



FULL LENGTH ARTICLE

Weakened humoral and cellular immune response to the inactivated COVID-19 vaccines in Chinese individuals with obesity/overweight

Qian Zhu^{a,1}, Yingzhi Zhang^{a,1}, Juan Kang^{a,1}, Zhiwei Chen^a,
Mingli Peng^a, Min Chen^a, Gaoli Zhang^a, Dejuan Xiang^a,
Shuang Xiao^a, Hu Li^a, Ying Mei^b, Jie Yang^b, Xiaoya Qi^b,
Dachuan Cai^{a,**}, Hong Ren^{a,*}

^a Department of Infectious Diseases, Key Laboratory of Molecular Biology for Infectious Diseases (Ministry of Education), Institute for Viral Hepatitis, The Second Affiliated Hospital, Chongqing Medical University, Chongqing 400061, China

^b Health Management Center, The Second Affiliated Hospital of Chongqing Medical University, Chongqing 400061, China

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Abstract Inactivated COVID-19 vaccines have been widely used to vaccinate the Chinese population. However, limited literature exists to explore the effect of obesity on the humoral and cellular immune response to these vaccines. In this study, 132 high BMI (Body mass index) (obesity and overweight, BMI ≥ 24 kg/m²) and 82 normal BMI (BMI < 24 kg/m²) participants were enrolled. Adverse events (AEs), Spike receptor-binding domain IgG antibody (anti-RBD-IgG), neutralizing antibodies (NAbs), and specific B-cell and T-cell responses were evaluated 21–105 days after full-course inactivated COVID-19 vaccination. The overall incidence of AEs was similar in individuals with and without obesity/overweight. No serious vaccine-related AEs occurred. Individuals with obesity/overweight had a reduced seropositivity rate of NAbs compared to those with normal BMI. Anti-RBD-IgG and NAbs titers in the high BMI group were significantly lower than those in the normal BMI group. The frequencies of RBD-specific

* Corresponding author. No. 288, Tianwen Avenue, Chayuan, Nan'an District, Chongqing 401336, China.

** Corresponding author.

E-mail addresses: cqmuCDC@cqmu.edu.cn (D. Cai), renhong0531@cqmu.edu.cn (H. Ren).

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¹ These authors have contributed equally to this work.

memory B cells (MBCs) and the numbers of spike-specific TNF- α + spot-forming cells (SFCs) in individuals with obesity/overweight were reduced compared with those noted in individuals without obesity/overweight. A similar trend of weakened humoral responses was also observed in individuals with central obesity. Our study results suggested that inactivated COVID-19 vaccines were safe and well tolerated but induced poor humoral and cellular immune responses in Chinese individuals with obesity/overweight.

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Introduction

The pandemic of coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is causing severe health problems and economic burdens worldwide. Obesity has been reported as a risk factor for a more severe course and outcomes of COVID-19, such as increased rates of hospitalization, ICU admission, and mortality.^{1,2} This evidence suggests that individuals with obesity should be prioritized for COVID-19 vaccination. According to the emerging clinical data, three FDA-approved SARS-CoV-2 vaccines (Pfizer-BioNTech, Moderna, and Johnson & Johnson) are widely used in the obese population in the USA and some European countries.³

Inactivated COVID-19 vaccines (BBIBP-CorV, CoronaVac) have been widely used to vaccinate the Chinese population in China mainland. However, limited literature exists to explore the effect of obesity on the safety and immune response of these vaccines. A study evaluated the effectiveness of these vaccines and found that obesity might be a risk factor for decreased antibody titers.⁴ To the best of our knowledge, past studies have demonstrated associations between obesity and impaired immune responses to influenza, hepatitis B, tetanus, and rabies vaccines.^{5–8} Therefore, related data about inactivated COVID-19 vaccines for Chinese people with obesity are needed and encouraged, especially targeted studies on different obesity subtypes or different patterns of body fat distribution.³

The purpose of this study was to evaluate the safety profile and provide new insights into inactivated COVID-19 vaccine-induced humoral and cellular immune responses in Chinese individuals with obesity/overweight.

Material and methods

Human subjects and clinical samples

This study was approved by the Ethics Committee of the Second Affiliated Hospital of Chongqing Medical University and conformed with the ethical guidelines of the Declaration of Helsinki. In this study, 132 individuals with obesity/overweight and 82 individuals with normal BMI were enrolled between August 16, 2021 and October 14, 2021. According to the Chinese BMI classification criteria recommended in the expert consensus on body weight

management among patients with overweight or obesity (2021),⁹ obesity is defined as BMI ≥ 28 kg/m², and overweight is defined as 24 kg/m² $\leq$ BMI < 28 kg/m². Normal BMI was defined as BMI < 24 kg/m². Central obesity is defined as a waist circumference ≥ 90 cm for men or > 85 cm for women. All enrolled human subjects met the following inclusion criteria: (i) age above 18 years; (ii) completed full-course vaccination with BBIBP-CorV/CoronaVac for more than 21 days. The exclusion criteria included (i) individuals with a history of SARS-CoV-2 infection or a history of contact with a confirmed or suspected COVID-19 patient; (ii) coinfection with hepatitis B virus, hepatitis C virus, and HIV; (iii) a history of malignant tumor, renal failure, and other immune diseases; (iv) undergoing any immunosuppressant treatment; and (v) pregnancy. All human subjects were recruited from the health management center of the Second Affiliated Hospital of Chongqing Medical University. All human subjects provided signed informed consent before enrollment. This study has been registered at ClinicalTrials.gov (NCT05043272), and the follow-up is ongoing.

Data collection

Demographic information and clinical data of participants were obtained by electronic medical records. Vaccine type, vaccination time, and adverse events within 7 days or 30 days were all recorded by questionnaires. We defined 21–45 days after the second dose as 1 month, 46–75 days as 2 months, and 76–105 days as 3 months in the study. Adverse events included local adverse events (pain, swelling, itch, induration, and redness) and systemic adverse events (fatigue, dizziness, somnolence, cough, fever, diarrhea, laryngeal pain, muscle pain, rhinorrhea, nausea, chest distress, chest pain, abdominal pain, chills, constipation, elevated blood pressure, headache, inappetence, palpitation, pruritus, and rash). All participants' peripheral blood samples were collected 21–105 days after full-course COVID-19 vaccination for laboratory tests. The study design was summarized in Fig. 1.

Evaluation of spike protein receptor-binding domain IgG antibody

Indirect ELISA was used to detect IgG-binding antibodies against the RBD antigen of SARS-CoV-2 (Sino Biological, Beijing, China) (Supplementary Methods). The detection limit for the anti-RBD-IgG antibody test was 1:50 for the

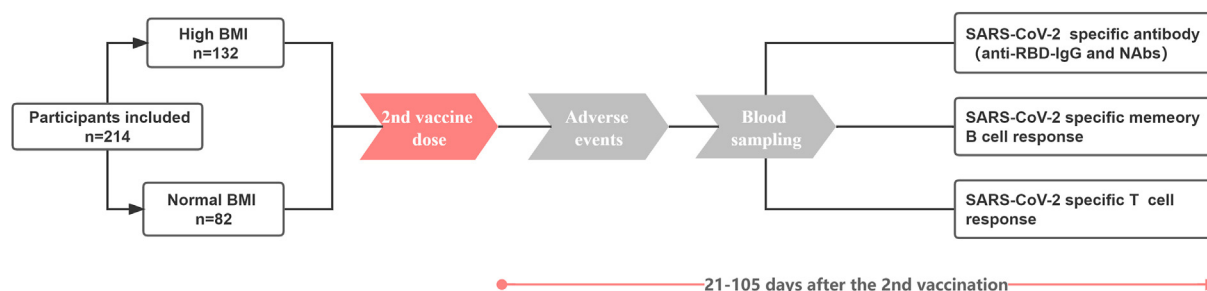


Figure 1 The flowchart of the study design.

inactivated COVID-19 vaccine. Seropositivity was defined as anti-RBD-IgG antibody titers greater than 1:50. Undetectable antibody titers in plasma were assigned values of 1:25 for calculation.

Evaluation of neutralizing antibody (RBD-ACE2 blocking antibody)

The neutralizing antibody was assayed by competitive ELISA (Sino Biological, Beijing, China) ([Supplementary Methods](#)). The detection limit for the neutralizing antibody test was 1:5 for the inactivated COVID-19 vaccine. Neutralizing antibody titers $\geq 1:5$ were considered to indicate seropositivity. Undetectable antibody titers in plasma were assigned values of 1:2.5 for calculation.

Detection of SARS-CoV-2-specific B cells and regulatory T cells by flow cytometry

According to the manufacturer's instructions, peripheral blood mononuclear cells (PBMCs) were isolated from heparinized whole blood and stained for 30 min at 4 °C using an antigen probe and conjugated antibodies ([Supplementary Methods](#)). Samples were evaluated by flow cytometry (Beckman Coulter, CytoFLEX) and analyzed by FlowJo (Treestar, 10.0.7r2).

Detection of spike-specific IFN- γ and TNF- α by FluoroSpot assay

Enumeration of cells secreting IFN- γ and tumor necrosis factor- α (TNF- α) against SARS-CoV-2 spike protein was conducted using a FluoroSpot kit (FSP-0109-2/FSP-0109-10, Mabtech, Sweden) according to the manufacturer's instructions ([Supplementary methods](#)). Plates were analyzed using an automated FluoroSpot reader (Elispot Reader, AID, Germany).

Statistical analysis

The Chi-square test and Fisher's exact test were used for categorical variables. The Mann-Whitney *U* test and Kruskal-Wallis test were used to compare two groups and multiple groups for continuous variables, respectively. All results of multiple comparisons were corrected using Bonferroni's correction. Geometric mean titers (GMTs) and their corresponding 95% confidential intervals (CIs) were

calculated based on the standard normal distribution of the log-transformed antibody titers. A two-sided *P* value < 0.05 was considered statistically significant. SPSS (IBM, 22.0.0) was used for statistical analysis. GraphPad Prism (GraphPad Software Inc., 8.0.0) was used for plotting.

Results

Characteristics of all participants

A total of 132 individuals with high BMI (obesity or overweight) and 82 individuals with normal BMI were enrolled in this study. Participants ranged in age from 18 to 75 years. As shown in [Table S1](#), 56.1% and 42.7% of males were in the high BMI group and normal BMI group, respectively. The age and sex distribution in the two groups were comparable (age, *P* = 0.603; sex, *P* = 0.057) ([Table S1](#)). No significant difference in the interval time (1, 2, and 3 months) from the second dose vaccination to sample collection was noted between the two groups (*P* = 0.482) ([Table S1](#)).

Adverse events of inactivated COVID-19 vaccines in all participants

The inactivated vaccines were well tolerated, and none of the participants had serious adverse events (grade 3 and 4 adverse events). Nineteen (13.9%) of 132 participants in the high BMI group and 12 (14.6%) of 82 participants in the normal BMI group had at least one adverse event within 7 days of receiving inactivated vaccines with no significant difference noted between groups ([Table S2](#)). All adverse events were mild (grade 1 or 2 adverse events). In participants with high BMI, the most common local adverse events were injection-site pain (7.3%) and injection-site swelling (3.6%), whereas the most common systemic adverse events were fatigue (1.4%) and dizziness (1.4%). When the observation was prolonged to 30 days, no new adverse events occurred ([Table S2](#)).

Specific antibody responses to inactivated COVID-19 vaccines in individuals with obesity/overweight

Overall, the seropositivity rate of anti-RBD-IgG was high in both groups, with 96.7% in the high BMI group and 98.8% in the normal BMI group ([Fig. 2A](#), left panel). However, GMTs of anti-RBD-IgG were significantly lower in the high BMI group compared with the normal BMI group [209.7 (95%CI

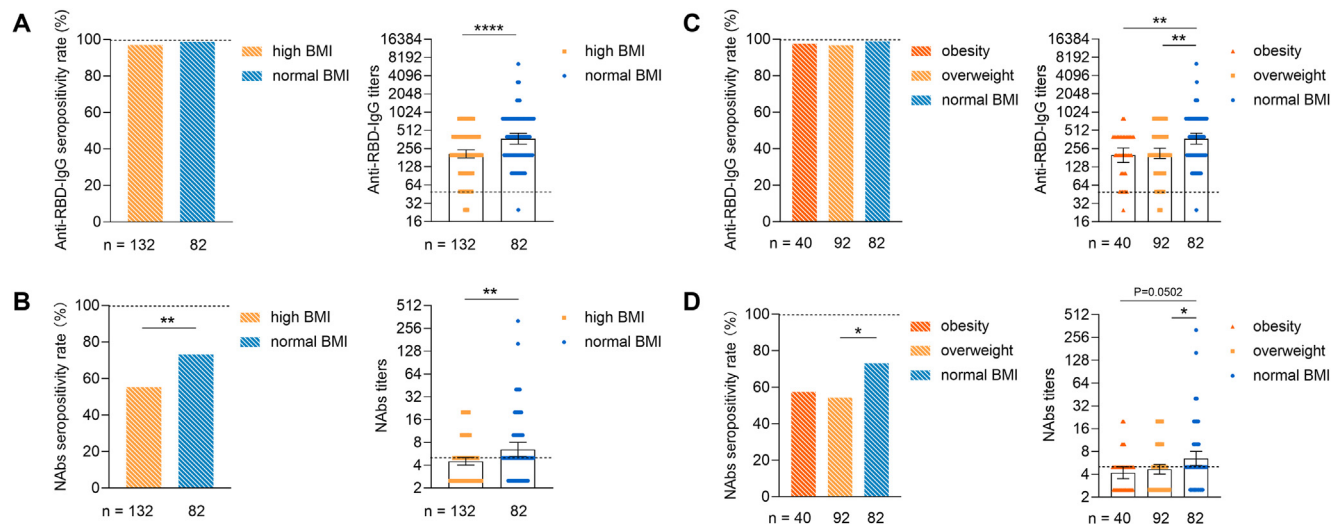


Figure 2 Antibody responses to inactivated COVID-19 vaccines in obesity and overweight individuals. (A, B) The seropositivity rate and antibody titers of anti-RBD-IgG (A) and NAbS (B) in individuals with high BMI and normal BMI. (C, D) The seropositivity rate and antibody titers of anti-RBD-IgG (C) and NAbS (D) in individuals with obesity, overweight and normal BMI. The error bars in antibody titers indicate the 95%CI of the GMTs. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$. High BMI, BMI ≥ 24 kg/m²; normal BMI, BMI < 24 kg/m². CI, confidential interval; anti-RBD-IgG, spike receptor-binding domain IgG antibody; GMTs, geometric mean titers; NAbS, neutralizing antibodies.

179.0–245.6) vs. 373.8 (303.6–460.3), $P < 0.001$] (Fig. 2A, right panel). As a critical antibody against SARS-CoV-2, NAbS were also analyzed in this study. The seropositivity rate of NAbS showed a significant difference between the two groups (55.3% in individuals with high BMI and 73.2% in individuals with normal BMI, $P = 0.010$) (Fig. 2B, left panel). Moreover, NAb titers in the high BMI groups were also remarkably lower than those in the normal BMI group [4.5 (95%CI 4.0–5.1) vs. 6.5 (5.2–8.0), $P = 0.005$] (Fig. 2B, right panel). As expected, the two types of antibodies were correlated ($r^2 = 0.604$, $P < 0.001$) (Fig. S1).

Next, we further compared the antibody responses in individuals with obesity, overweight or normal BMI, which was consistent with the overall trend. The seropositivity rates of anti-RBD-IgG in the obesity, overweight and normal BMI groups were 97.50%, 96.7%, and 98.8%, respectively (Fig. 2C, left panel). The obesity and overweight groups had lower anti-RBD-IgG titers compared with the normal BMI group [200.0 (151.9–263.3) vs. 214.0 (175.9–260.4) vs. 373.8 (303.6–460.3), $P = 0.001$], but no difference was observed between the subgroups (Fig. 2C, right panel). The seropositivity rates of NAbS in the three groups were 57.5%, 54.4%, and 73.2%, respectively (Fig. 2D, left panel). The NAbS titers in individuals with obesity and overweight were also lower than those in individuals with normal BMI [4.2 (3.5–5.0) vs. 4.7 (4.0–5.4) vs. 6.5 (5.2–8.0), $P = 0.050$] but similar between subgroups (Fig. 2D, right panel).

Finally, we analyzed antibody responses to inactivated vaccines in female and male participants and in older and young participants. In the subgroup analysis based on sex, females tended to have higher anti-RBD-IgG and NAb titers than males in the normal BMI group (Fig. S2). In the subgroup analysis based on age, elderly individuals (≥ 50 years) had lower antibody titers and seropositivity rates of NAbS than young individuals (< 50 years) in the normal BMI group (Fig. S3).

In summary, the antibody responses to inactivated vaccines in individuals with obesity/overweight were poorer than those in individuals with normal BMI.

Specific antibody responses to inactivated COVID-19 vaccines in individuals with obesity/overweight over time

To observe the effect of antibody responses over time, we established subgroup analyses for 1 month, 2 months, and 3 months. Although no significant difference was observed at 2 months ($P = 0.354$), anti-RBD-IgG titers in the high BMI group at other time points were significantly reduced ($P = 0.002$ at 1 month, $P = 0.002$ at 3 months) (Fig. 3A, right panel). It is worth noting that the NAb seropositivity rate in the high BMI group decreased faster than that in the normal BMI group, and the seropositivity rate at 3 months was significantly lower (26.7% vs. 65.2%, $P = 0.002$) (Fig. 3B, left panel). NAb titers also showed a similar trend, but a significant difference was only observed at 3 months ($P = 0.003$) (Fig. 3B, right panel). No significant differences in antibody titer or seropositivity rate were observed between the obesity group and the overweight group (Fig. 3C, D).

In general, the antibody responses to inactivated COVID-19 vaccines in individuals with obesity/overweight showed a downward trend over time.

Specific memory B-cell responses to inactivated COVID-19 vaccines in individuals with obesity/overweight

To further evaluate the humoral immune responses induced by inactivated vaccines in the obesity and overweight groups, we analyzed B cells from the three groups by flow cytometry. Notably, the frequency of RBD⁺ CD27⁺

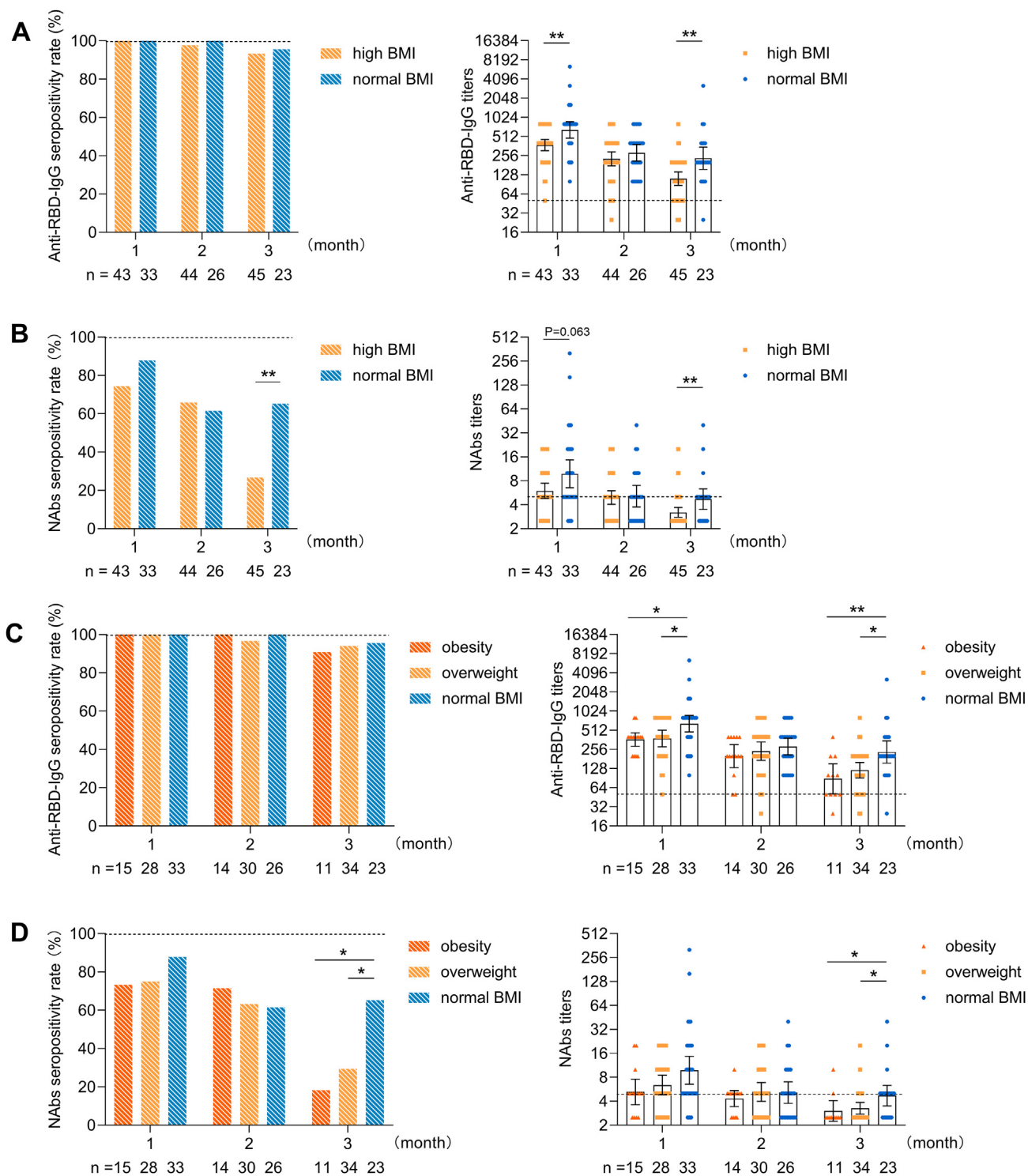


Figure 3 Antibody responses to inactivated COVID-19 vaccines in obesity and overweight over time. (A, B) The seropositivity rate and GMTs of anti-RBD-IgG (A) and NAb (B) in high BMI and normal BMI individuals at 1 month, 2 months, and 3 months. (C, D) The seropositivity rate and GMTs of anti-RBD-IgG (C) and NAb (D) in individuals with obesity, overweight, and normal BMI at 1 month, 2 months, and 3 months. The error bars in antibody titers indicate the 95%CI of the GMTs. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$. High BMI, BMI ≥ 24 kg/m²; normal BMI, BMI < 24 kg/m². CI, confidential interval; anti-RBD-IgG, spike receptor-binding domain IgG antibody; GMTs, geometric mean titers; NAb, neutralizing antibodies.

memory B cells (MBCs) within RBD⁺ B cells in the high BMI group was lower (35.7% vs. 44.1%, $P = 0.015$) (Fig. 4A, left panel). In the specific MBC subsets, we found that the frequency of activated MBCs (actMBCs) in the high BMI group was significantly lower (14.7% vs. 17.7%, $P = 0.022$). Resting MBCs (rMBCs) showed the same decreasing trend (20.8% vs. 22.3%, $P = 0.053$). However, the high BMI group had a higher frequency of intermediate MBCs (intMBCs) than the normal BMI group (42.6% vs. 39.2%, $P = 0.074$) (Fig. 4A, right panel). Furthermore, the frequencies of RBD-specific CD38⁺ CD27⁺ MBCs and CD38⁺ actMBCs were

significantly reduced in the high BMI group (CD38⁺ CD27⁺ MBCs, 2.21% vs. 3.24%, $P = 0.001$; CD38⁺ actMBCs, 4.86% vs. 6.16%, $P = 0.007$) (Fig. 4B). The gating strategy and representative results are shown in Figure S4.

Although there was no significant difference, BMI subgroup analysis also showed a trend of lower frequencies of RBD-specific CD27⁺ MBCs, actMBCs, and rMBCs but higher frequencies of intMBCs in the obesity and overweight groups (Fig. 4C). In addition, the frequencies of CD38⁺ CD27⁺ MBCs and CD38⁺ actMBCs in the obesity and overweight groups decreased significantly (Fig. 4D).

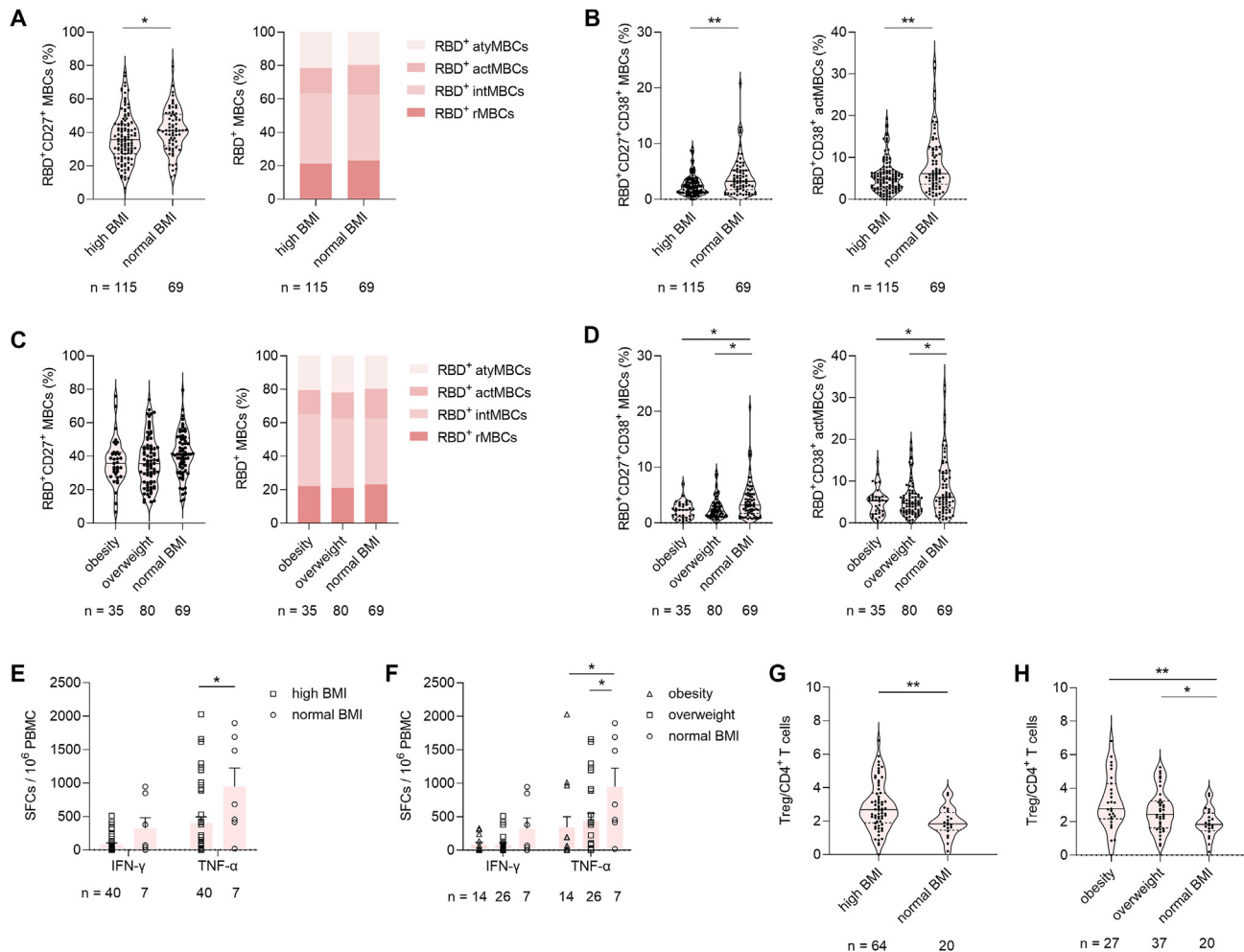


Figure 4 RBD-specific memory B-cell responses and T-cell responses to inactivated COVID-19 vaccines in obesity and overweight. (A) The frequencies of RBD⁺ CD27⁺ MBCs (left panel), and the percentage of rMBCs, intMBCs, actMBCs, atyMBCs in total RBD⁺ MBCs (right panel) in high BMI and normal BMI individuals. (B) The frequencies of RBD-specific CD38⁺ CD27⁺ MBCs (left panel) and CD38⁺ actMBCs (right panel) in high BMI and normal BMI individuals. (C) The frequencies of RBD⁺ CD27⁺ MBCs (left panel), and the percentage of rMBCs, intMBCs, actMBCs, atyMBCs in total RBD⁺ MBCs (right panel) in obesity, overweight, and normal BMI individuals. (D) The frequencies of RBD-specific CD38⁺ CD27⁺ MBCs (left panel) and CD38⁺ actMBCs (right panel) in obesity, overweight, and normal BMI individuals. The error bars represent median (IQR). (E) The number of spike-specific IFN- γ ⁺ SFCs and TNF- α ⁺ SFCs per 10⁶ PBMC in high BMI and normal BMI individuals. (F) The number of spike-specific IFN- γ ⁺ SFCs and TNF- α ⁺ SFCs per 10⁶ PBMC in obesity, overweight, and normal BMI groups. The error bars represent mean (SEM). (G) The frequency of Tregs within CD4⁺ T cells in high BMI and normal BMI individuals. (H) The frequency of Tregs within CD4⁺ T cells in obesity, overweight, and normal BMI groups. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$. actMBCs, activated MBCs; atyMBCs, atypical MBCs; intMBCs, intermediate MBCs; MBCs, memory B cells; IQR, interquartile range; PBMC, peripheral blood mononuclear cell; rMBCs, resting MBCs; SFC, spot-forming cell; SEM, standard error of mean; Treg, regulatory T cell.

The analysis of subgroups by time points also showed a similar trend of lower frequencies of RBD-specific CD27⁺ MBCs, actMBCs, rMBCs, and CD38⁺ CD27⁺ MBCs, and CD38⁺ actMBCs in individuals with obesity/overweight; however, the significant difference was observed only at 2 months and 3 months (Fig. S5).

In summary, the durable humoral immune response to inactivated COVID-19 vaccines in individuals with obesity/overweight was weakened.

T-cell responses to inactivated COVID-19 vaccines in individuals with obesity/overweight

We next evaluated the specific cellular immune response to inactivated COVID-19 vaccines in obese/overweight participants. Fluorospot assay results showed that the number of spike-specific TNF- α ⁺ spot-forming cells (SFCs) decreased significantly in the high BMI group. Spike-specific IFN- γ ⁺ SFCs showed the same trend, but no significant difference was observed (Fig. 4E). The BMI subgroup analysis also demonstrated lower TNF- α ⁺ SFCs in the obesity and overweight groups (Fig. 4F).

We also measured regulatory T cells (Tregs) by flow cytometry, and the results showed that the frequency of Tregs within CD4⁺ T cells was significantly greater in individuals with a high BMI (Fig. 4G). Similar trends were displayed in the obesity and overweight subgroups (Fig. 4H). The gating strategy and representative results are shown in Figure S6.

Specific humoral immune response to inactivated COVID-19 vaccines in individuals with central obesity

To observe the humoral immune response to inactivated COVID-19 vaccines in individuals with different patterns of body fat distribution, we also analyzed the antibody responses and RBD-specific MBCs in individuals with central obesity. The seropositivity rates of anti-RBD-IgG in individuals with central obesity and noncentral obesity were 96.4% and 98.7%, respectively (Fig. 5A, left panel). During the observation period, the anti-RBD-IgG titer in the central obesity group was obviously lower than that in the noncentral obesity group [192.6 (151.8–244.2) vs. 309.1 (246.7–387.3), $P = 0.008$] (Fig. 5A, right panel). The seropositivity rates of NABs in individuals with central obesity and noncentral obesity were 60.0% and 66.7%, respectively (Fig. 5B, left panel). The titers of NABs also showed the same trend [4.5 (3.8–5.3) vs. 5.5 (4.6–6.6)] (Fig. 5B, right panel). No differences in the frequencies of RBD-specific CD27⁺ MBCs and subsets (rMBC, actMBC, and intMBC) were noted between the central obesity and noncentral obesity groups (Fig. S7A). However, participants with central obesity had lower frequencies of RBD-specific CD38⁺ actMBCs (5.43% vs. 3.95%, $P = 0.003$) than those without central obesity (Fig. S7B).

Taken together, individuals with central obesity may have worse humoral immune responses to inactivated COVID-19 vaccines than those without central obesity.

Discussion

The main finding of our study was that the inactivated COVID-19 vaccines were safe and well tolerated with relatively mild adverse events in Chinese individuals. However, full-course inactivated COVID-19 vaccination induced a poor humoral and cellular immune response in Chinese individuals with obesity/overweight.

In this study, the AE rate was 13.9% in the high BMI group and 14.6% in the normal BMI group within 7 days of receiving inactivated vaccines. All AEs were mild and moderate, and the most common local AE was injection-site pain, which was consistent with a clinical trial of inactivated COVID-19 vaccines.^{10,11} This finding demonstrates that vaccination with inactivated vaccines is safe and well tolerated in Chinese individuals with a high BMI.

Next, we evaluated the antibody responses among individuals with obesity/overweight. The overall NAb seropositivity rates in the obesity group and the overweight group were 57.5% and 54.4%, respectively, which were significantly lower than that in the normal BMI group (73.20%). A sharp reduction in NAb seropositivity over time was observed in the high BMI group at 3 months with a seropositivity rate of only 26.7%. This finding indicates that individuals with obesity/overweight may have worse antibody responses than individuals with normal BMI. Considering that NABs are critical against live SARS-CoV-2, a long-term follow-up study for this population is needed. In addition, the GMTs of anti-RBD-IgG and NAB in all participants were reduced over time, but GMTs were significantly reduced in the obesity and overweight groups compared with the normal BMI group. Similar results were reported for mRNA vaccines and in other regions. Pellini¹² recruited 252 healthcare workers in Italy and analyzed the antibody titers 21 days after the first dose of BNT162b2 vaccination. They found that the antibody levels detected in underweight and normal-weight individuals were increased, and normal body weight was positively correlated with antibody response. A Turkish study⁴ found that individuals of young age ($P < 0.01$), female sex ($P < 0.01$), and not overweight or obese ($P = 0.020$) exhibited a significant IgG response to the SARS-CoV-2 inactivated vaccine. The latest study found that in the vaccinated cohort, there were increased risks of severe COVID-19 outcomes for people with obesity compared with the vaccinated population with a healthy weight.¹³ In fact, antibody titers may play an important role in the protection from SARS-CoV-2 infection and severe COVID-19 outcomes. A recent study reported that the occurrence of breakthrough infections with SARS-CoV-2 was correlated with lower neutralizing antibody titers during the peri-infection period.¹⁴ In summary, inactivated COVID-19 vaccines induced a poor antibody response in Chinese individuals with obesity/overweight; thus, more concern should be given to this special population.

Furthermore, we analyzed the RBD-specific B-cell response and spike-specific T-cell response because many studies have identified protective epitopes on the S-RBD protein, and most human-neutralizing monoclonal antibodies target this domain.^{15,16} MBCs and subsets are associated with protection from the reinfection of antigens. The rMBCs can persist for a long time and rapidly

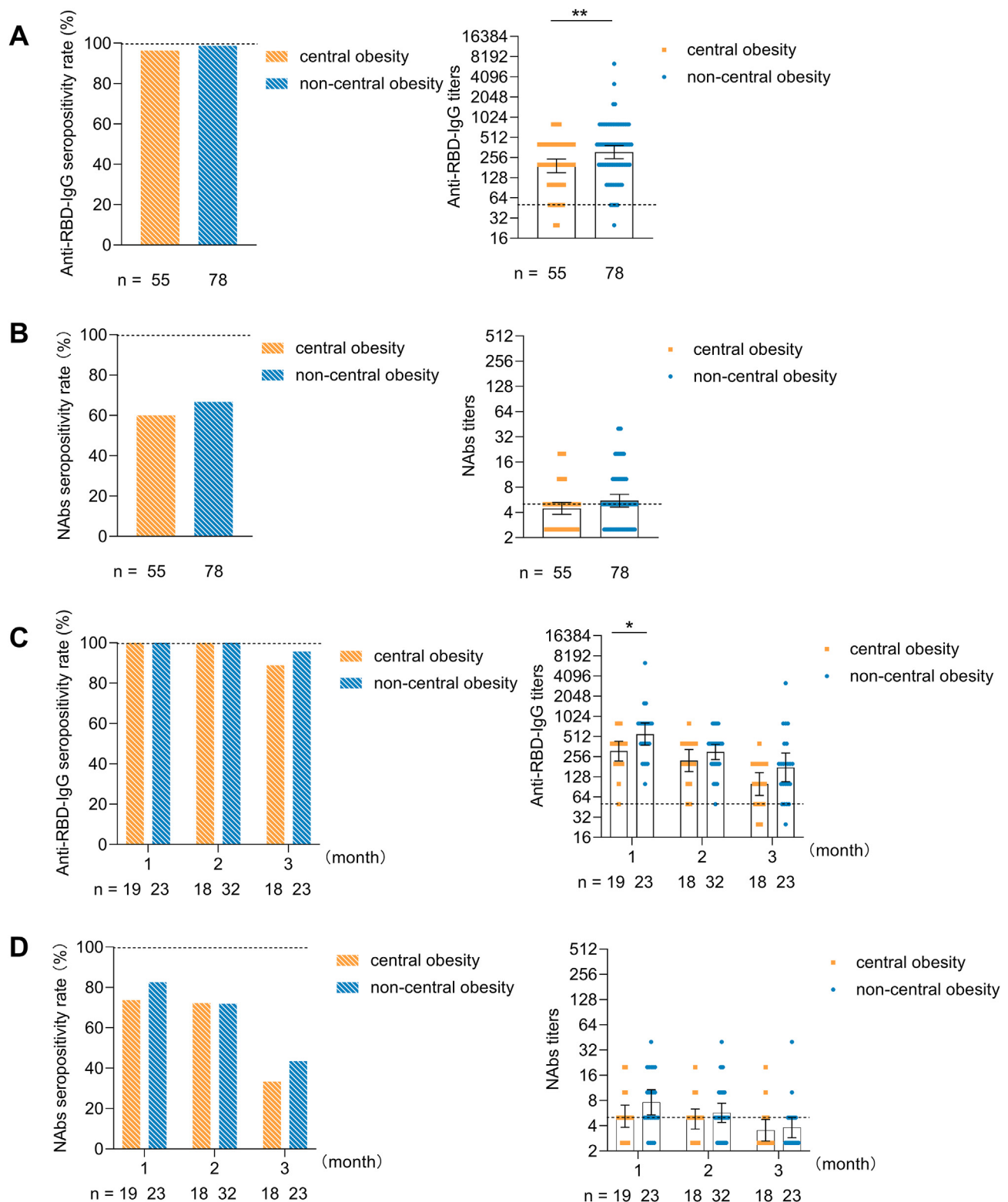


Figure 5 Antibody responses to inactivated COVID-19 vaccines in central obesity and noncentral obesity. (A, B) The seropositivity rate and antibody titers of anti-RBD-IgG (A) and NAbs (B) in central obesity and noncentral obesity individuals. (C, D) The seropositivity rate and antibody titers of anti-RBD-IgG (C) and NAbs (D) in central obesity and noncentral obesity individuals at 1 month, 2 months, and 3 months. The error bars in antibody titers indicate the 95%CI of the GMTs. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$. CI, confidential interval; anti-RBD-IgG, spike receptor-binding domain IgG antibody; NAbs, neutralizing antibodies.

respond upon rechallenge with the same pathogen. ActMBCs are potential plasma cell precursors that represent the earliest population to migrate from the peripheral blood from germinal centers.¹⁷ IntMBCs likely represent a transitional state between MBC subsets. Our study showed that participants with obesity/overweight had a lower frequency of RBD-specific MBCs, which suggests that the durable humoral immune response may be impaired. Individuals with high BMI had lower frequencies of rMBCs and actMBCs but higher frequencies of intMBCs. A recent study reported a decreased frequency of rMBCs but increased frequencies of intMBCs and actMBCs in mild COVID-19 patients, which likely represents ongoing immune activation after SARS-CoV-2 infection.¹⁸ In addition, individuals with high BMI had a lower frequency of CD38⁺ CD27⁺ MBCs, which are also known as antibody-secreting cells (ASCs). Thus, this discrepancy indicated that B-cell immune reactivation after full-course vaccination with inactivated COVID-19 vaccines may be impaired in our studied subjects. Indeed, a decreased B-cell response has been observed in obese individuals on other vaccines. A small human cohort study¹⁹ reported that after influenza vaccination, obesity was associated with reduced antibody titers and decreased frequency of class-switched MBCs as well as increased frequency of exhausted MBCs in both young and elderly patients. Beyond humoral responses, successful protection against SARS-CoV-2 infection can be accomplished by cellular immune responses, including CD4⁺ T cells, CD8⁺ T cells, and their corresponding memory subsets.²⁰ A recent study showed that T-cell activation was reduced in morbidly obese patients following double vaccination with BNT162b2.²¹ Reduced IFN- γ and TNF- α production in stimulated polyclonal T cells from subjects with obesity demonstrated an impaired T-cell antiviral immune response to influenza.²² These functional defects in T cells were consistent with our findings on inactivated COVID-19 vaccines in participants with obesity. Recently published studies hypothesize that obesity can cause chronic, low-grade inflammation, which may lead to T and B-cell defects, thus interfering with the immunogenicity of the COVID-19 vaccine.²³

Considering that the data about the immune response to inactivated COVID-19 vaccines under different body fat distribution patterns are deficient in Asian populations, we compared the humoral responses to inactivated COVID-19 vaccines in Chinese individuals with and without central obesity. Our results showed that compared with the noncentral obesity group, the central obesity group had a weaker antibody response. The frequencies of RBD-specific CD38⁺ actMBCs in people with central obesity were significantly lower. Watanabe's study²⁴ also showed similar results, namely, a higher waist circumference was associated with a lower antibody titer. In summary, this result demonstrated that compared to individuals with noncentral obesity, Chinese individuals with central obesity had weaker humoral responses to inactivated COVID-19 vaccines.

One of the limitations of our study is that these are preliminary results of a cross-sectional study. However, the study is ongoing, and further follow-up data will be reported in future publications. Another limitation is that we do not test the effectiveness of vaccines on circulating virus variants due to insufficient serum.

In conclusion, our results indicate that inactivated COVID-19 vaccines are safe and well tolerated but induce poor humoral and cellular immune responses in Chinese individuals with obesity/overweight. A large population-based cohort is necessary to further investigate the association between BMI and the effectiveness of COVID-19 vaccination. It is worth noting that our study outcomes disseminate the evidence to support the vaccination of COVID-19 booster doses for populations with obesity/overweight.

Author contributions

Concept and design: Hong Ren, Dachuan Cai. Funding acquisition: Hong Ren, Mingli Peng, Min Chen. Participant recruitment: Qian Zhu, Yingzhi Zhang, Juan Kang, Mingli Peng, Min Chen, Ying Mei, Jie Yang, Xiaoya Qi. Experiment execution: Yingzhi Zhang, Dejuan Xiang, Shuang Xiao, Gaoli Zhang. Acquisition, analysis, or interpretation of data: Yingzhi Zhang, Qian Zhu, Juan Kang, Zhiwei Chen, Min Chen, Hu Li, Mingli Peng, Dachuan Cai, Hong Ren. Drafting and critical revision of the manuscript: Qian Zhu, Yingzhi Zhang, Juan Kang, Zhiwei Chen, Dachuan Cai, Hong Ren. All authors were involved in writing the paper and had final approval of the submitted and published versions.

Conflict of interests

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.gendis.2022.10.023>.

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