The Lancet

Prognostic factors for severity and mortality in patients infected with COVID-19: A systematic review

--Manuscript Draft--

Manuscript Number:	THELANCET-D-20-13074
Article Type:	FT to NT Article (INTERNAL USE ONLY)
Keywords:	COVID-19; severe acute respiratory syndrome coronavirus 2; Coronavirus Infections; Systematic review; prognosis; prognostic factor
Corresponding Author:	Ariel Izcovich, Ph.D Hospital Alemán de Buenos Aires Buenos Aires, Buenos Aires ARGENTINA
First Author:	Ariel Izcovich, Ph.D
Order of Authors:	Ariel Izcovich, Ph.D
	Martín Alberto Ragusa, MD
	Fernando Tortosa, MD
	María Andrea Lavena Marzio, MD
	Camila Agnoletti, MD
	Agustín Bengolea, MD
	Agustina Ceirano, MD
	Federico Espinosa, MD
	Ezequiel Saavedra, MD
	Verónica Sanguine, MD
	Alfredo Tassara, MD
	Candelaria Cid, MD
	Hugo Norberto Catalano, PhD
	Arnav Agarwal, MD
	Farid Foroutan, PhD
	Gabriel Rada, MD
Manuscript Region of Origin:	ARGENTINA
Abstract:	Background The objective of our systematic review is to identify prognostic factors that may be used in decision-making related to the care of patients infected with COVID-19. Methods We conducted highly sensitive searches in PubMed/MEDLINE, the Cochrane Central Register of Controlled Trials (CENTRAL) and Embase. The searches covered the period from the inception date of each database until April 28, 2020. No study design, publication status or language restriction were applied. We included studies that assessed patients with confirmed or suspected SARS-CoV-2 infection and examined one or more prognostic factors for mortality or disease severity. Reviewers working in pairs independently screened studies for eligibility, extracted data and assessed the risk of bias. We performed meta-analyses and used GRADE to assess the certainty of the evidence for each prognostic factor and outcome. Findings We included 207 studies and found high or moderate certainty that the following 49 variables provide valuable prognostic information on mortality and/or severe disease in patients with COVID-19 infection: Demographic factors (age, male sex, smoking), patient history factors (comorbidities, cerebrovascular disease, chronic obstructive pulmonary disease, chronic kidney disease, cardiovascular disease, cardiac

	arrhythmia, arterial hypertension, diabetes, dementia, cancer and dyslipidemia), physical examination factors (respiratory failure, low blood pressure, hypoxemia, tachycardia, dyspnea, anorexia, tachypnea, haemoptysis, abdominal pain, fatigue, fever and myalgia or arthralgia), laboratory factors (high blood procalcitonin, myocardial injury markers, high blood White Blood Cell count (WBC), high blood lactate, low blood platelet count, plasma creatinine increase, high blood D-dimer, high blood lactate dehydrogenase (LDH), high blood C-reactive protein (CRP), decrease in lymphocyte count, high blood aspartate aminotransferase (AST), decrease in blood albumin, high blood interleukin-6 (IL-6), high blood neutrophil count, high blood B-type natriuretic peptide (BNP), high blood urea nitrogen (BUN), high blood creatine kinase (CK), high blood bilirubin and high erythrocyte sedimentation rate (ESR)), radiological factors (consolidative infiltrate and pleural effusion) and high SOFA score. Interpretation Identified prognostic factors can help clinicians and policy makers in tailoring management strategies for patients with COVID-19 infection while researchers can utilise our findings to develop multivariable prognostic models that could eventually facilitate decision-making and improve patient important outcomes. Funding None

Prognostic factors for severity and mortality in patients infected with COVID-19: A systematic review

Authors:

Ariel Izcovich, PhD
ORCID iD:0000-0001-9053-4396
Servicio de clínica médica del Hospital Alemán, Buenos Aires, Argentina
Pueyrredón 1640, Buenos Aires, Argentina

Martín Ragusa, MD
ORCID : 0000-0002-3182-8041
Servicio de clínica medica del Hospital Alemán, Buenos Aires, Argentina
Pueyrredón 1640, Buenos Aires, Argentina
Servicio de clínica médica del Hospital Fernández, Buenos Aires, Argentina

Fernando Tortosa, MD
ORCID: 0000-0002-0303-6055
Departamento Médico. Hospital "Ramón Carrillo",
Av. Moreno 601, San Carlos de Bariloche, Rio Negro, Argentina.

María Andrea Lavena Marzio, MD
ORCID: 0000-0002-3692-8981
Servicio de clínica medica del Hospital Alemán, Buenos Aires, Argentina
Pueyrredón 1640, Buenos Aires, Argentina

Camila Agnoletti, MD
ORCID: 0000-0001-5995-9097
Servicio de clínica medica del Hospital Alemán, Buenos Aires, Argentina
Pueyrredón 1640, Buenos Aires, Argentina

Agustín Bengolea, MD
ORCID: 0000-0001-5741-5221
Servicio de clínica medica del Hospital Alemán, Buenos Aires, Argentina
Pueyrredón 1640, Buenos Aires, Argentina

Agustina Ceirano, MD
ORCID: 0000-0003-1083-6787
Servicio de clínica medica del Hospital Alemán, Buenos Aires, Argentina
Pueyrredón 1640, Buenos Aires, Argentina

Federico Espinosa, MD
ORCID: 0000-0001-9255-7583
Servicio de clínica medica del Hospital Alemán, Buenos Aires, Argentina
Pueyrredón 1640, Buenos Aires, Argentina

Ezequiel Saavedra, MD
ORCID: 0000-0001-7833-8130
Servicio de clínica medica del Hospital Alemán, Buenos Aires, Argentina
Pueyrredón 1640, Buenos Aires, Argentina

Verónica Sanguine, MD
ORCID: 0000-0002-4842-0528
Dirección Nacional de Calidad en Servicios de Salud y Regulación Sanitaria- Ministerio de Salud de la Nación, Argentina

Alfredo Tassara, MD
ORCID: 0000-0001-6093-2692
Servicio de clínica medica del Hospital Alemán, Buenos Aires, Argentina
Pueyrredón 1640, Buenos Aires, Argentina

Candelaria Cid, MD
ORCID: 0000-0002-9377-6259
Servicio de clínica medica del Hospital Alemán, Buenos Aires, Argentina
Pueyrredón 1640, Buenos Aires, Argentina

Hugo N. Catalano, PhD
ORCID : 0000-0001-5359-6141
Servicio de clínica medica del Hospital Alemán, Buenos Aires, Argentina
Pueyrredón 1640, Buenos Aires, Argentina

Arnav Agarwal, MD
ORCID : 0000-0002-0931-7851
Department of Medicine, University of Toronto
27 King's College Cir, Toronto, Ontario, Canada

Farid Foroutan, PhD
ORCID: 0000-0002-1029-1812
Ted Rogers Centre for Heart Research, University Health Network
661 University Ave, Toronto, Ontario, Canada

Gabriel Rada, MD
ORCID: 0000-0003-2435-0710
Fundación Epistemonikos
Holanda 895, Providencia, Santiago, Chile
UC Evidence Center, Cochrane Chile Associated Center, Pontificia Universidad Católica de Chile
Diagonal Paraguay 476, Santiago, Chile
Internal Medicine Department, Faculty of Medicine, Pontificia Universidad Católica de Chile, Santiago, Chile
Lira 44, Santiago, Chile

Corresponding author:
Ariel Izcovich
Email address: ariel.izcovich@gmail.com
Postal address: Pueyrredón 1640, Buenos Aires, Argentina

Abstract word number: 350
Complete text word number: 4057
Tables: 1
Figures: 1
Supplemental Files: 4
References: 253

Keywords
COVID-19, severe acute respiratory syndrome coronavirus 2, Coronavirus Infections, Systematic review, prognosis, prognostic factor

Summary

Background

The objective of our systematic review is to identify prognostic factors that may be used in decision-making related to the care of patients infected with COVID-19.

Methods

We conducted highly sensitive searches in PubMed/MEDLINE, the Cochrane Central Register of Controlled Trials (CENTRAL) and Embase. The searches covered the period from the inception date of each database until April 28, 2020. No study design, publication status or language restriction were applied.

We included studies that assessed patients with confirmed or suspected SARS-CoV-2 infection and examined one or more prognostic factors for mortality or disease severity.

Reviewers working in pairs independently screened studies for eligibility, extracted data and assessed the risk of bias. We performed meta-analyses and used GRADE to assess the certainty of the evidence for each prognostic factor and outcome.

Findings

We included 207 studies and found high or moderate certainty that the following 49 variables provide valuable prognostic information on mortality and/or severe disease in patients with COVID-19 infection: Demographic factors (age, male sex, smoking), patient history factors (comorbidities, cerebrovascular disease, chronic obstructive pulmonary disease, chronic kidney disease, cardiovascular disease, cardiac arrhythmia, arterial hypertension, diabetes, dementia, cancer and dyslipidemia), physical examination factors (respiratory failure, low blood pressure, hypoxemia, tachycardia, dyspnea, anorexia, tachypnea, haemoptysis, abdominal pain, fatigue, fever and myalgia or arthralgia), laboratory factors (high blood procalcitonin, myocardial injury markers, high blood White Blood Cell count (WBC), high blood lactate, low blood platelet count, plasma creatinine increase, high blood D-dimer, high blood lactate dehydrogenase (LDH), high blood C-reactive protein (CRP), decrease in lymphocyte count, high blood aspartate aminotransferase (AST), decrease in blood albumin, high blood interleukin-6 (IL-6), high blood neutrophil count, high blood B-type natriuretic peptide (BNP), high blood urea nitrogen (BUN), high blood creatine kinase (CK), high blood bilirubin and high erythrocyte sedimentation rate (ESR)), radiological factors (consolidative infiltrate and pleural effusion) and high SOFA score.

Interpretation

Identified prognostic factors can help clinicians and policy makers in tailoring management strategies for patients with COVID-19 infection while researchers can utilise our findings to develop multivariable prognostic models that could eventually facilitate decision-making and improve patient important outcomes.

Funding

None

Research in context

Evidence before this study

We conducted highly sensitive searches in PubMed/MEDLINE, the Cochrane Central Register of Controlled Trials (CENTRAL) and Embase. The searches covered the period from the inception date of each database until April 28, 2020. No study design, publication status or language restriction were applied.

Previous related reviews have proposed multiple predictors of outcome in COVID-19 infected patients. However, the absolute risk modification attributed to the exposure to these potential prognostic factors and the certainty on those estimates has not been robustly evaluated.

Added value of this study

We did a systematic review of 207 studies across 12 countries and four continents, including 75607 patients with COVID-19. By following the GRADE approach, we identified 49 predictors of mortality and/or severe disease, in patients with COVID-19 infection, for which there is moderate or high certainty of the evidence. We selected two clinical scenarios (patients with non-severe COVID-19 infection and patients with severe COVID-19 infection) in which prognostic information could impact decision-making and provided estimates of the absolute risk modification that can be attributed to every identified prognostic factor.

Implications of all available evidence

Identified prognostic factors may guide the stratification of patients with SARS-CoV-2 infection based on their risk of severe disease or death. This risk stratification may subsequently guide optimised management and resource utilisation strategies in the care of these patients. Additionally, these variables can be incorporated to multivariable prognostic models that could eventually probe to facilitate decision-making and improve patient important outcomes.

Introduction

COVID-19 is an infection caused by the SARS-CoV-2 coronavirus.[1] It was first identified in Wuhan, China, on December 31, 2019;[2] five months later, more than six million cases had been identified across 215 countries.[3] On March 11, 2020, WHO characterised the COVID-19 outbreak as a pandemic.[1] While the majority of cases present with mild symptoms, a minority progress to acute respiratory illness and hypoxia requiring hospitalization, and a subset develop acute respiratory distress syndrome, multi-organ failure or have fatal outcomes.[4] The case fatality rate reported across countries, settings and age groups is highly variable, ranging from about 0.5% to 10%.[5] In hospitalised patients it has been reported to be higher than 20%.[6]

Prognostic factors (stand-alone or combined in risk assessment models) may guide the stratification of patients with SARS-CoV-2 infection based on their risk of severe disease or death. This risk stratification may subsequently guide optimised management and resource utilisation strategies in the care of these patients.

Although multiple prognostic factors have been proposed and some have been accepted as "established" by the scientific community (i.e age), the predictive value of most of these potential prognostic factors has not been robustly evaluated and remains uncertain. As pointed out by Wynants et.al: "unreliable predictors could cause more harm than benefit in guiding clinical decisions".[7] For example, aggressive and risky interventions might be attempted if the risk of poor outcomes are inaccurately defined as high based on unreliable predictors.

Using innovative and agile processes supported by advanced evidence synthesis tools and collaborative efforts across several international research groups, this systematic review aims to provide a rigorous summary of the evidence available on prognostic factors that can may be used in decision-making related to the care of patients infected with COVID-19.

Methods

Protocol registration

We published[8] and registered the protocol for this systematic review with PROSPERO (CRD42020178802).

Search strategy

We conducted highly sensitive searches in PubMed/MEDLINE, the Cochrane Central Register of Controlled Trials (CENTRAL) and Embase. The searches covered the period from the inception date of each database until April 28, 2020. No study design, publication status or language restriction were applied.
Detailed strategies for each database are reported in the online supplement.
In order to identify articles that might have been missed in the electronic searches, we reviewed the reference list of each included study and performed cross citation in Google Scholar using each included study as the index reference.

Study selection

Four reviewers working independently and in duplicate, performed study selection, including screening of titles and abstracts and of potentially eligible full-text articles. Reviewers resolved disagreements by discussion.

We included studies examining individual prognostic factors or risk assessment models based on the typologies of prognosis proposed by Iorio and colleagues[9] and the PROGnosis RESearch Strategy (PROGRESS) Group framework[10] without applying any restrictions based on analytical methods (i.e performing multivariable analysis).
Specifically, we included studies that evaluated patients with confirmed infection with SARS-CoV-2 regardless of the healthcare setting (i.e ambulatory or inpatients) and of baseline disease severity. We investigated all prognostic factors reported by individual studies and compared patients exposed with patients unexposed to each one of those factors. We considered studies that assessed mortality or severe COVID-19 disease as outcomes and accepted the author's definitions of the latter. When severe COVID-19 disease was reported as a multi-categorical scale, we used the most severe category. Additionally, when severe COVID-19 disease was not reported as an outcome, we considered ICU requirement, invasive mechanical ventilation (IVM) and acute respiratory distress syndrome (ARDS) as surrogate outcomes.

Data extraction
For each eligible study, five pairs of reviewers, independently, abstracted the following information on study characteristics (year of publication, country, medical center and time period in which the study was conducted); population characteristics (sample size, context in which the study was conducted and other population characteristics); description of prognostic factors and outcomes and their definitions; and studies results (measures of association or crude event rates for every candidate prognostic factor and outcome reported).

Risk of bias assessment
Two reviewers assessed the risk of bias of individual included studies independently and in duplicate. Discrepancies were resolved by consensus. We used the Quality in Prognosis Studies (QUIPS) tool for prognostic factor studies.[11] For "study confounding summary" and "statistical analysis and presentation domains", in order to assess adequacy of the multivariable models, we considered appropriate model adjustment as based on inclusion of age, one comorbidity (e.g diabetes) and one parameter of disease severity (e.g. respiratory rate) at minimum.

Data synthesis and analysis
We presented the results of individual prognostic factors in both tabular and narrative formats. We standardized the units of measurement for each prognostic factor, unifying the direction of the predictors and adjusting the weights of the studies, and calculated crude effect estimates when not provided.[12] When possible, we meta-analysed all prognostic factors whose association with the selected outcomes of interest was explored and were reported by more than one study. We used the generic inverse variance-based method to produce an overall measure of association and random-effect models based on the DerSimonian-Laird method provided by the metafor package for R software.[13]

For every candidate prognostic factor, we presented the measure of association as odds ratios (ORs) and their corresponding 95% confidence intervals (CI). In studies that reported the measure of association as a hazard ratio (HR) or risk ratio (RR), we converted them to ORs using the baseline risk (death rate or incidence of severe COVID-19 out of the total sample) reported in the studies.[14,15] For dichotomous variables, we used the crude event rate to calculate ORs when

no measures of association were provided. We excluded information on continuous variables for which no measures of association were available. We also calculated absolute risk differences (RDs) that can be attributed to every individual candidate prognostic factor by applying the ORs to estimated baseline risks (see below "Baseline risks"). When the same candidate prognostic factor was assessed in alternative ways (e.g. dichotomic and continuous) we used the one for which we found better certainty of evidence.

For every explored candidate variable, we performed sensitivity analysis excluding high risk of bias studies and studies that did not report adjusted estimates. In cases where the effect estimates provided by the primary analysis and the sensitivity analysis significantly differed, we either presented the moderate/low risk of bias – adjusted estimates or the primary analysis estimates but rated down certainty of the evidence because for risk of bias (see below).

Assessment of certainty of the evidence

We assessed certainty of the evidence for each candidate prognostic factor, by outcome, based on the GRADE approach.[16] The approach considers the following domains: risk of bias, indirectness, inconsistency, imprecision, and publication bias. We produced summary of findings tables and rated the certainty of the evidence as high, moderate, low or very low depending on the grading of the individual domains.[16] See online supplementary materials for a detailed description of the certainty of the evidence assessment.

Result interpretation

To define which candidate variables provide valuable prognostic information we adopted a minimally contextualized approach.[17] To this end, we arbitrarily set thresholds to define important incremental increase in the risk of our outcomes. In setting those thresholds we aimed to define the minimal incremental increase in the risk of mortality or severe COVID-19 disease that could be interpreted as valuable prognostic information without considering the potential consequences of using that information in healthcare decision-making. These thresholds represent the line that separates a risk increase that is trivial from a small but important risk increase. We set those thresholds in 0.5% increase in mortality and 1% increase insevere COVID-19 disease. We performed a sensitivity analysis in which we adopted a purely non-contextualized approach[17] to assess mortality outcome. In doing so we only considered the relative measures of association and used an OR of 1 as the threshold for minimal important risk increment.

Baseline risks

To define baseline risks we selected clinical scenarios based in the severity categories proposed by WHO.[18] To assess the prognostic value on mortality, we used the clinical scenario of a patient infected with COVID-19 with severe but not critical disease. We identified one study informing prognosis in this specific subgroup with a mortality risk of 9%.[19] However, as we identified significant variability in mortality risks reported for similar clinical scenarios, we performed a sensitivity analysis using a baseline risk of 26% as reported by a large cohort of non-ICU inpatients treated in 255 sites across 36 countries.[6]

To assess the prognostic value on severe COVID-19 disease, we used the clinical scenario of a patient infected with COVID-19 with non-severe disease. We identified 7 studies informing prognosis in this specific subgroup with a median risk of progression to severe or critical state of

13%.[20-26] We calculated baseline risks (risks in patients not exposed to the prognostic factor) by also considering the prevalence of every prognostic factor and the estimates of association.[27] When prevalence of prognostic factors was not available we used described baseline risks (9% for mortality and 13 % for severe COVID-19 disease).

Update of this systematic review

An artificial intelligence algorithm deployed in the Coronavirus/COVID-19 topic of the L·OVE platform (https://app.iloveevidence.com/loves/5e6fdb9669c00e4ac072701d) will provide instant notification of articles with a high likelihood of eligibility. These will be screened by paired reviewers iteratively and will conduct data extraction and iterative updates of estimates for selected prognostic factors accordingly. We will consider resubmission to a journal if there is a substantial modification on the measure of association or the certainty of the evidence for a given prognostic factor such that it is clinically significant, at the discretion of the reviewer team. This review is part of a larger project established to produce multiple parallel systematic reviews relevant to COVID-19.[28]

Results

Figure 1 illustrates the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram. Our search identified 7631 citations of which we included 569 studies for full text assessment. 207 studies fulfilled the inclusion criteria.[20,22-24,26,29-230] These 207 studies, with sample sizes from 10 to 8910, enrolled a total of 75607 patients and were conducted in 12 different countries (China , USA, Canada, Spain, France, Turkey, Korea, Japan, Italy, Germany, India and Singapore).

Supplementary table 1 describes the characteristics of the included studies reporting on mortality and/or severe COVID-19 disease. Regarding candidate prognostic factors, of the 207 included studies, 184 (88·9%) reported socio-demographic variables, 180 (86·9%) comorbidities, 178 (86%) clinical findings, 176 (85%) laboratory findings and 106 (51·3%) imaging findings. The outcomes reported were mortality in 116 (56%) and progression to severe/critical status in 131 (63·3%). In 78 (37·7%) of the included studies a multivariable analysis was performed. In the 150 studies in which the severity of included patients was described the mean proportion of patients in each category was: non-severe disease 63·8%, severe disease 22·6%, critical disease 13·6%·

Risk of bias was high across most identified studies· Among the 207 included studies only 7 were judged as low risk of bias[20,23,55,56,58,129,141] as the remaining presented important limitations in at least one domain or item· Most frequent were retrospective design, which may have introduced classification bias, and lack or inappropriate adjusted analysis. Supplementary table 2 provides detailed judgements for each of the risk of bias domains criteria.

Prognostic factors for mortality

We investigated 96 candidate prognostic factors for mortality from 116 studies including 57044 patients· Supplementary table 3 provides a summary of findings for all the candidate prognostic factors.

We found high or moderate certainty that the following 35 variables provide valuable prognostic information on mortality outcome (table 1):

Demographic factors

Age per 10 years increase (OR 1·8, 95% CI 1·54 to 2·1; RD 6·1%, 95% CI 4·2 to 8·2%), male sex (OR 1·72, 95% CI 1·5% to 1·98; RD 5%, 95% CI 4 to 7%) and active smoker (OR 1·57, 95%CI 1·19 to 2·07; RD 4·3%, 95%CI 1·5 to 7·5%).

Medical illness and patient history factors
Any chronic condition or comorbidity (OR 3·3, 95% CI 2·18 to 5; RD 10·3%, 95% CI 6·8 to 13·4%), cerebrovascular disease (OR 2·85, 95% CI 2·02 to 4·01; RD 12·6%, 95% CI 7·5 to 18·5%), chronic obstructive pulmonary disease (COPD) (OR 2·43, 95% CI 1·88 to 3·14; RD 9·8%, 95% CI 6·4 to 13·6%), chronic kidney disease (CKD), (OR 2·27, 95% CI 1·69 to 3·05; RD 8·8%, 95% CI 5·1 to 12·9%), cardiovascular disease (OR 2·12, 95% CI 1·77 to 2·56; RD 7·5%, 95% CI 5·4 to 9·7%), cardiac arrhythmia (OR 2·13, 95% CI 1·72 to 2·65; RD 6·5%, 95% CI 4·7 to 8·4%), arterial hypertension (OR, 2·02, 95% CI 1·71 to 2·38; RD 6%, 95% CI 4·5 to 7·33), diabetes (OR 1·84, 95% CI 1·61 to 2·1; RD 5·6%, 95% CI 4·3 to 7%), dementia (OR 1·54, 95% CI 1·31 to 1·81; RD 4·2%, 95% CI 2·5 to 6·2%), obesity (OR 1·41, 95% CI 1·15 to 1·74; RD 3·1%, 95% CI 1·2 to 5·1%), cancer (OR 1·35, 95% CI 1·17 to 1·55; RD 2·7%, 95% CI 1·4 to 4·2) and dyslipidemia (OR 1·26, 95%CI 1·06-1·5; RD 2·1%, 95%CI 0·5% to 3·9%).

Physical examination factors
Respiratory failure (OR 21·17, 95% CI 4·9 to 91·3; RD 20·3%, 95% CI 13·4% to 22·4%), low blood pressure (OR 6·7, 95% CI 3·14 to 14·33; RD 30·9%, 95% CI 14·7% to 49·6%), hypoxemia (OR 5·46, 95% CI 2·05 to 14·53; RD 6·7%, 95% CI 4·2% to 7·7%), tachycardia (OR 2·61, 95% CI 1·62 to 4·22; RD 11·5%, 95% CI 4·8% to 20·4%), dyspnea (OR 3·45, 95% CI 2·72 to 4·38; RD 8·9%, 95% CI 7·5% to 10·2%), anorexia (OR 2·16, 95% CI 1·14 to 4·12; RD 7%, 95% CI 1·1% to 13·1%) and tachypnea (OR 1·21, 95%CI 1·12 to 1·31; RD 1·4%, 95% CI 0·9% to 1·9%).

Laboratory factors
High blood procalcitonin (OR 12·42, 95% CI 7·18 to 21·5; RD 32·3%, 95% CI 25% to 38·1%), myocardial injury markers (OR 10·89, 95% CI 5·39 to 22·04; RD 16·9%, 95% CI 13·4% to 19%), high white blood cell count (WBC) (OR 4·06, 95% CI 2·7 to 6·12; RD 16·9%, 95% CI 11% to 23·3%), high blood lactate (OR 3·66, 95% CI 2·26 to 5·94; RD 14·3%, 95% CI 8·3% to 20·6%), low platelet count (OR 5·43, 95% CI 2·55 to 11·56; RD 14·3%, 95% CI 8·3% to 18·6%), high blood D-dimer (OR 4·81, 95% CI 3·15 to 7·34; RD 11·2%, 95% CI 8·8% to 13·1%), high blood lactate dehydrogenase (LDH) (OR 4·09, 95% CI 1·18 to 14·17; RD 10·4%, 95% CI 1·4% to 15·3%), high blood c-reactive protein (CRP) (OR 6·6, 95% CI 3·36 to 12·99; RD 7·9%, 95% CI 6·4% to 8·7%), decrease in lymphocyte count (OR 3·57, 95% CI 2 to 6·67; RD 17·1%, 95% CI 7·5% to 30·7%), high blood aspartate aminotransferase (AST) (OR 3·5, 95% CI 1·59-7·71; RD 11·1%, 95% CI 4% to 16·8%), decrease in blood albumin (OR 1·53, 95% CI 1·32 to 1·78; RD 4·2%, 95% CI 2·5% to 6%) and increase in plasma creatinine (OR 1·14, 95%CI 1·02 to 1·28; RD 1·1%, 95% CI 0·2% to 2·3%).

Others
SOFA score> 2 (OR 1·97, 95% CI 1·22 to 3·2; RD 7·3%, 95% CI 1·8% to 15%).

Prognostic factors for severe COVID-19 disease

We investigated 96 candidate prognostic factors for severe COVID-19 disease from 131 studies including 28538 patients· Supplementary table 3 provides a summary of findings for all the candidate prognostic factors.

In addition to identified prognostic factors for mortality, we found high or moderate certainty that the following 14 variables provide valuable prognostic information on severe COVID-19 disease outcome (table 1):

Physical examination factors
Haemoptysis (OR 4·39, 95% CI 2·18 to 8·81; RD 25·9%, 95% CI 11·4% to 42·1%), abdominal pain (OR 1·95, 95% CI 1·36 to 1·79; RD 9·4%, 95% CI 4% to 15·8%), fatigue (OR 1·41, 95% CI 1·19 to 1·68; RD 3·9%, 95% CI 2% to 5·9%), fever (OR 1·84, 95% CI 1·54 to 2·21; RD 6·1%, 95% CI 4·5% to 7·6%) and myalgia or arthralgia (OR 1·29, 95% CI 1·03 to 1·61; RD 3%, 95%CI 0·3% to 5·9%).

Laboratory factors
High neutrophil count (OR 5·66, 95% CI 3·71 to 8·63; RD 22%, 95% CI 17% to 27%), high blood B-type natriuretic peptide (BNP) (OR 4·99, 95% CI 3·2 to 7·77; RD 21·5%, 95% CI 15·5% to 26·7%), High blood urea nitrogen (BUN) (OR 3·66, 95% CI 2·82 to 4·74; RD 19·1%, 95% CI 14·8% to 23·4%), high blood creatine kinase (CK) (OR 3·1, 95% CI 2·32 to 4·16; RD 16·5%, 95% CI 11·7% to 21·6%), high blood bilirubin (OR 2·94, 95% CI 2·18 to 3·97; RD 16·8%, 95% CI 11·3% to 22·9%), high blood interleukin-6 (IL-6) (OR 7·36, 95% CI 2·97 to 18·27; RD 13·3%, 95% CI 8·5% to 15·9%), high erythrocyte sedimentation rate (ESR) (OR 3·08, 95% CI 2·04 to 4·65; RD 9·4%, 95% CI 6·7% to 11·3%).

Radiological factors
Consolidative infiltrate (OR 2·46, 95% CI 1·54 to 3·93; RD 12%, 95% CI 5·4% to 18·8%) and pleural effusion (OR 3·31, 95% CI 2·03 to 5·38; RD 19%, 95% CI 10% to 30%).

Other analysed variables
The remaining variables analysed were: asthma, tuberculosis, HIV infection, immunocompromise, autoimmune disease, malnutrition, chronic liver disease, thyroid disease, chronic gastric disease, chest pain, high fever, cough, rhinorrhea, odynophagia, conjunctivitis, sputum production, enlarged lymph nodes, rash, headache, vomits, diarrhea, anemia, low WBC, low neutrophil count, glomerular filtration rate, blood urea, cystatin C, prothrombin time, APTT time, ferritin, cholinesterase, alanine aminotransferase (ALT), blood fibrinogen degradation products, globulin, prealbumin, blood glucose, alfa-HBDH, low density lipoprotein (LDL), triglycerides, any abnormal radiologic finding, radiological interstitial pattern, ground glass opacity, crazy paving pattern, radiological evidence of enlarged lymph nodes, bilateral radiological compromise, APACHE, qSOFA. For all of these variables we found low or very low certainty evidence both for mortality and severe COVID-19 disease. Hence, it is uncertain if these variables provide prognostic value in the context of COVID-19 infected patients.

Additional analysis
We performed a sensitivity analysis on mortality outcome using a non-contextualized approach and assuming adjusted estimates as at low risk of being biased (less demanding risk of bias approximation in comparison with the primary analysis) (see methods, risk of bias assessment in

supplementary materials). The results were similar to the primary analysis. However our certainty increased to moderate or high for some prognostic factors for which we had very low or low certainty: Chest pain, cough, sputum production, anemia, high ferritin, high ALT, increase in blood glucose and high APACHE score.

A second sensitivity analysis in which we set a significantly higher baseline mortality risk (26%) for patients with severe but non-critical COVID-19 disease did not show differences with the primary analysis.

Discussion

In this systematic review we evaluated prognostic factors for poor outcome in patients with covid-19 infection. We found 49 variables that provide valuable prognostic information for mortality and/or severe COVID-19 disease. Identified prognostic factors include socio-demographic characteristics (age, male sex and smoking) medical illness and patients history information (comorbidities including chronic respiratory, cardiac and endocrinologic conditions), physical examination findings (respiratory failure related symptoms as well as general clinical condition deterioration), laboratory (multiple biomarkers and alterations in basic laboratory tests) and radiological findings (consolidation pattern and pleural effusion) (table 1).

Our systematic review has a number of strengths. First, it provides the most comprehensive and trustworthy body of evidence up to date as it includes a significant number of studies not included in prior reviews. Secondly, we followed the GRADE approach to summarize and rate the certainty on the evidence. And thirdly, we presented our results both as relative estimates of association as well as absolute risk differences and used the latter to interpret and analyse our results. We consider that the absolute risk modification that can be attributed to a prognostic factor is a critical piece of information for those aiming to make decisions using prognostic information.

Regarding limitations, most of the studies included in this review were not published in peer review journals (only as preprint) at the time we performed the search. We identified most of those studies by cross reference search in google scholar, but it is possible that some may have not been detected by our search strategy. Additionally, given the high publication speed of COVID-19 studies it is probable that new relevant information not included in our review is available at the time our review is published. We aim to address this issue by updating our results in the short term. Although we made efforts to identify data duplication, in many instances it was not clear if studies reported, totally or partially, on the same cohorts of patients hence we assume there is a considerable chance of some degree of data overlap between included publications. Significant variability in study design, study type, patient eligibility criteria, prognostic factor definition and outcome definition was observed, however, given the huge amount of information analysed, it was not feasible to explore subgroup effects accounting for those differences.

In analysing our results we implemented a minimally contextualized approach for which we arbitrarily set thresholds to define the minimal important risk difference necessary to assume valuable prognostic information. As the degree of contextualization was minimal, we set very low thresholds (near the point of no effect). We acknowledge that readers might find those thresholds inappropriate, hence we also provided relative estimates of association which can be used with alternative thresholds or analytical approximations (e.g partially contextualized approach).

We identified multiple systematic reviews addressing prognostic factors in patients with COVID-19 infection.[231-250] All analysed certain prognostic factors or groups or prognostic factors that we included in the present review, and measured mortality and/or disease severity as outcomes. Most of the reported results are in consonance with our findings with only a few exceptions. Kumar et.al[245] reported diarrhea, productive cough and high ALT as prognostic factors however we found low certainty evidence on those variables in our primary analysis. Wang et.al[248] reported no association between chronic kidney disease and malignancy with poor outcomes in COVID-19 patients however we found that both conditions are associated with an increased risk of mortality and severe COVID-19 disease. Other significant differences of our review in relation to these prior reviews include multiple characteristics that were previously not identified as prognostic factors. In contrast to previous reviews, here we provide both relative and absolute estimates of risk and provide our certainty in those estimates.
Significant information has been published since our search was finalized. An update of the ISARIC registry[251] including 15194 hospitalised patients discharged or dead, the openSAFELY registry[252] included 17425445 adults potentially exposed to COVID-19 infection and a Chinese registry[253] that included 44672 patients with COVID-19. These studies identified the following variables as prognostic factors for COVID-19 related mortality: Age, sex (male), obesity, cardiovascular disease, diabetes, arterial hypertension, dyslipidemia, COPD, smoking, malignancy, cerebrovascular disease, dementia and chronic kidney disease. All these variables were captured by our analysis as predictors of COVID-19 related mortality or severe COVID-19 disease for which moderate or high certainty evidence exists. In addition, other prognostic factors were identified by these studies: race (not white)[252] and deprivation,[252] two variables we did not explore, and immunocompromise,[252] asthma,[252] autoimmune diseases,[252] and chronic liver disease,[251,252] four variables for which we found low certainty evidence.

Our approach considered two clinical scenarios in which we assumed that the prognostic information of each predictor for each outcome could potentially impact decision-making. In patients presenting with mild disease, predicting the risk of progression to severe status could support decisions on the level of healthcare required and more extensive follow up strategies. In the same way, in patients presenting with severe disease, predicting mortality risk could support the use of certain, more aggressive, therapeutic interventions. Clinicians or decision-makers can use our results to tailor management strategies for patients with COVID-19. However, to what extent accounting for these prognostic factors will improve clinically important outcomes is a question that cannot be addressed with our results. Furthermore using information on multiple individual prognostic factors for outcome prediction is challenging. Multivariable models provide a solution to this limitation, however, considering the high demand for accurate risk prediction models for patients with COVID-19,[7] our work can also provide solid grounds for development of these prognostic tools.

We have identified a set of variables that provide valuable prognostic information in patients with COVID-19 infection. Clinicians and policy makers can use our results to tailor management strategies for patients with this condition while researchers can utilise our findings to develop multivariable prognostic models that could eventually facilitate decision-making and improve patient important outcomes.

Contributors
AI conceived the study. AI and MR designed the study. AI and MR screened titles and abstracts for inclusion. AI, MR, FT, ALM, CA, AB, AC, FE, EZ, VS extracted data. AI, MR analysed and interpreted the results. FF and AA helped with assessment of certainty of the evidence. AI wrote the first draft, which all authors revised for critical content. All authors approved the final manuscript. AI and MR are the guarantors. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

Declaration of interests
All authors have completed the ICMJE uniform disclosure form at http://www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years, no other relationships or activities that could appear to have influenced the submitted work.

Acknowledgments
None

Data sharing
The study protocol is available online at https://www.medrxiv.org/content/10.1101/2020.04.08.20056598v1. Most included studies are publically available. Additional data are available upon reasonable request.

The lead author (the manuscript's guarantor) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

References

1. World Health Organization. Director-General's remarks at the media briefing on 2019-nCoV on 11 February 2020. World Health Organization 2020. https://www.who.int/dg/speeches/detail/who-director-general-s-remarks-at-the-media-briefing-on-2019-ncov-on-11-february-2020
2. Hui DS, Azhar Ei, Madani TA, et al. The continuing 2019-nCoV epidemic threat of novel coronaviruses to global health - The latest 2019 novel coronavirus outbreak in Wuhan, China. *Int J Infect Dis* 2020; **91**: 264-266.
3. Worldometer. COVID-19 coronavirus pandemic. 2020. https://www.worldometers.info/coronavirus/ (accessed June 2, 2020).
4. Hu Y, Sun J, Dai Z, et al. Prevalence and Severity of Coronavirus Disease 2019 (COVID-19): A Systematic Review and Meta-Analysis. *J Clin Virol* 2020; **127**: 104371.
5. Centre for Evidence-Based Medicine. Global Covid-19 Case Fatality Rates. https://www.cebm.net/covid-19/global-covid-19-case-fatality-rates/ (accessed April 6, 2020).
6. International Severe Acute Respiratory and Emerging Infections Consortium (ISARIC). COVID-19 Report: 19 May 2020. https://media.tghn.org/medialibrary/2020/05/ISARIC_Data_Platform_COVID-19_Report_19MAY20.pdf. (accessed June 2, 2020)
7. Wynants L, Van Calster B, Bonten MMJ, et al. Prediction models for diagnosis and prognosis of Covid-19 infection: Systematic review and critical appraisal. *BMJ-Brit Med J* 2020; **369**:m1328.
8. Izcovich A, Ragusa M, Sanguine V, Tortosa F, Espinosa F, Agnoletti C, et al. Prognostic factors for severity and mortality in patients infected with COVID-19: A living systematic review protocol. *medRxiv* 2020; published online April 11. https://doi.org/10.1101/2020.04.08.20056598 [preprint].
9. Iorio A, Spencer FA, Falavigna M, et al. Use of GRADE for assessment of evidence about prognosis: Rating confidence in estimates of event rates in broad categories of patients. *BMJ-Brit Med J* 2015; **350**:h870.
10. Hemingway H, Croft P, Perel P, et al. Prognosis research strategy (PROGRESS) 1: A framework for researching clinical outcomes. *BMJ-Brit Med J* 2013; **346**: e5595.
11. Hayden JA, Van Der Windt DA, Cartwright JL, Cote P, Bombardier C. Assessing bias in studies of prognostic factors. *Ann Intern Med* 2013; **158**(4): 280-286.
12. Ahn S, Fessler JA. Standard errors of mean, variance, and standard deviation estimators. 2003. Available from: https://doi.org/10.1037/e572902006-006
13. Viechtbauer W. Conducting meta-analyses in R with the metafor package. *J Stat Softw* 2010; **36** (3).
14. Grant RL. Converting an odds ratio to a range of plausible relative risks for better communication of research findings. *BMJ-Brit Med J* 2014; **348**: f7450.
15. Wang Z. Converting odds ratio to relative risk in cohort studies with partial data information. *J Stat Softw* 2013; **55** (5).
16. Farid F, Guyatt G, Zuk V, et al. GRADE Guidelines 28: Use of GRADE for the assessment of evidence about prognostic factors: Rating certainty in identification of groups of patients with different absolute risks. *J Clin Epidemiol* 2020; **121**: 60-70.

17. Hultcrantz M, Rind D, Akl EA, T, et al. The GRADE Working Group clarifies the construct of certainty of evidence. *J Clin Epidemiol*. 2017; **87**: 4–13.
18. WHO. Clinical management of COVID-19 (interim guidance). https://www.who.int/publications-detail/clinical-management-of-covid-19. (accessed on June 2, 2020)
19. Hu L, Chen S, Fu Y, et al. Risk factors associated with clinical outcomes in 323 COVID-19 patients in Wuhan, China. *medRxiv* 2020; published online March 30. https://doi.org/10.1101/2020.03.25.20037721 [preprint].
20. Bai X, Fang C, Zhou Y, et al. Predicting COVID-19 malignant progression with AI techniques. *medRxiv* 2020; published online March 27. https://doi.org/10.1101/2020.03.20.20037325 [preprint].
21. Yan L, Zhang H-T, Goncalves J, et al. A machine learning-based model for survival prediction in patients with severe COVID-19 infection. *medRxiv* 2020; published online March 17. https://doi.org/10.1101/2020.02.27.20028027 [preprint].
22. Dong J, Zhang D, Xu J, et al. prediction for progression risk in patients with COVID-19 pneumonia: The CALL score. *Clin Infect Dis* 2020; published online April 09. https://doi.org/10.1093/cid/ciaa414
23. Bi Q, Hong C, Meng J, et al. Characterization of clinical progression of COVID-19 patients in Shenzhen, China. *medRxiv* 2020; published online May 13. https://doi.org/10.1101/2020.04.22.20076190 [preprint].
24. Li X, Xu S, Yu M, et al. Risk factors for severity and mortality in adult COVID-19 inpatients in Wuhan. *J Allergy Clin Immunol* 2020; **S0091-6749**(20): 30495-4.
25. Wang X, Fang J, Zhu Y, et al. Clinical characteristics of non-critically ill patients with novel coronavirus infection (COVID-19) in a Fangcang hospital. *Clin Microbiol Infect* 2020; published online April 03. https://doi.org/10.1016/j.cmi.2020.03.032
26. Gong J, Ou J, Qiu X, et al. A tool to early predict severe 2019-novel coronavirus pneumonia (COVID-19) : A multicenter study using the risk nomogram in Wuhan and Guangdong, China. *medRxiv* 2020; published online April 22. https://doi.org/10.1101/2020.03.17.20037515 [preprint].
27. Farid F, Iorio A, Thabane L, Guyatt G. Calculation of absolute risk for important outcomes in patients with and without a prognostic factor of interest. *J Clin Epidemiol* 2020; **117**: 46–51.
28. Rada G, Verdugo-Paiva F, Ávila C, et al; COVID-19 L·OVE Working Group. Evidence synthesis relevant to COVID-19: A protocol for multiple systematic reviews and overviews of systematic reviews. *Medwave* 2020; **20**(3): e7867.
29. Argenziano MG, Bruce SL, Slater CL, et al. Characterization and clinical course of 1000 Patients with COVID-19 in New York: Retrospective case series. *medRxiv* 2020; published online May 07. https://doi.org/10.1101/2020.04.20.20072116 [preprint].
30. Auld S, Caridi-Scheible M, Blum JM, et al. ICU and ventilator mortality among critically ill adults with COVID-19. *medRxiv* 2020; published online April 26. https://doi.org/10.1101/2020.04.23.20076737 [preprint].
31. Bai T, Tu S, Wei Y, et al. Clinical and laboratory factors predicting the prognosis of patients with COVID-19: An analysis of 127 patients in Wuhan, China. *SSRN* 2020; published online March 5. http://dx.doi.org/10.2139/ssrn.3546118 [preprint].

32. Benelli G, Buscarini E, Canetta C, et al. SARS-COV-2 comorbidity network and outcome in hospitalized patients in Crema, Italy. *medRxiv* 2020; published online April 30. https://doi.org/10.1101/2020.04.14.20053090 [preprint].
33. Cai Q, Huang D, Ou P, et al. COVID-19 in a designated infectious diseases hospital outside Hubei province, China. *Allergy* 2020; **00**: 1-11.
34. Cao M, Zhang D, Wang Y, et al. Clinical features of patients infected with the 2019 novel coronavirus (COVID-19) in Shanghai, China. *medRxiv* 2020; published online March 06. https://doi.org/10.1101/2020.03.04.20030395 [preprint].
35. Cao W. Clinical features and laboratory inspection of novel coronavirus pneumonia (COVID-19) in Xiangyang, Hubei. *medRxiv* 2020; published online February 25. https://doi.org/10.1101/2020.02.23.20026963 [preprint].
36. Chao C, Meiping C, Yiting L, et al. Clinical features and predictors for patients with severe SARS-CoV-2 pneumonia: A retrospective multicenter cohort study. *SSRN* 2020; published online March 31. http://doi.org/10.2139/ssrn.3556663 [preprint].
37. Chen G, Wu D, Guo W, et al. Clinical and immunologic features in severe and moderate forms of coronavirus disease 2019. *medRxiv* 2020; published online February 19. https://doi.org/10.1101/2020.02.16.20023903 [preprint].
38. Chen J, Pan H, Wang Y, et al. Clinical characteristics of critically ill patients with SARS-CoV-2 infected pneumonia (COVID-19) in Wenzhou, China: A retrospective, single-center, descriptive study. *SSRN* 2020; published online April 20. https://doi.org/10.2139/ssrn.3571553 [preprint].
39. Chen J, Qi T, Liu L, et al. Clinical progression of patients with COVID-19 in Shanghai, China. *J Infect* 2020; **80**: e1-e6.
40. Chen L, Liu HG, Liu W, et ali. Analysis of clinical features of 29 patients with 2019 novel coronavirus pneumonia. *Zhonghua Jie He He Hu Xi Za Zhi (Chinese journal of tuberculosis and respiratory diseases)* 2020;**43**(0):E005. https://doi.org/10.3760/cma.j.issn.1001-0939.2020.0005
41. Chen M, Tu C, Tan C, et al. Key to successful treatment of COVID-19: Accurate identification of severe risks and early intervention of disease progression. *medRxiv* 2020; published online April 11. https://doi.org/10.1101/2020.04.06.20054890 [preprint].
42. Chen M, Yongzhen F, Xiaoyan W, et al. Clinical characteristics and risk factors for fatal outcome in patients with 2019-coronavirus infected disease (COVID-19) in Wuhan, China. *SSRN* 2020; published online March 03. https://doi.org/10.2139/ssrn.3546069 [preprint].
43. Chen R, Liang W, Jiang M, et al. Risk factors of fatal outcome in hospitalized subjects with coronavirus disease 2019 from a nationwide analysis in China. *Chest* 2020; published online April 15. https://doi.org/10.1016/j.chest.2020.04.010
44. Chen TL, Dai Z, Mo P, et al. Clinical characteristics and outcomes of older patients with coronavirus disease 2019 (COVID-19) in Wuhan, China (2019): A single-centered, retrospective study. *J Gerontol* 2020; published online April 11. https://doi.org/10.1093/gerona/glaa089
45. Chen W, Chen C, Huang L, et al. Clinical characteristics of 85 patients infected by SARS-CoV-2 in Guangxi, China. *SSRN* 2020; published online April 01. https://doi.org/10.2139/ssrn.3559599 [preprint].

46. Chen X, Liu Z. Early prediction of mortality risk among severe COVID-19 patients using machine learning. *medRxiv* 2020; published online April 19. https://doi.org/10.1101/2020.04.13.20064329 [preprint].
47. Chen X, Zhang Y, Zhu B, et al. Associations of clinical characteristics and antiviral drugs with viral RNA clearance in patients with COVID-19 in Guangzhou, China. *SSRN* 2020; published online April 14. https://doi.org/10.2139/ssrn.3566234 [preprint].
48. Chen X, Zhao B, Qu Y, et al. Detectable serum SARS-CoV-2 viral load (RNAaemia) is closely associated with drastically elevated Interleukin 6 (IL-6) level in critically ill COVID-19 patients. *medRxiv* 2020; published online March 03. https://doi.org/10.1101/2020.02.29.20029520 [preprint].
49. Chen X, Zheng F, Qing Y, et al. Epidemiological and clinical features of 291 cases with coronavirus disease 2019 in areas adjacent to Hubei, China: A double-center observational study. *medRxiv* 2020; published online March 06. https://doi.org/10.1101/2020.03.03.20030353 [preprint].
50. Chen Y, Zhang K, Zhu G, et al. Clinical characteristics and current treatment of critically ill patients with COVID-19 outside Wuhan, China: A multicenter, retrospective, observational study.*SSRN* 2020; published online March 23. https://doi.org/10.2139/ssrn.3551426 [preprint].
51. Cheng Y, Luo R, Wang K, et al. Kidney impairment is associated with in-hospital death of COVID-19 patients. *medRxiv* 2020; published online February 20. https://doi.org/10.1101/2020.02.18.20023242 [preprint].
52. Chu J, Yang N, Wei Y, et al. Clinical characteristics of 54 medical staff with COVID-19: A retrospective study in a single center in Wuhan, China. *J Med Virol* 2020; **92**(7): 807-813
53. Colaneri M, Sacchi P, Zuccaro V, et al. Clinical characteristics of coronavirus disease (COVID-19) early findings from a teaching hospital in Pavia, North Italy, 21 to 28 February 2020. *Euro Surveill* 2020; **25**(16).
54. Colombi D, Bodini FC, Petrini M, et al. Well-aerated lung on admitting chest CT to predict adverse outcome in COVID-19 pneumonia. *Radiology* 2020; published online April 17. https://doi.org/10.1148/radiol.2020201433
55. Cumming MJ, Baldwin MR, Abrams D, et al. Epidemiology, clinical course, and outcomes of critically ill adults with COVID-19 in New York City: A prospective cohort study. *medRxiv* 2020; published online April 20. https://doi.org/10.1101/2020.04.15.20067157 [preprint].
56. Docherty AB, Harrison EM, Green CA, Hardwick HE, Pius R, Norman L, et al. Features of 16,749 hospitalised UK patients with COVID-19 using the ISARIC WHO Clinical Characterisation Protocol. *medRxiv* 2020; published online April 28. https://doi.org/10.1101/2020.04.23.20076042 [preprint].
57. Dreher M, Kersten A, Bickenbach J, et al. The characteristics of 50 hospitalized COVID-19 patients with and without ARDS. *Dtsch Arztebl Int* 2020; **117**: 271-8.
58. Du R-H, Liang L-R, Yang C-Q, et al. Predictors of mortality for patients with COVID-19 pneumonia caused by SARS-CoV-2: A prospective cohort study. *Eur Respir J* 2020; **55**: 2000524.
59. Duan Q, Guo G, Ren Y, et al. Treatment outcomes, influence factors of 116 hospitalized COVID-19 patients with longer/prolonged treatment course in Wuhan, China. *SSRN* 2020; published online March 13. https://doi.org/10.2139/ssrn.3550017 [preprint].

60. Fan J, Hui W, Guangming Y, et al. Low-density lipoprotein is a potential predictor of poor prognosis in patients with coronavirus disease 2019. *Metabolism* 2020; **107**:154-243.
61. Fan T, Hao B, Yang S, et al. Clinical characteristics of COVID-19 and establishment of a disease risk prediction model. *SSRN* 2020; published online March 31. https://doi.org/10.2139/ssrn.3556660 [preprint].
62. Fang L, Lin L, MengDa X, et al. Prognostic value of interleukin-6, C-reactive protein, and procalcitonin in patients with COVID-19. *J Clin Virol* 2020; 127:104370.
63. Fei J, Lin F, Ying L, et al. Reduction of lymphocyte at early stage elevates severity and death risk of COVID-19 patients: A hospital-based case-cohort study. *medRxiv* 2020; published online April 06. https://doi.org/10.1101/2020.04.02.20050955 [preprint].
64. Feng Y, Yun L, Tao B, et al. COVID-19 with different severity: A multi-center study of clinical features. *Am J Respir Crit Care Med* 2020; **201**(11): 1380-1388. https://doi.org/10.1164/rccm.202002-0445OC
65. Feng Z, Yu Q, Yao S, et al. Early prediction of disease progression in 2019 novel coronavirus pneumonia patients outside Wuhan with CT and clinical characteristics. *medRxiv* 2020; published online February 23. https://doi.org/10.1101/2020.02.19.20025296 [preprint].
66. Fu L, Fei J, Xiang HX, et al. Analysis of death risk factors among 200 COVID-19 patients in Wuhan, China: A hospital-based case-cohort study. *SSRN* 2020; published online March 23. https://doi.org/10.2139/ssrn.3551430 [preprint].
67. Fu L, Fei J, Xu S, et al. Acute liver injury and its association with death risk of patients with COVID-19: A hospital-based prospective case-cohort study.*medRxiv* 2020; published online April 06. https://doi.org/10.1101/2020.04.02.20050997 [preprint].
68. Gao L, Jiang D, Wen XS, et al. Prognostic value of NT-ProBNP in patients with severe COVID-19. *Respir Res* 2020; **21**: 83.
69. Gao Y, Li T, Han M, et al. Diagnostic utility of clinical laboratory data determinations for patients with the severe COVID-19. *J Med Virol* 2020; **92**(7): 791-796.
70. Grasselli G, Zangrillo A, Zanella A, et al. Baseline characteristics and outcomes of 1591 patients infected with SARS-CoV-2 admitted to ICUs of the Lombardy Region, Italy. *JAMA* 2020; **323**(16):1574-1581.
71. Gu T, Chu Q, Yu Z, et al. History of coronary heart disease increases the mortality rate of coronavirus disease 2019 (COVID-19) patients: A nested case-control study based on publicly reported confirmed cases in Mainland China. *medRxiv* 2020; published online April 03. https://doi.org/10.1101/2020.03.23.20041848 [preprint].
72. Guan W, Liang W, Zhao Y, et al. Comorbidity and its impact on 1590 Patients with Covid-19 in China: A nationwide analysis. *Eur Respir J* 2020; **55**: 2000547.
73. Guan W, Ni Z, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med* 2020; **382**: 1708-1720.
74. Guo Tao, Fan Y, Chen M, et al. Cardiovascular implications of fatal outcomes of patients with coronavirus disease 2019 (COVID-19). *JAMA Cardiol* 2020; published online March 27. https://doi.org/10.1001/jamacardio.2020.1017
75. Guo TM, Tong Y, Chen J, Huang L, Cheng B, Zhoue J. Clinical features predicting mortality risk in older patients with COVID-19. *SSRN* 2020; published online April 14. https://doi.org/10.2139/ssrn.3569846 [preprint].

76. Guo W, Li M, Dong Y, et al. Diabetes is a risk factor for the progression and prognosis of COVID-19. *Diabetes Metab Res Rev* 2020. https://doi.org/10.1002/dmrr.3319
77. Han H, Xie L, Liu R et al. Analysis of heart injury laboratory parameters in 273 COVID-19 patients in one hospital in Wuhan, China. *J M Virol* 2020; **92**(7): 819-823
78. Han M, Zhang Y, Liu Z, et al. Assessing SARS-CoV-2 RNA levels and lymphocyte/T cell counts in COVID-19 patients revealed initial immune status of patients as a major determinant of disease severity. *SSRN* 2020; published online March 31. http://dx.doi.org/10.2139/ssrn.3556670 [preprint].
79. Han Y, Zhang H, Mu S, et al. Lactate dehydrogenase, a risk factor of severe COVID-19 patients. *medRxiv* 2020; published online March 27. https://doi.org/10.1101/2020.03.24.20040162 [preprint].
80. He W, Chen L, Chen L, et al. Clinical characteristics and outcome of 31 cases with Covid-19 diagnosed in haematology units in Wuhan, China: A retrospective cohort study. *SSRN* 2020; published online March 24. https://doi.org/10.2139/ssrn.3558004 [preprint].
81. He XW, Lai JS, Cheng J, et al. Impact of complicated myocardial injury on the clinical outcome of severe or critically ill COVID-19 Patients. *Zhonghua Xin Xue Guan Bing Za Zhi (Chinese journal of cardiovascular diseases)* 2020; **48**(0):E011. Published online March 14. https://doi.org/10.3760/cma.j.cn112148-20200228-00137
82. Herold T, Jurinovic V, Arnreich C, et al. Level of IL-6 predicts respiratory failure in hospitalized symptomatic COVID-19 patients.*medRxiv* 2020; published online April 10. https://doi.org/10.1101/2020.04.01.20047381 [preprint].
83. Hu B, Wang D, Hu C, et al. Clinical features of critically ill patients with COVID-19 infection in China. *Research Square* 2020; published online March 08. https://doi.org/10.21203/rs.3.rs-16250/v1 [preprint].
84. Hu L, Chen S, Fu Y, et al. Risk factors associated with clinical outcomes in 323 COVID-19 patients in Wuhan, China. *medRxiv* 2020; published online March 30. https://doi.org/10.1101/2020.03.25.20037721 [preprint].
85. Hu X, Zeng W, Zhang Y, et al. CT imaging features of different clinical types of COVID-19: a chinese multicenter study. *SSRN* 2020; published online March 13. http://dx.doi.org/10.2139/ssrn.3550043 [preprint].
86. Hu Z, Gan J, Li J, et al. Leucocyte subsets effectively predict the clinical outcome of patients with COVID-19 pneumonia: A retrospective case-control study. *SSRN* 2020; published online April 1. https://doi.org/10.2139/ssrn.3559566 [preprint].
87. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020; **395**: 497-506.
88. Huang H, Cai H, Li Y, et al. Prognostic factors for COVID-19 pneumonia progression to severe symptom based on the earlier clinical features: A retrospective analysis. *medRxiv* 2020; published online March 30. https://doi.org/10.1101/2020.03.28.20045989 [preprint].
89. Huang M, Yang Y, Shang F, et al. Early and critical care in severe patients with COVID-19 in Jiangsu Province, China: A descriptive study. *SSRN* 2020; published online March 3. https://doi.org/10.2139/ssrn.3546056 [preprint].
90. Jiang X, Tao J, Wu H, et al. Clinical features and management of severe COVID-19: A retrospective study in Wuxi, Jiangsu Province, China. *medRxiv* 2020; published online April 14. https://doi.org/10.1101/2020.04.10.20060335 [preprint].

91. Jin JM, Bai P, He W, et al. Gender differences in patients with COVID-19: Focus on severity and mortality. *medRxiv* 2020; published online March 05. https://doi.org/10.1101/2020.02.23.20026864 [preprint].
92. Jin X, Lian JS, Hu JH, et al. Epidemiological, clinical and virological characteristics of 74 cases of coronavirus-infected disease 2019 (COVID-19) with gastrointestinal symptoms. *Gut* 2020; **69**: 1002-1009.
93. Kalligeros M, Shehadeh F, Mylona EK, et al. Association of obesity with disease severity among patients with COVID- 19. *Obesity* 2020; published online April 30. https://doi.org/10.1002/oby.22859
94. Kuang Y, He S, Lin S, et al. Clinical characteristics and CT manifestations of 143 hospitalized patients with 2019 novel coronavirus disease (COVID-19) outside Wuhan: A multi-center study in Taizhou City, Zhejiang, China. *SSRN* 2020; published online March 31. http://dx.doi.org/10.2139/ssrn.3556667 [preprint].
95. Lee HY, Ahn J, Kang CK, et al. Association of angiotensin II receptor blockers and angiotensin-converting enzyme inhibitors on COVID-19-related outcome. *SSRN* 2020; published online April 14. https://doi.org/10.2139/ssrn.3569837 [preprint].
96. Lei L, Gao JY. Clinical characteristics of 51 patients discharged from hospital with COVID-19 in Chongqing, China. *medRxiv* 2020; published online February 23. https://doi.org/10.1101/2020.02.20.20025536 [preprint].
97. Lei S, Jiang F, Su W, et al. Clinical characteristics and outcomes of patients undergoing surgeries during the incubation period of COVID-19 infection. *EClinicalMedicine* 2020; **21**: 100331.
98. Li H, Xiang X, Ren H, et al. Serum amyloid A is a biomarker of severe coronavirus disease and poor prognosis. *J Infect* 202; **80**: 646-655.
99. Li J, Long X, Luo H, et al. Clinical characteristics of deceased patients infected with SARS-CoV-2 in Wuhan, China. *SSRN* 2020; published online March 3. https://doi.org/10.2139/ssrn.3546043 [preprint].
100. Li J, Li M, Zheng S, et al. Leukopenia predicts risk for death in critically ill patients with COVID-19 in Wuhan, China: A single-centered, retrospective study. SSRN 2020; published online . https://doi.org/10.2139/ssrn.3555248
101. Li J, Wang X, Chen J, Zhang H, Deng A. Association of renin-angiotensin system inhibitors with severity or risk of death in patients with hypertension hospitalized for coronavirus disease 2019 (COVID-19) infection in Wuhan, China. *JAMA Cardiol* 2020; published online April 23. https://doi.org/10.1001/jamacardio.2020.1624
102. Li K, Wu J, Wu F, et al. PMID - 32118615. The clinical and chest CT features associated with severe and critical COVID-19 pneumonia. *Invest Radiol* 2020; **55**(6): 327-331.
103. Li Y, Wang Z, Hui Yan, et al. Clinical characteristics of 77 novel coronavirus 2019 infected patients with respiratory failure in the terminal stage in Wuhan. *SSRN* 2020; published online March 17. https://doi.org/10.2139/ssrn.3551325 [preprint].
104. Li Y-K, Peng S, Li L-Q, et al. Clinical and transmission characteristics of Covid-19 - A retrospective study of 25 cases from a single thoracic surgery department. *Curr Med Sci* 2020; **40**(2): 295-300.
105. Lian J, Jin X, Hao S, et al. Analysis of epidemiological and clinical features in older patients with coronavirus disease 2019 (COVID-19) out of Wuhan. *Clin Infect Dis* 2020; published online March 25. https://doi.org/10.1093/cid/ciaa242

106. Liang W, Guan W, Chen R, et al. Cancer patients in SARS-CoV-2 infection: A nationwide analysis in China. *Lancet Oncol* 2020; **21**: 335-337.
107. Liao X, Chen H, Wang B, et al. Critical care for severe COVID-19: A population-based study from a province with low case-fatality rate in China. *medRxiv* 2020; published online April 21. https://doi.org/10.1101/2020.03.22.20041277 [preprint].
108. Liu F, Xu A, Zhang Y, et al. Patients of COVID-19 may benefit from sustained lopinavir-combined regimen and the increase of eosinophil may predict the outcome of COVID-19 progression. *Int J Infect Dis* 2020; **95**: 183-191.
109. Liu J, Tu C, Zhu M, et al. Exploring the law of development and prognostic factors of common and severe COVID-19: A retrospective case-control study in 122 patients with complete course of disease. *SSRN* 2020; published online March 24. http://dx.doi.org/10.2139/ssrn.3555209 [preprint].
110. Liu J, Li S, Liu J, et al. Longitudinal characteristics of lymphocyte responses and cytokine profiles in the peripheral blood of SARS-CoV-2 infected patients. *medRxiv* 2020; published online February 22. https://doi.org/10.1101/2020.02.16.20023671 [preprint].
111. Liu J, Liu Y, Xiang P, et al. Neutrophil-to-Lymphocyte ratio predicts severe illness patients with 2019 novel coronavirus in the early stage. *medRxiv* 2020; published online February 12. https://doi.org/10.1101/2020.02.10.20021584 [preprint].
112. Liu K-C, Xu P, Lv W-F, et al CT Manifestations of coronavirus disease-2019: A retrospective analysis of 73 cases by disease severity. *Eur J Radiol* 2020; **126**: 108941.
113. Liu R, Ming X, Xu O, et al. Association of cardiovascular manifestations with in-hospital outcomes in patients with COVID-19: A hospital staff data. *medRxiv* 2020; published online March 12. https://doi.org/10.1101/2020.02.29.20029348 [preprint].
114. Liu T, Zhang J, Yang Y, et al. The potential role of IL-6 in monitoring severe case of coronavirus disease 2019. *medRxiv* 2020; published online March 10. https://doi.org/10.1101/2020.03.01.20029769 [preprint].
115. Liu W, Tao ZW, Wang L, et al. Analysis of factors associated with disease outcomes in hospitalized patients with 2019 novel coronavirus disease. *Chin Med J* 2020; **133**(9):1032-1038.
116. Liu Y, Mao B, Liang S, et al. Association between age and clinical characteristics and outcomes of coronavirus disease 2019. *SSRN* 2020; published online March 31. http://dx.doi.org/10.2139/ssrn.3556689 [preprint].
117. Liu Y, Bi L, Chen Y, et al. Active or latent tuberculosis increases susceptibility to COVID-19 and disease severity. *medRxiv* 2020; published online March 16. https://doi.org/10.1101/2020.03.10.20033795 [preprint].
118. Liu Y, Du X, Chen J, et al. Neutrophil-to-Lymphocyte Ratio as an independent risk factor for mortality in hospitalized patients with COVID-19. *J Infect* 2020; **81**: e6-e12.
119. Liu Y, Sun W, Guo Y, et al. Association between platelet parameters and mortality in coronavirus disease 2019: Retrospective cohort study. *Platelets* 2020; **31**: 490-496.
120. Liu Y, Sun W, Li J, et al. Clinical features and progression of acute respiratory distress syndrome in coronavirus disease 2019. *medRxiv* 2020; published online Febraury 27. https://doi.org/10.1101/2020.02.17.20024166 [preprint].

121. Liu Y, Yang Y, Zhang C, et al. Clinical and biochemical indexes from 2019-NCoV infected patients linked to viral loads and lung injury. *Sci China Life Sci* 2020; **63**(3): 364-374.
122. Lu J, Hu S, Fan R, et al. ACP Risk Grade: A simple mortality index for patients with confirmed or suspected severe acute respiratory syndrome coronavirus 2 disease (COVID-19) during the early stage of outbreak in Wuhan, China. *medRxiv* 2020; published online Febraury 23. https://doi.org/10.1101/2020.02.20.20025510 [preprint].
123. Luo XM, Zhou W, Yan X, et al. Prognostic value of C-Reactive Protein in patients with COVID-19. *medRxiv* 2020; published online March 23. https://doi.org/10.1101/2020.03.21.20040360 [preprint].
124. Luo XM, Zhou W, Xia H, et al. Characteristics of SARS-CoV-2 infected patients with clinical outcome during epidemic ongoing outbreak in Wuhan, China. *SSRN* 2020; published online March 24. https://doi.org/10.2139/ssrn.3552812 [preprint].
125. Lv X, Song C, Luo T, et al. Clinical characteristics between COVID-19 patients in and outside Wuhan: A multiple-centered retrospective study. *SSRN* 2020; published online April 23. https://doi.org/10.2139/ssrn.3572907 [preprint].
126. Ma J, Yin J, Qian Y, and Yuan Wu. Clinical characteristics and prognosis in cancer patients with COVID-19: A single center's retrospective study. *J Infec* 2020; published online April 14. https://doi.org/10.1016/j.jinf.2020.04.006
127. Ma KL, Liu ZH, Cao C, et al. COVID-19 myocarditis and severity factors： an adult cohort study. *medRxiv* 2020; published online March 23. https://doi.org/10.1101/2020.03.19.20034124 [preprint].
128. Ma Y, Shi N, Fan Y, et al. Predictive value of the neutrophil-to-lymphocyte ratio(NLR) for diagnosis and worse clinical course of the COVID-19: Findings from ten provinces in China. *SSRN* 2020; published online April 14. http://dx.doi.org/10.2139/ssrn.3569838 [preprint].
129. Mehra MR, Desai SS, Kuy SR, Henry TD, Patel AN. Cardiovascular disease, drug therapy, and mortality in Covid-19. *N Engl J Med* 2020; published online May 01. https://doi.org/10.1056/NEJMoa2007621
130. Mo P, Xing Y, Xiao Y, et al. Clinical characteristics of refractory COVID-19 pneumonia in Wuhan, China. *Clin Infect Dis* 2020, published online March 16. https://doi.org/10.1093/cid/ciaa270
131. Niu S, Tian S, Lou J, et al. Clinical characteristics of older patients infected with COVID-19: A descriptive study. *Arch Gerontol Geriatr* 2020; **89**: 104058.
132. Pan L, Mu M, Yang P, et al. Clinical characteristics of COVID-19 patients with digestive symptoms in Hubei, China: A descriptive, cross-sectional, multicenter study. *Am J Gastroenterol* 2020, **115**(5): 766-773.
133. Paranjpe I, Russak A, De Freitas JK, et al. Clinical characteristics of hospitalized Covid-19 patients in New York City. *medRxiv* 2020; published online April 26. https://doi.org/10.1101/2020.04.19.20062117 [preprint].
134. Peng YD, Meng K., Guan HQ, et al. Clinical characteristics and outcomes of 112 cardiovascular disease patients infected by 2019-NCoV. *Zhonghua Xin Xue Guan Bing Za Zhi (Chinese journal of cardiovascular diseases)* 2020; **48**: E004.
135. Qi D, Yan X, Tang X, et al. Epidemiological and clinical features of 2019-NCoV acute respiratory disease cases in Chongqing Municipality, China: A retrospective,

descriptive, multiple-center study. *medRxiv* 2020; published online March 20. https://doi.org/10.1101/2020.03.01.20029397 [preprint].
136. Qi X, Jiang Z, YU Q, et al. Machine learning-based CT radiomics model for predicting hospital stay in patients with pneumonia associated with SARS-CoV-2 infection: a multicenter study. *medRxiv* 2020; published online March 03. https://doi.org/10.1101/2020.02.29.20029603 [preprint].
137. Qin X, Qiu S, Yuan Y, et al. Clinical characteristics and treatment of patients infected with COVID-19 in Shishou, China. *SSRN* 2020; published online February 20. https://doi.org/10.2139/ssrn.3541147 [preprint].
138. Qu R, Ling Y, Zhang YH, et al. Platelet-to-lymphocyte ratio is associated with prognosis in patients with corona virus disease-19. *J Med Virol* 2020; **2020**: 1-9.
139. Ran J, Dai B, Wang D, and Li XM. Clinical predictors of severity based on an analysis of data of COVID-19 pneumonia. *SSRN* 2020; published online April 01. https://doi.org/10.2139/ssrn.3559525 [preprint].
140. Rentsch CT, Kidwai-Khan F, Tate JP, et al. Covid-19 testing, hospital admission, and intensive care among 2,026,227 United States veterans aged 54-75 years. *medRxiv* 2020; published online April 14. https://doi.org/10.1101/2020.04.09.20059964 [preprint].
141. Rossi PG, Marino M, Formisano D, et al. Characteristics and outcomes of a cohort of SARS-CoV-2 patients in the province of Reggio Emilia, Italy. *medRxiv* 2020, published online April 16. https://doi.org/10.1101/2020.04.13.20063545 [preprint].
142. Ruan Q, Yang K, Wang W, Jiang L, Song J. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. *Intensive Care Med* 2020; 4**6(**5): 846-848.
143. Sarkar J, and Chakrabarti P. A machine learning model reveals older age and delayed hospitalization as predictors of mortality in patients with COVID-19. *medRxiv* 2020; published online March 30. https://doi.org/10.1101/2020.03.25.20043331 [preprint].
144. Shi H, He L, Sun W, et al. Clinical characteristics and prognostic factors of 148 COVID-19 cases in a secondary epidemic area. *SSRN* 2020; published online April 23. https://doi.org/10.2139/ssrn.3572911 [preprint].
145. Shi S, Qin M, Shen B, et al. Association of cardiac injury with mortality in hospitalized patients with COVID-19 in Wuhan, China. *JAMA Cardiol* 2020; published online March 25. https://doi.org/10.1001/jamacardio.2020.0950
146. Shi W, Peng X, Liu T, et al. Deep learning-based quantitative computed tomography model in predicting the severity of COVID-19: A retrospective study in 196 patients. *SSRN* 2020; published online March 03. https://doi.org/10.2139/ssrn.3546089 [preprint].
147. Shi Y, Yu X, Zhao Hong, Wang Hao, Zhao R, Sheng J. Host susceptibility to severe COVID-19 and establishment of a host risk score: Findings of 487 cases outside Wuhan. *Crit Care* 2020; **24**: 108.
148. Song CY, Xu J, He JQ, Lu YQ. COVID-19 early warning score: A multi-parameter screening tool to identify highly suspected patients. *medRxiv* 2020, published online March 08. https://doi.org/10.1101/2020.03.05.20031906 [preprint].
149. Sun F, Kou S, Wang S, et al. Medication patterns and disease progression among 165 patients with coronavirus disease 2019 (COVID-19) in Wuhan, China: A single-

centered, retrospective, observational study. SSRN 2020; published online March 17. https://doi.org/10.2139/ssrn.3551323 [preprint].
150. Sun X, Wang J, Liu Z, et al. Characteristics of patients with COVID-19 pneumonia admitted to the intensive care unit and predictors of mortality in Wuhan, China: A single-centered retrospective cohort study. *SSRN* 2020; published online April 06. https://doi.org/10.2139/ssrn.3559629 [preprint].
151. Sun Y, Dong Y, Wang Y, et al. Characteristics and prognostic factors of disease severity in patients with COVID-19: the Beijing experience. *J Autoimmun* 2020; published online April 24. https://doi.org/10.1016/j.jaut.2020.102473
152. Tabata S, Imai K, Kawano S, et al. Non-severe vs severe symptomatic COVID-19: 104 cases from the outbreak on the cruise ship 'Diamond Princess' in Japan. *SSRN* 2020; published online April 07. https://doi.org/10.1101/2020.03.18.20038125 [preprint].
153. Tan L, Wang Q, Zhang D, et al. Lymphopenia predicts disease severity of COVID-19: A descriptive and predictive study. *Signal Transduct Target Ther* 2020; **5**: 33.
154. Tang N, Li D, Wang X, Sun Z. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. *J Thromb Haemost* 2020; **18**(4): 844-847.
155. Tian S, Hu N, Lou J, et al. Characteristics of COVID-19 infection in Beijing. *J Infect* 2020; **80**(4): 401–6.
156. Tu WJ, Cao J, Yu L, Hu X, Liu Q. Clinicolaboratory study of 25 fatal cases of COVID-19 in Wuhan. *Intensive Care Med* 2020; published online April 06. https://doi.org/10.1007/s00134-020-06023-4
157. Wan S, Yi Q, Fan S, et al. Relationships among lymphocyte subsets, cytokines, and the pulmonary inflammation index in coronavirus (COVID- 19) infected patients. *Br J Haematol* 2020; **189**(3):428-437.
158. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA* 2020; **323**(11): 1061–1069.
159. Wang D, Yin Y, Hu C, et al. Clinical course and outcome of 107 patients infected with the novel coronavirus, SARS-CoV-2, discharged from two hospitals in Wuhan, China. *Crit Care* 2020; **24**: 188.
160. Wang G, Wu C, Zhang Q, et al. Epidemiological and clinical features of coronavirus cisease 2019 (COVID-19) in Changsha, China. *SSRN* 2020; published online March 10. https://doi.org/10.2139/ssrn.3548770 [preprint].
161. Wang L, He W, Yu X, etal. Coronavirus disease 2019 in elderly patients: characteristics and prognostic factors based on 4-week follow-up. *J Infect* 2020; **80**: 639-645.
162. Wang L, He WB, Yu XM, Liu HF, Zhou WJ, Jiang H. Prognostic value of myocardial injury in patients with COVID-19. *Zhonghua Yan Ke Za Zhi (Chinese journal of ophthalmology)* 2020; **56**.
163. Wang L, Li X, Chen H, et al. Coronavirus disease 19 infection does not result in acute kidney injury: An analysis of 116 hospitalized patients from Wuhan, China. *Am J Nephrol* 2020; **51**: 343–348.

164. Wang L, Zou A, Wang J, et al. Matrix analysis of clinical characteristics and dynamic observation of immunological features in 90 cases of COVID-19. *SSRN* 2020, published online April 02. https://doi.org/10.2139/ssrn.3556688 [preprint].
165. Wang R, Pan M, Zhang X, et al. Epidemiological and clinical features of 125 hospitalized patients with COVID-19 in Fuyang, Anhui, China. *Int J Infect Dis* 2020; **95**: 421-428.
166. Wang X, Fang J, Zhu Y, et al. Clinical characteristics of non-critically ill patients with novel coronavirus infection (COVID-19) in a Fangcang hospital. *Clin Microbiol Infect* 2020; **S1198-743X**(20): 30177-4.
167. Wang Y, Luo H, Liu S, et al. Respiratory failure among patients with COVID-19 in Jiangsu province, China: A multicentre retrospective cohort study. *SSRN* 2020; published online March 24. https://doi.org/10.2139/ssrn.3552836 [preprint].
168. Wang Y, Lu X, Chen H, et al. Clinical course and outcomes of 344 intensive care patients with COVID-19. *Am J Respir Crit Care Med* 2020; **201**(11): 1430-34.
169. Wang Y, Zhou Y, Yang Z, Xia D, Geng S. Clinical characteristics of patients with severe pneumonia caused by the 2019 novel coronavirus in Wuhan, China. *medRxiv* 2020; published online March 03. https://doi.org/10.1101/2020.03.02.20029306 [preprint].
170. Wang Z, Yang B, Li Q, Wen L, Zhang R. Clinical features of 69 cases with coronavirus disease 2019 in Wuhan, China. *Clin Infect Dis* 2020; published online March 16. https://doi.org/10.1093/cid/ciaa272
171. Wen C, Yali Q, Zirui G, et al. Prevalence of acute kidney injury in severe and critical COVID-19 patients in Wuhan, China. *SSRN* 2020; published online March 24. https://doi.org/10.2139/ssrn.3555223 [preprint].
172. Wen Y, Wei L, Li Y, et al. Epidemiological and clinical characteristics of COVID-19 in Shenzhen, the largest migrant city of China. *medRxiv* 2020; published online March 23. https://doi.org/10.1101/2020.03.22.20035246 [preprint].
173. Wang S, Chen Z, Lin Y, et al. Epidemical and clinical characteristics of 165 patients infected with SARS-CoV-2 in Fujian province, China. *SSRN* 2020; published online March 23. https://doi.org/10.2139/ssrn.3551402 [preprint].
174. Wu C, Chen X, Cai Y, et al. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. *JAMA Intern Med* 2020; published online March 13. https://doi.org/10.1001/jamainternmed.2020.0994.
175. Wu J, Li W, Shi X, et al. Early antiviral treatment contributes to alleviate the severity and improve the prognosis of patients with novel coronavirus disease (COVID-19). *J Intern Med* 2020; published online March 27. https://doi.org/10.1111/joim.13063
176. Xie H, Zhao J, Lian N, Lin S, Xie Q, Zhuo H. Clinical characteristics of non-ICU hospitalized patients with coronavirus disease 2019 and liver injury: A retrospective study. *Liver Int* 2020; **40**: 1321–1326.
177. Xie J, Covassin N, Fan Z, et al. Association between hypoxemia and mortality in patients with COVID-1. *Mayo Clin Proc* 2020; **95**(6): 1138-1147.
178. Xie J, Hungerford D, Chen H, et al. Development and external validation of a prognostic multivariable model on admission for hospitalized patients with COVID-19. *medRxiv* 2020; published online April 07. https://doi.org/10.1101/2020.03.28.20045997 [preprint].

179. Xu S, Fu L, Fei J, et al. Acute kidney injury at early stage as a negative prognostic indicator of patients with COVID-19: A hospital-based retrospective analysis. *medRxiv* 2020; published online March 26. https://doi.org/10.1101/2020.03.24.20042408 [preprint].
180. Xu W, Qu S, Xing M, et al. Epidemiologic features and clinical findings of COVID-19-infected patients in Suzhou. *SSRN* 2020; published online March 18. http://dx.doi.org/10.2139/ssrn.3551352 [preprint].
181. Xu Y, Xu Z, Liu X, et al. Clinical findings in critical ill patients infected with SARS-Cov-2 in Guangdong province, China: A multi-center, retrospective, observational study. *medRxiv* 2020; published online March 06. https://doi.org/10.1101/2020.03.03.20030668 [preprint].
182. Xu YH, Dong JH, An WM, et al. Clinical and computed tomographic imaging features of novel coronavirus pneumonia caused by SARS-CoV-2. *J Infect*. 2020; **80**(4): 394–400.
183. Yan S, Song X, Lin F, et al. Clinical characteristics of coronavirus disease 2019 in Hainan, China. *medRxiv* 2020; published online March 23. https://doi.org/10.1101/2020.03.19.20038539 [preprint].
184. Yan X, Wang C, Peng D, et al. Clinical features, treatment and outcomes of 218 patients with COVID-19: A retrospective, multicenter study based on clinical classification. *SSRN* 2020; published online April 06. https://doi.org/10.2139/ssrn.3559594 [preprint].
185. Yang AP, Liu JP, Tao WQ, Li HM. The diagnostic and predictive role of NLR, d-NLR and PLR in COVID-19 patients. *Int Immunopharmacol* 2020; **84**: 106504.
186. Yang G, Tan Z, Zhou L, et al. Angiotensin II receptor blockers and angiotensin-converting enzyme inhibitors usage is associated with improved inflammatory status and clinical outcomes in COVID-19 patients with hypertension. *medRxiv* 2020; published online April 04. https://doi.org/10.1101/2020.03.31.20038935 [preprint].
187. Yang JK, Jin JM, Liu S, et al. Blood glucose is a representative of the clustered indicators of multi-organ injury for predicting mortality of COVID-19 in Wuhan, China. *SSRN* 2020; published online April 14. https://doi.org/10.2139/ssrn.3569852 [preprint].
188. Yang L, Lei Y, Zhang R, et al. Epidemiological and clinical features of 200 hospitalized patients with corona virus disease 2019 in Yichang, China: A descriptive study. *J Clin Virol* 2020; **129**: 104475.
189. Yang X, Yang Q, Wang Y, et al. Thrombocytopenia and its association with mortality in patients with COVID- 19. *J Thromb Haemos*t, 2020; **00**: 1-4.
190. Yang X, Yu Y, Xu J, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: A single-centered, retrospective, observational study. *Lancet Respir* Med 2020; **8**(5): 475- 481.
191. Yin Y, Zhou S, Zhang X, et al. Critically ill patients with COVID-19 in China: A multicenter retrospective observational study. *SSRN* 2020; published online April 07. https://doi.org/10.2139/ssrn.3562469 [preprint].
192. Young BE, Ong SWX., Kalimuddin S, et al. Epidemiologic features and clinical course of patients infected with SARS-CoV-2 in Singapore. *JAMA*. 2020; **323**(15): 1488- 1494.

193. Yu C, Lei Q, Li W, Wang X, Liu W, Li W. Epidemiological and clinical characteristics of 1663 hospitalized patients infected with COVID-19 in Wuhan, China. *SSRN* 2020; published online April 08. https://doi.org/10.2139/ssrn.3562482 [preprint].
194. Yu M, Xu D, Lan L, et al. Thin-section chest CT imaging of coronavirus disease 2019 pneumonia: Comparison between patients with mild and severe disease. *Radiology* 2020; **2**: 2.
195. Yu T, Cai S, Zheng Z, et al. Association between clinical manifestations and prognosis in patients with COVID-19. *Clin Ther* 2020; published online April 27. https://doi.org/10.1016/j.clinthera.2020.04.009
196. Yuan M, Yin W, Tao Z, Tan W, Hu Y. Association of radiologic findings with mortality of patients infected with 2019 novel coronavirus in Wuhan, China. *PLoS One* 2020; **15**(3): e0230548.
197. Zhang L, Yan X, Fan Q, et al. D- dimer levels on admission to predict in-hospital mortality in patients with Covid- 19. *J Thromb Haemost* 2020; **18**: 1324-1329.
198. Zeng L, Li J, Liao M, et al. Risk assessment of progression to severe conditions for patients with COVID-19 pneumonia: A single-center retrospective study. *medRxiv* 2020; published online March 30. https://doi.org/10.1101/2020.03.25.20043166 [preprint].
199. Zeng Z, Sha T, Zhang Y, et al. Hypertension in patients hospitalized with COVID-19 in Wuhan, China: A single-center retrospective observational study. *medRxiv* 2020; published online April 11. https://doi.org/10.1101/2020.04.06.20054825 [preprint].
200. Zhang F, Yang D, Li J, et al. Myocardial injury is associated with in-hospital mortality of confirmed or suspected COVID-19 in Wuhan, China: A single center retrospective cohort study. *medRxiv* 2020; published online March 24. https://doi.org/10.1101/2020.03.21.20040121 [preprint].
201. Zhang G, Chang H, Linjie L, et al. Clinical features and outcomes of 221 patients with COVID-19 in Wuhan, China. *medRxiv* 2020; published online March 06. https://doi.org/10.1101/2020.03.02.20030452 [preprint].
202. Zhang G, Zhang J, Wang B, et al. Analysis of clinical characteristics and laboratory findings of 95 cases of 2019 novel coronavirus pneumonia in Wuhan, China: A retrospective analysis. *Respir Res* 2020; **21:** 74.
203. Zhang H, Xiaoying W, Zongqiang F, et al. Potential factors for prediction of disease severity of COVID-19 patients. *medRxiv* 2020; published online March 23. https://doi.org/10.1101/2020.03.20.20039818 [preprint].
204. Zhang H-Y, Wang L-W, Chen Y-Y, et al. A Multicentre Study of 2019 Novel Coronavirus Disease Outcomes of Cancer Patients in Wuhan, China. *medRxiv* 2020; published online April 15. https://doi.org/10.1101/2020.03.21.20037127 [preprint].
205. Zhang J, Peng L, Morong W, et al. The clinical data from 19 critically ill patients with coronavirus disease 2019: A single-centered, retrospective, observational study. *J Publ Health* 2020; published online April 21. https://doi.org/10.1007/s10389-020-01291-2
206. Zhang JJ, Dong X, Cao Y, et al. Clinical characteristics of 140 patients infected with SARS- CoV- 2 in Wuhan, China. *Eur J Allergy Clin Immunol* 2020; **00**: 1–12.

207. Zhang L, Tao B, Yu J, et al. Digestive involvement of the coronavirus disease 2019: Need attention on the "gut-type" in the novel coronaviral infection. *SSRN* 2020; published online April 06. https://doi.org/10.2139/ssrn.3559590 [preprint].
208. Zhang L, Tao B, Yu J, et al. Diarrhea in patients with coronavirus disease 2019: Clinical characteristics, outcomes and implications. *SSRN* 2020; published online April 09. https://doi.org/10.2139/ssrn.3566201 [preprint].
209. Zhang L, Wenwu S, Liangkai C, et al. Clinical features and a simple model for predicting the mortality of coronavirus disease 2019 patients on admission. *SSRN* 2020; published online March 23. https://doi.org/10.2139/ssrn.3551386 [preprint].
210. Zhang L, Zhu F, Xie L, et al. Clinical characteristics of COVID-19-infected cancer patients: A retrospective case study in three hospitals within Wuhan, China. *Ann Oncol* 2020; published online March 25. https://doi.org/10.1016/j.annonc.2020.03.296
211. Zhang P, Zhu L, Cai J, et al. Association of inpatient use of angiotensin converting enzyme inhibitors and angiotensin II receptor blockers with mortality among patients with hypertension. *Circ Res AHA* 2020; **126** (12):1671-1681.
212. Zhang R, Huangqing O, Lingli F, et al. CT features of SARS-CoV-2 pneumonia according to clinical presentation: A retrospective analysis of 120 consecutive patients from Wuhan City. *Eur Radiol* 2020; published online April 11. https://doi.org/10.1007/s00330-020-06854-1
213. Zhang S, Guo M, Duan L, et al. Short term outcomes and risk factors for mortality in patients with COVID-19 in Wuhan, China: A retrospective study. *SSRN* 2020; published online March 23. http://dx.doi.org/10.2139/ssrn.3551390 [preprint].
214. Zhang S, Zhao J, Wu Z, et al. Potential predictors for disease progression and medication evaluation of 2019 novel coronavirus-infected pneumonia in Wuhan, China. *SSRN* 2020; published online March 23. https://doi.org/10.2139/ssrn.3551399 [preprint].
215. Zhang X, Guo W, Hua J, et al. The incidence, risk factors and clinical outcomes of acute kidney injury in critically ill patients with COVID-19: A multicenter study. *SSRN* 2020; published online April 23. http://dx.doi.org/10.2139/ssrn.3572908 [preprint].
216. Zhang X, Huan C, Jianhua H, et al. Epidemiological, clinical characteristics of cases of SARS-CoV-2 infection with abnormal imaging findings. *Int J Infect Dis* 2020; **94**: 81–87.
217. Zhang Y, Yanhui C, Minxue S, et al. Comorbid diabetes mellitus was associated with poorer prognosis in patients with COVID-19: A retrospective cohort study. *medRxiv* 2020; published online March 26. https://doi.org/10.1101/2020.03.24.20042358 [preprint].
218. Zhao, W, Zheng Z, Qizhi Y, Xie X, Liu J. Clinical outcomes of patients with 2019-NCoV: A preliminary summary. *SSRN* 2020; published online February 25. https://doi.org/10.2139/ssrn.3542167 [preprint].
219. Zhao W, Shikai Y, Xiangyi Z, et al. Clinical characteristics and durations of hospitalized patients with COVID-19 in Beijing: A retrospective cohort study. *medRxiv* 2020; published online March 30. https://doi.org/10.1101/2020.03.13.20035436 [preprint].
220. Zhen L, Ming W, Jiwei Y, et al. Caution on kidney dysfunctions of COVID-19 patients. *medRxiv* 2020; published online March 27. https://doi.org/10.1101/2020.02.08.20021212 [preprint].

221. Zheng F, Tang W, Li H,Huang YX, Xie YL, Zhou ZG. Clinical characteristics of 161 cases of corona virus disease 2019 (COVID-19) in Changsha. *Eur Rev Med Pharmacol Sci* 2020; **24**(6): 3404–10.
222. Zheng X, Jiehua C, Lisi D, et al. Clinical features and risk factors for the severity of inpatients with COVID-19: A retrospective cohort study. *SSRN* 2020; published online April 6. https://doi.org/10.2139/ssrn.3562460 [preprint].
223. Zhou B, She J, Wang Y, Ma X. The clinical characteristics of myocardial injury in severe and very severe patients with 2019 novel coronavirus disease. *SSRN* 2020; published online February 19. https://doi.org/10.2139/ssrn.3539668 [preprint].
224. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: A retrospective cohort study. *Lancet* 2020; **395**: 1054-62.
225. Zhou H, Zhang Z, Fan H, et al. Urinalysis, but not blood biochemistry, detects the early renal-impairment in patients with COVID-19. *SSRN* 2020; published online April 16. http://dx.doi.org/10.2139/ssrn.3569863 [preprint].
226. Zhou H, Wanxin C, Ziping L, et al. Delayed-phase thrombocytopenia in patients of coronavirus disease 2019 (COVID-19). *medRxiv* 2020; published online April 15. https://doi.org/10.1101/2020.04.11.20059170 [preprint].
227. Zhou M, Xu J, Hao X, et al. A 'Burning Point' is found before the composite end point event happened in critically ill patients with COVID-19: A multicenter retrospective study. *SSRN* 2020; published online April 20 . https://ssrn.com/abstract=3572864 [preprint].
228. Zhou Y, Zhen Y, Yanan G, et al. A new predictor of disease severity in patients with COVID-19 in Wuhan, China. *Respir Med* 2020; published online March 27. https://doi.org/10.1101/2020.03.24.20042119 [preprint].
229. Zhu B, Chunguo J, Xiaokai F, et al. Correlation between fasting blood glucose level at admission and mortality in COVID-19 patients: A retrospective study. *BMC Infect Dis* 2020; published online March 24. https://doi.org/10.21203/rs.3.rs-18484/v1 [preprint].
230. Zhu Q, Zhao S, Lai X, et al. Dose-response association between risk factors and incidence of COVID-19 in 325 hospitalized patients: A multicenter retrospective cohort study. *SSRN* 2020; published online April 08. https://doi.org/10.2139/ssrn.3562478 [preprint].
231. Li B, Yang J, Zhao F,et al. Prevalence and impact of cardiovascular metabolic diseases on COVID-19 in China. *Clin Res Cardiol* 2020; **109**: 531–538.
232. Lippi G, Lavie CJ, Sanchis-Gomar F. Cardiac troponin I in patients with coronavirus disease 2019 (COVID-19): Evidence from a meta-analysis. *Prog Cardiovasc Dis* 2020; published online March 10. https://doi.org/10.1016/j.pcad.2020.03.001
233. Lippi G, Plebani M. Procalcitonin in patients with severe coronavirus disease 2019 (COVID-19): A meta-analysis. *Clin Chim Acta* 2020; **505**: 190-191.
234. Ji W, Zhang J, Bishnu G, et al. Comparison of severe and non-severe COVID-19 pneumonia: Review and meta-analysis. *medRxiv 202*0; published online March 09. https://doi.org/10.1101/2020.03.04.20030965 [preprint].
235. Jain V, and Yuan J-M. Systematic review and meta-analysis of predictive symptoms and comorbidities for severe COVID-19 infection. *medRxiv* 2020; published online March 16. https://doi.org/10.1101/2020.03.15.20035360 [preprint].

236. Lippi G, and Henry BM. Active smoking is not associated with severity of coronavirus disease 2019 (COVID-19). *Eur J Intern Med* 2020; **75**: 107-108.
237. Lippi G, Henry BM. Chronic obstructive pulmonary disease is associated with severe coronavirus disease 2019 (COVID-19). *Respir Med* 2020; **167**: 105941.
238. Lippi G, Plebani M, and Henry BM. Thrombocytopenia is associated with severe coronavirus disease 2019 (COVID-19) infections: A meta-analysis. *Clin Chim Acta* 2020; **506**:145-148.
239. Zhao X, Zhang B, Li P, et al. Incidence, clinical characteristics and prognostic factor of patients with COVID-19: A systematic review and meta-analysis. *medRxiv* 2020; published online March 20. https://doi.org/10.1101/2020.03.17.20037572 [preprint].
240. Ebrahimi M, Saki A, and Rahim F. Laboratory findings, signs and symptoms, clinical outcomes of patients with COVID-19 infection: An updated systematic reeview and meta-analysis. *medRxiv* 2020; published online March 30. https://doi.org/10.1101/2020.03.25.20043703 [preprint].
241. Henry BM, Lippi G. Chronic kidney disease is associated with severe coronavirus disease 2019 (COVID-19) infection. *Int Urol Nephrol* 2020; **52**:1193-1194.
242. Wang B, Li B, Lu Z, Huang Y. Does comorbidity increase the risk of patients with COVID-19: Evidence from meta-analysis. *Aging* 2020; **12**(7).
243. Xiong M, Liang X, Wei YD. Changes in blood coagulation in patients with severe coronavirus disease 2019 (COVID- 19): A meta- analysis. *Br J Haematol* 2020; published online May 14. https://doi.org/10.1111/bjh.16725
244. Santoso A, Pranata R, Wibowo A, et al. Cardiac injury is associated with mortality and critically ill pneumonia in COVID-19: A meta-analysis. *Am J Emerg Med* 2020; published online April 19. https://doi.org/10.1016/j.ajem.2020.04.052
245. Kumar A, Arora A, Sharma P, et al. Clinical features of COVID-19 and factors associated with severe clinical course: A systematic review and meta-analysis. *SSRN* 2020; published online April 21. https://doi.org/10.2139/ssrn.3566166 [preprint].
246. Ali A, Mohamed S, Elkhidir I, et al. The association of lymphocyte count and levels of CRP, D-Dimer, and LDH with severe coronavirus disease 2019 (COVID-19): A meta-analysis. *medRxiv* 2020; published online April 24. https://doi.org/10.1101/2020.04.20.20072801 [preprint].
247. Aggarwal G, Lippi G, Michael Henry B. Cerebrovascular disease is associated with an increased disease severity in patients with coronavirus disease 2019 (COVID-19): A pooled analysis of published literature. *Int J Stroke* 2020; **15**: 4.
248. Wang X, Fang X, Cai Z, et al. Comorbid chronic diseases and acute organ injuries are strongly correlated with disease severity and mortality among COVID-19 patients: A systematic review and meta-analysis. *Research* 2020; **2020**:2402961.
249. Han P, Diao K, Pang T, Huang S, Yang Z. Comparison of clinical features between critically and non-critically Ill patients in SARS and COVID-19: A systematic review and meta-analysis. *SSRN* 2020; published online April 09. https://doi.org/10.2139/ssrn.3566133 [preprint].
250. Zheng Z, Peng F, Xu B, et al. Risk factors of critical & mortal COVID-19 cases: A systematic literature review and meta-analysis. *J Infect* 2020; **15**: 12.

251. Docherty AB, Harrison EM, Green CA, et al. Features of 20 133 UK patients in hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: prospective observational cohort study. *BMJ-Brit Med J*; **369**: m1985.
252. The OpenSAFELY Collaborative, Williamson E, Walker AJ, Bhaskaran KJ, et al. OpenSAFELY: Factors associated with COVID-19-related hospital death in the linked electronic health records of 17 million adult NHS patients. *medRxiv* 2020; published online May 07. https://doi.org/10.1101/2020.05.06.20092999 [preprint].
253. Deng G, Yin M, Chen X, Zeng F. Clinical determinants for fatality of 44,672 patients with COVID-19. *Crit Care*. 2020; **24**(1): 179.

Figures and tables

Figure 1. PRISMA (preferred reporting items for systematic reviews and meta-analyses) flowchart of study inclusions
and exclusions.

Table 1. Prognostic factors for mortality and/or severe COVID-19 disease

Figure 1.

PRISMA Flow Diagram

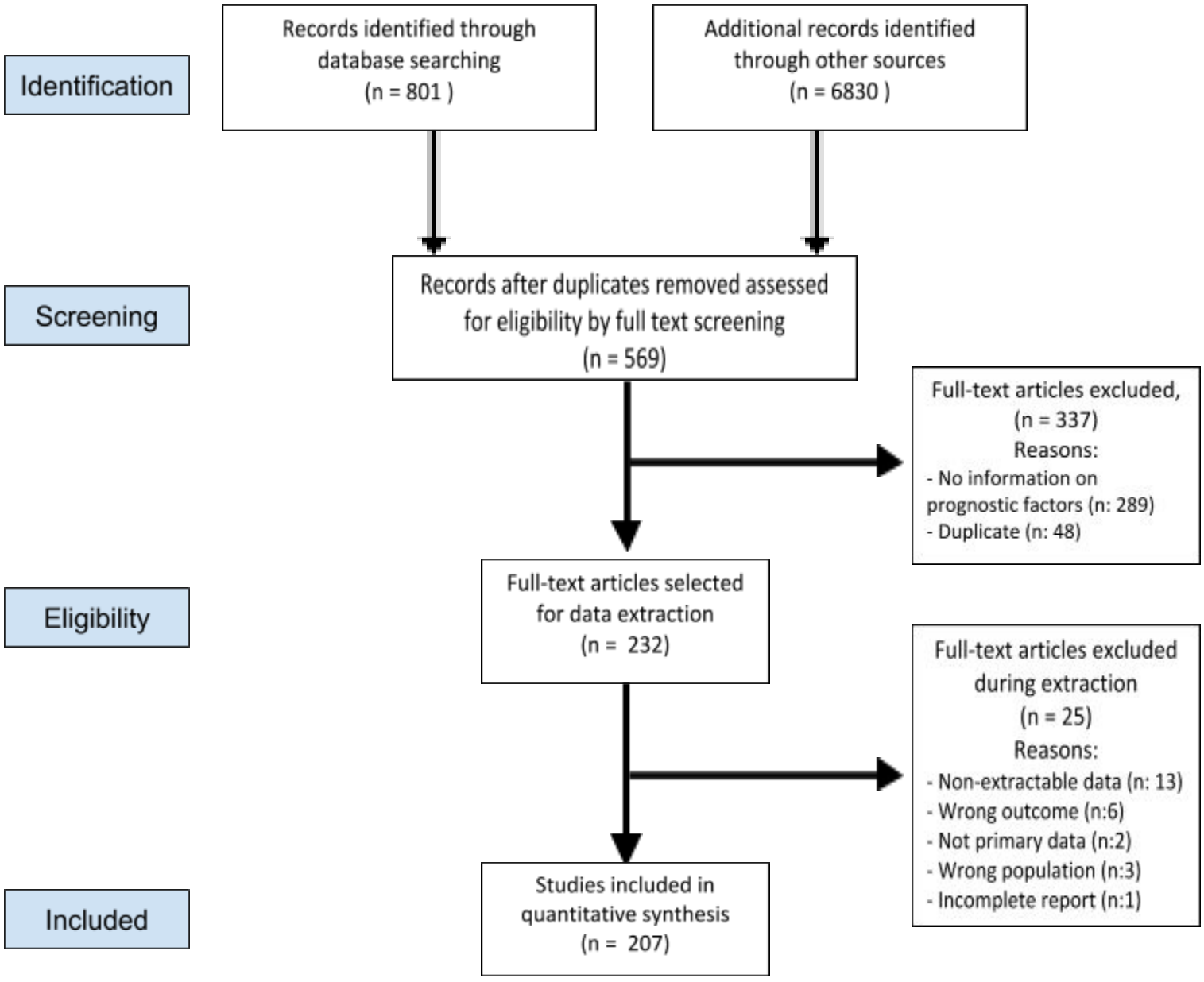

Table 1· Prognostic factors for mortality and/or severe COVID-19 disease

Prognostic factor	Mortality					Severe COVID-19 disease				
	Number of patients (studies)	Odds ratio (95%CI)	Risk without prognostic factor	Risk with prognostic factor	Certainty of the evidence	Number of patients (studies)	Odds ratio (95%CI)	Risk without prognostic factor	Risk with prognostic factor	Certainty of the evidence
Socio-demographic characteristics										
Age Definition: 10 years increase	11962 (19)	1·80 (1·54-2·10)	9%	15·1%	⊕⊕⊕⊕ HIGH	14456 (53)	1·63 (1·47-1·80)	13%	19·6%	⊕⊕⊕⊕ HIGH
			6·1% increase in mortality. Between 4·2% more and 8·2% more					6·6% increase in severe COVID-19 disease. Between 5% more and 8·2% more		
Sex Definition: Male	31948 (58)	1·72 (1·5-1·98)	8%	13%	⊕⊕⊕◯ MODERATE[d]	25032 (122)	1·53 (1·4-1·67)	10·8%	15·5%	⊕⊕⊕⊕ HIGH
			5% increase in mortality. Between 4% more and 7% more					4·7% increase in severe COVID-19 disease. Between 3·7% more and 5·6% more		
Smoking Definition: Active, present smoker	12025 (16)	1·57 (1·19-2·07)	8·7%	13%	⊕⊕⊕⊕ HIGH	9147 (45)	1·65 (1·25-2·17)	12·1%	18·4%	⊕⊕⊕◯ MODERATE [d]
			4·3% increase in mortality. Between 1·5% more and 7·5% more					6·3% increase in severe COVID-19 disease. Between 2·7% more and 10·2% more		
Medical illness and patient history										
Any chronic condition or comorbidities	4406 (16)	3·3 (2·18-5)	5·9%	16·2%	⊕⊕⊕◯ MODERATE [a]	6640 (40)	3·16 (2·71-3·68)	8·2%	20·1%	⊕⊕⊕⊕ HIGH

			10·3% increase in mortality. Between 6·8% more and 13·4% more				12% increase in severe COVID-19 disease. Between 10·6% more and 13·2% more		
Cerebrovascular disease Definition: History of stroke or CNS disease	15294 (26)	2·85 (2·02-4·01)	8·7%	21·3%	⊕⊕⊕⊕ HIGH	11050 (42)	2·67 (1·84-3·87)	12·7%	27·8%	⊕⊕⊕◯ MODERATE [d]
			12·6% increase in mortality. Between 7·5% more and 18·5% more					15·1% increase in severe COVID-19 disease. Between 8·4% more and 22·8% more		
COPD	34759 (41)	2·43 (1·88-3·14)	8·5%	18·4%	⊕⊕⊕⊕ HIGH	15468 (65)	2·7 (2·14-3·4)	12·6%	27·9%	⊕⊕⊕⊕ HIGH
			9·8% increase in mortality. Between 6·4% more and 13·6% more					15·3% increase in severe COVID-19 disease. Between 11% more and 20% more		
Chronic kidney disease Definition: KDIGO definition of CKD	23448 (28)	2·27 (1·69-3·05)	8·5%	17·2%	⊕⊕⊕⊕ HIGH	12056 (42)	2·21 (1·51-3·24)	12·8%	24·5%	⊕⊕◯◯ LOW [a,d]
			8·8% increase in mortality. Between 5·1% more and 12·9% more					11·7% increase in severe COVID-19 disease. Between 5·4% more and 19·2% more		
Cardiovascular disease Definition: Coronary heart disease or congestive heart failure	37156 (51)	2·12 (1·77-2·56)	8·1%	15·5%	⊕⊕⊕◯ MODERATE [d]	16679 (73)	3·34 (2·71-4·1)	12·2%	31·3%	⊕⊕⊕◯ MODERATE [d]
			7·5% increase in mortality. Between 5·4% more and 9·7% more					19·1% increase in severe COVID-19 disease. Between 15·1% more and 23·1% more		
Cardiac arrhythmia	12729 (6)	2·13 (1·72-2·65)	7%	13·6%	⊕⊕⊕⊕ HIGH	747 (4)	16·51 (6·69-40·77)	6·5%	35·5%	⊕⊕◯◯ LOW [a,c,e]
			6·5% increase in mortality. Between 4·7% more and 8·4% more					29% increase in severe COVID-19 disease. Between 22·6% more and 32·3% more		

Arterial hypertension	31341 (52)	2·02 (1·71-2·38)	7%	13%	⊕⊕⊕⊕ HIGH	20817 (94)	2·5 (2·21-2·92)	11·1%	23·3%	⊕⊕⊕◯ MODERATE[d]
			6% increase in mortality. Between 4·5% more and 7·3% more					12·1% increase in severe COVID-19 disease. Between 10·4% more and 14·4% more		
Diabetes	30303 (52)	1·84 (1·61-2·1)	7·9%	13·6%	⊕⊕⊕⊕ HIGH	21381 (97)	2·51 (2·2-2·87)	12%	25·2%	⊕⊕⊕⊕ HIGH
			5·6% increase in mortality. Between 4·3% more and 7% more					13·2% increase in severe COVID-19 disease. Between 11% more and 15·5% more		
Dementia	8922 (3)	1·54 (1·31-1·81)	9%	13·2%	⊕⊕⊕⊕ HIGH	0 (0)	NA	NA	NA	NA
			4·2% increase in mortality. Between 2·5% more and 6·2% more					NA		
Obesity: BMI > 25-30	9127 (3)	1·41 (1·15-1·74)	8·5%	11·5%	⊕⊕⊕⊕ HIGH	1140 (8)	3·74 (2·37-5·89)	10·2%	35%	⊕⊕⊕⊕ HIGH
			3·1% increase in mortality. Between 1·2% more and 5·1% more					24·8% increase in severe COVID-19 disease. Between 1·4% more and 42·2% more		
Cancer Definition: Solid or active haematologic cancer	22734 (25)	1·35 (1·17-1·55)	8·9%	11·6%	⊕⊕⊕⊕ HIGH	15156 (58)	2·06 (1·64-2·58)	12·8%	23·2%	⊕⊕⊕◯ MODERATE[d]
			2·7% increase in mortality. Between 1·4% more and 4·2% more					10·4% increase in severe COVID-19 disease. Between 6·6% more and 14·5% more		
Dyslipidemia	11273 (4)	1·26 (1·06-1·5)	8·9%	11%	⊕⊕⊕◯ MODERATE[b]	559 (4)	0·63 (0·22-1·83)	13·1%	8·7%	⊕⊕◯◯ LOW [a,b]

			2·1% increase in mortality. Between 0·5% more and 3·9% more				4·4% decrease in severe COVID-19 disease. Between 10% less and 8·3% more		
Clinical signs/symptoms									
Respiratory failure Definition: increased respiratory rate, abnormal blood gases (hypoxemia, hypercapnia, or both), and evidence of increased work of breathing	1887 (8)	21·17 (4·9-91·3)	3·1%	23·4%	⊕⊕⊕◯ MODERATE[a]	1156 (7)	23·21 (12·07 - 44·62)	NA	NA	NA
			20·3% increase in mortality. Between 13·4% more and 22·4% more					NA		
Low blood pressure Definition SBP less than 90-100 mmHg	1269 (2)	6·7 (3·14-14·33)	9%	39·9%	⊕⊕⊕◯ MODERATE[a]	480 (2)	1·29 (0·72-2·29)	NA	NA	NA
			30·9% increase in mortality. Between 14·7% more and 49·6% more					NA		
Hypoxemia Definition: Low digital saturation (below 90-93%)	1047 (5)	5·46 (2·05-14·53)	2·3%	9·1%	⊕⊕⊕◯ MODERATE[a]	1331 (5)	4·69 (1·56-14·09)	NA	NA	NA
			6·7% increase in mortality. Between 4·2% more and 7·7% more					NA		
Tachycardia Definition: More than 90-100 bpm	1269 (2)	2·61 (1·62-4·22)	9%	20·5%	⊕⊕⊕◯ MODERATE[a]	78 (1)	1·54 (0·31-7·58)	13%	18·7%	⊕◯◯◯ VERY LOW[a,f]
			11·5% increase in mortality. Between 4·8% more and 20·4% more					5·7 % increase in severe COVID-19 disease. Between 8·6% less and 40·1% more		

Dyspnea Definition: Dyspnea or shortness of breath	6613 (28)	3·45 (2·72-4·38)	4·9%	13·8%	⊕⊕⊕⊕ HIGH	16803 (78)	4·23 (3·32-5·38)	9·3%	27·8%	⊕⊕◯◯ LOW[a,d]
			8·9% increase in mortality. Between 7·5% more and 10·2% more					18·5 % increase in severe COVID-19 disease. Between 15·4% more and 21·3% more		
Anorexia	1483 (8)	2·16 (1·14-4·12)	7·3%	14·4%	⊕⊕⊕◯ MODERATE[c]	5495 (26)	2·86 (2·16-3·84)	10·4%	24%	⊕⊕⊕◯ MODERATE[a]
			7% increase in mortality. Between 1·1% more and 13·1% more					13·6% increase in severe COVID-19 disease. Between 9·8% more and 17·5% more		
Tachypnea Definition: More than 20-24 bpm	202 (1)	1·21 (1·12-1·31)	7·6%	9%	⊕⊕⊕◯ MODERATE[a]	518 (7)	7·51 (1·66-33·91)	13%	52·9%	⊕⊕⊕◯ MODERATE[d]
			1·4% increase in mortality. Between 0·9% more and 1·9% more					39·9% increase in severe COVID-19 disease. Between 6·9% more and 70·5% more		
Haemoptysis	781 (5)	2·91 (0·74-11·4)	8·3%	20·6%	⊕⊕◯◯ LOW[a,b]	3317 (14)	4·39 (2·18--8·81)	12·7%	38·6%	⊕⊕⊕◯ MODERATE[a]
			12·3% increase in mortality. Between 2·2% less and 34·6% more					25·9% increase in severe COVID-19 disease. Between 11·4% more and 42·1% more		
Abdominal pain	1127 (5)	1·06 (0·53-2·11)	9%	9·5%	⊕⊕◯◯ LOW[a,b]	4896 (22)	1·95 (1·36-2·79)	12·7%	22%	⊕⊕⊕◯ MODERATE[a]
			5% increase in mortality. Between 4% less and 8% more					9·4% increase in severe COVID-19 disease. Between 4% more and 15·8% more		
Fatigue	3725 (21)	1·66 (1·27-2·17)	7·1%	11·1%	⊕⊕◯◯ LOW[a,d]	13262 (71)	1·41 (1·19-1·68)	11·6%	15·5%	⊕⊕⊕◯ MODERATE[d]

			4% increase in mortality. Between 1·9% more and 5·9% more·					3·9% increase in severe COVID-19 disease. Between 2% more and 5·9% more·		
Fever· Definition: More than 37·5°C	6154 (31)	1·04 (0·77-1·4)	8·7%	9·1%	⊕⊕◯◯ LOW[a,b]	20026 (102)	1·84 (1·54-2·21)	9·3%	15·4%	⊕⊕⊕◯ MODERATE[d]
			0·3% increase in mortality. Between 2·3% less and 2·5% more					6·1% increase in severe COVID-19 disease. Between 4·5% more and 7·6% more		
Myalgia/arthralgia Definition: myalgia or arthralgias	3436 (18)	0·96 (0·77-1·23)	9·1%	8·7%	⊕⊕◯◯ LOW[a,b]	13814 (61)	1·29 (1·03-1·61)	12·5%	15·6%	⊕⊕⊕◯ MODERATE[d]
			0·3% decrease in mortality. Between 2% less and 1·8% more					3% increase in severe COVID-19 disease. Between 0·3% more and 5·9% more		
Laboratory measures										
High blood procalcitonin Definition: More than 0·01-05 ng/ml	4735 (10)	12·42 (7·18-21·5)	6·3%	38·5%	⊕⊕⊕◯ MODERATE[c]	7923 (28)	5·13 (3·16-8·35)	10·6%	35·4%	⊕⊕◯◯ LOW[a,d]
			32·3% increase in mortality. Between 25% more and 38·1% more					24·8% increase in severe COVID-19 disease. Between 16·7% more and 32·3% more		
Myocardial injury Definition: Reported as myocardial injury or as increase in blood troponins	3855 (21)	10·89 (5·39-22·04)	3·5%	20·4%	⊕⊕⊕◯ MODERATE[d]	3627 (20)	10 (6·84-14·62)	11·1%	51·3%	⊕⊕⊕⊕ HIGH
			16·9% increase in mortality. Between 13·4% more and 19% more					40·2% increase in severe COVID-19 disease. Between 33·1% more and 46·4% more		
High WBC Definition: greater than	2870 (10)	4·06 (2·7-6·12)	7·8%	24·7%	⊕⊕⊕◯ MODERATE[d]	9331 (32)	4·67 (3·17-6·88)	11·2%	35·6%	⊕⊕⊕⊕ HIGH

10·0 x 10^9/L			16·9% increase in mortality. Between 11% more and 23·3% more					24·3% increase in severe COVID-19 disease. Between 17·3% more and 31·2% more		
High blood lactate: Definition More than 1·5-2·2 mmol/L	1078 (1)	3·66 (2·26-5·94)	7·3%	21·7%	⊕⊕⊕◯ MODERATE[a]	812 (3)	3·74 (0·69-20·16)	12·1%	33·3%	⊕◯◯◯ VERY LOW [a,b,d]
			14·3% increase in mortality. Between 8·3% more and 20·6% more					21·2% increase in severe COVID-19 disease. Between 3·7% less and 51·4% more		
Low platelet count Definition: Less than 100-150 x 10^9/L	3676 (10)	5·43 (2·55-11·56)	5%	19·3%	⊕⊕⊕⊕ HIGH	8081 (32)	1·93 (1·52-2·46)	11·1%	19·2%	⊕⊕◯◯ LOW[a,d]
			14·3% increase in mortality. Between 8·3% more and 18·6% more					8% increase in severe COVID-19 disease. Between 5% more and 11·1% more		
High blood D-dimer Definition: More than 500-1000 ng/ml	4361 (17)	4·81 (3·15-7·34)	4·3%	15·6%	⊕⊕⊕◯ MODERATE[d]	6356 (24)	3·27 (2·46-4·36)	8·2%	20·7%	⊕⊕⊕◯ MODERATE[d]
			11·2% increase in mortality. Between 8·8% more and 13·1% more					12·5% increase in severe COVID-19 disease. Between 9·8% more and 14·8% more		
High blood LDH Definition: More than 240-250 U/L	1440 (6)	4·09 (1·18-14·17)	4·7%	15·2%	⊕⊕⊕◯ MODERATE[d]	7955 (26)	4·48 (3·21-6·25)	7·8%	23·9%	⊕⊕⊕◯ MODERATE[d]
			10·4% increase in mortality. Between 1·4% more and 15·3% more					16·2% increase in severe COVID-19 disease. Between 13·1% more and 18·8% more		
High blood CRP Definition:	2107 (8)	6·6 (3·36-12·99)	2·3%	10·3%	⊕⊕⊕◯ MODERATE[d]	9094 (37)	4·5 (3·1-6·23)	6·3%	19·5%	⊕⊕⊕⊕ HIGH

More than 1-100 mg/l			7·9% increase in mortality. Between 6·4% more and 8·7% more				13·2% increase in severe COVID-19 disease. Between 10·8% more and 14·9% more		
Decrease in Lymphocyte count Definition: per 1 x 10^9 U/L decrease	544(3)	3·57 (2-6·67)	9%	26·1%	⊕⊕⊕◯ MODERATE[d]	1909 (7)	2·28 (1·21-4·30)	13%	25·4%	⊕⊕⊕◯ MODERATE[d]
			17·1% increase in mortality. Between 7·5% more and 30·7% more					12·4% increase in severe COVID-19 disease. Between 2·3% more and 26·1% more		
High blood AST level Definition: More than 32-40 U/l	2969 (7)	3·5 (1·59-7·71)	6%	17·1%	⊕⊕⊕◯ MODERATE[d]	9179 (32)	3·41 (2·7-4·3)	9·9%	25·8%	⊕⊕⊕◯ MODERATE[a]
			11·1% increase in mortality. Between 4% more and 16·8% more					15·8% increase in severe COVID-19 disease. Between 12·7% more and 18·8% more		
Decrease in blood albumin: Definition: 20 g/L decrease	336 (3)	1·53 (1·32-1·78)	9%	13·2%	⊕⊕⊕◯ MODERATE[c]	1266 (5)	1·11 (1·01-1·21)	13%	14·2%	⊕⊕⊕◯ MODERATE[b]
			4·2% increase in mortality. Between 2·5% more and 6% more					1·2% increase in severe COVID-19 disease. Between 0·1% more and 2·3% more		
Increase in plasma creatinine Definition: per 1 mg% increase	1508 (9)	1·14 (1·02-1·28)	9%	10·1%	⊕⊕⊕◯ MODERATE[b]	1116 (4)	1·89 (0·87-4·10)	13%	22%	⊕⊕⊕◯ MODERATE[b]
			1·1% increase in mortality. Between 0·2% more and 2·3% more					9% increase in severe COVID-19 disease. Between 1·5% less and 25% more		
High Neutrophil count Definition: greater than 6·3 x 10^9/L	727 (2)	6·78 (3·07-14·97)	5·2%	23%	⊕⊕◯◯ LOW[a,c]	4945 (16)	5·66 (3·71-8·63)	9%	31%	⊕⊕⊕◯ MODERATE[a]
			17·8% increase in mortality. Between 10% more and 23% more					22% increase in severe COVID-19 disease. Between 17% more and 27% more		

High blood BNP: More than 500-900 pg/mL	1283 (6)	3·27 (1·24-8·63)	7%	19%	⊕⊕◯◯ LOW[a,d]	1086 (1)	4·99 (3·2-7·77)	9·4%	30·9%	⊕⊕⊕◯ MODERATE[a]
			12% increase in mortality. Between 1·9% more and 21·9% more					21·5% increase in severe COVID-19 disease. Between 15·5% more and 26·7% more		
High BUN Definition: mmol/L, > 5·2-9·5	1258 (2)	10·56 (6·76-16·48)	5·2%	29·6%	⊕⊕◯◯ LOW[a,c,e]	3890 (10)	3·66 (2·82-4·74)	11·1%	30·2%	⊕⊕⊕◯ MODERATE[a]
			24·4% increase in mortality. Between 20·2% more and 27·7% more					19·1% increase in severe COVID-19 disease. Between 14·8% more and 23·4% more		
High blood CPK Definition: More than 185-200 U/L	407 (3)	1·35 (0·58-3·14)	8·8%	11·5%	⊕⊕◯◯ LOW[a,b]	3292 (13)	3·1 (2·32-4·16)	11·5%	28·1%	⊕⊕⊕◯ MODERATE[a]
			2·7% increase in mortality. Between 3·7% less and 13% more					16·5% increase in severe COVID-19 disease. Between 11·7% more and 21·6% more		
High blood total bilirubin Definition: More than 17-21 pg/ml	2715 (3)	3·03 (1·87-4·92)	8·1%	20·7%	⊕⊕◯◯ LOW[a,c]	5098 (14)	2·94 (2·18--3·97)	12·5%	29·3%	⊕⊕⊕◯ MODERATE[a]
			12·6% increase in mortality. Between 6·3% more and 19·9% more					16·8% increase in severe COVID-19 disease. Between 11·3% more and 22·9% more		
High blood interleukin-6 Definition: More than 5-20 pg/ml	436 (4)	1·31 (0·14-12·27)	8·1%	10·3%	⊕⊕◯◯ LOW[a,b]	1211 (7)	7·36 (2·97-18·27)	6·5%	26·2%	⊕⊕⊕◯ MODERATE[a]
			2·2% increase in mortality. Between 11·6% less and 15% more					19·7% increase severe COVID-19 disease. Between 12·2% more and 23·9% more		

High ESR Definition More than 10-20 mm/H	628 (3)	0·89 (0·54-1·45)	9·7%	8·7%	⊕⊕◯◯ LOW[a,b]	2557 (12)	3·08 (2·04-4·65)	6·6%	15·6%	⊕⊕⊕◯ MODERATE[a]
			1% decrease in mortality. Between 5·6% less and 2·8% more					9·4% increase in severe COVID-19 disease. Between 6·7% more and 11·3% more		
Radiological signs										
Pleural effusion Definition: X ray or CT assessment	820 (5)	1·38 (0·63-3·06)	8·8%	11·7%	⊕⊕◯◯ LOW[a,b]	5289 (23)	3·31 (2·03-5·38)	12·5%	32%	⊕⊕⊕◯ MODERATE[d]
			3% decrease in mortality. Between 3% less and 13% more					19% increase in severe COVID-19 disease. Between 10% more and 30% more		
Consolidation pattern Definition: X ray or CT assessment	795 (4)	1·93 (1·31-2·84)	7·5%	13%	⊕⊕◯◯ LOW[a,c]	6133 (27)	2·46 (1·54-3·93)	11·2%	23·2%	⊕⊕⊕◯ MODERATE[d]
			5·8% increase in mortality. Between 2·3% more and 9·4% more					12% increase in severe COVID-19 disease. Between 5·4% more and 18·8% more		
Others										
High SOFA score Definition: More than 2	585 (3)	1·97 (1·22-3·2)	9%	16·3%	⊕⊕⊕◯ MODERATE[d]	92 (2)	21·31 (6·26-72·6)	13%	76·1%	⊕⊕◯◯ LOW[a,c]
			7·3% increase in mortality. Between 1·8% more and 15% more					63% increase in severe COVID-19 disease. Between 35·3% more and 78·6% more		

Glossary

FDP: Fibrin Degradation Product

PT: prothrombin time
APTT: activated partial thromboplastin time
APACHE: Acute Physiology And Chronic Health Evaluation II
SOFA: The sequential organ failure assessment score
qSOFA: quick sepsis related organ failure assessment
AST: Aspartate aminotransferase
ALT: Alanine aminotransferase
BUN: Blood urea nitrogen

Explanations

a. Risk of bias due to study limitations (unadjusted estimates, inappropriate prognostic factor or outcome assessment, inappropriate population inclusion criteria, study attrition)
b. Imprecision: confidence interval includes significant and non-significant risk increase
c. Imprecision due to fragility: less than 200 events
d. Inconsistency: unexplained visual heterogeneity
e. Risk of selective reporting: most of the pooled estimate weight from studies that performed multivariable analysis but did not report adjusted estimates·
f. Very serious imprecision: very wide confidence interval

Supplementary materials

Methods

Search strategy

Search strategy for Pubmed/MEDLINE
Search date: 29.04.2020
#1 coronavir*
#2 coronovirus*
#3 "corona virus"
#4 "virus corona"
#5 "corono virus"
#6 "virus corono"
#7 hcov*
#8 "covid-19"
#9 covid19*
#10 "covid 19"
#11 “2019-nCoV“
#12 cv19*
#13 "cv-19"
#14 "cv 19"
#15 "n-cov"
#16 ncov*
#17 "sars-cov-2"
#18 wuhan* AND (virus OR viruses OR viral)
#19 covid* AND (virus OR viruses OR viral)
#20 "sars-cov"
#21 "sars cov"
#22 "sars-coronavirus"
#23 "severe acute respiratory syndrome"
#24 "mers-cov"
#25 "mers cov"
#26 "middle east respiratory syndrome"
#27 "middle-east respiratory syndrome"
#28 "covid-19-related"
#29 "SARS-CoV-2-related"
#30 "SARS-CoV2-related"
#31 "2019-nCoV-related"
#32 "cv-19-related"
#33 "n-cov-related"
#34 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33
#35 incidence[MeSH:noexp]
#36 mortality[MeSH Terms]
#37 follow up studies[MeSH:noexp]
#38 prognos*[Text Word]

#39 predict*[Text Word]
#40 course*[Text Word]
#41 #35 OR #36 OR #37 OR #38 OR #39 OR #40
#42 ("2019/10/01"[Date - Publication] : "3000"[Date - Publication]
#43 #34 AND #41 AND #42

Search strategy for EMBASE (Elsevier)
Search date:29.04.2020
#1. coronovirus*
#2. coronavir*
#3. 'corona virus'
#4. 'virus corona'
#5. 'corono virus'
#6. 'virus corono'
#7. hcov*
#8. 'covid-19'
#9. covid19*
#10. 'covid 19'
#11. '2019-ncov'
#12. cv19*
#13. 'cv-19'
#14. 'cv 19'
#15. 'n-cov'
#16. ncov*
#17. 'sars-cov-2'
#18. wuhan*:ti,ab AND (virus OR viruses OR viral)
#19. covid* AND (virus OR viruses OR viral)
#20. 'sars-cov'
#21. 'sars cov'
#22. 'sars-coronavirus'
#23. 'severe acute respiratory syndrome'
#24. 'mers-cov'
#25. 'mers cov'
#26. 'middle east respiratory syndrome'
#27. 'middle-east respiratory syndrome'
#28. "covid-19-related"
#29. "SARS-CoV-2-related"
#30. "SARS-CoV2-related"
#31. "2019-nCoV-related"
#32. "cv-19-related"
#33. "n-cov-related"
#34. #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33
#35.'incidence'/de
#36. mortality:lnk
#37. 'follow up studies'/de
#38. prognos*:ti,ab,kw
#39. predict*:ti,ab,kw

#40. course*:ti,ab,kw
#41. #35 OR #36 OR #37 OR #38 OR #39 OR #40
#42.2020:py
#43. #34 AND #41 AND #42

Search strategy for CENTRAL (The Cochrane Library)
Search date:29.04.2020
#1 coronavir*:ti,ab,kw
#2 coronovirus*:ti,ab,kw
#3 "corona virus":ti,ab,kw
#4 "virus corona":ti,ab,kw
#5 "corono virus":ti,ab,kw
#6 "virus corono":ti,ab,kw
#7 hcov*:ti,ab,kw
#8 "covid-19":ti,ab,kw
#9 covid19*:ti,ab,kw
#10 "covid 19":ti,ab,kw
#11 “2019-nCoV“:ti,ab,kw
#12 cv19* :ti,ab,kw
#13 "cv-19":ti,ab,kw
#14 "cv 19":ti,ab,kw
#15 "n-cov":ti,ab,kw
#16 ncov*:ti,ab,kw
#17 "sars-cov-2"
#18 (wuhan* AND (virus OR viruses OR viral):ti,ab,kw
#19 covid* AND (virus OR viruses OR viral):ti,ab,kw
#20 "sars-cov":ti,ab,kw
#21 "sars cov" :ti,ab,kw
#22 "sars-coronavirus":ti,ab,kw
#23 "severe acute respiratory syndrome":ti,ab,kw
#24 "mers-cov":ti,ab,kw
#25 "mers cov":ti,ab,kw
#26 "middle east respiratory syndrome":ti,ab,kw
#27 "middle-east respiratory syndrome":ti,ab,kw
#28 "covid-19-related":ti,ab,kw
#29 "SARS-CoV-2-related":ti,ab,kw
#30 "SARS-CoV2-related":ti,ab,kw
#31 "2019-nCoV-related":ti,ab,kw
#32 "cv-19-related":ti,ab,kw
#33 "n-cov-related":ti,ab,kw
#34 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33
#35 MeSH descriptor: [Incidence] this term only
#36 MeSH descriptor: [Mortality] explode all trees
#37 MeSH descriptor: [Follow-Up Studies] this term only
#38 (prognos*):ti,ab,kw
#39 (predict*):ti,ab,kw
#40 (course*):ti,ab,kw

#41 #35 OR #36 OR #37 OR #38 OR #39 OR #40
#42 2020
#43 #34 AND #41 AND #42

Certainty of the evidence assessment

Risk of bias

We used the Quality in Prognosis Studies tool (QUIPS) for prognostic factor studies.[11] To be rated as low risk of bias studies needed to be prospective, have appropriately assessed prognostic factors and outcomes and analyzed the information by considering at least age, one comorbidity and one parameter of disease severity as potential confounders. To be rated as moderate risk of bias studies needed to have appropriately assessed prognostic factors and outcomes and analyzed the information by considering at least one of the pre-defined core set of variables: age, one comorbidity or one parameter of disease severity as potential confounders. The remaining studies were categorized as high risk of bias. RoB was assessed on an study basis but the domain related to considering potential confounder was also assessed on a prognostic factor basis as some studies provided adjusted estimates for some but not all prognostic factors. For the primary analysis we downgraded the certainty of the evidence for risk of bias when no studies with moderate or low risk of bias providing adjusted estimates were available or when subgroup analysis showed inconsistency between moderate/low risk of bias adjusted estimates and and high risk of bias studies and the overall pooled estimate of effects was used. We also performed a sensitivity analysis in which we downgraded for risk of bias only when adjusted estimates were not available or when subgroup analysis showed inconsistency between adjusted and unadjusted estimates and the overall pooled estimate was used.

Inconsistency

We used visual inspection of the forest plots and the I2 statistic to assess inconsistency. In doing so we considered the variability in point estimates and confidence interval overlap in relation to the thresholds set (see contextualization).

Imprecision

We rated down for imprecision when the 95%CI of the pooled estimates crossed the thresholds set (see contextualization). Additionally, we rated down for imprecision if the number of events was less than 200 as we assumed that the optimal information size was not met.[s1]

Selective reporting bias

In cases when most of the weight of the pooled estimates were provided by studies in which a multivariable analysis was performed but no adjusted estimates were provided for that particular variable, we considered rating down for selective reporting.

Publication bias

Given the nature of our research question (no interventions involved) and the facilities for reporting research results in this specific context (most of identified studies were published as preprint at the moment we performed the search). We assumed that publication bias was not a major issue and did not explore it while addressing certainty of the evidence.

References

s1. Guyatt GH, Oxman AD, Kunz R, et al. GRADE Guidelines 6. Rating the Quality of Evidence—Imprecision. *J Clin Epidemiol* 2011; 64(12): 1283–93. https://doi.org/10.1016/j.jclinepi.2011.01.012

Supplementary table 1

Supplementary table 2

Supplementary table 3