Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

from group B−, was diagnosed 6 months following the second dose and presented with mild headache symptoms for 2 days. Her specific antibody levels taken 2 months thereafter remained nonprotective. The second patient (F,38) from group B+/smB− and $CD19^+B$% less than 6% was diagnosed with having COVID-19 6 months after the second dose and presented with mild headache symptoms and fever for 2 days, with seroconversion 2 months after infection (516.10 AU/mL).

Furthermore, 11 patients received the third dose, 10 of whom produced protective antibodies with levels ranging from179 to 9972 AU/mL when measured 14 to 85 days postvaccination. Interestingly, patient (M,51) from group B− did not initially respond but developed a protective level after the third dose, whereas patient F,66 (group B+/smB−) with B% less than 6% remained seronegative after the third dose. Patient (F,62) from group B+/smB− had protective levels after the third dose and was diagnosed by polymerase chain reaction with COVID-19 36 days afterward. She also had mild disease manifestations and her antibody levels increased to 17,289 AU/mL 2 months postinfection.

Although this study is limited by the small cohort, it is the only study to date that made correlations between EUROClass classification and the humoral response to vaccination, and it is the first study to monitor the response of patients with CVID to the third BNT162b2 dose. Hence, our observations may have implications for the future treatment of patients with CVID in the era of COVID-19 pandemic. Patient (F,38) from group B− developed protective specific antibodies only after infection, which confirms the findings of Pulvirenti et al[6] that SARS-CoV-2 infection in patients with CVID causes a more efficient classical memory B cell response than BNT162b2 vaccine. After receiving the 2-dose BNT262b2 regimen, 2 patients were infected by SARS-CoV-2; however, despite having unprotective levels of specific antibodies preinfection, they only developed mild disease. Interestingly, one of our patients (F,30), who maintained to have negative serology result after infection, developed only mild COVID-19 with no post-acute COVID sequelae. This suggests that although the 2-dose BNT162b2 regimen does not increase the humoral response, it may still elicit robust antigen-specific CD8+ and T_H1-type CD4+ T-cell responses.[7] A recent study supports this theory and showed that two-thirds of their vaccinated patients with CVID indeed developed S-peptide–specific T-cell response.[8]

The results of the third BNT162b2 dose suggest that some patients with CVID may need a few BNT162b2 doses to achieve antigen exposure that produces or preserves good humoral response. Therefore, we should consider giving booster doses to patients with CVID earlier than 5 months after the second dose.

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Coronavirus disease 2019–related anxiety is associated with uncontrolled asthma in adults

There is evidence that the coronavirus disease 2019 (COVID-19) pandemic, its mitigation strategies, and resulting life changes are associated with detrimental effects on physical and mental health. Adults in the United States were 3 times more likely to meet the criteria for moderate or serious mental distress in April 2020 than in 2018 (70.4% vs 22.0%).[1] Although there is evidence linking stress with asthma exacerbation,[2] studies addressing the impact of the COVID-19 pandemic on anxiety among adults with asthma are limited. We evaluated the associations of COVID-19–related anxiety with asthma control in adults.

An online, cross-sectional study was conducted with US adults (≥ 18 years old) with a current self-reported physician diagnosis of asthma.[3] Study invitations were shared online (eg, social media, e-mail contacts in the networks of the researchers, ResearchMatch), and participants opted in for an incentive drawing.[3] Anxiety was

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measured using a 5-point Likert scale to capture participants' responses to 8 questions on participants' experiences in the previous 2 weeks.[4] These questions were developed in the Coronavirus Health and Impact Survey Initiative, which was launched early in the pandemic.[5] Responses were summed for a score ranging from 8 to 40 with higher values indicating higher anxiety. Anxiety scores were first dichotomized at the median (22) as high (above median) or low (at or below median) and then categorized into quartiles (8-17, 18-22, 23-26, and 27-40) to evaluate the dose-response association of anxiety with uncontrolled asthma. Participants also completed the asthma control test (ACT) and answered questions about health care utilization and the level of life changes during the pandemic. The study was approved by the University of Kansas Medical Center's institutional review board.

As of December 19, 2020, 909 surveys were received, of which 873 had complete data on the main variables. The χ^2 statistics were used to evaluate associations of anxiety (high vs low) with participant characteristics. Binary logistic regression models evaluated associations of anxiety level as a dichotomous variable or as an ordinal variable (quartiles) with uncontrolled asthma (ACT score ≤ 19). Multiple logistic regression analysis was performed to adjust for potential confounding variables identified a priori, including age, education, sex, race or ethnicity, residential area, home ownership, and having confirmed/suspected COVID-19. Statistical analysis was performed in SAS 9.4 (SAS Institute, Cary, North Carolina), and a *P* value less than .05 indicated statistical significance.

Participants were mostly of female sex (83%), White (80%), urban (60%), with at least a college degree (69%), and mean age of 45 plus or minus 15 years. Among the participants, 13% and 15% self-quarantined with and without COVID-19 symptoms, respectively; 14% lost their job; 21% had reduced ability to earn money; 25% had confirmed or suspected COVID-19; and 2% were hospitalized owing to COVID-19. Almost 57% had a self-reported asthma episode or attack since the pandemic, 29% contacted their health care provider for urgent symptoms, and 43% had uncontrolled asthma (ACT ≤ 19).

Most participants reported being worried about themselves and family and friends becoming infected with COVID-19 and about their own physical and mental/emotional health. Almost 48% of the participants had high anxiety score. Less educated and those who were renting or living with family or friends were more likely to experience significantly ($P < .01$) higher levels of anxiety. Furthermore, participants who self-quarantined, those who had confirmed or suspected COVID-19, and those exposed to others with confirmed or suspected COVID-19 reported significantly ($P < .05$) higher levels of anxiety.

Participants with higher anxiety levels were more likely to report having uncontrolled asthma (Fig 1). In adjusted multiple logistic regression models, participants with high anxiety were twice as likely to have uncontrolled asthma compared with counterparts reporting low levels of anxiety (odds ratio, 2.00; 95% confidence interval [CI], 1.45-2.74). In additional analyses treating anxiety as an ordinal variable (quartiles), we observed a significant dose-response direct relationship of COVID-19–related anxiety with the odds of uncontrolled asthma ($P < .001$). Compared with participants in the lowest anxiety quartile, the odds of uncontrolled asthma were 1.64 (95% CI, 1.06-2.53), 1.78 (95% CI, 1.12-2.85), and 3.83 (95% CI, 2.41-6.09) for those in the second, third, and fourth anxiety quartiles, respectively, after adjusting for covariates including having confirmed or suspected COVID-19.

Adults with asthma are substantially affected by the pandemic, experiencing high levels of anxiety. For example, findings from a national sample of adults in the United States suggest increased physical and mental symptoms among those with chronic respiratory conditions during the COVID-19 pandemic as compared with others.[6] Our study, with a geographically diverse adult asthma population and differing levels of asthma control, supports these findings and reveals a detrimental dose-response effect of COVID-19–related anxiety on asthma control. Acute stress is associated with an increase in sympathetic nervous system responses, cortisol, and inflammatory responses in people with asthma.[7] Chronic negative stress may affect asthma in multiple ways. Chen and Miller[2] postulate that chronic stress affects asthma by altering the magnitude of airway inflammatory response to irritants, allergens, and infections. Others revealed that chronic negative stress induces inflammatory changes that reduce glucocorticoid receptor responsiveness.[8] Both of these mechanisms can lead to difficult-to-treat, uncontrolled asthma. Our study has the typical limitations of the cross-sectional design, including the inability to rule out whether poor asthma control leads to increased

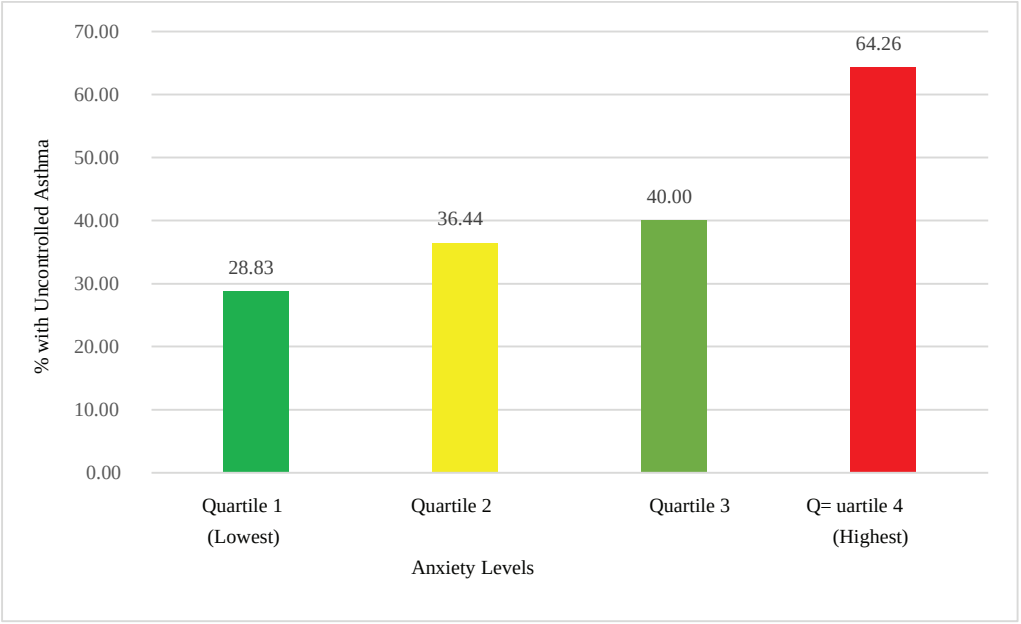

Figure 1. Percentage with uncontrolled asthma by anxiety levels (quartiles). *P* values for overall differences and for a dose-response association were less than .001.

anxiety (ie, reverse causation), selection bias, and relying on self-report of asthma. Furthermore, the anxiety scale used was developed during the emerging COVID-19 crisis to provide researchers with consistent measurement tools. Therefore, our findings should be interpreted with caution as reliability, validity, and cut points of the instrument have not yet been established. In addition, we could not assess whether COVID-19–related anxiety was additive to existing chronic anxiety or whether anxiety and asthma symptoms were confused. Moreover, although we were able to achieve geographic diversity in our sample, well-educated White women were overrepresented.

The COVID-19 pandemic has disproportionately affected people with chronic diseases, including asthma; these impacts were both physically and psychologically. Although asthma-related emergency department visits and hospitalizations seemed to be lower during COVID-19, we must consider the avoidant healthcare behaviors people developed during the COVID-19 pandemic. Our findings underscore the need for health care providers to assess for the ongoing psychological impact of the pandemic and refer to mental health specialists. Equally important are efforts among policymakers to improve access to mental health services for all, especially during a pandemic.

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The Probiotics in Pediatric Asthma Management (PROPAM) study

A Post Hoc analysis in allergic children

Type 2 inflammation is prevalent in children with asthma and increases susceptibility to respiratory infections.[1] Furthermore, acute airway infections usually precede asthma exacerbations in children.[2] Consequently, an ideal therapeutic strategy should be targeted to dampen inflammation and prevent infections. There is also evidence to suggest that children with asthma have intestinal and respiratory dysbiosis that promotes airway inflammation and allergy.[3] It is speculated that probiotics could restore "eubiosis," dampen inflammation, and prevent infections.[4] In fact, several studies have explored the effects of probiotics in allergic diseases, including asthma.[5]

Bifidobacterium breve B632 and *Ligilactobacillus salivarius* LS01 are probiotic strains with immunomodulatory activity.[6] In this regard, the PROPAM (PRObiotics in Pediatric Asthma Management) study provided evidence that a probiotic mixture containing both strains, significantly reduced the number of asthma exacerbations in children with asthma, who were evaluated in a pediatric primary-care setting ($P < 0.001$).[7]

Because allergy represents a main pathogenic factor in asthma, this post hoc analysis tested the hypothesis that allergic children could also respond to the probiotic supplementation.

The major outcome of the PROPAM study was the reduction of asthma exacerbations. A parental study described the methodology in detail.[7]

Participant children were included in this analysis based on documented allergy, including house dust mite (HDM) allergy. Children attended primary-care–pediatric clinics and were considered allergic if symptoms occurred after exposure to the sensitizing allergen.[8] Allergy was defined as presence of allergen-specific immunoglobulin (Ig)E, documented by skin-prick test (a wheal 3 mm or larger than the negative control was considered positive; the extracts were manufactured by Lofarma, Milan, Italy) or by serum assessment (ImmunoCap; Thermo Fisher, Milan, Italy) according to validated criteria.[9]

The probiotic mixture supplementation lasted 4 months. The probiotic mixture or placebo was taken twice daily (1 sachet in the morning and 1 in the evening) for 8 weeks and subsequently once daily for a another 8 weeks. The parents signed an informed consent form.

The Ethics Committee of Napoli 3 Sud NHS approved the study procedure on April 12, 2017 (N. 45/21/04/2017), and the study was registered on ClinicalTrials.gov (NCT04289441). Eleven Italian primary-care pediatricians, resident in the Campania region of southern Italy, identified the participants for the study.

A multivariate logistic regression model was applied to identify all factors significantly associated with the occurrence of asthma exacerbation. Results were expressed as odds ratio with 95% confidence intervals.

Table 1 reports the main findings. Allergic children were 164 (38.8% of the total per protocol population of the PROPAM study) of 422 children. Their mean age was 8.8 (SD + 3.31) years old; 60 (36.6%) were girls and 104 (63.4%) boys. In this subgroup, 16 were

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