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To the editor:

Studies have shown patients can experience post-acute COVID-19 syndrome, characterized by the persistence of symptoms ≥4 weeks after initial infection with COVID-19, for ≤1 year [1–5]. We sought to gain further perspective by conducting a 2-year follow-up study of patients diagnosed with COVID-19 to evaluate long-term sequelae.

This is a prospective, longitudinal, Institutional Review Board–approved cohort study consisting of patients diagnosed with COVID-19 infection in March and April of 2020 in the St. Joseph’s Health Network. The individuals with confirmed SARS-CoV-2, who were either hospitalized or tested positive in the outpatient setting, were included. The patients <18 years of age or those with cognitive impairment were excluded. Informed consent was obtained over telephone and participants were contacted during March and April of 2021 to complete a comprehensive questionnaire to evaluate for persistent symptoms after their initial diagnosis with COVID-19. The patients who reported persistence of symptoms at a 1-year follow-up were contacted again at a 2-year follow-up in March of 2022 to assess for persistence of COVID-19–related symptoms. Logistic regression analysis was performed to identify predictors of symptom persistence and the McNemar test was used to compare the duration of symptoms among those surveyed both years.

Five hundred patients were invited, of which 173 participated, including 91 patients who were previously hospitalized. The mean age was 51.5 years old, with an age range of 18 to 95, of whom 49.42% were male. The most common ethnicity was Hispanic (46.24%) and the most common comorbidity was hypertension (39.5%) (Table 1). At 12 months follow-up 50.8% of the patients experienced at least one persistent symptom (Fig. 1A); the most common symptoms were shortness of breath (25%), fatigue (24%), anxiety (21%), difficulty focusing/brain fog (18%), body aches (18%), and headaches (16%) (Fig. 1B). At 24 months follow-up, 23.1% of the patients experienced at least one persistent symptom (Fig. 1A); the most common symptoms being shortness of breath (13.2%), fatigue (12.1%), difficulty focusing/brain fog (10.4%), memory loss (9.2%), and anxiety (8.1%) (Fig. 1B). Thirteen patients were lost to follow-up from year 1 to year 2.

Anxiety (p: 0.001), headaches (p: 0.002), shortness of breath (p: 0.012), and fatigue (p: 0.049) were most likely to improve between the 1- to 2-year follow-ups. Logistic regression analysis adjusted for age, gender, obesity, and comorbidities (at least 1) was used for the comparison of men to women and inpatients to outpatients. Wilcoxon rank sum test or Fisher’s exact test were used for the continuous and categorical comparisons of the two groups. At 1-year follow-up, women were more likely than men to have persistent symptoms (62.9% vs 38.1%, respectively, p: 0.001). At 2-year follow-up, women again were more likely than men to have at least one persistent symptom (53.6% vs 31.3%, respectively, p: 0.048). The proportion of those with persistent symptoms was similar between inpatients and outpatients (52.9% vs 48.0%, respectively, p: 0.052), although there appeared to be a trend toward higher rates among inpatients.
Two years after infection, 23.1% of patients still experienced at least one persistent symptom. At 1- and 2-years follow-up, shortness of breath and fatigue were the most common symptoms. In other studies, fatigue and shortness of breath were similarly found to be amongst the most commonly reported symptoms after 1 year [1–5]. The symptoms most likely to improve between years 1 and 2 were anxiety, headaches, shortness of breath, and fatigue. Women were more likely to have persistent symptoms at 2 years compared with men. Women have been found to experience more persistent symptoms in other studies as well [4,5].

To our knowledge this was the first U.S. study to describe the duration and symptomatology of COVID-19 in patients over a 2-year follow-up period. Most of the patients had reduction and resolution in their symptoms over the 2-year period; however, nearly a quarter of patients still experience persistent symptoms. The study limitations included a small patient sample, self-recall bias, loss of patients to follow-up, and being a single centre study. The study would have benefited from more frequent follow-up intervals to provide a more accurate timeline of symptom recovery. The aetiology and treatment of post-acute COVID-19 syndrome remains poorly defined. With over half a billion people infected worldwide, thousands of new infections daily, and waning protection from immunization or prior infection, a global public health crisis could be looming. For millions of patients, post-acute COVID-19 syndrome can significantly impair cognitive function, quality of life, and the ability to work at full capacity for years to come [1–4]. These points highlighted the urgent need for larger scale studies to better understand and effectively treat this post viral phenomenon.

Transparency declaration
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Author contributions
CM was responsible for concept and design. CM, SN, SC, SR, GH, and HJ were responsible for acquisition, analysis, and interpretation of data. CM, SN, and HJ drafted the manuscript. HJ was responsible for statistical analysis.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cmi.2022.06.008.

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