

Atypical symptoms, SARS-CoV-2 test results, and immunization rates in 456 residents from eight nursing homes facing a COVID-19 outbreak

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Running title: Atypical symptoms in COVID-19 nursing home residents

Key words: COVID-19, testing for SARS-CoV-2, nursing homes, rRT-PCR, symptoms, antibodies, immunization, older people.

Key points:

- Anorexia, behavioural change, exhaustion, malaise, and falls are possible COVID-19 symptoms in nursing home residents
- Positive and negative predictive values of SARS-CoV-2 immunization by rRT-PCR are 95.2% and 92.4% in nursing home residents. 61% of residents tested negative by rRT-PCR who developed SARS-CoV-2 immunization had symptoms consistent with COVID-10

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Abstract

Background: Frail older persons may have an atypical presentation of COVID-19. The value of rRT-PCR testing for identifying SARS-CoV-2 nursing homes (NH) residents is not known.

Objective: To determine whether (i) atypical symptoms may predict rRT-PCR results and (ii) rRT-PCR results may predict immunization against SARS-CoV-2 in NH residents.

Design: A retrospective longitudinal study.

Setting: eight NHs with at least ten rRT-PCR-positive residents.

Subjects: 456 residents.

Methods: Typical and atypical symptoms recorded in residents' files during the 14 days before and after rRT-PCR testing were analyzed. Residents underwent blood testing for IgG-SARS-CoV-2 nucleocapsid protein 6 to 8 weeks after testing. Univariate and multivariate analyses compared symptoms and immunization rates in rRT-PCR-positive and negative residents.

Results: 161 residents had a positive rRT-PCR (35.3%), 17.4% of whom were asymptomatic before testing. Temperature $>37.8^{\circ}\text{C}$, oxygen saturation $<90\%$, unexplained anorexia, behavioural change, exhaustion, malaise, and falls before testing were independent predictors of a further positive rRT-PCR. Among the rRT-PCR-positive residents, 95.2% developed SARS-CoV-2 antibodies vs 7.6% in the rRT-PCR-negative residents. Among the residents with a negative rRT-PCR, those who developed SARS-CoV-2 antibodies more often had typical or atypical symptoms ($p=0.02$ and <0.01 , respectively).

Conclusion: This study supports a strategy based on (i) testing residents with typical or unexplained atypical symptoms for an early identification of the first SARS-CoV-2 cases, (ii) rT-PCR testing for identifying COVID-19 residents, (iii) repeated wide-facility testing (including asymptomatic cases) as soon as a resident is tested positive for SARS-CoV-2, and (iv) implementing SARS-CoV-2 infection control measures in rRT-PCR-negative residents when they have unexplained typical or atypical symptoms.

Abbreviations

AUC: area under the curve

COVID-19: Coronavirus 19

NH: Nursing home

rRT-PCR: Real-time reverse-transcriptase polymerase chain reaction for SARS-CoV-2

Introduction

Nursing home (NH) residents represent more than one third of COVID-19-related deaths in the Western countries. NHs are closed environments that are very conducive to outbreaks. Their residents are extremely vulnerable to severe forms of COVID-19, with a mortality rate exceeding 25 % [1-3]. The strategy used to prevent COVID-19 outbreaks in NHs was initially based on: (i) a daily screening of symptoms consistent with COVID-19 in residents, staff members, and visitors, (ii) nasopharyngeal testing using the real-time reverse-transcriptase polymerase chain reaction (rRT-PCR) for SARS-CoV-2 in symptomatic subjects, and (iii) the implementation of appropriate infection prevention and control measures [4-6]. In a NH facing a COVID-19 outbreak, over half of the rRT-PCR-positive residents were asymptomatic at the time of testing [7]. This major finding led to the addition of the following recommendation: rRT-PCR testing of all residents, including the asymptomatic ones, for all new identified cases, and repeat testing until no new cases are identified [5,6].

The high percentage of asymptomatic rRT-PCR-positive residents found in Aron's study [7] may have been overestimated, since some atypical symptoms, further attributed to COVID-19 in frail older people [8-20], were not considered. It is also possible that some of the symptomatic residents with repeated negative rRT-PCR test results for SARS-CoV-2 may have developed antibodies a few weeks later.

In March 2020, the Health Agency of the French Occitanie region recommended the following: (i) to make a daily report of any unusual and unexplained symptoms in the NH residents' files, (ii) to perform an rRT-PCR test in residents presenting unusual symptoms without any obvious cause, (iii) to perform an rRT-PCR test on all residents, including those asymptomatic, in the case of a positive test result in a resident, (iv) to repeat testing in all residents tested negative

once every 7 days until no new cases were identified for at least 14 days, and (v) to implement appropriate infection prevention and control measures in residents with positive rRT-PCR testing or with unexplained symptoms, even if repeated testing was negative [21]. COVID-19 support platforms were concomitantly set up in proximity hospitals to help NHs to follow regional guidance [22]. In May 2020, the same Agency recommended to perform SARS-CoV-2 serology in residents of NHs having faced a COVID-19 outbreak in order to better prepare for a new outbreak.

The objectives of this study, conducted in NHs facing a COVID-19 outbreak, were to determine (i) the phenotype of rRT-PCR-positive and negative residents, (ii) whether typical and atypical symptoms differ between rRT-PCR-positive and negative residents, and (iii) how well rRT-PCR testing results can predict immunization against SARS-CoV-2 in NH residents.

Methods

Design of the study

A retrospective longitudinal study was carried out in NHs having faced a SARS-CoV-2 outbreak in the Occitanie region between March 3 and June 10, 2020. This analysis was based on symptoms prospectively recorded by doctors or nurses in the residents' files, in accordance with the Occitanie Health Agency guidance.

Setting

NHs reporting ten or more residents with a positive rRT-PCR result in the Occitanie region (Appendix 1).

Participants

As soon as COVID-19 was diagnosed in at least one NH resident, all residents and/or their relatives were informed of the regional guidance to reduce SARS-CoV-2 dissemination in NHs.

When the COVID-19 outbreak was controlled in the NH, all residents and/or their relatives were informed that the residents' anonymized clinical and biological data would be used for research purposes. None of them disagreed. This study was approved by the Institutional Review Board of the Montpellier hospital (IRB-MTP_2020_06_202000534).

Outcomes

The symptoms noted by the doctors or nurses in the residents' medical files (by using their usual medical information intelligence software) were retrospectively analyzed by two doctors who were not aware of the rRT-PCR and blood test results. Recorded symptoms included: (i) typical COVID-19 symptoms: temperature $> 100^{\circ}\text{F}$ (37.8°C), cough, shortness of breath or respiratory rate $> 24/\text{min}$, and oxygen saturation $< 90\%$, (ii) atypical symptoms: chills without fever, malaise, behavioural change (including delirium, unusual apathy, aggressiveness, or opposition to care), unusual rhinorrhea, nasal congestion, sore throat, myalgia, exhaustion, dizziness, headache, nausea, diarrhea, falls, livedo, anorexia, and hypothermia, and (iii) residents' characteristics including age, gender, length of stay at facility < 90 or ≥ 90 days, as well as chronic comorbidities, including heart diseases requiring at least one medication, treated diabetes mellitus, history of stroke, kidney insufficiency (creatinine clearance < 30 ml/min), hemodialysis, body mass index > 25 kg/m² (overweight) or < 18.5 kg/m² (malnutrition), moderate or severe cognitive decline according to the NH medical coordinator, use of antipsychotic drugs, and smoking habits.

Nasopharyngeal testing for SARS-CoV-2 using rRT-PCR was performed in all residents as soon as a first resident was tested positive in the NH. Testing was repeated weekly in all previously negative residents until no new cases were identified for at least 14 days in the NH and in all positive residents until rRT-PCR became negative.

All residents underwent blood testing for SARS-CoV-2 nucleocapsid protein IgG using an enzyme-linked immunosorbent assay 6 to 8 weeks after the last resident was tested positive for SARS-CoV-2 in the NH [23].

Statistical analysis

Qualitative variables were described with frequency and proportions for each category. The description of quantitative variables was performed using mean and standard deviation and/or median, minimum and maximum values. Characteristics of positive or negative rRT-PCR residents were compared using Student's or Wilcoxon-Mann-Whitney tests for quantitative variables according to the distribution, and Chi-2 or Fisher exact tests for qualitative variables. Symptoms that were distributed differently between positive and negative rRT-PCR residents ($p < 0.20$) were entered into a multivariate logistic regression analysis. A backward selection of variables was applied using the Akaike Information Criterion [24]. The significance of removing a variable from the logistic model was determined by the maximum likelihood ratio

test. The goodness-of-fit of the models was assessed using the Hosmer and Lemeshow Chi-square test as well as the Area Under the receiver operating characteristic Curve (AUC) and its 95% confidence interval. An AUC equal to 0.5 suggests a non-discriminatory model; between 0.7 and 0.8, that discrimination is acceptable; and between 0.8 and 0.9, that it is excellent [25]. The adjusted odds-ratios (OR) and their 95% confidence intervals were reported. No imputation method was used to handle missing data. The statistical significance threshold was set at 5%. Analyses were performed using SAS Enterprise Guide, v7.3 (SAS Institute Inc, Cary, NC, USA).

Results

Characteristics of the NHs

Among the 99 NHs of the area, 37 had at least one rRT-PCR-positive resident and 212 residents had positive rRT-PCR test results between March 3 and June 10, 2020. Ten NHs reported at least ten cases of rRT-PCR-positive residents but 2 had missing data. In the eight remaining NHs, all 456 residents were included in the analysis: 161 tested positive for SARS-CoV-2 (35.3%; range: 15.7 to 54.7%) and there was no drop out (Appendix 1).

Demographic characteristics of residents

Residents with a positive rRT-PCR test more often had cardiovascular or renal diseases, or a severe cognitive impairment. Preexisting lung disease was not a risk factor for positive rRT-PCR testing (Table 1).

Symptoms during the 14 days prior to the testing

Typical symptoms were significantly more common in rRT-PCR-positive residents than in negative ones (on average, 1.9 typical symptoms vs 0.4 in negative residents, respectively, $p < 0.0001$). There was a significantly greater number of typical symptoms in rRT-PCR-positive residents ($p < 0.0001$). Temperature $> 100^{\circ}\text{F}$ (37.8°C), cough, oxygen saturation $< 90\%$ and respiratory rate $> 24/\text{min}$ were all more prevalent in rRT-PCR-positive residents than in those who tested negative ($p < 0.0001$) (Table 2, Appendix 2).

Atypical symptoms were also significantly more common in rRT-PCR-positive residents than in those who tested negative (on average, 1.9 typical symptoms vs 0.6, respectively, $p < 0.0001$). There was a significantly greater number of atypical symptoms in rRT-PCR-positive residents

than in the negative ones ($p < 0.0001$). The most prevalent atypical symptoms observed in rRT-PCR-positive residents were exhaustion, falls, behavioural change, anorexia, muscle pain, chills, sore throat, and malaise. Diarrhea was more prevalent in rRT-PCR-positive residents but its prevalence was also high in residents who tested negative (Table 2, Appendix 2).

Among the 28 rRT-PCR-positive residents who were asymptomatic before testing (Table 3): (i) 14 (50%) remained asymptomatic in the 14 days following the positive testing, (ii) 11 (39.3%), 5 (17.9%), and 4 (14.3%) had at least one, two or three typical symptoms, and (iii) 6 had at least one atypical symptom (21.4%). In the rRT-PCR-negative residents who were asymptomatic before testing, 150 (90.9%) remained asymptomatic after testing (Appendix 3).

Symptoms of rRT-PCR-positive and negative residents are displayed in Appendix 3. Table 4 displays symptoms associated with a positive result for SARS-CoV-2 in the univariate and multivariate analyses. In the multivariate analysis, the symptoms associated with a positive rRT-PCR result were anorexia, exhaustion, falls/malaise, temperature $> 37^{\circ}\text{C}$, oxygen saturation $< 90\%$, and behavioural change. The model AUC was 0.82.

Immunization against SARS-CoV-2 in NH residents, depending on rRT-PCR test results

A positive rRT-PCR result predicted the development of SARS-CoV-2 IgG in 95.2% of cases [Positive Predictive Value IC95%: 93.1%-97.3%]. A negative rRT-PCR result predicted the lack of immunization against SARS-CoV-2 in 92.4% of cases [Negative Predictive value IC95%: 89.8%-94.9%]. Among the 21 residents who repeatedly tested negative for SARS-CoV-2, those who developed antibodies against SARS-CoV-2 had more often a respiratory symptom and more often atypical symptoms, including especially diarrhea, hypothermia, behavioural change, and falls (Table 5). All asymptomatic rRT-PCR-positive residents developed antibodies against SARS-CoV-2.

Death and hospitalization rate

A higher rate of hospitalization and death was observed in residents with positive rRT-PCR testing (Appendix 1).

Discussion

The main results of this study are: (i) nasopharyngeal rRT-PCR testing has a high value in predicting immunization against SARS-CoV-2; (ii) even when taking into account atypical

symptoms, 17.4% of the PCR-positive residents are asymptomatic in the 14 days before testing; (iii) besides typical symptoms (fever, oxygen saturation < 90%, but not cough), anorexia, behavioural change, exhaustion, malaise, and falls in the 14 days before testing are independent predictors of a positive rRT-PCR test and (iv) 61.9% of residents who developed antibodies while having repeated negative rRT-PCR results had at least one typical or atypical symptom over the follow-up period.

Our study has several strengths. First, it was conducted in a large sample of NH residents who were tested across eight NHs facing a severe COVID-19 outbreak. Second, all residents were studied and there was no drop out during the study. Third, ascertainment of typical and atypical symptoms was almost complete since all studied NHs followed the regional Health Agency guidance published in March 2020. This guidance recommends to record systematically on residents' files all unexplained symptoms - even those unusual for COVID-19 - and to test residents for SARS-CoV-2 by rRT-PCR at the slightest doubt. Because atypical symptoms reported as COVID-19 symptoms in frail older persons are very common in NH residents, the assessment of typical and atypical symptoms in both residents tested positive and negative by rRT-PCR allowed us to determine whether typical and atypical symptoms are predictors of a positive testing for SARS-CoV-2 in NH residents. Fourth, the rRT-PCR positive or negative results were ascertained in all residents with no selection bias since the facility-wide testing was (i) implemented in all residents, even when asymptomatic, (ii) repeated in all negative residents until no new cases were diagnosed for at least 14 days and (iii) repeated in all positive residents until their test results became negative [5,6]. Fifth, IgG against SARS-CoV-2 were measured in all residents, and the period during which this study was conducted (March to June 2020, i.e. during the "first wave" of the epidemic in our region) allowed us to ascertain a recent contact with SARS-CoV-2 in residents. rRT-PCR testing and immunization against SARS-CoV-2 were performed in all residents, enabling the estimation of the negative predictive value of rRT-PCR testing in NH residents.

The present study does however have some limitations. First, doctors and nurses may have missed some symptoms that were not recorded in residents' files. However, the high AUC value of our model (0.82) suggests that typical and atypical symptoms retained in the multivariate analysis predict a great part of rRT-PCR test results in the studied residents. On the contrary, it is possible that symptoms may have been overreported during that period of high anxiety in staff members. However, this bias does not affect the multivariate model since

symptoms were probably overreported with the same magnitude in residents further tested positive and negative. Second, the study was conducted in NHs facing a COVID-19 outbreak. Therefore, whether our results can be extrapolated to COVID-19 residents from NHs less severely affected by the epidemic remains to be confirmed. In fact, the presence of a large number of cases in a NH can induce a high “viral load” in the facility and a greater risk of repeated viral contacts that could modify residents’ symptoms and perhaps the development of antibodies.

The main difference between our results and those of previous ones is the proportion of asymptomatic rRT-PCR-positive residents, which was 56% (27 out of 48 residents) in Arons’ study [7] vs 17.4% (28 out 161) in ours. The difference is probably partly due to the atypical symptoms considered in our study (including exhaustion, falls, behavioural change, diarrhea, and anorexia) that have been shown to be possible COVID-19 symptoms in frail older subjects [8-21, 26].

The results of the present study may have several possible implications.

The present study allows us to estimate the negative predictive value of rT-PCR testing, showing that 7.6% of the residents who repeatedly tested negative for SARS-CoV-2 developed antibodies against SARS-CoV-2. Among those 7.6% of residents with “false negative results”, a large part of them (61.9%) had at least one respiratory or atypical symptom that was not explained by another obvious cause in the 14 days before or after the first testing. This result suggests that SARS-CoV-2 infection prevention and control measures should be implemented in rRT-PCR-negative residents when they have typical or atypical symptoms consistent with COVID-19 (especially diarrhea, hypothermia, behavioural change, malaise or falls)[27], even if it remains to be determined whether residents tested repeatedly negative but developing SARS-CoV-2 IgG may participate in virus transmission.

The percentage of NH residents tested positive for SARS-CoV-2 who developed SARS-CoV-2 IgG was very high (95.2%). All 28 asymptomatic rRT-PCR-positive residents developed SARS-CoV-2 IgG in the present study, suggesting the lack of “false-positive results” in the residents of our sample. Because Arons *et al.* showed that a major part of asymptomatic rRT-PCR-positive residents have a viable virus [7], the present result further confirms that the same infection prevention and control measures should be implemented in residents tested positive for SARS-CoV-2, whether symptomatic or not.

The excellent value of rRT-PCR to predict immunization against SARS-CoV-2 strongly legitimates the strategy to diagnose COVID-19 in NH residents recommended in the US and in Europe that is based on rRT-PCR testing [5,6]. Most rRT-PCR-positive residents (95.2%) and 7.6% of rRT-PCR-negative residents developed SARS-CoV-2 IgG. It remains to be determined whether the development of antibodies against SARS-CoV-2 is long-lasting in immunized residents, therefore protecting them against a new infection, and whether the determination of the serologic status of residents may help to better prepare NHs to prevent a new COVID-19 outbreak.

Even if the number of asymptomatic rRT-PCR-positive residents is lower in the present study than in other studies, the presence of asymptomatic forms of COVID-19 in residents legitimates US and EuGMS guidance that recommends (i) testing all NH residents, even if asymptomatic, as soon as a new case of COVID-19 is diagnosed, (ii) repeating tests in all previously negative subjects once a week until the testing identifies no new COVID-19 cases for at least 14 days and (iii) performing appropriate infection and prevention measures [5,6].

The present study demonstrates that atypical symptoms have to be added to the list of symptoms that should be daily screened to identify the first SARS-CoV-2 residents as early as possible. Assessment of atypical symptoms adds to the prediction of COVID-19 infection in residents tested repeatedly negative by rRT-PCR (see above) and, above all, adds strongly to the prediction of a positive rRT-PCR testing in NH residents. Indeed, among symptoms already reported as being consistent with COVID-19 in frail older persons [8-20], anorexia, behavioural change, exhaustion, malaise, and falls in the 14 days before testing were predictors of a positive rRT-PCR testing, and this independently of typical symptoms (fever, oxygen desaturation, but not cough) in our multivariate model. Since atypical symptoms can accompany infectious situations in general, the present results suggest that measures to prevent infectious diseases in NH residents, including influenza and pneumococcal vaccinations, should be implemented more than ever when SARS-CoV-2 circulates in the community. This could reduce the risk of confusion between symptoms linked to COVID-19 and to other infectious diseases, also because some patients with COVID-19 have had pneumonia [28].

The rate of death in infected residents was high (19.2%), but lower than in previous studies [3]. It remains to be determined whether the high hospitalization rate (25.6%), aimed at reducing the workload of staff members [6], may have participated in this relatively low mortality rate.

Conclusions and Implications

The present study strongly supports (i) a strategy based on rRT-PCR for an early identification of SARS-CoV-2 in NH residents, (ii) that NH residents with unusual fatigue, behavioural change, anorexia, malaise or falls should be tested by rRT-PCR for an early identification of the first SARS-CoV-2 cases, (iii) that facility-wide testing should include asymptomatic residents when a first SARS-CoV-2 case is identified, (iv) that rRT-PCR-negative residents with unexplained respiratory symptom, diarrhea, hypothermia, behavioural change, or falls should be managed, as a precaution, as SARS-CoV-2 residents, even if it remains to be determined whether they may participate in SARS-CoV-2 transmission and (v) that immunization is quite systematic in residents tested positive for SARS-CoV-2. Whether immunization may protect residents against a new SARS-CoV-2 infection remains to be elucidated.

UNCORRECTED MANUSCRIPT

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Table 1. Demographic characteristics, coexisting conditions, prognosis, and seroconversion level of the 456 studied residents.

Characteristics	SARS-CoV-2 Test Results		P value
	Negative (N – 295)	Positive (N – 161)	
Women/men - no. (%)	211/84 (71.5/28.5)	116/45 (72.0/27.9)	0.91
Mean age (\pm SD) - year	86.2 (9.3)	87.4 (7.9)	0.36
Length of stay at facility <90 days before testing - no. (%)	16 (5.5)	12 (7.5)	0.39
Coexisting conditions - no. (%)			
Any coexisting condition	266 (90.2)	159 (98.8)	0.0005
Chronic lung disease	63 (21.5)	27 (16.8)	0.23
Diabetes	64 (21.8)	27 (16.8)	0.20
Cardiovascular disease	193 (65.9)	124 (77.0)	0.01
Cerebrovascular accident	46 (15.7)	35 (21.7)	0.11
Renal disease	56 (19.1)	60 (37.3)	< 0.0001
Received hemodialysis	4 (1.4)	1 (0.6)	0.66
Obesity	29 (10.0)	19 (11.8)	0.55
Moderate cognitive impairment	105 (36.1)	58 (36.0)	0.99
Severe cognitive impairment	104 (35.5)	81 (50.6)	<0.001
Malnutrition	33 (28.7)	29 (36.2)	0.27
Antipsychotic drug consumption	40 (23.5)	18 (25.7)	0.72
Tobacco consumption	4 (3.4)	3 (4.5)	0.71
Hospitalization	19 (6.4)	40 (24.8)	< 0.0001
Death	15 (5.1)	31 (19.2)	< 0.0001
SARS-CoV-2 antibodies	21 (7.6)	119 (95.2)	< 0.0001

Table 2. Reported Symptoms in Residents during the 14 days before testing.

Symptoms during the past 14 days	SARS-CoV-2 Test Results		<i>P</i> Value
	Negative (N – 295)	Positive (N – 161)	
Typical symptoms - no. (%)			
At least one symptom	75 (25.4)	113 (70.2)	< 0.0001
At least two symptoms	29 (9.8)	77 (47.8)	< 0.0001
At least three symptoms	9 (3.0)	55 (34.2)	< 0.0001
Number of typical symptoms - mean (SD)	0.41 (0.9)	1.86 (1.7)	< 0.0001
Temperature > 100°F (37.8°C)	36 (12.2)	91 (56.5)	< 0.0001
Cough	37 (12.5)	54 (33.5)	< 0.0001
Oxygen saturation < 90%	27 (9.1)	63 (39.2)	< 0.0001
Respiratory rate over 24/min	8 (2.7)	45 (27.9)	< 0.0001
Atypical symptoms - no. (%)			
At least one symptom	102 (34.6)	119 (73.9)	< 0.0001
At least two symptoms	47 (15.9)	79 (49.1)	< 0.0001
At least three symptoms	12 (4.1)	52 (32.3)	< 0.0001
Number of atypical symptoms	0.6 (0.9)	1.9 (1.8)	< 0.0001
Exhaustion	33 (11.2)	72 (44.7)	< 0.0001
Falls	23 (7.8)	37 (23.0)	< 0.0001
Behavioural disorder	14 (4.7)	30 (18.6)	< 0.0001
Anorexia	4 (1.4)	22 (13.7)	< 0.0001
Muscle pain	1 (0.3)	18 (11.2)	< 0.0001
Chills	2 (0.7)	13 (8.1)	< 0.0001
Sore throat	0 (0.0)	6 (3.7)	0.002
Malaise	1 (0.3)	6 (3.7)	0.009
Diarrhea	45 (15.2)	37 (23.0)	0.04
Hypothermia	18 (6.1)	17 (10.6)	0.09

Table 3. Any symptoms (typical or atypical) reported in residents during the 14 days before testing

Symptoms during the past 14 days	SARS-CoV-2 test results		<i>P</i> Value
	Negative (N – 295)	Positive (N – 161)	
Any typical or atypical symptoms - no. (%)			
At least one symptom	130 (44.1)	133 (82.6)	< 0.0001
At least two symptoms	83 (28.14)	118 (73.3)	< 0.0001
At least three symptoms	34 (11.5)	95 (59.0)	< 0.0001
Number of symptoms - mean (SD)	0.99 (1.5)	3.75 (3.0)	< 0.0001

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Table 4. Symptoms discriminating residents with positive vs negative rRT-PCR testing in the univariate and multivariate analyses

Parameters	Univariate analysis			Multivariate analysis		
	OR	95% CI	P Value	OR	95% CI	P Value
Temperature > 100°F (37.8°C)	9.3	[5.9-14.9]	<0.0001	4.9	[2.9-8.4]	<0.0001
Cough	3.5	[2.2-5.7]	<0.0001			
Shortness of breath or respiratory rate > 24/min	8.3	[4.4-15.6]	<.0001			
Oxygen saturation < 90%	6.4	[3.8-10.6]	<0.0001	2.7	[1.5-5.0]	0.01
Chills	12.9	[2.9-57.8]	0.0009			
Rhinorrhea	1.1	[0.4-3.6]	0.81			
Muscle pain	37.0	[4.9-279.8]	0.0005			
Exhaustion	6.4	[4.0-10.3]	<.0001	2.5	[1.4-4.5]	0.002
Headaches	1.4	[0.3-6.2]	0.7			
Nausea	1.7	[0.6-4.4]	0.31			
Diarrhoea	1.7	[1.0-2.7]	0.04			
Behavioural disorder	4.6	[2.4-9.0]	<0.0001	2.5	[1.1-5.6]	0.02
Skin symptom	3.7	[0.7-20.6]	0.13			
Anorexia	11.5	[3.9-34.0]	<0.0001	5.7	[1.7-18.9]	0.004
Hypothermia	1.8	[0.9-3.6]	0.09			
Malaise or fall	3.7	[2.2-6.5]	<0.0001	2.6	[1.4-5.1]	0.004

Table 5. Reported symptoms during the 14 days before rRT-PCR testing in residents tested negative for SARS-CoV-2: comparison of residents with positive vs those with negative SARS-CoV-2 immunization

Symptoms during the past 14 days	SARS-CoV-2 Immunization		<i>P</i> Value
	Negative (N – 256)	Positive (N – 21)	
Typical symptoms - no. (%)			
At least one symptom	71 (27.7)	11 (52.4)	0.02
Number of typical symptoms - mean (SD)	0.38 (0.7)	0.95 (1.3)	0.01
Shortness of breath	12 (4.7)	5 (23.8)	< 0.01
Respiratory rate over 24/min	6 (2.3)	3 (14.3)	0.02
Atypical symptoms - no. (%)			
At least one symptom	96 (37.5)	14 (66.7)	< 0.01
At least two symptoms	44 (17.2)	11 (52.4)	
At least three symptoms	16 (6.2)	7 (33.3)	
Number of atypical symptoms	0.64 (1.0)	1.9 (1.9)	< 0.01
Exhaustion	34 (13.3)	72 (28.6)	0.1
Falls	31 (12.1)	6 (28.6)	0.04
Behavioural disorder	12 (4.7)	4 (19.0)	0.02
Anorexia	5 (1.9)	2 (9.5)	0.09
Chills	0 (0.7)	1 (4.8)	0.08
Malaise	0 (0.7)	1 (4.8)	0.08
Diarrhea	42 (16.4)	9 (42.9)	<0.01
Hypothermia	11 (4.3)	5 (23.8)	<0.01