Sero-survey on Long-term Care Facility Residents Reveals Increased Risk of Sub-optimal Antibody Response to BNT162B2: Implications for Breakthrough Prevention

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Sero-survey on long-term care facility residents reveals increased risk of sub-optimal antibody response to BNT162B2: implications for breakthrough prevention

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Key words: SARS-CoV-2, Long Term Care Facilities, aging, comorbidities, S-IgG antibodies.

26 **ABSTRACT**

27 **Background:** The impact of coronavirus disease 2019 caused by Severe Acute Respiratory Syndrome
28 Coronavirus 2 on hosts of Long Term Care Facilities (LTCFs) has been dramatic at global scale as aging and
29 comorbidities pose individuals at increased risk of severe disease and death.

30 **Methods:** Aim of this study was to evaluate SARS-CoV-2 S-IgG antibodies titers in 478 residents and 649
31 health care workers of the largest Italian nurse facility two months after the complete vaccination with
32 BNT162B2. Associations among host-related factors and predictors of humoral response were investigated.

33 **Results:** By stratifying levels of humoral responses, we found that 62.1%, 21.6%, 12.1% and 4.2% of hosts has
34 high ($>1,000$ BAU/ml), medium (101-1,000), low (1-100) and null (<1 BAU/mL) S-IgG titers, respectively. Hosts
35 with previous COVID-19 and those with SARS-CoV-2 N-IgG positive serology showed higher level of
36 serological response ($p<0.001$ and $p<0.001$, respectively), while the administration of corticosteroid or cancer
37 diminished all levels of specific antibodies ($p=0.019$ and $p=0.004$). Significant associations were observed for
38 these parameters in those with suboptimal response ($p<0.001$, $p<0.001$, $p=0.028$ and $p=0.005$) and with a
39 null one ($p=0.005$, $p<0.001$ and $p=0.039$). Predictors of an increased risk of null response were advanced age,
40 corticosteroid therapy and diabetes mellitus ($p=0.025$, $p=0.017$ and $p=0.037$). In contrast, previous diagnosis
41 of COVID-19 resulted strongly associated with a reduced risk of null response to vaccination ($p<0.001$).

42 **Conclusions:** SARS-CoV-2 specific antibodies in elderly individuals need to be measured to consider a third
43 dose of vaccine after mass vaccination for prevention of reinfections in LTCFs despite the maintenance of
44 barrier measures.

45 **INTRODUCTION**

46 The coronavirus disease 2019 (COVID-19) pandemic, which started in late 2019 in China, continues to spread
47 worldwide, despite the adoption of personal protective equipment (PPE), subsequent lockdowns, prolonged
48 control measures implemented in most developed countries and unprecedented vaccination campaigns. The
49 impact of COVID-19 on older people living in nursing Long Term Care Facilities (LTCFs) has been particularly
50 devastating at national and international scales [1]. Living in community, the lack of diagnostic tools as well

51 as PPE for hosts and health care workers (HCWs) and the health vulnerabilities of the elderly, all contributed
52 to the spread and lethality of the virus in the setting of Nurse Facilities (NFs). In addition, conditions like
53 frailty, dependence, dementia or high burden of comorbidities are responsible of high incidence of disease
54 susceptibility and mortality. By July 2021, the highest mortality rate among older people (aged >75 years),
55 has reached 48.7% of confirmed cases as reported by New York City Health (Worldometer. Age, sex, existing
56 conditions of COVID-19 cases and deaths ([https://www.worldometers.info/coronavirus/coronavirus-age-](https://www.worldometers.info/coronavirus/coronavirus-age-sex-demographics/)
57 [sex-demographics/](https://www.worldometers.info/coronavirus/coronavirus-age-sex-demographics/) (accessed July 8, 2021). In parallel, Italian data from the Istituto Superiore di Sanità (from
58 February 2020 to May 2021) indicate that the overall mortality rate, defined as number of deaths over the
59 total of residents, was 9.1% (<https://www.epicentro.iss.it/coronavirus/pdf>).
60 Age, concomitant pathologies and immunosenescence are recognized as the main factors that influence the
61 risk of severe morbidity and death. Among these it has been proven that deterioration of both humoral and
62 cellular immune responses and alteration of lymph node architecture play a major role in the failure to
63 contrast pathogens and related morbidity [2]. Indeed, immune responses may be affected both by
64 aforementioned factors and other common events related to senescence, such as the alteration of metabolic
65 processes, blood circulation, gas exchanges and organ function. Lower responses to influenza virus,
66 *Streptococcus pneumoniae* and some Flaviviruses have been demonstrate in elderly compared to younger
67 adults [3-8].
68 For these reasons elderly and hosts of nursing facility, as well as HCWs taking care of them, have been
69 prioritized to be vaccinated as soon as vaccines became available (December 27, 2020).
70 Several reports indicate that vaccination of old age is showing to protect from severe disease, and risk of
71 death by conferring a degree of humoral immunity [9-15].
72 Here, we present data obtained in the largest NH facility in Milan, the Italian city early hit by SARS-CoV-2
73 pandemic. We demonstrate differences between elderly vaccinees over the age of 70 and young vaccinees
74 below 60 years by investigating differences in antibody titers by age, and we identify factors related to
75 humoral responses after the second dose of mRNA BNT162b2 vaccine. Implications of this study may be

76 important to reinforce protective measures in NHs as well as to pose the need of to identify effective
77 vaccination strategies in frail residents, including additional doses and/or switch to different vaccines.

78 **METHODS**

79 **Study population**

80 The study was conducted at the Pio Albergo Trivulzio, the main LTCF in Milan, hosting about 500 aged
81 residents and hiring about 700 HCW. Four hundred and seventy-eight LTCF residents and 649 HCWs were
82 studied. HCWs included nurses, doctors, healthcare technicians, health service assistant, cleaners, laboratory
83 and administrative staff.

84 First dose administration of BNT162b2 vaccine started in the structure on December, 27 and occurred until
85 January, 31. Second dose was administered at 21 days and was completed on February 25.

86 Around two months after the second dose, a blood sample was obtained for routine assessment of laboratory
87 parameters and a 500 µl were stored at -20° for SARS-CoV-2 antibody quantifications.

88 HCWs were vaccine administered and tested in parallel according to an informed consent.

89 Samples were concomitantly screened for SARS-Cov-2 nucleocapsid protein (N-IgG) to capture possible
90 asymptomatic infection or assess the persistence of specific antibodies in previously infected subjects. All
91 data used in this study were previously anonymized as required by the Italian Data Protection Code
92 (Legislative Decree196/2003) and the general authorizations issued by the Data Protection Authority. Ethics
93 Committee approval was deemed unnecessary because, under Italian law, it is only required in the case of
94 prospective clinical trials of medical products for clinical use (Art. 6 and Art. 9 of Legislative Decree 211/2003).

95 All patients gave their written informed consent to the medical procedures/interventions carried out for
96 routine treatment purposes. The study was conducted in compliance with Good Clinical Practice and the
97 declaration of Helsinki.

98 **SARS-CoV-2 antibody assays**

99 We used Elecsys Anti-SARS-CoV-2 S (Roche), an immunoassay for the quantitative determination *in vitro* of
100 total antibodies to the SARS-CoV-2 spike (S) protein receptor binding domain (RBD) in human serum and

101 plasma. The assay cut off is >0.8 BAU/ml reported by manufacturer. Elecsys Anti-SARS-CoV-2 S assay
102 manufacturer reports a sensitivity of 98.8 % (95 % CI: 98.1 – 99.3 %) and a specificity of 95 % (CI: 99.7 –
103 100 %).

104 Response to vaccination in residents was classified as high, medium, low and null response by stratifying the
105 level of anti-S IgG values in 4 levels: >1,000, 101-1,000, 1-100 and <1 BAU/mL, respectively.

106 Elecsys Anti-SARS-CoV-2 (Roche), an immunoassay for the in vitro quantitative determination of antibodies
107 to the SARS-CoV-2 N protein in human serum and plasma was used with a sensitivity of 99.5% (CI: 97.0-100 %)
108 and a specificity of 99.80% (CI: 99.69-99.88).

109 **Statistical analysis**

110 Parametric tests (t test and ANOVA), nonparametric tests (Mann–Whitney and Kruskal–Wallis) and the
111 Pearson χ^2 test (or Fisher exact test, when necessary) were used to compare normally distributed, non-
112 normally distributed continuous, and categorical variables of patients, respectively. The primary endpoint
113 was the risk of null response to vaccine, evaluated by means of a logistic regression model, also correcting
114 for gender, age, comorbidities and immune modulatory treatments. Also, previous diagnosis of COVID-19
115 and positive anti-nucleocapsid serology were included as correlates in the analysis in two different models,
116 due to their strong reciprocal association. We evaluated their combined effect over the risk of null response
117 to vaccination stratifying the population based on previous clinical and serological evidence of SARS-CoV-2
118 exposure.

119 **RESULTS**

120 **Participant characteristics**

121 **Hosts**

122 The main demographic and clinical characteristics of 478 analyzed LTCF subjects are shown in Table 1. The
123 majority of residents were females (81%) with an age higher than 80 years old (n=345, 72.2%). SARS-COV-2
124 anti-nucleocapsid antibodies determination was available for 455 subjects and resulted positive in 268 cases

125 (58.9%). Among these, 143 hosts (53.4%) did not show clinical signs of infection in the past, while 7 patients
126 with documented clinical COVID-19 resulted negative for serology (7/187, 3.7%).

127 A large majority (n=413, 86.4%) of residents presented at least one morbidity, being affected by dementia,
128 the most common syndrome, in 58.6% of cases. Almost all hosts received polytherapies for chronic diseases
129 (hypertension, heart disease, lung disease, diabetes and cancer). Anticoagulant or corticosteroid therapy
130 resulted administered in 114/478 (23.8%) and 19/478 (4.0%), respectively.

131 **HCWs**

132 Among the 649 HCWs, the majority of subjects were females (n=464, 71.5%) with a median age of 49 years
133 (IQR: 34-55). In detail, the age classes were as follow: 15.1% (n=98), 18.2% (n=118), 21.6% (n=140), 36.8%
134 (n=239) and 8.3% (n=54) for ≥ 30 , 31-40, 41-50, 51-60 and >60 years, respectively. About one third of subjects
135 (27.3%, n=113) presented at least one comorbidity, while 14 presented two of them. HCWs with a previous
136 exposure to SARS-CoV-2 were 124 (19.1%) as detected by nasopharyngeal swab (data not shown).

137 **Vaccine-associated side effects**

138 No major vaccine associated side effects occurred either in residents or in HCWs. Minor effects such as site
139 of injection pain, fatigue, malaise, headache, nausea or skin rash, muscle and joint pain, fever were reported
140 in about 10% and 16% of individuals, respectively.

141 **Serological response to vaccine**

142 **Hosts**

143 Overall, we detected anti-S-IgG antibodies in 95.8% of hosts receiving two doses of BNT162b2 vaccine.
144 According to level of response, high, medium and low titers were present in 62.1% (n=297), 21.6% (n=103)
145 and 12.1% (n=58) of cases, respectively.

146 Median level of anti-S IgG of 7.500, corresponding to the upper limit of quantification of the assay (IQR:
147 848- >7.500 BAU/mL) after a median time of 64 days from the second dose (IQR 63-65 days).

148 We first investigated the associations among main epidemiological and clinical characteristics and levels of
149 response to vaccination. The results are reported in Table 2.

150 A weak association for null response was observed for female compared to male sex (4.9% vs. 1.1%, $p=0.050$)
151 and diabetes (10.4% vs. 3% $p=0.052$). A significantly higher response was detected for host with previous
152 COVID-19 and for those with SARS-CoV-2 N-IgG serology considering all level of serological response ($p<0.001$
153 and $p<0.001$). In contrast, the administration of corticosteroid diminished all levels of specific antibodies
154 ($p=0.019$). Significant associations were observed for these parameters in those with suboptimal response
155 ($p<0.001$, $p<0.001$ and $p=0.028$) and with a null one ($p=0.005$, $p<0.001$ and $p=0.039$).
156 Among subjects with a previous COVID-19 clinical diagnosis, we did not find any case of null response to
157 vaccine, either in those with positive or negative nucleocapsid serology (0/125 and 0/7, respectively).
158 Differently, among hosts without a documented previous diagnosis of COVID-19, null response to vaccine
159 was lower in those with positive nucleocapsid serology when compared to subjects with negative serology:
160 0.7% (1/143) vs. 10.6% (19/180), respectively ($p<0.001$) (data not shown).

161 LTCF residents with neoplastic disease showed a significant difference in the distribution of antibody
162 response considering all levels ($p=0.004$) and suboptimal response ($p=0.005$) but not null response.

163 **HCWs**

164 Regarding the response to vaccination, 66.1% (n=429) of subjects showed high titers and 33% (n=214)
165 medium titers. A suboptimal response was observed in 6 subjects (0.9%), of whom 2 were null responder.
166 The median level of anti-S IgG in HCW was 1.789 (IQR: 754->7.500), markedly lower compared to hosts,
167 according to the lower percentage of previously infection in these subjects. A significantly different
168 distribution of response was detected for age classes both considering all titer strata ($p<0.001$) and null
169 response ($p=0.040$). Null responders were present only in subjects with more than 60 years (n=2, 3.7%). A
170 significantly different distribution of response was present for previous COVID-19 only considering all strata
171 of antibody titers ($p<0.001$), as the only two non-responders did not experience COVID-19 (data not shown).

172 **Predictors of responses in LTCF hosts and HCWs**

173 We then studied predictors of null response to SARS-CoV-2 vaccination by univariate and multivariate logistic
174 regression analysis. Firstly, the advanced age resulted strongly associated with an increased risk of null

175 response ($p=0.005$ and $p=0.025$ in univariate and multivariate analysis, respectively). In addition,
176 corticosteroid therapy resulted associated with no anti-spike antibody titers in both analyses ($p=0.17$ and
177 $p=0.042$). Diabetes mellitus resulted significantly associated with a higher risk of null response only in the
178 multivariate analysis ($p=0.037$).

179 Further, previous diagnosis of COVID-19 resulted strongly associated with a reduced risk of null response to
180 vaccination ($p<0.001$). No association was observed for cancer and female sex either in the univariate or
181 multivariate analyses.

182 When evaluating positive anti-nucleocapsid serology instead of COVID-19 clinical diagnosis, the former
183 resulted associated with a lower risk of null response to vaccine, both in the univariate (OR 0.035, 95% CI:
184 0.01-0.26) and in the multivariate analysis (OR 0.051, 95% CI 0.01-0.42), with no impact on significance of
185 other covariates (data not shown).

186 As for HCW univariate and multivariate analyses did not show any factor associated with null response to
187 vaccination (data not shown).

188 **DISCUSSION**

189 Surveys are of great importance to define the serological effects to COVID19 vaccine in real world population,
190 particularly in fragile individuals. In general, quantification of the antibody response to SARS-CoV-2
191 vaccination is highly relevant for identifying possible vaccine failure (i.e the risk of breakthrough infection)
192 and estimating level and time of protection. However, thresholds for positivity and cut off values provided
193 by different assay manufacturers differ and their diagnostic value is not yet established and standardized at
194 present. Although total anti-spike titers may be not indicative of sufficient inhibitory capacities, vaccination-
195 induced antibody titers may be used as surrogate marker from which a protection correlate could be
196 estimated [16, 17].

197 Several papers addressed the efficacy of different SARS-CoV-2 vaccines either through Phase II and III of
198 clinical trials [18-20] or field investigations [9-11]. Few of them detailed data regarding elderly and persons
199 living in nurse facility [12-15] and outbreaks after the first and second dose were reported [21-23]. At

200 present, cohorts <16 years or >80 years who might show reduced vaccine reactivity are limited. We report
201 a large sero-survey in residents of the largest LTCF of Italy where SARS-CoV-2 could spread because of late
202 warning and lack of PPE and diagnostic tools. Our data indicate that full vaccination either in LTCF hosts and
203 HCWs elicits a humoral response in above 96% of individuals accordingly with published papers.
204 Nevertheless, while the majority of both elderly vaccinees and HCWs raised high responses after their second
205 vaccination dose, a highest percentage of hosts showed a lower or null response when compared to HCW
206 (14.2% vs. 0.9%). The main differences between the two groups of vaccinated individuals are likely a
207 consequence of immunosenescence, which describes the phenomenon of reduced adaptive immune
208 responses in hosts. Previous data reported that titers of S-IgG antibodies are significantly lower in elderly
209 persons [18]. Accordingly, our regression analysis in LTCF residents indicates that aging is strongly associated
210 with an increased risk of null response.

211 Noteworthy, our findings suggest that comorbidities and their treatment may impact humoral responses as
212 detected by several significant associations, even though only diabetes and corticosteroid therapy confer an
213 increased risk of unresponsiveness. Limited numbers of LTCF hosts with other morbidities such cancer and
214 diseases of the immune system prevent us to detect other associations impacting antibody response. To our
215 knowledge no similar data are yet available in elderly persons.

216 Our study population includes older adults living in assisted structures and their care providers, with or
217 without a history of natural infection with SARS-CoV-2. As already reported, individuals having a history of
218 natural infection or positive serology have higher antibody levels and an enhanced response to vaccination,
219 even after a single dose [24]. Indeed, in our case-file both prevalence of diagnosed COVID-19 and median
220 titers of S-IgG were higher in hosts compared to HCWs (56% vs. 19.1% and 7.500 vs. 1.789 BAU/mL,
221 respectively). Consequently, both N-IgG positive results and previous COVID-19 resulted predictive factors of
222 positive response to vaccination.

223 Although serological assays may still need to be standardized, compared and interpreted in the light of large
224 population results, they allow to preliminarily evaluate levels of protection conferred by SARS-CoV-2

225 vaccines. As demonstrated for other vaccine campaigns, vaccination of old individuals often fails to induce
226 high titers of antibodies or fully protective immunity as quality and quantity of antibody titers may be
227 markedly inferior in elderly compared to adults [2-8, 13, 25].

228 The major limitation of our study is that we measured spike (S) protein RBD antibodies, stratifying the level
229 of response in high, medium, inadequate and null instead of evaluating neutralizing antibodies that are
230 considered the better correlate of protection. Further differences in humoral response may be underscored
231 in our study as a high percentage of values are above the upper limit of the assay quantification. We could
232 not address this point by dilution experiments because of the large number of studied subjects. In addition,
233 we measured S-IgG antibodies around two months after the vaccine administration. It is conceivable that
234 antibodies titers could be above the ELISA dynamic range. Future studies to monitor antibody levels will
235 clarify the dynamic of antibody mount and decay.

236 Our considerations are based on the hypothesis anti-SARS-CoV-2 antibodies are the major correlate of
237 protection. Indeed, immunity is a complex phenomenon where both humoral and cellular responses are
238 interdependent involving both innate and adaptive immunity. Further studies will be essential to understand
239 type and function of antibodies produced after vaccination, the neutralizing capacity of the antibodies along
240 with the persistence of their protective effects. Therefore, information regarding S-IgG levels are as much
241 crucial as the identification of SARS-CoV-2 emerging variants that may elude protection conferred by
242 vaccines. Although the effectiveness of mRNA vaccines may be inferred by screening methods based on
243 sources of population-based data, we believe that accurate results from standardized assays are essential at
244 individual level to protect elderly hosts from SARS-CoV-2 reinfection [26].

245 Old subjects who have been heavily hit by the SARS-CoV-2 pandemic need to be protected through general
246 prevention actions and specific measures that include early vaccine administration and testing of their effects
247 on humoral responses. Furthermore, as demonstrated in individuals with solid organ transplantation [27], a
248 3rd dose of homologous vaccine needs to be administered in unresponsive populations.

249 **ABBREVIATIONS**

250 **LTCFs:** Long Term Care Facilities

251 **COVID-19:** Coronavirus disease 2019

252 **PPE:** Protective Equipment

253 **HCWs:** Health Care Workers

254 **NFs:** Nurse Facilities

255 **S:** Spike protein

256 **RBD:** Receptor Binding Domain

257 **N:** Nucleocapsid protein

258 **IQR:** Inter-Quartile Range

259 **COPD:** Chronic Obstructive Pulmonary Disease

260 **CI:** Confidence Interval

261 **OR:** Odd Ratio

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264 **AUTHORS' CONTRIBUTIONS**

265 BC, RV, AG, PLR, MD, FP and GC collected the serological and clinical data. MF performed the statistical
266 analysis. AL and CB wrote the first version of the article. All the authors contributed to the final version of
267 the manuscript.

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269 No external funding was received.

270 **AVAILABILITY OF DATA AND MATERIALS**

271 All data generated or analysed during this study are included in this published article and its supplementary
272 information files.

273 **DECLARATIONS**

274 **Ethics approval and consent to participate**

275 All data used in this study were previously anonymized as required by the Italian Data Protection Code
276 (Legislative Decree196/2003) and the general authorizations issued by the Data Protection Authority. Ethics
277 Committee approval was deemed unnecessary because, under Italian law, it is only required in the case of
278 prospective clinical trials of medical products for clinical use (Art. 6 and Art. 9 of Legislative Decree 211/2003).
279 All patients gave their written informed consent to the medical procedures/interventions carried out for
280 routine treatment purposes. The study was conducted in compliance with Good Clinical Practice and the
281 declaration of Helsinki.

282 **Consent for publication**

283 Not applicable.

284 **Competing interests**

285 The authors declare that they have no competing interests.

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371 **Table 1.** Characteristics of 478 subjects undergoing to SARS-CoV-2 vaccination in a long-term care
372 facility. Categorical variables are expressed as % (N), continuous variables as median value (Inter-
373 quartile range).

	n (%)
Gender, female	81.0 (387)
Age, years (IQR)	87 (82-92)
Age distribution	
<70 years	5.0 (24)
70-80 years	11.1 (53)
80-90 years	47.5 (227)
>90 years	36.4 (174)
Previous Covid-19	29.7 (142)
Diabetes	15.5 (74)
Cancer	4.8 (23)
Malnutrition	15.5 (74)
Heart Disease	4.0 (19)
COPD ^a	13.4 (64)
Cerebral stroke	15.7 (75)
Dementia	58.6 (280)
Autoimmune disease	1.0 (5)
Gastrointestinal/Liver Disease	1.3 (6)
Chronic kidney disease	1.7 (8)
Anemia	5.6 (27)
Immunosuppressive therapy	0.6 (3)
Anticoagulant therapy	23.8 (114)
O2 therapy	4.8 (23)
Corticosteroid therapy	4.0 (19)
Previous positive anti-nucleocapsid serology	58.9 (268/455)
Anti-spike antibodies median titre (IQR)	>7500 (848-7500)

374 ^aChronic obstructive pulmonary disease

375 **Table 2.** Response to SARS-CoV-2 vaccination among 478 patients living in a long-term care facility, according to the main epidemiological and clinical characteristics showing
376 significant associations and differences among groups. Pearson χ^2 test was used to compare categorical variables of patients in the study groups.

		Grade of response to SARS-CoV-2 vaccine, % (n)				Comparison of response distribution, p-value		
		High response n=297	Medium response n=103	Low response n=58	Null response n=20	Overall*	Suboptimal response**	Null response***
Gender	Females	61.7 (239)	22.5 (87)	10.9 (42)	4.9 (19)	ns	ns	0.050
	Males	63.7 (58)	17.6 (16)	17.6 (16)	1.1 (1)			
Age groups, years	<70	58.3 (14)	29.2 (7)	8.3 (2)	4.2 (1)	ns	ns	0.061
	70-80	62.3 (33)	20.8 (11)	113.2 (7)	3.8 (2)			
	80-90	63.4 (144)	50.0 (22)	11.9 (27)	2.6 (6)			
	>90	60.9 (106)	20.1 (35)	12.6 (22)	6.3 (11)			
Previous Covid-19	No	49.1 (165)	28.9 (97)	16.1 (54)	5.9 (20)	<0.001	<0.001	0.005
	Yes	92.9 (132)	4.2 (6)	2.8 (4)	0.0 (0)			
Anti-Nucleocapsid serology	Neg	17.1 (32)	47.6 (89)	25.1 (47)	10.2 (19)	<0.001	<0.001	<0.001
	Pos	98.1 (263)	1.1 (3)	0.4 (1)	0.4 (1)			
Diabetes	No	64.1 (259)	20.9 (85)	12.0 (48)	3.0 (12)	0.077	ns	0.052
	Yes	51.9 (38)	24.7 (18)	13.0 (10)	10.4 (8)			
Cancer	No	63.9 (291)	21.1 (96)	11.0 (50)	4.0 (18)	0.004	0.005	ns
	Yes	29.2 (7)	29.2 (7)	33.3 (8)	8.3 (2)			
Corticosteroid therapy	No	63.2 (290)	21.3 (98)	12.0 (55)	3.5 (16)	0.019	0.028	0.039
	Yes	36.8 (7)	26.3 (5)	15.8 (3)	21.0 (4)			

377 * Overall p-value: comparison between all the response groups

378 ** Suboptimal response p-value: comparison of low-null response vs. medium-high response

379 *** Null response p-value: comparison of null response vs. all the other responses grouped together

Table 3. Logistic regression model evaluating the risk of null response to SARS-CoV-2 vaccination among 478 patients living in a long-term care facility.

	Univariate analysis			Multivariate analysis		
	p	OR ^a	95% CI ^b	p	OR	95% CI
Age, per 10 year higher	0.005	2.988	1.40-6.39	0.025	2.630	1.13-6.14
Gender, females vs. males	0.123	4.905	0.65-37.0	0.292	3.103	0.38-25.50
Previous Covid-19	0.000	0.103	0.01-0.12	0.000	0.126	0.02-0.23
Diabetes mellitus	0.060	2.613	0.96-7.11	0.037	3.415	1.08-10.8
Cancer	0.936	1.088	0.14-8.53	0.377	0.357	0.04-3.51
Corticosteroid therapy	0.017	3.246	1.23-8.54	0.042	4.964	1.06-23.52

^a Confidence interval

^b Odd ratio