observed among 44.1% of patients. The Figure shows that a high proportion of individuals still reported fatigue (53.1%), dyspnea (43.4%), joint pain, (27.3%) and chest pain (21.7%).

Discussion | This study found that in patients who had recovered from COVID-19, 87.4% reported persistence of at least 1 symptom, particularly fatigue and dyspnea. Limitations of the study include the lack of information on symptom history before acute COVID-19 illness and the lack of details on symptom severity. Furthermore, this is a single-center study with a relatively small number of patients and without a control group of patients discharged for other reasons. Patients with community-acquired pneumonia can also have persistent symptoms, suggesting that these findings may not be exclusive to COVID-19.6

Clinicians and researchers have focused on the acute phase of COVID-19, but continued monitoring after discharge for long-lasting effects is needed.

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Concept and design: All authors.

Drafting of the manuscript: Carfi, Landi.

Critical revision of the manuscript for important intellectual content: Bernabei, Landi.

Statistical analysis: Carfi.

Supervision: Bernabei, Landi.

Conflict of Interest Disclosures: None reported.

Additional Information: The members of the Gemelli Against COVID-19 Post-Acute Care Study Group are listed in reference 5.


Trends in Daily Use of Biotin Supplements Among US Adults, 1999-2016

Over-the-counter biotin supplements, especially in high doses (≥5 mg/d, or 166-fold greater than the dietary recommendation of 30 μg/d), are widely available and marketed as having health benefits such as stimulating growth of hair and nails. The US Food and Drug Administration (FDA) issued a safety communication in 2017 warning that high-dosage biotin supplement use may interfere with laboratory test accuracy.1 To understand the potential clinical implications of high-dosage biotin supplement use, we characterized the prevalence and trends in use of 1 mg/d or greater and 5 mg/d or greater of biotin among US adults from 1999 to 2016. A biotin dosage of 1 mg/d or greater was chosen because lower dosages (<1 mg/d) are unlikely to interfere with laboratory tests; a dosage of 5 mg/d or greater was studied because biotin supplements for hair and nail growth often contain 5 mg/d or more.

Methods | Repeated cross-sectional surveys from the nationally representative National Health and Nutrition Examination Survey (NHANES) were used to assess trends in self-reported biotin supplement use of 1 mg/d or greater and 5 mg/d or greater from 1999 to 2016 (9 survey cycles). In each cycle, NHANES sampled noninstitutionalized US residents through a complex, stratified, multistage probability sampling design with certain populations overrepresented (overall response, 74%).2 Participants provided informed consent.2 Because the data are publicly available and anonymized, the
Table. Trends in Self-reported Biotin Supplement Use ≥1 mg/d in the National Health and Nutrition Examination Survey, 1999-2016

<table>
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</tr>
</thead>
<tbody>
<tr>
<td>In survey cycle</td>
<td>4580</td>
<td>5080</td>
<td>4796</td>
<td>4636</td>
<td>5873</td>
<td>6145</td>
<td>5499</td>
<td>5702</td>
<td>5647</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Consuming ≥1 mg/d biotin</td>
<td>4</td>
<td>11</td>
<td>5</td>
<td>15</td>
<td>28</td>
<td>30</td>
<td>50</td>
<td>103</td>
<td>145</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Linear and quadratic $P$ values for trend. NA indicates not applicable (subgroups with ≥1 survey cycles with no observed outcomes).

Data reported as 0 refer to a prevalence estimate of 0% to <0.1%. Relative standard error (standard error/prevalence)×100 is greater than 30%, indicating that the estimates are unstable due to low numbers of biotin users in these cells.

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Participants self-reported race/ethnicity according to survey categories, assessed to capture differences in health and supplement use by race/ethnicity and to provide nationally representative estimates.

Study limitations include self-reported biotin use and poor precision due to small numbers of biotin users in some subgroups.
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Acquisition, analysis, or interpretation of data: Li, Rooney, Burmeister, Lutsey.

Drafting of the manuscript: Li.

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: Rooney, Lutsey.

Administrative, technical, or material support: Li, Lutsey.

Supervision: Li.

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COMMENT & RESPONSE

Need for Additional Trials of Vitamin C for Sepsis
To the Editor: Since a single-center, 94-patient, uncontrolled observational study of the combination therapy of vitamin C, thiamine, and hydrocortisone reported a 32% absolute mortality reduction in patients with sepsis in 2017, several investigators have tested vitamin C and combination therapy in clinical trials. The recently published Vitamin C, Hydrocortisone and Thiamine in Patients With Septic Shock (VITAMINS) trial reported no difference in the primary outcome of time alive and free of vasopressors.2 We agree that the results of the VITAMINS trial should temper enthusiasm for the use of vitamin C therapy outside of clinical trials, which some had adopted after the 2017 report.

However, in the accompanying editorial on the VITAMINS trial, Dr Kalil reported a large number of trials registered on ClinicalTrials.gov and stated that “considering the available evidence...there is insufficient equipoise to continue enrolling more patients in sepsis trials involving high-dose vitamin C administration.”3 We disagree. First, preclinical studies indicate that high-dose vitamin C has strong biologic plausibility to improve outcomes in sepsis.4 Second, the multicenter phase 2 randomized clinical trial of higher-dose vitamin C (CITRIS-ALI; 200 mg/kg per day) in 167 patients with sepsis and acute respiratory distress syndrome (ARDS) reported a significant reduction in mortality, although this was a secondary outcome.5 Third, the design and size of the VITAMINS trial was not robust enough to make conclusions regarding efficacy. The trial was unblinded, the number of enrolled patients (n = 216) was modest, and the comparison group was treated with hydrocortisone, which may have confounded interpretation of the results. Fourth, of 28 trials that we reviewed in ClinicalTrials.gov (using the search terms sepsis and vitamin C), 50% have a planned recruitment of fewer than 100 patients, and an additional 36% plan to enroll fewer than 250 patients; 76% are single-center trials. Thus, most of these trials will be underpowered and will lack external validity. In contrast, a randomized, blinded, multicenter trial in North America is ongoing (LOVIT; Canadian Critical Care Trials Group). This trial will enroll large numbers of patients with sepsis and ARDS and test the higher dose of vitamin C used in CITRIS-ALI. We believe additional rigorous trials are needed to test the potential efficacy of vitamin C in patients with sepsis and ARDS.

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