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MAJOR ARTICLE

Prevalence of SARS-CoV-2 in Household Members and Other Close Contacts of COVID-19 Cases: A Serologic Study in Canton of Vaud, Switzerland

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Background. Research on severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) transmission within households and other close settings using serological testing is scarce.

Methods. We invited coronavirus disease 2019 (COVID-19) cases diagnosed between February 27 and April 1, 2020, in Canton of Vaud, Switzerland, to participate, along with household members and other close contacts. Anti-SARS-CoV-2 immunoglobulin G antibodies were measured using a Luminex immunoassay. We estimated factors associated with serological status using generalized estimating equations.

Results. Overall, 219 cases, 302 household members, and 69 other close contacts participated between May 4 and June 27, 2020. More than half of household members (57.2%; 95% CI, 49.7%–64.3%) had developed a serologic response to SARS-CoV-2, while 19.0% (95% CI, 10.0%–33.2%) of other close contacts were seropositive. After adjusting for individual and household characteristics, infection risk was higher in household members aged ≥65 years than in younger adults (adjusted odds ratio [aOR], 3.63; 95% CI, 1.05–12.60) and in those not strictly adhering to simple hygiene rules like hand washing (aOR, 1.80; 95% CI, 1.02–3.17). The risk was lower when more than 5 people outside home were met during semiconfinement, compared with none (aOR, 0.35; 95% CI, 0.16–0.74). Individual risk of household members to be seropositive was lower in large households (22% less per each additional person).

Conclusions. During semiconfinement, household members of a COVID-19 case were at very high risk of getting infected, 3 times more than close contacts outside home. This highlights the need to provide clear messages on protective measures applicable at home. For elderly couples, who were especially at risk, providing external support for daily basic activities is essential.

Keywords. COVID-19; household; SARS-CoV-2; serology; transmission.

The understanding of transmission patterns is especially critical to guide interventions aiming at limiting the occurrence of new cases of coronavirus disease 2019 (COVID-19). In this respect, transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in promiscuous settings such as households is of particular interest and is at the core of the early investigation protocols provided by the World Health Organization (WHO Unity Studies) to address the many unknowns related to the COVID-19 pandemic [1, 2].

Studies dealing with the transmission of SARS-CoV-2 within households have found secondary attack rates (SARs) ranging from 3.9% to 44.6%, reflecting heterogeneous settings and study designs [3]. The evidence regarding transmission to close contacts outside the household tends to show lower SARs (from 0.7% to 5.1%), but attack rates above 50% have been reported in certain circumstances [4–8]. Most studies conducted so far are based on the identification of active disease through nucleic acid amplification tests (NAATs), whose sensitivity can be hampered by various factors [9].

The availability of serological assays allows the identification of past infection and thus provides key input into our understanding of the epidemiology of SARS-CoV-2. Nevertheless, studies on SARS-CoV-2 transmission in close settings using serological testing remain scarce. So far, most of them found SARs close to

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35% within households [10–13]. However, none of them includes a thorough investigation of factors associated with seropositivity. Regarding close contacts outside the household, research shows SARs ranging from 0% to 13.7%, but study designs and settings are disparate [12, 14–16]. Furthermore, the amount of available serological assays is quickly growing, often with limited external validation of their accuracy, and concerns are emerging regarding their accuracy in the setting of seroepidemiological studies because of the lower median level of antibodies in participants compared with clinical studies [17].

This work was part of *SerocoViD*, a community-based seroepidemiological study of SARS-CoV-2 infection conducted in Canton of Vaud, Switzerland, embedded within a nationwide program, Corona Immunitas [18]. Taking advantage of prior development and validation of a highly sensitive serological assay carried out locally [19], the objective was to determine the prevalence of anti-SARS-CoV-2 immunoglobulin G (IgG) antibodies among household members and other close contacts of COVID-19 cases and to identify factors associated with seropositivity in these highly exposed people.

METHODS

Study Design and Participants

SerocoViD is a cross-sectional community-based seroepidemiological study of SARS-CoV-2 infection conducted in Canton of Vaud (French-speaking region of Switzerland, 806 088 inhabitants on December 31, 2019). The study was launched at the end of April 2020, coinciding with the easing of semiconfinement measures taken in Switzerland in mid-March.

From February 27 (first confirmed case in Canton of Vaud) to March 4, 2020, all COVID-19 cases underwent contact tracing by local authorities. At that time, a close contact was any individual who had been within 2 m of an infected person for at least 15 minutes, starting 24 hours before illness onset. Given the exponential growth of the number of cases, contact tracing was stopped from week 2 of the epidemic. For the same reason, from March 9, 2020, diagnostic testing was limited to health care personal, hospitalized people, and individuals at increased risk for severe illness in the entire country.

We sampled confirmed COVID-19 cases from the cantonal registry (total n ≈ 3700). With the exception of 3 people (1 deceased, 2 who returned home abroad), all confirmed cases from week 1 were invited to participate in the study (n = 13), along with their close contacts identified by contact tracing (n = 117). Additionally, all cases aged between 6 months and 19 years (n = 66) and a random sample of noninstitutionalized cases aged ≥20 years (n = 368) who were tested positive during weeks 2–5 (from March 5 to April 1, 2020) were invited to take part in the study. In order to extend the age range of confirmed cases for whom a contact tracing procedure had been performed, the study team conducted complementary tracing procedures for 3 adolescent cases, thus identifying 20 additional close contacts outside the household.

Overall, this resulted in the solicitation of 447 confirmed cases (hereafter called index cases) and 137 close contacts not belonging to the households of the index cases. Moreover, index case participants were asked to invite all their household members aged ≥6 months to take part in the study. Because of testing restrictions, index cases were not necessarily the first infected in their household, but those fulfilling testing criteria. All index cases were diagnosed using NAAT.

Patient Consent Statement

The Cantonal Ethics Committee of Vaud, Switzerland, approved the protocol (ID 2020-00887), and written consent was obtained from participants.

Procedures

Index cases and their close contacts, identified by contact tracing, were invited by letters. Participants completed registration for the study and answered the study questionnaire (available in French and English) via an online platform. The questionnaire covered the following topics: sociodemographic information, medical history, history of symptoms compatible with COVID-19 and use of health services, living conditions and household characteristics, contacts with other people in private and professional settings, and compliance with measures aimed at controlling the epidemic. The full questionnaire is available in the Supplementary Data.

Study visits took place in 4 centers distributed over the cantonal territory between May 4 and June 27, 2020. A venous blood sample was collected to proceed with serological testing. We offered a home visit by a mobile study team to people at increased risk for severe illness from COVID-19. All participants (or their legal representative) provided written informed consent.

Detection of Anti-SARS-CoV-2 Antibodies

We measured anti-SARS-CoV-2 IgG antibodies targeting the spike (S) protein in its native trimeric form using a Luminex immunoassay. This test was developed by the Lausanne University Hospital, Switzerland, in collaboration with the École Polytechnique Fédérale de Lausanne (EPFL), and compared with 5 commercially available immunoassays detecting IgG against the N protein and the monomeric moieties of the S1 protein [19]. The in-house Luminex S protein trimer IgG assay was 99.2% specific in sera from people infected with prepandemic coronaviruses or from patients with autoimmune diseases, and it proved to be more sensitive (96.7%) than commercial tests in hospitalized patients with moderate to severe disease 16 to 33 days postsymptoms. The threshold for a positive result was defined at an antibody Multiplex Fluorescent Immunoassay (MFI) ratio of ≥6.

Statistical Analysis

We calculated the proportion of index cases with a positive serology test result and computed a Clopper-Pearson 95% CI. Significant clustering of infections within households has been reported in previous research [20]. In order to account for correlation between close contacts of the same index case, we used generalized estimating equations (GEEs) with an exchangeable correlation structure to estimate the seroprevalence and corresponding 95% CI among contacts. Odds ratios (ORs) were computed to measure the strength of the association between each independent variable and the serology test result. We used GEEs to account for correlation between contacts of the same index case and calculated ORs with their 95% CIs and *P* values using a logit link function. Finally, a multivariable regression model using GEE was fitted to measure the adjusted association of individual and household characteristics with serology test results among household members. Considering the potential influence of past diagnostic testing for SARS-CoV-2 on the reporting of symptoms, we proceeded to a sensitivity analysis among contacts not reporting previous nasal or throat swabbing. We performed statistical analysis using Stata/IC, version 16.1. There was no imputation of missing values.

RESULTS

Two-hundred nineteen index cases (49.0%), aged 2 to 90 years (mean [SD], 48.7 [19.3] years), participated in the study, of whom 55.7% considered themselves women. They reported 421 household members, of whom 302 (71.7%), aged 1 to 87 years (mean [SD], 37.0 [21.3] years), took part in the study. Sixty-nine (50.4%) close contacts outside the household, aged 9 to 85 years (mean [SD], 47.8 [17.0] years), participated.

Prevalence of Seropositivity in the Different Groups

Most index cases (215/219, 98.2%) had a positive serological test result (95% CI, 95.4%–99.5%) (Figure 1). The crude proportion of positives was 53.0% in household members (160/302) and 17.4% among close contacts outside the household (12/69). When taking into account correlation, the seroprevalence was 57.2% in household members (95% CI, 49.7%–64.3%) and 19.0% in close contacts outside the household (95% CI, 10.0%–33.2%).

Unadjusted Association of Individual and Household Characteristics With Seropositivity (Bivariable Analysis)

A higher proportion of household members aged 65 to 75 (85.7%) and ≥75 (83.3%) were seropositive (Table 1). No association between serological test result and gender or level of education was found (Figure 2). Household members currently smoking had lower odds of infection than nonsmokers in bivariable analysis (unadjusted OR, 0.56; 95% CI, 0.32–0.96). In close contacts outside the household, seroprevalence was 30.3% and 5.7% in overweight/obese and normal/underweight

Figure 1. Percentage of participants with a positive serology test result, by type of participant. Index cases: crude proportion, calculation of 95% confidence interval using the Clopper-Pearson method. For household members and close contacts outside the household, proportion and corresponding 95% confidence interval were estimated using GEEs (exchangeable correlation structure). Abbreviation: GEEs, generalized estimating equations.

participants, respectively, but no association was found in household members. Close contacts not strictly adhering to simple hygiene rules tended to have higher odds of infection (Table 2, Figure 2). We found no association between serology and compliance with social distancing rules. Positive test results were less frequent in household members who had met more than 5 people per week during the semiconfinement compared with none (unadjusted OR, 0.42; 95% CI, 0.22–0.78), but there was no association with the number of close encounters with symptomatic individuals. In bivariable analysis, seroprevalence significantly decreased with increasing household size. We found that 66.1% of participants living with 1 other person only (the index COVID-19 case) had a positive test result, contrasting with participants living with ≥5 people, who showed a 26.0% risk of being seropositive (unadjusted OR, 0.19; 95% CI, 0.06–0.62). There was an inverse relationship between household size and mean age of participants in the household (Supplementary Table 1).

Adjusted Association of Individual and Household Characteristics With Seropositivity (Multivariable Analysis)

We finally estimated the adjusted association of individual and household characteristics with serology test results among household members (Table 3). The odds of infection were almost 4 times higher in household members aged ≥65 than in the younger age group (adjusted OR, 3.63; 95% CI, 1.05–12.60). The association of current smoking with negative serology observed in bivariable analysis faded in the multivariable model (adjusted OR, 0.73; 95% CI, 0.38–1.39). Although overweight/obesity tended to be associated with higher odds of infection, this association was not statistically significant at the .05 level. In comparison with bivariable analysis, we observed a

Table 1. Serology Test Result According to General Characteristics and Medical History, Stratified by Type of Participant (Unadjusted Results)

	Index Cases (n = 219)	Household Members (n = 302)			Close Contacts Outside the Household (n = 69)		
	No. (%) Seropositive	No. (%) Seropositive	Unadjusted OR [95% CI]	*P* Value	No. (%) Seropositive	Unadjusted OR [95% CI]	*P* Value
All participants	215/219 (98.2)	160/302 (53.0)			12/69 (17.4)		
Age				.119			.928
6 mo–<5 y	1/2 (50.0)	5/11 (45.5)	0.92 [0.37–2.29]		No participant	..	
5 y–<10 y	1/1 (100.0)	12/22 (54.6)	1.16 [0.55–2.44]		0/1 (0.0)	..	
10 y–<15 y	2/2 (100.0)	15/32 (46.9)	0.93 [0.49–1.75]		0/3 (0.0)	..	
15 y–<20 y	20/21 (95.2)	9/19 (47.4)	1.17 [0.56–2.45]		0/2 (0.0)	..	
20 y–<40 y	42/43 (97.7)	37/76 (48.7)	Reference		3/15 (20.0)	Reference	
40 y–<65 y	103/104 (99.0)	60/116 (51.7)	0.83 [0.52–1.30]		7/38 (18.4)	0.92 [0.22–3.87]	
65 y–<75 y	31/31 (100.0)	12/14 (85.7)	3.98 [1.03–15.44]		2/9 (22.2)	1.32 [0.16–11.00]	
≥75 y	15/15 (100.0)	10/12 (83.3)	5.25 [1.16–23.72]		0/1 (0.0)	..	
Gender				.164			.124
Male	94/96 (97.9)	74/146 (50.7)	Reference		8/30 (26.7)	Reference	
Female	120/122 (98.4)	86/156 (55.1)	1.27 [0.91–1.76]		4/39 (10.3)	0.36 [0.10–1.32]	
Other	1/1 (100.0)	No participant	..		No participant	..	
Current smoker[a]				.034			.825
No	191/194 (98.5)	142/256 (55.5)	Reference		10/59 (17.0)	Reference	
Yes	23/24 (95.8)	18/46 (39.1)	0.56 [0.32–0.96]		2/9 (22.2)	1.21 [0.22–6.53]	
Weight status				.146			.011
Normal or underweight	104/106 (98.1)	92/184 (50.0)	Reference		2/35 (5.7)	Reference	
Overweight or obese	110/112 (98.2)	66/111 (59.5)	1.37 [0.90–2.09]		10/33 (30.3)	6.74 [1.54–29.50]	
Adult participants only							
Education				.196			.423
Lower secondary or less	21/21 (100.0)	21/33 (63.6)	Reference		3/10 (30.0)	Reference	
Upper secondary	58/59 (98.3)	46/82 (56.1)	0.93 [0.46–1.90]		5/23 (21.7)	0.64 [0.13–3.21]	
Tertiary	108/109 (99.1)	51/100 (51.0)	0.61 [0.30–1.24]		4/30 (13.3)	0.33 [0.06–1.83]	
Chronic medical conditions[b]				.037			.148
None	131/133 (98.5)	86/169 (50.9)	Reference		6/44 (13.6)	Reference	
≥1	58/58 (100.0)	32/47 (68.1)	1.94 [1.04–3.62]		6/19 (31.6)	2.48 [0.73–8.48]	
Hypertension				.110			.034
No	152/154 (98.7)	95/182 (52.2)	Reference		7/50 (14.0)	Reference	
Yes	36/36 (100.0)	21/31 (67.7)	1.81 [0.87–3.74]		5/11 (45.5)	4.48 [1.12–18.01]	
Diabetes				.489			.082
No	169/171 (98.8)	111/206 (53.9)	Reference		10/57 (17.5)	Reference	
Yes	15/15 (100.0)	4/6 (66.7)	1.75 [0.36–8.48]		2/3 (66.7)	8.59 [0.76–96.92]	
Cardiovascular disease				.239			..
No	170/172 (98.8)	103/196 (52.6)	Reference		12/58 (20.7)	..	
Yes	12/12 (100.0)	9/12 (75.0)	2.03 [0.62–6.62]		0/2 (0.0)	..	
Kidney disease							
No	181/183 (98.9)	115/212 (54.3)	..		12/60 (20.0)	..	
Yes	3/3 (100.0)	No participant	..		0/1 (0.0)	..	
Chronic respiratory disease				.196			..
No	177/179 (98.9)	106/202 (52.5)	Reference		12/59 (20.3)	..	
Yes	7/7 (100.0)	4/5 (80.0)	3.79 [0.50–28.52]		0/2 (0.0)	..	
Immunodeficiency				.596			..
No	174/176 (98.9)	110/202 (54.5)	Reference		12/58 (20.7)	..	
Yes	12/12 (100.0)	4/9 (44.4)	0.74 [0.25–2.23]		0/3 (0.0)	..	
Cancer							
No	177/179 (98.9)	113/209 (54.1)	..		12/58 (20.7)	..	
Yes	4/4 (100.0)	No participant	..		0/2 (0.0)	..	
Other chronic condition				.325			..
No	159/160 (99.4)	97/184 (52.7)	Reference		12/55 (21.8)	..	
Yes	24/25 (96.0)	18/28 (64.3)	1.49 [0.68–3.27]		0/7 (0.0)	..	

Calculation of odds ratio and *P* value: correlation between close contacts of the same index case taken into account using GEE (exchangeable correlation structure, logit link function).

Abbreviations: GEE, generalized estimating equation; OR, odds ratio.

[a]Children aged <12 considered nonsmokers.

[b]Among all following conditions, except "other chronic condition."

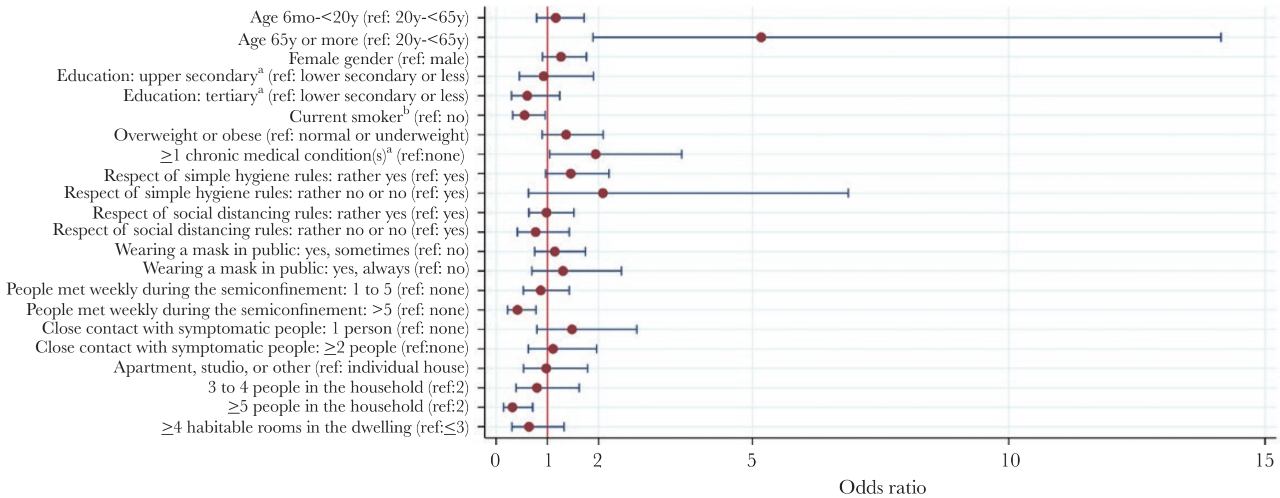

Figure 2. Unadjusted association between characteristics of household members of index cases and seropositivity (bivariable analysis). For calculation of odds ratio, the correlation between household members of the same index case was taken into account using GEEs (exchangeable correlation structure, logit link function). Error bars represent the limits of the 95% confidence interval for the odds ratio. [a]Adult participants only. [b]Children aged <12 considered nonsmokers. Abbreviation: GEEs, generalized estimating equations.

strengthening of the relationship between the absence of strict adherence to simple hygiene rules and positive serology testing (adjusted OR, 1.80; 95% CI, 1.02–3.17). However, there was no indication of a link with adherence to social distancing rules or mask wearing. The association of a greater number of social contacts during the semiconfinement with lower odds of infection was confirmed in multivariable analysis (adjusted OR, 0.35; 95% CI, 0.16–0.74). On the other hand, close encounters with symptomatic individuals tended to be associated with positive serology, but this tendency was not statistically significant at the .05 level. Household characteristics did not show a significant association with serological test result. Adding characteristics of the index case to the model (age, gender) yielded comparable estimates (results not shown).

Prevalence and Clinical Presentation of Flu-Like Episodes and Use of Health Services

The occurrence of ≥1 flu-like episode since the end of February 2020 was strongly associated with positive serological testing, both in household members (OR, 3.55; 95% CI, 2.37–5.32) (Table 4) and close contacts outside the household (OR, 8.64; 95% CI, 1.77–42.12). The proportion of asymptomatic seropositive individuals (ie, not reporting any flu-like episode) was 21.4% in household members and 16.7% in close contacts outside the household. With the exception of chest pain, all reported symptoms were associated with a positive serology. This was particularly evident in household members mentioning new-onset anosmia or ageusia, of whom 92.8% were seropositive (OR, 6.24; 95% CI, 3.46–11.24). When limiting the analysis to participants not reporting previous nasal or throat swabbing, the strength of the association between symptoms and serology generally increased (Supplementary Table 2). Half the seropositive household members not mentioning prior PCR testing reported tiredness (49.6%) (Figure 3), followed by headache (44.1%), cough (37.1%), fever (36.8%), aching muscles or joints (36.6%), and anosmia or ageusia (35.9%). Gastrointestinal symptoms were infrequent. Half of the seropositive household members (46.3%) reported contact with a medical provider, and 6.3% were hospitalized. Figures were comparable among seropositive close contacts outside the household (41.7% and 8.3%, respectively). However, the hospitalization rate was higher in index cases (14.7%).

DISCUSSION

More than 1 in 2 participants living with a confirmed COVID-19 case developed a serologic response to SARS-CoV-2, while 1 in 5 close contacts outside the household was seropositive. Our findings confirm that households represent high-risk transmission settings [4, 5, 8, 12, 21–23]. The SAR we observed is substantially higher than those reported in previous seroepidemiological studies, including a large nationwide survey conducted in Spain (37.4%) and a retrospective cohort study conducted in Singapore (11%, estimation based on Bayesian modeling) [11–13, 23]. One study disclosed an SAR of 80% in household members of essential workers, but the estimation was based on 30 participants only [10]. Besides serological testing characteristics, differences could be due to variable average household sizes (2.2 members in Switzerland vs 2.6 in Spain) [24], unequal adoption of protective behaviors within households [25], or different levels of confinement. Regarding close contacts outside the household, previous seroepidemiological studies have provided SAR estimations

Table 2. Serology Test Result According to Adherence to Measures Aimed at Decreasing Transmission, Contacts With Other People, and Living Conditions, Stratified by Type of Participant (Unadjusted Results)

	Household Members (n = 302)			Close Contacts Outside the Household (n = 69)		
	No. (%) Seropositive	Unadjusted OR [95% CI]	*P* Value	No. (%) Seropositive	Unadjusted OR [95% CI]	*P* Value
Respect of measures and contacts with other people						
Respect of simple hygiene rules (washing hands regularly, sneezing into the elbow, etc.)			.123			.272
Yes	114/215 (53.0)	Reference		8/56 (14.3)	Reference	
Rather yes	40/74 (54.1)	1.46 [0.97–2.20]		4/13 (30.8)	2.22 [0.54–9.21]	
Rather no or no	4/9 (44.4)	2.08 [0.63–6.87]		No participant	..	
Respect of social distancing rules (physical distancing, avoid shaking hands or kissing, etc.)			.868			.114
Yes	87/157 (55.4)	Reference		7/53 (13.2)	Reference	
Rather yes	56/105 (53.3)	0.99 [0.64–1.52]		5/15 (33.3)	2.94 [0.77–11.23]	
Rather no or no	15/36 (41.7)	0.77 [0.42–1.43]		0/1 (0.0)	..	
Wearing a mask in public			.657			.093
No	79/163 (48.5)	Reference		5/38 (13.2)	Reference	
Yes, sometimes	54/98 (55.1)	1.15 [0.75–1.74]		2/17 (11.8)	1.06 [0.21–5.35]	
Yes, always	27/40 (67.5)	1.31 [0.70–2.45]		5/13 (38.5)	4.36 [1.06–17.83]	
Weekly No. of people who met outside home during the semiconfinement			.009			.761
0	65/100 (65.0)	Reference		2/17 (11.8)	Reference	
1–5	73/140 (52.1)	0.87 [0.53–1.43]		6/34 (17.7)	1.26 [0.25–6.35]	
>5	21/61 (34.4)	0.42 [0.22–0.78]		4/17 (23.5)	1.86 [0.32–10.75]	
Close contact with people outside the home having symptoms suggestive of COVID-19, No. of people			.456			.099
0	127/233 (54.5)	Reference		2/14 (14.3)	Reference	
1	17/34 (50.0)	1.48 [0.80–2.75]		5/42 (11.9)	0.88 [0.15–5.01]	
≥2	16/35 (45.7)	1.11 [0.63–1.96]		5/12 (41.7)	4.36 [0.68–27.99]	
Living conditions and household characteristics[a]						
Housing type[b]			.946			
Individual house	83/158 (52.5)	Reference				
Apartment, studio, or other	77/144 (53.5)	0.98 [0.54–1.79]				
No. of people in the household[b]			.046			
2	39/59 (66.1)	Reference				
3	31/51 (60.8)	0.82 [0.35–1.93]				
4	44/74 (59.5)	0.78 [0.34–1.77]				
5	33/68 (48.5)	0.43 [0.17–1.06]				
≥6	13/50 (26.0)	0.19 [0.06–0.62]				
No. of habitable rooms (besides kitchen) in the dwelling[c]			.441			
≤3	35/54 (64.8)	Reference				
4–6	96/183 (52.5)	0.67 [0.32–1.40]				
≥7	29/65 (44.6)	0.55 [0.21–1.47]				

All participants, including children and teens. Calculation of odds ratio and *P* value: correlation between close contacts of the same index case taken into account using GEE (exchangeable correlation structure, logit link function).

Abbreviations: COVID-19, coronavirus disease 2019; GEE, generalized estimating equation; OR, odds ratio.

[a]Not relevant for close contacts outside the household.

[b]Answer of the index case taken for all household members.

[c]Answer of the index case taken for all household members, except 2 households where information from the index case was missing (mean of answers reported by other household members taken instead).

ranging from 0% to 13.7% [12, 14–16, 23]. The heterogeneity of results could reflect different study designs and settings and varying adherence to public health protective recommendations [25]. The strong difference observed between the prevalence in household members and in close contacts outside the home is probably due the fact that contacts at home are closer and last longer than those that occur outside, due to the difficulty of applying social distancing in limited spaces and with family members. Moreover, simple hygiene rules may be more neglected at home, maybe due to a feeling of security.

We found that older household members were at particularly high risk, corroborating the findings of previous research

Table 3. Adjusted Association of Individual and Household Characteristics With Serology Test Result Among Household Members

	Adjusted OR [95% CI]	*P* Value
Characteristics of household member		
Age (ref: 20 y–<65 y)		
6 mo–<20 y	0.92 [0.54–1.59]	.775
≥65 y	3.63 [1.05–12.60]	.042
Gender (ref: male)		
Female	1.37 [0.90–2.08]	.137
Current smoker[a] (ref: no)		
Yes	0.73 [0.38–1.39]	.339
Weight status (ref: normal or underweight)		
Overweight or obese	1.48 [0.90–2.43]	.125
Respect of simple hygiene rules (washing hands regularly, sneezing into the elbow, etc.) (ref: yes)		
Rather yes, rather no, or no	1.80 [1.02–3.17]	.041
Respect of social distancing rules (physical distancing, avoid shaking hands or kissing, etc.) (ref: yes)		
Rather yes, rather no, or no	1.06 [0.62–1.82]	.831
Wearing a mask in public (ref: no)		
Yes, sometimes	1.02 [0.61–1.72]	.926
Yes, always	0.94 [0.43–2.09]	.885
Weekly No. of people met outside home during semiconfinement (ref: 0)		
1–5	0.70 [0.40–1.21]	.201
>5	0.35 [0.16–0.74]	.006
Close contact with people outside home having symptoms suggestive of COVID-19, No. of people (ref: none)		
1	1.29 [0.62–2.67]	.495
≥2	1.72 [0.86–3.45]	.125
Characteristics of household		
Highest education level among adult household members (ref: lower secondary or less)		
Upper secondary	1.08 [0.21–5.54]	.922
Tertiary	1.64 [0.34–7.95]	.541
Housing type[b] (ref: individual house)		
Apartment, studio, or other	0.87 [0.39–1.95]	.738
No. of people in the household[b]		
1-person increase	0.78 [0.56–1.08]	.135
No. of habitable rooms (besides kitchen) in the dwelling[c]		
1-room increase	0.98 [0.76–1.25]	.843
Mean age of participating household members[d]		
1-y increase	1.00 [0.97–1.04]	.793

Multivariable regression model; 291/302 household members included in model. Within-household correlation taken into account using GEE (exchangeable correlation structure, logit link function). The variable "chronic medical conditions," which was not available for children and teens, was not included in the model.

Abbreviations: COVID-19, coronavirus disease 2019; GEE, generalized estimating equation; OR, odds ratio.

[a]Children aged <12 considered nonsmokers.

[b]Answer of the index case taken for all household members.

[c]Answer of the index case taken for all household members, except 2 households where information from the index case was missing (mean of answers reported by other household members taken instead).

[d]Given the association between household size and mean age of participating household members, this variable was included in the model.

on transmission using NAAT [8, 26, 27]. This association was not found for close contacts outside the home. This suggests that elderly couples are even less able to apply protective measures at home, due to their high level of mutual dependency. There was no difference in infection susceptibility according to gender, which is in line with other works [5, 23, 26]. The impact of smoking on the risk of SARS-CoV-2 infection is a controversial issue [28]. Although household members currently smoking were less frequently positive, this association vanished in multivariable analysis, suggesting that it may be confounded by other factors. The importance of hygiene measures to avoid transmission within the household is confirmed by our observations [29]. Mask wearing in public and respect of social distancing rules, which is particularly difficult when living under the same roof, were not associated with infection risk in households. In contrast, the association of a greater number of social contacts with a lower probability of infection seems surprising in the first place. In fact, our study took place during a period of semiconfinement, during which most people stayed at home, except those who had to go out to work in essential sectors. Our findings thus show that the individual risk of being infected is higher when staying at home than when working

Table 4. Serology Test Result According to Symptoms and Use of Health Services Since the End of February 2020, Stratified by Type of Participant

	Index Cases (n = 219)	Household Members (n = 302)			Close Contacts Outside the Household (n = 69)		
	No. (%) Seropositive	No. (%) Seropositive	Odds Ratio [95% CI]	*P* Value	No. (%) Seropositive	Odds Ratio [95% CI]	*P* Value
Symptoms							
Flu-like episodes				.000			.008
0	25/26 (96.2)	34/117 (29.1)	Reference		2/39 (5.1)	Reference	
≥1	190/193 (98.5)	125/184 (67.9)	3.55 [2.37–5.32]		10/29 (34.5)	8.64 [1.77–42.12]	
Cough				.001			.003
No	58/58 (100.0)	84/192 (43.8)	Reference		5/53 (9.4)	Reference	
Yes	157/161 (97.5)	76/110 (69.1)	2.07 [1.36–3.15]		7/16 (43.8)	7.76 [2.02–29.84]	
Runny or stuffy nose, sneezing				.001			.008
No	105/107 (98.1)	93/208 (44.7)	Reference		5/52 (9.6)	Reference	
Yes	110/112 (98.2)	67/94 (71.3)	2.18 [1.38–3.44]		7/17 (41.2)	6.33 [1.64–24.46]	
Sore throat				.049			.729
No	137/140 (97.9)	109/224 (48.7)	Reference		8/52 (15.4)	Reference	
Yes	78/79 (98.7)	51/78 (65.4)	1.53 [1.00–2.33]		4/17 (23.5)	1.27 [0.33–4.84]	
Dyspnea				.000			.203
No	123/125 (98.4)	108/235 (46.0)	Reference		9/61 (14.8)	Reference	
Yes	92/94 (97.9)	52/67 (77.6)	2.86 [1.74–4.70]		3/8 (37.5)	2.82 [0.57–13.97]	
Feeling of fever				.000			.901
No	93/95 (97.9)	87/206 (42.2)	Reference		9/54 (16.7)	Reference	
Yes	122/124 (98.4)	73/96 (76.0)	2.74 [1.71–4.40]		3/15 (20.0)	1.09 [0.27–4.44]	
Temperature ≥37.5°C (measured)				.000			.007
No	80/82 (97.6)	82/209 (39.2)	Reference		8/63 (12.7)	Reference	
Yes	135/137 (98.5)	78/93 (83.9)	4.64 [2.82–7.65]		4/6 (66.7)	12.61 [1.98–80.32]	
Headache				.000			.001
No	79/81 (97.5)	76/180 (42.2)	Reference		4/52 (7.7)	Reference	
Yes	136/138 (98.6)	84/122 (68.9)	2.14 [1.43–3.19]		8/17 (47.1)	10.29 [2.55–41.62]	
Pain in muscles, joints				.000			.940
No	86/89 (96.6)	88/203 (43.4)	Reference		10/58 (17.2)	Reference	
Yes	129/130 (99.2)	72/99 (72.7)	2.44 [1.61–3.70]		2/11 (18.2)	0.94 [0.18–4.84]	
Chest pain				.444			.018
No	150/152 (98.7)	131/258 (50.8)	Reference		7/58 (12.1)	Reference	
Yes	65/67 (97.0)	29/44 (65.9)	1.23 [0.72–2.09]		5/11 (45.5)	5.56 [1.34–23.07]	
Tiredness, exhaustion				.000			.001
No	31/33 (93.9)	62/162 (38.3)	Reference		3/49 (6.1)	Reference	
Yes	184/186 (98.9)	98/140 (70.0)	2.66 [1.79–3.95]		9/20 (45.0)	11.03 [2.64–45.97]	
Appetite loss				.000			.003
No	89/93 (95.7)	104/237 (43.9)	Reference		7/61 (11.5)	Reference	
Yes	126/126 (100.0)	56/65 (86.2)	4.52 [2.50–8.17]		5/8 (62.5)	11.30 [2.28–55.89]	
Nausea, vomiting				.004			.181
No	178/182 (97.8)	138/275 (50.2)	Reference		11/67 (16.4)	Reference	
Yes	37/37 (100.0)	22/27 (81.5)	2.93 [1.40–6.13]		1/2 (50.0)	6.51 [0.42–101.56]	
Diarrhea				.001			.475
No	154/157 (98.1)	123/250 (49.2)	Reference		10/62 (16.1)	Reference	
Yes	61/62 (98.4)	37/52 (71.2)	2.37 [1.41–3.99]		2/7 (28.6)	1.90 [0.33–11.00]	
Belly pain				.002			.530
No	175/178 (98.3)	134/267 (50.2)	Reference		10/62 (16.1)	Reference	
Yes	40/41 (97.6)	26/35 (74.3)	2.76 [1.44–5.28]		2/7 (28.6)	1.75 [0.31–10.01]	
Sudden loss of smell or taste				.000			.001
No	74/77 (96.1)	96/233 (41.2)	Reference		6/62 (9.7)	Reference	
Yes	141/142 (99.3)	64/69 (92.8)	6.24 [3.46–11.24]		6/7 (85.7)	65.25 [5.47–779.10]	
Use of health services							
Contact with a medical provider				.000			.027
No	28/28 (100.0)	86/209 (41.2)	Reference		7/57 (12.3)	Reference	

Table 4. Continued

	Index Cases (n = 219)	Household Members (n = 302)			Close Contacts Outside the Household (n = 69)		
	No. (%) Seropositive	No. (%) Seropositive	Odds Ratio [95% CI]	*P* Value	No. (%) Seropositive	Odds Ratio [95% CI]	*P* Value
Yes	185/189 (97.9)	74/93 (79.6)	3.61 [2.19–5.95]		5/12 (41.7)	4.62 [1.20–17.86]	
Nasal or throat swabbing to detect SARS-CoV-2				.000			.002
No	([a])	110/240 (45.8)	Reference		7/63 (11.1)	Reference	
Yes	([a])	50/62 (80.7)	2.74 [1.61–4.65]		5/6 (83.3)	38.52 [3.95–375.53]	
Test result for SARS-CoV-2[b]							
Negative or unknown	([a])	5/16 (31.3)	..		4/5 (80.0)	..	
Positive	([a])	45/46 (97.8)	..		1/1 (100.0)	..	
Hospitalization				.028			..
No	181/185 (97.8)	150/291 (51.6)	Reference		11/68 (16.2)	..	
Yes	32/32 (100.0)	10/11 (90.9)	4.96 [1.19–20.62]		1/1 (100.0)	..	
Admission to the ICU				..			..
No	203/207 (98.1)	158/300 (52.7)	..		12/69 (17.4)	..	
Yes	10/10 (100.0)	2/2 (100.0)	..		No participant	..	
Intubation				..			..
No	210/214 (98.1)	160/302 (53.0)	..		12/69 (17.4)	..	
Yes	3/3 (100.0)	No participant	..		No participant	..	

All participants, including children and teens. Calculation of odds ratio and *P* value: correlation between close contacts of the same index case taken into account using GEEs (exchangeable correlation structure, logit link function).

Abbreviations: GEEs, generalized estimating equations; ICU, intensive care unit; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

[a]Index cases all tested positive.

[b]Nucleic acid amplification test.

outside, with the aim of confinement (or quarantine) being to break the transmission chain. We have thus to accept that this works well but at the price of a higher risk for household members of COVID-19 cases to be infected. Like previous studies, we found an inverse relationship between household size and the proportion of seropositive household members

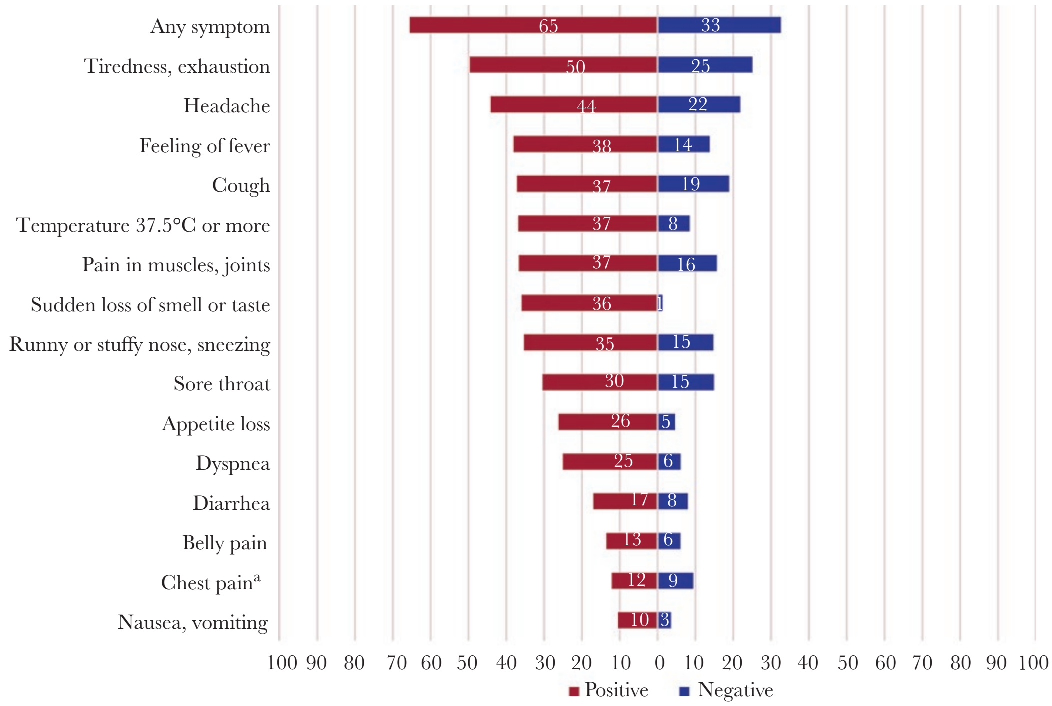

Figure 3. Percentage of household members reporting specific symptoms, according to serology test result (household members not reporting prior nasal or throat swabbing to detect severe acute respiratory syndrome coronavirus 2). The correlation between household members of the same index case was taken into account using GEEs (exchangeable correlation structure). [a]Difference not statistically significant at the .05 level. Abbreviation: GEEs, generalized estimating equations.

[26, 27]. This seems counterintuitive, as prevalence of infectious diseases is well known to be associated with crowded housing. However, having many in a household decreases mutual dependency and thus decreases close contacts. This association was weakened by inclusion of the mean age of household members in the multivariable model, suggesting that the apparent protective effect of a high number of household members could reflect the fact that large families are, on average, younger. However, disentangling the respective contributions of household size and age distribution of household members remains difficult.

Regarding the clinical presentation of COVID-19, the proportion of asymptomatic seropositive individuals was close to the findings of Pollán and colleagues in Spain (28.5%) [12]. Even if not specific, a large number of symptoms were still associated with SARS-CoV-2 infection, especially new-onset smell and/or taste disturbance, confirming the clinical utility of this symptom in suspicion of COVID-19 [30]. Interestingly, the prevalence of flu-like symptoms was high also in seronegative people, maybe because the first epidemic wave occurred just after the winter, when other respiratory infections were still quite prevalent.

Limitations need to be acknowledged. The Swiss testing policy during the first epidemic wave, which limited diagnostic testing mainly to individuals at increased risk for severe illness, made the sample of index cases not representative of all cases that occurred in the community during this period. Index cases were thus not necessarily the first infected in their household, but those fulfilling testing criteria. However, this would be especially problematic if the purpose were to identify factors associated with infectivity of the index case, which we deliberately avoided.

Incidence of new COVID-19 cases remains high worldwide, and prevention of transmission is, for now, the only way to tackle the pandemic. If concerns regarding the transmission of SARS-CoV-2 in shops, restaurants, and public gatherings are justified, our findings emphasize that the risk of being infected is much higher at home. However, this remains overlooked in collective awareness and public health discourse, precisely because quarantine and confinement are methods used to break the transmission chain. Early testing of the first case in a household is important to support immediate self-isolation within the house. Our results suggest in particular that it is essential for noninstitutionalized elderly couples to receive strong external support for daily basic needs during the infectious period of the index case. Further research is needed to determine the efficacy and acceptability of specific measures aimed at limiting SARS-CoV-2 transmission within households and at motivating early testing and self-isolation.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

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Data sharing. All data and materials used in this work are accessible to researchers upon reasonable request for data sharing to the corresponding author.

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