

## LETTER TO THE EDITOR

# Reply to Jakovac: About COVID-19 and vitamin D

Angelo Facchiano,<sup>1\*</sup> Antonio Facchiano,<sup>2\*</sup> Manuela Bartoli,<sup>3</sup> Alberto Ricci,<sup>4</sup> and Francesco Facchiano<sup>5\*</sup>

<sup>1</sup>National Research Council, CNR-ISA, Avellino, Italy; <sup>2</sup>Istituto Dermopatico dell'Immacolata, IDI-IRCCS Rome, Italy;

<sup>3</sup>Department of Ophthalmology, Medical College of Georgia, Augusta University, Augusta, Georgia; <sup>4</sup>Department of Clinical and Molecular Medicine, Division of Respiratory Diseases, Sant'Andrea Hospital, Sapienza University of Rome, Rome, Italy; and <sup>5</sup>Department of Oncology and Molecular Medicine, Istituto Superiore di Sanità, Rome, Italy

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TO THE EDITOR: In response to the letter from Jakovac entitled: "COVID-19 and vitamin D—Is there a link and an opportunity for intervention?" (3) we want to highlight the large meta-analysis published in 2017 reporting a systematic review of randomized controlled trials indicating that vitamin D (VitD) supplementation reduced the risk of acute respiratory tract infections (10). These results support the potential beneficial impact of VitD supplementation against acute respiratory tract infections, but also analyze dosage and point out the importance of considering VitD baseline levels. Another interesting issue supporting the tight correlation between VitD and coronavirus disease (COVID-19) stems from the observation that anosmia and ageusia are early symptoms in COVID-19 patients (6, 8). Of interest, anosmia and/or ageusia were detected in subjects with VitD deficiency (1, 4), thus implying that COVID-19 infections could be associated with or lead to VitD deficiency. Additional evidence rises from the observation that patients with Kallmann syndrome, a rare congenital form of hypogonadotropic hypogonadism, have symptoms common to COVID-19 patients, namely hypo- or anosmia and higher frequency in men, and also low VitD levels (2). A tight correlation between sex hormones and VitD supplementation was recently reported by a study correlating the hormone-modulated expression of a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) receptor (ACE2) and hypovitaminosis D (5). Severe deficiency of VitD is widespread across the world, and VitD has a role in several cellular-mediated responses to pathogens (7), therefore its supplementation may be a simple and cost-effective way to minimize respiratory exacerbation in fragile population (9). Overall, these studies strongly support a possible preventive and/or therapeutic role of VitD in patients with COVID-19 as reported by Jakovac's letter and underline the need of collecting appropriate data from patients and further epidemiological studies to correlate COVID-19 infection and clinical progression to the hormonal assets of patients. Currently, there are 11 clinical trials listed in the clinical trial registry of the National Institutes of Health (NIH) (clinicaltrials.gov) aimed at testing VitD supplementation in COVID-19 patients in combination with other drugs and comparing high doses versus standard doses. There is no doubt that the results of these trials will be key to the validation of this adjunctive treatment for COVID-19 patients.

\* Angelo Facchiano, Antonio Facchiano, and F. Facchiano contributed equally to this work.

Correspondence: Francesco Facchiano (francesco.facchiano@iss.it).

## DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

## AUTHOR CONTRIBUTIONS

F.F., Angelo Facchiano, and Antonio Facchiano conceived and designed the study; F.F., Angelo Facchiano, Antonio Facchiano, M.B., and A.R. drafted manuscript; F.F., Angelo Facchiano, Antonio Facchiano, M.B., and A.R. edited and revised manuscript; F.F., Angelo Facchiano, Antonio Facchiano, M.B., and A.R. approved final version of manuscript.

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