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Research paper

Exposures associated with SARS-CoV-2 infection in France: A nationwide online case-control study

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SUMMARY

Background: We aimed to assess the role of different setting and activities in acquiring SARS-CoV-2 infection.
Methods: In this nationwide case-control study, cases were SARS-CoV-2 infected adults recruited between 27 October and 30 November 2020. Controls were individuals from the Ipsos market research database matched to cases by age, sex, region, population density and time period. Participants completed an online questionnaire on recent activity-related exposures.
Findings: Among 3426 cases and 1713 controls, in multivariable analysis, we found an increased risk of infection associated with any additional person living in the household (adjusted-OR: 1·16; 95%CI: 1·11-1·21); having children attending day-care (aOR: 1·31; 95%CI: 1·02-1·62), kindergarten (aOR: 1·27; 95%CI: 1·09-1·45), middle school (aOR: 1·30; 95%CI: 1·15-1·47), or high school (aOR: 1·18; 95%CI: 1·05-1·34); with attending professional (aOR: 1·15; 95%CI: 1·04-1·26) or private gatherings (aOR: 1·57; 95%CI: 1·45-1·71); and with having frequented bars and restaurants (aOR: 1·95; 95%CI: 1·76-2·15), or having practiced indoor sports activities (aOR: 1·36; 95%CI: 1·15-1·62). We found no increase in risk associated with frequenting shops, cultural or religious gatherings, or with transportation, except for carpooling (aOR: 1·47; 95%CI: 1·28-1·69). Teleworking was associated with decreased risk of infection (aOR: 0·65; 95%CI: 0·56-0·75).
Interpretation: Places and activities during which infection prevention and control measures may be difficult to fully enforce were those with increased risk of infection. Children attending day-care, kindergarten, middle and high schools, but not primary schools, were potential sources of infection for the household.
Funding: Institut Pasteur, Research & Action Emerging Infectious Diseases (REACTing), Fondation de France (Alliance" Tous unis contre le virus").

1. Introduction

One year after the first cases of coronavirus disease 2019 (COVID-19) were reported in Wuhan [1], China, the COVID-19 pandemic continues, with considerable public health, economic and societal impacts. Many countries, particularly those in Europe, managed to bring transmission to low levels in the spring of 2020 through the introduction of strict and wide-reaching public health and social measures [2,3]. However, since the fall, these same countries have faced continued resurgence in transmission and have introduced curfews and stay-at-home orders as means to control viral spread. Stay-at-home orders have proved to be effective at reducing SARS-CoV-2 transmission [2,3] but at a very high cost to society. A better

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Research in Context

Evidence before this study

Despite the continued resurgence in cases of COVID-19 in many parts of the world, the settings which facilitate SARS-COV-2 transmission have not been well described in the literature. SARS-CoV-2 is transmitted through close contact, large droplets, aerosols and contaminated surfaces. Outbreak investigations have identified transmission linked to bars and restaurants, air travel, cruise ships, buses, choir practices, fitness classes and indoor sport, religious gatherings, nursing homes, food processing plants, schools, homeless shelters, and worker dormitories. Although outbreak investigations offer insight into where and how transmission is occuring, they are prone to selection bias. For example outbreaks are more likely to be detected in certain crowded settings in which people know who infected them. Furthermore, they cannot be used to determine the frequency and relative risks of infection by setting, which are essential to inform more targeted control strategies. Therefore, alternative designs are required, such as case-control studies. We searched PubMed for non-healthcare based case-control studies on SARS-CoV-2 infection published between 31 December 2019 and 31 March 2021. We identified only one other relevant study which was conducted in the United States of America and found that having frequented bars and restaurants to be risk factors for SARS-CoV-2 infection.

Added value of this study

In multivariable analysis, we found an increased risk of infection for a having a larger household; having children in the household attend kindergarten or school in person, with the exception of primary school; attending professional or private gatherings; having frequented bars and restaurants and having practiced sports indoors. Various means of public transport were found not to have an increased risk of infection, with the exception of carpooling. Equally, neither shops nor cultural or religious gatherings were associated with an increased risk of infection. We found that complete or partial teleworking had lower risk of infection compared to working in an office.

Implications of all the available evidence

The places and activities that appear to have facilitated SARS-CoV-2 infection despite the public health and social measures implemented at the national level are those in which adherence to infection prevention and control measures is conceiveably more difficult. In these settings, ongoing reinforcement of hand and respiratory hygiene, physical distancing, mask wearing and adequate ventilation of indoor settings remains critical to reducing viral circulation.

understanding of where transmission is occurring more frequently would enable more refined and targeted public health and social measures, likely at a lower economic cost compared to the blunt and wide-reaching measures, such as stay-at-home orders.

SARS-CoV-2 is transmitted through close contact, large droplets, aerosols and contaminated surfaces [4,5]. Outbreak investigations have identified transmission linked to bars and restaurants [6–10], air travel [11,12], cruise ships [13], buses [14], choir practices [15], fitness classes and indoor sport [9,10,16], religious gatherings [17], nursing homes [18], food processing plants [19], schools [20], homeless shelters [21], and worker dormitories [22]. Although outbreak investigations offer insight into where and how transmission is occurring, they are prone to selection bias. For example, outbreaks are more likely to be detected and described in certain crowded settings in which people know who infected them. Furthermore, they cannot be used to determine the frequency and the relative risks of infection by setting, which are essential to inform more targeted control strategies. Therefore, alternative designs are required, such as case-control studies [23], or mobility networks models [24]. To further understand the places and activities facilitating transmission, we present here the findings of a large case-control study conducted in October and November 2020 in France.

2. Methods

2.1. Study design and participants

In this case-control study, cases and controls were selected from two different national databases. Cases were obtained through the database from the Caisse Nationale d'Assurance Maladie (CNAM), a national health insurance agency which receives notification of all cases of COVID-19 in France. Potential cases for our study were all those diagnosed with COVID-19 and with an e-mail address with the national health insurance agency (55% of the adult French population).

Based on the characteristics of cases, Ipsos, a French market research and public opinion specialist company, selected controls at regular intervals from a panel representative of the French population using frequency-matching with cases on age (18-28, 29-58, 59+ years), sex, region, population density, and period of infection (before or during stay-at-home orders).

Controls reporting prior SARS-CoV-2 infection were not eligible for inclusion in the study. Further, health care workers were excluded as cases or controls, as they were assumed to have higher occupation-related exposure to SARS-CoV-2 compared to the general population.

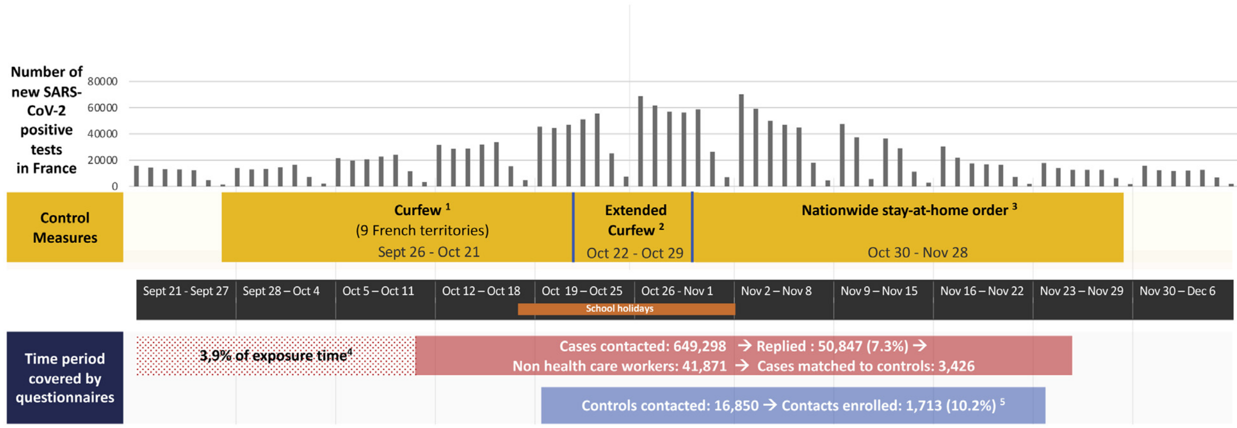
2.2. Data collection

Cases and controls were invited by email and received information online about the study before filling a questionnaire if they agreed to participate. The questionnaire covered sociodemographic characteristics (age, sex, region of residence, composition of the household, profession), exposure information related to place of work and means of transportation, places visited, type of leisure or sporting activities. Questionnaires covered the 10 days preceding symptom onset for cases (or testing if asymptomatic), and the 10 days preceding inclusion for controls. The Figure shows the timeline of the epidemic curve of positive SARS-CoV-2 cases in France, as well as the periods covering the different control measures, and the exposure period covered by the questionnaires sent to study participants. Cases with onset of symptoms, or testing if asymptomatic, prior to 4 November were considered presumably infected prior to the stay-at-home order period which ended on 30 October (median incubation period for SARS-CoV-2 infection is estimated at five days [25]), and the remaining were considered infected during the period of the stay-at-home order.

2.3. Statistical analyses

Our primary objective was to determine the association between various exposures and SARS-CoV-2 infection.

Due to cost consideration in recruiting controls, and requirements of matching them with cases on age, sex, region, population density, and time period, only 1713 controls were available for 41,871 cases. To increase the readiness of the results and improve the quality of matching which proved difficult with the large imbalance between the number of cases and controls, we performed exact matching of two cases per control within each set of matching factors (age, sex, region, population density, and period of infection). In order to



[1] From Sept. 26 to Oct. 22 : In 9 French metropolitan areas, bars were closed at 10 pm, followed by complete closure of bars and the implementation of an evening curfew (9 pm to 6 am) from Oct 16.

[2] Oct. 22 : Extension of the curfew (9 pm to 6 am) to departments that account for 69% of the French population. During this time period, indoor sport facilities, restaurants, cafés, nonessential shops and cultural venues were open during the day in areas with a curfew and were continuously open everywhere else.

[3] Oct. 30 : Implementation of nationwide stay-at-home orders, closure of non-essential businesses and in-person classes at universities; schools and factories remained open

[4] Cases were first contacted on 27 October 2020. A small group of 1,653 cases, representing 3.9% of all 41,871 cases, indicated first day of symptoms before 19 October. The time period covered by their questionnaires is shown in light dotted pink to highlight the fact that they represented a small proportion of all person-time of exposure for cases. A sensitivity analysis in which they are removed from the pool of cases from which the 3,426 cases are selected for the logistic regression analysis shows no difference in the results (Table S3).

[5] The relatively low response rate among controls may be explained by the short time given to controls to reply before new controls are contacted to preserve the matching on time.

Fig. 1. Timeline showing the epidemic curve of positive SARS-CoV-2 cases in France, as well as the periods covering the different control measures in France, and the period covered by the questionnaires sent to the study participants.

minimize the impact of random variation in the selection of cases for available controls, we performed 1000 random sampling of two cases per control with replacement (bootstrapping) [26]. We then calculated the mean number of cases and controls for each exposure category over the 1000 databases. We also ran 1000 uni- and multivariable logistic regression analyses adjusting for the matching factors and potential confounders. We then computed the mean log-odds-ratio (OR), as well as the 2·5% and 97·5% quantiles log-OR for each exposure, before exponentiating them to obtain ORs and their 95% confidence intervals (CI). For age-adjustment, we used a finer age categorization (10-year age categories) than the one used for the frequency-matching process (18-28, 29-58, 59+ years). Interaction terms were used to explore whether the magnitude of the associations with SARS-CoV-2 infection for several exposures varied according to age categories, sex, population density, time period or profession.

All statistical analyses were performed using Stata 16.0 (StataCorp, College Station, TX, USA).

2.4. Ethical considerations

This study received ethical approval by the Comité de Protection des Personnes Sud Ouest et Outre Mer 1 on 21 September 2020. The data protection authority Commission Nationale de l'Informatique et des Libertés (CNIL) authorized the processing of data on 21 October 2020. Informed consent was obtained from all participants. The study is registered with ClinicalTrials.gov under the identifier NCT04607941.

2.5. Role of the funding source

The study was funded by Institut Pasteur and Research & Action Emerging Infectious Diseases (REACTing). AF's laboratory receives support from the Labex IBEID (ANR-10-LABX-62-IBEID) and the INCEPTION project (PIA/ANR-16-CONV-0005) for studies on emerging viruses. TC is funded by the Fondation de France (Alliance "Tous unis contre le virus").

3. Results

From 27 October to 30 November 2020, 694,298 individuals with a diagnosis of COVID-19 were contacted by e-mail by the insurance company, of which 50,847 (7.3%) replied. Of note, only individuals aged 18 years and older (roughly 85% of all cases) were eligible for the study, so that the true participation rate may be slightly higher. Among these, 8,976 were health care workers and not considered further in this study, leaving us with 41,871 cases. At regular intervals, controls were frequency-matched to the cases, so that 1713 controls were available out of the 16,850 contacted by the end of the study period (see Fig. 1).

Table S1 describes the socio-demographic characteristics of the study participants. When compared to the 1,076,284 adult (18 years and older) patients registered in the national COVID-19 database during the period 20 October – 30 November 2020, cases in our study were more likely to be females (65% compared to 55% in the national database), from the Eastern part of France - Grand Est and Bourgogne-Franche-Comté regions (29% versus 14%), in the age group 39-59 years (48% versus 34%), and less likely older than 69 years (4% versus 18%). Half of participants (50%) lived in cities of 100,000 or more inhabitants, and 27% were from rural areas. Applying a mean incubation period of SARS-CoV-2 of 5 days to all cases, infection was considered to have occurred before the introduction of stay-at-home orders for 44% of the participants, and during the stay-at-home orders for 56%. Table S2 compares the professional category of the highest income in the household of controls with that of the general population in France. It shows that controls were more likely to belong to higher professional categories (34% versus 20%), and less likely to come from intermediate jobs (22% versus 26%) and workers jobs (11% versus 19%).

Table 1 shows the professional category of the reference person in the household and household characteristics. The risk of infection increased with the number of people living in the home (aOR for one additional person living in the household: 1·16; 95% CI: 1·11-1·21), and with children in the household attending school or other educational institutions in person: high school (aOR: 1·18; 95%CI: 1·05-

Table 1
Household composition and characteristics associated with risk of SARS-CoV-2 infection.

	Cases (n=3426)	Controls (n=1713)	OR univariable *	OR multivariable **
Professional category of the reference person of the household, n (%)				
Intermediate profession	641 (18·7)	321 (18·7)	1 (ref)	1 (ref)
Independent profession	187 (5·5)	53 (3·1)	1·74 (1·49-2·04)	1·75 (1·46-2·08)
Senior executive	1132 (33·0)	434 (25·3)	1·30 (1·18-1·43)	1·27 (1·15-1·42)
Employee	583 (17·0)	360 (21·0)	0·79 (0·71-0·89)	0·86 (0·76-0·97)
Worker	353 (10·3)	104 (6·1)	1·69 (1·47-1·94)	1·83 (1·57-2·13)
Retired	380 (11·1)	314 (18·3)	0·69 (0·56-0·83)	0·90 (0·72-1·11)
Unemployed or inactive people	150 (4·4)	127 (7·4)	0·58 (0·49-0·70)	0·92 (0·75-1·13)
Housing type, n (%)				
House	2143 (62·6)	986 (57·6)	1 (ref)	1 (ref)
Apartment	1262 (36·8)	718 (41·9)	0·70 (0·64-0·75)	0·92 (0·83-1·02)
Shelters and nursing homes	21 (0·6)	9 (0·5)	1·01 (0·56-1·66)	1·49 (0·84-2·37)
Number of persons in the household, n (%)				
1	510 (14·9)	368 (21·5)	1 (ref)	1 (ref)
2	1021 (29·8)	604 (35·3)	1·27 (1·14-1·41)	1·17 (1·04-1·31)
3	715 (20·9)	325 (19·0)	1·57 (1·40-1·76)	1·38 (1·21-1·58)
4	804 (23·5)	298 (17·4)	1·99 (1·76-2·22)	1·60 (1·35-1·87)
5	277 (8·1)	92 (5·4)	2·22 (1·91-2·59)	1·81 (1·44-2·25)
6+	99 (2·9)	26 (1·5)	2·89 (2·29-3·61)	2·33 (1·70-3·13)
Child in household attending day-care centre, n (%)				
No	3309 (96·6)	1687 (98·5)	1 (ref)	1 (ref)
Yes	117 (3·4)	26 (1·5)	1·59 (1·30-1·89)	1·31 (1·02-1·62)
Child in household looked after by a childminder, n (%)				
No	3297 (96·2)	1693 (98·8)	1 (ref)	1 (ref)
Yes	129 (3·8)	20 (1·2)	2·30 (1·89-2·75)	1·92 (1·54-2·36)
Child in household attending kindergarten, n (%)				
No	3061 (89·3)	1619 (94·5)	1 (ref)	1 (ref)
Yes	365 (10·7)	94 (5·5)	1·52 (1·34-1·70)	1·27 (1·09-1·45)
Child in household attending primary school, n (%)				
No	2826 (82·5)	1474 (86·0)	1 (ref)	1 (ref)
Yes	600 (17·5)	239 (14·0)	1·14 (1·03-1·24)	0·87 (0·77-0·99)
Child in household attending middle school, n (%)				
No	2814 (82·1)	1488 (86·9)	1 (ref)	1 (ref)
Yes	612 (17·9)	225 (13·1)	1·57 (1·42-1·73)	1·30 (1·15-1·47)
Child in household attending high school, n (%)				
No	2873 (83·9)	1481 (86·5)	1 (ref)	1 (ref)
Yes	553 (16·1)	232 (13·5)	1·40 (1·27-1·54)	1·18 (1·05-1·34)
Child in household attending college or university, n (%)				
No	3056 (89·2)	1525 (89·0)	1 (ref)	1 (ref)
Yes	370 (10·8)	188 (11·0)	1·07 (0·96-1·20)	0·93 (0·81-1·07)
Member of the household looking after a child/children (outside of the household) in day-care centre, n (%)				
No	3362 (98·1)	1700 (99·2)	1 (ref)	1 (ref)
Yes	64 (1·9)	13 (0·8)	2·21 (1·68-2·78)	1·95 (1·39-2·58)

* OR (95%CI) adjusted on the variables used for matching: age, region and population density of place of residence, sex and public health measures period (prior to or during stay-at-home orders)
** OR (95%CI) adjusted on age, region and population density of place of residence, sex, public health measures period (prior to or during stay-at-home orders), body mass index, professional category of the reference person of the household, type of housing, number of persons in the household, institutions attended by household children and children cared for outside the household (pre-kindergarten, kindergarten, primary school, middle school, high school), means of transportation (bus, tramway, metro and train), work-related exposure (office work, teleworking, in-person professional meeting), sports practice (indoors and outdoors), recent places visited, and attendance at private, cultural, school and religious gatherings.

1·34), middle school (aOR: 1·30; 95%CI: 1·15-1·47), kindergarten (aOR: 1·27; 95%CI: 1·09-1·45), day-care centre (aOR: 1·31; 95%CI: 1·02-1·62), childminder (aOR: 1·92; 95%CI: 1·54-2·36), with the exception of university students (aOR: 0·93; 95%CI: 0·81-1·07) and primary school pupils (aOR: 0·87; 95%CI: 0·77-0·99). Contact with a child or children from outside of the household attending a day-care centre was also associated with a higher risk of infection (aOR: 1·95; 95%CI: 1·39-2·58).

Table 2 describes the risks of infection associated with the work environment. When compared to working in an office, not working (aOR: 0·56; 95%CI: 0·48-0·65), not working in an office (aOR: 0·86; 95%CI: 0·76-0·96), and partial (aOR: 0·76; 95%CI: 0·66-0·87) or complete teleworking (aOR: 0·65; 95%CI: 0·56-0·75) were associated with a decreased risk of infection. In-person work-related meetings were associated with an increased risk of infection (aOR: 1·15; 95%CI: 1·04-1·26).

Public transportation was not associated with increased risk of infection, whereas carpooling (aOR: 1·47; 95%CI: 1·28-1·69) was associated with an increased risk of infection (Table 3). With respect to other activity-related exposures, private social gatherings (aOR: 1·57; 95%CI: 1·45-1·71) were associated with an increased risk, but not religious or cultural gatherings (Table 4). Indoor, but not outdoor, sports activities were associated with increased risk (aOR: 1·36; 95%CI: 1·15-1·62). Finally, frequenting bars or restaurants (aOR: 1·95; 95%CI: 1·76-2·15) were associated with increased risk, but not frequentation of any type of shops (including retail and convenience shops).

The main interactions we found concerned changes in risk associated with the start of the stay-at-home order. Details can be found in Table S4.

4. Discussion

This large case-control study allowed us to explore the risk of SARS-CoV-2 infection associated with various exposures in France in October and November 2020 – a period during which broad-

Table 2
Work environment exposures and risk of SARS-CoV-2 infection.

Items	Cases (n=3426)	Controls (n=1713)	OR univariable *	OR multivariable **
Professional activity, n (%)				
Office work without teleworking	665 (19·4)	249 (14·5)	1 (ref)	1 (ref)
Not working	753 (22·0)	553 (32·3)	0·55 (0·49-0·62)	0·56 (0·48-0·65)
Working but no office work	1115 (32·5)	504 (29·4)	0·82 (0·74-0·90)	0·86 (0·76-0·96)
Office work with partial teleworking	494 (14·4)	212 (12·4)	0·85 (0·75-0·96)	0·76 (0·66-0·87)
Office work with complete teleworking	399 (11·6)	195 (11·4)	0·75 (0·66-0·84)	0·65 (0·56-0·75)
Number of days spent at workplace, n (%)				
Did not visit workplace	2050 (59·9)	984 (57·4)	1 (ref)	
1 - 2 days	281 (8·2)	135 (7·9)	0·86 (0·76-0·97)	
3 – 4 days	272 (7·9)	136 (7·9)	0·82 (0·71-0·92)	
5 +	822 (24·0)	458 (26·7)	0·74 (0·68-0·80)	
In-person professional meeting, n (%)				
No	2459 (71·8)	1352 (78·9)	1 (ref)	1 (ref)
Yes	967 (28·2)	361 (21·1)	1·38 (1·27-1·49)	1·15 (1·04-1·26)

* OR (95%CI) adjusted on the variables used for matching: age, region and population density of place of residence, sex and public health measures period (prior to or during stay-at-home orders)
** OR (95%CI) adjusted on age, region and population density of place of residence, sex, public health measures period (prior to or during stay-at-home orders), body mass index, professional category of the reference person of the household, type of housing, number of persons in the household, institutions attended by household children and children cared for outside the household (pre-kindergarten, kindergarten, primary school, middle school, high school), means of transportation (bus, tramway, metro and train), work related-exposure (office work, teleworking, in-person professional meeting), sports practice (indoors and outdoors), recent places visited, attendance at private, cultural, school and religious gatherings.

reaching public health and social measures were implemented. We found an increased risk of infection associated with having a larger household, having children attending school or other educational institutions in person (with the exception of primary schools), attending professional or private gatherings, frequenting bars and restaurants and practicing indoor sports activities. We found no increase in risk associated with frequenting shops, attending cultural or religious gatherings, or with transportation, except for carpooling. Risk of infection varied by profession, but both partial and complete teleworking were associated with a decreased risk of infection.

The public health and social measures that were in place during the study period mainly concerned the closure of indoor sports facilities and bars in the main cities of France in October, and were expanded to include the closure of restaurants, non-essential businesses and in person-classes at universities across the country in November. For most activities and places, the level of exposure was more than 5% of controls, allowing us to identify as statistically significant increases in the risk of infection of 30% or more for these exposures.

The findings of the study are consistent with our knowledge on SARS-CoV-2 transmission and support current infection prevention and control measures specific to SARS-CoV-2. Places at increased risk for transmission were indoor areas in which adherence to these measures may be difficult (households, bars, restaurants, indoor

Table 3
Usual means of transportation and travel exposures and risk of SARS-CoV-2 infection.

Items	Cases (n=3426)	Controls (n=1713)	OR univariable *	OR multivariable **
Carpooling, n (%)				
No	3127 (91·3)	1616 (94·3)	1 (ref)	1 (ref)
Yes	299 (8·7)	97 (5·7)	1·58 (1·39-1·77)	1·47 (1·28-1·69)
Bus, n (%)				
No	3152 (92·0)	1501 (87·6)	1 (ref)	1 (ref)
Yes	274 (8·0)	212 (12·4)	0·58 (0·51-0·66)	0·65 (0·56-0·75)
Tramway, n (%)				
No	3269 (95·4)	1600 (93·4)	1 (ref)	1 (ref)
Yes	157 (4·6)	113 (6·6)	0·63 (0·53-0·75)	0·77 (0·64-0·93)
Metro (subway), n (%)				
No	3148 (91·9)	1555 (90·8)	1 (ref)	1 (ref)
Yes	278 (8·1)	158 (9·2)	0·81 (0·70-0·93)	0·92 (0·79-1·10)
Train, n (%)				
No	3238 (94·5)	1622 (94·7)	1 (ref)	1 (ref)
Yes	188 (5·5)	91 (5·3)	0·96 (0·81-1·12)	1·03 (0·86-1·25)
Travel abroad, n (%)				
No	3316 (96·8)	1684 (98·3)	1 (ref)	1 (ref)
Yes	110 (3·2)	29 (1·7)	1·89 (1·53-2·29)	1·55 (1·22-1·92)
Travel outside region of residency, n (%)				
No	2852 (83·2)	1488 (86·9)	1 (ref)	1 (ref)
Yes	574 (16·8)	225 (13·1)	1·33 (1·21-1·46)	1·07 (0·95-1·19)

* OR (95%CI) adjusted on the variables used for matching: age, region and population density of place of residence, sex and public health measures period (prior to or during stay-at-home orders)
** OR (95%CI) adjusted on age, region and population density of place of residence, sex, public health measures period (prior to or during stay-at-home orders), body mass index, professional category of the reference person of the household, type of housing, number of persons in the household, institutions attended by household children and children cared for outside the household (pre-kindergarten, kindergarten, primary school, middle school, high school), means of transportation (bus, tramway, metro and train), work -related exposure(office work, teleworking, in-person professional meeting), sports practice (indoors and outdoors), recent places visited, attendance at private, cultural, school and religious gatherings.

Table 4
Gatherings, recent places visited and leisure activities and risk of SARS-CoV-2 infection.

Items	Cases (n=3426)	Controls (n=1713)	OR univariable *	OR multivariable **
Private social gathering (friends or extended family), n (%)				
No	1873 (54·7)	1146 (66·9)	1 (ref)	1 (ref)
Yes	1553 (45·3)	567 (33·1)	1·65 (1·53-1·77)	1·57 (1·45-1·71)
Religious gathering, n (%)				
No	3328 (97·1)	1669 (97·4)	1 (ref)	1 (ref)
Yes	98 (2·9)	44 (2·6)	1·29 (1·05-1·56)	1·08 (0·84-1·35)
Cultural gathering, n (%)				
No	3246 (94·7)	1634 (95·4)	1 (ref)	1 (ref)
Yes	180 (5·3)	79 (4·6)	1·18 (1·01-1·37)	0·96 (0·79-1·15)
School or university courses, n (%)				
No	3225 (94·1)	1553 (90·7)	1 (ref)	1 (ref)
Yes	201 (5·9)	160 (9·3)	0·56 (0·49-0·65)	0·51 (0·43-0·60)
Outdoor sports activities, n (%)				
No	3076 (89·8)	1496 (87·3)	1 (ref)	1 (ref)
Yes	350 (10·2)	217 (12·7)	0·77 (0·68-0·86)	0·66 (0·57-0·75)
Indoor sports activities, n (%)				
No	3222 (94·0)	1648 (96·2)	1 (ref)	1 (ref)
Yes	204 (6·0)	65 (3·8)	1·57 (1·37-1·82)	1·36 (1·15-1·62)
Bars or restaurants, n (%)				
No	2516 (73·4)	1444 (84·3)	1 (ref)	1 (ref)
Yes	910 (26·6)	269 (15·7)	2·00 (1·85-2·18)	1·95 (1·76-2·15)
Bars, n (%)				
No	2975 (86·8)	1644 (96·0)	1 (ref)	
Yes	219 (6·4)	69 (4·0)	1·75 (1·52-2·03)	
Missing values	232 (6·8)	0 (0·0)	-	
Restaurants, n (%)				
No	2452 (71·6)	1460 (85·2)	1 (ref)	
Yes	742 (21·7)	253 (14·8)	1·90 (1·74-2·08)	
Missing values	232 (6·8)	0 (0·0)	-	
Nightclub, raves or parties, n (%)				
No	3344 (97·6)	1688 (98·5)	1 (ref)	1 (ref)
Yes	82 (2·4)	25 (1·5)	1·47 (1·16-1·82)	1·15 (0·86-1·51)
Shops (retail and convenience shops), n (%)				
No	658 (19·2)	308 (18·0)	1 (ref)	1 (ref)
Yes	2768 (80·8)	1405 (82·0)	0·92 (0·84-1·01)	0·83 (0·76-0·92)

* OR (95%CI) adjusted on the variables used for matching: age, region and population density of place of residence, sex and public health measures period (prior to or during stay-at-home orders)
** OR (95%CI) adjusted on age, region and population density of place of residence, sex, public health measures period (prior to or during stay-at-home orders), body mass index, professional category of the reference person of the household, type of housing, number of persons in the household, institutions attended by household children and children cared for outside the household (pre-kindergarten, kindergarten, primary school, middle school, high school), means of transportation (bus, tramway, metro and train), work-related exposure (office work, teleworking, in-person professional meeting), sports practice (indoors and outdoors), recent places visited, attendance at private, cultural, school and religious gatherings.

sports facilities), whereas places in which these measures can be fully applied were not at increased risk for transmission (public transportation, shops, cultural or religious gatherings). Households, bars, restaurants, and indoor sports facilities have been previously found associated with increased risk of transmission in numerous studies [6–10,23,27]. Our finding that public transportation was not a place of transmission is at odds with earlier studies in subways [28], buses [14] and airplanes [11,12]. This may be explained by the methodology used (the study of the New York subway was based on an ecological correlation between turnstile entries and COVID-19 incidence data), the nature of trips (bus and airplane rides suggest long seating times next to another person with meals and therefore mask removal), the timing of the study (holidays and stay-at-home orders) during which fewer people use public transportation, or the fact that during short commutes on public transportation, masks can be worn for the duration of the travel and there is often limited interaction between passengers. Results regarding religious gatherings, cultural gatherings, or university courses should be considered cautiously though due to the low number of people attending these places during the study period.

Household size, as in other studies [29,30], was associated with increased risk of infection. Independently of household size, having children attending day-care centres (age 0-3 years) kindergarten (age 3-6 years), middle school, or high school was associated with an increased risk of infection. This finding, also recently reported in other studies [31,32] suggests that children may be infected in these school facilities, or during activities linked to these facilities, and bring the virus back into the home setting in which adherence to infection prevention and control measures is low [33]. It is important to differentiate the possibility of outbreaks in schools [20,34,35], which have largely been limited so far [36], from the risk of silent spread from the school to the household setting in which frequent, close contact may facilitate transmission. Household members older than 50 years, or with co-morbidities, should be aware of this risk and be strict on barrier measures whenever possible with school-aged children, particularly if the latter are symptomatic. Primary school-aged children did not carry an increased risk of infection for their relatives. Aside from random variation, this may reflect their lower susceptibility to infection, or less efficient onwards transmission, compared to older age groups [37-39]. This less efficient onwards transmission did not apply to children aged under 6, for whom close physical interactions in the household are likely more frequent compared to primary school-aged children. University students did not appear to increase the risk of their relatives. However, this finding corresponds to a time period during which in-person learning was limited (October 2020) and then completely restricted (November 2020) across universities in France. Of interest, in person school and university courses, corresponding mainly to continuing education in this adult population, were not associated with increased risk of infection.

Partial and complete teleworking were found to be protective, compared to in-person office work, confirming the pertinence of favouring teleworking as a public health measure to reduce viral circulation [40].

This study has several limitations. We cannot rule out past or current asymptomatic infections among the controls. This may have led to an underestimation of the strength of some associations reported in the study. The findings should be interpreted in the context of the public health and social measures that were implemented in France during the study period, which likely influenced the exposures of participants. Another issue is the extent to which the source population for cases and controls was the same. Cases were recruited nationwide, and controls were selected from a panel from a market and public opinion research company, which can be considered to be reasonably representative of the French population. However, the low completion rate of the online questionnaire for both cases and controls is such that we cannot exclude the presence of selection biases towards younger, more female, wealthier, and more health-conscious participants. The online questionnaire may also have prevented those with limited internet access and/or command of the French language from participating in the study. Information as to the ethnicity of participants was not able to be collected. Some of these biases have likely been attenuated through multivariable analysis, and the overall consistency of the findings with those in the published literature increase our confidence in the results. Although we adjusted in the multivariable analysis for numerous variables that may act as potential confounders, we agree that some confounding remains, as shown for instance by the negative association between taking the bus or the tramway, or visiting shops, and becoming infected by SARS-CoV-2. We preferred therefore to report that there was no increase in risk, rather than saying that there was a decreased risk, associated with these practices. It will be important that similar studies are performed in other settings (e.g., emergency rooms of hospitals, or general practitioners), so that factors associated with SARS-CoV-2 transmission in other population groups can be studied as well.

Overall, this study complements our knowledge on SARS-CoV-2 transmission beyond what was already known from outbreak investigations. It generally supports the idea that settings in which adherence to SARS-CoV-2 infection prevention and control measures, including hand and respiratory hygiene, physical distancing, mask wearing and adequate ventilation of indoor settings, is critical to controlling viral circulation, as places at risk for transmission were indoor areas in which adherence to such measures is conceivably more difficult. Having children attend to kindergarten or middle- or high- school was associated with increased risk of infection and understanding whether viral acquisition takes place in or outside school will be important to identify ways to minimize transmission related to this setting. These findings should be used to guide the refinement of public health measures to reduce transmission as countries struggle to preserve both health and economies. This study continues and may serve as a monitoring tool to evaluate the risk of infection related to different activities in various settings until the epidemic is controlled.

Contributors

AF, SG, TC, LS, FO, CD, FC, SC, A Mailles, and DLB designed the investigation.

SG, TC, LS, AF, AS, A Mailles, and DLB developed the study questionnaire.

FO, CD, CB, AD, SM and A Maurizot managed the data collection online.

OC and CVP oversaw the adherence of the study to the regulatory requirements.

LS and TC oversaw the collection of the data and maintained the database.

LS, TC, JP and AF performed the statistical analyses.

SG, RG, TC and AF drafted the first versions of the manuscript.

All authors critically reviewed and approved the final version of the manuscript.

Data availability statement

The data that support the findings of this study are available from the Caisse Nationale d'Assurance Maladie, a national health insurance agency in France and from Ipsos, a French market research and public opinion specialist company. Restrictions apply to the availability of these data, which were used under authorized agreement for this study by the data protection authority Commission Nationale de l'Informatique et des Libertés (CNIL). Access to these data would therefore require prior authorization by the CNIL.

Declaration of Competing interests

AF and SC are members of the COVID-19 Scientific Advisory Council to the Government of France. All other authors have nothing to declare.

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Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.lanepe.2021.100148.

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