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Prognostic factors for adverse outcomes in patients with COVID-19: A field-wide systematic review and meta-analysis

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Short title: Prognostic factors in COVID-19 patients

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ABSTRACT

Introduction: The individual prognostic factors for COVID-19 are unclear. For this reason, we aimed to present a state-of-the-art systematic review and meta-analysis on the prognostic factors for adverse outcomes in COVID-19 patients.

Methods: We systematically reviewed PubMed from January 1, 2020 to July 26, 2020 to identify non-overlapping studies examining the association of any prognostic factor with any adverse outcome in patients with COVID-19. Random-effects meta-analysis was performed, and between-study heterogeneity was quantified using I^2 metric. Presence of small-study effects was assessed by applying the Egger's regression test.

Results: We identified 428 eligible articles, which were used in a total of 263 meta-analyses examining the association of 91 unique prognostic factors with 11 outcomes. Angiotensin-converting enzyme inhibitors, obstructive sleep apnea, pharyngalgia, history of venous thromboembolism, sex, coronary heart disease, cancer, chronic liver disease, chronic obstructive pulmonary disease, dementia, any immunosuppressive medication, peripheral arterial disease, rheumatological disease and smoking were associated with at least one outcome and had >1000 events, P-value <0.005, I^2 <50%, 95% prediction interval excluding the null value, and absence of small-study effects in the respective meta-analysis. The risk of bias assessment using the Quality In Prognosis Studies tool indicated high risk of bias in 302 of 428 articles for study participation, 389 articles for adjustment for other prognostic factors, and 396 articles for statistical analysis and reporting.

Conclusions: Our findings could be used for prognostic model building and guide patients' selection for randomized clinical trials.

1 INTRODUCTION

In December 2019, a cluster of pneumonia cases was reported in Wuhan, China, and subsequent epidemiological tracking identified a novel coronavirus (Severe Acute Respiratory Syndrome-Coronavirus-2, SARS-CoV-2) as the cause.[1] The SARS-CoV-2 has spread across all continents since then and caused a public health crisis.[2] As of February 2021, there have been more than 100 million confirmed cases with coronavirus disease 2019 (COVID-19) and more than 2 million deaths according to World Health Organization.[3]

The ongoing public health emergency necessitates the discovery of reliable prognostic factors to guide clinical decision making and treatment plan tailored to the patient characteristics. These prognostic factors could also improve the design and analysis of future clinical trials and suggest novel insights on molecular pathways of the disease.[4,5]

There is a growing body of literature on COVID-19 patients, examining prognostic features of the disease. However, clinical decision-making and research guidance is often based on narrative reviews or low-quality studies.[6] There is yet no published effort to critically and systematically summarize the epidemiological evidence on the entire prognostic factor landscape for multiple adverse outcomes in COVID-19 patients. Our study aims to fill this gap by conducting the first comprehensive systematic review, critical appraisal and (in case of sufficient data) meta-analysis of all prognostic factors in patients with COVID-19 by applying state-of-the-art approaches.

2 METHODS

We followed the MOOSE (*Meta-analyses of Observational Studies in Epidemiology*) guideline and the latest guidance of the Prognosis Methods Group of the Cochrane Collaboration to design and report our meta-analysis.[7,8] We designed the research question and data extraction of this systematic review according to the modified checklist for critical appraisal and data extraction for systematic reviews of prognostic factor research (CHARMS-PF).[5,9] A protocol for this systematic review was published on *Open Science Foundation* (osf.io/382wj).

2.1 Literature search

We systematically searched PubMed from January 1, 2020 to July 26, 2020 to identify all studies examining any prognostic factor of any adverse outcome in patients with COVID-19. Our search algorithm was based on LitCovid[10,11] and was the following: "coronavirus"[All Fields] OR "SARS-CoV-2"[All Fields] OR "cov"[All Fields] OR "2019-SARS-CoV-2"[All Fields] OR "COVID-19"[All Fields] OR "SARS-CoV-2"[All Fields]. The literature search was performed by two independent researchers (VB, LB). We additionally performed a reference screening of the eligible articles to identify additional potentially eligible articles.

2.2 Eligibility criteria

We considered as eligible observational studies or clinical trials that included patients with SARS-CoV-2 infection (defined by real-time polymerase chain reaction testing or standardized clinical/radiological criteria) and examined the effect of any prognostic factor on any outcome. We considered eligible any outcome that was relevant

to patients if its definition and measurement was standardized or explicitly defined. We excluded outcomes measured at the time of diagnosis or hospital admission, and prognostic factors measured after diagnosis or hospital admission, to ensure temporality between prognostic factor and outcome.

Prognostic factor was defined as "any measure that, among people with a given health condition, is associated with a subsequent clinical outcome."[12] We considered all types of prognostic factors including demographic and anthropometric individual characteristics, biomarkers, symptoms, clinical signs, medical history and comorbid diseases, medications, and findings in chest imaging. **Table 1** shows a detailed description of the PICOTS (Population, Index prognostic factor, Comparator prognostic factor, Outcome, Timing, Setting) system.[5,9,13]

2.3 Data Extraction

Data extraction was performed independently by two researchers (VB, LB) following the CHARMS checklist.[5,9] From each article, we extracted the first author, the year and the journal of publication, the geographic region and the involved hospital, the recruitment period, the examined prognostic factors, and the examined outcomes and their definition. For each prognostic factor, we extracted the reported measure of association (i.e., odds ratio, risk ratio, or hazard ratio) and the level of comparison. We extracted both univariable and multivariable prognostic factor's effect estimates, whenever available.[5,8]

2.4 Risk of bias assessment

The presence of bias in the eligible studies was assessed independently by two researchers (VB, LB) using the Quality In Prognosis Studies (QUIPS) tool. QUIPS assesses 6 domains: participation, attrition, prognostic factor measurement, adjustment for other prognostic factors, outcome measurement and analysis and reporting.[5,14] In each one domain apart from adjustment for other prognostic factors, risk of bias was assessed as low, moderate, or high based on a prespecified set of questions.

2.5 Statistical Analysis

In the absence of a reported prognostic effect size, we calculated the univariable odds ratio (OR) and its standard error from the reported 2 × 2 contingency table. When zero counts occurred in a cell of the contingency table, we applied the Haldane-Anscombe correction.[15]

For associations examined in at least 5 studies, we estimated the summary effect estimate and its 95% confidence interval (CI) applying the DerSimonian and Laird random-effects model, because methodological heterogeneity was expected between the eligible studies.[16,17] To minimize the effect of different outcome definitions on between-study heterogeneity, we combined only studies using the same outcome definition. A statistically significant effect was claimed at P-value <0.05. Also, between-study heterogeneity was quantified by the I^2 statistic.[18,19] Values greater than 50% and 75% were judged as large and very large heterogeneity, respectively.

We estimated the 95% prediction interval, which further accounts the uncertainty for the effect that would be expected in a new study addressing the same association.[16] We

assessed whether there was evidence for small-study effects with the Egger's regression asymmetry test.[20] The presence of small-study effects was based on a statistically significant Egger's test at P-value <0.10 combined by a more conservative effect in the largest study of the meta-analysis compared to the effect in the random-effects meta-analysis.

We performed three sensitivity analyses to explore potential sources of between-study heterogeneity by excluding (a) studies presenting hazard ratios, (b) studies with a sample smaller than 100 COVID-19 patients, and (c) studies including only individuals with specific comorbidities. Then, we estimated the Spearman correlation coefficient to examine the correlation of effect estimate, I^2 statistic and P-value in the main analysis and the sensitivity analyses.

We also examined which associations presented a highly significant effect at P-value <0.005, absence of large or very large between-study heterogeneity (i.e., I^2 <50%), 95% prediction interval excluding the null value, and more than 1000 events. The rationale for the use of a strict P-value threshold is based on current recommendations to avoid false-positive findings.[21–23]

Statistical analysis was performed on *R Statistical Software version 3.6.3* (Foundation for Statistical Computing, Vienna, Austria) and the packages "*metafor*" and "*metareg*" were used for all analyses. Additional details on the eligibility criteria, the data extraction process, and the risk of bias assessment are presented in the supplementary material.

3 RESULTS

3.1 Description of eligible articles

We screened a total of 36,661 articles, and we identified 428 eligible articles that were published between January 1, 2020 and July 26, 2020 and were included in a meta-analysis (**Figure 1**). The majority of the included studies were from China (n=106), USA (n=98), Italy (n=65), Spain (n=34), France (n=26) and UK (n=20).

3.2 Risk of bias assessment

424 of 428 articles (99%) that participated in at least one meta-analysis were graded as having high risk of bias in at least one domain (**Figure 2**). To specify on domains, high risk of bias was present in 302 articles (71%) for study participation, one article for study attrition (0.2%), 255 articles (60%) for prognostic factor measurement, 19 articles (4%) for outcome measurement, and 396 articles (93%) for statistical analysis and reporting. Also, 389 articles (91%) did not present a prognostic factor's effect estimate that was adjusted for other prognostic factors. The detailed assessment of the eligible articles per domain is presented in **Supplementary Table 1**.

3.3 Description of clinical outcomes and prognostic factors

We performed a total of 263 meta-analyses focused on risk for mortality (n=89 meta-analyses), ICU admission (n=48 meta-analyses), hospital admission (n=50 meta-analyses), two composite outcomes (n=24 meta-analyses), invasive mechanical ventilation (n=23 meta-analyses), acute kidney injury (n=9 meta-analyses), venous thromboembolism (n=6 meta-analyses), pulmonary embolism (n=5 meta-analyses), acute

respiratory distress syndrome (n=5 meta-analyses), and deep venous thrombosis (n=4 meta-analyses).

Overall, we evaluated 91 unique prognostic factors which were categorized into seven categories: biomarkers (n=16 meta-analyses, 11 unique factors), comorbidities (n=120 meta-analyses, 30 unique factors), imaging markers (n=7 meta-analyses, 4 unique factors), demographic characteristics (n=25 meta-analyses, 3 unique factors), environmental factors (n=8 meta-analyses, 2 unique factors), medications (n=28 meta-analyses, 12 unique factors), and symptoms or clinical signs (n=59 meta-analyses, 29 unique factors).

3.4 Findings from meta-analyses

The median number of studies per meta-analysis was 9 (interquartile range [IQR], 6 – 14), the median number of events per meta-analysis was 1195 (IQR, 514 – 2937) and the median number of COVID-19 participants per meta-analysis was 5131 (IQR, 2394 – 13,395). One hundred and fifty-seven of 263 meta-analyses (60%) included more than 1000 events. One hundred and forty-nine of 263 meta-analyses (57%) presented a statistically significant effect at P-value <0.05, whereas 119 of them had a P-value <0.005.

One hundred and thirty-seven of 263 meta-analyses (52%) presented large or very large between-study heterogeneity (I^2 >50%). Forty-eight of 263 meta-analyses (18%) presented a 95% prediction interval that excluded the null value. Also, 18 of 263 meta-analyses (7%) presented evidence for small-study effects. The results of the meta-analyses for the 263 associations are available in **Supplementary Table 2**.

A forest plot of the 29 associations with more than 1000 events, P-value <0.005, I^2 <50%, and no evidence of small-study effects is presented in **Figure 3**. Of the 149 statistically significant meta-analyses at P-value <0.05, 16 meta-analyses included more than 1000 events, had a P-value <0.005 in random-effects model, I^2 <50%, 95% prediction interval excluding the null value and absence of small-study effects. These meta-analyses examined the effect of obstructive sleep apnea (OR, 2.11; 95% CI, 1.54 – 2.89), and history of VTE (OR, 2.35; 95% CI, 1.75 – 3.14) on risk of hospitalization, the effect of female sex (OR, 0.53; 95% CI, 0.46 – 0.59) on risk of ICU admission, the effect of coronary heart disease (OR, 1.69; 95% CI, 1.43 – 1.99) on risk of acute kidney injury, the effect of cancer (OR, 1.57; 95% CI, 1.25 – 1.98) and female sex (OR, 0.62; 95% CI, 0.55 – 0.71) on risk of invasive mechanical ventilation, and the effect of ACEi (OR, 1.38; 95% CI, 1.20 – 1.59), cancer (OR, 2.14; 95% CI, 1.86 – 2.45), chronic liver disease (OR, 1.46; 95% CI, 1.24 – 1.72), COPD (OR, 2.19; 95% CI, 1.88 – 2.55), dementia (OR, 3.12; 95% CI, 2.50 – 3.90), any immunosuppressive medication (OR, 1.22; 95% CI, 1.12 – 1.34), peripheral arterial disease (OR, 2.07; 95% CI, 1.55 – 2.75), pharyngalgia (OR, 0.58; 95% CI, 0.46 – 0.71), rheumatological disease (OR, 1.41; 95% CI, 1.27 – 1.57), and smoking (OR, 1.50; 95% CI, 1.35 – 1.66) on risk of mortality. Thirteen additional meta-analyses fulfilled the aforementioned characteristics with the exception of a 95% prediction interval that included the null value. These meta-analyses assessed the effect of ACEi on risk of hospitalization, the effect of cardiovascular disease, chronic kidney disease, chronic lung disease, and diabetes mellitus on risk of ICU admission, the effect of ACEi/ARBs and sex on risk of acute kidney injury, the effect of BMI on risk of invasive mechanical ventilation, the effect of chronic kidney disease and sex on the risk

of a composite outcome (defined as ICU admission or death), and the effect of ARBs, insulin and low white blood cells count on risk of mortality. These 29 associations are visualized in a Sankey diagram (**Figure 4**).

3.5 Sensitivity analyses

We repeated 57 meta-analyses after excluding the studies that reported hazard ratios (HR) without information on 2 × 2 contingency table (**Supplementary Table 3**). Overall, we observed high correlation of summary effect estimates (rho = 0.98, P <0.05), P-values (rho = 0.96, P <0.05), and I^2 statistics (rho = 0.95, P <0.05) before and after the exclusion of these studies.

A total of 192 meta-analyses were repeated after the exclusion of studies with less than 100 COVID-19 participants (**Supplementary Table 4**). Overall, we observed high correlation of summary effect estimates (rho = 0.99, P <0.05), P-values (rho = 0.96, P-value <0.05), and I^2 statistics (rho = 0.96, P-value <0.05) before and after the exclusion of these studies.

A total of 103 meta-analyses were repeated after the exclusion of studies including only COVID-19 patients with a specific comorbid disorder (**Supplementary Table 5**). Overall, we observed high correlation of summary effect estimate (rho = 0.99, P <0.05), P-value (rho = 0.98, P-value <0.05), and I^2 statistic (rho = 0.98, P-value <0.05) before and after the exclusion of these studies.

4 DISCUSSION

We conducted a comprehensive systematic review, and meta-analysis to present an overview of the prognostic factors associated with any adverse outcome in patients diagnosed with COVID-19. We applied state-of-the-art approaches to combine the data from more than 420 studies by following the relevant methodological guidance. In our research effort, we considered more than 260 associations covering a wide range of predictors for multiple outcomes in COVID-19 patients. More than half of these associations presented a nominally significant effect, and only 16 of them provided strong evidence in terms of sample size, statistical significance, consistency, and lack of small-study effects. Below, we discuss the findings of our research effort with a focus on the most credible predictors, and the potential biases in these associations.

4.1 Principal findings in context

Our risk of bias assessment indicated that almost all the eligible studies included in our systematic review presented high risk of bias in at least one domain of QUIPS tool. Most articles had high risk of bias in the domains of participation and statistical analysis and presented several statistical pitfalls, including absence of a regression technique or inappropriate modelling strategy and handling of missing data, and poor reporting of the time horizon of prediction. In accordance with the systematic review of prognostic and diagnostic models for COVID-19,[24] our systematic review of individual prognostic factors also indicated poor reporting of the length of follow-up, exclusion of participants who still had the disease at the end of the study period and inappropriate statistical methods. Our meta-analyses focused on unadjusted effect estimates, indicating that the

prognostic effect of some prognostic factors is likely to become smaller if they were included in a multivariable prediction model.[5] We could not combine adjusted effect estimates, because they were only scarcely reported in the literature. Whenever adjusted effect estimates were presented, selection of covariates was not consistent among different studies, whereas the selection of covariates in the multivariable model either was not clearly described in the eligible studies or was inappropriately based on the results of univariable modelling. An additional observation of our systematic review, corroborating the poor research practices in this field, was the substantial use of overlapping populations to examine the same or correlated prognostic factors and/or outcomes in different articles.[25–27]

Age and sex constitute known prognostic factors for many chronic diseases. Our analysis confirms that age is a prognostic factor related to hospitalization, and mortality, with a linear dose-response association with mortality. Although large between-study heterogeneity was observed in these meta-analyses, 95% prediction intervals excluded the null value. Also, sex was identified as a prognostic factor for ICU admission, acute kidney injury, invasive mechanical ventilation, and composite outcome (defined as ICU admission, and death) in male compared to female patients. In these associations small or moderate between-study heterogeneity was observed, but 95% prediction intervals included the null value for acute kidney injury, and composite outcome. The strong association of age and sex with adverse outcomes in COVID-19 patients indicates that they should be considered in multivariable prognostic models as covariates.

Symptoms and clinical signs associated with adverse events in COVID-19 patients could be used as “red flags” for patients requiring enhanced monitoring or treatment.[28]

Dyspnea was a predictor of hospitalization, oxygen saturation was a predictor of mortality, and both associations presented large between-study heterogeneity with 95% prediction intervals excluding the null value. Also, pharyngalgia was a predictor of hospitalization with absence of large between-study heterogeneity and 95% prediction interval excluding the null value. Additionally, smoking could be considered a prognostic factor of clinical deterioration because available evidence showed a consistent association of smoking with risk of mortality.

Almost half of the meta-analyses examined comorbid diseases as prognostic factors of COVID-19 outcomes. SARS-CoV-2 causes systemic inflammation and multi-organ damage outside the respiratory system, therefore patients with pre-existing chronic disorders of these organs may be more prone to organ insufficiency.[29] The most consistent evidence for a prognostic role were obstructive sleep apnea, venous thromboembolism, cardiovascular disease, chronic kidney disease, chronic lung disease, diabetes mellitus, obesity, cancer, chronic liver disease, COPD, dementia, peripheral arterial disease and rheumatological disease, which predicted the occurrence of at least one prognostic outcome. An important limitation of the studies examining the prognostic effect of comorbid diseases was the vague reporting of their definition and ascertainment. This research practice could cause considerable heterogeneity, but we could not test this hypothesis in subgroup analyses. For example, presence of cardiovascular disease, chronic lung disease, chronic liver disease, and any comorbidity constitute disease groups which might include different diseases across studies.

Twelve medications were considered as prognostic factors for COVID-19 patients. More than half of the relevant meta-analyses examined the prognostic significance of

ACE inhibitors and ARBs. ACE inhibitors were identified as predictors of hospitalization and mortality, ARBs were predictors of mortality, and the use of either ACE inhibitors or ARBs presented consistent evidence for an association with acute kidney injury. Among the rest of the medications, use of any immunosuppressive medication and insulin presented consistent evidence as predictors of mortality.

A total of 16 meta-analyses were performed for serum biomarkers and two adverse outcomes (i.e., mortality and ICU admission). Almost all these meta-analyses had a small sample. Only leukopenia presented consistent evidence for prediction of mortality, but the 95% prediction interval included the null value. Although the majority of eligible studies dichotomized continuous biomarkers, many of them used standardized cutpoints. However, several studies did not report the cutpoint they used, rendering this information ineligible for inclusion in meta-analysis. According to published guidance, we only combined studies that reported the cutpoint used, and used the same cutpoint, to avoid heterogeneity and to increase interpretability of results.

4.2 Comparison with other studies

Our findings on the low study quality are in accordance with other published systematic reviews that appraised published studies on COVID-19. A meta-epidemiological study that assessed all literature related to SARS-CoV-2 during the first semester of the pandemic showed that the majority of research was composed by articles without original data and assessed all the studies that contained original data and were published during that period as high risk of bias.[6] Moreover, a living systematic review and network meta-analysis of clinical treatment studies on COVID-19 patients and a recent systematic review of treatment studies of chloroquine and hydroxychloroquine

also highlighted low methodological quality of published studies.[30,31] Furthermore, a systematic review of all prediction models, diagnostic and prognostic, for COVID-19 patients assessed all models as high risk of bias and highlighted the use of improper statistical analysis.[24]

4.3 Recommendations and policy implications

There is a growing body of epidemiological studies examining prognostic factors of the COVID-19. Due to the great significance of answering clinical questions related to prognosis of COVID-19, it is important to highlight the limitations and the gaps of the existing literature to improve the design and the validity of upcoming studies on COVID-19 prognosis. An important issue that should be raised is the need for adequate and transparent reporting of methodology and findings in future studies to improve the applicability of the evidence. The reporting of the methods and results of future studies could be improved by following the STROBE statement and PROGRESS framework.[12,32] Future studies should include a detailed description of the recruitment process and sample selection, apply an appropriate regression modelling technique for the statistical analysis and present prognostic effects adjusted at least for age and sex. The time horizon for the prediction should be clearly reported and hazard ratios should be the effect size metric of choice, because odds ratios and risk ratios are sensitive to changes based on the time horizon of the prediction contributing to between-study heterogeneity. Also, selective reporting of findings should be avoided to minimize the effect of publication bias in the reported associations.

Based on a recently published comprehensive systematic review of COVID-19 related prediction models, the selection of predictors for model building is more

appropriate to be based on previous literature than on a purely data driven approach.[24] Considering that our meta-analyses synthesized unadjusted prognostic effect estimates, our findings do highlight the prognostic factors that could constitute good predictors for adverse events in patients with COVID-19. Our findings could be used as a pool for candidate predictors in future efforts to develop a new prediction model or update existing ones for COVID-19 patients.

4.4 Strengths and limitations

The major strength of our study is that it provides an overall mapping, and statistical synthesis of all published studies examining prognostic factors for multiple health outcomes in COVID-19 patients. We especially focused on including only studies with non-overlapping populations in each meta-analysis. This was achieved through detailed scrutinization of the methodology of eligible articles to capture the period of recruitment, and the hospital setting of each study. Furthermore, we enhanced our systematic review and meta-analysis by a risk of bias assessment using QUIPS tool to identify the domains that could introduce bias to the prognostic factor's effect estimates.

However, our study has some limitations. We observed high risk of bias in at least one domain in almost all the studies, and this fact could lead to biased prognostic factor's effect estimates in the meta-analyses. Furthermore, half of the meta-analyses presented large between-study heterogeneity, but sources of heterogeneity could not be adequately explored due to poor reporting in the majority of articles. Potential sources of heterogeneity include different sampling methods and duration of follow up, varying diagnostic criteria of COVID-19, inclusion of COVID-19 patients of various severity groups or stages of disease and use of different treatment regimens between studies.

Incomplete reporting did not allow us to examine the effect of these characteristics by subgroup analyses, sensitivity analyses or meta-regression in the summary effect of the meta-analyses. Moreover, a meta-analysis was not feasible for outcomes that were not defined in a standardized manner across different studies, such as progression of COVID-19, acute myocardial injury, and acute liver injury.

5 Conclusions

Our article systematically identified and assessed all the published studies examining prognostic factors for adverse outcomes in patients with COVID-19 published until the end of July 2020. We made an exhaustive and comprehensive effort to assess the quality of the studies and to exclude all possible duplicate studies and studies including overlapping population to avoid inflation of the reported summary effects. Our findings could facilitate the selection of candidate predictors for development or update of multivariable prognostic models.

Contributors:

VB and LB conceived and designed the study, did the literature search, the data extraction, and the statistical analyses. VB, LB, IT and EE and wrote the first draft. MvS and KGMM critically commented on the first draft. All the authors wrote the final version of the manuscript. LB accepts full responsibility for the work and conduct of the study, had access to the data, and controlled the decision to publish. The corresponding author attests that all listed authors meet authorship criteria and that no other meeting the criteria have been omitted. VB and LB are the guarantors.

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Ethical approval:

Not needed.

Data sharing:

Additional data for the eligible studies are available on request from the corresponding author at lazaros.belbasis@gmail.com.

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Figure 1. Flow chart of literature search for individual prognostic factors in patients with COVID-19.

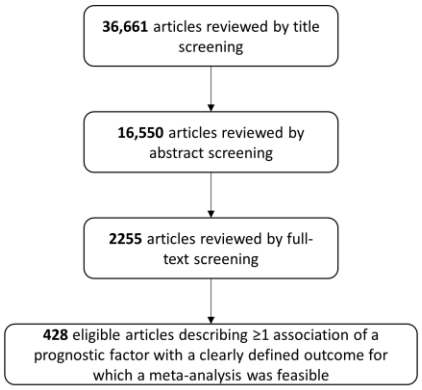


Figure 2. Risk of bias assessment (using QUIPS) based on six domains across 428 eligible articles for adverse outcomes in patients with COVID-19.

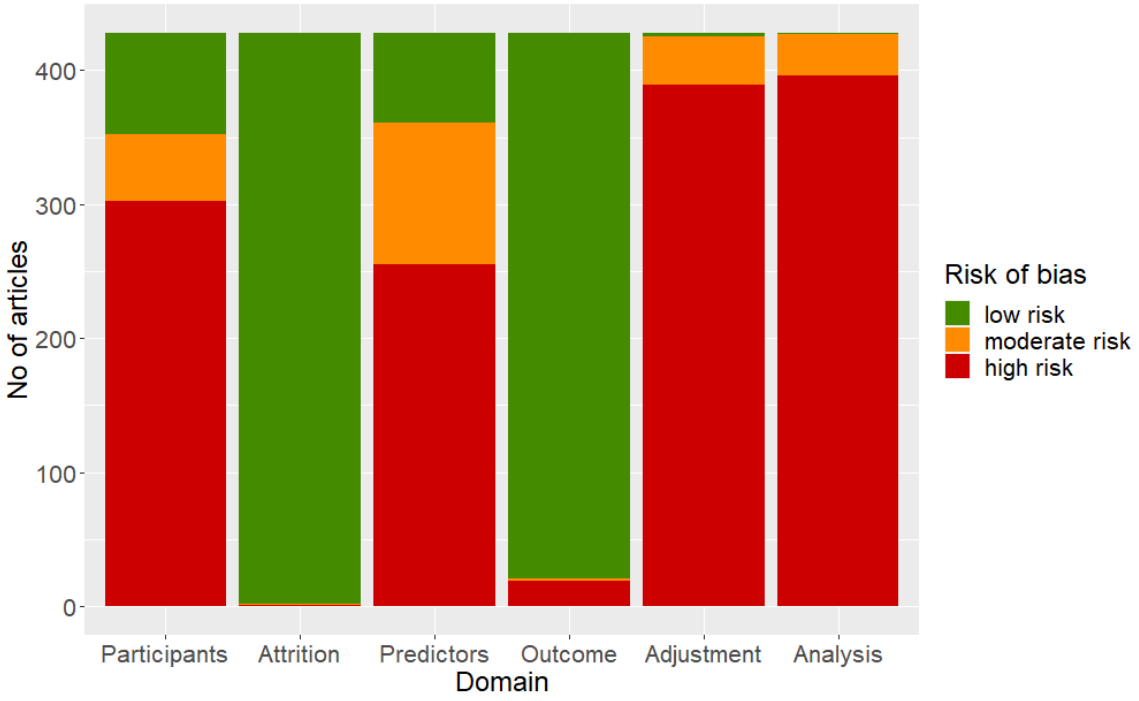
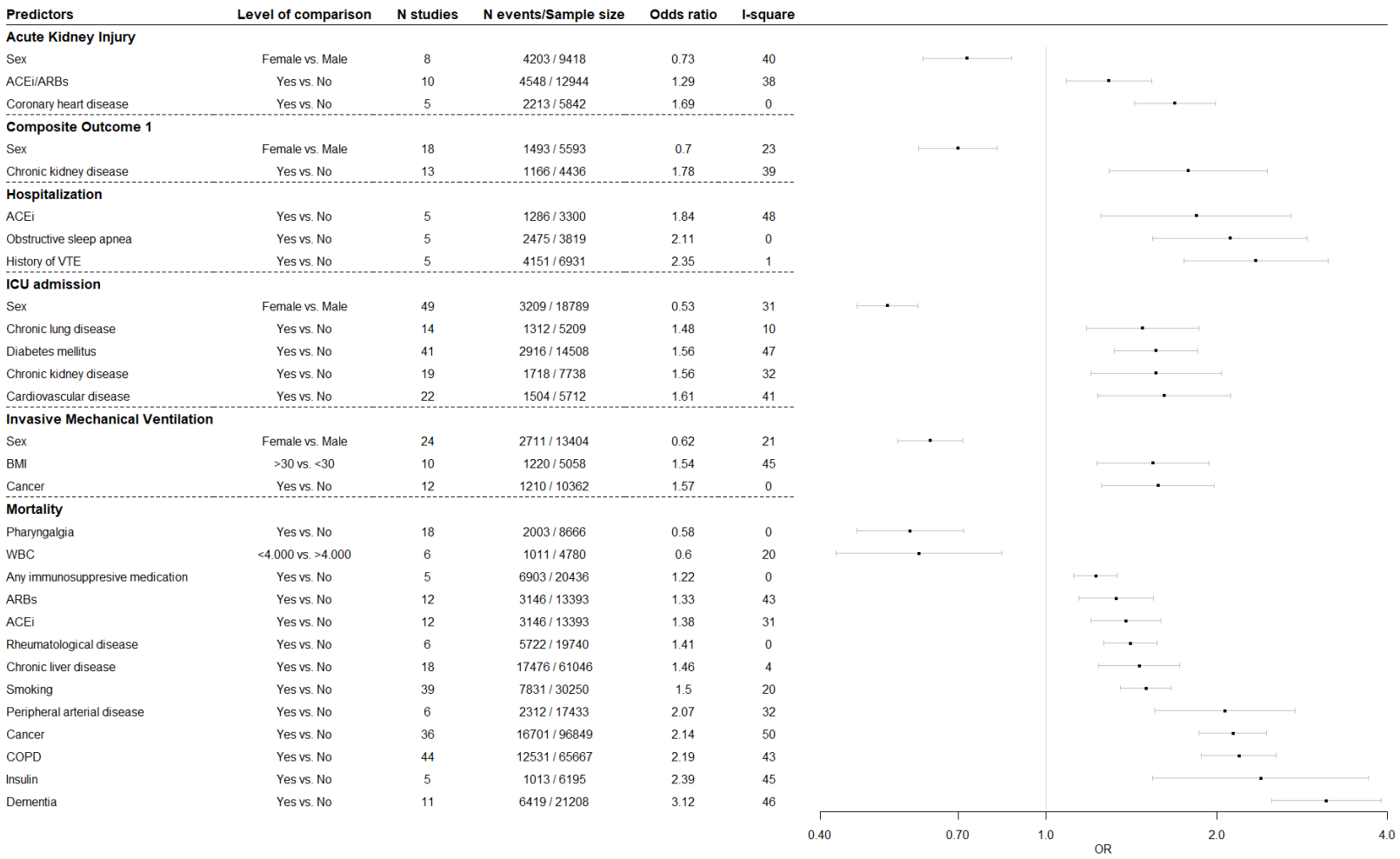


Figure 3. Forest plot of the 29 associations that had more than 1000 events, P-value <0.005, I^2 <50%, absence of small-study effects.



Predictors	Level of comparison	N studies	N events/Sample size	Odds ratio	I-square
Acute Kidney Injury					
Sex	Female vs. Male	8	4203 / 9418	0.73	40
ACEi/ARBs	Yes vs. No	10	4548 / 12944	1.29	38
Coronary heart disease	Yes vs. No	5	2213 / 5842	1.69	0
Composite Outcome 1					
Sex	Female vs. Male	18	1493 / 5593	0.7	23
Chronic kidney disease	Yes vs. No	13	1166 / 4436	1.78	39
Hospitalization					
ACEi	Yes vs. No	5	1286 / 3300	1.84	48
Obstructive sleep apnea	Yes vs. No	5	2475 / 3819	2.11	0
History of VTE	Yes vs. No	5	4151 / 6931	2.35	1
ICU admission					
Sex	Female vs. Male	49	3209 / 18789	0.53	31
Chronic lung disease	Yes vs. No	14	1312 / 5209	1.48	10
Diabetes mellitus	Yes vs. No	41	2916 / 14508	1.56	47
Chronic kidney disease	Yes vs. No	19	1718 / 7738	1.56	32
Cardiovascular disease	Yes vs. No	22	1504 / 5712	1.61	41
Invasive Mechanical Ventilation					
Sex	Female vs. Male	24	2711 / 13404	0.62	21
BMI	>30 vs. <30	10	1220 / 5058	1.54	45
Cancer	Yes vs. No	12	1210 / 10362	1.57	0
Mortality					
Pharyngalgia	Yes vs. No	18	2003 / 8666	0.58	0
WBC	<4.000 vs. >4.000	6	1011 / 4780	0.6	20
Any immunosuppresive medication	Yes vs. No	5	6903 / 20436	1.22	0
ARBs	Yes vs. No	12	3146 / 13393	1.33	43
ACEi	Yes vs. No	12	3146 / 13393	1.38	31
Rheumatological disease	Yes vs. No	6	5722 / 19740	1.41	0
Chronic liver disease	Yes vs. No	18	17476 / 61046	1.46	4
Smoking	Yes vs. No	39	7831 / 30250	1.5	20
Peripheral arterial disease	Yes vs. No	6	2312 / 17433	2.07	32
Cancer	Yes vs. No	36	16701 / 96849	2.14	50
COPD	Yes vs. No	44	12531 / 65667	2.19	43
Insulin	Yes vs. No	5	1013 / 6195	2.39	45
Dementia	Yes vs. No	11	6419 / 21208	3.12	46

Figure 4. Sankey diagram presenting the 29 statistically significant associations at P-value <0.005 that had more than 1000 events, I^2 <50%, absence of small-study effects.

The thickness of each line connecting a prognostic factor with an outcome depends on the number of studies examining this association.

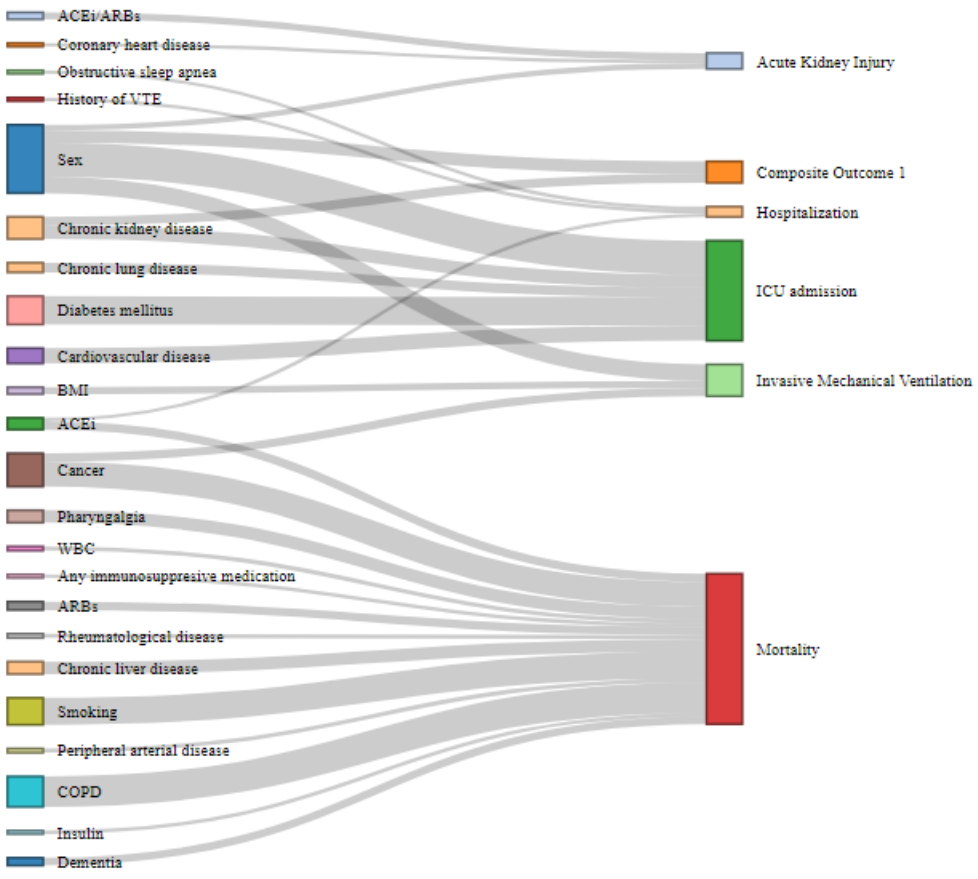


Table 1. Key items for framing aim, search strategy, and study inclusion and exclusion criteria for systematic review, following PICOTS guidance.

Item	**Definition**
Population	Patients diagnosed with COVID-19
Index prognostic factors	Any variable that was measured upon hospital admission or diagnosis of COVID-19 and was examined for an association with any adverse event
Comparator prognostic factors	Not applicable
Outcomes	Any clearly defined adverse event in patients with COVID-19
Timing	Prognostic factors measured upon diagnosis of COVID-19 or hospital admission, and predicting any time horizon of the adverse outcomes
Setting	Patients visiting ambulatory healthcare facilities, patients admitted to hospital, or patients visiting emergency department

Supplementary material

Supplementary methods

Supplementary Table 1. Risk of bias assessment using QUIPS tool for the 428 eligible articles that participated in the meta-analyses.

Supplementary Table 2. Results of the 263 meta-analyses for predictors of clinical outcomes in patients with COVID-19.

Supplementary Table 3. Results of the sensitivity analysis excluding the studies that reported hazard ratios.

Supplementary Table 4. Results of the sensitivity analysis excluding the studies with less than 100 COVID-19 participants.

Supplementary Table 5. Results of the sensitivity analysis excluding the studies including only COVID-19 patients with a specific comorbid disorder.

Supplementary references

Supplementary methods

Eligibility criteria

We excluded studies that examined the diagnostic factors distinguishing COVID-19 pneumonia and community-acquired pneumonia; the prognostic factors for infections by other coronaviruses; and the predictors of a positive result in testing for SARS-COV-2 in patients suspected for COVID-19. Moreover, we excluded studies that performed propensity score matching, because this approach is appropriate for causal inference rather than prediction. We excluded case-series including less than 20 COVID-19 patients, and studies published in languages other than English.

Data extraction

If the handling of a prognostic factor (i.e., dichotomous, categorical, or continuous) was not reported, we did not extract this association. For dichotomized continuous prognostic factors, we extracted the cut-off value. Also, when a measure of association was not reported, for binary factors, we extracted the number of individuals with the factor present in both patients with and without the outcome. For studies conducted in the same geographic region, we compared hospitals and recruitment periods to ensure that fully independent populations will be included in each meta-analysis. When multiple studies with potentially overlapping samples examined the same association, we kept the study that had the largest sample size for the corresponding meta-analysis.

Risk of bias assessment

We also assessed whether the eligible studies applied a multivariable analysis in which they adjusted the associations of specific prognostic factors for other prognostic factors. For studies examining multiple prognostic factors and/or

outcomes, we assessed the pertinent question with the highest risk of bias grade for the ascertainment of the prognostic factor and outcome. The eligible studies were assessed on the basis of the prognostic factors and the outcomes that participated in a meta-analysis.

Supplementary Table 1. Risk of bias assessment using QUIPS tool for the 428 eligible articles that participated in the meta-analyses.

First Author, Year	Country	Study participation	Study attrition	Prognostic factor measurement	Outcome measurement	Adjustment for other prognostic factors	Statistical analysis and reporting
Abrishami et al, 2020 [1]	Iran	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Abrishami et al, 2020 [2]	Iran	High risk	Low risk	High risk	Low risk	High risk	High risk
Adegunsoye et al, 2020 [3]	USA	Moderate risk	Low risk	Low risk	Low risk	Moderate risk	High risk
Aggarwal et al, 2020 [4]	India	High risk	Low risk	High risk	Low risk	High risk	High risk
Alberici et al, 2020 [5]	Italy	Moderate risk	Low risk	High risk	Low risk	High risk	High risk
Alkundi et al, 2020 [6]	UK	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Allocca et al, 2020 [7]	Italy	High risk	Low risk	High risk	High risk	High risk	High risk
Aloisio et al, 2020 [8]	Italy	High risk	Low risk	High risk	Low risk	High risk	High risk
Aloisio et al, 2020 [9]	Italy	High risk	Low risk	Low risk	Low risk	High risk	High risk
Al-Salameh et al, 2020 [10]	France	Low risk	Low risk	Moderate risk	Low risk	High risk	High risk
Al-Samkari et al, 2020 [11]	USA	High risk	Low risk	High risk	Low risk	High risk	High risk
Amit et al, 2020 [12]	Israel	High risk	Low risk	High risk	Low risk	High risk	High risk
Antinori et al, 2020 [13]	Italy	High risk	Low risk	High risk	Low risk	High risk	High risk
Antony et al, 2020 [14]	USA	High risk	Low risk	Low risk	Low risk	High risk	High risk
Arapovic et al, 2020 [15]	Bosnia-Herzegovina	High risk	Low risk	Low risk	Low risk	High risk	High risk
Argenziano et al, 2020 [16]	USA	Moderate risk	Low risk	High risk	Low risk	High risk	High risk
Arlet et al, 2020 [17]	France	High risk	Low risk	Low risk	Low risk	High risk	High risk
Artifoni et al, 2020 [18]	France	High risk	Low risk	High risk	Low risk	High risk	High risk
Assaad et al, 2020 [19]	France	Moderate risk	Low risk	Low risk	Low risk	High risk	Moderate risk
Auld et al, 2020 [20]	USA	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Ayanian et al, 2020 [21]	USA	High risk	Low risk	High risk	Low risk	High risk	High risk
Ayerbe et al, 2020 [22]	Spain	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Azar et al, 2020 [23]	USA	Low risk	Low risk	High risk	Low risk	High risk	High risk
Baqui et al, 2020 [24]	Brazil	High risk	Low risk	High risk	Low risk	High risk	High risk
Barbero et al, 2020 [25]	Spain	Moderate risk	Low risk	High risk	Low risk	High risk	High risk
Barman et al, 2020 [26]	Turkey	High risk	Low risk	Low risk	Low risk	High risk	Moderate risk
Barrasa et al, 2020 [27]	Spain	Low risk	Low risk	Low risk	Low risk	High risk	High risk
Bavaro et al, 2020 [28]	Italy	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Bazzan et al, 2020 [29]	Italy	High risk	Low risk	Low risk	Low risk	High risk	High risk
Bean et al, 2020 [30]	UK	Low risk	Low risk	Low risk	Low risk	Moderate risk	High risk
Bellelli et al, 2020 [31]	Italy	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Benoy et al, 2020 [32]	Netherlands	High risk	Low risk	High risk	Low risk	High risk	High risk
Benussi et al, 2020 [33]	Italy	High risk	Low risk	Low risk	Low risk	High risk	High risk
Bhargava et al, 2020 [34]	USA	High risk	Low risk	High risk	Low risk	High risk	High risk

First Author, Year	Country	Study participation	Study attrition	Prognostic factor measurement	Outcome measurement	Adjustment for other prognostic factors	Statistical analysis and reporting
Bhatla et al, 2020 [35]	USA	Low risk	Low risk	High risk	Low risk	High risk	High risk
Biagi et al, 2020 [36]	Italy	Low risk	Low risk	Low risk	Low risk	High risk	High risk
Bianchetti et al, 2020 [37]	Italy	Moderate risk	Low risk	Moderate risk	Low risk	Moderate risk	High risk
Bolondi et al, 2020 [38]	Italy	High risk	Low risk	Low risk	Low risk	High risk	High risk
Bonetti et al, 2020 [39]	Italy	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Borghesi et al, 2020 [40]	Italy	High risk	Low risk	High risk	Low risk	High risk	High risk
Borobia et al, 2020 [41]	Spain	High risk	Low risk	High risk	Low risk	High risk	High risk
Boscolo et al, 2020 [42]	Italy	High risk	Low risk	High risk	Low risk	High risk	High risk
Bossini et al, 2020 [43]	Italy	Moderate risk	Low risk	High risk	Low risk	High risk	High risk
Bravi et al, 2020 [44]	Italy	Low risk	Low risk	Moderate risk	Low risk	High risk	High risk
Brill et al, 2020 [45]	UK	High risk	Low risk	High risk	Low risk	High risk	High risk
Brouns et al, 2020 [46]	Netherlands	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Bruno et al, 2020 [47]	Italy	Low risk	Low risk	Low risk	Low risk	High risk	High risk
Buckner et al, 2020 [48]	USA	Low risk	Low risk	High risk	Low risk	High risk	High risk
Buscarini et al, 2020 [49]	Italy	Moderate risk	Low risk	High risk	Low risk	High risk	High risk
Busetto et al, 2020 [50]	Italy	Low risk	Low risk	High risk	Low risk	Moderate risk	High risk
Cabezudo-García et al, 2020 [51]	Spain	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Cai et al, 2020 [52]	China	High risk	Low risk	High risk	Low risk	High risk	High risk
Cao et al, 2020 [53]	China	Low risk	Low risk	Low risk	Low risk	High risk	High risk
Cariou et al, 2020 [54]	France	High risk	Low risk	High risk	Low risk	High risk	High risk
Carlino et al, 2020 [55]	Italy	High risk	Low risk	High risk	Low risk	High risk	High risk
Carrasco et al, 2020 [56]	Spain	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Caussy et al, 2020 [57]	France	High risk	Low risk	High risk	Low risk	High risk	High risk
Ceano-Vivas et al, 2020 [58]	Spain	Moderate risk	Low risk	High risk	Low risk	High risk	High risk
Cecconi et al, 2020 [59]	Italy	Low risk	Low risk	High risk	Low risk	High risk	Moderate risk
Cen et al, 2020 [60]	China	High risk	Low risk	High risk	Low risk	High risk	High risk
Chamorro-Pareja et al, 2020 [61]	USA	High risk	Low risk	Low risk	Low risk	High risk	High risk
Chan et al, 2020 [62]	Singapore	High risk	Low risk	Low risk	Low risk	High risk	High risk
Chao et al, 2020 [63]	USA	High risk	Low risk	High risk	Low risk	High risk	High risk
Chaudhry et al, 2020 [64]	USA	High risk	Low risk	High risk	Low risk	High risk	High risk
Chen et al, 2020 [65]	China	High risk	Low risk	High risk	Low risk	High risk	High risk
Chen et al, 2020 [66]	China	High risk	Low risk	High risk	Low risk	High risk	High risk
Chen et al, 2020 [67]	China	High risk	Low risk	High risk	Low risk	High risk	High risk
Chen et al, 2020 [68]	China	High risk	Low risk	High risk	Low risk	High risk	High risk
Chen et al, 2020 [69]	China	High risk	Low risk	High risk	Low risk	High risk	High risk
Chen et al, 2020 [70]	China	High risk	Low risk	High risk	Low risk	High risk	Moderate risk
Chen et al, 2021 [71]	China	High risk	Low risk	Moderate risk	Moderate risk	High risk	High risk

First Author, Year	Country	Study participation	Study attrition	Prognostic factor measurement	Outcome measurement	Adjustment for other prognostic factors	Statistical analysis and reporting
Chen et al, 2020 [72]	China	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Chen et al, 2020 [73]	China	High risk	Low risk	Moderate risk	Low risk	Moderate risk	High risk
Cheng et al, 2020 [74]	China	Low risk	Low risk	Low risk	Low risk	High risk	Moderate risk
Chhiba et al, 2020 [75]	USA	Low risk	Low risk	Moderate risk	Low risk	Moderate risk	Moderate risk
Cholankeril et al, 2020 [76]	USA	High risk	Low risk	High risk	Low risk	High risk	High risk
Chougar et al, 2020 [77]	France	High risk	Low risk	High risk	Low risk	High risk	High risk
Chung et al, 2020 [78]	Korea	High risk	Low risk	Moderate risk	High risk	High risk	High risk
Ciceri et al, 2020 [79]	Italy	High risk	Low risk	High risk	Low risk	High risk	High risk
Colombi et al, 2020 [80]	Italy	High risk	Low risk	High risk	Low risk	High risk	High risk
Conversano et al, 2020 [81]	Italy	Low risk	Moderate risk	Low risk	Low risk	High risk	High risk
Covino et al, 2020 [82]	Italy	Moderate risk	Low risk	High risk	Low risk	High risk	High risk
Criel et al, 2020 [83]	Belgium	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
d'Alessandro et al, 2020 [84]	Italy	High risk	Low risk	Low risk	Low risk	High risk	High risk
Davies et al, 2020 [85]	UK	High risk	Low risk	Low risk	Low risk	High risk	High risk
De Smet et al, 2020 [86]	Belgium	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Deiana et al, 2020 [87]	Italy	High risk	Low risk	Low risk	Low risk	High risk	High risk
Del Amo et al, 2020 [88]	Spain	Low risk	Low risk	Low risk	Low risk	High risk	High risk
Della-Torre et al, 2020 [89]	Italy	High risk	Low risk	High risk	Low risk	High risk	High risk
Demelo-Rodríguez et al, 2020 [90]	Spain	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Deng et al, 2020 [91]	China	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Deng et al, 2020 [92]	China	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Deng et al, 2020 [93]	China	High risk	Low risk	High risk	Low risk	High risk	High risk
Denova-Gutiérrez et al, 2020 [94]	Mexico	Moderate risk	Low risk	High risk	Low risk	High risk	High risk
Desborough et al, 2020 [95]	UK	High risk	Low risk	Moderate risk	High risk	High risk	High risk
Di Bella et al, 2020 [96]	Italy	High risk	Low risk	High risk	Low risk	High risk	High risk
Ding et al, 2020 [97]	China	High risk	Low risk	High risk	Low risk	High risk	High risk
Docherty et al, 2020 [98]	UK	Low risk	Low risk	High risk	Low risk	High risk	Moderate risk
Dreher et al, 2020 [99]	Germany	High risk	Low risk	High risk	Low risk	High risk	High risk
D'Silva et al, 2020 [100]	USA	High risk	Low risk	High risk	Low risk	High risk	High risk
Du et al, 2020 [101]	China	High risk	Low risk	High risk	Low risk	High risk	High risk
Du et al, 2020 [102]	China	Moderate risk	Low risk	High risk	Low risk	High risk	High risk
Duanmu et al, 2020 [103]	USA	High risk	Low risk	High risk	Low risk	High risk	High risk
Dudoignon et al, 2020 [104]	France	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Dufour et al, 2020 [105]	Belgium	High risk	Low risk	High risk	Low risk	High risk	High risk
Ebinger et al, 2020 [106]	USA	Low risk	Low risk	High risk	Low risk	High risk	High risk
Escalera-Antezana et al, 2020 [107]	Bolivia	Low risk	Low risk	Moderate risk	Low risk	High risk	High risk
Fang et al, 2020 [108]	UK	High risk	Low risk	Moderate risk	Low risk	High risk	High risk

First Author, Year	Country	Study participation	Study attrition	Prognostic factor measurement	Outcome measurement	Adjustment for other prognostic factors	Statistical analysis and reporting
Fauvel et al, 2020 [109]	France	High risk	Low risk	High risk	High risk	High risk	High risk
Felice et al, 2020 [110]	Italy	Moderate risk	Low risk	Low risk	High risk	High risk	High risk
Feng et al, 2020 [111]	China	High risk	Low risk	Low risk	Low risk	High risk	High risk
Ferguson et al, 2020 [112]	USA	Low risk	Low risk	Moderate risk	Low risk	High risk	High risk
Ferm et al, 2020 [113]	USA	High risk	Low risk	High risk	Low risk	High risk	High risk
Fernández-Cruz et al, 2020 [114]	Spain	High risk	Low risk	High risk	Low risk	High risk	High risk
Ferrante et al, 2020 [115]	Italy	High risk	Low risk	High risk	Low risk	High risk	Moderate risk
Fisher et al, 2020 [116]	USA	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Fogarty et al, 2020 [117]	Ireland	Low risk	Low risk	Moderate risk	Low risk	High risk	High risk
Fominskiy et al, 2021 [118]	Italy	Low risk	Low risk	Moderate risk	Low risk	High risk	High risk
Fosbøl et al, 2020 [119]	Denmark	Low risk	Low risk	Low risk	Low risk	Low risk	Moderate risk
Foster et al, 2020 [120]	USA	Moderate risk	Low risk	High risk	Low risk	High risk	High risk
Fox et al, 2020 [121]	UK	High risk	Low risk	High risk	Low risk	High risk	High risk
Francone et al, 2020 [122]	Italy	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Götzinger et al, 2020 [123]	Europe	High risk	Low risk	High risk	Low risk	High risk	High risk
Gallo et al, 2020 [124]	Italy	Moderate risk	Low risk	High risk	Low risk	High risk	High risk
Gao et al, 2020 [125]	China	High risk	Low risk	Moderate risk	Low risk	High risk	Moderate risk
Gao et al, 2020 [126]	China	Low risk	Low risk	High risk	Low risk	High risk	High risk
Gao et al, 2020 [127]	China	High risk	Low risk	High risk	Low risk	High risk	High risk
Garcia-Pachon et al, 2020 [128]	Spain	Low risk	Low risk	Moderate risk	Low risk	High risk	High risk
Gavin et al, 2020 [129]	USA	Low risk	Low risk	High risk	Low risk	High risk	High risk
Gayam et al, 2021 [130]	USA	High risk	Low risk	High risk	Low risk	High risk	High risk
Gazzaruso et al, 2020 [131]	Italy	High risk	Low risk	Low risk	Low risk	High risk	High risk
Gervaise et al, 2020 [132]	France	High risk	Low risk	Low risk	Low risk	High risk	High risk
Gervasoni et al, 2020 [133]	Italy	Moderate risk	Low risk	Low risk	High risk	High risk	High risk
Giacomelli et al, 2020 [134]	Italy	Low risk	Low risk	High risk	Low risk	High risk	High risk
Gidari et al, 2020 [135]	Italy	Moderate risk	Low risk	Moderate risk	Low risk	High risk	High risk
Giusti et al, 2020 [136]	Italy	High risk	Low risk	Low risk	Low risk	High risk	High risk
Goicoechea et al, 2020 [137]	Spain	Moderate risk	Low risk	High risk	Low risk	High risk	High risk
Gold et al, 2020 [138]	USA	High risk	Low risk	Low risk	Low risk	High risk	High risk
Golpe et al, 2020 [139]	Spain	High risk	Low risk	High risk	Low risk	Moderate risk	Moderate risk
Golpe et al, 2020 [140]	Spain	Moderate risk	Low risk	Moderate risk	Low risk	Moderate risk	Moderate risk
Goshua et al, 2020 [141]	USA	High risk	Low risk	High risk	Low risk	High risk	High risk
Goyal et al, 2020 [142]	USA	Low risk	Low risk	High risk	Low risk	High risk	High risk
Goyal et al, 2020 [143]	USA	High risk	Low risk	High risk	Low risk	Moderate risk	Moderate risk
Grandmaison et al, 2020 [144]	Switzerland	High risk	Low risk	Moderate risk	Moderate risk	High risk	High risk
Grasseli et al, 2020 [145]	Italy	High risk	Low risk	High risk	Low risk	High risk	High risk
Gregoriano et al, 2020 [146]	Switzerland	Low risk	Low risk	High risk	Low risk	High risk	Moderate risk

First Author, Year	Country	Study participation	Study attrition	Prognostic factor measurement	Outcome measurement	Adjustment for other prognostic factors	Statistical analysis and reporting
Guan et al, 2020 [147]	China	High risk	Low risk	Low risk	Low risk	High risk	High risk
Gupta et al, 2020 [148]	USA	Low risk	Low risk	High risk	Low risk	Moderate risk	Moderate risk
Hajifathalian et al, 2020 [149]	USA	Low risk	Low risk	High risk	Low risk	High risk	High risk
Hajifathalian et al, 2020 [150]	USA	High risk	Low risk	High risk	Low risk	High risk	Moderate risk
Halasz et al, 2020 [151]	Italy	Moderate risk	Low risk	High risk	Low risk	High risk	High risk
Halvatsiotis et al, 2020 [152]	Greece	High risk	Low risk	High risk	Low risk	High risk	High risk
Harmouch et al, 2020 [153]	USA	High risk	Low risk	High risk	Low risk	High risk	High risk
Hattori et al, 2021 [154]	Japan	High risk	Low risk	Low risk	High risk	High risk	High risk
Hengeveld et al, 2020 [155]	Netherlands	Moderate risk	Low risk	High risk	Low risk	High risk	High risk
Herold et al, 2020 [156]	Germany	High risk	Low risk	High risk	Low risk	High risk	High risk
Hewitt et al, 2020 [157]	UK, Italy	High risk	Low risk	High risk	Low risk	Moderate risk	Moderate risk
Hippensteel et al, 2020 [158]	USA	High risk	Low risk	High risk	High risk	High risk	High risk
Hirsch et al, 2020 [159]	USA	High risk	Low risk	Moderate risk	Low risk	Moderate risk	High risk
Holt et al, 2020 [160]	Denmark	Low risk	Low risk	Low risk	Low risk	High risk	High risk
Hong et al, 2020 [161]	Korea	Moderate risk	Low risk	High risk	Low risk	High risk	High risk
Horby et al, 2020 [162]	UK	Moderate risk	Low risk	High risk	Low risk	High risk	High risk
Hottz et al, 2020 [163]	Brazil	High risk	Low risk	High risk	Low risk	High risk	High risk
Hsu et al, 2020 [164]	USA	Moderate risk	Low risk	High risk	Low risk	High risk	High risk
Hu et al, 2020 [165]	China	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Huang et al, 2020 [166]	China	Low risk	Low risk	High risk	Low risk	High risk	High risk
Huang et al, 2020 [167]	China	High risk	Low risk	High risk	Low risk	High risk	High risk
Huang et al, 2020 [168]	China	High risk	Low risk	High risk	Low risk	High risk	High risk
Huang et al, 2020 [169]	China	High risk	Low risk	High risk	Low risk	High risk	High risk
Hur et al, 2020 [170]	USA	High risk	Low risk	High risk	Low risk	High risk	High risk
Husain-Syed et al, 2020 [171]	Germany	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Hwang et al, 2020 [172]	Korea	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Iaccarino et al, 2020 [173]	Italy	High risk	Low risk	High risk	Low risk	High risk	High risk
Imam et al, 2020 [174]	USA	High risk	Low risk	High risk	High risk	High risk	High risk
Imam et al, 2020 [175]	USA	High risk	Low risk	High risk	Low risk	High risk	High risk
Inciardi et al, 2020 [176]	Italy	High risk	Low risk	High risk	Low risk	High risk	High risk
Israelsen et al, 2020 [177]	Denmark	Low risk	Low risk	High risk	Low risk	High risk	High risk
Izquierdo-Domínguez et al, 2020 [178]	Spain	High risk	Low risk	High risk	Low risk	High risk	High risk
Jalili et al, 2021 [179]	Iran	Low risk	Low risk	High risk	Low risk	High risk	High risk
Jang et al, 2020 [180]	Korea	High risk	Low risk	High risk	Low risk	High risk	High risk
Javanian et al, 2020 [181]	Iran	High risk	Low risk	High risk	Low risk	High risk	High risk
Jiang et al, 2020 [182]	China	High risk	Low risk	High risk	Low risk	High risk	High risk
Jordan et al, 2020 [183]	USA	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Jung et al, 2020 [184]	Korea	Low risk	Low risk	Low risk	Low risk	Moderate risk	High risk

First Author, Year	Country	Study participation	Study attrition	Prognostic factor measurement	Outcome measurement	Adjustment for other prognostic factors	Statistical analysis and reporting
Kalan et al, 2020 [185]	Iran	High risk	Low risk	High risk	Low risk	High risk	High risk
Kalligeros et al, 2020 [186]	USA	Low risk	Low risk	High risk	Low risk	High risk	High risk
Karmen-Tuohy et al, 2020 [187]	USA	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Kayem et al, 2020 [188]	France	High risk	Low risk	High risk	High risk	High risk	High risk
Kebisek et al, 2020 [189]	USA	Low risk	Low risk	High risk	Low risk	High risk	High risk
Khalil et al, 2020 [190]	UK	High risk	Low risk	High risk	Low risk	High risk	High risk
Khamis et al, 2020 [191]	Oman	Moderate risk	Low risk	High risk	Low risk	High risk	High risk
Khamis et al, 2020 [192]	Oman	Low risk	Low risk	Low risk	Low risk	High risk	High risk
Killerby et al, 2020 [193]	USA	High risk	Low risk	High risk	Low risk	High risk	High risk
Kim et al, 2020 [194]	Korea	Low risk	Low risk	Moderate risk	Low risk	Moderate risk	High risk
Kim et al, 2020 [195]	USA	High risk	Low risk	High risk	Low risk	Low risk	Moderate risk
King et al, 2020 [196]	USA	High risk	Low risk	High risk	Low risk	High risk	High risk
Klang et al, 2020 [197]	USA	High risk	Low risk	High risk	Low risk	Moderate risk	High risk
Klok et al, 2020 [198]	Netherlands	High risk	Low risk	Low risk	Low risk	High risk	High risk
Knights et al, 2020 [199]	UK	High risk	Low risk	High risk	Low risk	High risk	High risk
Knorr et al, 2020 [200]	USA	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Koleilat et al, 2021 [201]	USA	High risk	Low risk	Moderate risk	High risk	High risk	High risk
Korkmaz et al, 2020 [202]	Turkey	High risk	Low risk	High risk	Low risk	High risk	High risk
Kormann et al, 2020 [203]	France	High risk	Low risk	High risk	Low risk	High risk	High risk
Kragholm et al, 2020 [204]	Denmark	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Krishnan et al, 2020 [205]	USA	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Kuno et al, 2020 [206]	USA	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Lagadinou et al, 2020 [207]	Greece	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Lagi et al, 2020 [208]	Italy	Moderate risk	Low risk	High risk	Low risk	High risk	High risk
Larsen et al, 2020 [209]	France	High risk	Low risk	High risk	Low risk	High risk	High risk
Larson et al, 2020 [210]	USA	Moderate risk	Low risk	High risk	Low risk	High risk	High risk
Lee et al, 2020 [211]	UK	Moderate risk	Low risk	Moderate risk	Low risk	High risk	High risk
Lee et al, 2020 [212]	Korea	Moderate risk	Low risk	High risk	Low risk	High risk	High risk
Lee et al, 2020 [213]	Korea	High risk	Low risk	High risk	Low risk	High risk	High risk
Lee et al, 2020 [214]	USA	High risk	Low risk	High risk	Low risk	High risk	High risk
Li et al, 2020 [215]	China	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Li et al, 2020 [216]	China	Low risk	Low risk	Moderate risk	Low risk	High risk	Moderate risk
Li et al, 2020 [217]	China	High risk	Low risk	High risk	Low risk	Moderate risk	High risk
Li et al, 2020 [218]	China	Low risk	Low risk	High risk	Low risk	High risk	High risk
Li et al, 2020 [219]	China	High risk	Low risk	Low risk	Low risk	High risk	High risk
Li et al, 2020 [220]	China	High risk	Low risk	High risk	Low risk	High risk	High risk
Li et al, 2020 [221]	China	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Liabeuf et al, 2020 [222]	France	High risk	Low risk	High risk	Low risk	High risk	High risk
Lim et al, 2020 [223]	Korea	High risk	Low risk	Moderate risk	Low risk	High risk	High risk

First Author, Year	Country	Study participation	Study attrition	Prognostic factor measurement	Outcome measurement	Adjustment for other prognostic factors	Statistical analysis and reporting
Lin et al, 2021 [224]	China	High risk	Low risk	High risk	Low risk	High risk	Moderate risk
Liu et al, 2020 [225]	China	High risk	Low risk	High risk	Low risk	High risk	High risk
Liu et al, 2020 [226]	China	High risk	Low risk	High risk	Low risk	High risk	High risk
Liu et al, 2020 [227]	China	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Liu et al, 2020 [228]	China	High risk	Low risk	High risk	Low risk	High risk	High risk
Liu et al, 2020 [229]	China	High risk	Low risk	High risk	Low risk	High risk	High risk
Liu et al, 2020 [230]	Hong Kong	High risk	Low risk	High risk	Low risk	High risk	High risk
Liu et al, 2020 [231]	China	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Liu et al, 2020 [232]	China	High risk	Low risk	High risk	Low risk	High risk	High risk
Lodigiani et al, 2020 [233]	Italy	Moderate risk	Low risk	High risk	Low risk	High risk	High risk
Loonstra et al, 2020 [234]	Netherlands	High risk	Low risk	High risk	Low risk	High risk	High risk
Lopez-Otero et al, 2021 [235]	Spain	Low risk	Low risk	Low risk	Low risk	Moderate risk	High risk
Lorente-Ros et al, 2020 [236]	Spain	Moderate risk	Low risk	Moderate risk	Low risk	High risk	Moderate risk
Louapre et al, 2020 [237]	France	High risk	Low risk	High risk	Low risk	High risk	High risk
Luan et al, 2020 [238]	China	High risk	Low risk	High risk	Low risk	High risk	High risk
Lubetzky et al, 2020 [239]	USA	High risk	Low risk	High risk	Low risk	High risk	High risk
Lumbreras-Marquez et al, 2020 [240]	Mexico	Low risk	Low risk	High risk	Low risk	High risk	High risk
Luo et al, 2020 [241]	China	High risk	Low risk	High risk	Low risk	High risk	High risk
Luo et al, 2020 [242]	USA	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Luo et al, 2020 [243]	China	High risk	Low risk	High risk	Low risk	High risk	High risk
Lynch et al, 2020 [244]	USA	High risk	Low risk	High risk	Low risk	High risk	High risk
Ma et al, 2020 [245]	China	High risk	Low risk	High risk	Low risk	High risk	High risk
Maatman et al, 2020 [246]	USA	High risk	Low risk	High risk	High risk	High risk	High risk
Macera et al, 2020 [247]	Italy	High risk	Low risk	High risk	Low risk	High risk	High risk
Mahdavinia et al, 2020 [248]	USA	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Malberti et al, 2020 [249]	Italy	High risk	Low risk	Low risk	Low risk	Moderate risk	High risk
Mani et al, 2020 [250]	USA	High risk	Low risk	High risk	Low risk	High risk	High risk
Mannheim et al, 2020 [251]	USA	High risk	Low risk	High risk	Low risk	High risk	High risk
Maquet et al, 2020 [252]	France	Low risk	Low risk	Low risk	Low risk	Moderate risk	High risk
Martín-Moro et al, 2020 [253]	Spain	Moderate risk	Low risk	High risk	Low risk	High risk	High risk
Martín-Sánchez et al, 2020 [254]	Spain	Low risk	Low risk	Low risk	Low risk	High risk	High risk
Marta-Enguita et al, 2020 [255]	Spain	High risk	Low risk	High risk	Low risk	High risk	High risk
Marzolini et al, 2020 [256]	Switzerland	High risk	Low risk	Low risk	Low risk	High risk	High risk
Masetti et al, 2020 [257]	Italy	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
McCullough et al, 2020 [258]	USA	High risk	Low risk	High risk	Low risk	High risk	High risk
Medetalibeyoğlu et al, 2020 [259]	Turkey	High risk	Low risk	Low risk	Low risk	High risk	High risk
Mendoza et al, 2020 [260]	Spain	High risk	Low risk	High risk	Low risk	High risk	High risk

First Author, Year	Country	Study participation	Study attrition	Prognostic factor measurement	Outcome measurement	Adjustment for other prognostic factors	Statistical analysis and reporting
Merzon et al, 2020 [261]	Israel	High risk	Low risk	High risk	Low risk	Moderate risk	High risk
Mestre-Gómez et al, 2021 [262]	Spain	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Meszaros et al, 2020 [263]	France	High risk	Low risk	Low risk	Low risk	High risk	High risk
Middeldorp et al, 2020 [264]	Netherlands	Moderate risk	Low risk	Moderate risk	Low risk	High risk	High risk
Mikami et al, 2021 [265]	USA	Moderate risk	Low risk	High risk	Low risk	High risk	High risk
Mishra et al, 2020 [266]	India	High risk	Low risk	Low risk	Low risk	High risk	Moderate risk
Miyashita et al, 2020 [267]	USA	Moderate risk	Low risk	Moderate risk	Low risk	High risk	High risk
Miyashita et al, 2020 [268]	USA	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Moghaddam et al, 2020 [269]	Germany	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Montagnani et al, 2020 [270]	Italy	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Montastruc et al, 2020 [271]	France	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Montopoli et al, 2020 [272]	Italy	High risk	Low risk	Low risk	Low risk	High risk	High risk
Moreno-Perez et al, 2020 [273]	Spain	High risk	Low risk	High risk	Low risk	High risk	High risk
Moriconi et al, 2020 [274]	Italy	Low risk	Low risk	High risk	Low risk	High risk	High risk
Morrison et al, 2020 [275]	USA	High risk	Low risk	High risk	Low risk	High risk	High risk
Myers et al, 2020 [276]	USA	High risk	Low risk	High risk	Low risk	High risk	High risk
Myrstad et al, 2020 [277]	Norway	High risk	Low risk	High risk	Low risk	High risk	High risk
Nahum et al, 2020 [278]	France	Low risk	Low risk	Moderate risk	Low risk	High risk	High risk
Nathwani et al, 2020 [279]	UK	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Nie et al, 2020 [280]	China	High risk	Low risk	High risk	Low risk	High risk	High risk
Nie et al, 2020 [281]	China	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Nikpouraghdam et al, 2020 [282]	Iran	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Nobel et al, 2020 [283]	USA	High risk	Low risk	High risk	Low risk	High risk	High risk
Nowak et al, 2020 [284]	Poland	Low risk	Low risk	High risk	Low risk	High risk	High risk
Nuno et al, 2020 [285]	Spain	High risk	Low risk	High risk	Low risk	High risk	High risk
Okoh et al, 2020 [286]	USA	High risk	Low risk	High risk	Low risk	High risk	High risk
Ortiz-Brizuela et al, 2020 [287]	Mexico	Low risk	Low risk	High risk	Low risk	High risk	High risk
Oussalah et al, 2020 [288]	France	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Paderno et al, 2020 [289]	Italy	High risk	Low risk	High risk	Low risk	High risk	High risk
Palaiodimos et al, 2020 [290]	USA	High risk	Low risk	High risk	Low risk	High risk	High risk
Panagiotou et al, 2020 [291]	UK	High risk	Low risk	High risk	Low risk	High risk	High risk
Panepinto et al, 2020 [292]	USA	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Parrotta et al, 2020 [293]	USA	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Patel et al, 2020 [294]	UK	High risk	Low risk	High risk	Low risk	High risk	High risk
Patell et al, 2020 [295]	USA	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Pelayo et al, 2020 [296]	USA	High risk	Low risk	Moderate risk	Low risk	Moderate risk	High risk
Pellaud et al, 2020 [297]	Switzerland	Low risk	Low risk	High risk	Low risk	High risk	High risk
Peng et al, 2020 [298]	China	High risk	Low risk	Low risk	Low risk	High risk	High risk

First Author, Year	Country	Study participation	Study attrition	Prognostic factor measurement	Outcome measurement	Adjustment for other prognostic factors	Statistical analysis and reporting
Pereira et al, 2020 [299]	USA	Moderate risk	Low risk	Moderate risk	Low risk	High risk	High risk
Pérez-Sáez et al, 2020 [300]	Spain	High risk	Low risk	High risk	Low risk	High risk	High risk
Petersen et al, 2020 [301]	Germany	High risk	Low risk	Low risk	Low risk	High risk	High risk
Petrilli et al, 2020 [302]	USA	Moderate risk	Low risk	Moderate risk	Low risk	High risk	High risk
Pettit et al, 2020 [303]	USA	High risk	Low risk	High risk	High risk	Moderate risk	High risk
Piano et al, 2020 [304]	Italy	High risk	Low risk	High risk	Low risk	High risk	High risk
Pinto et al, 2020 [305]	Italy	Low risk	Low risk	Low risk	Low risk	Moderate risk	High risk
Poblador-Plou et al, 2020 [306]	Spain	Low risk	Low risk	High risk	Low risk	Moderate risk	High risk
Ponziani et al, 2020 [307]	Italy	Low risk	Low risk	High risk	Low risk	High risk	High risk
Poyiadji et al, 2020 [308]	USA	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Qian et al, 2020 [309]	China	Low risk	Low risk	Low risk	Low risk	High risk	High risk
Qin et al, 2020 [310]	China	Moderate risk	Low risk	Moderate risk	Low risk	High risk	High risk
Qin et al, 2020 [311]	China	High risk	Low risk	High risk	Low risk	Moderate risk	Moderate risk
Quartuccio et al, 2020 [312]	Italy	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Ramachandran et al, 2020 [313]	USA	High risk	High risk	High risk	Low risk	High risk	High risk
Raoufi et al, 2020 [314]	Iran	High risk	Low risk	High risk	Low risk	High risk	High risk
Rastad et al, 2020 [315]	Iran	High risk	Low risk	High risk	Low risk	High risk	High risk
Rath et al, 2020 [316]	Germany	Low risk	Low risk	High risk	Low risk	High risk	High risk
Redd et al, 2020 [317]	USA	Low risk	Low risk	High risk	Low risk	High risk	High risk
Ren et al, 2020 [318]	China	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Richardson et al, 2020 [319]	USA	Low risk	Low risk	Moderate risk	Low risk	High risk	High risk
Rivera-Izquierdo et al, 2020 [320]	Spain	High risk	Low risk	High risk	Low risk	High risk	High risk
Rivera-Izquierdo et al, 2020 [321]	Spain	High risk	Low risk	High risk	Low risk	High risk	Moderate risk
Robilotti et al, 2020 [322]	USA	Moderate risk	Low risk	High risk	Low risk	High risk	High risk
Rogado et al, 2020 [323]	Spain	Moderate risk	Low risk	High risk	Low risk	High risk	High risk
Roman et al, 2020 [324]	Spain	High risk	Low risk	High risk	Low risk	High risk	Moderate risk
Rosenberg et al, 2020 [325]	USA	Moderate risk	Low risk	High risk	Low risk	High risk	High risk
Rossi et al, 2020 [326]	Italy	Moderate risk	Low risk	Moderate risk	Low risk	High risk	High risk
Rottoli et al, 2020 [327]	Italy	High risk	Low risk	High risk	Low risk	Moderate risk	High risk
Rubin et al, 2020 [328]	France	Moderate risk	Low risk	Low risk	Low risk	High risk	High risk
Russo et al, 2020 [329]	Italy	High risk	Low risk	High risk	Low risk	High risk	High risk
Sabri et al, 2020 [330]	Iran	High risk	Low risk	High risk	Low risk	High risk	High risk
Salacup et al, 2020 [331]	USA	High risk	Low risk	High risk	Low risk	Moderate risk	High risk
Saluja et al, 2020 [332]	India	High risk	Low risk	Low risk	Low risk	High risk	High risk
Sanchez-Pina et al, 2020 [333]	Spain	Moderate risk	Low risk	High risk	Low risk	High risk	High risk
Santoliquido et al, 2020 [334]	Italy	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Sardu et al, 2020 [335]	Italy	High risk	Low risk	Moderate risk	Low risk	High risk	High risk

First Author, Year	Country	Study participation	Study attrition	Prognostic factor measurement	Outcome measurement	Adjustment for other prognostic factors	Statistical analysis and reporting
Sardu et al, 2020 [336]	Italy	High risk	Low risk	Low risk	High risk	High risk	High risk
Satici et al, 2020 [337]	Turkey	Low risk	Low risk	High risk	Low risk	High risk	High risk
Secco et al, 2020 [338]	Italy	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Selcuk et al, 2020 [339]	Turkey	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Semenova et al, 2020 [340]	Kazakhstan	Low risk	Low risk	Low risk	Low risk	High risk	High risk
Shah et al, 2020 [341]	UK	High risk	Low risk	High risk	Low risk	High risk	High risk
Shah et al, 2020 [342]	USA	High risk	Low risk	High risk	Low risk	Moderate risk	High risk
Shahriarirad et al, 2020 [343]	Iran	Low risk	Low risk	High risk	Low risk	High risk	High risk
Shang et al, 2020 [344]	China	High risk	Low risk	Low risk	Low risk	High risk	High risk
Shekhar et al, 2020 [345]	USA	Low risk	Low risk	High risk	Low risk	High risk	High risk
Shen et al, 2020 [346]	China	High risk	Low risk	High risk	Low risk	High risk	High risk
Shi et al, 2020 [347]	China	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Simmonet et al, 2020 [348]	France	Low risk	Low risk	Moderate risk	Low risk	Moderate risk	High risk
Singer et al, 2020 [349]	USA	Low risk	Low risk	High risk	Low risk	High risk	High risk
Smadja et al, 2020 [350]	France	High risk	Low risk	High risk	Low risk	High risk	High risk
Smith et al, 2020 [351]	USA	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Soares et al, 2020 [352]	Brazil	High risk	Low risk	High risk	Low risk	Moderate risk	High risk
Sohaib Asghar et al, 2020 [353]	Pakistan	Low risk	Low risk	High risk	Low risk	High risk	High risk
Solaimanzadeh et al, 2020 [354]	USA	High risk	Low risk	Low risk	Low risk	High risk	High risk
Somers et al, 2020 [355]	Michigan	High risk	Low risk	High risk	Low risk	High risk	Moderate risk
Sousa et al, 2020 [356]	Brazil	Low risk	Low risk	Moderate risk	Low risk	Moderate risk	High risk
Stevens et al, 2021 [357]	USA	High risk	Low risk	High risk	Low risk	High risk	High risk
Stoneham et al, 2020 [358]	UK	High risk	Low risk	Moderate risk	High risk	High risk	High risk
Stroppa et al, 2020 [359]	Italy	Moderate risk	Low risk	High risk	Low risk	High risk	High risk
Suleyman et al, 2020 [360]	USA	Low risk	Low risk	High risk	Low risk	High risk	High risk
Sun et al, 2020 [361]	China	High risk	Low risk	High risk	Low risk	High risk	High risk
Sun et al, 2020 [362]	China	High risk	Low risk	High risk	Low risk	High risk	High risk
Sun et al, 2020 [363]	China	High risk	Low risk	High risk	Low risk	High risk	High risk
Tambe et al, 2020 [364]	India	Low risk	Low risk	Moderate risk	Low risk	High risk	High risk
Tan et al, 2020 [365]	China	High risk	Low risk	Low risk	Low risk	High risk	High risk
Tan et al, 2020 [366]	UK	High risk	Low risk	Moderate risk	Low risk	Moderate risk	Moderate risk
Tanriverdi et al, 2020 [367]	Turkey	High risk	Low risk	High risk	Low risk	High risk	High risk
Tatum et al, 2020 [368]	USA	High risk	Low risk	High risk	Low risk	High risk	High risk
Tenforde et al, 2020 [369]	USA	High risk	Low risk	High risk	Low risk	High risk	High risk
Tharakan et al, 2020 [370]	USA	High risk	Low risk	Low risk	Low risk	High risk	High risk
Tomlins et al, 2020 [371]	UK	Low risk	Low risk	High risk	Low risk	High risk	High risk
Toussie et al, 2020 [372]	USA	Moderate risk	Low risk	High risk	Low risk	High risk	High risk
Trimaille et al, 2020 [373]	France	Moderate risk	Low risk	High risk	High risk	High risk	High risk
Trujillo et al, 2020 [374]	Spain	Moderate risk	Low risk	High risk	Low risk	High risk	High risk

First Author, Year	Country	Study participation	Study attrition	Prognostic factor measurement	Outcome measurement	Adjustment for other prognostic factors	Statistical analysis and reporting
Urra et al, 2020 [375]	Spain	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Valeri et al, 2020 [376]	USA	Moderate risk	Low risk	High risk	Low risk	High risk	High risk
van Gerwen et al, 2020 [377]	USA	High risk	Low risk	High risk	Low risk	Moderate risk	High risk
Villard et al, 2020 [378]	France	High risk	Low risk	High risk	High risk	High risk	High risk
Vivanti et al, 2020 [379]	France	Low risk	Low risk	High risk	Low risk	High risk	High risk
Wan et al, 2020 [380]	China	High risk	Low risk	High risk	Low risk	High risk	High risk
Wang et al, 2020 [381]	China	Low risk	Low risk	High risk	Low risk	High risk	High risk
Wang et al, 2020 [382]	China	Low risk	Low risk	High risk	Low risk	High risk	High risk
Wang et al, 2020 [383]	China	Low risk	Low risk	High risk	Low risk	High risk	High risk
Wang et al, 2020 [384]	China	High risk	Low risk	High risk	Low risk	High risk	High risk
Wang et al, 2020 [385]	China	High risk	Low risk	High risk	Low risk	High risk	High risk
Wang et al, 2020 [386]	China	High risk	Low risk	High risk	Low risk	High risk	High risk
Wang et al, 2020 [387]	China	High risk	Low risk	High risk	Low risk	High risk	High risk
Wang et al, 2020 [388]	China	High risk	Low risk	High risk	Low risk	High risk	High risk
Wang et al, 2020 [389]	China	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Wang et al, 2020 [390]	USA	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Whyte et al, 2020 [391]	UK	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Wu et al, 2020 [392]	China	High risk	Low risk	High risk	Low risk	High risk	Moderate risk
Wu et al, 2020 [393]	China	High risk	Low risk	Low risk	Low risk	High risk	High risk
Xu et al, 2020 [394]	China	High risk	Low risk	High risk	Low risk	High risk	High risk
Xu et al, 2020 [395]	China	High risk	Low risk	High risk	Low risk	High risk	High risk
Xu et al, 2020 [396]	China	High risk	Low risk	Low risk	Low risk	High risk	High risk
Yan et al, 2020 [397]	USA	High risk	Low risk	High risk	Low risk	High risk	High risk
Yan et al, 2020 [398]	China	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Yang et al, 2020 [399]	China	High risk	Low risk	High risk	Low risk	High risk	High risk
Yang et al, 2020 [400]	China	High risk	Low risk	Low risk	Low risk	High risk	High risk
Yang et al, 2020 [401]	China	High risk	Low risk	High risk	Low risk	High risk	High risk
Yang et al, 2020 [402]	USA	High risk	Low risk	Low risk	Low risk	High risk	High risk
Yao et al, 2020 [403]	China	Low risk	Low risk	High risk	Low risk	High risk	High risk
Yao et al, 2020 [404]	China	High risk	Low risk	Low risk	Low risk	High risk	High risk
Yarza et al, 2020 [405]	Spain	High risk	Low risk	High risk	High risk	High risk	High risk
Ye et al, 2020 [406]	China	Moderate risk	Low risk	Moderate risk	Low risk	High risk	High risk
Ye et al, 2020 [407]	China	High risk	Low risk	High risk	Low risk	High risk	High risk
Yip et al, 2020 [408]	Hong Kong	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Yu et al, 2020 [409]	China	High risk	Low risk	High risk	Low risk	High risk	High risk
Yu et al, 2020 [410]	China	High risk	Low risk	High risk	Low risk	High risk	High risk
Yuan et al, 2020 [411]	China	High risk	Low risk	High risk	Low risk	High risk	High risk
Zeng et al, 2020 [412]	China	High risk	Low risk	High risk	Low risk	High risk	High risk
Zeng et al, 2020 [413]	China	High risk	Low risk	Moderate risk	Low risk	High risk	Moderate risk

First Author, Year	Country	Study participation	Study attrition	Prognostic factor measurement	Outcome measurement	Adjustment for other prognostic factors	Statistical analysis and reporting
Zhang et al, 2020 [414]	China	High risk	Low risk	Moderate risk	Low risk	Moderate risk	Moderate risk
Zhang et al, 2020 [415]	China	Low risk	Low risk	High risk	Low risk	High risk	High risk
Zhang et al, 2020 [416]	China	High risk	Low risk	Moderate risk	High risk	High risk	High risk
Zhang et al, 2020 [417]	China	High risk	Low risk	High risk	Low risk	High risk	High risk
Zhang et al, 2020 [418]	China	High risk	Low risk	High risk	Low risk	High risk	High risk
Zhang et al, 2020 [419]	China	High risk	Low risk	High risk	Low risk	High risk	High risk
Zhang et al, 2020 [420]	China	High risk	Low risk	High risk	Low risk	High risk	High risk
Zhao et al, 2020 [421]	China	High risk	Low risk	Low risk	Low risk	High risk	High risk
Zheng et al, 2020 [422]	China	High risk	Low risk	High risk	Low risk	High risk	High risk
Zheng et al, 2020 [423]	China	High risk	Low risk	High risk	Low risk	Moderate risk	Moderate risk
Zhou et al, 2020 [424]	China	High risk	Low risk	High risk	Low risk	High risk	High risk
Zhou et al, 2020 [425]	China	High risk	Low risk	High risk	Low risk	High risk	High risk
Zhou et al, 2020 [426]	China	High risk	Low risk	Low risk	Low risk	Moderate risk	High risk
Zhu et al, 2020 [427]	China	High risk	Low risk	Moderate risk	Low risk	High risk	High risk
Zou et al, 2020 [428]	China	High risk	Low risk	High risk	Low risk	High risk	High risk

Note: For studies examining multiple prognostic factors and/or outcomes, we assessed the pertinent question with the highest risk of bias grade for the ascertainment of the prognostic factor and outcome.

Supplementary Table 2. Results of the 263 meta-analyses for predictors of clinical outcomes in patients with COVID-19.

Category of predictor	Predictor	Level of comparison	N events/N participants	N studies	RE summary OR (95% CI)	P-value	I^2	95% PI	Egger's test P-value
Acute Kidney Injury									
Comorbidities	Cancer	Yes vs. No	4123/10,960	6	1.55 (1.07 - 2.25)	1.98×10^{-2}	37	0.63 - 3.83	0.082†
Comorbidities	Chronic kidney disease	Yes vs. No	2173/4992	5	2.46 (1.75 - 3.46)	2.54×10^{-7}	28	1.04 - 5.81	0.053†
Comorbidities	COPD	Yes vs. No	2213/5842	5	1.34 (0.83 - 2.18)	2.31×10^{-1}	23	0.40 - 4.47	0.236
Comorbidities	Coronary heart disease	Yes vs. No	2213/5842	5	1.69 (1.43 - 1.99)	4.90×10^{-10}	0	1.29 - 2.20	0.201
Comorbidities	Diabetes mellitus	Yes vs. No	4938/20,881	12	1.95 (1.57 - 2.43)	1.43×10^{-9}	73	1.04 - 3.69	0.396
Comorbidities	Heart failure	Yes vs. No	4062/9228	5	2.26 (1.50 - 3.41)	9.95×10^{-5}	52	0.71 - 7.15	0.727
Comorbidities	Hypertension	Yes vs. No	2842/13,088*	9	2.26 (1.69 - 3.03)	4.87×10^{-8}	73	0.99 - 5.16	0.343
Demographics	Sex	Female vs. Male	4203/9418	8	0.73 (0.61 - 0.87)	4.82×10^{-4}	40	0.49 - 1.07	0.247
Medications	ACEi/ARBs	Yes vs. No	4548/12,944*	10	1.29 (1.08 - 1.53)	4.06×10^{-3}	38	0.87 - 1.92	0.260
Acute Respiratory Distress Syndrome									
Comorbidities	Diabetes mellitus	Yes vs. No	957/8366	9	2.33 (1.77 - 3.06)	1.87×10^{-9}	26	1.30 - 4.16	0.849
Comorbidities	Hypertension	Yes vs. No	494/5980*	9	2.13 (1.50 - 3.03)	2.23×10^{-5}	66	0.81 - 5.64	0.113
Demographics	Sex	Female vs. Male	366/1186	7	0.78 (0.48 - 1.25)	3.00×10^{-1}	61	0.19 - 3.14	0.076
Environmental factors	Smoking	Yes vs. No	189/481	5	0.73 (0.39 - 1.38)	3.38×10^{-1}	0	0.26 - 2.05	0.641
Medications	ACEi/ARBs	Yes vs. No	252/2015*	8	0.80 (0.62 - 1.03)	7.90×10^{-2}	0	0.58 - 1.09	0.546
Composite Outcome 1 (ICU admission or Death)									
Comorbidities	Any comorbidity	Yes vs. No	400/1077	7	1.50 (1.11 - 2.03)	8.00×10^{-3}	0	1.01 - 2.22	0.337
Comorbidities	BMI	>30 kg/m^2 vs. <30 kg/m^2	562/1595	6	1.20 (0.96 - 1.50)	1.01×10^{-1}	0	0.88 - 1.64	0.781
Comorbidities	Cancer	Yes vs. No	1098/4129	13	1.49 (1.02 - 2.19)	4.10×10^{-2}	53	0.49 - 4.56	0.835
Comorbidities	Cardiovascular disease	Yes vs. No	739/3129	8	1.74 (1.06 - 2.86)	2.90×10^{-2}	78	0.38 - 7.95	0.146
Comorbidities	Chronic kidney disease	Yes vs. No	1166/4436	13	1.78 (1.29 - 2.46)	4.26×10^{-4}	39	0.77 - 4.11	0.961
Comorbidities	COPD	Yes vs. No	732/3234	8	2.04 (1.30 - 3.19)	1.98×10^{-3}	51	0.62 - 6.71	0.672
Comorbidities	Coronary heart disease	Yes vs. No	420/1276	5	2.38 (1.37 - 4.13)	2.16×10^{-3}	68	0.38 - 14.95	0.386
Comorbidities	Diabetes mellitus	Yes vs. No	1327/4910	15	1.85 (1.42 - 2.42)	5.51×10^{-6}	59	0.80 - 4.30	0.691
Comorbidities	Heart failure	Yes vs. No	340/866	5	0.83 (0.50 - 1.39)	4.86×10^{-1}	1	0.35 - 1.96	0.895
Comorbidities	Hypertension	Yes vs. No	1073/4313	13	1.68 (1.13 - 2.48)	9.72×10^{-3}	81	0.42 - 6.75	0.254
Comorbidities	Solid organ transplantation	Yes vs. No	478/1284	5	1.09 (0.53 - 2.24)	8.19×10^{-1}	0	0.34 - 3.52	0.889
Demographics	Age	per 1 year increase	578/1663	5	1.015 (1.003 - 1.028)	1.70×10^{-2}	58	0.977 - 1.055	0.788
Demographics	Sex	Female vs. Male	1493/5593	18	0.70 (0.60 - 0.82)	1.12×10^{-5}	23	0.48 - 1.02	0.935
Environmental factors	Smoking	Yes vs. No	359/961	8	1.20 (0.82 - 1.74)	3.49×10^{-1}	0	0.75 - 1.90	0.692
Medications	ACEi	Yes vs. No	586/2867	5	1.44 (0.86 - 2.39)	1.63×10^{-1}	70	0.27 - 7.67	0.384
Medications	ACEi/ARBs	Yes vs. No	1591/7694	6	1.67 (0.92 - 3.01)	8.93×10^{-2}	94	0.22 - 12.87	0.540
Medications	ARBs	Yes vs. No	586/2867	5	1.23 (0.69 - 2.20)	4.86×10^{-1}	77	0.18 - 8.53	0.241

Category of predictor	Predictor	Level of comparison	N events/N participants	N studies	RE summary OR (95% CI)	P-value	I^2	95% PI	Egger's test P-value
Symptoms/signs	Cough	Yes vs. No	449/1330	7	0.89 (0.63 - 1.26)	5.11×10^{-1}	40	0.38 - 2.08	0.555
Symptoms/signs	Dyspnea	Yes vs. No	475/1380	7	2.15 (1.67 - 2.77)	2.15×10^{-9}	1	1.52 - 3.04	0.449
Symptoms/signs	Fever	Yes vs. No	790/2381	9	1.18 (0.82 - 1.71)	3.71×10^{-1}	51	0.45 - 3.11	0.731
Composite Outcome 2 (ICU admission, Mechanical Ventilation or Death)									
Comorbidities	Any comorbidity	Yes vs. No	1084/4633*	7	2.90 (1.72 - 4.90)	7.03×10^{-5}	67	0.63 - 13.31	0.048†
Comorbidities	Diabetes mellitus	Yes vs. No	1422/5658	9	2.09 (1.18 - 3.71)	1.14×10^{-2}	88	0.30 - 14.41	0.310
Comorbidities	Hypertension	Yes vs. No	1373/5673	9	2.51 (1.58 - 3.98)	9.94×10^{-5}	82	0.57 - 11.08	0.161
Demographics	Sex	Female vs. Male	1384/5679	7	0.91 (0.69 - 1.20)	4.97×10^{-1}	50	0.45 - 1.85	0.168
Deep Venous Thrombosis									
Comorbidities	Cancer	Yes vs. No	193/1038	7	1.16 (0.59 - 2.28)	6.76×10^{-1}	5	0.40 - 3.30	0.188
Comorbidities	Diabetes mellitus	Yes vs. No	202/532	6	1.08 (0.64 - 1.83)	7.61×10^{-1}	0	0.52 - 2.28	0.656
Comorbidities	Hypertension	Yes vs. No	202/532	6	0.98 (0.64 - 1.50)	9.38×10^{-1}	0	0.54 - 1.79	0.347
Demographics	Sex	Female vs. Male	225/688	7	0.86 (0.59 - 1.26)	4.31×10^{-1}	0	0.52 - 1.41	0.517
Hospitalization									
Comorbidities	Any comorbidity	Yes vs. No	8851/17,459	22	4.13 (3.33 - 5.12)	2.46×10^{-38}	75	1.93 - 8.86	0.311
Comorbidities	Asthma	Yes vs. No	10,189/19,312*	19	1.15 (0.96 - 1.37)	1.37×10^{-1}	52	0.66 - 2.00	0.689
Comorbidities	BMI	>30 kg/m^2 vs. <30 kg/m^2	10,382/17,298	12	1.49 (1.20 - 1.84)	2.58×10^{-4}	82	0.75 - 2.96	0.485
Comorbidities	Cancer	Yes vs. No	14,320/28,846*	21	2.42 (1.78 - 3.28)	1.63×10^{-8}	83	0.75 - 7.82	0.832
Comorbidities	Cardiovascular disease	Yes vs. No	6571/23,556**	19	3.40 (2.64 - 4.38)	2.39×10^{-21}	80	1.42 - 8.11	0.462
Comorbidities	Cerebrovascular disease	Yes vs. No	4464/7353	5	7.92 (3.18 - 19.70)	8.54×10^{-6}	74	0.40 - 156.32	0.550
Comorbidities	Chronic kidney disease	Yes vs. No	14,066/35,627	19	5.17 (3.81 - 7.03)	6.48×10^{-26}	80	1.68 - 15.94	0.675
Comorbidities	Chronic lung disease	Yes vs. No	2958/15,984*	18	1.98 (1.46 - 2.69)	1.29×10^{-5}	55	0.80 - 4.90	0.607
Comorbidities	COPD	Yes vs. No	9018/17,335*	14	3.38 (2.31 - 4.94)	3.25×10^{-10}	70	0.96 - 11.95	0.344
Comorbidities	Coronary heart disease	Yes vs. No	10,082/18,493	13	3.47 (2.44 - 4.94)	4.86×10^{-12}	83	1.02 - 11.82	0.190
Comorbidities	Diabetes mellitus	Yes vs. No	14,927/39,014**	33	3.71 (3.17 - 4.34)	2.80×10^{-60}	72	1.94 - 7.09	0.774
Comorbidities	Dyslipidemia	Yes vs. No	2973/6886	6	2.43 (1.58 - 3.75)	5.84×10^{-5}	60	0.75 - 7.93	0.574
Comorbidities	Heart failure	Yes vs. No	9859/18,444*	14	6.74 (4.17 - 10.88)	6.34×10^{-15}	81	1.27 - 35.83	0.554
Comorbidities	History of VTE	Yes vs. No	4151/6931	5	2.35 (1.75 - 3.14)	1.25×10^{-8}	1	1.43 - 3.83	0.243
Comorbidities	HIV infection	Yes vs. No	6258/11,362	6	1.31 (0.98 - 1.75)	6.77×10^{-2}	0	0.87 - 1.97	0.781
Comorbidities	Hypertension	Yes vs. No	13,532/27,541**	30	3.70 (3.10 - 4.41)	4.17×10^{-48}	84	1.67 - 8.18	0.519
Comorbidities	Immunocompromised state	Yes vs. No	2308/4753	6	1.70 (0.95 - 3.04)	7.17×10^{-2}	45	0.37 - 7.81	0.201
Comorbidities	Obesity	Yes vs. No	5938/19,788	10	2.10 (1.67 - 2.65)	3.16×10^{-10}	51	1.14 - 3.86	0.180
Comorbidities	Obstructive sleep apnea	Yes vs. No	2475/3819	5	2.11 (1.54 - 2.89)	3.14×10^{-6}	0	1.27 - 3.51	0.248
Comorbidities	Rheumatological disease	Yes vs. No	1569/2500	5	1.52 (0.97 - 2.39)	6.88×10^{-2}	0	0.73 - 3.17	0.019†
Comorbidities	Solid organ transplantation	Yes vs. No	1644/2599	5	2.90 (0.98 - 8.58)	5.41×10^{-2}	38	0.15 - 56.74	0.531
Demographics	Age	>60 vs. <60	6226/20,704	10	4.12 (3.02 - 5.61)	2.66×10^{-19}	90	1.57 - 10.81	0.656
Demographics	Age	>65 vs. <65	6306/11,907	11	4.83 (3.03 - 7.70)	3.53×10^{-11}	94	0.84 - 27.87	0.329
Demographics	Age	Per 1 year increase	372/1360	5	1.057 (1.036 - 1.077)	2.77×10^{-8}	62	0.993 - 1.124	0.810

Category of predictor	Predictor	Level of comparison	N events/N participants	N studies	RE summary OR (95% CI)	P-value	I^2	95% PI	Egger's test P-value
Demographics	Nursing home	Yes vs. No	2261/5607	5	6.25 (0.75 - 52.47)	9.11×10^{-2}	94	0.002 - 17536.89	0.231
Demographics	Sex	Female vs. Male	16,662/42,229***	44	0.61 (0.54 - 0.69)	6.68×10^{-16}	79	0.33 - 1.12	0.497
Environmental factors	Smoking	Yes vs. No	10,954/29,237*	20	1.54 (1.23 - 1.94)	2.12×10^{-4}	78	0.68 - 3.51	0.354
Imaging markers	Bilateral involvement	Yes vs. No	1249/1697	7	5.93 (3.01 - 11.70)	2.74×10^{-7}	57	0.97 - 36.44	0.872
Imaging markers	Ground-glass opacity	Yes vs. No	144/234	5	0.44 (0.19 - 1.01)	5.33×10^{-2}	0	0.11 - 1.70	0.468
Medications	ACEi	Yes vs. No	1286/3300	5	1.84 (1.25 - 2.71)	2.00×10^{-3}	48	0.60 - 5.60	0.570
Medications	ACEi/ARBs	Yes vs. No	5491/11,784	10	1.90 (1.50 - 2.41)	1.20×10^{-7}	75	0.93 - 3.90	0.286
Medications	Any immunosuppressive medication	Yes vs. No	1133/1847	5	2.23 (1.22 - 4.08)	9.08×10^{-3}	0	0.84 - 5.95	0.796
Medications	ARBs	Yes vs. No	1286/3300	5	1.49 (0.83 - 2.70)	1.83×10^{-1}	84	0.18 - 12.21	0.092
Symptoms/signs	Ageusia	Yes vs. No	2145/3729	10	0.40 (0.24 - 0.65)	2.25×10^{-4}	79	0.08 - 1.96	0.804
Symptoms/signs	Anorexia	Yes vs. No	1156/1686	5	1.68 (0.98 - 2.86)	5.69×10^{-2}	38	0.40 - 7.05	0.744
Symptoms/signs	Anosmia	Yes vs. No	2190/3818	11	0.35 (0.22 - 0.56)	9.58×10^{-6}	75	0.08 - 1.52	0.863
Symptoms/signs	Chest pain	Yes vs. No	286/845	5	1.17 (0.83 - 1.64)	3.65×10^{-1}	0	0.67 - 2.03	0.554
Symptoms/signs	Cough	Yes vs. No	4847/17,617	20	1.26 (0.94 - 1.69)	1.16×10^{-1}	83	0.41 - 3.92	0.393
Symptoms/signs	Diarrhea	Yes vs. No	3933/16,149	17	1.33 (0.98 - 1.79)	6.57×10^{-2}	77	0.47 - 3.75	0.232
Symptoms/signs	Dyspnea	Yes vs. No	4840/17,566	19	3.47 (2.74 - 4.38)	1.69×10^{-25}	73	1.59 - 7.55	0.596
Symptoms/signs	Fatigue	Yes vs. No	1345/3157	9	1.37 (0.72 - 2.61)	3.41×10^{-1}	87	0.17 - 11.22	0.562
Symptoms/signs	Fever	Yes vs. No	4867/18,220	21	2.10 (1.53 - 2.88)	4.05×10^{-6}	86	0.58 - 7.55	0.087†
Symptoms/signs	GI symptoms	Yes vs. No	627/1882	8	1.77 (0.92 - 3.38)	8.51×10^{-2}	73	0.26 – 12.00	0.339
Symptoms/signs	Headache	Yes vs. No	2425/13,973	14	0.55 (0.37 - 0.80)	1.85×10^{-3}	80	0.15 - 1.95	0.013
Symptoms/signs	Myalgia	Yes vs. No	1042/2178	11	0.82 (0.49 - 1.35)	4.26×10^{-1}	77	0.17 - 3.99	0.396
Symptoms/signs	Nasal congestion	Yes vs. No	815/1673	7	0.48 (0.37 - 0.61)	6.58×10^{-9}	0	0.34 - 0.66	0.596
Symptoms/signs	Nausea	Yes vs. No	1524/2496	6	1.37 (0.99 - 1.90)	5.76×10^{-2}	37	0.62 - 3.06	0.280
Symptoms/signs	Pharyngalgia	Yes vs. No	2659/13,672	12	0.48 (0.32 - 0.71)	2.71×10^{-4}	74	0.14 - 1.60	0.272
Symptoms/signs	Rhinorrhea	Yes vs. No	2078/12,281	9	0.61 (0.37 - 0.99)	4.68×10^{-2}	54	0.19 – 2.00	0.013
Symptoms/signs	Vomiting	Yes vs. No	1443/2499	8	1.58 (1.15 - 2.19)	5.21×10^{-3}	9	0.93 - 2.71	0.025†
ICU admission									
Biomarkers	Creatinine	133 µmol/L vs. 133 µmol/L	280/886	5	1.22 (0.34 - 4.34)	7.64×10^{-1}	74	0.02 - 93.63	0.707
Biomarkers	LDH	>250 U/L vs. <250 U/L	249/1048	6	8.64 (3.17 - 23.55)	2.46×10^{-5}	66	0.43 - 173.03	0.262
Biomarkers	Lymphocytes	<1.000 /µL vs. >1.000 /µL	314/1241	8	4.41 (2.12 - 9.17)	6.89×10^{-5}	73	0.47 - 41.51	0.005†
Biomarkers	Procalcitonin	>0.5 ng/ml vs. <0.5 ng/ml	405/1237	6	3.15 (1.68 - 5.92)	3.59×10^{-4}	64	0.50 - 19.81	0.700
Biomarkers	WBC	<4.000 /µL vs. >4.000 /µL	195/429	6	0.73 (0.36 - 1.48)	3.79×10^{-1}	0	0.27 - 1.98	0.366
Comorbidities	Any comorbidity	Yes vs. No	1703/6867	16	2.07 (1.45 - 2.96)	6.41×10^{-5}	74	0.56 - 7.64	0.429
Comorbidities	Asthma	Yes vs. No	708/2567	10	1.08 (0.80 - 1.47)	6.05×10^{-1}	4	0.71 - 1.65	0.947

Category of predictor	Predictor	Level of comparison	N events/N participants	N studies	RE summary OR (95% CI)	P-value	I^2	95% PI	Egger's test P-value
Comorbidities	Autoimmune diseases/ Rheumatological diseases	Yes vs. No	1214/4538	5	1.47 (0.74 - 2.93)	2.75×10^{-1}	53	0.19 - 11.67	0.719
Comorbidities	BMI	>30 kg/m^2 vs. <30 kg/m^2	1289/4707	11	1.93 (1.42 - 2.63)	3.04×10^{-5}	67	0.74 - 5.06	0.090†
Comorbidities	Cancer	Yes vs. No	2714/11,770	31	1.06 (0.80 - 1.42)	6.70×10^{-1}	50	0.37 - 3.05	0.025
Comorbidities	Cardiovascular disease	Yes vs. No	1504/5712	22	1.61 (1.23 - 2.11)	5.04×10^{-4}	41	0.77 - 3.36	0.571
Comorbidities	Cerebrovascular disease	Yes vs. No	952/4836	10	1.01 (0.62 - 1.64)	9.78×10^{-1}	58	0.27 - 3.79	0.185
Comorbidities	Chronic kidney disease	Yes vs. No	1718/7738	19	1.56 (1.20 - 2.04)	9.22×10^{-4}	32	0.82 - 3.00	0.506
Comorbidities	Chronic liver disease	Yes vs. No	302/1633	11	1.87 (1.09 - 3.22)	2.34×10^{-2}	0	1.00 - 3.50	0.189
Comorbidities	Chronic lung disease	Yes vs. No	1312/5209	14	1.48 (1.18 - 1.86)	7.92×10^{-4}	10	1.00 - 2.20	0.482
Comorbidities	Cirrhosis	Yes vs. No	496/1648	5	1.15 (0.59 - 2.22)	6.82×10^{-1}	0	0.39 - 3.34	0.551
Comorbidities	COPD	Yes vs. No	1131/5463	17	1.41 (1.01 - 1.97)	4.48×10^{-2}	32	0.60 - 3.31	0.311
Comorbidities	Coronary heart disease	Yes vs. No	1151/5779	14	1.42 (0.98 - 2.04)	6.37×10^{-2}	59	0.46 - 4.33	0.611
Comorbidities	Diabetes mellitus	Yes vs. No	2916/14,508	41	1.56 (1.32 - 1.85)	2.56×10^{-7}	47	0.82 - 2.98	0.372
Comorbidities	Dyslipidemia	Yes vs. No	490/2386	8	0.87 (0.55 - 1.36)	5.37×10^{-1}	53	0.26 - 2.88	0.380
Comorbidities	Heart failure	Yes vs. No	1076/4900	10	1.27 (0.88 - 1.85)	2.03×10^{-1}	53	0.46 - 3.55	0.322
Comorbidities	HIV infection	Yes vs. No	378/1684	5	1.27 (0.64 - 2.52)	4.88×10^{-1}	0	0.42 - 3.86	0.455
Comorbidities	Hypertension	Yes vs. No	2895/14,803	41	1.73 (1.41 - 2.12)	1.58×10^{-7}	71	0.65 - 4.63	0.040†
Comorbidities	Obesity	Yes vs. No	935/5348	11	1.61 (0.90 - 2.87)	1.08×10^{-1}	76	0.27 - 9.73	0.011
Comorbidities	Obstructive sleep apnea	Yes vs. No	511/2236	5	1.62 (1.16 - 2.26)	4.63×10^{-3}	0	0.94 - 2.79	0.562
Comorbidities	Solid organ transplantation	Yes vs. No	516/1670	5	1.14 (0.63 - 2.05)	6.69×10^{-1}	0	0.44 - 2.95	0.971
Demographics	Age	>60 vs. <60	470/3099	9	1.95 (1.25 - 3.06)	3.43×10^{-3}	69	0.50 - 7.55	0.120
Demographics	Age	>65 vs. <65	1870/9500	13	1.33 (0.91 - 1.94)	1.43×10^{-1}	88	0.34 - 5.12	0.897
Demographics	Age	Per 1 year increase	780/2769*	6	1.005 (0.99 - 1.02)	5.00×10^{-1}	80	0.957 - 1.055	0.117
Demographics	Sex	Female vs. Male	3209/18,789*	49	0.53 (0.46 - 0.59)	1.43×10^{-24}	31	0.34 - 0.82	0.497
Environmental factors	Smoking	Yes vs. No	1624/7286*	18	1.19 (1.03 - 1.39)	2.30×10^{-2}	3	0.97 - 1.48	0.320
Imaging markers	Bilateral involvement	Yes vs. No	426/1362	9	2.73 (1.51 - 4.94)	9.13×10^{-4}	52	0.60 - 12.41	0.590
Medications	ACEi	Yes vs. No	1199/5402	8	1.01 (0.81 - 1.27)	9.05×10^{-1}	21	0.64 - 1.60	0.534
Medications	ACEi/ARBs	Yes vs. No	1819/9880	12	1.20 (0.83 - 1.74)	3.28×10^{-1}	85	0.35 - 4.13	0.296
Medications	ARBs	Yes vs. No	1138/5014	7	1.08 (0.82 - 1.42)	5.80×10^{-1}	36	0.57 - 2.05	0.320
Medications	Statins	Yes vs. No	353/1072	5	1.17 (0.88 - 1.55)	2.77×10^{-1}	0	0.74 - 1.84	0.160
Symptoms/signs	Chest pain	Yes vs. No	278/1556	6	1.14 (0.64 - 2.05)	6.51×10^{-1}	35	0.28 - 4.65	0.620
Symptoms/signs	Cough	Yes vs. No	840/2902	23	0.95 (0.78 - 1.15)	5.95×10^{-1}	0	0.77 - 1.16	0.568
Symptoms/signs	Diarrhea	Yes vs. No	727/2549	17	0.97 (0.78 - 1.21)	7.85×10^{-1}	0	0.76 - 1.23	0.657
Symptoms/signs	Dyspnea	Yes vs. No	989/3287	24	4.31 (2.77 - 6.71)	9.31×10^{-11}	77	0.67 - 27.79	0.006†
Symptoms/signs	Expectoration	Yes vs. No	446/1680	10	0.76 (0.53 - 1.09)	1.34×10^{-1}	9	0.43 - 1.35	0.821
Symptoms/signs	Fatigue	Yes vs. No	222/993	8	1.07 (0.65 - 1.76)	7.92×10^{-1}	49	0.27 - 4.16	0.890
Symptoms/signs	Fever	Yes vs. No	1051/4102	26	1.09 (0.89 - 1.34)	4.06×10^{-1}	4	0.80 - 1.49	0.262
Symptoms/signs	GI symptoms	Yes vs. No	313/2402	8	1.11 (0.73 - 1.68)	6.32×10^{-1}	40	0.40 - 3.07	0.903

Category of predictor	Predictor	Level of comparison	N events/N participants	N studies	RE summary OR (95% CI)	P-value	I^2	95% PI	Egger's test P-value
Symptoms/signs	Headache	Yes vs. No	829/2867	19	0.62 (0.47 - 0.82)	7.09×10^{-4}	0	0.46 - 0.84	0.730
Symptoms/signs	Myalgia	Yes vs. No	493/1773	11	0.93 (0.63 - 1.37)	7.03×10^{-1}	39	0.35 - 2.46	0.267
Symptoms/signs	Nausea/Vomiting	Yes vs. No	371/1581	7	0.62 (0.30 - 1.27)	1.91×10^{-1}	41	0.11 - 3.59	0.288
Symptoms/signs	Pharyngalgia	Yes vs. No	456/1929	11	1.26 (0.82 - 1.95)	2.92×10^{-1}	27	0.48 - 3.30	0.306
Invasive Mechanical Ventilation									
Comorbidities	Any comorbidity	Yes vs. No	1838/9474	7	1.17 (0.81 - 1.68)	3.99×10^{-1}	73	0.43 - 3.19	0.054
Comorbidities	Asthma	Yes vs. No	1077/5131	9	1.04 (0.84 - 1.30)	6.96×10^{-1}	0	0.80 - 1.36	0.380
Comorbidities	BMI	>30 kg/m^2 vs. <30 kg/m^2	1220/5058	10	1.54 (1.23 - 1.93)	1.66×10^{-4}	45	0.87 - 2.74	0.661
Comorbidities	Cancer	Yes vs. No	1210/10,362	12	1.57 (1.25 - 1.98)	1.02×10^{-4}	0	1.21 - 2.04	0.043
Comorbidities	Cardiovascular disease	Yes vs. No	1424/8466	8	1.16 (0.64 - 2.10)	6.17×10^{-1}	87	0.17 - 7.77	0.039
Comorbidities	Cerebrovascular disease	Yes vs. No	866/5729	7	1.39 (0.79 - 2.47)	2.54×10^{-1}	64	0.26 - 7.39	0.462
Comorbidities	Chronic kidney disease	Yes vs. No	2148/11,766	10	1.36 (0.91 - 2.04)	1.38×10^{-1}	80	0.37 - 4.98	0.258
Comorbidities	Chronic lung disease	Yes vs. No	1586/8382	9	1.17 (0.68 - 2.00)	5.72×10^{-1}	83	0.20 - 6.66	0.003
Comorbidities	COPD	Yes vs. No	906/4418	9	1.58 (0.92 - 2.69)	9.59×10^{-2}	67	0.32 - 7.73	0.954
Comorbidities	Coronary heart disease	Yes vs. No	969/10,641	8	1.81 (1.37 - 2.40)	3.68×10^{-5}	24	1.00 - 3.27	0.247
Comorbidities	Diabetes mellitus	Yes vs. No	3248/24,541	26	1.64 (1.33 - 2.02)	3.65×10^{-6}	75	0.68 - 3.92	0.266
Comorbidities	Heart failure	Yes vs. No	1036/10,213	8	1.41 (0.89 - 2.22)	1.41×10^{-1}	64	0.38 - 5.26	0.011
Comorbidities	HIV infection	Yes vs. No	1302/7359	6	1.44 (0.77 - 2.68)	2.54×10^{-1}	0	0.59 - 3.47	0.866
Comorbidities	Hypertension	Yes vs. No	1992/14,928	21	1.70 (1.39 - 2.08)	2.25×10^{-7}	61	0.83 - 3.48	0.230
Comorbidities	Solid organ transplantation	Yes vs. No	261/828	5	1.32 (0.73 - 2.40)	3.63×10^{-1}	0	0.50 - 3.48	0.953
Demographics	Age	>60 vs. <60	877/4220	5	1.66 (1.33 - 2.07)	9.28×10^{-6}	32	0.92 - 2.97	0.368
Demographics	Age	>65 vs. <65	1277/14,042	10	1.74 (1.14 - 2.66)	9.68×10^{-3}	85	0.46 - 6.67	0.826
Demographics	Sex	Female vs. Male	2711/13,404	24	0.62 (0.55 - 0.71)	2.46×10^{-12}	21	0.46 - 0.85	0.720
Environmental factors	Smoking	Yes vs. No	1105/5471	10	1.15 (0.94 - 1.40)	1.75×10^{-1}	18	0.78 - 1.68	0.677
Medications	ACEi	Yes vs. No	361/2614	5	1.28 (0.91 - 1.82)	1.57×10^{-1}	0	0.73 - 2.25	0.006
Medications	ACEi/ARBs	Yes vs. No	536/4116	10	1.18 (0.81 - 1.73)	3.92×10^{-1}	56	0.40 - 3.49	0.372
Medications	ARBs	Yes vs. No	361/2614	5	1.46 (1.04 - 2.06)	2.87×10^{-2}	12	0.71 - 3.03	0.852
Symptoms/signs	Fever	Yes vs. No	438/1391	6	0.95 (0.69 - 1.29)	7.26×10^{-1}	25	0.47 - 1.90	0.937
Mortality									
Biomarkers	ALT	>40 U/L vs. <40 U/L	1155/5829	6	1.47 (1.12 - 1.93)	5.07×10^{-3}	49	0.72 - 3.02	0.088†
Biomarkers	AST	>40 U/L vs. <40 U/L	1182/5950	7	2.42 (1.70 - 3.44)	8.19×10^{-7}	72	0.86 - 6.82	0.570
Biomarkers	CRP	>10 mg/L vs. <10 mg/L	508/3914	7	7.09 (3.14 - 16.00)	2.37×10^{-6}	63	0.72 - 69.46	0.752
Biomarkers	D-dimers	>0.5 µg/mL vs. <0.5 µg/mL	591/3936	9	3.47 (2.25 - 5.36)	1.98×10^{-8}	63	1.02 - 11.78	0.015†
Biomarkers	LDH	>250 U/L vs. <250 U/L	523/4185	10	3.72 (1.74 - 7.93)	6.80×10^{-4}	83	0.28 - 49.38	0.244
Biomarkers	Lymphocytes	<1.000 /µL vs.	367/1733	5	3.18 (1.33 - 7.58)	9.22×10^{-3}	87	0.14 - 72.75	0.587

Category of predictor	Predictor	Level of comparison	N events/N participants	N studies	RE summary OR (95% CI)	P-value	I^2	95% PI	Egger's test P-value
		>1.000 /μL							
Biomarkers	Neutrophils	>6.300 /μL vs. <6.300 /μL	317/1906	5	5.66 (3.42 - 9.37)	1.50×10^{-11}	72	1.00 - 31.96	0.312
Biomarkers	Platelets	<150.000 /μL vs. >150.000 /μL	226/2017	8	2.31 (1.39 - 3.84)	1.26×10^{-3}	55	0.57 - 9.32	0.233
Biomarkers	Procalcitonin	>0.5 ng/ml vs. <0.5 ng/ml	815/3848	7	5.36 (2.67 - 10.74)	2.27×10^{-6}	69	0.69 - 41.81	0.799
Biomarkers	WBC	<4.000 /μL vs. >4.000 /μL	1011/4780	6	0.60 (0.43 - 0.84)	2.65×10^{-3}	20	0.29 - 1.21	0.532
Biomarkers	WBC	>10.000 /μL vs. <10.000 /μL	500/4309	7	6.35 (2.58 - 15.61)	5.77×10^{-5}	90	0.31 - 128.62	0.509
Comorbidities	Any comorbidity	Yes vs. No	14,625/62,464	31	3.54 (2.84 - 4.41)	1.64×10^{-29}	87	1.44 - 8.70	0.006†
Comorbidities	Any neurological disease	Yes vs. No	8569/23,631	7	3.68 (2.28 - 5.96)	1.12×10^{-7}	92	0.79 - 17.08	0.145
Comorbidities	Asthma	Yes vs. No	17,046/70,521	28	0.90 (0.76 - 1.07)	2.41×10^{-1}	53	0.51 - 1.58	0.657
Comorbidities	Atrial fibrillation	Yes vs. No	869/3633	9	2.20 (1.43 - 3.37)	3.03×10^{-4}	40	0.78 - 6.24	0.680
Comorbidities	BMI	>30 kg/m^2 vs. <30 kg/m^2	2619/13,340	25	0.96 (0.80 - 1.13)	6.00×10^{-1}	52	0.53 - 1.72	0.320
Comorbidities	BMI	Per 1 kg/m^2 increase	585/3362	9	0.991 (0.972 - 1.009)	3.27×10^{-1}	31	0.95 - 1.033	0.867
Comorbidities	Cancer	Yes vs. No	16,701/96,849	36	2.14 (1.86 - 2.45)	1.69×10^{-27}	50	1.30 - 3.52	0.262
Comorbidities	Cardiovascular disease	Yes vs. No	14,794/77,260	27	3.10 (2.38 - 4.04)	6.75×10^{-17}	94	0.95 - 10.15	0.244
Comorbidities	Cerebrovascular disease	Yes vs. No	2533/17,662	31	2.89 (2.26 - 3.69)	1.90×10^{-17}	55	1.10 - 7.58	0.167
Comorbidities	Chronic kidney disease	Yes vs. No	18,219/90,951	51	3.01 (2.52 - 3.60)	9.39×10^{-34}	80	1.14 - 7.98	0.107
Comorbidities	Chronic liver disease	Yes vs. No	17,476/61,046	18	1.46 (1.24 - 1.72)	5.95×10^{-6}	4	1.15 - 1.84	0.399
Comorbidities	Chronic lung disease	Yes vs. No	6534/41,381	15	2.35 (1.85 - 3.00)	4.36×10^{-12}	71	1.10 - 5.02	0.315
Comorbidities	Cirrhosis	Yes vs. No	567/4448	6	1.41 (0.83 - 2.39)	2.06×10^{-1}	0	0.66 - 2.98	0.262
Comorbidities	COPD	Yes vs. No	12,531/65,667	44	2.19 (1.88 - 2.55)	8.08×10^{-24}	43	1.20 - 4.00	0.277
Comorbidities	Coronary heart disease	Yes vs. No	5068/35,417	42	2.84 (2.44 - 3.29)	8.44×10^{-43}	54	1.48 - 5.44	0.327
Comorbidities	Dementia	Yes vs. No	6419/21,208	11	3.12 (2.50 - 3.90)	1.62×10^{-23}	46	1.86 - 5.23	0.619
Comorbidities	Diabetes mellitus	Yes vs. No	17,994/116,666	53	2.15 (1.84 - 2.52)	1.87×10^{-21}	89	0.82 - 5.67	0.057†
Comorbidities	Dyslipidemia	Yes vs. No	4899/19,680	19	1.34 (1.05 - 1.70)	1.70×10^{-2}	72	0.60 - 2.97	0.083
Comorbidities	Heart failure	Yes vs. No	4287/39,794	32	3.74 (2.80 - 5.01)	6.57×10^{-19}	84	0.86 - 16.36	0.998
Comorbidities	Hematological malignancy	Yes vs. No	6471/24,427	6	2.11 (1.63 - 2.72)	9.34×10^{-9}	33	1.16 - 3.85	0.021†
Comorbidities	History of VTE	Yes vs. No	972/4252	7	1.52 (1.06 - 2.19)	2.43×10^{-2}	13	0.78 - 2.96	0.102
Comorbidities	HIV infection	Yes vs. No	6921/25,340	9	0.81 (0.52 - 1.25)	3.45×10^{-1}	15	0.37 - 1.80	0.241
Comorbidities	Hypertension	Yes vs. No	9169/73,066*	68	2.22 (1.95 - 2.53)	2.66×10^{-32}	77	0.96 - 5.11	0.132
Comorbidities	Immunocompromised state	Yes vs. No	4187/11,789	12	2.05 (1.37 - 3.05)	4.51×10^{-4}	58	0.66 - 6.35	0.810
Comorbidities	Obesity	Yes vs. No	6735/25,894	15	1.27 (0.94 - 1.71)	1.13×10^{-1}	76	0.51 - 3.17	0.426
Comorbidities	Obstructive sleep apnea	Yes vs. No	568/3827	7	1.41 (1.08 - 1.85)	1.11×10^{-2}	0	1.00 - 2.01	0.713
Comorbidities	Peripheral arterial disease	Yes vs. No	2312/17,433	6	2.07 (1.55 - 2.75)	6.08×10^{-7}	32	1.05 - 4.06	0.466

Category of predictor	Predictor	Level of comparison	N events/N participants	N studies	RE summary OR (95% CI)	P-value	I^2	95% PI	Egger's test P-value
Comorbidities	Rheumatological disease	Yes vs. No	5722/19,740	6	1.41 (1.27 - 1.57)	4.64×10^{-10}	0	1.21 - 1.64	0.755
Comorbidities	Tuberculosis	Yes vs. No	903/5268	5	1.88 (0.70 - 5.07)	2.12×10^{-1}	0	0.38 - 9.40	0.525
Demographics	Age	>60 vs. <60	9803/96,805	24	9.23 (7.20 - 11.83)	8.75×10^{-69}	87	3.19 - 26.67	0.392
Demographics	Age	>65 vs. <65	5752/31,564	22	5.52 (3.94 - 7.75)	4.69×10^{-23}	92	1.34 - 22.76	0.739
Demographics	Age	Per 1 year increase	2236/13,397	33	1.072 (1.063 - 1.081)	1.17×10^{-57}	74	1.029 - 1.116	0.290
Demographics	Nursing home	Yes vs. No	1123/6665	11	2.41 (1.25 - 4.64)	8.78×10^{-3}	88	0.23 - 24.92	0.022†
Demographics	Sex	Female vs. Male	24,317/190,180	71	0.71 (0.65 - 0.78)	3.37×10^{-14}	74	0.46 - 1.12	0.704
Environmental factors	Alcohol drinking	Yes vs. No	993/6321	6	0.99 (0.72 - 1.34)	9.27×10^{-1}	0	0.64 - 1.53	0.497
Environmental factors	Smoking	Yes vs. No	7831/30,250	39	1.50 (1.35 - 1.66)	1.41×10^{-14}	20	1.15 - 1.95	0.155
Imaging markers	Bilateral involvement	Yes vs. No	1195/6784	25	1.39 (1.02 - 1.89)	3.70×10^{-2}	55	0.48 - 4.04	0.004†
Imaging markers	Consolidation	Yes vs. No	477/3169	9	1.52 (1.05 - 2.22)	2.79×10^{-2}	45	0.59 - 3.94	0.440
Imaging markers	Ground-glass opacity	Yes vs. No	729/4958	12	0.96 (0.65 - 1.43)	8.56×10^{-1}	58	0.32 - 2.90	0.042
Imaging markers	Pleural effusion	Yes vs. No	210/660	7	1.61 (0.80 - 3.24)	1.80×10^{-1}	25	0.36 - 7.29	0.548
Medications	ACEi	Yes vs. No	3146/13,393	12	1.38 (1.20 - 1.59)	7.03×10^{-6}	31	1.01 - 1.89	0.020
Medications	ACEi/ARBs	Yes vs. No	3375/23,303	28	1.31 (1.02 - 1.67)	3.16×10^{-2}	83	0.45 - 3.83	0.063
Medications	Anticoagulant therapy	Yes vs. No	1825/4837	10	1.14 (0.87 - 1.49)	3.39×10^{-1}	30	0.65 - 2.00	0.228
Medications	Antiplatelet therapy	Yes vs. No	1010/2127	5	1.21 (0.75 - 1.95)	4.45×10^{-1}	53	0.29 - 5.06	0.017
Medications	Any immunosuppressive medication	Yes vs. No	6903/20,436	5	1.22 (1.12 - 1.34)	7.99×10^{-6}	0	1.06 - 1.41	0.107
Medications	ARBs	Yes vs. No	3146/13,393	12	1.33 (1.14 - 1.55)	2.25×10^{-4}	43	0.92 - 1.92	0.101
Medications	Beta-blockers	Yes vs. No	2690/10,327	8	1.98 (1.53 - 2.57)	2.64×10^{-7}	78	0.94 - 4.18	0.622
Medications	Calcium channel blockers	Yes vs. No	1150/7198	7	1.27 (0.80 - 2.02)	3.10×10^{-1}	71	0.33 - 4.89	0.200
Medications	Chemotherapy	Yes vs. No	1052/3124	5	1.12 (0.61 - 2.06)	7.11×10^{-1}	55	0.19 - 6.58	0.479
Medications	Insulin	Yes vs. No	1013/6195	5	2.39 (1.54 - 3.71)	9.92×10^{-5}	45	0.71 - 8.06	0.719
Medications	Oral corticosteroids	Yes vs. No	898/2563	5	1.00 (0.49 - 2.04)	9.92×10^{-1}	32	0.15 - 6.56	0.016
Medications	Statins	Yes vs. No	1842/5553	6	1.56 (1.27 - 1.90)	1.75×10^{-5}	55	0.92 - 2.62	0.144
Symptoms/signs	Abdominal pain	Yes vs. No	219/2157	8	1.04 (0.53 – 2.05)	9.00×10^{-1}	0	0.45 – 2.42	0.387
Symptoms/signs	Altered mental status	Yes vs. No	6727/33,241	10	4.38 (2.53 - 7.58)	1.23×10^{-7}	87	0.78 - 24.54	0.545
Symptoms/signs	Anorexia	Yes vs. No	692/5095	12	1.54 (0.92 - 2.58)	9.83×10^{-2}	67	0.32 - 7.44	0.407
Symptoms/signs	Anosmia/Ageusia	Yes vs. No	293/2116	5	0.42 (0.23 - 0.77)	5.41×10^{-3}	0	0.15 - 1.13	0.618
Symptoms/signs	Arthralgia/Myalgia	Yes vs. No	906/3753	6	0.56 (0.46 - 0.70)	8.43×10^{-8}	0	0.42 - 0.76	0.272
Symptoms/signs	Chest pain	Yes vs. No	580/6353	14	1.07 (0.70 - 1.62)	7.65×10^{-1}	31	0.38 - 2.98	0.394
Symptoms/signs	Chills	Yes vs. No	1093/4858	7	0.85 (0.51 - 1.42)	5.39×10^{-1}	63	0.23 - 3.11	0.681
Symptoms/signs	Cough	Yes vs. No	8825/44,947	33	0.82 (0.71 - 0.95)	7.40×10^{-3}	57	0.50 - 1.35	0.211
Symptoms/signs	Diarrhea	Yes vs. No	2696/12,241	23	0.71 (0.55 - 0.92)	1.00×10^{-2}	49	0.33 - 1.54	0.323
Symptoms/signs	Dizziness	Yes vs. No	240/3019	9	1.57 (0.99 - 2.49)	5.66×10^{-2}	0	0.90 - 2.73	0.752
Symptoms/signs	Dyspnea	Yes vs. No	8780/44,683	31	2.70 (2.16 - 3.39)	6.83×10^{-18}	86	0.99 - 7.41	0.027†
Symptoms/signs	Expectoration	Yes vs. No	2038/11,156	19	1.25 (1.03 - 1.53)	2.58×10^{-2}	33	0.77 - 2.05	0.894
Symptoms/signs	Fatigue	Yes vs. No	2169/13,648	22	1.03 (0.81 - 1.32)	7.86×10^{-1}	64	0.45 - 2.36	0.490

Category of predictor	Predictor	Level of comparison	N events/N participants	N studies	RE summary OR (95% CI)	P-value	I^2	95% PI	Egger's test P-value
Symptoms/signs	Fever	Yes vs. No	9444/73,576	28	0.92 (0.75 - 1.13)	4.25×10^{-1}	83	0.40 - 2.12	0.269
Symptoms/signs	GI symptoms	Yes vs. No	1661/34,470	14	1.02 (0.76 - 1.36)	9.09×10^{-1}	70	0.38 - 2.74	0.339
Symptoms/signs	Headache	Yes vs. No	2685/13,997	23	0.56 (0.39 - 0.81)	1.91×10^{-3}	64	0.16 - 1.96	0.238
Symptoms/signs	Heart rate	>100 bpm vs. <100 bpm	214/666	5	1.81 (1.24 - 2.65)	2.28×10^{-3}	0	0.97 - 3.36	0.067
Symptoms/signs	Hemoptysis	Yes vs. No	1079/3413	8	1.00 (0.62 - 1.62)	9.95×10^{-1}	0	0.55 - 1.82	0.932
Symptoms/signs	Myalgia	Yes vs. No	7126/38,321	17	0.62 (0.45 - 0.86)	3.61×10^{-3}	78	0.21 - 1.84	0.198
Symptoms/signs	Nausea	Yes vs. No	491/3364	8	0.99 (0.57 - 1.74)	9.78×10^{-1}	43	0.24 - 4.13	0.760
Symptoms/signs	Nausea/Vomiting	Yes vs. No	1800/8849	10	0.80 (0.60 - 1.08)	1.46×10^{-1}	38	0.41 - 1.60	0.048
Symptoms/signs	Pharyngalgia	Yes vs. No	2003/8666	18	0.58 (0.46 - 0.71)	5.04×10^{-7}	0	0.46 - 0.73	0.316
Symptoms/signs	Respiratory rate	>24 bpm vs. <24 bpm	1211/5496	6	4.50 (2.38 - 8.54)	4.02×10^{-6}	87	0.59 - 34.10	0.931
Symptoms/signs	Rhinorrhea	Yes vs. No	913/4933	6	0.63 (0.38 - 1.04)	7.16×10^{-2}	15	0.22 - 1.79	0.077
Symptoms/signs	SpO2	<90 % vs. >90 %	1267/6448	7	4.37 (2.98 - 6.42)	5.08×10^{-14}	70	1.43 - 13.4	0.861
Symptoms/signs	Vomiting	Yes vs. No	438/3225	8	1.19 (0.72 - 1.96)	4.89×10^{-1}	2	0.61 - 2.33	0.649
Pulmonary Embolism									
Comorbidities	Cancer	Yes vs. No	299/2291	6	0.95 (0.41 - 2.19)	9.03×10^{-1}	58	0.09 - 10.14	0.517
Comorbidities	COPD	Yes vs. No	253/1745	5	0.99 (0.59 - 1.66)	9.72×10^{-1}	0	0.43 - 2.28	0.739
Comorbidities	Diabetes mellitus	Yes vs. No	253/1740	5	0.86 (0.62 - 1.19)	3.68×10^{-1}	0	0.51 - 1.46	0.984
Comorbidities	Hypertension	Yes vs. No	253/1735	5	0.87 (0.66 - 1.15)	3.36×10^{-1}	0	0.55 - 1.38	0.754
Demographics	Sex	Female vs. Male	305/1965	6	0.71 (0.54 - 0.93)	1.30×10^{-2}	0	0.48 - 1.04	0.113
Venous Thromboembolism									
Comorbidities	Cancer	Yes vs. No	144/644	7	1.63 (0.76 - 3.50)	2.10×10^{-1}	0	0.60 - 4.44	0.321
Comorbidities	Chronic kidney disease	Yes vs. No	142/653	6	0.61 (0.30 - 1.24)	1.73×10^{-1}	0	0.22 - 1.68	0.231
Comorbidities	Diabetes mellitus	Yes vs. No	158/724	7	0.87 (0.54 - 1.40)	5.65×10^{-1}	14	0.36 - 2.12	0.169
Comorbidities	Hypertension	Yes vs. No	113/570	5	0.75 (0.39 - 1.42)	3.74×10^{-1}	44	0.12 - 4.69	0.499
Demographics	Sex	Female vs. Male	214/951	9	0.71 (0.51 - 0.99)	4.22×10^{-2}	0	0.47 - 1.06	0.167
Environmental factors	Smoking	Yes vs. No	127/595	5	0.69 (0.34 - 1.43)	3.23×10^{-1}	11	0.16 - 3.03	0.955

* One study did not report the number of cases and/or total number of participants.

** Two studies did not report the number of cases and/or total number of participants.

*** Three studies did not report the number of cases and/or total number of participants.

† The annotated meta-analyses fulfilled the criteria for the presence of small-study effects (a statistically significant Egger's test at P-value <0.10 and a more conservative effect in the largest study than in the random-effects meta-analysis.

Abbreviations: ACEi = angiotensin-converting enzyme inhibitors, ALT = alanine aminotransferase, ARBs = angiotensin II receptor blockers, AST = aspartate aminotransferase, BMI = body mass index, bpm = breaths per minute (for respiratory rate) or beats per minute (for heart rate), CI = confidence interval, COPD = chronic obstructive pulmonary disease, CRP = C-reactive protein, GI = gastrointestinal, HIV = human immunodeficiency virus, LDH = lactate dehydrogenase, OR = odds ratio, PI = prediction interval, RE = random-effects, SpO_2 = blood oxygen saturation, VTE = venous thromboembolism, WBC = white blood cells

Supplementary Table 3. Results of the sensitivity analysis excluding the studies that reported hazard ratios.

Predictors	Level of comparison	N events/N participants	N studies	RE summary OR (95% CI)	P-value	I^2	95% PI
Acute Kidney Injury							
ACEi/ARBs	Yes vs. No	4548/11,816	9	1.29 (1.07 - 1.56)	7.40×10^{-3}	43	0.83 - 2.01
Hypertension	Yes vs. No	2842/9658	8	2.02 (1.54 - 2.65)	4.52×10^{-7}	63	1.01 - 4.04
Acute Respiratory Distress Syndrome							
ACEi/ARBs	Yes vs. No	252/887	7	0.88 (0.63 - 1.22)	4.42×10^{-1}	0	0.57 - 1.36
Hypertension	Yes vs. No	494/2550	8	1.83 (1.11 - 3.01)	1.76×10^{-2}	69	0.42 - 7.91
Composite Outcome 1 (ICU admission or Death)							
Age	Per 1 year increase	508/1424	4	1.013 (0.996 - 1.031)	1.29×10^{-1}	68	0.947 - 1.085
Any comorbidity	Yes vs. No	330/838	6	1.35 (0.95 - 1.92)	9.54×10^{-2}	0	0.82 - 2.22
Cancer	Yes vs. No	1028/3890	12	1.53 (1.00 - 2.35)	4.97×10^{-2}	56	0.45 - 5.28
Chronic kidney disease	Yes vs. No	1096/4197	12	1.78 (1.24 - 2.55)	1.76×10^{-3}	45	0.68 - 4.65
COPD	Yes vs. No	662/2995	7	2.18 (1.31 - 3.63)	2.79×10^{-3}	51	0.56 - 8.42
Coronary heart disease	Yes vs. No	350/1037	4	2.54 (1.15 - 5.61)	2.17×10^{-2}	76	0.08 - 80.52
Cough	Yes vs. No	379/1091	6	0.89 (0.58 - 1.36)	5.86×10^{-1}	49	0.28 - 2.82
Diabetes mellitus	Yes vs. No	1257/4671	14	1.92 (1.45 - 2.55)	6.68×10^{-6}	60	0.80 - 4.63
Fever	Yes vs. No	720/2142	8	1.26 (0.81 - 1.97)	3.09×10^{-1}	54	0.38 - 4.16
Hypertension	Yes vs. No	1003/4074	12	1.69 (1.10 - 2.60)	1.63×10^{-2}	82	0.38 - 7.60
Sex	Female vs. Male	1423/5354	17	0.70 (0.59 - 0.83)	5.32×10^{-5}	27	0.46 - 1.07
Composite Outcome 2 (ICU admission, Mechanical Ventilation or Death)							
Any comorbidity	Yes vs. No	1084/4282	5	3.11 (1.58 - 6.14)	1.08×10^{-3}	75	0.32 - 30.01
Hospitalization							
Age	Per 1 year increase	258/854	4	1.059 (1.029 - 1.09)	8.37×10^{-5}	69	0.939 - 1.194
ICU admission							
Age	>60 vs. <60	440/2882	8	1.96 (1.18 - 3.26)	9.54×10^{-3}	73	0.42 - 9.09
Age	>65 vs. <65	1815/9039	12	1.19 (0.81 - 1.74)	3.80×10^{-1}	87	0.32 - 4.35
Any comorbidity	Yes vs. No	1673/6650	15	2.02 (1.39 - 2.94)	2.48×10^{-4}	75	0.52 - 7.79
GI symptoms	Yes vs. No	283/2185	7	0.95 (0.69 - 1.30)	7.28×10^{-1}	3	0.59 - 1.51
Lymphocytes	<1.000 /μL vs. >1.000 /μL	284/1024	7	4.52 (1.90 - 10.74)	6.26×10^{-4}	73	0.31 - 64.97
Sex	Female vs. Male	3179/18,572	48	0.53 (0.46 - 0.60)	1.84×10^{-23}	32	0.33 - 0.83
Invasive Mechanical Ventilation							
Age	>65 vs. <65	1226/13,035	9	1.50 (0.99 - 2.26)	5.54×10^{-2}	82	0.43 - 5.22
Cerebrovascular disease	Yes vs. No	815/4722	6	1.23 (0.68 - 2.22)	4.99×10^{-1}	62	0.22 - 6.94
Chronic kidney disease	Yes vs. No	2097/10,759	9	1.30 (0.86 - 1.99)	2.17×10^{-1}	82	0.33 - 5.08
Coronary heart disease	Yes vs. No	918/9634	7	1.79 (1.46 - 2.20)	2.08×10^{-8}	0	1.37 - 2.34

Predictors	Level of comparison	N events/N participants	N studies	RE summary OR (95% CI)	P-value	I^2	95% PI
Diabetes mellitus	Yes vs. No	3197/23,534	25	1.62 (1.30 - 2.00)	1.18×10^{-5}	75	0.67 - 3.91
Sex	Female vs. Male	2660/12,397	23	0.64 (0.57 - 0.73)	3.12×10^{-12}	14	0.50 - 0.83
Smoking	Yes vs. No	1054/4464	9	1.13 (0.96 - 1.32)	1.38×10^{-1}	0	0.93 - 1.36
Mortality							
ACEi	Yes vs. No	2310/11,678	11	1.31 (1.11 - 1.55)	1.42×10^{-3}	18	0.95 - 1.80
ACEi/ARBs	Yes vs. No	3136/21,468	26	1.36 (1.05 - 1.75)	1.90×10^{-2}	83	0.46 - 3.97
Age	>60 vs. <60	9783/96,415	23	8.96 (6.97 - 11.51)	7.95×10^{-66}	88	3.11 - 25.80
Age	>65 vs. <65	5639/30,863	21	5.85 (4.13 - 8.28)	3.00×10^{-23}	92	1.42 - 24.06
Age	per 1 year increase	1453/8793	23	1.078 (1.065 - 1.092)	4.20×10^{-32}	77	1.022 - 1.137
Anticoagulant therapy	Yes vs. No	948/2938	8	1.02 (0.61 - 1.69)	9.53×10^{-1}	39	0.30 - 3.44
Antiplatelet therapy	Yes vs. No	174/412	4	0.99 (0.61 - 1.60)	9.76×10^{-1}	0	0.35 - 2.85
Any immunosuppresive medication	Yes vs. No	6067/18,721	4	1.24 (1.12 - 1.39)	6.60×10^{-5}	0	0.98 - 1.58
ARBs	Yes vs. No	2310/11,678	11	1.25 (1.01 - 1.55)	3.61×10^{-2}	48	0.73 - 2.14
AST	>40 U/L vs. <40 U/L	1167/5818	6	2.63 (1.86 - 3.73)	5.60×10^{-8}	72	0.92 - 7.56
Asthma	Yes vs. No	17,000/70,367	27	0.88 (0.74 - 1.05)	1.46×10^{-1}	52	0.51 - 1.52
Beta-blockers	Yes vs. No	1854/8612	7	2.13 (1.63 - 2.78)	3.49×10^{-8}	59	1.05 - 4.31
BMI	Per 1 unit increase	480/2891	7	0.997 (0.972 - 1.023)	8.25×10^{-1}	42	0.938 - 1.06
Cerebrovascular disease	Yes vs. No	2465/17,330	30	2.92 (2.25 - 3.78)	4.86×10^{-16}	57	1.06 - 8.06
Chronic kidney disease	Yes vs. No	18,097/90,588	49	3.06 (2.54 - 3.67)	5.91×10^{-33}	80	1.15 - 8.13
Coronary heart disease	Yes vs. No	5050/35,363	41	2.84 (2.44 - 3.31)	1.25×10^{-41}	55	1.47 - 5.50
D-dimers	>0.5 μg/mL vs. <0.5 μg/mL	488/3329	8	3.76 (2.18 - 6.48)	1.89×10^{-6}	66	0.79 - 17.8
Diabetes mellitus	Yes vs. No	17,948/116,512	52	2.16 (1.84 - 2.54)	2.85×10^{-21}	90	0.82 - 5.72
Heart failure	Yes vs. No	4241/39,640	31	3.82 (2.83 - 5.15)	1.67×10^{-18}	85	0.86 - 17.03
Hypertension	Yes vs. No	8983/68,775	65	2.24 (1.95 - 2.57)	7.21×10^{-30}	78	0.95 - 5.28
LDH	>250 U/L vs. <250 U/L	508/4053	9	3.81 (1.68 - 8.62)	1.37×10^{-3}	85	0.24 - 60.13
Neutrophils	>6.300 /μL vs. <6.300 /μL	241/1697	4	6.79 (4.31 - 10.7)	1.39×10^{-16}	51	1.21 - 38.13
Obstructive sleep apnea	Yes vs. No	522/3673	6	1.42 (1.05 - 1.91)	2.19×10^{-2}	0	0.93 - 2.16
Peripheral arterial disease	Yes vs. No	2244/17,101	5	2.06 (1.46 - 2.91)	4.26×10^{-5}	44	0.79 - 5.38
Sex	Female vs. Male	18,946/175,565	67	0.70 (0.64 - 0.77)	7.96×10^{-14}	70	0.44 - 1.12
Smoking	Yes vs. No	7673/29,370	37	1.50 (1.34 - 1.67)	7.66×10^{-13}	23	1.12 - 2.00
Statins	Yes vs. No	1006/3838	5	1.35 (0.93 - 1.96)	1.13×10^{-1}	58	0.45 - 4.06

Supplementary Table 4. Results of the sensitivity analysis excluding the studies with less than 100 COVID-19 participants.

Predictors	Level of comparison	N events/N participants	N studies	RE summary OR (95% CI)	P-value	I^2	95% PI
Acute Kidney Injury							
ACEi/ARBs	Yes vs. No	4438/12774	7	1.27 (1.06 - 1.53)	1.08×10^{-2}	51	0.79 - 2.06
Cancer	Yes vs. No	4025/10813	4	1.50 (1.03 - 2.20)	3.63×10^{-2}	50	0.36 - 6.27
Diabetes mellitus	Yes vs. No	4828/20711	9	1.99 (1.59 - 2.49)	2.16×10^{-9}	79	1.01 - 3.94
Heart failure	Yes vs. No	4036/9177	4	2.27 (1.45 - 3.56)	3.61×10^{-4}	64	0.40 - 12.80
Hypertension	Yes vs. No	2732/12918	6	2.41 (1.78 - 3.25)	9.98×10^{-9}	78	0.96 - 6.02
Sex	Female vs. Male	4036/9177	4	0.74 (0.63 - 0.87)	2.80×10^{-4}	49	0.42 - 1.31
Acute Respiratory Distress Syndrome							
ACEi/ARBs	Yes vs. No	163/1740	4	0.80 (0.61 - 1.05)	1.05×10^{-1}	0	0.44 - 1.45
Diabetes mellitus	Yes vs. No	793/8070	4	2.34 (1.55 - 3.54)	5.76×10^{-5}	59	0.46 - 11.85
Hypertension	Yes vs. No	330/5684	4	3.00 (2.27 - 3.97)	1.56×10^{-14}	58	1.00 – 9.00
Composite Outcome 1 (ICU admission or Death)							
ACEi/ARBs	Yes vs. No	1541/7551	4	2.03 (1.02 - 4.02)	4.26×10^{-2}	96	0.08 – 54.00
Age	Per 1 year increase	543/1564	4	1.015 (1.002 - 1.029)	2.33×10^{-2}	68	0.961 - 1.072
Any comorbidity	Yes vs. No	334/919	5	1.48 (1.07 - 2.05)	1.79×10^{-2}	0	0.87 - 2.52
BMI	>30 kg/m^2 vs. <30 kg/m^2	484/1403	4	1.15 (0.91 - 1.45)	2.53×10^{-1}	0	0.68 - 1.92
Cancer	Yes vs. No	1033/3920	10	1.47 (0.98 - 2.20)	6.35×10^{-2}	56	0.46 - 4.64
Cardiovascular disease	Yes vs. No	709/3019	6	1.83 (1.04 - 3.20)	3.62×10^{-2}	83	0.29 - 11.42
Chronic kidney disease	Yes vs. No	1093/4178	9	1.81 (1.25 - 2.60)	1.57×10^{-3}	51	0.67 - 4.88
COPD	Yes vs. No	682/3069	6	1.86 (1.18 - 2.93)	7.91×10^{-3}	54	0.51 - 6.75
Coronary heart disease	Yes vs. No	385/1177	4	2.79 (1.53 - 5.09)	8.20×10^{-4}	70	0.22 - 34.76
Cough	Yes vs. No	386/1145	4	0.80 (0.62 - 1.03)	8.62×10^{-2}	0	0.45 - 1.40
Diabetes mellitus	Yes vs. No	1254/4649	11	1.90 (1.40 - 2.57)	3.59×10^{-5}	69	0.72 - 5.03
Dyspnea	Yes vs. No	412/1195	4	2.01 (1.54 - 2.62)	2.08×10^{-7}	0	1.13 - 3.58
Fever	Yes vs. No	692/2097	5	1.17 (0.75 - 1.82)	4.92×10^{-1}	61	0.30 - 4.57
Heart failure	Yes vs. No	305/767	4	0.87 (0.49 - 1.52)	6.22×10^{-1}	11	0.19 - 3.91
Hypertension	Yes vs. No	1000/4052	9	1.80 (1.15 - 2.83)	1.05×10^{-2}	86	0.38 - 8.59
Sex	Female vs. Male	1354/5174	12	0.69 (0.60 - 0.79)	7.36×10^{-8}	0	0.59 - 0.80
Composite Outcome 2 (ICU admission, Mechanical Ventilation, or Death)							
Any comorbidity	Yes vs. No	1072/4601	6	2.78 (1.62 - 4.74)	1.91×10^{-4}	71	0.53 - 14.43
Diabetes mellitus	Yes vs. No	1383/5536	7	1.94 (1.03 - 3.67)	4.13×10^{-2}	90	0.22 - 16.90
Hypertension	Yes vs. No	1334/5551	7	2.50 (1.49 - 4.19)	5.43×10^{-4}	86	0.46 - 13.65
Sex	Female vs. Male	1345/5557	5	0.91 (0.66 - 1.26)	5.68×10^{-1}	66	0.32 - 2.58
Deep Venous Thrombosis							
Cancer	Yes vs. No	116/832	4	0.96 (0.44 - 2.11)	9.24×10^{-1}	0	0.17 - 5.40
Hospitalization							
ACEi/ARBs	Yes vs. No	5455/11726	9	1.90 (1.49 - 2.43)	3.20×10^{-7}	78	0.89 - 4.05

Predictors	Level of comparison	N events/N participants	N studies	RE summary OR (95% CI)	P-value	I^2	95% PI
Age	>60 vs. <60	6204/20616	8	4.00 (2.91 - 5.49)	1.00×10^{-17}	92	1.43 - 11.14
Age	>65 vs. <65	6256/11845	10	4.98 (3.08 - 8.06)	5.85×10^{-11}	95	0.82 - 30.12
Age	Per 1 year increase	358/1319	4	1.056 (1.033 - 1.080)	1.22×10^{-6}	71	0.961 - 1.161
Ageusia	Yes vs. No	2085/3555	7	0.35 (0.20 - 0.61)	2.10×10^{-4}	85	0.05 - 2.29
Anosmia	Yes vs. No	2086/3563	7	0.29 (0.17 - 0.47)	9.73×10^{-7}	82	0.05 - 1.49
Any comorbidity	Yes vs. No	8651/16922	13	4.27 (3.40 - 5.37)	8.48×10^{-36}	82	1.96 - 9.34
Asthma	Yes vs. No	10076/18988	14	1.09 (0.90 - 1.31)	3.89×10^{-1}	56	0.62 - 1.91
BMI	>30 kg/m^2 vs. <30 kg/m^2	10340/17207	11	1.43 (1.16 - 1.77)	8.10×10^{-4}	83	0.73 - 2.82
Cancer	Yes vs. No	14175/28548	16	2.49 (1.78 - 3.48)	1.05×10^{-7}	87	0.72 - 8.62
Cardiovascular disease	Yes vs. No	6522/23458	16	3.29 (2.50 - 4.33)	1.27×10^{-17}	82	1.32 - 8.18
Chronic kidney disease	Yes vs. No	14050/35587	18	5.24 (3.85 - 7.14)	6.55×10^{-26}	81	1.68 - 16.31
Chronic lung disease	Yes vs. No	2829/15650	12	2.00 (1.41 - 2.83)	9.04×10^{-5}	66	0.72 - 5.54
COPD	Yes vs. No	8961/17241	12	3.61 (2.50 - 5.21)	6.38×10^{-12}	64	1.19 - 10.97
Coronary heart disease	Yes vs. No	10002/18347	11	3.64 (2.51 - 5.30)	1.18×10^{-11}	85	1.01 - 13.1
Cough	Yes vs. No	4638/17110	12	1.25 (0.89 - 1.76)	1.95×10^{-1}	89	0.37 - 4.25
Diabetes mellitus	Yes vs. No	14735/38591	26	3.72 (3.15 - 4.40)	2.65×10^{-53}	77	1.89 - 7.33
Diarrhea	Yes vs. No	3769/15733	10	1.38 (1.00 - 1.91)	5.34×10^{-2}	85	0.44 - 4.30
Dyslipidemia	Yes vs. No	2913/6728	4	2.71 (1.66 - 4.44)	7.25×10^{-5}	68	0.39 - 18.94
Dyspnea	Yes vs. No	4638/17110	12	3.53 (2.83 - 4.40)	4.07×10^{-29}	76	1.71 - 7.28
Fatigue	Yes vs. No	1277/2946	5	1.46 (0.64 - 3.32)	3.71×10^{-1}	93	0.06 - 33.34
Fever	Yes vs. No	4657/17707	13	2.11 (1.48 - 3.00)	3.26×10^{-5}	89	0.57 - 7.85
GI symptoms	Yes vs. No	506/1613	4	1.67 (0.70 - 3.98)	2.45×10^{-1}	87	0.03 - 82.42
Headache	Yes vs. No	2286/13599	8	0.40 (0.28 - 0.58)	1.17×10^{-6}	81	0.13 - 1.30
Heart failure	Yes vs. No	9779/18298	11	6.11 (3.61 - 10.35)	1.74×10^{-11}	84	1.04 - 35.89
Hypertension	Yes vs. No	13340/27118	23	3.77 (3.13 - 4.56)	2.23×10^{-43}	88	1.65 - 8.61
Immunocompromised state	Yes vs. No	2300/4696	5	1.70 (0.91 - 3.18)	9.43×10^{-2}	55	0.25 - 11.74
Myalgia	Yes vs. No	843/1794	5	0.64 (0.35 - 1.14)	1.29×10^{-1}	86	0.07 - 5.58
Nasal congestion	Yes vs. No	804/1590	5	0.48 (0.37 - 0.62)	9.65×10^{-9}	0	0.32 - 0.72
Nausea	Yes vs. No	1497/2380	4	1.32 (0.92 - 1.91)	1.37×10^{-1}	55	0.32 - 5.53
Pharyngalgia	Yes vs. No	2561/13385	7	0.45 (0.28 - 0.71)	5.99×10^{-4}	84	0.10 - 2.01
Rhinorrhea	Yes vs. No	1967/11996	4	0.47 (0.25 - 0.85)	1.29×10^{-2}	68	0.05 - 4.55
Sex	Female vs. Male	16435/41698	32	0.60 (0.53 - 0.68)	6.68×10^{-15}	83	0.32 - 1.11
Smoking	Yes vs. No	10879/29086	18	1.55 (1.23 - 1.96)	2.58×10^{-4}	80	0.67 - 3.59
Solid organ transplantation	Yes vs. No	1611/2541	4	2.86 (0.80 - 10.22)	1.06×10^{-1}	53	0.02 - 384.59
Vomiting	Yes vs. No	1391/2322	5	1.42 (1.04 - 1.94)	2.82×10^{-2}	0	0.85 - 2.35
ICU admission							
ACEi	Yes vs. No	1171/5256	6	1.01 (0.77 - 1.33)	9.49×10^{-1}	42	0.50 - 2.04
ACEi/ARBs	Yes vs. No	1779/9711	9	1.19 (0.79 - 1.79)	3.99×10^{-1}	89	0.30 - 4.66
Age	>65 vs. <65	1827/9289	10	1.34 (0.90 - 1.99)	1.53×10^{-1}	90	0.33 - 5.46
Age	Per 1 year increase	780/2673	5	0.999 (0.987 - 1.011)	8.28×10^{-1}	69	0.959 - 1.040

Predictors	Level of comparison	N events/N participants	N studies	RE summary OR (95% CI)	P-value	I^2	95% PI
Any comorbidity	Yes vs. No	1637/6614	12	2.17 (1.44 - 3.27)	2.21×10^{-4}	80	0.50 - 9.35
ARBs	Yes vs. No	1110/4868	5	1.04 (0.75 - 1.45)	7.93×10^{-1}	56	0.39 - 2.82
Asthma	Yes vs. No	639/2348	6	1.04 (0.70 - 1.54)	8.48×10^{-1}	27	0.43 - 2.53
Autoimmune diseases/ Rheumatological diseases	Yes vs. No	1196/4473	4	1.07 (0.71 - 1.61)	7.51×10^{-1}	0	0.44 - 2.62
Bilateral involvement	Yes vs. No	319/1070	4	3.13 (1.67 - 5.88)	3.82×10^{-4}	48	0.34 - 29.19
BMI	>30 kg/m^2 vs. <30 kg/m^2	1273/4615	10	1.94 (1.40 - 2.68)	7.03×10^{-5}	70	0.70 - 5.39
Cancer	Yes vs. No	2520/11354	23	1.00 (0.74 - 1.36)	9.86×10^{-1}	59	0.33 - 3.07
Cardiovascular disease	Yes vs. No	1312/5156	13	1.47 (1.11 - 1.94)	7.25×10^{-3}	47	0.72 - 3.00
Cerebrovascular disease	Yes vs. No	854/4514	6	1.08 (0.63 - 1.86)	7.82×10^{-1}	71	0.20 - 5.78
Chronic kidney disease	Yes vs. No	1623/7408	13	1.59 (1.18 - 2.13)	2.23×10^{-3}	49	0.72 - 3.49
Chronic liver disease	Yes vs. No	193/1297	5	2.05 (1.14 - 3.70)	1.67×10^{-2}	0	0.79 - 5.35
Chronic lung disease	Yes vs. No	1239/4927	9	1.52 (1.12 - 2.04)	6.37×10^{-3}	33	0.77 - 2.98
Cirrhosis	Yes vs. No	462/1598	4	1.11 (0.56 - 2.17)	7.71×10^{-1}	0	0.25 - 4.85
COPD	Yes vs. No	1046/5256	13	1.33 (0.95 - 1.86)	9.12×10^{-2}	34	0.58 - 3.05
Coronary heart disease	Yes vs. No	1054/5466	8	1.26 (0.83 - 1.91)	2.72×10^{-1}	73	0.33 - 4.77
Cough	Yes vs. No	541/2108	8	1.02 (0.82 - 1.27)	8.46×10^{-1}	0	0.78 - 1.34
Diabetes mellitus	Yes vs. No	2635/13691	26	1.53 (1.28 - 1.84)	3.33×10^{-6}	57	0.79 - 2.97
Diarrhea	Yes vs. No	569/2086	8	1.01 (0.79 - 1.29)	9.66×10^{-1}	2	0.72 - 1.41
Dyslipidemia	Yes vs. No	383/2140	4	0.83 (0.44 - 1.58)	5.79×10^{-1}	77	0.05 - 13.45
Dyspnea	Yes vs. No	689/2493	9	3.99 (2.09 - 7.60)	2.59×10^{-5}	88	0.42 - 38.17
Expectoration	Yes vs. No	370/1391	5	0.79 (0.50 - 1.24)	3.02×10^{-1}	29	0.25 - 2.49
Fatigue	Yes vs. No	192/881	6	1.06 (0.58 - 1.92)	8.58×10^{-1}	62	0.17 - 6.52
Fever	Yes vs. No	752/3294	11	1.07 (0.79 - 1.45)	6.61×10^{-1}	33	0.53 - 2.15
GI symptoms	Yes vs. No	269/2286	5	1.11 (0.64 - 1.94)	7.06×10^{-1}	63	0.19 - 6.59
Headache	Yes vs. No	588/2341	9	0.64 (0.46 - 0.87)	5.17×10^{-3}	0	0.44 - 0.93
Heart failure	Yes vs. No	1007/4760	8	1.28 (0.86 - 1.91)	2.29×10^{-1}	62	0.39 - 4.15
HIV infection	Yes vs. No	339/1527	3	1.15 (0.49 - 2.68)	7.54×10^{-1}	0	0.005 - 280.92
Hypertension	Yes vs. No	2601/13888	25	1.78 (1.40 - 2.26)	1.91×10^{-6}	80	0.63 - 5.06
Myalgia	Yes vs. No	379/1412	5	0.95 (0.59 - 1.53)	8.46×10^{-1}	48	0.24 - 3.85
Nausea/Vomiting	Yes vs. No	312/1344	4	0.85 (0.28 - 2.56)	7.66×10^{-1}	64	0.01 - 71.89
Obesity	Yes vs. No	781/5071	6	1.31 (0.63 - 2.7)	4.70×10^{-1}	83	0.13 - 13.12
Pharyngalgia	Yes vs. No	377/1622	6	1.21 (0.63 - 2.31)	5.64×10^{-1}	56	0.20 - 7.48
Procalcitonin	>0.5 ng/ml vs. <0.5 ng/ml	365/1162	4	3.11 (1.55 - 6.24)	1.44×10^{-3}	75	0.15 - 63.87
Sex	Female vs. Male	2852/17684	32	0.53 (0.45 - 0.61)	2.91×10^{-17}	50	0.30 - 0.93
Smoking	Yes vs. No	1570/6914	13	1.20 (1.04 - 1.37)	1.09×10^{-2}	0	1.02 - 1.40
Solid organ transplantation	Yes vs. No	490/1576	4	1.17 (0.64 - 2.13)	6.03×10^{-1}	0	0.32 - 4.36
Invasive Mechanical Ventilation							
ACEi/ARBs	Yes vs. No	517/3968	8	1.24 (0.82 - 1.87)	3.04×10^{-1}	62	0.37 - 4.13
Age	>65 vs. <65	1179/13839	7	1.81 (1.17 - 2.80)	8.09×10^{-3}	88	0.41 - 7.91

Predictors	Level of comparison	N events/N participants	N studies	RE summary OR (95% CI)	P-value	I^2	95% PI
Any comorbidity	Yes vs. No	1786/9323	5	1.07 (0.75 - 1.51)	7.16×10^{-1}	75	0.35 - 3.27
Asthma	Yes vs. No	1006/5040	8	1.04 (0.83 - 1.29)	7.47×10^{-1}	0	0.79 - 1.36
BMI	>30 kg/m^2 vs. <30 kg/m^2	1211/4966	9	1.57 (1.25 - 1.97)	9.58×10^{-5}	47	0.88 - 2.81
Cancer	Yes vs. No	1189/10335	11	1.59 (1.27 – 2.00)	7.17×10^{-5}	0	1.22 - 2.08
Cardiovascular disease	Yes vs. No	1422/8367	7	1.11 (0.61 - 2.02)	7.24×10^{-1}	88	0.15 - 8.19
Chronic lung disease	Yes vs. No	1557/8307	7	1.09 (0.62 - 1.91)	7.77×10^{-1}	86	0.16 - 7.31
COPD	Yes vs. No	853/4271	7	1.71 (0.95 - 3.08)	7.60×10^{-2}	72	0.28 - 10.41
Coronary heart disease	Yes vs. No	939/10555	7	1.80 (1.32 - 2.45)	2.10×10^{-4}	34	0.87 - 3.72
Diabetes mellitus	Yes vs. No	3106/24237	22	1.71 (1.37 - 2.13)	1.98×10^{-6}	78	0.70 - 4.18
Fever	Yes vs. No	423/1357	5	0.92 (0.70 - 1.20)	5.40×10^{-1}	5	0.57 - 1.49
Heart failure	Yes vs. No	1022/10190	7	1.46 (0.93 - 2.30)	9.77×10^{-2}	66	0.38 - 5.61
HIV infection	Yes vs. No	1292/7296	5	1.27 (0.63 - 2.55)	5.04×10^{-1}	0	0.41 - 3.95
Hypertension	Yes vs. No	1851/14624	17	1.69 (1.36 - 2.11)	2.44×10^{-6}	67	0.79 - 3.63
Sex	Female vs. Male	2537/12927	16	0.62 (0.55 - 0.70)	1.98×10^{-13}	20	0.47 - 0.81
Mortality							
Abdominal pain	Yes vs. No	175/1919	5	1.14 (0.47 - 2.77)	7.68×10^{-1}	0	0.27 - 4.81
ACEi	Yes vs. No	3086/13195	9	1.38 (1.18 - 1.62)	7.50×10^{-5}	45	0.94 - 2.03
ACEi/ARBs	Yes vs. No	3284/22879	21	1.29 (1.00 - 1.66)	5.33×10^{-2}	86	0.44 - 3.80
Age	>60 vs. <60	9780/96705	22	9.59 (7.46 - 12.34)	1.64×10^{-69}	88	3.31 - 27.77
Age	>65 vs. <65	5706/31260	17	6.43 (4.53 - 9.11)	1.62×10^{-25}	93	1.57 - 26.25
Age	Per 1 year increase	2090/12958	26	1.073 (1.063 - 1.082)	1.12×10^{-54}	78	1.03 - 1.118
Altered mental status	Yes vs. No	6651/32870	5	6.11 (3.16 - 11.82)	7.29×10^{-8}	92	0.60 - 62.08
Anorexia	Yes vs. No	659/4921	10	1.43 (0.81 - 2.54)	2.14×10^{-1}	71	0.25 - 8.08
Anticoagulant therapy	Yes vs. No	1729/4598	6	1.28 (1.11 - 1.48)	8.07×10^{-4}	0	1.04 - 1.57
Any comorbidity	Yes vs. No	14510/61938	23	3.68 (2.92 - 4.65)	7.09×10^{-28}	90	1.48 - 9.19
Any immunosuppresive medication	Yes vs. No	6883/20338	4	1.22 (1.12 - 1.33)	9.60×10^{-6}	0	1.01 - 1.48
Any neurological disease	Yes vs. No	8549/23533	6	3.41 (2.08 - 5.62)	1.30×10^{-6}	93	0.66 - 17.69
ARBs	Yes vs. No	3086/13195	9	1.33 (1.13 - 1.57)	7.38×10^{-4}	56	0.86 - 2.05
Arthralgia/Myalgia	Yes vs. No	896/3676	5	0.55 (0.45 - 0.68)	3.57×10^{-8}	0	0.39 - 0.78
Asthma	Yes vs. No	16985/70354	26	0.90 (0.75 - 1.07)	2.34×10^{-1}	56	0.50 - 1.61
Atrial fibrillation	Yes vs. No	832/3498	7	2.03 (1.26 - 3.26)	3.36×10^{-3}	41	0.63 - 6.52
Beta-blockers	Yes vs. No	2659/10257	7	1.94 (1.48 - 2.55)	1.45×10^{-6}	81	0.87 - 4.33
Bilateral involvement	Yes vs. No	1004/6041	13	1.13 (0.82 - 1.56)	4.51×10^{-1}	58	0.43 - 2.94
BMI	>30 kg/m^2 vs. <30 kg/m^2	2478/12825	19	0.94 (0.78 - 1.12)	4.69×10^{-1}	57	0.52 - 1.69
BMI	Per 1 kg/m^2 increase	561/3263	7	0.992 (0.975 - 1.009)	3.37×10^{-1}	26	0.955 - 1.029
Calcium channel blockers	Yes vs. No	1103/7133	6	1.67 (1.30 - 2.14)	4.57×10^{-5}	18	1.00 - 2.78
Cancer	Yes vs. No	16628/96639	32	2.15 (1.88 - 2.47)	1.67×10^{-28}	51	1.32 - 3.51
Cardiovascular disease	Yes vs. No	14682/76858	20	3.72 (2.81 - 4.93)	6.10×10^{-20}	95	1.11 - 12.43
Cerebrovascular disease	Yes vs. No	2367/17176	24	3.13 (2.41 - 4.07)	1.72×10^{-17}	60	1.16 - 8.43

Predictors	Level of comparison	N events/N participants	N studies	RE summary OR (95% CI)	P-value	I^2	95% PI
Chest pain	Yes vs. No	490/6051	10	1.01 (0.64 - 1.61)	9.57×10^{-1}	37	0.33 - 3.15
Chills	Yes vs. No	1088/4815	6	0.88 (0.52 - 1.48)	6.19×10^{-1}	68	0.21 - 3.68
Chronic kidney disease	Yes vs. No	18124/90607	46	3.05 (2.54 - 3.65)	2.37×10^{-33}	81	1.15 - 8.09
Chronic liver disease	Yes vs. No	17426/60743	14	1.44 (1.20 - 1.74)	1.16×10^{-4}	16	1.01 - 2.06
Chronic lung disease	Yes vs. No	6524/41304	14	2.39 (1.87 - 3.05)	2.31×10^{-12}	72	1.11 - 5.13
Consolidation	Yes vs. No	433/2898	5	1.61 (1.21 - 2.14)	9.61×10^{-4}	18	0.85 - 3.07
COPD	Yes vs. No	12409/65294	37	2.22 (1.89 - 2.62)	3.80×10^{-22}	51	1.16 - 4.27
Coronary heart disease	Yes vs. No	4953/35011	36	2.87 (2.46 - 3.35)	3.16×10^{-41}	57	1.49 - 5.54
Cough	Yes vs. No	8651/44314	21	0.80 (0.69 - 0.92)	2.76×10^{-3}	66	0.48 - 1.31
CRP	>10 mg/L vs. <10 mg/L	486/3822	6	7.27 (2.95 - 17.91)	1.64×10^{-5}	69	0.50 - 105.30
Dementia	Yes vs. No	6342/20991	8	3.26 (2.62 - 4.06)	7.19×10^{-26}	48	1.94 - 5.47
Diabetes mellitus	Yes vs. No	17863/116246	45	2.15 (1.82 - 2.53)	7.54×10^{-20}	91	0.80 - 5.74
Diarrhea	Yes vs. No	2602/11763	15	0.63 (0.48 - 0.82)	8.47×10^{-4}	56	0.29 - 1.37
Dizziness	Yes vs. No	216/2889	7	1.47 (0.87 - 2.50)	1.52×10^{-1}	0	0.73 - 2.95
Dyslipidemia	Yes vs. No	4854/19494	16	1.37 (1.08 - 1.74)	1.05×10^{-2}	74	0.62 - 3.01
Dyspnea	Yes vs. No	8625/44052	20	2.44 (1.92 - 3.10)	3.48×10^{-13}	89	0.91 - 6.57
Expectoration	Yes vs. No	1953/10754	12	1.31 (1.03 - 1.66)	2.52×10^{-2}	54	0.69 - 2.49
Fatigue	Yes vs. No	2077/13231	15	0.99 (0.75 - 1.29)	9.16×10^{-1}	73	0.40 - 2.42
Fever	Yes vs. No	9332/73102	20	0.91 (0.73 - 1.13)	3.85×10^{-1}	87	0.39 - 2.14
Ground-glass opacity	Yes vs. No	702/4702	8	0.84 (0.57 - 1.24)	3.76×10^{-1}	61	0.28 - 2.50
Headache	Yes vs. No	2627/13720	19	0.57 (0.39 - 0.85)	5.12×10^{-3}	69	0.15 - 2.14
Heart failure	Yes vs. No	4232/39632	30	3.95 (2.95 - 5.29)	3.06×10^{-20}	84	0.94 - 16.69
Hemoptysis	Yes vs. No	1046/3239	6	0.95 (0.57 - 1.59)	8.50×10^{-1}	0	0.46 - 1.97
History of VTE	Yes vs. No	936/4123	5	1.44 (0.96 - 2.15)	7.96×10^{-2}	20	0.56 - 3.66
Hypertension	Yes vs. No	8869/72042	51	2.41 (2.10 - 2.77)	2.68×10^{-36}	80	1.08 - 5.37
Immunocompromised state	Yes vs. No	4157/11617	10	2.10 (1.38 - 3.19)	5.32×10^{-4}	65	0.61 - 7.23
LDH	>250 U/L vs. <250 U/L	453/3967	6	6.12 (2.60 - 14.38)	3.30×10^{-5}	86	0.32 - 115.85
Myalgia	Yes vs. No	7087/38122	14	0.62 (0.44 - 0.87)	5.50×10^{-3}	82	0.20 - 1.95
Nausea	Yes vs. No	486/3321	7	0.97 (0.53 - 1.77)	9.18×10^{-1}	50	0.19 - 4.95
Nausea/Vomiting	Yes vs. No	1780/8754	9	0.77 (0.57 - 1.02)	6.77×10^{-2}	36	0.40 - 1.47
Nursing home	Yes vs. No	1071/6438	8	2.63 (1.20 - 5.77)	1.55×10^{-2}	91	0.17 - 41.6
Obesity	Yes vs. No	6657/25618	10	1.31 (0.95 - 1.82)	1.01×10^{-1}	83	0.48 - 3.63
Obstructive sleep apnea	Yes vs. No	548/3732	6	1.42 (1.08 - 1.86)	1.16×10^{-2}	0	0.97 - 2.08
Peripheral arterial disease	Yes vs. No	2288/17376	5	2.14 (1.64 - 2.78)	1.87×10^{-8}	26	1.10 - 4.15
Pharyngalgia	Yes vs. No	1944/8383	14	0.56 (0.45 - 0.70)	3.73×10^{-7}	0	0.44 - 0.72
Platelets	<150.000 /μL vs. >150.000 /μL	175/1821	5	2.70 (1.40 - 5.20)	3.14×10^{-3}	67	0.32 - 22.93
Procalcitonin	>0.5 ng/ml vs. <0.5 ng/ml	793/3766	5	6.57 (2.85 - 15.11)	9.57×10^{-6}	77	0.39 - 109.33
Respiratory rate	>24 bpm vs. <24 bpm	1201/5419	5	5.02 (2.58 - 9.77)	2.04×10^{-6}	89	0.49 - 51.78
Rhinorrhea	Yes vs. No	899/4894	5	0.49 (0.36 - 0.66)	3.99×10^{-6}	0	0.30 - 0.80

Predictors	Level of comparison	N events/N participants	N studies	RE summary OR (95% CI)	P-value	I^2	95% PI
Sex	Female vs. Male	24048/189232	53	0.71 (0.65 - 0.78)	2.01×10^{-13}	79	0.46 - 1.12
Smoking	Yes vs. No	7754/29951	34	1.50 (1.35 - 1.68)	8.72×10^{-14}	24	1.14 - 1.99
SpO2	<90 % vs. >90 %	1249/6330	5	4.08 (2.79 - 5.97)	3.70×10^{-13}	76	1.09 - 15.29
Statins	Yes vs. No	1811/5483	5	1.60 (1.31 - 1.95)	4.60×10^{-6}	58	0.89 - 2.84
Vomiting	Yes vs. No	416/3045	6	0.97 (0.55 - 1.71)	9.27×10^{-1}	0	0.44 - 2.16
WBC	<4.000 /µL vs. >4.000 /µL	1006/4737	5	0.58 (0.40 - 0.84)	3.75×10^{-3}	31	0.22 - 1.50
WBC	>10.000 /µL vs. <10.000 /µL	495/4266	6	7.27 (2.89 - 18.29)	2.47×10^{-5}	92	0.28 - 186.15
Pulmonary Embolism							
Cancer	Yes vs. No	262/2180	4	0.89 (0.36 - 2.22)	8.03×10^{-1}	68	0.02 - 40.10

Supplementary Table 5. Results of the sensitivity analysis excluding the studies including only COVID-19 patients with a specific comorbid disorder.

Predictors	Level of comparison	N events/N participants	N studies	RE summary OR (95% CI)	P-value	I^2	95% PI
Acute Respiratory Distress Syndrome							
ACEi/ARBs	Yes vs. No	228/1952	7	0.80 (0.62 - 1.04)	9.23×10^{-2}	0	0.57 - 1.12
Diabetes mellitus	Yes vs. No	861/8201	6	2.38 (1.64 - 3.46)	5.49×10^{-6}	49	0.88 - 6.44
Hypertension	Yes vs. No	398/5815	6	2.57 (1.83 - 3.61)	5.37×10^{-8}	66	0.95 - 6.92
Sex	Female vs. Male	342/1123	6	0.76 (0.45 - 1.29)	3.08×10^{-1}	66	0.15 - 3.89
Smoking	Yes vs. No	165/418	4	0.60 (0.27 - 1.34)	2.16×10^{-1}	0	0.10 - 3.51
Composite Outcome 1 (ICU admission or Death)							
Any comorbidity	Yes vs. No	367/1002	6	1.53 (1.11 - 2.09)	8.64×10^{-3}	0	0.98 - 2.38
Cough	Yes vs. No	416/1255	6	0.78 (0.61 - 1.00)	4.80×10^{-2}	0	0.55 - 1.11
Dyspnea	Yes vs. No	442/1305	6	2.02 (1.57 - 2.61)	5.92×10^{-8}	0	1.41 - 2.90
Fever	Yes vs. No	757/2306	8	1.11 (0.76 - 1.64)	5.83×10^{-1}	52	0.41 - 3.06
Sex	Female vs. Male	1460/5518	17	0.69 (0.59 - 0.81)	3.65×10^{-6}	21	0.48 - 0.98
Smoking	Yes vs. No	336/904	7	1.19 (0.80 - 1.77)	3.79×10^{-1}	0	0.71 - 2.00
Composite Outcome 2 (ICU admission, Mechanical Ventilation or Death)							
Diabetes mellitus	Yes vs. No	1395/5568	8	2.20 (1.17 - 4.13)	1.38×10^{-2}	89	0.27 - 18.02
Hypertension	Yes vs. No	1346/5583	8	2.63 (1.59 - 4.34)	1.62×10^{-4}	84	0.52 - 13.19
Sex	Female vs. Male	1357/5589	6	0.91 (0.67 - 1.23)	5.46×10^{-1}	58	0.39 - 2.12
Hospitalization							
Age	>60 vs. <60	6075/20,468	9	4.38 (3.18 - 6.04)	1.70×10^{-19}	90	1.64 - 11.73
Any comorbidity	Yes vs. No	8742/17,028	19	4.14 (3.31 - 5.19)	3.60×10^{-35}	77	1.92 - 8.97
Bilateral involvement	Yes vs. No	1159/1571	5	8.25 (3.36 - 20.25)	4.04×10^{-6}	62	0.53 - 128.4
Cancer	Yes vs. No	14,263/28,752	20	2.52 (1.85 - 3.43)	5.27×10^{-9}	84	0.78 - 8.13
Cardiovascular disease	Yes vs. No	6429/23,087	17	3.34 (2.56 - 4.36)	9.50×10^{-19}	82	1.36 - 8.19
Chronic lung disease	Yes vs. No	2793/15,463	15	1.89 (1.37 - 2.63)	1.30×10^{-4}	56	0.76 - 4.73
COPD	Yes vs. No	8961/17,241	13	3.80 (2.70 - 5.36)	2.67×10^{-14}	63	1.31 - 11.06
Coronary heart disease	Yes vs. No	10,002/18,347	11	3.64 (2.51 - 5.30)	1.18×10^{-11}	85	1.01 - 13.10
Diabetes mellitus	Yes vs. No	14,762/38,493	30	3.69 (3.14 - 4.34)	4.93×10^{-56}	74	1.90 - 7.17
Fatigue	Yes vs. No	1310/3110	8	1.39 (0.70 - 2.77)	3.51×10^{-1}	88	0.15 - 13.14
GI symptoms	Yes vs. No	525/1735	6	1.89 (0.91 - 3.89)	8.56×10^{-2}	80	0.19 - 18.87
Heart failure	Yes vs. No	9779/18,298	12	6.65 (4.02 - 11.01)	1.74×10^{-13}	84	1.16 - 38.22
Hypertension	Yes vs. No	13,440/27,367	28	3.72 (3.11 - 4.46)	3.52×10^{-46}	85	1.67 - 8.32
Myalgia	Yes vs. No	940/2031	9	0.68 (0.42 - 1.12)	1.34×10^{-1}	77	0.15 - 3.18
Obesity	Yes vs. No	5796/19,319	8	2.15 (1.68 - 2.77)	1.96×10^{-9}	56	1.11 - 4.20

Predictors	Level of comparison	N events/N participants	N studies	RE summary OR (95% CI)	P-value	I^2	95% PI
Sex	Female vs. Male	16,297/41,341	37	0.63 (0.55 - 0.71)	4.50×10^{-13}	82	0.34 - 1.17
Smoking	Yes vs. No	10,789/28,717	17	1.63 (1.28 - 2.07)	6.07×10^{-5}	80	0.71 - 3.75
ICU admission							
Age	>60 vs. <60	455/2948	8	1.99 (1.22 - 3.24)	5.75×10^{-3}	73	0.45 - 8.81
Age	>65 vs. <65	1853/9417	12	1.29 (0.88 - 1.89)	1.87×10^{-1}	89	0.33 - 5.05
Chest pain	Yes vs. No	264/1528	5	1.23 (0.73 - 2.08)	4.46×10^{-1}	27	0.33 - 4.53
Chronic liver disease	Yes vs. No	288/1605	10	1.89 (1.10 - 3.27)	2.21×10^{-2}	0	1.00 - 3.60
Chronic lung disease	Yes vs. No	1298/5181	13	1.50 (1.16 - 1.94)	2.03×10^{-3}	16	0.92 - 2.45
Cough	Yes vs. No	826/2874	22	0.94 (0.78 - 1.15)	5.60×10^{-1}	0	0.77 - 1.16
Diarrhea	Yes vs. No	713/2521	16	0.99 (0.80 - 1.24)	9.49×10^{-1}	0	0.78 - 1.26
Dyspnea	Yes vs. No	975/3259	23	4.25 (2.71 - 6.68)	3.44×10^{-10}	78	0.65 - 27.95
Expectoration	Yes vs. No	432/1652	9	0.76 (0.51 - 1.14)	1.86×10^{-1}	19	0.35 - 1.67
Fatigue	Yes vs. No	208/965	7	1.02 (0.60 - 1.74)	9.36×10^{-1}	55	0.22 - 4.71
Fever	Yes vs. No	1037/4074	25	1.08 (0.88 - 1.32)	4.51×10^{-1}	4	0.80 - 1.46
Headache	Yes vs. No	815/2839	18	0.61 (0.46 - 0.81)	5.16×10^{-4}	0	0.45 - 0.83
Sex	Female vs. Male	3194/18,638	48	0.52 (0.46 - 0.59)	6.38×10^{-27}	27	0.35 - 0.78
Invasive Mechanical Ventilation							
ACEi/ARBs	Yes vs. No	528/4068	9	1.18 (0.79 - 1.77)	4.19×10^{-1}	61	0.37 - 3.81
Age	>65 vs. <65	1268/13,959	9	1.68 (1.10 - 2.55)	1.58×10^{-2}	86	0.43 - 6.53
Chronic lung disease	Yes vs. No	1578/8334	8	1.14 (0.65 - 1.98)	6.54×10^{-1}	85	0.18 - 6.99
Solid organ transplantation	Yes vs. No	253/780	4	1.36 (0.64 - 2.88)	4.22×10^{-1}	18	0.15 - 12.3
Mortality							
Abdominal pain	Yes vs. No	214/2114	7	1.00 (0.50 - 2.03)	9.92×10^{-1}	0	0.40 - 2.52
ACEi/ARBs	Yes vs. No	3345/23,201	26	1.29 (1.01 - 1.64)	4.37×10^{-2}	84	0.44 - 3.72
Age	>60 vs. <60	9780/96,705	22	9.59 (7.46 - 12.34)	1.64×10^{-69}	88	3.31 - 27.77
Age	>65 vs. <65	5741/31,456	20	5.50 (3.90 - 7.77)	2.92×10^{-22}	93	1.31 - 23.10
Age	Per 1 year increase	2206/13,307	31	1.072 (1.063 - 1.081)	2.66×10^{-58}	74	1.030 - 1.116
Altered mental status	Yes vs. No	6720/33,221	9	4.53 (2.58 - 7.96)	1.52×10^{-7}	88	0.76 - 27.04
Anosmia/Ageusia	Yes vs. No	279/2077	4	0.43 (0.23 - 0.80)	8.30×10^{-3}	0	0.11 - 1.70
Anticoagulant therapy	Yes vs. No	1729/4552	6	1.28 (1.11 - 1.47)	8.21×10^{-4}	0	1.04 - 1.56
Antiplatelet therapy	Yes vs. No	979/2057	4	1.36 (0.86 - 2.16)	1.84×10^{-1}	48	0.25 - 7.50
Any comorbidity	Yes vs. No	14,596/62,373	28	3.57 (2.86 - 4.46)	3.68×10^{-29}	88	1.45 - 8.76
AST	>40 U/L vs. <40 U/L	1167/5818	6	2.63 (1.86 - 3.73)	5.60×10^{-8}	72	0.92 - 7.56
Atrial fibrillation	Yes vs. No	858/3597	8	2.27 (1.42 - 3.62)	5.78×10^{-4}	47	0.69 - 7.52
Beta-blockers	Yes vs. No	2624/10,144	6	2.04 (1.54 - 2.70)	5.86×10^{-7}	83	0.85 - 4.86
Bilateral involvement	Yes vs. No	1108/6466	18	1.31 (0.95 - 1.82)	1.02×10^{-1}	59	0.45 - 3.81
BMI	>30 kg/m^2 vs. <30 kg/m^2	2562/13,190	23	0.92 (0.78 - 1.09)	3.51×10^{-1}	50	0.53 - 1.60
BMI	Per 1 kg/m^2	566/3308	8	0.99 (0.974 - 1.007)	2.54×10^{-1}	21	0.958 - 1.024

Predictors	Level of comparison	N events/N participants	N studies	RE summary OR (95% CI)	P-value	I^2	95% PI
Cancer	Yes vs. No	16,659/96,716	34	2.14 (1.86 - 2.45)	6.63×10^{-28}	50	1.31 - 3.49
Cardiovascular disease	Yes vs. No	14,764/77,158	25	3.27 (2.50 - 4.27)	4.88×10^{-18}	94	1.00 - 10.72
Cerebrovascular disease	Yes vs. No	2454/17,301	28	3.01 (2.33 - 3.90)	4.11×10^{-17}	58	1.11 - 8.21
Chills	Yes vs. No	1088/4815	6	0.88 (0.52 - 1.48)	6.19×10^{-1}	68	0.21 - 3.68
Chronic kidney disease	Yes vs. No	18,118/90,660	47	3.11 (2.59 - 3.73)	6.98×10^{-34}	81	1.16 - 8.30
Chronic liver disease	Yes vs. No	17,463/60,995	17	1.45 (1.22 - 1.73)	2.78×10^{-5}	9	1.08 - 1.96
Chronic lung disease	Yes vs. No	6499/41,268	14	2.42 (1.89 - 3.11)	3.29×10^{-12}	72	1.12 - 5.25
Consolidation	Yes vs. No	459/3075	7	1.62 (1.12 - 2.35)	1.08×10^{-2}	45	0.62 - 4.23
COPD	Yes vs. No	12,238/64,682	39	2.23 (1.90 - 2.63)	4.85×10^{-22}	48	1.17 - 4.28
Coronary heart disease	Yes vs. No	5014/35,251	40	2.85 (2.45 - 3.31)	2.60×10^{-42}	55	1.49 - 5.47
Cough	Yes vs. No	8723/44,659	26	0.79 (0.69 - 0.91)	1.44×10^{-3}	60	0.49 - 1.28
Dementia	Yes vs. No	6384/21,095	10	3.09 (2.48 - 3.86)	2.36×10^{-23}	48	1.84 - 5.21
Diabetes mellitus	Yes vs. No	17,922/11,6431	49	2.18 (1.86 - 2.56)	2.80×10^{-21}	90	0.82 - 5.78
Diarrhea	Yes vs. No	2670/12,139	20	0.67 (0.52 - 0.87)	2.76×10^{-3}	49	0.32 - 1.42
Dyslipidemia	Yes vs. No	4857/19,574	17	1.39 (1.09 - 1.78)	7.70×10^{-3}	73	0.63 - 3.09
Dyspnea	Yes vs. No	8710/44,491	26	2.69 (2.13 - 3.41)	1.63×10^{-16}	88	0.98 - 7.39
Expectoration	Yes vs. No	2001/11,035	16	1.25 (1.00 - 1.55)	4.75×10^{-2}	44	0.70 - 2.21
Fatigue	Yes vs. No	2148/13,581	20	1.03 (0.80 - 1.32)	8.39×10^{-1}	67	0.44 - 2.39
Fever	Yes vs. No	9407/73,477	25	0.94 (0.77 - 1.16)	5.64×10^{-1}	85	0.41 - 2.18
Ground-glass opacity	Yes vs. No	711/4864	10	0.83 (0.58 - 1.19)	3.06×10^{-1}	50	0.33 - 2.10
Headache	Yes vs. No	2666/13,915	21	0.56 (0.39 - 0.81)	1.92×10^{-3}	66	0.16 - 1.96
Heart failure	Yes vs. No	4252/39,681	31	3.76 (2.80 - 5.05)	1.77×10^{-18}	85	0.85 - 16.63
History of VTE	Yes vs. No	931/4087	5	1.28 (0.91 - 1.80)	1.57×10^{-1}	0	0.73 - 2.23
Hypertension	Yes vs. No	9075/72,781	62	2.23 (1.95 - 2.56)	4.63×10^{-31}	79	0.96 - 5.18
Insulin	Yes vs. No	978/6082	4	2.57 (1.58 - 4.18)	1.52×10^{-4}	54	0.42 - 15.68
LDH	>250 U/L vs. <250 U/L	469/3951	7	5.38 (2.28 - 12.69)	1.20×10^{-4}	85	0.32 - 91.50
Nausea	Yes vs. No	486/3321	7	0.97 (0.53 - 1.77)	9.18×10^{-1}	50	0.19 - 4.95
Obesity	Yes vs. No	6716/25,849	14	1.29 (0.95 - 1.74)	9.70×10^{-2}	78	0.51 - 3.28
Peripheral arterial disease	Yes vs. No	2288/17,376	5	2.14 (1.64 - 2.78)	1.87×10^{-8}	26	1.10 - 4.15
Pharyngalgia	Yes vs. No	1983/8578	16	0.56 (0.45 - 0.69)	1.53×10^{-7}	0	0.44 - 0.71
Platelets	<150.000 /μL vs. >150.000 /μL	197/1917	6	2.35 (1.24 - 4.43)	8.44×10^{-3}	66	0.35 - 15.95
Pleural effusion	Yes vs. No	192/601	6	1.40 (0.72 - 2.74)	3.23×10^{-1}	17	0.36 - 5.40
Rhinorrhea	Yes vs. No	899/4894	5	0.49 (0.36 - 0.66)	3.99×10^{-6}	0	0.30 - 0.80
Sex	Female vs. Male	24,174/189,620	63	0.72 (0.65 - 0.78)	1.53×10^{-13}	76	0.46 - 1.12
Smoking	Yes vs. No	7787/30,112	37	1.50 (1.35 - 1.67)	2.91×10^{-14}	22	1.14 - 1.98
SpO2	<90 % vs. >90 %	1254/6397	6	4.27 (2.85 - 6.39)	1.71×10^{-12}	75	1.22 - 14.95
Statins	Yes vs. No	1776/5370	4	1.56 (1.26 - 1.93)	3.99×10^{-5}	66	0.68 - 3.57
WBC	<4.000 /μL vs. >4.000	1006/4737	5	0.58 (0.40 - 0.84)	3.75×10^{-3}	31	0.22 - 1.50

Predictors	Level of comparison	N events/N participants	N studies	RE summary OR (95% CI)	P-value	I^2	95% PI
	/μL						
WBC	>10.000 /μL vs. <10.000 /μL	495/4266	6	7.27 (2.89 - 18.29)	2.47×10^{-5}	92	0.28 - 186.15

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