Incidence of long Covid-19 in people with previous SARS-Cov2 infection: a systematic review and meta-analysis of 120,970 patients

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Abstract

Background: The long-term consequences of the coronavirus disease 19 (COVID-19) are likely to be frequent but results hitherto are inconclusive. Therefore, we aimed to define the incidence of long-term COVID signs and symptoms as defined by the World Health Organization , using a systematic review and meta-analysis of observational studies.

Methods: A systematic search in several databases was carried out up to 12 January 2022 for observational studies reporting the cumulative incidence of long COVID signs and symptoms divided according to body systems affected. Data are reported as incidence and 95% confidence intervals (CIs). Several sensitivity and meta-regression analyses were performed.

Findings: Among 11,162 papers initially screened, 196 were included, consisting of 120,970 participants (mean age: 52.3 years; 48.8% females) who were followed-up for a median of six months. The incidence of any long COVID symptomatology was 56.9% (95%CI: 52.2-61.6). General long COVID signs and symptoms were the most frequent (incidence of 31%) and digestive issues the least frequent (7.7%). The presence of any, neurological, general and cardiovascular long COVID symptomatology was most frequent in females. Higher mean age was associated with higher incidence of psychiatric, respiratory, general, digestive and skin conditions. The incidence of long COVID symptomatology was different according to continent, age and follow-up length.

Interpretation: Long COVID is a common condition in patients who have been infected with SARS-CoV-2,regardless of the severity of the acute illness, indicating the need for more cohort studies on this topic.

Key words: COVID-19; long COVID; systematic review, cohort, SARS-CoV-2.

Introduction

Since the beginning of the COVID-19 pandemic on 8 March 2020, more than 500 million cases of SARS-CoV-2 infection have been reported worldwide with a daily global increase of approximately 500,000 cases per day.[1] While global health strategies, vaccines, antivirals and new monoclonal antibodies have significantly reduced COVID-19 mortality and severe illness, long consequences after the acute phase of the disease remain an unresolved issue.

During the first pandemic wave, several articles highlighted the possible medium-to long-term devasting consequences of SARS-CoV2 infection, for patients and healthcare systems [2, 3]. Article conclusions were based on follow-up studies of people who had coronavirus infections including SARS-CoV-1 in 2003 and MERS-CoV in 2012 [4, 5] and who, after months and years of follow-up, still had symptoms and signs linked to previous infection. There is an increasing body of global literature reporting the long-term sequelae of patients with previous SARS-CoV-2 infection.[2, 3] Reported symptoms vary and include, for example, dyspnea, hair loss, anxiety, depression, asthenia, fatigue and loss of appetite.[2, 3]

Furthermore, the terminology relating to long COVID in the literature is not standardized. Researchers have used different terms to describe the prolonged symptoms following COVID-19 disease, for example: Long COVID, Long-haulers, Post-acute COVID-19 syndrome, and Chronic COVID-19. Moreover, different time cut-offs have been used (from 2-3 weeks to months after COVID-19).[4] In October 2021, the World Health Organization (WHO) defined the long COVID as "a condition that occurs in individuals with a history of probable or confirmed SARS-CoV-2 infection, usually 3 months from the onset of COVID-19 with symptoms that last for at least 2 months and cannot be explained by an alternative diagnosis". [5] The real number of people living with long COVID is unknown, as well as the real incidence and which organs or systems are most frequently involved. Knowing the real incidence of long COVID is critical for addressing the problem and examining possible therapeutic approaches, preventative efforts, and global health policy. The

definition and inclusion criteria of previous studies on long/post COVID conditions may have masked the true burden. However, to explain the real incidence without the confounding influence of different follow-up lengths, we used the WHO definition. Importantly, our study is the first to include exclusively papers using the WHO proposed period to define long COVID.[6-9]

Given this background, we carried out a systematic review and meta-analysis regarding the incidence of signs and symptoms typical of long COVID, with a minimum follow-up time longer than at least 3 months and according to the WHO definition.

Materials and methods

Protocol registration

This study was conducted following the recommendations in the Cochrane handbook for systematic literature reviews to conduct the screening and selection of studies.[10] The original protocol was registered in https://osf.io/5b2tv.

This systematic review and meta-analysis was reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, updated version to 2021.[11]

Research question

The research question for this systematic review is: "What is the incidence of long COVID signs and symptoms?" To guide the identification of adequate keywords to build search strategies to search bibliographic databases, the research question was framed into the PICO(S) (Participants, Intervention, Comparison, Outcome, Study design) format: (P) laboratory confirmed and/or clinically diagnosed COVID-19: long COVID was defined as the presence of signs and/or symptoms after three months and lasting at least two months and that cannot be explained by other medical conditions, in agreement with the indications of the WHO [5]; (I): none; (C) none; (O) incidence of signs and symptoms of long COVID; (S) observational studies.

Information sources and search strategies

We searched Medline (via Ovid) and Web of Science from database inception to 12 January 2022, through OVID. The search for individual studies in these bibliographic databases was supplemented by a manual search of references included in relevant systematic reviews already published regarding this topic.

Considering the main PICOS elements, we built the following search strategy for Medline: "("COVID-19" OR "Novel Coronavirus–Infected Pneumonia" OR "2019 novel coronavirus" OR

“2019-nCoV” OR “SARS-CoV-2”) AND (“lingering symptoms” OR “persistent symptoms” OR “long-term symptoms” OR "long-term Covid" OR “long-term” OR “long term” OR “long”)”. Then we adapted the search strategy for Web of Science.

The management of potentially eligible references was carried out using the Rayyan website (https://www.rayyan.ai/).

Eligibility Criteria

Inclusion criteria comprised the following: (1) observational studies (case-control, cohort, longitudinal studies); (2) studies that investigated the diagnosis of long COVID according to the criteria mentioned previously. ; (3) presence of long COVID for at least 12 weeks.[5] Only articles written in English were included.

Studies with a follow-up shorter than 12 weeks or with an unclear follow-up, case series and case reports were excluded.

Study selection

We followed the recommendations reported in the Cochrane handbook for Systematic reviews to select studies that were finally included in this review.[10] The selection of the articles was performed independently by six authors (OT, AB, LD, DFB, RB, VG), in couples. The agreement within the couples, evaluated with the K was 0.85 in couple 1, 0.81 in couple 2, and 0.86 in couple 3. Consensus meetings were held with all reviewers to discuss the studies for which divergent selection decisions were made. Two additional senior members (NV, FDG) of the review team were involved, when necessary. The studies selection process involved, first, a selection based on title and/or abstracts, then a selection of studies retrieved from this first step based on the full-text manuscripts.

Data collection and data items

We collected the following information: data regarding the identification of the manuscript (e.g., first author name and affiliation, year of publication, journal name, title of the manuscript), data on the characteristics of the population considered (e.g., sample size, mean age, location, gender, etc.), setting (e.g., hospital, intensive care unit, etc.), method of follow-up visit, follow-up in months, type of diagnosis of COVID-19, and signs and symptoms recorded during the follow-up period. These data were collected using a standard data extraction form. The data extraction was carried out independently by the six authors, in couples, with one author for each couple extracting the data and the other checking, with the senior authors checking the quality of the data extraction.

Risk of bias evaluation

The Newcastle-Ottawa Scale (NOS) was used to assess the study quality/risk of bias.[12] The NOS assigns a maximum of 9 points based on three quality parameters: selection, comparability, and outcome. The evaluation was made by one author and checked by another, independently. The risk of bias was then categorized as high (<5/9 points), moderate (6-7), or low (8-9).[13] The investigators solved any discrepancies by jointly re-assessing an article (NV, AB and FDG).

Data synthesis

Signs and symptoms were grouped into anatomical clusters, i.e., neurological, dermatological, and psychiatric conditions. The cumulative incidence of symptoms and 95% confidence intervals (CIs) were estimated using a meta-analysis, under a random-effect model.[14] Heterogeneity between estimates was assessed using the I^2 statistic. In case of an I^2 over 50% a series of meta-regression analyses (taking as moderators if the participants were hospitalized, the percentage of females, and the mean age of the sample size) was conducted. Several sensitivity analyses (continent, mean age, using the WHO classification in children, adults, older people [15], follow-up period, stayed in intensive care unit, hospitalized, type of follow-up, and risk of bias) were also conducted.[16]

Moderators and strata were chosen based on clinical judgment. Publication bias was assessed by visually inspecting funnel plots and using Egger bias test, with a p-value <0.05 indicative of possible publication bias.[17]

All analyses were performed using “metaprop”, a command available in STATA 14.0

Results

Search results

As shown in **Supplementary Figure 1**, among 11,167 records initially screened, 346 full-texts were retrieved, with a final selection of 196 articles (see the list in **Supplementary Table 1**).

Descriptive characteristics

As shown in **Supplementary Table 2**, the 196 studies included 120,970 participants (median per study: 190 participants, range: 17 to 31,013) with a mean age of 52.3 years. The participants were more frequently males (percentage of females=48.8%) ($p<0.0001$, Chi Square test). The majority of the studies took place in Europe (n=126, 64.3%), and used the polymerase chain reaction for the identification of SARS-CoV-2 (n=185, 94.4%). Furthermore, most studies considered only hospitalized patients (n=128, 65.3%) including people admitted to intensive care unit (n=101, 51.5%). Follow-up with a median of six months (range: 3-12 months) was predominantly conducted via outpatients' visits (n=86, 43.9%). Among the 196 articles included, only two reported data on the vaccination status against SARS-CoV-2.

Risk of bias

As reported in **Supplementary Table 2**, the risk of bias, evaluated with the NOS, was overall low in 129 (65.8) studies and moderate for the other works included. No study was at high risk of bias evaluated as a NOS score less than 5.

Incidence of long COVID signs and symptoms

Figure 1 and **Table 1** show the incidence of long COVID signs and symptoms. In the 196 studies included, comprising 120,970 people, the cumulative incidence of any long COVID symptomatology was 56.9% (95%CI: 52.2-61.6).

By grouping into anatomical clusters, we observed that in 156 cohorts (106,284 participants), the overall incidence of neurological signs/symptoms was 19.7% (95%CI: 17.4-22.1). In this cluster the most frequent sign/symptom was difficulty in concentrating (14.6%), and the least frequent was seizures (0.6%). The incidence of headache, taste and smell disorders, cognitive impairment, memory deficits, dizziness, and cramps were over 10%. Psychiatric conditions affected 20.3% of the participants (95%CI: 17.4-23.3), in 117 cohorts and for a total of 65,156 people. All the four signs and symptoms considered in this cluster (post-traumatic stress disorder [PTSD], depression, sleep disorder, anxiety) had an incidence over 10%.

Respiratory conditions affected approximately one quarter of the participants with long COVID (154 cohorts, 101,849 participants, 24.5%; 95%CI: 21.3-27.9). Among the respiratory signs or symptoms, the most frequent was dyspnea (142 cohorts, 97,065 participants, incidence of 24.1%). Mobility impairment disorders affected 13.7% (10.6-17.2) of the 19,747 participants included in 34 different cohorts, with a decreased exercise tolerance (incidence of 16.6%), being the most frequent. Heart conditions were also particularly frequent, affecting 11.0% of the participants. Palpitations were identified in 11.2% of the 32,784 participants considered. Among the clusters considered, digestive (incidence: 7.7%; 95%CI: 6.4-9.1) and skin disorders (incidence: 8.5%, 95%CI: 6.8-10.3) were the least represented.

Finally, general signs and symptoms, i.e., not includible in any of the clusters cited before, affected approximately one third of the 113,802 people included in 166 cohorts. Of particular interest, fatigue affected 31.4% (95%CI: 27.1-35.8) of the people included, being the most common symptom in the general cluster.

Meta-regression analyses

Considering the incidence of signs and symptoms clusters, all were affected by a high heterogeneity (I^2=99%). Therefore, we tried to explain the heterogeneity observed using a series of meta-regression and sensitivity analyses.

Supplementary Table 3 shows the meta-regression analyses. Higher percentage of females moderated the onset of any, neurological, general and cardiovascular long COVID symptomatology. Each increase in one percent of females in the sample size was associated with a small increase in any long COVID symptomatology (beta=0.02±0.01; p=0.047), neurological (beta=0.003±0.0009; p=0.001), general (beta=0.02±0.01; p=0.05), and cardiovascular (beta=0.003±0.0009; p=0.001) signs and symptoms. However, this moderator explained only a small proportion of the heterogeneity of the various outcomes (less than 10%, except for cardiovascular outcomes) (**Supplementary Table 3**).

Finally, higher mean age of the cohorts included was associated with higher incidence of psychiatric (beta =0.003±0.001; p=0.007), respiratory (beta=0.004±0.001; p=0.009), general (beta =0.004±0.002; p=0.03), digestive (beta =0.002±0.0009; p=0.04) and skin conditions (beta =0.002±0.0009; p=0.02) (**Supplementary Table 3**). Again, except for the last outcome, higher mean age explained only a small proportion of the heterogeneity found in the various outcomes.

Sensitivity analyses

Supplementary Table 4 shows the cumulative incidence stratified by some potential factors, i.e., continent, mean age and follow-up. Overall, the incidence of any long COVID was significantly higher in studies carried out in Oceania (63.4%) vs. Europe (48.5%) (p for the interaction <0.0001), whilst no significant differences were observed by mean age or by follow-up. When considering neurological conditions, the incidence was, again, significantly higher in Oceania and in Europe compared to North America (with an incidence almost doubled). Moreover, the incidence of neurological conditions was significantly higher in adults than in children (p for interaction=0.03)

and in studies having a follow-up of 3 months compared to those with a longer follow-up (**Supplementary Table 4**). Similarly, psychiatric conditions affected more frequently African participants than Asians (p for the interaction <0.0001) and participants older than 60 years, with an incidence approximately four times higher than children/youth. Similarly, respiratory conditions were more frequent in Europe than in the other continents and in the studies with a follow-up of 3 months. Another point of importance is that the incidence of mobility issues was significantly higher in adults than the other ages considered and in studies having a follow-up over six months. Finally, general and cardiovascular symptomatology was higher in studies carried out in Africa than in other continents and in adults (**Supplementary Table 4**).

Finally, **Supplementary Table 5** reports the data stratified by ICU admission, hospitalization status, type of follow-up, and presence of risk of bias. Overall, patients previously admitted in ICU reported a significantly lower incidence of neurological conditions and mobility issues than their counterparts. Similarly, patients not hospitalized reported a significantly higher presence of neurological and psychiatric conditions. When considering the type of follow-up method used for evaluating long COVID symptomatology patients interviewed in person usually reported lower incidence of several long COVID signs and symptoms. Finally, considering the presence of risk of bias, we observed a significantly higher incidence of neurological, psychiatric, respiratory, cardiovascular, digestive, skin conditions and mobility issues in studies having a moderate risk of bias compared to low.

Discussion

According to the WHO definition for long COVID, we carried out a systematic review of all the studies reporting data on long COVID symptomatology including 196 studies for a total of 120,970 patients with a previous SARS-CoV-2 infection. A key finding of this study was that more than half of the patients previously having COVID-19 had some form of long COVID symptomology, further strengthening the importance of this emergent condition.

Comparing our results with those reported in three previously published systematic reviews with meta-analyses [3, 18, 19], we observed that the incidence of any sign or symptom of long COVID remained high when only including studies having a follow-up of at least three months according to the new WHO definition. [5] Respiratory symptomatology, such as dyspnea, and general signs and symptoms, such as fatigue, may affect between one quarter to one third of all long CVOID patients. Moreover, different inclusion/exclusion criteria indicated that long COVID is a long term condition that will likely be experienced over coming years and with current limited therapeutical options.[20] These findings support the idea that COVID-19 could lead to persistence of symptoms even after the end of acute infection, as has already been demonstrated for SARS-CoV-1 and MERS-CoV. In 2003, after the end of the outbreak of SARS-CoV-1, Herridge *et al.* evaluated the respiratory function of 109 survivors at 3, 6 and 12 months after discharge, reporting a relevant reduction in respiratory function and quality of life.[21] Most patients had also extrapulmonary conditions, with muscle wasting and fatigue being the most frequent, similar to long COVID.[21] In addition, Ahmed *et al*. conducted a systematic review and meta-analysis investigating persistent symptoms of both SARS-CoV-1 and MERS-COV, demonstrating that up to 6 months after discharge impaired respiratory function was present in 27% of patients, PTSD in 39%, depression in 33%, and anxiety in 30%. Moreover, a reduction in exercise capacity was noted with a mean 6-min walking distance of 461 m in the cohort of patients analyzed.[22] It is important to remark that some studies demonstrated the persistence of symptoms for several years from SARS-CoV-1 infection. In particular, Ngai *et al*. performed a respiratory function-test 2 years after discharge on 55 SARS-CoV-1 infected patients,

showing a significant impairment of diffusing capacity of the lungs for carbon monoxide (DLCO), exercise capacity and health status, with a more marked adverse impact among health care workers.[23] Moldofsky *et al.*, evaluated the neuropsychiatric disorders that occurred in SARS-CoV-1-infected patients, demonstrating that chronic fatigue, pain, weakness, depression, and sleep disturbance, were still present over a 20-months follow-up. [24] This evidence suggests that for COVID-19 we should expect similar long-term consequences.

Another result of importance of our systematic review and meta-analysis was that long COVID signs and symptoms, and particularly general, neurological, and cardiovascular symptoms, were more frequent in females than in males supporting other literature which found that females appear to be at higher risk of long COVID than males, even though females are less represented in the present systematic review. [25] Moreover, higher mean age also represents an important risk factor to develop long COVID symptoms, particularly general, psychiatric, respiratory, digestive, and skin issues indicating that long COVID could be of epidemiological importance in older people. Sudre *et al.* in a cohort of 558 patients described a greater risk for people aged over 70 years of developing ongoing symptoms. Indeed, 22% of people aged over 70 reported symptoms lasting 4 weeks or more, compared to 10% of patients aged 18 to 49 years.[26] Notably, in our systematic review, there was not an increased risk of long COVID for patients who had been hospitalized or had stayed in intensive care units, contrary to what is reported by Jovanoski *et al*., who described an increased risk of respiratory, cardiovascular, and mental health outcomes up to 6 months after discharge in patients hospitalized with severe/critical COVID-19.[27] Overall, these findings indicate that people living in the community and not hospitalized can have a similar incidence of long COVID symptomatology, demonstrating the importance of follow-up among these patients.

Furthermore, the incidence of any and general signs and symptoms was significantly higher in Oceania, whilst respiratory symptoms were more commonly reported in Europe and Africa. North America reported the lowest incidence among all categories of symptoms. Even if a definitive conclusion cannot be drawn, we can hypothesize that genetic and environmental factors can justify

these different incidences. We can also report that this difference is partially ascribable to the process of symptoms' definition and perception, and data collection across countries that could greatly vary. However, future studies are needed to better understand these significant differences. Among all the results reported in the sensitivity analyses, we would like to underline the importance of mobility issues that were more frequent in adults than in the other ages. Since mobility issues are often a precursor to disability, our meta-analysis further indicates the need to approach long COVID with non-pharmacological approaches, such as promoting physical activity.[28] When stratifying patients for mean age, it is interesting that children and adolescents presented long COVID symptoms, particularly respiratory and general symptoms: taken together, these significant findings encourage follow-up of children previously affected by COVID-19 for better understanding of the long-term sequalae of this condition.

In the opinion of the present authors, long COVID represents a major public-health problem, both because of its incidence in patients with SARS-CoV-2 infection and because of the lack of effective therapeutic strategies to date. Published literature regarding the possible treatment is still limited, and studies published until now were limited by lack of homogeneity owing to varying study designs, settings, populations, follow-up period and symptoms description. Potentially, mass vaccination and the use of new therapies aimed at rapidly reducing viral load and limiting disease progression could play a crucial role in preventing long COVID and long-term symptoms persistence, but future studies are urgently needed. In addition to characteristics of patients, the SARS-CoV-2 variant of concern involved in acute infection is often missing, but it may also play an important role in the type of symptoms that occur in long COVID.

The results of our systematic review with meta-analysis must be interpreted within its limitations. First, some long COVID symptoms may be missing because they were not identified and not investigated in patient questionnaires. This limitation determines the need to standardize questionnaires and to better define some symptoms: for example, the symptom "fatigue" may be exaggerated by some patients or underestimated by others. The use of objective and precise scales,

such as, the Visual Analogue Scale for pain or the Fatigue Assessment Scale for fatigue would facilitate harmonization of symptom descriptions. The studies included in this meta-analysis often used only self-reported information or physical examination. Second, all the outcomes were characterized by a high heterogeneity, only partly explained by our meta-regression or sensitivity analyses. These findings suggest that other factors are probably important in determining a higher or lower incidence of long COVID. Unfortunately, we were not able to explore the role of vaccinations on the incidence of long COVID: further studies are urgently needed in this sense. Another important problem is the presence of publication bias in our findings, likely owing to the choice to screen papers written only in English and the fact that only two databases were screened.[29] Finally, the maximum follow-up reported by the studies included in our systematic review was only one year. Future studies are needed regarding long-term consequences of COVID-19.

In conclusion, our systematic review and meta-analysis indicates that long COVID is a common condition in patients who have been infected with SARS-CoV-2 and often regardless of the severity of the acute illness. Therefore, more long-term studies are needed to understand the real long-term impact on quality of life, but also to develop optimal therapeutic and long COVID prevention strategies.

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Author Contributions

F.D.G. and N.V. conceived the study topic and design. A.B., L.D., D.F.B., F.D.G, O.T., V.G. and R.B. carried out the study selection and data extraction. The data were analysed by N.V. and the manuscript drafted by F.D.G, A.B. and N.V.

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Figure 1 Incidence of long COVID signs and symptoms

Table 1. Cumulative incidence of long COVID signs and symptoms

System	Number of cohorts	Total sample size	Cumulative incidence	95% CI
Any	**196**	**120970**	**56.9**	**52.2-61.6**
Neurological	**156**	**106284**	**19.7**	**17.4-22.1**
Headache	104	87599	12.4	10.5-14.4
Taste disorder (ageusia or dysgeusia)	116	62510	12.8	10.7-15.0
Smell disorder (anosmia)	117	93929	13.1	11.1-15.3
Cognitive impairment	44	21300	13.5	10.5-16.8
Memory deficits	48	18348	13.5	10.5-16.9
Difficulty concentrating	58	30380	14.6	11.7-17.9
Dizziness	46	27737	10.8	8.3-13.7
Tremors	8	4078	3.4	1.4-6.2
Seizures	4	9325	0.6	0.0-2.1
Cramps	6	790	12.0	5.2-21.0
Visual impairment	16	9963	4.6	2.5-7.2
Psychiatric	**117**	**65156**	**20.3**	**17.4-23.3**
PTSD	26	13167	13.6	8.9-19.3
Depression	74	43789	16.1	12.8-19.8
Sleep disorders	81	50757	17.8	14.8-21.0
Anxiety	85	46762	18.9	15.2-22.2
Respiratory	**154**	**101849**	**24.5**	**21.3-27.9**
Cough	108	86809	13.1	11.0-15.5
Dyspnea	142	97065	24.1	20.5-27.9
Oxygen use	4	400	4.3	2.4-6.7
Nasal congestion	36	48592	6.3	5.0-7.7
Voice change	14	10352	3.7	2.0-5.9
Mobility impairment	**34**	**19747**	**13.7**	**10.6-17.2**
Decreased exercise tolerance	12	6431	16.6	11.2-22.8
Mobility decline	19	13177	11.3	7.7-15.6
Functional impairment	10	6544	7.6	3.1-13.9
Heart	**95**	**54056**	**11.0**	**8.9-13.3**
Palpitations	55	32784	11.2	8.7-14.1
Chest pain	71	45894	10.6	8.2-13.3
Flushing	3	2349	3.1	0-11.2
Hypertension (new onset)	4	2136	6.4	1.5-14.3
Digestive	**99**	**80701**	**7.7**	**6.4-9.1**
Abdominal pain	47	61445	5.2	4.0-6.5
Diarrhea	77	72024	5.9	4.9-7.1
Vomit	40	28238	3.0	2.0-4.0
Loss of appetite	52	27034	7.1	5.2-9.4
Skin	**63**	**34224**	**8.5**	**6.8-10.3**
Rash	34	25796	4.1	2.9-5.5
Hair loss	52	28816	8.8	6.8-11.1
General	**166**	**113802**	**31.0**	**27.1-35.1**
Weight loss	16	11234	7.2	5.1-9.6

System	Number of cohorts	Total sample size	Cumulative incidence	95% CI
Myalgia	103	84678	15.5	13.0-18.3
Pain	48	28230	19.9	14.7-25.6
Flulike symptoms	1	97	16.5	9.7-25.4
Fever	45	55310	7.9	5.2-11.0
Fatigue	142	104766	31.4	27.1-35.8
Arthralgia	64	34941	15.0	11.6-18.9
Sore throat	49	63400	7.6	6.2-9.2
Sweats	9	9079	5.8	4.4-7.4
Poor QoL	7	3995	16.0	9.0-24.7
Conjunctivitis	14	7256	3.1	1.1-6.0

Data are reported as cumulative incidence with their 95% confidence intervals.

PTSD= Post-traumatic stress disorder, QoL= Quality of Life

Supplementary Table 1. List of references included in the systematic review and meta-analysis

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Supplementary Table 2. Descriptive characteristics of the studies included

Author, year	Sample size	Country	Methods for COVID19 diagnosis	Hospitalized	ICU	Follow-up (months)	Follow-up mode	Percentage females	Mean age	NOS
Abdelrahman,2021	172	Egypt	PCR	Hospital and non-hospital	No	10	Phone	65.7	42	7
Agergaard,2021	20	Denmark	PCR	Hospital and non-hospital	Yes	7	Outpatient visit	81.0	53	9
Albu,2021	41	Spain	PCR	Hospital and non-hospital	Yes	3	Outpatient visit	58.0	54	7
Anastasio,2021	379	Italy	PCR	Yes	Yes	4	Outpatient visit	54.0	56	7
Aranda, 2021	113	Spain	PCR	Yes	Yes	7	Outpatient visit	30.1	64	7
Arnold,2021	110	UK	PCR	Yes	No	4	Outpatient visit	40.0	55	7
Asadi-Pooya,2021	4681	Iran	PCR	Yes	Yes	6	Phone	47.1	52	7
Attuabi,2021	516	Denmark	PCR	Hospital and non-hospital	Yes	3	Outpatient visit	52.0	44	7

Author, year	Sample size	Country	Methods for COVID19 diagnosis	Hospitalized	ICU	Follow-up (months)	Follow-up mode	Percentage females	Mean age	NOS
August,2021	353	Germany	PCR	Yes	NA	6	Outpatient visit	56.0	54	8
Augustin, 2021	90	Germany	PCR	No	No	7	Outpatient visit	57.0	49	8
Becker, 2021	136	Switzerland	PCR	Yes	Yes	12	Outpatient visit	38.0	60	8
Bellan,2021	200	Italy	PCR	Yes	Yes	4	Outpatient visit	38.5	61	7
Bellan,2021	57	Italy	PCR	Yes	Yes	12	Outpatient visit	39.0	62	7
Bertlich,2021	43	Germany	PCR	Yes	No	6	Outpatient visit	34.0	65	7
Betschart,2021	247	Switzerland	PCR	Yes	NA	12	Outpatient visit	30.0	60	8
Blomberg,2021	91	Norway	PCR	Hospital and non-hospital	No	6	NA	53.0	46	8
Boari, 2021	183	Italy	PCR	Yes	Yes	4	Outpatient visit	41.0	58	8
Boscolo-Rizzo,2021	84	Italy	PCR	Yes	No	6	Phone	55.2	55	8
Bottemanne,2021	107	France	PCR	Yes	No	3	Outpatient visit	27.4	60	8
Bozzetti, 2021	704	Italy	PCR	Yes	Yes	6	Outpatient visit	32.0	63	8

Author, year	Sample size	Country	Methods for COVID19 diagnosis	Hospitalized	ICU	Follow-up (months)	Follow-up mode	Percentage females	Mean age	NOS
Bussiere,2021	1865	Canada	PCR	Yes	NA	4.8	in person interview	84.2	42	8
Buttery,2021	86	UK	PCR	Hospital and non-hospital	Yes	3	eletronic survey	77.0	46	6
Bylicki,2021	55	France	PCR	No	No	9	Outpatient visit	22.7	31	6
Capelli,2021	160	Italy	PCR	No	No	8	Phone	51.0	49	8
Caruso,2021	118	Italy	PCR	Yes	Yes	6	Outpatient visit	53.0	65	8
Cassar,2021	46	UK	PCR	Yes	Yes	6	Outpatient visit	41.0	55	8
Catalán,2021	76	Spain	PCR	Yes	Yes	12	Outpatient visit	38.0	62	6
Chand,2021	105	USA	PCR	Yes	Yes	7	Phone	52.0	54	6
Chaumont,2022	50	France	PCR	Yes	NA	6	Outpatient visit	40.0	66	8
Chen, 2021	715	China	PCR	Yes	Yes	7.5	Phone	48.7	69	8
Chowdhury,2021	313	Bangladesh	PCR	Yes	No	7	Phone	19.8	38	8
Clavario,2021	200	Italy	PCR	Yes	No	3	Outpatient visit	43.0	59	6

Author, year	Sample size	Country	Methods for COVID19 diagnosis	Hospitalized	ICU	Follow-up (months)	Follow-up mode	Percentage females	Mean age	NOS
Cristillo, 2021	18	Italy	PCR	Yes	No	6	Outpatient visit	26.7	65	8
Cristillo, 2022	106	Italy	PCR	Yes	No	6	Outpatient visit	27.7	63	8
Dai,2021	1415	China	PCR	Yes	No	6	Outpatient visit	50.0	48	8
Darcis, 2021	1697	Belgium	PCR	Yes	Yes	6	Outpatient visit	36.7	60	8
Darley, 2021	50	Australia	PCR	Yes	NA	8	Outpatient visit	39.0	47	7
De las Penas, 2021	199	Spain	PCR	Yes	Yes	7	Outpatient visit	39.8	52	8
De las Penas, 2021	97	Spain	PCR	Yes	Yes	7	Phone	37.9	70	8
De las Penas, 2021	435	Spain	PCR	Yes	Yes	8.5	Phone	46.5	60	8
De las Penas, 2021	264	Spain	PCR	Yes	Yes	8	Outpatient visit	46.5	61	8
De las Penas, 2021	1969	Spain	PCR	Yes	Yes	7.3	Phone	67.0	56	7
De las Penas, 2021	1593	Spain	PCR	Yes	Yes	8.4	Phone	46.5	61	8
De las Penas, 2021	1593	Spain	PCR	Yes	Yes	7	Phone	48.0	61	8
De las Penas, 2022	1969	Spain	PCR	Yes	Yes	8	Phone	45.0	61	8

Author, year	Sample size	Country	Methods for COVID19 diagnosis	Hospitalized	ICU	Follow-up (months)	Follow-up mode	Percentage females	Mean age	NOS
De las Penas, 2022	161	Spain	PCR	Yes	Yes	8	Phone	45.0	61	9
Del Brutto, 2021	1969	Ecuador	PCR	NA	NA	18	Outpatient visit	63.0	63	6
Dennis, 2021	1142	UK	PCR	Hospital and non-hospital	No	5	Outpatient visit	70.6	44	6
Diaz Fuentes, 2021	50	USA	PCR	Yes	Yes	3	Outpatient visit	53.0	60	8
D'souza,2021 (only abstract)	201	India	PCR	Yes	NA	6	Outpatient visit	NA	NA	6
Du,2022	111	China	PCR	Yes	No	6	Outpatient visit	38.0	54	8
Elkan, 2021	132	Israel	PCR	Yes	No	9	eletronic survey	56.0	58	8
Eloy,2021	19	France	PCR	Yes	Yes	6	eletronic survey	37.0	61	8
Evans,2021	66	UK	PCR	Yes	Yes	6	mixed	69.0	58	9
Fang, 2021	3060	China	PCR	Yes	Yes	12	Phone	52.1	68	6

Author, year	Sample size	Country	Methods for COVID19 diagnosis	Hospitalized	ICU	Follow-up (months)	Follow-up mode	Percentage females	Mean age	NOS
Ferrucci, 2022	767	Italy	PCR	Yes	Yes	5	Outpatient visit	26.3	56	6
Fink, 2021	1233	Brazil	PCR	Yes	No	4.4	Outpatient visit	58.0	15	8
Forster, 2022 (abstract)	76	German	PCR	Hospital and non-hospital	NA	3	NA	NA	NA	8
Fortini, 2021	53	Italy	PCR	Yes		4	Outpatient visit	47.5	68	7
Fortini, 2022	1459	Italy	PCR	Yes	No	12	Outpatient visit	53.0	71	8
Fortunato, 2022	46	Italy	PCR	No	No	12	Phone	53.9	43	8
Froidure, 2021	17	Belgium	PCR	Yes	Yes	3	Outpatient visit	31.0	60	6
Frontera, 2021	178	USA	PCR	Yes	Yes	6	Phone	35.0	69	8
Fumagalli, 2022	126	Italy	PCR	Yes	No	12	Phone	40.0	62	8
Gaber, 2021	382	UK	PCR	No	No	4	eletronic survey	83.0	NA	7
Galal,2021	402	Egypt	PCR	Yes	Yes	6	Outpatient visit	63.7	37	8
Gamberini, 2021	138	Italy	PCR	Yes	Yes	12	Outpatient visit	27.5	64	8

Author, year	Sample size	Country	Methods for COVID19 diagnosis	Hospitalized	ICU	Follow-up (months)	Follow-up mode	Percentage females	Mean age	NOS
Garcia-Abellan,2021	430	Spain	PCR	Yes	No	6	Outpatient visit	40.0	64	6
Garrigues,2021	178	France	PCR	Yes	Yes	4	Phone	38.5	63	6
Gautam,2021	146	UK	PCR	Yes	Yes	5	Outpatient visit	37.5	56	8
Gerard,2021	120	France	PCR	Yes	Yes	6	Outpatient visit	45.8	59	6
Gherlone,2021	200	Italy	PCR	Yes	Yes	4	Outpatient visit	25.0	63	8
Ghosn,2021	288	France	PCR	Yes	Yes	6	Outpatient visit	37.0	61	8
Goertz, 2021	122	Nederland and Belgium	PCR	Hospital and non-Hospital	NO	3	Phone	85.0	47	8
Gonzales-Hermosillo, 2021	1137	Mexico	PCR	Yes	Yes	3	Phone	34.6	51	8
Gonzalez,2021	123	Spain	PCR	Yes	Yes	3	Outpatient visit	25.8	60	8
Graham,2021	2113	USA	PCR	No	No	4	mixed	70.0	43	7
Gramaglia,2021	130	Italy	PCR	Yes	Yes	4	Phone	43.6	56	8

Author, year	Sample size	Country	Methods for COVID19 diagnosis	Hospitalized	ICU	Follow-up (months)	Follow-up mode	Percentage females	Mean age	NOS
Gudziol, 2021	62	Germany	PCR	No	NA	4	Outpatient visit	58.1	62	8
Han,2021	100	China	PCR	Hospital and non-hospital	Yes	6	Outpatient visit	30.0	54	6
Haung,2022	237	China	PCR	Yes	Yes	7	Outpatient visit	60.6	57,67	6
Heightman,2022	24	UK	PCR	Yes	NA	12	mixed	56.5	50	8
Hodgson,2021	114	Australia	PCR	Yes	Yes	6	Phone	41.5	61	6
Hopkins,2021	1325	UK	Lab confirmed	No	No	6	other	74.9	40	8
Horwitz, 2021	193	USA	PCR	Yes	Yes	6	eletronic survey	40.0	62	8
Hossain, 2021	126	Bangladesh	PCR	Hospital and non-hospital	Yes	3	Phone	27.6	39	8
Houben-Wilken, 2022	2198	Netherlands	PCR	Hospital and non-hospital	No	6	eletronic survey	82.8	50	8

Author, year	Sample size	Country	Methods for COVID19 diagnosis	Hospitalized	ICU	Follow-up (months)	Follow-up mode	Percentage females	Mean age	NOS
Huang ,2021	239	Cina	Lab confirmed	Yes		6	in person interview	47.0	59	8
Huang,2021	2469	Cina	Lab confirmed	Yes	Yes	6	mixed	48.0	57	7
Ishiyama, 2021	461	Japan	PCR	Yes	Yes	3	mixed	40.0	53	8
Jacobson 2021	95	USA	PCR	Yes	NA	4	Outpatient visit	47.0	43	9
Janiri, 2021	118	Italy	PCR	Yes	Yes	3	Outpatient visit	43.6	55	6
Karaarsian,2022	381	Turkey	Lab confirmed	Yes	Yes	3	Phone	40.5	53	6
Kayaaslan, 2022	285	Turkey	PCR	Yes	Yes	5	eletronic survey	43.6	45	8
Kim, 2022	291	Korea	PCR	Hospital and non-hospital	Yes	12	eletronic survey	68.0	37	6
Kim,2021	1007	Korea	PCR	Yes		6	eletronic survey	69.7	30	8

Author, year	Sample size	Country	Methods for COVID19 diagnosis	Hospitalized	ICU	Follow-up (months)	Follow-up mode	Percentage females	Mean age	NOS
Klein, 2021	241	Israel	PCR	Yes	No	6	eletronic survey	38.0	35	8
Knight,2021	5252	USA	PCR	Yes	Yes	6	eletronic survey	47	44	8
Kozak, 2021	103	Canada	PCR	Hospital and non-hospital	Yes	3	Outpatient visit	53.0	49	8
Kyzar, 2021	223	USA	PCR	Hospital and non-hospital	Yes	8	mixed	62.5	46	8
Lavergne SM, 2021	52	USA	PCR	Yes	No	6	in person interview	71.0	53	7
Leftin Dobkin, 2021	512	USA	PCR	Yes	No	3	Outpatient visit	58.6	13	8
Lemhofer, 2021	119	Germany	PCR	No	No	3	eletronic survey	59.2	50	9

Author, year	Sample size	Country	Methods for COVID19 diagnosis	Hospitalized	ICU	Follow-up (months)	Follow-up mode	Percentage females	Mean age	NOS
Leth, 2021	29	Denmark	PCR	Yes	Yes	3	mixed	57.0	58	6
Li, 2021	365	China	PCR	Yes	Yes	6	Outpatient visit	36.9	59	6
Liang,2020	365	China	PCR	Yes	Yes	3	Outpatient visit	72.0	41	8
Liao, 2022	49	China	PCR	Yes	Yes	12	Outpatient visit	80.5	39	6
Logue, 2021	236	USA	PCR	Hospital and non-hospital	Yes	6	mixed	57.1	48	8
Lombardo, 2021	141	Italy	PCR	Hospital and non-hospital	Yes	12	Phone	54.0	53	8
Lu, 2020	76	China	PCR	Yes	Yes	3	Outpatient visit	43.3	44	8
Maestre-Muniz, 2021	303	Spain	PCR	Hospital and non-hospital	Yes	12	Phone	49.3	65	8
Malinowska, 2021	1276	Poland	PCR	Hospital and non-hospital	No	6	Phone	43.3	53	8

Author, year	Sample size	Country	Methods for COVID19 diagnosis	Hospitalized	ICU	Follow-up (months)	Follow-up mode	Percentage females	Mean age	NOS
Mantovani, 2021	1276	Italy	PCR	Hospital and non-hospital	No	6	Outpatient visit	32.4	52	7
Martinez, 2021	177	Switzerland	PCR	Yes	No	3	eletronic survey	75.4	35	8
Mazza ,2022	303	italy	PCR	Yes	Yes	12	in person interview	32.0	59	9
Mazza, 2021	60	Italy	PCR	Yes	Yes	3	Outpatient visit	33.0	58	8
McCue, 2021	543	United Kingdom	PCR	Yes	Yes	3	other	23.0	57	8
McGroder, 2021	67	USA	PCR	Yes	Yes	4	Outpatient visit	39.0	54	8
McPeake, 2021	131	United Kingdom	PCR	Yes	Yes	5	Outpatient visit	34.4	59	8
Mechi, 2021	260	Iraq	PCR	Hospital and non-hospital	NA	9	Outpatient visit	64.0	52	8

Author, year	Sample size	Country	Methods for COVID19 diagnosis	Hospitalized	ICU	Follow-up (months)	Follow-up mode	Percentage females	Mean age	NOS
Meije, 2021	192	Spain	PCR	Yes	Yes	7	Phone			7
Mendez, 2022	226	Spain	PCR	Yes	Yes	12	Phone	42.1	58	8
Menges, 2021	24	Switzerland	PCR	Hospital and non-hospital		7	eletronic survey	49.7	47	8
Messin, 2021	76	France	PCR	Yes	Yes	6	Phone	59.5	52	6
Mirfazeli, 2022	93	Iran	PCR	Hospital and non-hospital	Yes	9	Phone	42.0	50	8
Miwa, 2021	112	Japan	PCR	Yes	Yes	3	Outpatient visit	17.6	63	8
Mohamed-Hussein, 2021	294	Egypt	PCR	Hospital and non-hospital	Yes	3	mixed	58.0	43	8
Moreno-Perez, 2021	171	Spain	PCR	Hospital and non-hospital	Yes	3	Outpatient visit	47.3	62	8
Morin, 2021	431	France	PCR	Yes	Yes	4	mixed	42.1	61	8
Munblit, 2021	74	Russia	PCR	Yes	No	8.3	Phone	51.1	56	7

Author, year	Sample size	Country	Methods for COVID19 diagnosis	Hospitalized	ICU	Follow-up (months)	Follow-up mode	Percentage females	Mean age	NOS
Munblit, 2021	95	Russia	PCR	Yes	Yes	7	Phone	51.1	56	8
Naik, 2021	17	India	Lab confirmed	Yes	NA	6	Phone	30.6	42	8
Nehme, 2021	262	Switzerland	PCR	No	No	9	Phone	60.9	42	6
Nguyen, 2021	277	France	PCR	Yes	Yes	7	Phone	55.0	38	8
Nguyen, 2022	277	France	PCR	Yes	Yes	11	Phone	68.0	42	8
Noviello,2021	244	Italy	PCR	Hospital and non-hospital	NA	5	other	40.0	44	8
Nune,2021 (abstract)	2649	UK	Lab confirmed	Yes	NA	9	NA	NA	NA	8
Och, 2021	2649	Poland	PCR	Yes	Yes	6	Phone	50.6	70	8
Ong, 2021	2243	Singapore	PCR	Yes	Yes	6	Outpatient visit	24.6	44	7
Orrù,2021	629	Italy	PCR	NA	NA	3	eletronic survey	82.0	44	8
Osmanov, 2022	629	Russia	PCR	Yes	Yes	5	Phone	52.1	10	8

Author, year	Sample size	Country	Methods for COVID19 diagnosis	Hospitalized	ICU	Follow-up (months)	Follow-up mode	Percentage females	Mean age	NOS
Otte, 2021	125	Germany	PCR	No	No	6	Outpatient visit	42.3	45	6
Parente-Arias, 2021	496	Spain	PCR			3	Phone	65.0	55	8
Parry, 2021	347	India	PCR	Hospital and non-hospital	Yes	3	Outpatient visit	38.3	52	6
Pasquini, 2021	271	Italy	PCR	Hospital and non-hospital	No	4	Outpatient visit	65.4	46	8
Peghin, 2021	73	Italy	PCR	Hospital and non-hospital	Yes	6	Phone	53.4	53	6
Pelà, 2021	183	Italy	PCR	Yes	Yes	5	Outpatient visit	40.0	60	8
Peluso, 2021	507	USA	PCR	Hospital and non-hospital	Yes	3	Outpatient visit	54.5	44	8
Pérez-Gonzàlez,2022	518	Spain	PCR	Yes	No	6	other	40.0	57	8
Petersen,2020	26	Faroe Island	PCR	No	No	4	Phone	98.0	40	8

Author, year	Sample size	Country	Methods for COVID19 diagnosis	Hospitalized	ICU	Follow-up (months)	Follow-up mode	Percentage females	Mean age	NOS
Petrocelli,2021	151	Italy	PCR	No	No	6	mixed	75.0	44	8
Pilotto, 2021	81	Italy	PCR	Yes	Yes	6	Phone	30.3	65	7
Qu,2021	26	China	PCR	Yes	Yes	3	Outpatient visit	50.0	48	8
Radtke, 2021	599	USA	PCR	No	No	3	Outpatient visit	54.0	11	8
Rass, 2021	599	Austria	PCR	Hospital and non-hospital	Yes	3	Outpatient visit	49.0	56	6
Rass,2022	160	Austria	Lab confirmed	Yes	Yes	12	other	33.0	54	6
Rauch, 2021	121	Germany	PCR	Hospital and non-hospital	Yes	6	Eletronic survey	68.5	NA	8
Rivera-Izquierdo, 2022	121	Spain	PCR	Yes	No	12	other	43.0	61	6
Roge, 2021	1583	Lettonia	PCR	Yes	NA	6	Outpatient visit	44.5	10	8
Romero-Duarte, 2021	248	Spain	PCR	Yes	Yes	6	Outpatient visit	46.3	63	8

Author, year	Sample size	Country	Methods for COVID19 diagnosis	Hospitalized	ICU	Follow-up (months)	Follow-up mode	Percentage females	Mean age	NOS
Romero-Duarte, 2021	187	SPAIN	PCR	Yes	Yes	5	In person interview	46.3	63	8
Sakurada, 2022	300	JAPAN	PCR	Hospital and non-hospital	Yes	3	Outpatient visit	55.4	39	8
Schambeck, 2021	56	Switzerland	PCR	Hospital and non-hospital	NA	9	Outpatient visit	41		8
Seang, 2022	540	FRANCE	PCR	Hospital and non-hospital	NA	6	In person interview	78.0	48	7
SeeBle, 2021	1355	GERMANY	PCR	Hospital and non-hospital	Yes	12	Outpatient visit	55.2	57	8
Shoucri, 2021	135	USA	PCR	Yes	Yes	6	Outpatient visit	40.8	36	8
Simani, 2021	81	Iran	PCR	Yes	Yes	12	Phone	33.3	55	6
Sonnweber,2021	127	Austria	PCR	Yes	Yes	3	Outpatient visit	43.0	57	6

Author, year	Sample size	Country	Methods for COVID19 diagnosis	Hospitalized	ICU	Follow-up (months)	Follow-up mode	Percentage females	Mean age	NOS
Soraas, 2021	906	HONG KONG	PCR	No	No	12	In person interview	68.0	44	8
Suarez-Robles,2020	797	Spain	PCR	Yes	Yes	3	Phone	54.0	59	9
Sykes, 2021	797	UK	PCR	Yes	Yes	4	In person interview	34.3	58	6
Szekely, 2021	65	Israel	LAB CONFIRMED	Yes	NA	3	Outpatient visit	44.0	52	6
Tabacof, 2022	44	USA	PCR	Hospital and non-hospital	NA	12	In person interview	69.0	44	8
Taboada, 2021	63	Spain	PCR	Yes	Yes	6	Outpatient visit	41.0	66	6
Taquet, 2021	146	NETHERLANDS	PCR	Hospital and non-hospital	Yes	6	In person interview	55.6	46	8

Author, year	Sample size	Country	Methods for COVID19 diagnosis	Hospitalized	ICU	Follow-up (months)	Follow-up mode	Percentage females	Mean age	NOS
Terlizzi, 2021	96	USA	PCR	Yes	Yes	6	In person interview	57.3	56	8
Titze-de-Akmeida, 2022	1190	BRAZIL	PCR	Hospital and non-hospital	Yes	8	phone and in person interview	61.0	41	8
Tleyjeh,2021	267	Saudi Arabia	PCR	Yes	No	4	Phone	23.0	52	8
Tleyleh, 2021	145	USA	PCR	Hospital and non-hospital	Yes	6	phone and in person interview	33.0	52	8
Todt, 2021	31013	Brazil	PCR	Yes	Yes	3	Phone	40.2	53	7
Tosato, 2021	134	ITALY	PCR	Yes	NA	3	In person interview	38.2	73	8
Trunfio,2021	387	Italy	PCR	Hospital and non-hospital	Yes	6	Outpatient visit	44.0	56	8

Author, year	Sample size	Country	Methods for COVID19 diagnosis	Hospitalized	ICU	Follow-up (months)	Follow-up mode	Percentage females	Mean age	NOS
Ugurlu,2021	129	Turkey	PCR	Yes	NA	3	Outpatient visit	53.0		6
Vaes, 2021	386	Netherlands	PCR	Hospital and non-hospital	Yes	6	eletronic survey	82.8	50	6
Vaira, 202	91	Italy	PCR	No	No	6	eletronic survey	76.3	38	6
van der Borst, 2020	273	Netherlands	PCR	Yes	Yes	3	Outpatient visit	40.0	59	9
Vassallini, 2021	499	Italy	PCR	Yes	Yes	3	Phone	46.0	53	6
Walle-Hansen,2021	362	Norway	PCR	Yes	Yes	6	Outpatient visit	43.0	74	6
Weber, 2021	125	USA	Lab confirmed	Hospital and non-hospital	Yes	6	mixed	51.2	61	8
Weng,2021	251	China	PCR	Yes	Yes	3	Phone	44.4	NA	6
Wisnivesky, 2021	165	USA	Lab confirmed	Hospital and non-hospital	Yes	6	in person interview	54.9	50	8

Author, year	Sample size	Country	Methods for COVID19 diagnosis	Hospitalized	ICU	Follow-up (months)	Follow-up mode	Percentage females	Mean age	NOS
Wynberg, 2021	165	Netherlands	PCR	Hospital and non-hospital	Yes	3	Outpatient visit	46.0	51	8
Xiong, 2021	200	China	PCR	Yes	Yes	3	Phone	54.5	52	8
Yin,2021	104	China	PCR	Yes	Yes	6	Outpatient visit	49.6	53,51	8
Zayet, 2021	1005	France	PCR	Hospital and non-hospital	Yes	9	mixed	63.8	49	8
Zhao,2021	239	China	PCR	Yes	Yes	12	Outpatient visit	40.0	48	7

ICU= Intensive Care Unit, NA= Not Available, PCR= Polymerase chain reaction, USA = United Stades of America, NOS= Newcastle Ottawa Scale.

Supplementary Table 3. Meta-regression analysis of long COVID signs and symptoms

	Hospitalized (yes vs. no)	% of females	Mean age
Any	NS	B=0.02 (0.01) P=0.047 R2=2.2	NS
Neurological	NS	B=0.003 (0.0009) P=0.001 R2=9.2	NS
Psychiatric	NS	NS	B=0.003 (0.001) P=0.007 R2=6.7
Respiratory	NS	NS	B=0.004 (0.001) P=0.009 R2=6.0
Mobility issues	NS	NS	NS
General	NS	B= 0.02 (0.01) P=0.05 R2=2.0	B=0.004 (0.002) P=0.03 R2=3.0
Cardiovascular	NS	B=0.003 (0.0009) P=0.001 R2=14.1	NS
Digestive	NS	NS	B=0.002 (0.0009) P=0.04 R2=5.0
Skin	NS	NS	B=0.002 (0.0009) P=0.02 R2=12.6

Data are reported as Beta (B) and their standard error and correspondent p-values and adjusted R2.

NS: not significant.

Supplementary Table 4. Cumulative incidence of long COVID by continent, mean age and follow-up

	Continent						Mean age			Follow-up		
Cluster	**North America**	**Europe**	**Asia**	**South America**	**Africa**	**Oceania**	**Children Youth (0-18)**	**Adults (18-60)**	**Older (>=60)**	**3 months**	**3-6 months**	**6-12 months**
Any	48.5*** (32.2-65.0)	58.7 (53.1-64.2)	54.3 (42.3-66.1)	55.2 (31.2-78.0)	60.2 (56.9-63.4)	63.4 (57.4-69.2)	72.0 (20.0-100)	58.0 (51.8-64.1)	56.2 (47.2-65.0)	60.7 (49.5-71.4)	56.0 (48.8-63.0)	56.1 (47.5-64.5)
Neurological	15.4*** (8.8-23.4)	23.0 (20.0-26.2)	8.9 (6.8-11.2)	30.9 (22.2-40.3)	11.9 (9.4-14.7)	34.0 (18.9-49.4)	8.8* (4.0-15.1)	20.3 (17.4-23.4)	18.8 (14.5-23.6)	20.0** (13.8-26.0)	20.1 (16.4-24.2)	14.0 (12.4-15.6)
Psychiatric	19.0*** (9.8-30.4)	21.4 (17.8-25.3)	15.0 (9.2-22.0)	26.8 (15.3-40.0)	41.6 (37.8-45.6)	-	5.0** (0.0-16.1)	19.6 (16.1-23.4)	20.7 (14.8-27.3)	20.0 (12.7-28.4)	19.4 (14.9-24.2)	21.7 (18.1-25.6)
Respiratory	21.9*** (12.1-33.6)	27.0 (23.4-30.8)	17.3 (13.0-22.0)	17.3 (4.8-35.0)	26.8 (23.4-30.5)	23.3 (18.3-28.7)	17.0 (4.2-35.2)	23.6 (19.5-27.9)	26.9 (20.9-33.4)	32.6*** (23.0-43.0)	21.7 (17.3-26.4)	22.9 (17.8-28.4)
Mobility issues	17.7 (4.8-36.1)	14.2 (10.3-18.5)	9.5 (6.0-13.7)	-	-	-	4.9*** (0.9-11.5)	17.3 (13.2-21.8)	8.8 (4.3-14.6)	13.9* (5.5-25.2)	11.5 (7.0-16.8)	16.3 (12.5-20.6)
General	20.0*** (11.6-30.0)	33.6 (29.2-38.2)	28.2 (20.6-36.5)	21.6 (5.6-43.9)	53.5 (49.5-57.5)	19.6 (15.0-24.7)	10.6*** (8.5-12.8)	31.1 (26.2-36.3)	31.2 (23.7-39.3)	36.6 (27.3-46.3)*	27.8 (22.5-32.3)	32.9 (25.4-40.8)
Cardiovascular	8.6 (3.8-15.0)***	10.5 (8.3-12.9)	11.1 (7.4-15.5)	-	33.1 (29.4-36.9)	10.7 (8.9-13.3)	1.9** (0.0-5.9)	11.3 (8.6-14.3)	9.6 (6.7-12.7)	14.4 (7.3-23.4)	10.7 (7.7-13.9)	8.9 (6.8-11.2)
Digestive	6.6*** (3.3-11.0)	8.4 (6.5-10.5)	4.8 (3.2-6.6)	4.0 (2.3-6.3)	36.9 (33.1-40.8)	3.1 (0.6-8.8)	1.5 (0.0-4.2)	6.9 (5.6-8.3)	10.4 (5.7-16.3)	12.1*** (7.4-17.8)	8.4 (6.1-11.0)	4.2 (3.2-5.4)
Skin	6.2 (3.3-9.9)	8.0 (6.2-9.9)	12.5	-	8.9	-	2.1*** (1.2-3.3)	8.4 (6.3-10.8)	13.2	6.8*** (3.4-11.3)	7.9 (5.4-10.9)	10.6 (7.9-13.7)

			(6.5-20.0)		(6.5-11.1)				(7.9-19.6)			

Notes: data are reported as cumulative incidence with their 95% confidence intervals. *, **, *** indicate between sub-groups interaction with a p-value <0.05, <0.001 and <0.0001, respectively.

Supplementary Table 5. Cumulative incidence of long COVID by previous intensive care unit admission, hospitalization, follow-up mode and risk of bias.

	ICU admission		Hospitalized			Type of follow-up					Risk of bias	
Cluster	**Yes**	**No**	**Mixed**	**Yes**	**No**	**Outpatient visit**	**Mixed**	**Phone**	**Electronic survey**	**In person interview**	**Moderate**	**Low**
Any	53.6 (46.0-61.1)	51.0 (42.2-59.8)	55.7 (46.3-65.1)	51.5 (45.0-58.1)	53.0 (38.5-67.4)	53.7*** (47.8-59.7)	55.6 (44.0-67.2)	50.1 (41.6-58.6)	52.9 (34.2-71.6)	36.3 (25.7-46.8)	51.9 (43.0-60.7)	52.3 (45.6-59.0)
Neurological	18.1* (16.4-19.8)	28.2 (20.0-36.5)	25.8*** (20.6-31.0)	16.7 (15.4-18.0)	35.4 (15.5-55.4)	24.8*** (21.6-28.1)	18.7 (13.5-23.8)	17.4 (15.0-20.0)	22.1 (17.7-26.6)	14.3 (11.1-17.4)	23.9*** (21.1-26.7)	18.9 (17.4-20.5)
Psychiatric	23.9 (21.0-26.7)	20.9 (15.2-26.6)	28.6** (22.3-34.9)	19.3 (17.7-21.0)	38.5 (27.1-50.0)	23.3** (20.3-26.3)	16.9 (10.3-23.4)	22.9 (19.1-26.8)	22.9 (18.4-27.3)	16.8 (9.3-24.4)	23.9*** (21.1-26-7)	18.9 (17.4-20.5)
Respiratory	28.1 (25.1-31.0)	29.2 (20.5-38.0)	25.1 (18.3-31.9)	27.7 (25.5-29.9)	29.1 (19.5-38.7)	31.3*** (26.9-35.6)	18.4 (9.8-27.1)	25.7 (20.2-31.2)	17.9 (13.8-22.0)	19.1 (14.2-24.0)	31.4*** (26.8-35.9)	23.4 (21.7-25.2)
Mobility issues	13.6*** (10.0-17.2)	23.9 (20.4-27.3)	20.2** (15.1-25.3)	11.3 (8.9-22.7)	18.4 (14.7-22.7)	22.4*** (17.0-27.7)	20.6 (18.9-22.6)	7.3 (3.7-10.9)	13.9 (8.9-18.8)	8.7 (4.0-13.4)	28.0*** (18.6-37.3)	11.7 (9.7-13.7)
General	34.0 (30.1-37.8)	32.6 (20.0-45.1)	34.1 (23.2-45.0)	32.8 (29.8-35.8)	38.5 (26.8-50.2)	35.5 (27.9-43.1)	28.2 (16.2-40.2)	35.6 (28.2-43.0)	29.0 (23.1-34.7)	25.7 (18.4-33.0)	34.9 (27.8-42.0)	31.5 (28.4-34.6)
Cardiovascular	10.9 (9.2-12.5)	16.1 (10.5-21.7)	17.1** (13.3-20.8)	9.9 (8.7-11.1)	16.0 (2.5-29.4)	16.8*** (14.0-20.0)	8.5 (3.5-13.5)	7.9 (5.6-10.1)	11.8 (7.8-15.8)	10.7 (6.9-14.5)	14.3** (11.0-17.6)	9.5 (8.6-10.4)
Digestive	9.0 (7.6-10.4)	8.0	9.6	7.2	11.4	11.2*** (8.8-13.5)	5.6	5.6	5.7 (4.1-7.3)	7.4 (5.3-9.5)	9.6** (7.4-11.7)	6.4

	ICU admission		Hospitalized			Type of follow-up					Risk of bias	
		(6.0-9.9)	(7.2-11.9)	(6.3-8.1)	(6.2-16.5)		(3.4-7.8)	(4.4-6.8)				(5.7-7.0)
Skin	10.0 (7.9-12.0)	11.3 (7.3-15.2)	8.3 (5.9-10.6)	9.5 (7.8-11.2)	6.1 (1.1-11.2)	9.8*** (7.5-12.0)	5.1 (0.4-9.8)	9.2 (6.5-11.8)	9.7 (4.9-14.6)	7.7 (3.0-12.4)	13.7*** (10.2-17.2)	6.8 (5.4-8.2)

Notes: data are reported as cumulative incidence with their 95% confidence intervals. *, **, *** indicate between sub-groups interaction with a p-value <0.05, <0.001 and <0.0001, respectively.

Supplementary Figure 1. PRISMA flow-chart