status

Among participants with SARS-CoV-2 infection (positive IgM or IgG or both, n=180), 67.6% reported no symptoms (Table 3). Among participants with symptomatic SARS-CoV-2 infections, the most common symptoms were fever, cough, headache and fatigue. Even if participants with a positive serological status reported Covid-19 syndrome (fever, cough, anosmia, headache notably) significantly more often than participants without serological immunity (Table 3), the frequency of symptoms reported did not appear to be strictly specific to SARS-CoV-2 infection.

Table 3: Symptoms reported in the last 3 months prior the serological test according to serological status (n=1241)

	Negative serological status n (%)	CI95% $	Positive serological status n (%)	CI95%$	P-value
Individuals missing symptom data (n=303)	302 (24.3%)		1 (0.1%)		
Individuals with symptom data (n=938)	759 (75.7%)		179 (99.9%)		
Asymptomatic patient	656 (86.4%)	(84.7 – 91.4)	121 (67.6%)	(65.8 – 71.5)	<0.001
Participants with symptoms	103 (13.6%)	(11.7 – 14.3)	58 (32.4%)	(30.6 – 34.1)	
Fever	42 (4.0%)	(2.1 – 4.1)	36 (18.0%)	(16.1 – 18.9)	<0.001
Cough	38 (3.7%)	(1.8 – 3.8)	28 (14.0%)	(12.1 – 14.6)	<0.001
Dyspnea	16 (1.5%)	(0.0 – 1.5)	8 (4.0%)	(2.1 – 4.1)	0.040
Headache	41 (3.9%)	(2.0 – 4.0)	36 (18.0%)	(16.2 – 18.9)	<0.001
Anosmia	15 (1.4%)	(0.0 – 1.4)	21 (10.5%)	(8.6 – 10.9)	<0.001
Rhinitis	39 (3.7%)	(1.8 – 3.8)	21 (10.5%)	(8.6 – 10.9)	<0.001
Fatigue	35 (3.4%)	(1.5 – 3.5)	38 (19.0%)	(17.1 – 20.0)	<0.001
Diarrhoea	15 (1.4%)	(0.0 – 1.4)	15 (7.5%)	(5.6 – 7.8)	<0.001
Joint pain	15 (1.4%)	(0.0 – 1.4)	19 (9.5%)	(7.6 – 10.0)	<0.001
Odynophagia	22 (2.1%)	(0.0 – 2.1)	14 (7.0%)	(5.1 – 7.3)	<0.001
Chills	21 (2.0%)	(0.0 – 2.0)	17 (8.5%)	(6.6 – 8.8)	<0.001
Mottling	1 (0.1%)	(0.0 – 0.1)	0 (0%)	(0.0 – 0.1)	0.999
Skin rash	1 (0.1%)	(0.0 – 0.1)	3 (1.5%)	(0.0 – 1.5)	0.014
Conjunctivitis	9 (0.8%)	(0.0 – 0.7)	8 (4.0%)	(2.1 – 4.1)	0.002
Other	5 (0.5%)	(0.0 – 0.4)	2 (1.0%)	(0.0 – 0.9)	0.316

CI95%: confidence interval at 95%
$: an exact test of a simple null hypothesis about the probability of success in a Bernoulli experiment was performed, with confidence level for the returned confidence interval.

DISCUSSION

The present study is the first to describe the dynamics of SARS-CoV-2 seroprevalence among a large cohort of 1241 homeless people living in Marseille, France. Analysis of data from homeless participants with positive serology results over time, revealed a high prevalence of asymptomatic infection and significant associations between positive serology and the lack of financial resources, being an isolated parent, having between 5 and 15 daily contacts, and the time spent in emergency shelters. Repeated seroprevalence studies enabled to estimate the cumulative incidence of SARS-CoV-2 infection in both asymptomatic and symptomatic people, offering valuable data to inform public health policy-makers [7,21]. In the general population, asymptomatic individuals represent up to 68% of SARS-CoV-2 infections [7,22] and contribute to the rapid spread of the disease [1]. In our study, the estimated prevalence of SARS-CoV-2 increased from 6.01% [4.68-7.34] in June to August to 18.86 % [16.00-21.72] in September to December and remained higher than in the general population. Indeed, a cross-sectional study evaluating the seroprevalence of SARS-CoV-2 antibodies across the general population in Marseille in May and November, 2020, found 3.0% [1.9-4.2] and 6.5% (CI95% 4.5 – 8.7), respectively. The increasing gap in seroprevalence between the general population and the homeless population may be due to a potential breakdown of protective measures for people in the most precarious situations [5]. The available data on homeless people comes from cross-sectional studies, that mainly found high seroprevalence [7,10,11]. However, the testing approach was different and concerned a population selected from one type of accommodation (mainly emergency shelters) and results also depend on the intensity of the local epidemic at the time of the survey. A lower infection rate with increasing age was reported in several population-based serological studies, which is not consistent with our findings [23,24]. We observed no differences, in univariate analysis, in estimated seropositivity for older participants or for participants who had comorbidities. These results suggest that aged homeless people at risk of severe COVID-19 disease may be infected by SARS CoV-2 at the same rate as other adults. The pandemic has played an important role in amplifying health inequalities that already existed [25,26]. Increasing evidence has emerged, highlighting that COVID-19 mortality is higher for those who are socioeconomically deprived. We reported in our findings, in addition to the poorest condition of homelessness, that not having financial resources during the pandemic crisis was also a risk factor of SARS-CoV-2 seroprevalence. The link between socioeconomic status and development of infectious disease is well documented, and the main mechanisms reported to be associated with higher occurrence rates of communicable diseases included poor housing, lack of education, nutritional deficiencies, poor work conditions and hygiene [27].

African homeless immigrants had higher SARS-CoV-2 prevalence rates in our study compared to other nationalities. This is despite the fact that North and Sub-Saharan Africans are grouped together for analysis in our study. These findings were consistent with French, English or US studies which reported higher seroprevalence rates and mortality in black ethnic groups [9,28,29]. The homeless are a heterogeneous population. Even if homeless people already face disparity in health outcomes in the current COVID-19 pandemic, African immigrants are a subgroup at even more risk. Thus, it could be important to generate accessible health information and preventive measures for this subgroup, adapted to their literacy and specific needs.

Our study reported lower SARS-CoV-2 infection rates in participants with mental disorders or substance abuse. This is surprising since substance use disorders have frequently been reported to increase the risk of infectious diseases and mental illness to impact awareness of vulnerability to infection and help-seeking when symptoms of COVID-19 develop [30,31]. Since social contacts are the way in which the infection is spread, this lower seroprevalence could be interpreted as a sign of exclusion of these particularly stigmatized people [32]. It should also be noted that in Marseille there are specific healthcare mobile teams for people suffering from mental disorders and substance abuse [33]. This type of specific program has previously reported positive results in pandemic context [34].

In line with the findings of other studies, we observed a considerable proportion of positive subjects (67.6%) with asymptomatic infection [22,35,36]. Some symptoms (fever, cough, headache or fatigue notably) were significantly associated with positive SARS-CoV-2 serology and should be repeated to people during interventions on prevention and information.

As previously described, smoking prevalence was lower in seropositive SARS-CoV-2 participants in our study [37]. Even if prevalence was lower, smoking was associated with an increased risk of hospitalization and morbidity [38]. In our study, a substantial proportion of participants reported alcohol and tobacco consumption. In homeless populations a large proportion of deaths are therefore substance-attributable [39].

Our study reinforces the negative role of overcrowded types of accommodation for homeless people, which increase SARS-CoV-2 transmission. In the USA and France, emergency shelters and their high population density appear to increase the risk of infection [7,11]. Indeed, the emergency shelters are short term shelters that can accommodate several hundred people in Marseille with common sanitary facilities [40]. Collective transitional shelters are longer term, smaller facilities offering more consistent social work. The first French lockdown was ordered on March 17, 2020, as emergency shelters are already full in normal times, hotels were required. In these hotels, people did not have kitchen facilities and often found themselves in high-density grouping areas, especially

at meal times or in the few outdoor spaces available [40]. Shelters should be considered as high-risk environments and stays there should be limited to the minimum. Providing adequate housing with individual bathroom facilities could be the most effective strategy for mitigating SARS-CoV-2 transmission in homeless communities, as was reported in a modeling study and by field healthcare workers [41,42]. Our findings also show an association with a high prevalence in shelters and hostels, which highlights the limits of individual preventive measures in transitional collective accommodations. These studies illustrate a good compliance with preventive measures, notably in collective accommodations, but these are clearly insufficient to limit the spread of infection. Homeless people in the pandemic must face concurrent risks: the risk of SARS-CoV-2 infection in shelters and collective accommodation, and the risk of the lack of access to food, water or hygiene products in more insecure housing conditions [43].

Throughout the course of the pandemic, healthcare and housing programs for homeless people have been modified. However, our results suggest that overcrowded and large emergency shelters or transitional accommodation including hostels increase the risk of SARS-CoV-2 transmission which pleads to adapt social and public health infrastructures towards good quality, smaller and semi-private accommodation. Holistic action (food, hygiene and financial support, health insurance, specific vaccination program…) must also be taken to ensure that the needs of these individuals are met sufficiently for them to be able to limit viral spread, survive this pandemic and be well enough equipped to endure the following economic crisis.
In addition, our findings highlight two other risk factors linked to socioeconomic inequalities: the lack of financial resource and being an isolated parent. Furthermore, people with low financial resources or single parents with one child are potentially more likely to seek outside support which may increase the risk of viral exposure, as it was previously described for people who have to work outside [44].

Strengths and limitations
Our study has number of strengths. Although studies have shown an increased risk of SARS-CoV-2 infection in homeless people, this is the first surveillance data from a cohort providing an incidence rate of seroconversion and comparing seroprevalence with the general population at two different time points. Our study described risk factors of SARS-CoV-2 infection in a large study population with high-quality and statistically robust methodology. Our findings quantify the excess risk associated with staying in emergency shelters. We also found evidence of SARS-CoV-2 infection among the most economically vulnerable (lack of financial resources, isolated parent) highlighting the need for a comprehensive and proactive approach including financial aid, food, water, adequate housing, mobile healthcare and social assistance for this vulnerable population.
Our study has also some limitations. Although it is representative of different homelessness categories (living in the street, slum, squat, emergency shelter or transitional accommodation), the sample was not randomly enrolled and therefore our findings may not reflect true seroprevalence, as a potential selection bias cannot be excluded. Characteristics of study participants upon inclusion and at the end of follow-up were also different, roofless and younger populations were most frequently lost to follow-up because of a higher mobility. We may also underestimate seroprevalence and false negative results cannot be excluded [45,46]. Finally, the serological tests between the general population and the homeless population were not exactly the same. This may account for some of the observed differences in seroprevalence rates between the two populations.

Policy implications and further research
There is growing evidence that, in addition to usual preventive measures, public policies should pay attention to adapt the type of accommodation and overall approach of precariousness. The findings of this study can guide European and other governments' disease control planning; to find optimal solutions to house people in less crowded accommodations, prioritizing individual rather than collective settings and a global approach, thus restricting transmission. To complete these results, future studies in this vulnerable population should assess the morbidity and mortality associated with SARS-CoV-2.

CONCLUSIONS
The longitudinal cohort of homeless people in Marseille revealed an increase in the seroprevalence of SARS-CoV-2 infection. This was higher than that observed in the general population and reflects precarious living conditions and inadequate types of accommodation for this vulnerable population.

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Data sharing statement
The datasets generated and analyzed during the current study are not publicly available due to special authorization to transfer databases given by the CNIL. Upon prior authorization by the CNIL, the dataset would be available from the corresponding author upon reasonable request. Additionally, the study protocol is available upon request. All data requests should be addressed to the corresponding author.

Ethical Approval
All participants provided a written informed consent. The COVIDHomeless study was designed and carried out in compliance with the Declaration of Helsinki and with legal and regulatory provisions. It was approved by the ethics committee on May 28, 2020 (CPP IDF VI - number 44-20; ID: 2020-AO1398-31). The database was anonymized and declared to the French data protection commission (*Commission Nationale de l'Informatique et des Libertés*, CNIL, n°2018172v0).

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Figure legend/caption

Figure 1: Seroprevalence rates during the two serological testing campaigns[$] in homeless people cohorts and results for the general population from the EpiCov study in Marseille.
*General population seroprevalence rate data come from the EpiCov study in Marseille. $: Bootstrap resampling approach with a set of 1,000 samples was used to create confidence intervals, accounting for variability in the sensitivity and specificity of the serological assay.

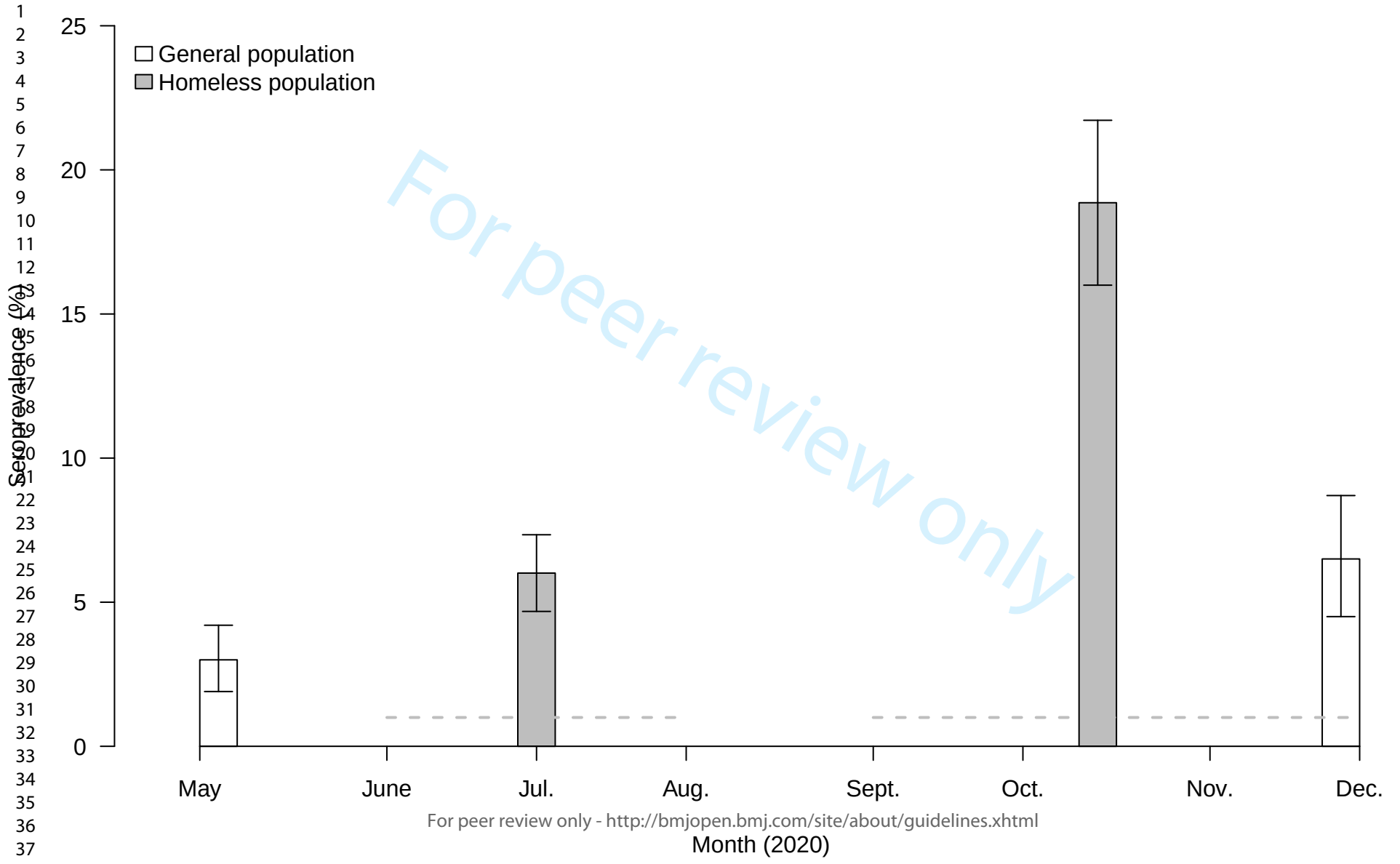
Figure 2: Risk of SARS-CoV-2 infection by type of housing for homeless participants estimated by the Kaplan-Meier method, including 95% CI. Censoring and number of participants at risk at different time points are indicated.

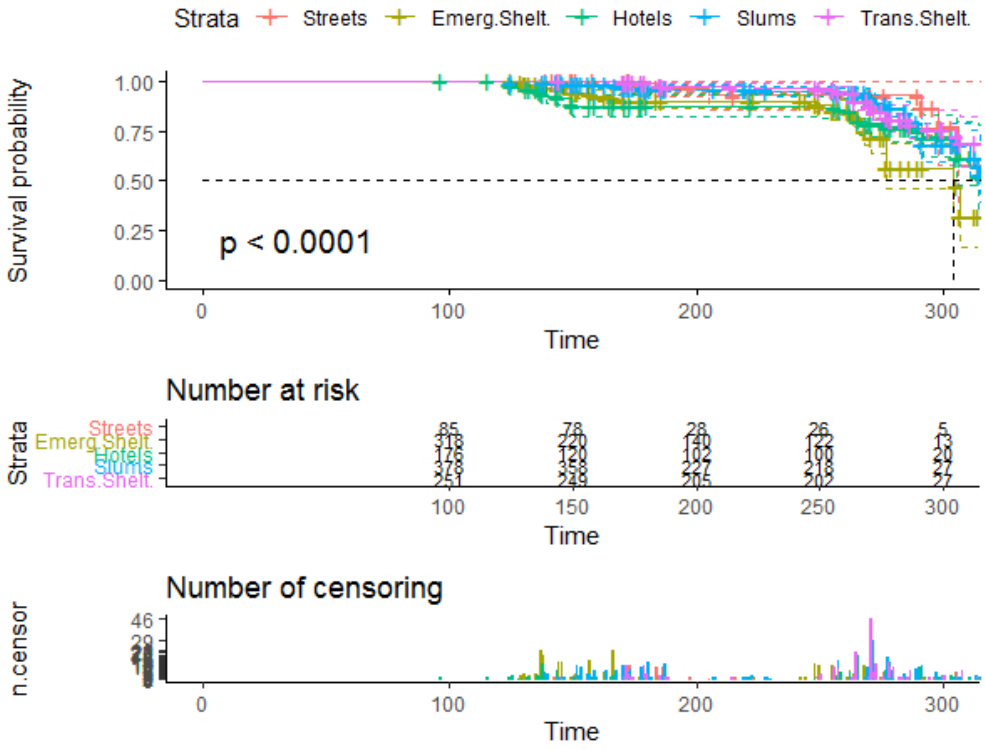
Street: people living rough (ETHOS1); Emerg.Shelt.: people living in emergency shelters (ETHOS2); Hostel: people living in hostels (ETHOS3); Slums: people living in slums or squats (ETHOS8); Trans.Shelt.: people living in transitional accommodation for the homeless (ETHOS4)

Figure 3: Cox multivariable logistic regression analysis of risk factors of SARS-CoV-2 seroprevalence in homeless people in Marseille
Having_Comorb_PsyAddic: Psychiatric or addictive comorbidities

Supplementary File 1: Representativeness of the sample
* *Adult homeless population living in the city of Marseille*. MDM (Médecins du Monde): Doctors of the World NGO; SIAO (Services intégrés de l'accueil et de l'orientation): Integrated reception and guidance services

Supplementary File 2: Cox multivariable logistic regression analysis of risk factors of SARS-CoV-2 seroprevalence in homeless people in Marseille adgusted on age and sex
Having_Comorb_PsyAddic: Psychiatric or addictive comorbidities

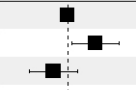




Risk of SARS-CoV-2 infection by type of housing for homeless participants estimated by the Kaplan-Meier method, including 95% CI. Censoring and number of participants at risk at different time points are indicated.Street: people living rough (ETHOS1); Emerg.Shelt.: people living in emergency shelters (ETHOS2); Hostel: people living in hostels (ETHOS3); Slums: people living in slums or squats (ETHOS8); Trans.Shelt.: people living in transitional accommodation for the homeless (ETHOS4)

157x124mm (96 x 96 DPI)

Variable		N	Hazard ratio	p
Household_status	Isolated adults	589	Reference	
	Isolated parent	121	1.64 (1.07, 2.52)	0.024
	Family	338	0.78 (0.50, 1.20)	0.255
Percent_time_shelter	<=33	764	Reference	
	33 to 66	139	1.70 (1.11, 2.62)	0.016
	>=66	145	1.93 (1.18, 3.15)	0.009
Difficulty_access_hygiene_products	No,never,rarely	685	Reference	
	Yes,always,often	363	0.75 (0.50, 1.12)	0.160
Having_FinancialResources	No	459	Reference	
	Yes	589	0.70 (0.51, 0.97)	0.033
Tobacco	Non smoker	452	Reference	
	Smoker	596	0.46 (0.32, 0.65)	<0.001
Having_Comorb_PsyAddic	No	784	Reference	
	Yes	264	0.52 (0.32, 0.85)	0.009
Number_Daily_contact	<=5	634	Reference	
	5-15	319	1.84 (1.27, 2.67)	0.001
	>15	95	1.45 (0.69, 3.04)	0.331



Cox multivariable logistic regression analysis of risk factors of SARS-CoV-2 seroprevalence in homeless people in MarseilleHaving_Comorb_PsyAddic: Psychiatric or addictive comorbidities

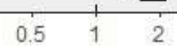
274x147mm (96 x 96 DPI)

Supplementary Table 1: Representativeness of the sample

Type of accommodation	Estimation of the target population*	Source	Number of effectively enrolled people
Squats or slums (Ethos 8)	619 to 817	NGO (MDM - Doctors of the World) – April 2020	363
Emergency shelters (Ethos 2)	795	Official administrative data (SIAO) – April 2020	358
Collective transitional shelters (Ethos 3)	634	Official administrative data (SIAO) – April 2020	196
Hostels mobilized during the covid crisis (Ethos 2)	893	Official administrative data (Service+) – July 2020	197
Street (Ethos 1)	?	No usable source of data	98

* *Adult homeless population living in the city of Marseille*. MDM (Médecins du Monde): Doctors of the World NGO; SIAO (Services intégrés de l'accueil et de l'orientation): Integrated reception and guidance services

Variable		N	Hazard ratio	p
Sex		1048	1.12 (0.75, 1.68)	0.576
Age		1048	1.21 (0.69, 2.13)	0.503
Household_status	Isolated adults	589	Reference	
	Isolated parent	121	1.62 (1.05, 2.49)	0.028
	Family	338	0.75 (0.48, 1.17)	0.207
Percent_time_shelter	<=33	764	Reference	
	>=66	145	1.90 (1.13, 3.18)	0.015
	33 to 66	139	1.73 (1.11, 2.68)	0.015
Difficultyaccess_hygiene	No,never,rarely	685	Reference	
	Yes,always,often	363	0.74 (0.50, 1.12)	0.154
Have_FinancialResource	No	459	Reference	
	Yes	589	0.71 (0.51, 0.98)	0.037
Tobacco	Non smoker	452	Reference	
	Smoker	596	0.47 (0.32, 0.67)	<0.001
Have_Comorb_PsyAddic	No	784	Reference	
	Yes	264	0.52 (0.32, 0.84)	0.008
Number_Daily_contact	<=5	634	Reference	
	>15	95	1.47 (0.70, 3.09)	0.311
	5-15	319	1.86 (1.28, 2.70)	0.001



STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	3
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3-4
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	3
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*4*
Bias	9	Describe any efforts to address potential sources of bias	3-4
Study size	10	Explain how the study size was arrived at	3-4 and supl. file
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	3-4
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	4
		(*b*) Describe any methods used to examine subgroups and interactions	4
		(*c*) Explain how missing data were addressed	4
		(*d*) If applicable, explain how loss to follow-up was addressed	4
		(*e*) Describe any sensitivity analyses	4
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	3-4 and supl. file
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	5
		(b) Indicate number of participants with missing data for each variable of interest	5
		(c) Summarise follow-up time (eg, average and total amount)	5
Outcome data	15*	Report numbers of outcome events or summary measures over time	5
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	5-7
		(*b*) Report category boundaries when continuous variables were categorized	5-7
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	5-7
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	5
Discussion			
Key results	18	Summarise key results with reference to study objectives	8-9
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9
Generalisability	21	Discuss the generalisability (external validity) of the study results	9
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	12

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.