# Patient-Reported Symptoms and Sequelae 12 Months After COVID-19 in Hospitalized Adults: A Multicenter Long-Term Follow-Up Study

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**Objective:** Our knowledge on the long-term consequences of COVID-19 is still scarce despite the clinical relevance of persisting syndrome. The aim of this study was to analyze patient-reported outcomes, including assessment by specific questionnaires of health impairment and symptoms.

**Methods:** This is a prospective, observational and multicenter cohort study coordinated by Fondazione IRCSS Ca' Granda Ospedale Maggiore Policlinico di Milano and Istituto di Ricerche Farmacologiche Mario Negri IRCCS including eight hospitals located in North and Central Italy. A telephone interview to assess rehospitalization, access to health care resources, general health status subjective evaluation, and symptoms was performed at 12 months after the discharge in patients admitted to hospital because of COVID-19 from February 2020 to the end of May 2020.

**Results:** Among the 776 patients discharged alive, 44 (5.7%) died, 456 subjects (58.8%) completed the questionnaire and 276 (35.6%) were not reachable or refused to join the telephone interview. The mean age of the study population was 59.4 years (SD 14.1), 69.8% of individuals needed oxygen support during hospitalization and 10.4% were admitted to ICU. Overall, 91.7% of participants reported at least one symptom/sequela at 12 months. Exertional dyspnea (71.7%), fatigue (54.6%), and gastrointestinal symptoms (32.8%) were the most reported ones. Health issues after discharge including hospitalization or access to emergency room were described by 19.4% of subjects. Female and presence of comorbidities were independent predictors

of health impairment and presence of $\geq 2$ symptoms/sequelae after 12 months from hospitalization for COVID-19.

**Conclusions:** Patient-reported symptoms and sequelae, principally dyspnea and fatigue, are found in most individuals even 12 months from COVID-19 hospitalization. Long-term follow-up based on patient-centered outcome can contribute to plan tailored interventions.

Keywords: long COVID-19, SARS-CoV-2, long-term sequelae, COVID-19, dyspnea

## INTRODUCTION

Since the first documented case of pneumonia related to SARS-CoV-2 in December 2019, progresses have been made on management of COVID-19.

However, researchers have focused mainly on the acute phase, attention has lately been shifting to post-COVID-19 signs and symptoms and, as a consequence, there is still very limited information on the sequalae of COVID-19 (1). The exact nature and prevalence of persistent symptoms after SARS-CoV-2 infection are not known, but an increasing number of studies are reporting a high incidence of sequelae during the convalescence months, defined as "*long-COVID-19*," which recently obtained a formal definition by WHO (2).
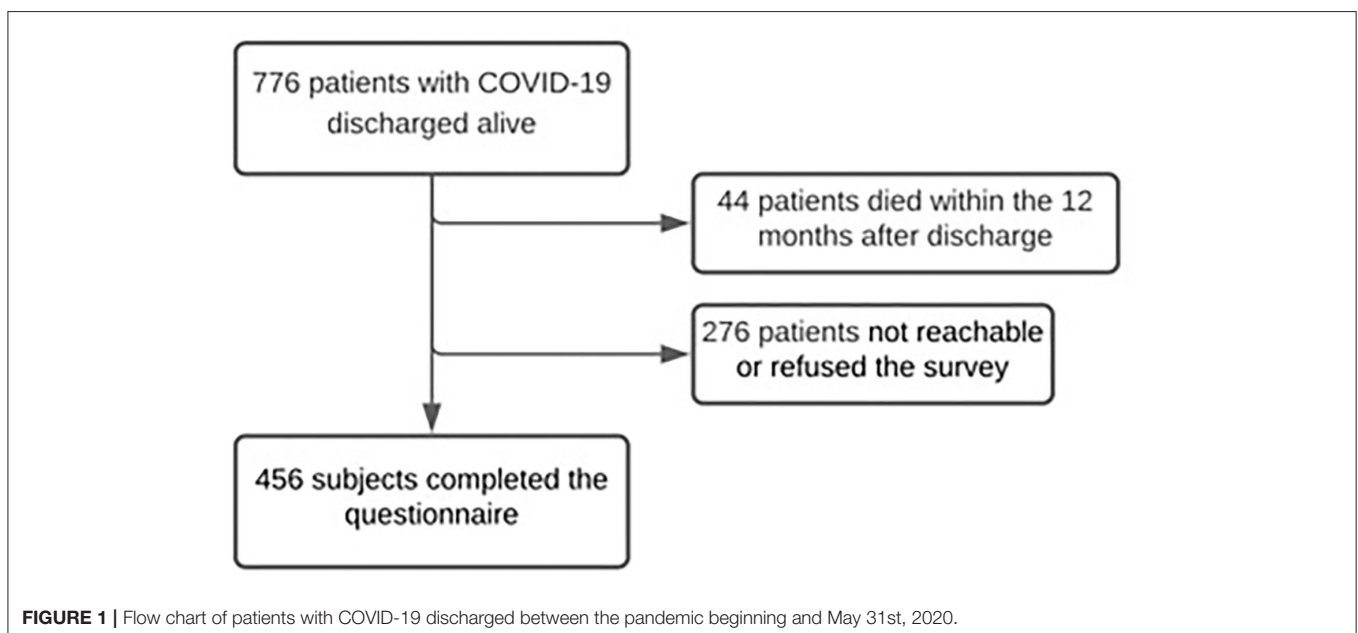
Long-COVID-19 sequelae were reported by several studies and range from cough, dyspnea, fatigue, chest pain, migraine but also neurocognitive symptoms such as depression, anxiety, and insomnia (3, 4). During early COVID-19 convalescence, these clinical sequelae seem to be related to gender, age, BMI, and clinical severity during hospitalization (5, 6).

Unfortunately, robust data are lacking in terms of duration of this syndrome, risk factors, long term differences among patients with severe COVID-19 and individuals who experienced only mild or no symptoms, best methods to follow those patients and potential treatment.

With that in mind, it is likely that patients recovering from COVID-19 might need support for a wide range of complications (7) and evidence shows that follow-up programs and rehabilitation services should be developed to address the impact of "*long haulers*" (8).

Studies published on long COVID-19 until now showed a high degree of heterogeneity. In particular they considered very different follow-up lengths, mainly from 3 to 6 months, discordant inclusion criteria with many cohorts involving both hospitalized and non-hospitalized patients, diverse signs and symptoms investigated and a different approach in patient assessment ranging from hospital visit, dedicated mobile phone applications and telephone interviews to collect self-reported symptoms (4–6, 8–18).

Here, we present a prospective study designed to assess a large class of patient-reported symptoms and sequelae in a homogenous cohort of hospitalized patients after 12 months of follow up.



FIGURE 1 | Flow chart of patients with COVID-19 discharged between the pandemic beginning and May 31st, 2020.

# METHODS

## Study Design and Participants

This is a prospective, observational and multicenter cohort study supported by Fondazione IRCSS Ca' Granda Ospedale Maggiore Policlinico di Milano and Istituto di Ricerche Farmacologiche Mario Negri IRCCS including eight hospitals located in North and Central Italy.

All consecutive adults with a positive RT-PCR result for SARS-CoV-2 admitted to eight hospitals located in North and Central Italy were enrolled in the COVID-19 Network cohort. Patients aged <18 years and pregnant women were excluded.

Data collected included age, sex, comorbidities, signs and symptoms of COVID-19 at admission, hospitalization length, ICU admission, acute complications during hospital stay, and destination after discharge. Acute complications during hospitalization included Acute Respiratory Distress Syndrome (ARDS), infections, Acute Kidney Injury (AKI), cardiologic events, metabolic, hepatic/gastrointestinal, haematologic or neurologic disorders, thrombosis, or acute ischemic-hemorrhagic events. A severity scale was used to stratify patients considering the oxygen support needed: grade 0 (oxygen support not required), grade 1 (oxygen through Venturi mask), and grade 2 [oxygen through High Flow Nasal Cannula (HFNC), CPAP or non-invasive ventilation].

## Outcomes

The follow up was proposed by telephone interview to all COVID-19 Network patients who were discharged alive between the beginning of the pandemic (last week of February 2020) and the 31st May 2020.

Four outcomes were assessed: (i) significant medical problems defined as need of hospitalization or emergency room (ER) access and cardio-neuro-vascular events after the discharge; (ii) patients' subjective perception of general health; (iii) symptoms (ageusia, anosmia, cough, dyspnea at rest, episodes of anxiety, exertional dyspnea (measured by the modified British Medical Research Council (mMRC) dyspnea scale (19), fatigue, gastrointestinal symptoms, headache, loss of appetite, myalgia, limitations on daily life activities, memory problems, sleep disorders); (iv) presence of a group of sequelae which include dyspnea at rest and exertional dyspnea, myalgia, and limitations on daily life activities that we arbitrarily grouped as "*disabling sequelae*" considering their impact on general health status and daily life.

Patient's subjective assessments was recorded on a 0–10 scale to evaluate the generic health status and capacity to appreciate smells and taste (0 = very poor, 10 = very good).

For the remaining symptoms and signs a 0–10 scale was employed where 0 = absence of the symptom and 10 = maximum intensity. A subjective score ≥5 was considered as presence of symptom.

For example, we asked patients direct question like: "*how would you score your state of health from 0 to 10 where 0 is a very bad state of health and 10 is a perfect state of health?*"

The same type of question was asked about the other signs or symptoms: *how would you score your loss of smells from 0 to 10 where 0 = absence of the symptom and 10=maximum subjective intensity?*

Outcomes were assessed at 12 months after discharge from COVID-19 hospitalization. Participants were asked to report

**TABLE 1** | Characteristics of patients hospitalized with COVID-19 and discharged alive who consented to follow up interview.

| | Value |
|---|---|
| **Total, *N*** | 456 |
| **Female, *N* (%)** | 168 (36.8%) |
| **Age, mean (SD)** | 59.4 (14.1) |
| **Age, range (*N*, %)** | |
| 18–44 | 62 (13.6%) |
| 45–64 | 225 (49.3%) |
| ≥65 | 169 (37.1%) |
| **Ethnicity, *N* (%)** | |
| Caucasian | 377 (87.7%) |
| Other | 53 (12.3%) |
| **Comorbidities, *N* (%)** | |
| Respiratory diseases | 52 (11.7%) |
| Cardiovascular diseases | 188 (42.2%) |
| Nephropathies | 16 (3.4%) |
| GI diseases and hepatopathies | 37 (8.3%) |
| Rheumatological diseases | 10 (2.3%) |
| Metabolic diseases | 81 (18.2%) |
| Neurologic diseases | 20 (4.5%) |
| Cancer | 16 (3.6%) |
| SOT and HSCT | 5 (1.1%) |
| **Number of comorbidities, *N* (%)** | |
| 0 | 176 (40.4%) |
| 1–2 | 197 (45.2%) |
| ≥3 | 63 (14.5%) |
| **Symptoms at COVID-19 onset, *N* (%)** | |
| Respiratory symptoms | 364 (80.4%) |
| Systemic symptoms* | 412 (90.4%) |
| Neurologic symptoms | 64 (14.4%) |
| GI symptoms | 85 (18.8%) |
| **Number of symptoms at COVID-19 onset, median (IQR)** | 3 (2–4) |
| **Hospitalization length, median (IQR)** | 12 (6–21) |
| **Hospitalization length, *N* (%)** | |
| <14 days | 242 (53.1%) |
| ≥14 days | 214 (46.9%) |
| **ICU admission, *N* (%)** | 46 (10.4%) |
| **Destination after discharge, *N* (%)** | |
| Home | 378 (84.4%) |
| Rehab facility/Long-term care | 70 (15.6%) |
| **Complications during hospital stay, *N* (%)** | 250 (55.0%) |
| **Severity scale, *N* (%)** | |
| 1 (H, no oxygen required) | 136 (30.2%) |
| 2 (H, $O_2$ max Venturi Mask) | 224 (49.7%) |
| 3 (H, HFNC or CPAP or NIV) | 91 (20.2%) |

current symptoms, i.e., those present in the previous 14 days, except for gastrointestinal symptoms whose presence had to be reported during the 12 months period (from discharge to administration of the questionnaire).

Patients who died during the 12 months from hospital discharge were identified through Regional Health Care System informatic tool.

Questionnaires were administered *via* telephone interviews run by a trained medical investigator. If the subject was unreachable at first call, three attempts were made.

Answers to the questionnaire were filled into the REDCap data capture tool.

The study protocol was approved by the institutional review board (Ethics Committee of Milano Area 2, number 556) and informed consent was provided by all study participants. All procedures were in accordance with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

## Statistics

The study population was described with means and standard deviations for continuous variables, and with frequencies and percentages for categorical variables. Characteristics of patients with and without interview were compared using Pearson's chi-squared for categorical variables and *t*-test for the continuous ones.

Logistic regressions were fitted to find which baseline and COVID-19 characteristic were associated with presence of the following outcomes at 12 months: health status deterioration, severe medical problems, and high frequency of sequelae. We first calculated different models corrected for age, sex, number of comorbidities, and ethnicity. Subsequently all significant ($p < 0.05$) variables were included in corrected models.

Statistical analyses were performed using Stata v.15.1 (Stata Corp, College Station, TX). In this study, we followed the strengthening the Reporting of observational studies in epidemiology (STROBE) guidelines (see **Supplementary Material**).

## RESULTS

A total of 776 patients admitted to hospital because of COVID-19 and discharged alive from February 28 to May 31, 2020 were included in the analysis. Forty-four subjects (5.7%) died during the 12 months after discharge and 276 (35.6%) subjects were unreachable or refused to join the telephone interview. Four hundred and fifty-six individuals completed the questionnaire (58.8%; **Figure 1**).
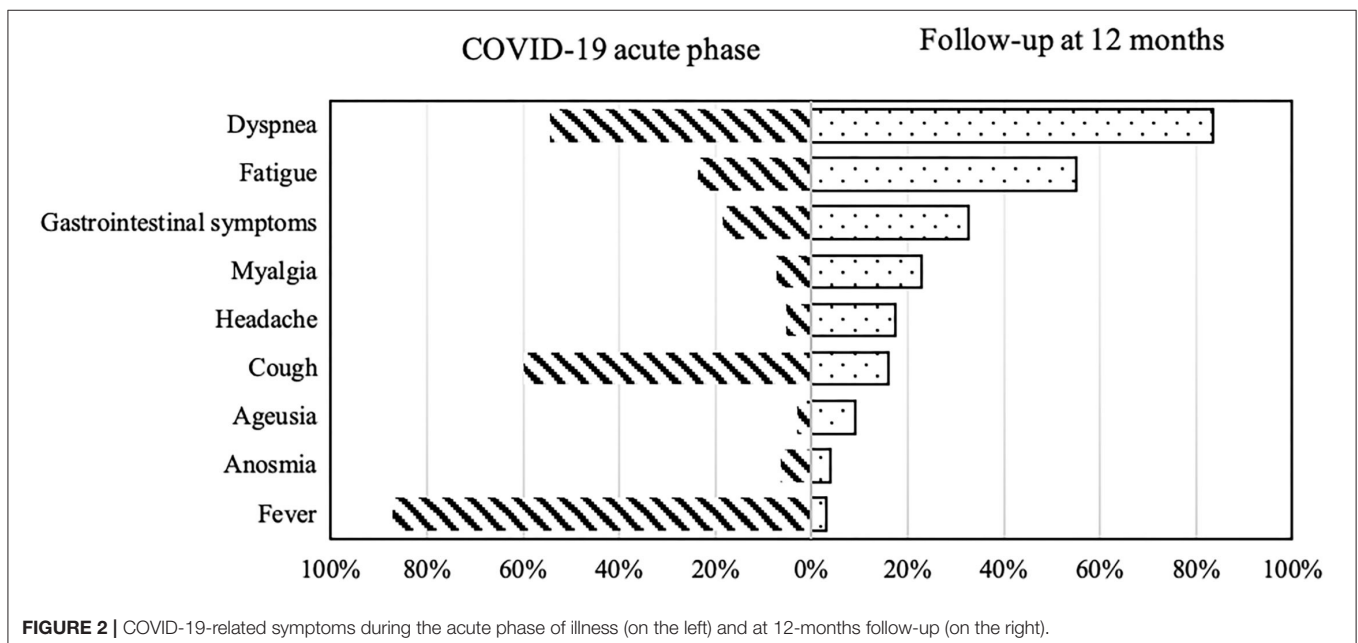
**Table 1** summarizes the demographic and clinical characteristics of the study population. Patients were mainly of Caucasian origin (87.7%) and male (63.2%). Mean age was 59.4 years (SD 14.1).

Nearly 60% of patients had at least one comorbidity with the 14.4% suffering from more than three comorbidities. Cardiovascular diseases were the most common health problem present (42.2%).

The median length of hospital stay was 12.0 (IQR 6.0–21.0) days and 46 subjects (10.4%) were admitted to the intensive care unit (ICU).

One hundred and thirty-six (30.2%) participants did not require oxygen support during their hospital stay, 224 (49.7%) required it through nasal cannula or Venturi mask and 91 (20.2%) needed high-flow oxygen support through HFNC, CPAP or non-invasive ventilation (**Table 1**).

We compared participants who joined the follow-up to those who were unreachable or refused to join the survey. In the latter



**FIGURE 2 |** COVID-19-related symptoms during the acute phase of illness (on the left) and at 12-months follow-up (on the right).

group mean age was significantly higher (64 years vs. 59 among the participants, $p < 0.001$). Patients who were unreachable or refused telephone interview were more frequently discharged to rehabilitation centers/nursing homes ($p < 0.001$), had a higher number of comorbidities ($p = 0.074$) and, specifically, had more neurologic ($p = 0.039$) or metabolic ($p = 0.018$) comorbidities, and suffered more from acute complications during the hospitalization in COVID-19 unit ($p = 0.044$) (**Supplementary Table S1**).

## Patient-Reported Symptoms and Sequelae at 12 Months

Overall, 91.7% of patients reported at least one persisting symptom/sequela 12 months after hospital discharge and 69.6% reported two or more symptoms.

Respiratory problems were the most reported symptoms/sequelae with 71.7% of participants suffering from exertional dyspnea (score $\geq 1$ in mMRC scale), while 12.5% of participants reported dyspnea at rest (**Figure 2**).

Other most common symptoms reported at 12 months were fatigue (54.6%), gastrointestinal symptoms (altered bowel habits and bloating) (32.8%), sleep disorders (32.4%), anxiety (23.2%), and myalgias (22.3%; **Table 2**).

When comparing participants with 0–1 persisting symptoms at 12 months to those who reported $\geq 2$ symptoms, predictors of $\geq 2$ symptoms reported were: female sex (aOR = 2.44, 95% CI: 1.45–4.1, and $p = 0.001$) and 1–2 comorbidities (aOR = 2.24, 95% CI: 1.32–3.8, and $p = 0.009$), while older age ($\geq 65$ years old) showed a protective role (aOR = 0.43, 95% CI: 0.19–0.99, and $p < 0.027$; **Figure 3**).

When all significant ($p < 0.05$) variables were included in a general multivariable model, female sex, older age, and the presence of 1–2 comorbidities at baseline were confirmed as independent predictors of $\geq 2$ symptoms (**Supplementary Table S2**).

About 81% patients reported at least one disabling sequela (dyspnea at rest, exertional dyspnea, myalgia, and limitations on daily life activities) and 30.1% reported two or more.

Female sex (aOR = 2.62, 95% CI: 1.64–4.17, and $p < 0.001$), 1–2 comorbidities at baseline (aOR = 1.19, 95% CI: 1.12–3.27, and $p = 0.048$), number of symptoms in the acute phase (aOR = 1.2, 95% CI: 1.02–1.41, and $p = 0.031$), presence of respiratory symptoms (aOR = 2.05, 95% CI: 1.07–3.93, and $p = 0.031$) and neurologic symptoms (aOR = 1.98, 95% CI: 1.04–3.76, and $p = 0.038$) during COVID-19 hospitalization were associated to the presence of two or more disabling sequelae (**Supplementary Table S3**).

## General Health Status at 12 Months

Self-perception of general health 12 months after COVID-19 discharge was poor (a score $< 5$) in 2.4% of patients whereas 31.7% reported an excellent health status (a score $\geq 9$) (**Figure 4**).

When comparing post- to pre-COVID19 scores of self-perception of general health, 55.5% of participants reported a lower score after COVID-19, while 44.5% described a stable or improved score (38.3% stable health status, 6.2% an improved health condition).

**TABLE 2 |** Persistent symptoms and sequelae investigated among patients with COVID-19, discharged alive and who agreed to follow up interview ($n = 456$).

| General health status after COVID-19, N (%) | Value |
| --- | --- |
| <5 | 11 (2.42%) |
| 5–6 | 65 (14.32%) |
| 7–8 | 234 (51.54%) |
| 9–10 | 144 (31.72%) |
| **Severe medical issues after COVID-19, N (%)** | 88 (19.38%) |
| ER admission | 47 (10.35%) |
| Hospitalization | 30 (6.61%) |
| - Respiratory problems | 5 (1.10%) |
| - Neurologic problems | 1 (0.22%) |
| - Psychiatric problem | 0 |
| - GI problems | 1 (0.22%) |
| - Hepatologic problems | 2 (0.44%) |
| - Cardiovascular problems | 17 (3.72%) |
| - Other | 15 (3.30%) |
| Other | 15 (3.30%) |
| **Respiratory symptoms, N (%)** | 57 (12.5%) |
| Dyspnea at rest ($\geq 5$) | |
| Exertional dyspnea | |
| - mMRC 0 | 128 (28.32%) |
| - mMRC $\geq 1$ | 324 (71.68%) |
| Cough | 73 (16.08%) |
| **GI symptoms, N (%)** | 149 (32.75%) |
| Altered gastrointestinal function (altered bowel habits and bloating) | |
| **Other symptoms, N (%)** | 18 (3.96%) |
| Smell disorder (<5) | |
| Taste disorder (<5) | 13 (2.86%) |
| Memory disorder (<5) | 15 (3.47%) |
| Fatigue | 230 (54.63%) |
| Headache | 73 (17.38%) |
| Sleep difficulties | 147 (32.38%) |
| Decreased appetite | 34 (7.49%) |
| Limitations to daily activities (limitations to daily activities + troubled walking) | 69 (16.35%) |
| Anxiety ($\geq 5$) | 104 (23.16%) |
| Myalgia | 94 (22.27%) |

Predictors significantly associated to health impairment were female sex (aOR = 2.08, 95% CI: 1.36–3.18, and $p = 0.001$), cardiovascular comorbidities (aOR = 1.85, 95% CI: 1.05–3.24, and $p = 0.032$), and a longer length of hospital stay (**Figure 4**).

When all significant ($p < 0.05$) variables were included in a general multivariable model, female sex, and hospitalization length remained as independent predictors of health impairment (**Supplementary Table S4**).

## Significant Medical Problems After Hospital Discharge

Overall, 19.4% of participants accessed to health care resources during the 12 months after discharge, including: access to ER (10.6% of patients) and need of hospitalization (6.6% of patients; **Table 2**).

A longer hospital stay during COVID-19 was associated to a higher incidence of significant medical problem after discharge (adjusted aOR = 1.02, 95% CI: 1.003–1.05, and $p = 0.023$) (**Supplementary Table S5**). No other characteristic was related to presence of significant problem during 12 months after hospital discharge.

## DISCUSSION

In the present study, we showed that ~90% of individuals admitted to hospital for COVID-19 still presents self-reported symptoms 12 months after discharge being respiratory symptoms and fatigue the most common reported sequelae.

To our knowledge, this is one of the largest multicentric and prospective studies on long COVID-19 among patients hospitalized with COVID-19 and followed up systematically after 12 months.

In comparison with other studies, we recorded a very high rate of sequelae. Notably, many of these studies included a large proportion of non-hospitalized patients (4, 6) and others excluded patients who required intubation/mechanical ventilation or reported comorbidities at baseline (11).

In our study, the high rate of COVID-19 patient-reported symptoms/sequelae can be also explained by the large number of areas covered by the survey: beyond respiratory symptoms and fatigue, patients frequently reported systemic symptoms, sleep disorders, and psychological distress.

Moreover, the approach based on subjects' perception we used in this study (telephone interview) and the psychological
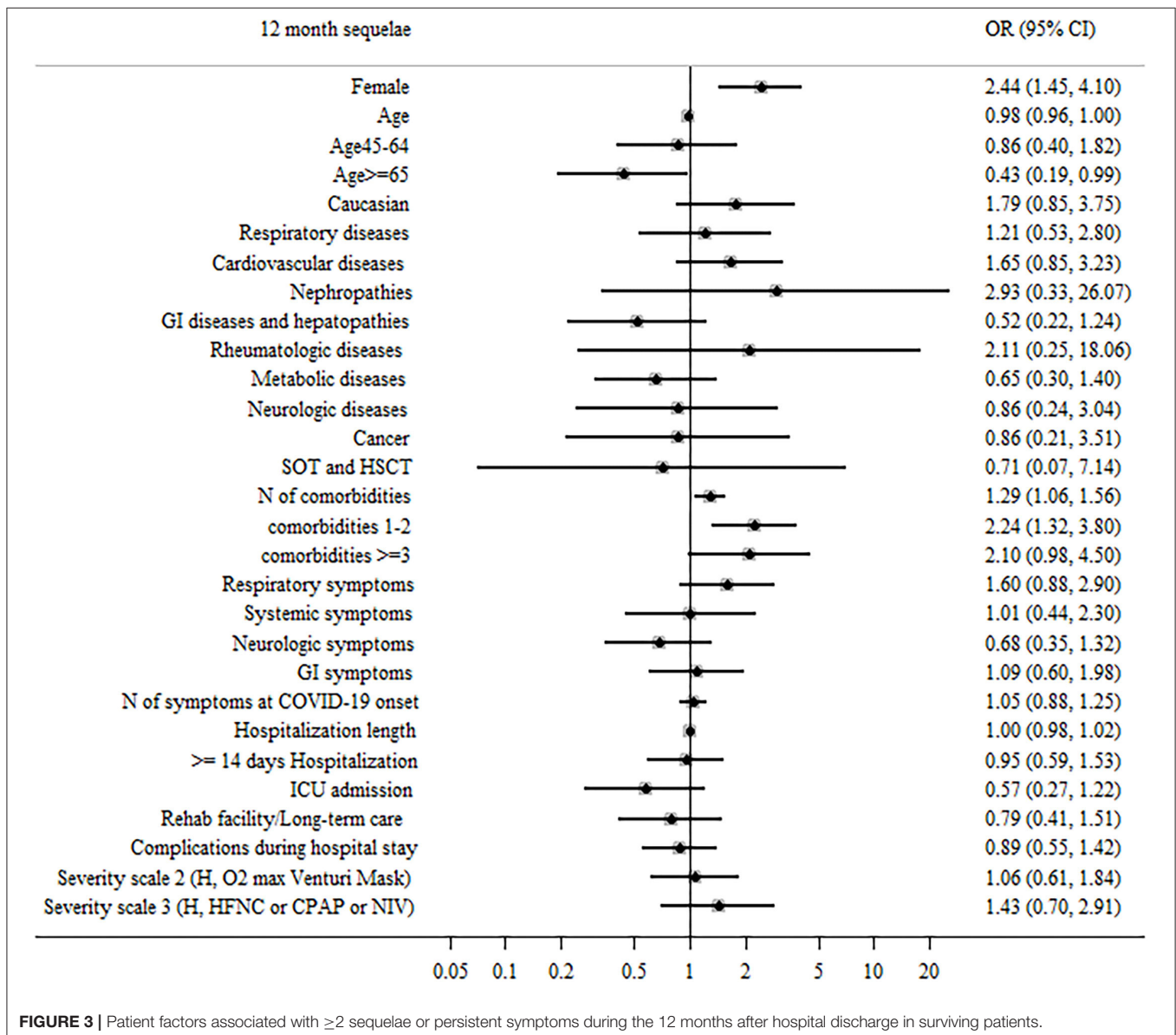


| 12 month sequelae | OR (95% CI) |
|---|---|
| Female | 2.44 (1.45, 4.10) |
| Age | 0.98 (0.96, 1.00) |
| Age45-64 | 0.86 (0.40, 1.82) |
| Age>=65 | 0.43 (0.19, 0.99) |
| Caucasian | 1.79 (0.85, 3.75) |
| Respiratory diseases | 1.21 (0.53, 2.80) |
| Cardiovascular diseases | 1.65 (0.85, 3.23) |
| Nephropathies | 2.93 (0.33, 26.07) |
| GI diseases and hepatopathies | 0.52 (0.22, 1.24) |
| Rheumatologic diseases | 2.11 (0.25, 18.06) |
| Metabolic diseases | 0.65 (0.30, 1.40) |
| Neurologic diseases | 0.86 (0.24, 3.04) |
| Cancer | 0.86 (0.21, 3.51) |
| SOT and HSCT | 0.71 (0.07, 7.14) |
| N of comorbidities | 1.29 (1.06, 1.56) |
| comorbidities 1-2 | 2.24 (1.32, 3.80) |
| comorbidities >=3 | 2.10 (0.98, 4.50) |
| Respiratory symptoms | 1.60 (0.88, 2.90) |
| Systemic symptoms | 1.01 (0.44, 2.30) |
| Neurologic symptoms | 0.68 (0.35, 1.32) |
| GI symptoms | 1.09 (0.60, 1.98) |
| N of symptoms at COVID-19 onset | 1.05 (0.88, 1.25) |
| Hospitalization length | 1.00 (0.98, 1.02) |
| >= 14 days Hospitalization | 0.95 (0.59, 1.53) |
| ICU admission | 0.57 (0.27, 1.22) |
| Rehab facility/Long-term care | 0.79 (0.41, 1.51) |
| Complications during hospital stay | 0.89 (0.55, 1.42) |
| Severity scale 2 (H, O2 max Venturi Mask) | 1.06 (0.61, 1.84) |
| Severity scale 3 (H, HFNC or CPAP or NIV) | 1.43 (0.70, 2.91) |

**FIGURE 3 |** Patient factors associated with ≥2 sequelae or persistent symptoms during the 12 months after hospital discharge in surviving patients.

**FIGURE 4 |** Patient factors associated with health status difference after 12 months—before COVID-19.
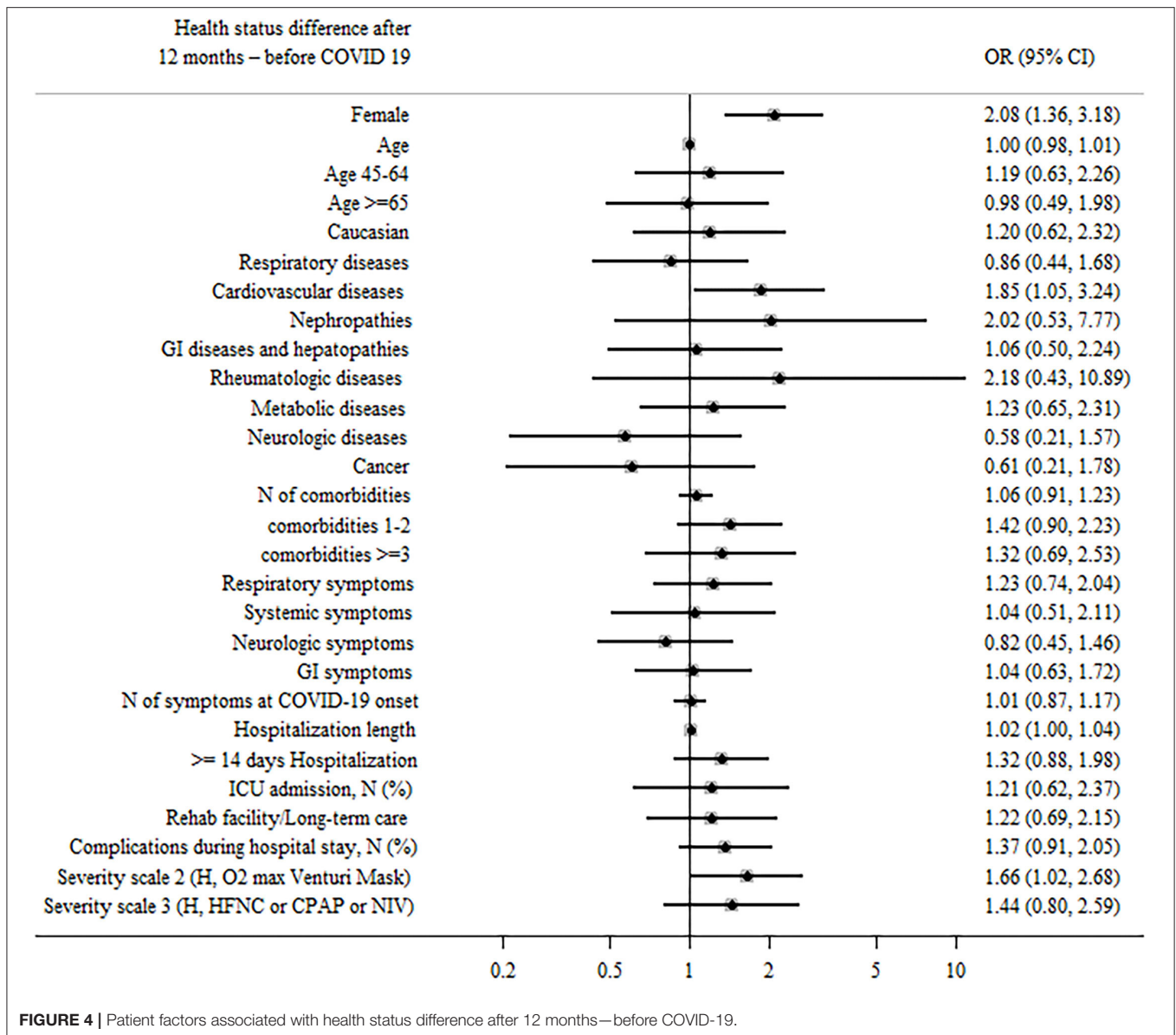
effects of the subsequent and concurrent COVID-19 waves could overestimate the presence of persisting symptoms.

As confirmed by other authors, female sex, and comorbidities were strongly related to long-COVID19 syndrome (4–6, 9, 12, 14, 17, 20, 21).

In order to explain the correlation between female sex and long COVID-19, physiological and social factors have been reported as possible drivers (15, 22). Nevertheless, Wu et al. (11) demonstrated that female sex strongly predicts impaired DLCO (diffusion lung capacity for carbon monoxide) at 12 months after discharge, suggesting that a physio-pathological process might be present. Moreover, Seeßle et al. proposes a potential role of autoimmunity disorders as co-factor in long COVID incidence and, if proven, it could partially explain the female predisposition to such a syndrome.

Interestingly, and in sharp contrast with other studies (6, 9, 23), age seems to have a protective role on self-perception of symptoms/sequelae after 12 months. A UK study on long COVID-19 supported this finding, indeed they reported that the prevalence of self-reported sequelae was greatest in people aged 35–69 years (24). It is possible that younger patients dedicate more attention to possible signs of health impairment (22), they are probably more reliable in the telephone interview and, at present, we cannot exclude that the development of long COVID could be secondary to an altered immune response possibly more pronounced in younger individuals.

In our study, more than 50% of patients referred health impairment after COVID-19. Interestingly, those subjects frequently present cardiovascular comorbidities. Therefore, the pre-existence of a cardiovascular disease might be a predictive

factor of a harder rehabilitation probably because of the effect of SARS-CoV-2 pneumonia on the cardiovascular system (25).

Interestingly, our findings show that the severity of acute COVID-19 (ICU stay, severity scale, and complications during hospitalization) does not have a significant impact on long COVID-19.

Thus far, available findings on long COVID-19 incidence do not differ so much between non-hospitalized subjects and hospitalized ones (6, 9, 17, 18). This data, shared by several groups, deserves attention and could be an interesting starting point for further analysis.

As experienced in many other contexts during the present pandemic, most studies dealing with post-COVID-19 have employed surveys by telephone call or mobile Apps (5, 6, 9, 16–18, 26, 27).

In our study, nearly 50% refused the survey or were not reachable but, unfortunately, we do not know the correct proportion of the two sub-population. Those people were fragile patients, older, and/or hosted in long-term rehabilitation centers.

In some studies, subjects with expected communication impairment were excluded (12, 26) allowing authors to be more selective and, consequently, the percentage of reported COVID-19 sequelae resulted lower. In conclusion, our findings are probably more representative of a younger and heathier population while fragile subjects are underrepresented in our study and in all similar ones. Targeted studies are needed.

Our study has several limitations. First, the absence of a control group and of an intermediate follow up time point makes it difficult to highlight improving or worsening trend.

Second, by focusing on hospitalized patients, symptoms reported after 12 months could be attributable to either COVID-19 or by the hospitalization, making it difficult to identify the direct consequence of COVID-19. Third, telephone interviews did not permit any objective measures of patient symptoms or signs but, conversely, self-reported symptoms could represent a selection tool to identify those patients who may benefit from an outpatient assessment.

By contrast, some strengths are evident. This is one of the few available prospective studies on COVID-19 follow-up which evaluated health status of a large and homogenous cohort of previously hospitalized patients at 12 months after discharge in Lombardy, one of the most affected regions in Europe during the first wave.

The questionnaire, within the limits of its structure, allowed to investigate many areas of one's health status.

Moreover, all data were collected prospectively, both during acute COVID-19 and during follow up in order to avoid possible bias during retrospective collection of hospitalization documents.

To conclude, in this study we highlighted the existence of a long COVID-19 pandemic lasting 12 months after hospitalization and emphasize the need to implement public-health strategies to manage this condition. Future studies are likely to clarify the chronic nature of long-COVID-19 and, consequently, the need for large-scale economic investments in terms of public health and social policies.

## DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

## ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Ethics Committee of Milano Area 2, number 556. The patients/participants provided their written informed consent to participate in this study.

## COVID-19 NETWORK" WORKING GROUP

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AC: conceptualization, data curation, and original draft writing. GV: original draft writing and data curation. GB: data curation and investigation. AN: conceptualization and methodology. MT: conceptualization, methodology, and formal analysis. AGa: methodology and formal analysis. AM: conceptualization and supervision. MM, CC, PBr, PBo, and MC: review, editing, and investigation. AGo: validation and supervision. AB: conceptualization, validation, and supervision. All authors contributed to the article and approved the submitted version.

## SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fmed.2022.834354/full#supplementary-material

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