Humoral and cellular immunogenicity of the BNT162b2 mRNA Covid-19 Vaccine in nursing home residents

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Dear Editor,

We read with interest the communication by Capetti et al.[1] Nursing home residents are particularly vulnerable to Covid-19 as a result of advanced age, frailty and presence of chronic medical conditions, and have been reported to account for 56% of all Covid-19 related deaths in Belgium.[2] Vaccines are known to be less immunogenic in nursing home residents, but the response to the severe acute respiratory syndrome coronavirus (SARS-CoV-2) vaccines has not been characterized in this population.[3] We therefore sought to determine the immunogenicity of the BNT162b2 mRNA Covid-19 Vaccine in nursing home residents in comparison to COVID-19-naïve healthcare workers four weeks after the first vaccine dose.

One-hundred consecutive residents from 2 Belgian long-term care facilities were studied after vaccination with 2 doses, administered with a 3-week interval. This study was approved by the local institutional review board, and written informed consent was obtained. We determined both humoral (antibodies against the receptor binding domain of S1 subunit of the spike protein, CMIA on Architect-I System from Abbott) and cellular (QuantiFERON SARS-CoV-2 Antigen 2, Qiagen) responses, as current evidence indicates that the immunological correlate of protective immunity requires a balance between neutralizing anti-S antibodies and Th1 responses.[4] COVID-19-experienced and COVID-19-naïve residents were segregated by presence (n=64) or absence (n=46) of antibodies against SARS-CoV-2 nucleocapsid (CMIA on Architect-I System from Abbott), based on the observations by Capetti et al.[1] Fifteen consecutive healthcare workers without spike antibodies before

vaccination were used as controls. Statistical testing was performed with the Kruskal-Wallis test followed by Dunn's multiple comparisons tests for continuous variables and Fisher's Exact tests for categorical variables.

The nursing home residents had a mean age of 86 years (range 56-109), were 71% female and 100% white. The median activities of daily living score according to a 6-item evaluation scale (Katz) was 17 on 24 (range 9-24), and 20% had mild and 38% had moderate or severe cognitive impairment (based on the mini-mental state examination score). Major comorbidities are available in Supplementary Table S1. Four weeks after the first vaccine dose medians of the antibody titers were 32226 AU/ml in COVID-19-experienced and 1762 AU/ml in COVID-19-naïve residents versus 8476 AU/ml in COVID-19-naïve healthcare workers (figure 1, panel A). Using a 1050 AU/ml cut-off, corresponding to a PRNT dilution of 1:80, an antibody response could be documented in 97% of COVID-19-experienced residents, 61% of COVID-19-naïve residents and 93% of COVID-19-naïve healthcare workers ($p < 0.001$). Medians of the interferon gamma responses were 0.89 IU/ml in COVID-19-experienced and 0.13 IU/ml in COVID-19-naïve residents versus 1.18 IU/ml in the COVID-19-naïve healthcare workers (figure 1, panel B). Using a cut-off of 0.15 IU/ml, a cellular response could be documented in 97% of COVID-19-experienced residents, 48% of COVID-19-naïve residents and 87% of COVID-19-naïve healthcare workers ($p < 0.001$). A combined humoral and cellular response was found in 97% of COVID-19-experienced residents, 37% of COVID-19-naïve residents and 87% of COVID-19-naïve healthcare workers (figure 1, panel C; $p < 0.001$).

Four weeks after the first vaccine dose, the humoral and cellular immunogenicity of the BNT162b2 mRNA vaccine was suboptimal in COVID-19-naïve nursing home

residents in comparison to COVID-19-naïve healthcare workers. Longitudinal studies are required to determine whether these differences are the result of a delayed or a quantitatively lower immune response and will be informative to tailor the optimal vaccination strategy in this vulnerable population.

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Disclosures

The authors declare no conflict of interest.

References

1. Capetti AF, Stangalini CA, Borgonovo F, et al. Impressive boosting of anti-S1/S2 IgG production in COVID-19-experienced patients after the first shot of the BNT162b2 mRNA COVID-19 Vaccine. Clin Infect Dis **2021**.
2. Sciensano. Surveillance in residential care centers. https://covid-19.sciensano.be/sites/default/files/Covid19/COVID-19_Surveillance_WZC.pdf. Accessed March 27, 2021.
3. Rolland Y, Cesari M, Morley JE, Merchant R, Vellas B. Editorial: COVID19 Vaccination in Frail People. Lots of Hope and Some Questions. J Nutr Health Aging **2021**; 25(2): 146-7.
4. Poland GA, Ovsyannikova IG, Kennedy RB. SARS-CoV-2 immunity: review and applications to phase 3 vaccine candidates. Lancet **2020**; 396(10262): 1595-606.

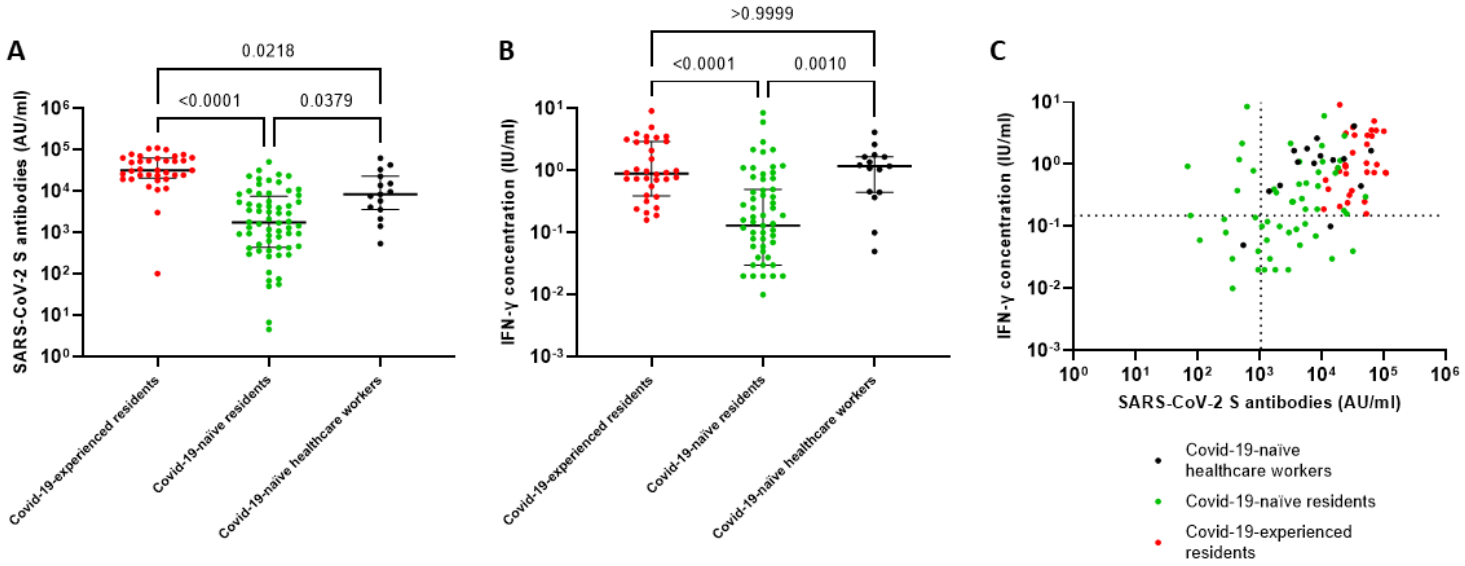
Figure 1 Legend

Panel A shows the quantitative SARS-CoV-2 spike antibody titers (assessed by means of CMLI and expressed as AU/ml) in 100 nursing home residents and 15 seronegative healthcare workers 4 weeks after the first of two doses of BNT162b2 mRNA Covid-19. Medians with interquartile ranges are shown.

Panel B shows the QuantiFERON response (assessed by means of ELISA and expressed as IU/ml) in 100 nursing home residents and 15 seronegative healthcare workers 4 weeks after the first of two doses of BNT162b2 mRNA Covid-19. Medians with interquartile ranges are shown.

Panel C shows the correlation between the QuantiFERON response and quantitative SARS-CoV-2 spike antibody titers. The dotted lines correspond to the cut-offs of 0.15 IU/ml and 1050 AU/ml respectively.

Figure 1


A
0.0218
<0.0001
0.0379
SARS-CoV-2 S antibodies (AU/ml)
Covid-19-experienced residents
Covid-19-naïve residents
Covid-19-naïve healthcare workers
B
>0.9999
<0.0001
0.0010
IFN-γ concentration (IU/ml)
Covid-19-experienced residents
Covid-19-naïve residents
Covid-19-naïve healthcare workers
C
IFN-γ concentration (IU/ml)
SARS-CoV-2 S antibodies (AU/ml)
Covid-19-naïve healthcare workers
Covid-19-naïve residents
Covid-19-experienced residents