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► **To cite this version:**

Hubert Blain, Yves Rolland, Edouard Tuillon, Nadia Giacosa, Mylène Albrand, et al.. Efficacy of a Test-Retest Strategy in Residents and Health Care Personnel of a Nursing Home Facing a COVID-19 Outbreak. *Journal of the American Medical Directors Association*, 2020, 21 (7), pp.933-936. 10.1016/j.jamda.2020.06.013 . hal-03081987

HAL Id: hal-03081987

<https://hal.umontpellier.fr/hal-03081987v1>

Submitted on 18 Jul 2022

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Efficacy of a Test-Retest Strategy in Residents and Health Care Personnel of a Nursing Home facing a COVID-19 Outbreak

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Running title: Testing Efficacy in a Nursing Home facing COVID-19

Key words: COVID-19, nursing home, rRT-PCR, antibodies against SARS-CoV-2

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

Conflicts of interest/Competing interests: Authors declare no conflicts of interest/Competing interests

The present study did not require ethical approval. All materials and data are available.

Word count: main text: 1578; abstract: 299. **References:** 5. **Graphics count:** 1 table, 1 figure.

Brief Summary :

A wide testing strategy is effective in detecting asymptomatic COVID-19 residents and HCP in a NH facing COVID-19 outbreak. Symptomatic residents and HCP as well as asymptomatic HCP with negative testing may also play a role in the virus spread within the NH.

Acknowledgements – The authors thank Anna Bedbrook for editorial assistance and all residents and health care personnel of the nursing home.

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Abstract

Objective: To assess the American Testing Guidance for Nursing Homes (NHs) - updated May 19, 2020 - with a new COVID-19 case.

Design: Case investigation.

Setting and Subjects: All 79 residents and 34 Health Care Personnel (HCP) of a NH.

Methods: 7 days after identification of a COVID-19 resident, all residents and HCP underwent rRT-PCR testing for SARS-CoV-2 with nasopharyngeal swabs. This was repeated weekly in all previously negative subjects until the testing identified no new cases and in all positive subjects until the testing was negative. COVID-19 infection prevention and control (IPC) measures were implemented in all residents and HCP with positive testing or with COVID-19 symptoms. Standard IPC was also implemented in all HCP. Six weeks after initial testing, all residents underwent testing for ELISA-based IgG antibodies directed against the SARS-CoV-2. Symptoms were serially recorded in residents and HCP.

Results: 36 residents had a positive RT-PCR at baseline and two at day 7. Six HCP had a positive RT-PCR at baseline and two at day 7. No new COVID-19 cases were diagnosed later. Among the SARS-CoV-2-positive cases, six residents (16%) and three HCP (37%) were asymptomatic during the 14 days before testing. Twenty-five residents (92.3%) and all 8 HCP (100%) with a positive RT-PCR developed IgG antibodies against SARS-CoV-2. Among the residents and HCP always having tested negative, 2 (5%) and 5 (11.5%) developed IgG antibodies against SARS-CoV-2. These 2 residents had typical COVID-19 symptoms before and after testing and 2/5 HCP were asymptomatic before and after testing.

Conclusions and Implications: This study shows the validity of the updated American Testing Guidance for Nursing Homes (NHs). It suggests implementing COVID-19 IPC in both residents and HCP with positive testing or COVID-19 symptoms and warns that asymptomatic HCP with repeated negative RT-PCR testing can develop antibodies against SARS-CoV-2.

Key words: COVID-19, nursing home, rRT-PCR, antibodies against SARS-CoV-2

Introduction

After identification of a COVID-19 case in a Nursing Home (NH), residents are at high risk of serious illness and death from COVID-19, with a rapid and widespread transmission of

34 SARS-CoV-2 .^{1,2} The standard COVID-19 diagnosis is based on SARS-CoV-2 nucleic acid
35 testing by real-time reverse-transcriptase polymerase chain reaction (RT-PCR).³ Residents
36 and health care personnel (HCP) with positive RT-PCR can be asymptomatic at the time of
37 testing and may contribute to transmission.² Control strategies focusing only on symptomatic
38 residents are therefore insufficient. This explains why the recent American Testing Guidance
39 for Nursing Homes recommends (i) testing of all residents and HCP in the NH if there is a
40 confirmed case of COVID-19 and (ii) repeated weekly testing of all previously negative
41 residents until no new cases of COVID-19 are detected for at least 14 days since the most
42 recent positive result.⁴

43 Seroconversion with SARS-CoV-2 antibodies generally occurs rapidly in adult subjects.⁵ The
44 immune response to viruses may be influenced by aging, and seroconversion in frail older
45 subjects is uncertain. It is unclear whether residents and HCP with repeated negative testing
46 may develop antibodies against SARS-CoV-2.

47 A study was carried out on all residents and HCP of a NH facing a COVID-19 outbreak. The
48 aim was to assess clinical and serological parameters for the efficacy of infection prevention
49 and control (IPC) measures adapted to (i) symptoms and (ii) results of repeated testing.

50 **Methods**

51 **Setting:** Single NH

52 **Participants:** From March 3rd to 6th, 2020, three NH residents were hospitalized for severe
53 non-respiratory COVID-19 symptoms. All three developed respiratory symptoms (cough with
54 fever and dyspnea) 7 to 10 days after admission, and RT-PCR following nasopharyngeal swab
55 test confirmed COVID-19. Seven days after the first diagnosis, all residents or HCP were
56 enrolled in the study.

57 No ethics committee was required as this is an observational study.

58

59 **Outcomes:** COVID-19 symptoms were examined for 14 days before the first test and then
60 followed daily for 6 weeks.

61 Nasopharyngeal testing for SARS-CoV-2 using rRT-PCR was performed in all residents and
62 HCP. It was repeated weekly in all previously negative subjects until no new cases were
63 identified and in all positive subjects until testing was negative.

64 COVID-19 IPC measures were applied in all residents and HCP with positive testing or with
65 new COVID-19 symptoms, including diarrhoea, delirium, or falls.

66 Six weeks after initial testing, all residents and HCP underwent blood testing for IgG
67 antibodies directed against the SARS-CoV-2 nucleocapsid protein using an ELISA CE-IVD
68 marked kit (ID screen[®] SARS-CoV-2-N IgG indirect ID. Vet, Montpellier, France).⁵

69 **Results**

70 **Residents**

71 Among the 79 residents, 38 (48%) had a positive RT-PCR (Table 1). 36 were diagnosed at
72 baseline and two at day 7. The residents who tested positive were distributed throughout the
73 4 floors of the NH (10, 9, 10, 9).

74 The mean age of residents was similar in positive and negative RT-PCR groups. Diabetes and
75 renal disease were more common in RT-PCR positive residents.

76 Thirteen residents died two to seven days after testing due to respiratory symptoms. Twelve
77 (7 men) had a positive RT-PCR. Six RT-PCR-positive residents (16%) were asymptomatic
78 before testing.

79 Six weeks after initial testing, seven residents still had at least one typical COVID-19
80 symptom (particularly fever or cough) or a significant functional impairment. Among them, 5
81 (83%) were RT-PCR-positive.

82 The RT-PCR test became negative 14, 21, or 28 days after initial positive testing in 2 (14%),
83 7 (27%), and 12 (46%) residents. In the 5 (19%) who still had positive RT-PCR 28 days after
84 initial testing, one recovered completely and 4 had long-lasting symptoms (fever and
85 hypothermia; shortness of breath; dry cough; impaired health status).

86 **Health Care Personnel**

87 Among the 34 HCP, 6 had positive RT-PCR at baseline and 2 at day 7 (23.5%). No new
88 COVID-19 diagnosis was made later. Two thirds of the positive RT-PCR HCP had COVID-
89 19 symptoms, often mild.

90 **Seroconversion**

91 Six weeks after nasopharyngeal testing, 25 residents (92.3%) and all 8 HCP (100%) with
92 positive RT-PCR developed SARS-CoV-2 IgG antibodies. Two (5%) RT-PCR negative
93 residents and 5 (11.5%) RT-PCR negative HCP developed antibodies. All 2 residents and 3/5
94 HCPs had typical COVID-19 symptoms.

95 **Discussion**

96 The present study shows the clinical efficacy of a symptom- and repeated testing-based
97 strategy in a NH facing a COVID-19 outbreak. This experience validates the American
98 Testing Guidance for Nursing Homes updated in May 2020.⁴

99 All residents and HCP were tested and there was no selection bias. This study was conducted
100 before any other COVID-19 cases had been detected in the county. The presence of
101 antibodies in residents and HCP is therefore almost certainly linked with the COVID-19
102 outbreak in that NH.

103 In the present study, 16% of residents and one third of HCP with positive RT-PCR were
104 asymptomatic in the 14 days before testing. This confirms that all residents and HCP should
105 be tested if there is a confirmed case of COVID-19, whatever the symptoms.⁴ Two residents
106 and two HCP who tested negative at baseline were tested positive for COVID-19 7 days after
107 baseline. This suggests that a repeated weekly testing of all previously negative residents and
108 HCP until no new COVID-19 cases are identified is also essential in preventing the SARS-
109 CoV-2 spread.⁴

110 Positive RT-PCR was associated with a severe prognosis (death in 32%), especially in men
111 (death in 58%), confirming previous studies.^{1,2} Among the 22 negative RT-PCR residents
112 presenting COVID-19 symptoms, one died and the others recovered completely, suggesting
113 that severe COVID-19 outcomes could be generally, but not always, predicted by positive
114 testing.

115 Testing remained positive for 3 weeks or more in two thirds of the RT-PCR positive residents.
116 One remained positive for 8 weeks, indicating that NHs facing a COVID-19 outbreak should
117 be prepared to maintain prolonged protective measures in residents tested positive for SARS-
118 CoV-2. In accordance with our regional guidelines⁶, this NH was considered to be COVID-
119 19-free when none of the residents and HCP were diagnosed within the 14 days after the last
120 positive result. COVID-19 free NHs apply regional recommended measures to prevent any
121 further COVID entrance and spread. In our Occitanie region, these measures include⁶: 1.
122 Checking that RT-PCR testing in HCP and visitors with COVID-19 symptoms or in those
123 having had contact with COVID-19 suspected or confirmed cases (daily screening) is
124 negative before entering the premises. 2. Checking that RT-PCR testing in all new residents
125 and in all residents having spent more than 24 h outside the NH (especially after
126 hospitalization) is negative before entering. 3. Checking that residents, HCP, and visitors
127 previously tested positive for COVID-19 meet all 3 follow-up NH entrance criteria: (i)
128 resolution of fever (without use of fever-reducing medications) and of other COVID-19
129 symptoms within the past 48 hours; (ii) two consecutive negative RT-PCR results collected
130 ≥ 24 hours apart, (iii) the first control test collected at least 7 days after the positive testing or
131 7 days after the first COVID-19 symptoms. 4. Obliging visitors allowed to enter the NH to
132 sign a charter in which they agree to adhere to standard and transmission-based precautions to
133 prevent COVID-19 spread in the NH (systematic face mask wearing, hand hygiene, and
134 especially social distancing) as well as a registry with contact details to facilitate testing and
135 contact tracing should a new case be diagnosed in the NH. 5. Admission to a private room and
136 14 days of isolation for every new resident and every resident having left the NH for at least
137 24h (especially after hospital stay). 6. Testing of every resident having left the NH for less
138 than 24 hours (especially for medical consultation) 5 to 7 days after a possible contact with
139 COVID-19. 7. Daily screening of all residents for COVID-19 symptoms (including atypical
140 symptoms) and testing if there is any doubt. 8. If regular testing of HCP, visitors, and
141 residents at high risk of encountering COVID-19 subjects outside the NH (health care
142 workers who have a care activity outside the NH, visitors of several NHs, hemodialysed
143 patients, etc...) can be justified in regions with moderate or substantial community
144 transmission, this measure is not recommended in our region in which community
145 transmission is now considered as low.

146 Residents and HCP with positive RT-PCR developed IgG antibodies against the SARS-CoV-
147 2 in 96% and 100%, respectively, suggesting that most frail older adults living in a NH, as
148 well as the HCP, can produce an antibody response against SARS-CoV-2.

149 Two residents (5%) with negative RT-PCR developed antibodies and all had fever or
150 respiratory symptoms consistent with COVID-19 in the 14 days before. This suggests that
151 residents with COVID-19 symptoms should benefit from the same IPC strategy as residents
152 with positive RT-PCR, even if tested negative. Five HCP with negative testing developed
153 antibodies against SARS-CoV-2 (11%) and some of them had no COVID-19 symptoms. This
154 suggests that if specific COVID-19 IPC measures must be implemented in HCP with
155 confirmed or suspected COVID-19, all HCP should wear a facemask, even if asymptomatic
156 and with negative testing.

157

158 **Conclusions and Implications**

159 The present study supports the recent American testing guidance for NHs. It demonstrates that
160 (i) testing all NH residents and HCP as soon as a new case of COVID-19 is diagnosed and (ii)
161 repeating tests in all previously negative subjects once a week until the testing identifies no
162 new COVID-19 cases is effective in detecting asymptomatic COVID-19 residents and HCP.
163 It also shows that (iii) proposing COVID-19 IPC measures in residents and HCP tested
164 positive or with COVID-19 symptoms and (iv) taking precautions in all other HCP should be
165 effective in blocking the dissemination of the virus in NHs facing a COVID-19 outbreak.

166

167 **Conflicts of Interest:** The authors declare no conflicts of interest/Competing interests

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192 **Table 1. Demographic Characteristics, Reported Symptoms at the Time of Initial**
 193 **Testing, and Occurrence of Antibodies against SARS-CoV-2 in Residents**

| Characteristics | SARS CoV-2 Test Results | | |
|--|-------------------------|--------------------|-----------------|
| | Positive (N=38) | Negative (N=41) | <i>P value*</i> |
| Overall | | | |
| Mean age (\pm SD) — yr | 86 (15,5) | 87 (9,8) | 0.95 |
| Length of stay at Facility < 90 days before testing —no. (%) | 4 (10) | 5 (12) | 1.00 |
| Coexisting conditions—no % | | | |
| Any coexisting condition | 38 (100) | 36 (88) | 0.06 |
| Chronic lung disease | 9 (23) | 9 (21) | 0.85 |
| Diabetes | 9 (24) | 3 (7) | 0.04 |
| Cardiovascular disease | 32 (84) | 32(78) | 0.49 |
| Cerebrovascular accident | 10 (26) | 9 (22) | 0.65 |
| Renal disease | 26 (68) | 7 (17) | <0.0001 |
| Received hemodialysis | 0 | 1 (2) | 1.00 |
| Cognitive impairment | | | |
| Moderate | 18 (47) | 20 (49) | 0.90 |
| Severe | 14 (37) | 3 (7) | 0.001 |
| Denutrition | 12 (32) | 14 (34) | 0.80 |
| Obesity | 10 (26) | 9 (22) | 0.65 |
| Symptoms during the past 14 days—no. (%) | | | |
| In symptomatic residents | 32 (84) | 22 (54) | <0.01 |
| At least one typical Covid 19 symptom | 28 (74) | 19 (46) | 0.01 |
| Temperature | 27 (71) | 14 (34) | 0.001 |
| Cough | 14 (37) | 10 (24) | 0.23 |
| Shortness of breath | 24 (63) | 6 (15) | <0.0001 |
| Saturation rate less than 90% | 21 (55) | 5 (12) | <0.0001 |
| Respiratory rate more than 24 | 21 (55) | 4 (10) | <0.0001 |
| Only atypical Covid 19 symptoms | 3 (8) | 3 (7) | 1.0000 |
| Asymptomatic residents | 6 (16) | 19 (46) | <0.01 |
| Deaths | 12 (32) | 1 (2) | <0.0001 |
| Antibodies against SARS CoV-2 | 25 (96) | 2 (5) | <0.0001 |

194
 195 ***P for chi-square test or Fisher's exact test if chi-square was not a valid test for categorical variables, and
 196 Student test for continuous variables.

Assessment of COVID-19 symptoms

3 cases hospitalized for atypical COVID-19 symptoms

COVID-19 diagnosis in the first 3 residents
Implementation of IPC measures in the NH

March 1, 2020

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14

28

April 6

13

April 20, 2020

Nasopharyngeal swab testing repeated every week in all previously negative residents and HCP until testing identified no new cases and in all positive subjects until testing was negative.

Blood testing for antibodies against SARS-CoV-2