Global Prevalence of Post COVID-19 Condition or Long COVID: A Meta-Analysis and Systematic Review

Running Title: Post COVID-19 Condition Meta-Analysis

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Summary:

After screening almost 4,500 articles and meta-analyzing 41 included studies, global pooled post COVID-19 condition prevalence is estimated to be 0.43 (95% CI: 0.39, 0.46), with those hospitalized experiencing a higher prevalence of 0.54 than those not hospitalized of 0.34.

Abstract

Introduction

This study aims to examine the worldwide prevalence of post COVID-19 condition, through a systematic review and meta-analysis.

Methods

PubMed, Embase, and iSearch were searched on July 5, 2021 with verification extending to March 13, 2022. Using a random effects framework with DerSimonian-Laird estimator, we meta-analyzed post COVID-19 condition prevalence at 28+ days from infection.

Results

50 studies were included, and 41 were meta-analyzed. Global estimated pooled prevalence of post COVID-19 condition was 0.43 (95% CI: 0.39,0.46). Hospitalized and non-hospitalized patients have estimates of 0.54 (95% CI: 0.44,0.63) and 0.34 (95% CI: 0.25,0.46), respectively. Regional prevalence estimates were Asia— 0.51 (95% CI: 0.37,0.65), Europe— 0.44 (95% CI: 0.32,0.56), and North America— 0.31 (95% CI: 0.21,0.43). Global prevalence for 30, 60, 90, and 120 days after infection were estimated to be 0.37 (95% CI: 0.26,0.49), 0.25 (95% CI: 0.15,0.38), 0.32 (95% CI: 0.14,0.57) and 0.49 (95% CI: 0.40,0.59), respectively. Fatigue was the most common symptom reported with a prevalence of 0.23 (95% CI: 0.17,0.30), followed by memory problems (0.14 [95% CI: 0.10,0.19]).

Discussion

This study finds post COVID-19 condition prevalence is substantial; the health effects of COVID-19 appear to be prolonged and can exert stress on the healthcare system.

Key Words

epidemiology; infectious diseases; post COVID-19 condition; PASC; Long-COVID

Key Points

Question

Among those infected with COVID-19, what is the global and regional prevalence of post COVID-19 condition?

Findings

Globally, the pooled post COVID-19 condition prevalence estimate was 0.43, whereas the estimates for patients who did and did not have to be hospitalized due to COVID-19 was 0.54 and 0.34, respectively. Regionally, estimated pooled prevalence from largest to smallest effect size were 0.51 for Asia, 0.44 for Europe, and 0.31 for North America. Global pooled prevalence for 30, 60, 90, and 120 days after index date were estimated to be 0.37, 0.25, 0.32, and 0.49, respectively. Among commonly reported post COVID-19 condition symptoms, fatigue and memory problems were reported most frequently, with a prevalence of 0.23 and 0.14.

Meaning

In follow-up studies of patients with COVID-19 infections, post COVID-19 condition was common both globally and across geographic regions, with studies from Asia reporting the highest prevalence.

MAIN TEXT

Introduction

Coronavirus Disease 2019 (COVID-19), a highly transmissible disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has presented extraordinary challenges to the global healthcare system. Worldwide, there have been over 470 million COVID-19 cases and over 6 million deaths, as of March 22, 2022.[1] In addition to the identified COVID-19 infections or reported cases, there is also a large fraction of covert infections due to a multitude of reasons including asymptomatic infections,[2] barrier to testing[3,4] and underreporting.[5,6] Indeed, a recent review estimated the worldwide pooled asymptomatic percentage of COVID-19 infections to be 35.1% (95% CI: 30.7 to 39.9%), as of August 2021.[7]

Although the vast majority of those infected survive with an ensuing case fatality rate of 1.3%, survivors of COVID-19 are known to be at-risk for a variety of sequelae— a condition that has been known as Post-Acute Sequelae of COVID-19 (PASC)[8] in the US, commonly referred to as long COVID.[9] Rigorously defining this condition proved elusive in the earlier stages of the pandemic. In the literature, the occurrence of long-term ailments of COVID-19 appears under many names including Long COVID, Post-Acute COVID-19 Syndrome (PACS)[10], Chronic COVID-19 Syndrome (CCS)[11], and Long Haul COVID-19[12]. In October 2021, the World Health Organization (WHO) proposed a clinical definition and a name "post COVID-19 condition" to unify various existing definitions.[13] Whereas previously the occurrence of long-term ailments of COVID-19 was commonly defined as new or persistent symptoms 4+ weeks from infection with SARS-CoV-2, it is now defined as "the 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".[14] Likewise, there now exists an ICD-10 code corresponding to post COVID-19 condition – U09.9.[15]

Carfi et al. were among the first to report on post COVID-19 condition, finding 87.4% of hospitalized patients had at least one persistent symptom at a mean of 60.3 days after symptom onset.[16] A recent meta-analysis estimated 80% of those infected with SARS-CoV-2 develop at least one long-term symptom.[17] Additionally, time since infection, acute phase severity, geographic region, and select sociodemographic characteristics, such as age and sex, are among the factors likely to influence post COVID-19 condition prevalence estimates.

At this juncture of being nearly two years into the COVID-19 pandemic, numerous large, high-quality studies on post COVID-19 condition, with substantial follow-up time, have been conducted. Expanding on previous meta-analyses hampered by smaller sample sizes and shorter follow-up times, this systematic review and meta-analysis aims to provide a comprehensive synthesis of information on prevalence and symptoms of post COVID-19 condition among those tested or diagnosed with COVID-19 to-date.

Methods

Search Strategy

We employed PICO and PRISMA frameworks to guide our entire research process (**eTable 1**).[18] The literature databases, PubMed and Embase for published articles, as well as iSearch for preprint articles from bioRxiv, medRxiv, SSRN, Research Square, and preprints.org, were searched on July 5, 2021, and search verification was extended through March 13, 2022. The search aimed to capture papers relating to post COVID-19 condition and that examine prevalence, risk factors, and/or duration, published during the years 2020-2022, and written in English. The full search strategy, including filters for each database, is presented in **eMethods 1**.

Screening Procedure

A two-step approach to screening was used with an initial title/abstract screening, followed by a full-text screening, and an ultimate discussion and re-examination to resolve conflicting marks. Screeners 1 and 2 performed both phases of the screening independently. Our inclusion criteria were as follows: (1) human study population with confirmed COVID-19 diagnosis through PCR test, antibody test, or a clinical diagnosis, (2) index date of first test/diagnosis, date of hospitalization, discharge date, or date of clinical recovery/negative test, (3) primary outcome must include prevalence, risk factors, duration, or symptoms of post COVID-19 condition, and (4) the follow-up time is at least 28 days after the index date. Regarding (4), we note that this search strategy was formulated before the WHO's definition was developed. At this time, four weeks was a common threshold used to define Long COVID. We excluded case studies, reviews, studies with imaging or molecular/cellular testing as primary results, and studies with only healthcare workers or residents of nursing homes/long-term care facilities. We also excluded studies that did not meet the sample size threshold of 323, pre-calculated herein, to ensure the included studies were adequately powered to achieve a margin of error of at least 0.05 on the provided prevalence estimate (**eMethods 2**).

Data Extraction

After studies were selected, the following relevant data elements were manually extracted by both screeners: article title, authors, date of publication, study purpose, study design, population, setting, country, sample size, method of COVID-19 confirmation, index date, follow-up time, demographic variables (i.e., age and sex), and outcomes examined.

Outcomes and measures

The primary outcome was the prevalence of post COVID-19 condition and symptoms at least 28 days after the index date. We defined post COVID-19 condition as having any symptoms, or at least one new or persisting symptom during the follow-up time. Furthermore, the follow-up time of COVID-19 patients across studies was divided into the following four groups: symptoms at 28-30 days (labeled as 30 days), 60 days, 90 days, and 120 days after the index date. Although our post COVID-19 condition definition diverges from the WHO's, we note that our estimates at 90 and 120 days may best reflect the current consensus definition. We combined similar symptoms into a broader concept. For example, we joined together dyspnea, shortness of breath, and problem of breathing reported in different studies into a broader symptom concept of dyspnea (**eTable 2**). Studies were classified into the following three groups based on the underlying study population: (1) studies with only non-hospitalized COVID-19 positive individuals, (2) studies with only hospitalized COVID-19 positive individuals, and (3) studies with a case-mix with hospitalized and non-hospitalized individuals. In addition to prevalence, we were also interested in the risk factors for post COVID-19 condition as secondary outcomes.

Statistical Analysis

Meta-analysis with random effects and generic inverse variance weighting was performed to estimate the prevalence of post COVID-19 condition and symptoms, for outcomes reported in at least five studies. The confidence interval was calculated incorporating between-study variance obtained by the DerSimonian-Laird (DL) estimator (**eMethods 3**). Heterogeneity among studies was reflected by the I^2 statistic, where I^2 between 75% and 100% indicates considerable heterogeneity. We further stratified our analysis by (1) study population type (only hospitalized, only non-hospitalized, or mixed hospitalized and non-hospitalized – see eFigure 1), (2) sex (female versus male), (3) follow-up time, (4) region (Asia, Europe, and USA). Another stratified analysis is presented in the supplement (**eFigure 2**) wherein pooled post COVID-19 condition prevalence is estimated (A) among studies considering this condition to be persisting symptoms (i.e., extended beyond a pre-specified number of days) and (B) among studies considering this condition to be at least one symptom or not recovered from COVID-19. All analyses were conducted in R (version 4.0.2) using packages meta[19,20] and metafor.[21]

For critical appraisal, we used a checklist-based tool from the Joanna Briggs Institute (JBI), corresponding to prevalence studies and hence, enabling assessment of risk of bias among the included study designs.[22] Assessment of publication bias was carried out visually by generating funnel plot and formally by conducting Egger's and Begg's tests for funnel plot asymmetry (**eMethods 4** and **eFigure 3**).

Results

Search Results

In our main literature search (July 2021), we identified 4,438 unique citations of which 270 had titles or abstracts that passed our criteria for a full-text assessment. After the full-text screen, we deemed 40 studies eligible for a qualitative synthesis, of which we further meta-analyzed reported measures from 33 with compatible outcomes. See the PRISMA flow diagram (**Figure 1**) and **eTable 3** for details concerning study inclusion/exclusion criteria. In efforts to further verify the search results, we performed a second literature search (August 2021), although no additional eligible studies were identified. However, we also performed a third search (March 2022), and 10 new studies were added (**eMethods 1** and **eFigure 4**).

Study Characteristics

Table 1 (and eTable 4) shows the characteristics of all 50 included articles. The studies comprised a total of 1,680,003 COVID-19 positive patients that we categorized into non-hospitalized (4,165 patients from 5 studies), hospitalized (67,161 patients from 22 studies), and any COVID-19 positive-patients regardless of hospitalization status (1,608,677 individuals from 23 studies). **Figure 1** and **eFigure 4B** lists additional study characteristics.

Prevalence of post COVID-19 condition

Among the 41 included studies in the quantitative synthesis, we meta-analyzed the 31 studies reporting an overall prevalence of post COVID-19 condition. Pooled global prevalence of post COVID-19 condition was estimated to be 0.43 (95% CI: 0.39, 0.46) (**Table 2**). Substantial heterogeneity was observed among the included studies (I^2 =100%, P < 0.001). Estimates ranged widely from 0.09 to 0.81 which may in part be driven by differences in terms of sex, region, COVID-19 study population, and follow-up time. For example, the studies that included only hospitalized cases tended to show higher post COVID-19 condition prevalence than non-hospitalized or the mix of hospitalized and non-hospitalized patients (**Figure 2**). To better understand the interplay of these factors with resulting prevalence estimates, we performed additional stratified meta-analyses (**Table 2**).

First, the pooled post COVID-19 condition prevalence in hospitalized patients of 0.54 (95% CI: 0.44, 0.63) compared to the estimates in non-hospitalized patients of 0.34 (95% CI: 0.25, 0.46) and in a mix of hospitalized and non-hospitalized COVID-19 patients of 0.33 (95% CI: 0.29, 0.37) revealed a sizeable difference, further distinguished by non-overlapping confidence intervals with the latter. However, we note that a wide range of estimates contributed to these groups (i.e., prevalence varied from 0.22 – 0.81 in hospitalized studies, 0.23 – 0.53 in non-hospitalized studies, 0.09 – 0.62 in the mixed group) (**eFigure 5B**).

Next, when focusing on sex, we estimated a pooled post COVID-19 condition prevalence in females of 0.49 (95% CI: 0.35, 0.63), which was higher than that in males of 0.37 (95% CI: 0.24, 0.51). Considering the same studies underly both strata, this imbalance was unlikely attributable to differences in the contributing studies (**eFigure 5A**).

Examining region-specific prevalences, pooled estimated prevalence of post COVID-19 condition was lower in the USA at 0.31 (95% CI: 0.21, 0.43) than in Europe at 0.44 (95% CI: 0.32, 0.56), while the highest estimated prevalence was in Asia at 0.51 (95% CI: 0.37, 0.65). Considerable within-region variation was observed among the included studies in that the corresponding ranges of prevalence estimates were generally wide, with Europe exhibiting the largest range of 0.09 – 0.81 (**eFigure 5C**).

Finally, we focused on estimating post COVID-19 condition prevalence stratified by follow-up time. With increasing follow-up time from 30 to 60 days after the index date, the estimated pooled prevalence of post COVID-19 condition decreased from 0.37 (95% CI: 0.26, 0.49) to 0.25 (95% CI: 0.15, 0.38). Pooled prevalence at 90 and 120 days after the index date increased to 0.32 (95% CI: 0.14, 0.57) and to 0.49 (95% CI: 0.40, 0.59), respectively (**eFigure 5D**). A possible reason for this comparatively high prevalence at 120 days of follow-up time is that the bulk of the studies underlying this estimate were concentrated on hospitalized populations (**eFigure 6**).

Significant levels of heterogeneity were present within each stratified meta-analysis. Post COVID-19 condition definition may affect observed heterogeneity (**eFigure 2**). Noting that the prevalence of each symptom varied, effect size of post COVID-19 condition prevalence estimates may differ in part due to the underlying symptoms assessed therein. Ultimately, these findings suggest that such variation may be indelible, as the definition of post COVID-19 condition itself, as well as other clinical and methodological subcomponents, were largely in-flux prior to the WHO clinical definition (October 2021).[23]

Prevalence of specific post COVID-19 condition symptoms

We assessed 23 symptoms reported across 36 studies (**Table 2**, **Figure 3**). Among the symptoms measured in our included studies, these 23 were meta-analyzed because each were reported in at least 5 separate studies. The five most prevalent symptoms were the following, with corresponding estimated pooled symptom-specific prevalence: fatigue at 0.23 (95% CI: 0.17, 0.30), memory problems at 0.14 (95% CI: 0.10, 0.19), dyspnea at 0.13 (95% CI: 0.11, 0.15), sleep problems at 0.11 (95% CI: 0.05, 0.23), and joint pain at 0.10 (95% CI: 0.04, 0.22) (**eFigure 7**). We note that a study by Orrū et al. from Italy tended to fall toward the higher end of the observed range for several symptom categories, and as such this outlying study (relative to the other underlying studies) may have skewed the resulting point estimates and confidence intervals to a degree.[24]

Risk factors for post COVID-19 condition

Although all included studies were screened for reported post COVID-19 condition risk factors, sex and pre-existing asthma were the only risk factors that were estimated in multiple studies and thus meta-analyzed. Female sex and pre-existing asthma had higher odds of having post COVID-19 condition with pooled estimated odds ratios (OR) of 1.57 (95% CI: 1.09, 2.26) and 2.15 (95% CI: 1.14, 4.05), respectively (see **eFigure 8**). Both meta-analyzed ORs were based on less than 5 studies and should thus be interpreted with caution. Among the studies that were not meta-analyzed, several found that individuals with more severe COVID-19 during the acute phase had higher risk of developing post COVID-19 condition.[25–30] Additionally, two studies found older age to be associated with post COVID-19 condition.[31,32] Other risk factors for post COVID-19 condition including number of symptoms during acute COVID-19,[16] fatigue[9], dyspnea,[9,33] muscle pain,[50] headache,[9,31] myalgia,[9] anosmia,[34] and pre-existing conditions such as obesity,[18,52] comorbidity,[45] and hypothyroidism[37] were reported to be positively associated with post COVID-19 condition (**eTable 5**).

A summary of the 9 studies not included in the meta-analysis and the two studies that measured duration of symptoms is included in **eResults 1** and **eTable 6**. Briefly, the latter two studies suggest select symptoms (e.g., fatigue, dyspnea, and headache) to be among the longest lasting (**eTable 6**). We note that these studies are limited by follow-up time (<6 months) and further complicated by post COVID-19 symptoms being known to relapse/recur.

Discussion

We screened nearly 4,500 articles and synthesized information from 50 studies including almost 1.7M individuals worldwide. The empirical findings suggest a global post COVID-19 condition prevalence of approximately 0.43 (or 43%). Based on a WHO estimate of 470 million worldwide COVID-19 infections, this global pooled post COVID-19 condition estimate indicates that around 200 million individuals currently experience or have previously experienced long-term health-related consequences of COVID-19. Individuals who were hospitalized during acute COVID-19 infection had higher post COVID-19 condition prevalence at 0.54, compared to non-hospitalized patients at 0.34. Female adults had both higher prevalence and risk of having post COVID-19 condition than male adults (0.49 vs 0.37). Corresponding regional prevalence estimates in Asia, Europe, and USA are approximately 0.51, 0.44, and 0.31, respectively. Prevalence estimates at 30, 60, 90, and 120 days are 0.37, 0.25, 0.32, and 0.49, respectively. While the 30-day estimate is most congruent with older definitions of post COVID-19 condition, the 90- and 120-day estimates likely best represent the WHO's current definition.[13]

Our global post COVID-19 condition estimate of 43% is considerably lower than the 80% figure provided by Lopez-Leon et al.[35] Their most prevalent sequela was fatigue at 58% which is concordant with fatigue being the most prevalent sequela at 23% in this study. In general, empirical symptom-specific prevalence estimates are lower in this study, although multiple estimates (e.g., for insomnia, memory problems, anxiety, depression) generally reconcile with the Lopez-Leon et al. review.[17] Similarly, when comparing to the Iqbal et al.[36] meta-analyzed symptom prevalence findings, the estimates herein are lower. A potential reasoning for this is the sample size threshold that we employed may have led to select studies being excluded that were conducted in early 2020 with smaller samples and focused mainly on sicker patients. We note that the three most common symptoms we find (fatigue, memory problems, dyspnea) are consistent with the three symptoms explicitly included in the WHO's definition.[13]

Our meta-analysis showed that female sex and pre-existing asthma correspond with higher proportions of post COVID-19 condition development. Outside of our meta-analysis, we also found age, acute phase symptoms and severity, hypothyroidism, obesity, hypertension, and other pre-existing conditions to be risk factors for post COVID-19 condition. Protective factors for post COVID-19 condition may also exist, as a recent study suggested vaccines may offer protection.[37] However, a large hospital-based study suggested the opposite.[38] As such, the interplay between COVID-19 vaccines and post COVID-19 condition is at-large yet to be determined. Additionally, the evolving SARS-CoV-2 variant landscape may bear implications for post COVID-19 condition prevalence, in that the Omicron variant tends to accompany milder acute symptoms in largely vaccinated or previously infected population,[39,40] which may result in less post COVID-19 symptom burden. We detected other risk factors for post COVID-19 condition, but they were not meta-analyzed because too few studies measured them. An increased number of acute-phase symptoms is associated with post COVID-19 condition; however, one study reported high prevalence of post COVID-19 condition in an asymptomatic subgroup.[41] Also, few studies examined the duration of post COVID-19 condition. A literature review of post-infection sequelae for other coronaviruses showed that fatigue, respiratory symptoms, and psychological symptoms were common among SARS and MERS survivors.[42] Tansey et al. reported improvements in quality of life measures among SARS survivors at the 3 month mark, but even at one year, there was not complete resolution.[43] Recent studies from Xie et al. find that, at one year, COVID-19 patients are at higher risk for cardiovascular disease and diabetes.[44,45] Our results suggest a non-trivial subset of patients experience post COVID-19 condition at 120+ days. Future research needs to further explore risk factors and duration, as these are generally critical components in screening patients for increased risk of developing post COVID-19 condition, and in devising an appropriate treatment protocol.

Limitations

First, we only considered studies written in English which may have excluded important studies written in other languages. Second, while our criteria for follow-up time and index date seem reasonable, there may be important results from studies using other criteria. For example, a large Danish cohort analyzed by Lund et al. was excluded due to follow-up time.[46] Third, bias in testing for COVID-19, especially in the early stages of the pandemic, might have affected the characteristics of the COVID-19 positive cohort.[47] In other words, patients without access to testing, patients without strong health-seeking behavior, and asymptomatic individuals are not blanketly reflected in the empirical findings. Additionally, included studies conducted in early 2020 may tend to be older and higher risk individuals, as testing among these groups was prioritized at that time. Fourth, our sample size criteria may have curtailed inclusion of early-pandemic studies, as sample sizes were generally smaller at that time. Fifth, in addition to the PICO and PRISMA search (July 2021), we updated our search twice (August 2021 and March 2022) in an effort to ensure our results were up-to-date. By restricting our update to include only papers published in high-profile journals, we may have missed notable studies. Sixth, some of the effects observed for hospitalized COVID-19 positive individuals are likely attributed to hospitalization (e.g., critical care myopathy), which may partially explain and confound the observed differences between hospitalized and non-hospitalized prevalence of post COVID-19 condition. Seventh, since the bulk of the included studies in the meta-analysis were performed prior to the WHO post COVID-19 condition definition issuance in October of 2021, the clinical definition is not comprehensively reflected in this meta-analysis.

Future studies may consider adhering to the WHO guidelines on post COVID-19 condition. Lastly, while our review included studies across 16+ countries, data from multiple regions are largely absent, notably, Africa, Central America, Oceania, and The Caribbean. Regarding the underrepresented region of Africa, a recent preprint from South Africa examining 1,873 COVID-19 positive adults found that 66.7% had one or more persistent symptoms at 3 months from hospital discharge, with highest reporting of fatigue, shortness of breath, and lack of concentration (Dryden et al., 2022).[48] Concerning existing inequities in healthcare access, we emphasize that stratifying post COVID-19 condition by race-ethnicity is a noteworthy gap in the literature. Regarding the age composition of the included articles, few children were included in the underlying sample. Future investigators may seek to further examine differences in post COVID-19 condition prevalence among such demographic subgroups.

Conclusions

Findings from this study provide insight into the empirical estimates of prevalence, symptoms, a limited set of risk factors, and duration of post COVID-19 condition, with an examination of differences by several factors including geography. We recommend continued attention be focused on identifying patients at-risk of developing post COVID-19 condition and on quantifying duration of symptoms. With an estimated 200 million individuals affected, post COVID-19 condition's impact on population health and the labor force is enormous. It is imperative that those affected are provided proper health, social, and economic protections.

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Figure Titles and Captions

Figure 1. PRISMA flow diagram.

Note: Additional study characteristics of all included studies are listed in the box in the bottom left.

Figure 2. Forest plot for worldwide post COVID-19 condition prevalence.

Notes: Prevalence estimates and 95% CIs are provided for each study with a relevant measure, and for the meta-analysis of all such studies. For individual studies, the horizontal line represents the estimate, whiskers represent the confidence interval, the size of the box represents the weight assigned to the study, and the color shading reflects the hospitalization status of the study population, as noted in the legend. For the pooled estimate, the width of the diamond represents the confidence interval. Meta-analyzed prevalence and 95% CIs are calculated using random-effects models with inverse variance weighting as described in the methods. Measures of heterogeneity of prevalence estimates are provided.

Figure 3. Forest plot for post COVID-19 condition prevalence by hospitalization status, region, follow-up time, and sex, as well as symptom-specific prevalence.

Notes: Pooled estimates and 95% CIs calculated from random-effect models with inverse variance weighting as described in methods. Pooled estimates with confidence intervals are provided on the left, and visualization of the intervals on the right.

Table 1. Summary of Included Studies*.

Region	Date of Publication	Authors	Study Design [a]	Population of Interest [b,c]	Setting	Country	Sample Size	Follow-up Time [f]	Age	Sex (% female)	Outcomes of Interest [e]
Asia	Dec 2020	Huang et al	AC	COVID-19+, hospitalized adults	Leishenshan Hospital (Wuhan)	China	464	4-6 months ***	57 (15-93) [c]	48.50%	Symptom prevalence, risk factors
	Jan 2021	Huang et al	AC	COVID-19+ adults	Jin Yin-tan Hospital (Wuhan)	China	1,733	186 (175-199) days [c] ****	57 (47-65) [c]	48%	Overall and symptom prevalence
	Jan 2021	Xiong et al	PC	COVID-19+, hospitalized adults	Renmin Hospital of Wuhan University	China	538	97 (95-102) days [c] ***	52 (41-62) [c]	54.50%	Overall and symptom prevalence
	Jan 2021	Zheng et al	CS	COVID-19+, hospitalized adults	Multicenter (hospitals in Wuhan)	China	574	241.79 (16.16) days [d] ****	57.7 (11.4) [d]	60.60%	Symptom prevalence
	Apr 2021	Shang et al	PC	COVID-19+, severe, hospitalized	Multicenter (3 hospitals in Wuhan)	China	796	6 months ***	62 (51-69) [c]	49.20%	Overall and symptom prevalence, risk factors
	Aug 2021	Huang et al	AC	COVID-19+, hospitalized	Jin Yin-tan Hospital (Wuhan)	China	1,276	6 months, 12 months****	59 (49-67) [c]	47.00%	Symptom prevalence, risk factors
	Sep 2021	Zhang et al	RC	COVID-19+, hospitalized adults	Multicenter (Huoshenshan and Taikang Tongji Hospital, Wuhan)	China	2,433	364 (357-371) days [c] ****	60 (49-68) [c]	50.50%	Overall and symptom prevalence, risk factors
	June 2021	Areekal et al	CS	COVID-19+, hospitalized, symptomatic adults	Government Medical College, Thrissur (Kerala)	India	335	28 days *	50.7 (15.7) [d]	48.10%	Overall and symptom prevalence, risk factors
	June 2021	Budhiraja et al	PC	COVID-19+, hospitalized	Multicenter (3 Hospitals in North India)	India	990	9 (4-12) months [d] ****	14.6% <=29 59.7% 30-59 25. 7% 60+	67.70%	Overall and symptom prevalence
	July 2021	Naik et al	PC	COVID-19+ adults	Tertiary Care Facility in New Delhi	India	1,234	91 (45-185) days [c] ***	41.4 (14.2) [d]	30.60%	Overall and symptom prevalence, risk factors, duration

Region	Date of Publication	Authors	Study Design [a]	Population of Interest [b,e]	Setting	Country	Sample Size	Follow-up Time [f]	Age	Sex (% female)	Outcomes of Interest [e]
	Mar 2021	Mannan et al	CS	COVID-19+, hospitalized	Multicenter (6 hospitals)	Bangladesh	1,021	4+ Weeks *	1.8% 0-9 4.9% 10-19 24.4% 20-29 30.4% 30-39 16.8% 40-49 12.4% 50-59 9.4% 60+	25%	Symptom prevalence
	Nov 2020	Sami et al	PC	COVID-19+, hospitalized adults	Khorshid Hospital (Isfahan)	Iran	452	4 weeks *	n/a	n/a	Symptom prevalence
	Aug 2021	Munblit et al	PC	COVID-19+, hospitalized adults	Multicenter (Sechenov University Hospital Network, Moscow)	Russia	2,649	218 (200-236) days [c] ****	56 (46-66) [c]	51.10%	Overall and symptom prevalence, risk factors
Europe	Jan 2021	Venturelli et al	PC	COVID-19+ adults	Papa Giovanni XXIII Hospital (Bergamo)	Italy	767	105 (84-127) days [c] ***	63 (13.6) [d]	32.90%	Overall and symptom prevalence
	Feb 2021	Soraas et al	PC	COVID-19+, non-hospitalized adults	Online Survey	Norway	588	248 (18) days [d] ****	48 [d]	57%	Overall and symptom prevalence
	Mar 2021	Morin et al	PC	COVID-19+, hospitalized adults	Bicêtre Hospital (Paris)	France	478	113 (94-128) days [c] ***	61 (16) [d]	42.10%	Overall and symptom prevalence
	Mar 2021	Lampl et al	RC	COVID-19+	Regensburg Public Health Department, Regensburg, Bavaria	Germany	419	6+ weeks *	44 (30-57) [c]	56.60%	Overall and symptom prevalence
	Mar 2021	Ayoubkhani et al	RC	COVID-19+, hospitalized	NHS hospitals in England	UK	47,780	140 (50) days [d] ***	64.5 (19.2) [d]	45%	Symptom prevalence
	Apr 2021	Lemhofer et al	CS	COVID-19+ adults with mild to moderate infection	Survey Administered by 2 Bavarian health departments	Germany	365	3 months+ ***	49.8 (16.9) [d]	58.50%	Overall and symptom prevalence

Region	Date of Publication	Authors	Study Design [a]	Population of Interest [b,e]	Setting	Country	Sample Size	Follow-up Time [f]	Age	Sex (% female)	Outcomes of Interest [e]
	May 2021	Orrù et al	CS	COVID-19+ adults plus COVID-19- controls	Online Survey (recruitment via social media or email)	Italy	507	1-3 months **	0.2% <20 12.23% 20-29 20.91% 30-39 30.77% 40-49 26.04% 50-59 8.24% 60-69 1.58% >70	82.05%	Symptom prevalence
	May 2021	Desgranges et al	PC	COVID-19+, symptomatic, outpatient adults with at least one risk factor for severe COVID-19	University hospital of Lausanne	Switzerland	418	105 (121-204) days [c] ***	41 (31-54) [c]	62%	Overall and symptom prevalence, risk factors
	June 2021	Peghin et al	AC	COVID-19+ adults	Udine Hospital	Italy	599	191 (172-204) days [c] ****	53(15.8) [d]	53.40%	Overall and symptom prevalence
	June 2021	Righi et al	PC	COVID-19+ adults	Verona University Hospital	Italy	448	6 weeks, 12 weeks **	56 (45-66) [c]	45.10%	Overall and symptom prevalence
	June 2021	Maestre-Muñiz et al	CS	COVID-19+ adults	Tomelloso General Hospital	Spain	543	12 months ****	n/a	n/a	Overall and symptom prevalence
	July 2021	Ghosn et al	PC	COVID-19+, hospitalized	Multicenter (French Covid Cohort)	France	1,137	3 months, 6 months ***	61 (51-71) [c]	37%	Symptom prevalence
	July 2021	Augustin et al	PC	COVID-19+, non-hospitalized adults	University Hospital Cologne	Germany	1.4 months: 958 4.3 months: 442 6.8 months: 353	1.4 (1-2) months, 4.3 (3-5) months, 6.8 (6-8) months [c] ****	43 (31-54) [c]	53.50%	Overall and symptom prevalence, risk factors
	July 2021	Menges et al	PC	COVID-19+ adults	Department of Health of the Canton of Zurich, Switzerland Surveillance	Switzerland	431	7.2 (5.9-10.3) months [c] ****	47 (33-58) [c]	50%	Overall and symptom prevalence, risk factors
	July 2021	Taylor et al	PC	COVID-19+, hospitalized	Barts Health NHS Trust (London)	UK	675	12+ weeks ***	n/a	42.10%	Symptom prevalence

Region	Date of Publication	Authors	Study Design [a]	Population of Interest [b,e]	Setting	Country	Sample Size	Follow-up Time [f]	Age	Sex (% female)	Outcomes of Interest [e]
	Aug 2021	Fernández-de-Las-Peñas et al	PC	COVID-19+, hospitalized	Multicenter	Spain	1,142	7 (0.6) months [d] ****	61 (17) [d]	48%	Overall and symptom prevalence
	Apr 2021	Whittaker et al	PC	COVID-19+ adults	Clinical Practice Research Database (CPRD) Aurum	UK	46,687	63 days (63-63) [c] **	38.6% 18-30 16.6% 31-40 15.7% 41-50 16% 51-60 7.4% 61-70 3.3% 71-80 2.4% >80	54.60%	Symptom prevalence
	Aug 2021	Søraas et al	PC	COVID-19+, non-hospitalized adults	Multicenter (Four laboratories in South-Eastern Norway)	Norway	794	3-8 months ****	49.6 (17.4) [d]	49.00%	Symptom prevalence
	Nov 2021	Matta et al	CS	COVID-19+ adults	CONSTANCES Cohort	France	26,823	10-12 months ****	49.4 (12.9) [d]	51.20%	Symptom prevalence, risk factors
	Nov 2021	Whittaker et al	PC	COVID-19+ adults	Clinical Practice Research Datalink (CPRD) Aurum	UK	456,002	9.2 months maximum, 3.5 (2.0-4.4) months [c] (community), 2.2 (1.3-3.5) months [c] (hospitalized) ****	43 (30-55) [c] (community), 61 (48-76) [c] (hospitalized)	55.60% (community), 49.40% (hospitalized)	Symptom prevalence
	Nov 2021	Evans et al	PC	COVID-19+, hospitalized adults	Multicenter (Post-hospitalisation COVID-19 study)	UK	1,170	2-7 months ****	57.9 (13.0) [d]	35.70%	Overall and symptom prevalence
	Nov 2021	Heightman et al	PC	COVID-19+, hospitalized adults	UCLH post-COVID-19 service	UK	547 (hospitalized only)	69 (51-111) days [c] **	58.3 (47.0-67.7) [c]	43%	Symptom prevalence
Americas	Dec 2020	Cirulli et al	PC	COVID-19+ adults	Surveyed participants from Helix DNA Discovery Project and Healthy Nevada Project	USA	357	30, 60, 90 days ***	n/a	n/a	Overall and symptom prevalence, risk factors
	Mar 2021	Hirschtick et al	CS	COVID-19+, symptomatic adults	Michigan Disease Surveillance System	USA	593	30, 60 days **	51.5 (15.8) [d]	56.10%	Overall prevalence

Region	Date of Publication	Authors	Study Design [a]	Population of Interest [b,c]	Setting	Country	Sample Size	Follow-up Time [f]	Age	Sex (% female)	Outcomes of Interest [e]
	Mar 2021	Spotnitz et al	RC	COVID-19+	ICM MarketScan Commercial Claims and Encounters, Optum Electronic Health Record, and Columbia University Irving Medican Center.	USA	448,176	30-180 days ***	n/a	n/a	Overall and symptom prevalence
	Mar 2021	Perlis et al	CS	COVID-19+, symptomatic	Online Survey with Non-Probability Sampling	USA	6,211	10 months ****	37.8 (12.2) [d]	45.10%	Overall and symptom prevalence, risk factors
	Mar 2021	Huang et al	RC	COVID-19+, non-hospitalized with 5+ year history in EHR system	UC CORDS (University of California Covid research data set)	USA	1,407	61+ days **	2% < 18 10% 18-29 16% 30-39 18% 40-49 21% 50-59 16% 60-69 12% 70-79 6% >= 80	58.90%	Symptom prevalence, risk factors
	Apr 2021	Damiano et al	PC	COVID-19+, hospitalized (moderate or severe Covid) adults	Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo	Brazil	425	207 (20.4) days [d] ****	55.7 (14.2) [d]	51.53%	Psychiatric and cognitive symptom prevalence
	Apr 2021	Chevinsky et al	PC	COVID-19+ adult inpatients and outpatients	Premier Healthcare Database Sepical COVID-19 Release (PHD-SR)	USA	Outpatients: 44,489 Inpatients: 27,284	31-60 days, 61-90 days, 91-120 days ***	Inpatients: 8.8% 18-39 10% 40-49 28.1% 50-64 22.1% 65-74 18% 75-84 13% >= 85 Outpatients: 35.7% 19-39 18.1% 40-49 25.9% 50-64 10.3% 65-74 6% 75-84 4% >= 85	52.5% (inpatients) 61.2% (outpatients)	Overall and symptom prevalence
	April 2021	Chopra et al	PC	COVID-19+, hospitalized	MI-COVID19 initiative (38 hospitals in Michigan)	USA	488	60 days **	62 (50-72) [c]	48.20%	Overall and symptom prevalence

Region	Date of Publication	Authors	Study Design [a]	Population of Interest [b,e]	Setting	Country	Sample Size	Follow-up Time [f]	Age	Sex (% female)	Outcomes of Interest [e]
	May 2021	Yomogida et al	PC	COVID-19+ adults	Long Beach Department of Health and Human Services Surveillance	USA	366	1 Month, 2 months, 10 weeks-5 months ***	11.4% 18-24 39.3% 25-39 30.2% 40-54 10.6% 55-64 8.2% 65+	56.40%	Overall and symptom prevalence, risk factors
	June 2021	Wong-Chew et al	PC	COVID-19+, hospitalized adults	Temporary Covid-19 Hospiital in Mexico City	Mexico	30 days: 1,303 90 days: 928	30, 90 days ***	n/a	n/a	Symptom prevalence, risk factors
	June 2021	Shoucri et al	RC	COVID-19+, hospitalized adults	New York-Presbyterian/Columbia University Irving Medical Center	USA	3 months: 488 6 months: 364	3, 6 months ***	3 months: 60 (47.8-71) 6 months: 61 (50.0-71) [c]	43.2% - 3 months 47.8% - 6 months	Symptom prevalence
	Dec 2021	Jovanoski et al	RC	COVID-19+	Optum de-identified COVID-19 EHR dataset	USA	57,748	30-90 days, 90-180 days ***	47.93 (18.76) [d]	53.30%	Symptom prevalence
Mix	Mar 2021	Sudre et al	PC	COVID-19+, symptomatic	COVID Symptom Study App	UK, Sweden, US	4,182	28-84 days **	42 (32-53) [c]	71.50%	Overall and symptom prevalence, risk factors, duration
	May 2021	Taquet et al	RC	COVID-19+, age 10+	TriNetX EHR Network	USA, others	236,379	6 months ***	46 (19.7) [d]	55.60%	Risk factors, duration
	Sep 2021	Taquet et al	RC	COVID-19+, age 10+	TriNetX EHR Network	USA, others	273,618	3-6 months ***	46.3 (19.8) [d]	55.60%	Overall and symptom prevalence

Note: No studies meeting our inclusion/exclusion criteria were returned by the search for regions: Africa, Central America, Middle East (with the exception of Iran), Oceania, and The Caribbean.

[*] A version of this table with linked references is available in the supplementary materials

[a] PS = Prospective Cohort, RS = Retrospective Cohort, CS = Cross-sectional, AC = Ambidirectional Cohort
[b] Not all inclusion/exclusion criteria listed
[c] Median (IQR) or Median (range)
[d] Mean (SD) or Mean (95% CI)
[e] Some studies included populations and outcomes outside the scope of this review.
[f] Asterisks denote length of follow-up time according to the following convention: [4 weeks, 8 weeks] - *, (8 weeks, 12 weeks] - **, (12 weeks, 6 months] - *** 6+ months - ****. If a study considered measurements at several follow-up times, the longest duration was used.

Table 2. Meta-analysis of pooled post COVID-19 condition prevalence with 95% CI in COVID-19 Positive Individuals[a]

		Post COVID-19 Condition Prevalence in COVID-19 Positive Individuals [95% CI]; (number of included studies)			
		Any*	**Mixed Hospitalized & Non-Hospitalized**	**Only Hospitalized**	**Only Not Hospitalized**
Overall Post COVID-19 Condition		0.43 [0.39; 0.46]; (31)	0.33 [0.29; 0.37]; (15)	0.54 [0.44; 0.63]; (14)	0.34 [0.25; 0.46]; (5)
Sex	Female	0.49 [0.35; 0.63]; (9)	0.43 [0.31; 0.56]; (6)	…	
	Male	0.37 [0.24; 0.51]; (9)	0.31 [0.22; 0.43]; (6)	…	
Region	Europe	0.44 [0.32; 0.56]; (13)	…	…	
	Asia	0.51 [0.37; 0.65]; (7)	…	…	
	USA	0.31 [0.21; 0.43]; (7)	…	…	
Follow-up time	30 days	0.37 [0.26; 0.49]; (10)	…	…	
	60 days	0.25 [0.15; 0.38]; (10)	…	…	
	90 days	0.32 [0.14; 0.57]; (9)	…	…	
	120 days	0.49 [0.40; 0.59]; (13)	0.39 [0.30; 0.49]; (4) [b]	0.58 [0.47; 0.68]; (8)	
General symptoms	Fatigue	0.23 [0.17; 0.30]; (28)	0.19 [0.14; 0.24]; (13)	0.29 [0.21; 0.40]; (11)	
	Tachycardia	0.06 [0.03; 0.11]; (9)	…	0.06 [0.04; 0.08]; (5)	
	Dizziness	0.05 [0.02; 0.09]; (7)	…	0.03 [0.01; 0.07]; (6)	
	Appetite	0.04 [0.02; 0.09]; (8)	…	0.03 [0.01; 0.07]; (6)	
	Sore throat	0.03 [0.02; 0.05]; (12)	…	0.02 [0.01; 0.08]; (6)	
	Fever	0.02 [0.01; 0.04]; (14)	0.02 [0.01; 0.04]; (6)	0.02 [0.00; 0.05]; (5)	
Neurologic symptoms	Memory problems	0.14 [0.10; 0.19]; (9)	…	0.12 [0.09; 0.17]; (6)	
	Sleep problems	0.11 [0.05; 0.23]; (15)	0.08 [0.01; 0.34]; (5)	0.13 [0.09; 0.20]; (9)	
	Concentration/ Confusion / Brain	0.09 [0.05; 0.15]; (13)	0.13 [0.04; 0.33]; (5)	0.06 [0.03; 0.12]; (7)	

	fog				
	Taste	0.08 [0.04; 0.13]; (10)	…	0.04 [0.02; 0.07]; (5)	
	Smell	0.07 [0.05; 0.11]; (15)	0.12 [0.06; 0.23]; (6)	0.05 [0.03; 0.07]; (8)	
	Smell or Taste	0.06 [0.02; 0.21]; (10)	0.04 [0.01; 0.23]; (5)	…	
	Headache	0.05 [0.03; 0.07]; (22)	0.04 [0.02; 0.07]; (10)	0.05 [0.02; 0.10]; (9)	
Respiratory symptoms	Dyspnea	0.13 [0.11; 0.15]; (28)	0.11 [0.09; 0.14]; (15)	0.17 [0.11; 0.25]; (9)	
	Cough	0.07 [0.05; 0.09]; (28)	0.05 [0.03; 0.08]; (12)	0.08 [0.05; 0.13]; (12)	
	Chest pain	0.05 [0.04; 0.07]; (16)	0.03 [0.02; 0.06]; (7)	0.07 [0.05; 0.10]; (9)	
Psychological symptoms	Anxiety	0.08 [0.04; 0.16]; (11)	0.12 [0.05; 0.25]; (6)	…	
	Depression	0.07 [0.03; 0.15]; (8)	0.13 [0.04; 0.34]; (5)	…	
Musculoskeletal symptoms	Joint pain	0.10 [0.04; 0.22]; (6)	…	…	
	Myalgia	0.06 [0.04; 0.09]; (19)	0.05 [0.03; 0.09]; (11)	0.07 [0.05; 0.10]; (8)	
Gastrointestinal symptoms	Abdominal pain	0.04 [0.01; 0.09]; (7)	…	…	
	Diarrhea	0.03 [0.01; 0.05]; (11)	…	0.02 [0.01; 0.04]; (7)	
Dermatologic symptoms	Hair loss	0.07 [0.02; 0.24]; (10)	…	0.13 [0.08; 0.21]; (6)	

* Includes studies that reported on only non-hospitalized, only hospitalized, or a mix of hospitalized & non-hospitalized COVID-19 positive patients.

[a] Pooled estimates and 95% CIs calculated from random-effect models with inverse variance weighting as described in methods. Prevalence is stratified by acute-phase hospitalization status. Estimates for the non-hospitalized population are not provided due to lack of sample size.

[b] Only 4 studies with mixed hospitalized and non-hospitalized population. This estimate should be interpreted with caution due to low sample size.

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Conflict of Interest Disclosures

Authors have no competing interests

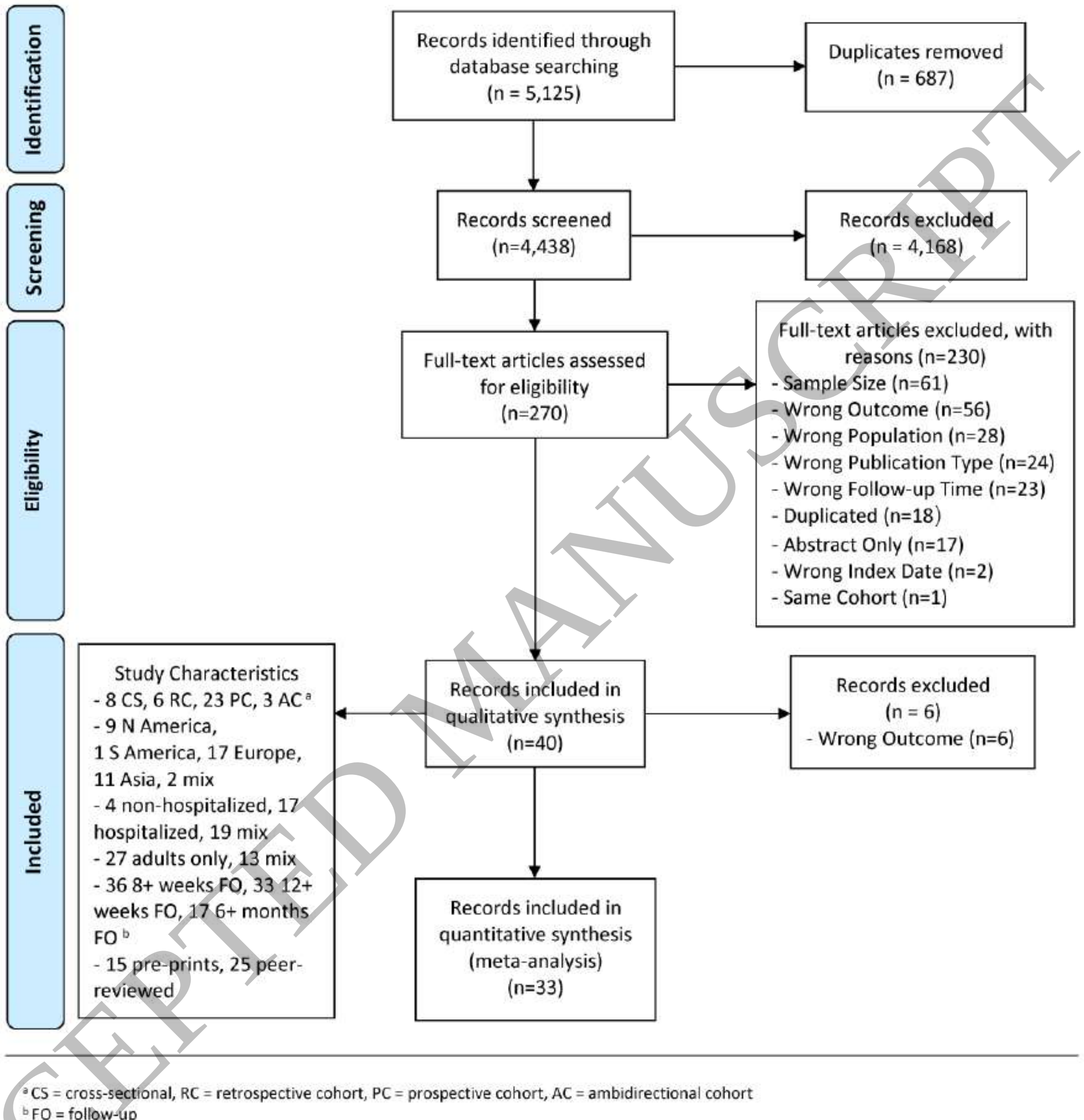

Figure 1
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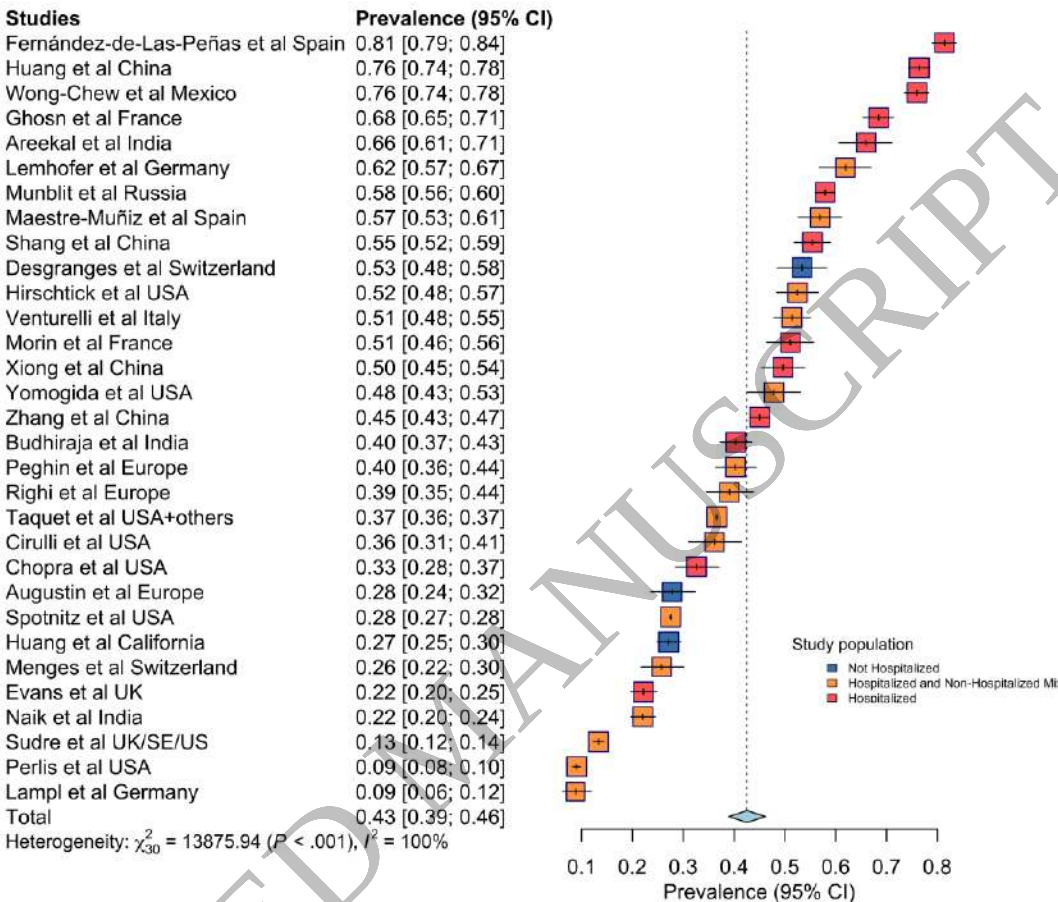

Figure 2
165x138 mm (0.2 x DPI)

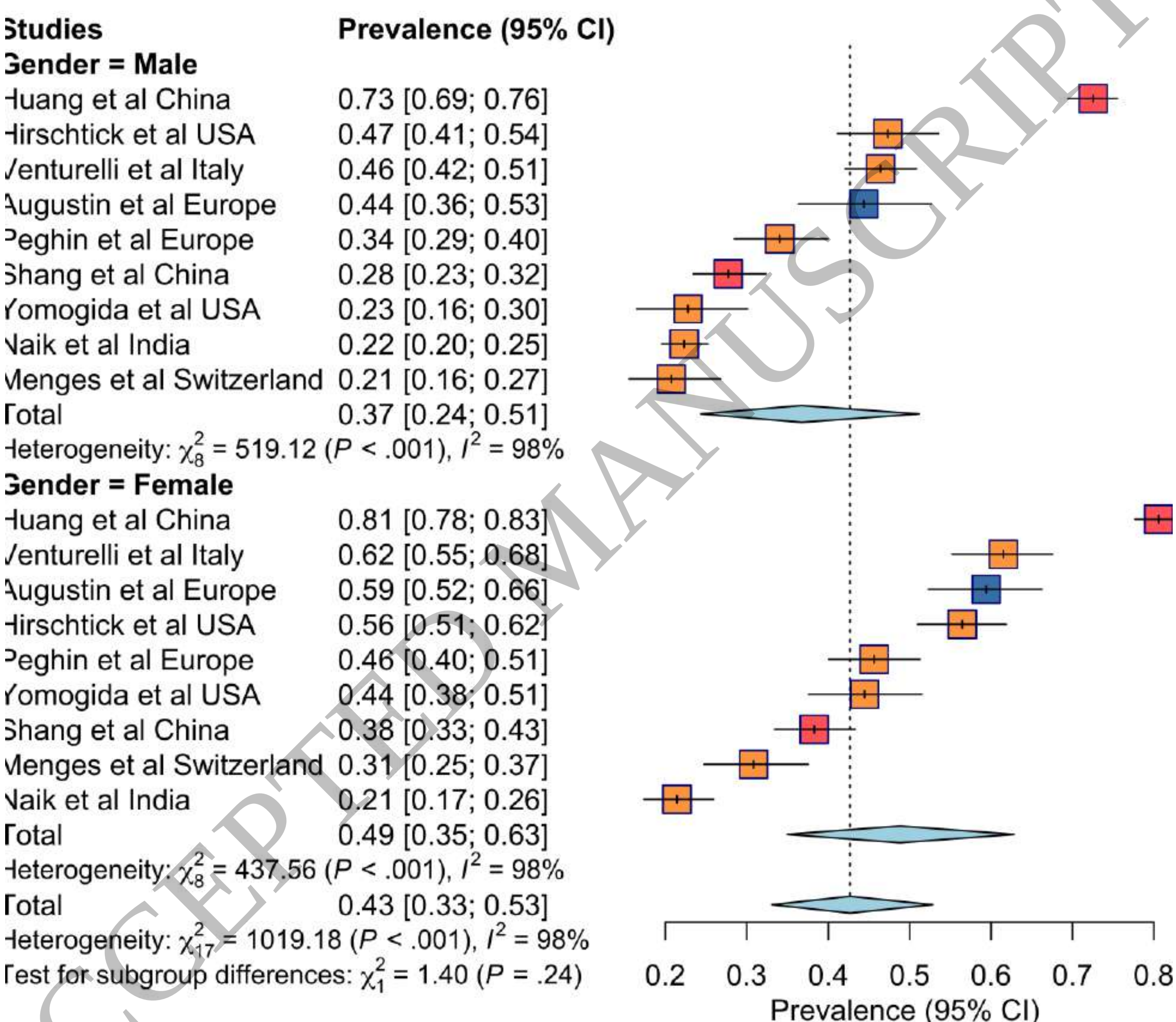

Figure 3

165x206 mm (0.2 x DPI)