Prevalence of comorbidities and their association with mortality in patients with COVID-19: A Systematic Review and Meta-analysis

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Abstract

Aims

COVID-19 is a global pandemic that as of the 4th May has registered over 3,585,711 confirmed cases and 248,780 deaths. This review aims to estimate the prevalence of both cardiometabolic and other co-morbidities in patients with COVID-19 infection, and to estimate the increased risk of severity and mortality in people with co-morbidities.

Materials and Methods

Medline, Scopus and the World Health Organisation (WHO) website for Global research on COVID-19 were searched from January 2019 up to April 23, 2020. Study inclusion was restricted to English language publications, original articles that reported prevalence of co-morbidities in individuals with COVID-19 disease, and case-series > 10 patients. 18 studies were selected for inclusion. Data were analysed using random effects meta-analysis models.

Results

Eighteen studies with a total of 14,558 individuals were identified. The pooled prevalence for co-morbidities in patients with COVID-19 disease was 22.9% (95% CI: 15.8 to 29.9) for hypertension; 11.5% (9.7 to 13.4) for diabetes; and 9.7% (6.8 to 12.6) for cardiovascular disease (CVD). For chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD), cerebrovascular disease, and cancer, the pooled prevalences were all less than 4%. With the exception of cerebrovascular disease, all other co-morbidities had a significantly increased risk for having severe COVID-19. In addition, the risk of mortality was significantly increased in individuals with CVD, COPD, CKD, cerebrovascular disease, and cancer.

Conclusions

In individuals with COVID-19, the presence of co-morbidities (both cardiometabolic and other) is associated with a higher risk of severe COVID-19 and mortality. These findings have important implications for the public health with regards to risk stratification and future planning.

Introduction

In December 2019, a new flu-like virus causing atypical pneumonia emerged, affecting many individuals in the city of Wuhan, China. The syndrome caused by this virus, later recognised as the coronavirus disease 2019 (COVID-19),[1] has now reached pandemic levels. As of 4th May 2020, there have been 3,585,711 confirmed cases of COVID-19 and 248,780 deaths reported worldwide.[2] COVID-19 cases has been classified as mild, moderate, and severe or critical.[3] In its mild form, symptoms are cough and fever, whilst imaging shows no signs of lung inflammation. Cases are classified as moderate if the patient has a fever, respiratory tract symptoms, and imaging shows visible lung inflammation. Severe cases of COVID-19 include adults with any of the following: shortness of breath (respiratory rate of greater than 30 breaths per minute), oxygen saturation <93% at rest, or arterial oxygen partial pressure <300mmHg.

Based on the early estimates by China's National Health Commission, of those who died from this outbreak 75% had pre-existing health conditions such as diabetes and cardiovascular disease.[4,5] Subsequently, other reports highlighted the high number of pre-existing health conditions in patients with COVID-19.[6,7] The overwhelming burden of COVID-19 has led to severe pressure on the capacity of healthcare systems, and has adversely affected health care workers.[8] It is vital to identify patients at the highest risk of morbidity and mortality to ensure that adequate advice is given to those most at risk, and also to enable them to shield themselves from the spread of this disease. Such information is also important for future risk stratification for any preventative therapies or vaccinations.

Current knowledge about this novel virus is rapidly evolving, warranting the need to update systematic reviews as more evidence becomes available. Previous systematic reviews focusing on co-morbidities have assessed prevalence of co-morbidities in COVID-19 patients, and

reported the increased odds of having co-morbidities in patients with severe COVID-19 compared to the non-severe stage.[9,10] This systematic review and meta-analysis has assessed the risk of severity and mortality in patients with cardiovascular and other comorbidities compared to those without, in patients with COVID-19, and in addition has updated the evidence on the prevalence of co-morbidities in this patient group.

Methods

Databases and Search Strategy

This study was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[11] and Meta-analyses Of Observational Studies in Epidemiology (MOOSE)[12] guidelines (completed checklists are provided in supplementary figures S1 and S2). The protocol for this systematic review and meta-analysis is registered at PROSPERO CRD42020175966.

Three authors (AKS, RS and AS) performed an initial systematic search on March 30, 2020; an updated search was conducted (by CG and SS) on April 23, 2020. Medline, Scopus and the World Health Organisation website on research into COVID-19[13] were searched, and the full search strategy is reported in online material (supplementary figure S3).

Eligibility Criteria and Study Selection

We retrieved all studies conducted in patients with COVID-19 that explicitly reported the detailed epidemiological characteristics, prevalence of comorbidities, severity of the disease, and in-hospital death outcomes. We excluded case reports, case series of less than 10 patients, studies that did not report prevalence of comorbidities, and studies not published in the English language. Studies that reported prevalence of co-morbidities but did not report mortality or severe COVID-19 were still included and incorporated in the meta-analyses of prevalences only.

An initial abstract and title screen was carried out by two authors (AKS and SS). The full text of studies that met our predefined inclusion criteria were screened by four authors (AKS, RS, AS, CG): those that entirely fulfilled our inclusion criteria were retrieved for further review. Where it was clear that the study cohorts overlapped (that is, the same hospital and time-period for cases were specified), then the largest study was selected for inclusion. If studies had an overlapping

cohort but reported the data for different analyses, they were both included in the systematic review but only analysed separately, with the studies contributing to different meta-analyses. Any ambiguity during study selection was resolved by discussion and consensus. A detailed PRISMA flow-diagram for the search strategy is included in figure 1.

Risk of Bias and Study Quality

The Newcastle-Ottawa Scale (NOS), proposed by Wells et al.[14] and designed to evaluate the quality of non-randomised studies, was employed to assess risk of bias. The NOS score consists of three categories: Selection, Comparability and Outcome. A study can be awarded from zero up to nine stars. Two reviewers independently assessed the studies for risk of bias using this score (SA and BC), and any disagreements were resolved through discussion.

Data Extraction and Statistical Analysis

Three authors (AKS, RS and CG) independently undertook data extraction according to The Cochrane Handbook guidelines.[15] Any disagreement was settled by consensus between all authors.

We calculated the estimated pooled prevalence of diabetes, hypertension, cardiovascular disease (CVD), chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD), cerebrovascular disease, and cancer in COVID-19 patients. We also calculated the estimated pooled relative risk of mortality and of contracting severe vs non-severe COVID-19[3] infection, related to each co-morbidity, using estimated risk ratios (RR) with 95% confidence intervals (95% CI). Different studies utilised different criteria to determine severity of disease, and these criteria are listed in the supplementary material (Table S1). Due to between study heterogeneity, all models were fitted assuming random-effects using the DerSimonian and Laird method.[15] This method is based on the inverse weighting approach, but incorporates an

adjustment to the study weights according to the extent of heterogeneity. Heterogeneity was assessed using Higgins I^2 statistic[16] and interpreted as low (I^2 <25%), moderate (I^2 between 25-50%) or high (I^2 >50%). Between study heterogeneity was investigated by fitting meta-regression models to assess the associations between study effect size with mean study age of patients (median age was used if mean was not reported) and sex (proportion of males). Meta-regression models were fitted using random effects univariable meta-regression models, with the study effect size as the dependent variable, and the study characteristic of interest as the independent variable.

We evaluated the potential for publication bias within meta-analyses by funnel plots and the Egger's test.[15] For meta-analyses where publication bias was found to be significant, the pooled effect size was recalculated using the "trim and fill" adjustment based on the Duval and Tweedle nonparametric method.[17] All analyses were carried out in Stata/IC 15.0 using the metan, metareg, and metatrim commands.

Results

Study Characteristics

The search strategy identified 797 studies, from which 128 were found to be duplicates, and 405 were non-clinical studies, review articles, commentaries, and guidelines. After full text review a further 146 studies were excluded, including 10 studies which had a cohort that overlapped with another larger study that was to be included in the analysis.[18-27] We included 18 studies with14,558 patients in this systematic review.[28-41] Four pairs of studies had overlapping cohorts,[(28,29),(37,42),(31,43),(33,44)], but reported on different outcomes and therefore were both included in the systematic review, but were not incorporated in the same meta-analyses. Characteristics of the included studies can be found in table 1.

The majority of studies (n=16) were based in China, 1 was from the USA, and 1 was from Italy. 17 studies were based on in-patients, whilst one study used data from infectious diseases registries.[30] Study size ranged from 41 participants up to 7,162. For the study based on registry data, only the sub-sample with information on the presence or absence of co-morbidities was included.[30] The proportion of males in studies varied between 44 to 82%, with most studies reporting more males than females. Age varied from a median of 47 to 63 years of age, with the oldest median age reported in a study carried out in Italy.[32] All studies were carried out in late 2019 to early 2020 (table 1). All studies scored at least seven on the Newcastle-Ottawa risk of bias scale (rated low risk of bias), with the majority scoring eight (supplementary Table S2).

Meta-analysis

The meta-analyses of co-morbidities in COVID-19 patients found an estimated 22.9% (95% CI 15.8 to 29.9) had hypertension; 11.5% (9.7 to 13.4) diabetes; 9.7% (6.8 to 12.6) CVD; 3.1% (1.0 to 5.2) COPD; 2.4% (1.5 to 3.2) CKD; 3.0% (1.8 to 4.2) cerebrovascular disease; and 3.9% (2.5

to 5.4) had cancer. All meta-analyses were based on a minimum of seven studies and between study heterogeneity varied from moderate to high (summary results of the meta-analyses are given in table 2, with full forest plots provided in supplementary figure S4). The meta-analyses showed that hypertension (RR 1.66 [95% CI: 1.32, 2.09]), diabetes (2.11 [1,40, 3.19], CVD (2.55 [1.85, 3.51], COPD (2.62 [2.31, 2.97], CKD (3.86 [2.32, 6.40]), and cancer (2.48 [1.46, 4.19]) were all significantly associated with a higher risk of severe COVID-19, compared to patients without comorbidities (figure 2, table 2). Cerebrovascular disease was the only co-morbidity assessed that was not significantly associated with severe COVID-19 (1.73 [0.74, 4.05]) but as only one study reported this data, this result may be due to the lack of evidence rather than no true association, and therefore further research is needed (figure 2, table 2).

Compared to individuals without comorbidities, the risk of death was significantly increased in those with CVD (RR 1.88 [95% CI: 1.41, 2.51], COPD (1.53 [1.03, 2.28]), CKD (1.84 [1.03, 3.30]), cerebrovascular disease (2.48 [2.14, 2.86]), and cancer (1.77 [1.08, 2.88]) (figure 3, table 2).

Results from the meta-regression analyses showed no statistically significant association between either mean study age or proportion of males, with estimated RRs for severity or mortality (supplementary table S3). In addition, although the risk of publication bias was found to be significant in four of the meta-analyses undertaken (table 2, funnel plots provided in supplementary material (figure S5)), when trim and fill analyses were applied no adjustments were made to the meta-analyses (no study estimates were trimmed or filled) and the results remained unchanged (supplementary table S4).

Discussion

This systematic review and meta-analyses showed that in patients with COVID-19, hypertension, diabetes, CVD, COPD, CKD and cancer, were associated with an increased risk of having severe COVID-19, and CVD, COPD, CKD, cerebrovascular disease, and cancer were also associated with an increased risk of mortality. These results are in line with other systematic reviews showing that patients who had severe COVID-19 had increased odds of having a co-morbidity.[10] To our knowledge, although two reviews have assessed risk of severe COVID-19 by co-morbidities (found on preprint databases), this is the first systematic review that has estimated the risk of mortality in COVID-19 patients, this is also the first review to assess increased risk of severe COVID-19 in CKD, cerebrovascular disease and cancer patients. We also estimated the prevalence of co-morbidities in a COVID-19 patient group, showing similar results to previous studies.[9]

This meta-analysis included 18 studies and over 14,000 patients. The methods used throughout were robust, with a comprehensive search strategy of multiple databases, and a minimum of two researchers selecting studies and extracting data. Some limitations should be considered while interpreting this study. Due to local policies for testing COVID-19, and the fact that some studies only included cases admitted to hospital, cases selected for individual studies may not represent all the regional infected population, especially for asymptomatic cases. Therefore the true prevalence and marginal distributions of comorbidities among COVID-19 patients remain unknown. The prevalences and relative risks reported in this review therefore need to be interpreted with caution, and may not reflect true population rates. A further limitation is that 16 out of the 18 studies were from China, as this is where the outbreak began, which limits the generalizability of the results. In addition, although we removed studies that clearly had overlapping cohorts, in that they named the same hospital and time-period, it was not possible

to identify possible overlap between all studies. In particular the large China wide study by Guan et al[6] of laboratory confirmed COVID-19 cases, may include individuals reported in other smaller hospital based studies carried out in the same country. This review has gone further than previous systematic reviews to remove overlapping cohorts though, with many current reviews not addressing the issue and including all published studies.

This review was also limited by the reporting of co-morbidities in the included studies, in particular in the registry study[30] where only a proportion of participants could be included in this meta-analysis due to missing information on co-morbidities. In addition, we did not have data on multi-morbidities, with many of these chronic conditions co-existing, which would have been useful to assess. From this analysis, it is unclear whether the risk of severity of COVID-19 or mortality, are related to poor level of blood pressure or glucose control in individuals with co-morbidities, but again the data was not available to assess this fully. Recent reports have also highlighted possible ethnic differences, with black minority ethnic groups being more affected with severe disease, but our review was mostly limited to studies carried out in China, and results were not reported by ethnicity, so we were unable to investigate this here.[45] In addition there has been recent speculation about obesity being associated with severe COVID-19, after results from a single-centre study of 124 patients,[46] although a recent report from the UK Intensive Care Audit contradicted these results and suggested that the BMI of critically ill patients with COVID-19 is similar to the general population.[45] Unfortunately, only one study in our included papers had data on BMI, so we could not investigate this relationship in our review.

Finally four of the meta-analyses carried out were statistically significant for publication bias as tested for using the Egger's test, although this test does display a high type 1 error rate[17] and when trim and fill was undertaken no study estimates were removed or added. The results from the meta-analyses where publication bias was found to be significant should still be interpreted with caution.

Five recent meta-analyses (two as yet only available on pre-print websites) have assessed the prevalence of co-morbidities in people with COVID-19.[9,10,47-49] Three systematic reviews, with search dates finishing between the end of February and the 5th March, found similar results to those reported here, but with fewer studies.[9,10,49] Emani et al, Li et al, and Yang et al included 10, 6 and 9 studies respectively, and reported hypertension prevalence in COVID-19 patients of between 16 to 17.1%, diabetes between 8 and 9.7% and CVD between 5 and 12%. These results are complementary to what has been reported here, which is unsurprising given that the reviews contain many of the same studies. The results presented here though are based on more data (13 or 14 studies), with greater care taken to remove cohorts that overlap from the review. Jain et al[48] identified 7 studies (1813 COVID-19 patients) for their systematic review, and showed CVD, COPD and hypertension were associated with a significantly increased odds of both severe disease and ICU admission, but found diabetes was only borderline for a significant association with severity of COVID-19 disease. Chen et al pooled results from 9 studies and reported a significant association between disease severity and hypertension (OR 2.3; 95% CI 1.76-3.00), diabetes (2.67; 1.91-3.74), and CHD (2.85, 1.68-4.84). The results complement those reported here, although this synthesis has included more studies and assessed more co-morbidities as risk factors. This is the first review to have shown an association between CKD and cancer, and severe COVID-19 disease; and to show an association between CKD, cerebrovascular disease and cancer, and mortality from COVID-19.

The results of this review should aid in identifying individuals most at risk of severe complications from COVID-19, and hence is useful for public health messaging on social distancing and self-isolation. This review has updated the evidence on the association between co-morbidities and COVID-19, and identified further vulnerable groups including patients with CKD and cancer. In light of this evidence policy makers should give clear guidance to these

groups that they are at increased risk from severe COVID-19. The results of this analysis should also help with the targeting of people for ongoing trials, and inform policy makers as to which groups should be prioritised if a vaccination becomes available. The high mortality associated with COVID-19 in these chronic conditions calls for an increased emphasis on future preventative therapies and vaccination programmes for these groups, in addition to the traditional risk prevention.

Conclusions

In summary, this systematic review and meta-analysis has identified that the presence of co-morbidities such as diabetes, hypertension, CVD, and COPD in individuals with COVID-19 is associated with an approximate two-fold increased risk of developing severe symptoms and mortality.

Contributors: AKS, RS, AK, CLG and KK conceived the idea of the study; AKS. RS, AK, CLG and SS carried out the literature search, screened the studies, and undertook data extraction, and this was checked by YC. CLG and AKS carried out the statistical analysis. BC and YC carried out the risk of bias scoring. CLG, KK, FZ, SS and MJD interpreted the findings; and CLG, AKS, and KK drafted the manuscript, CLG produced the figures. SS, FZ, BC, YC, KK, RS, AK and MJD critically reviewed the manuscript, and CLG, AKS and KK revised the manuscript for final submission. All authors have approved the final draft of the manuscript. The corresponding author (KK) attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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Transparency Declaration: The lead author (AKS) affirms that this 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.

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Data Sharing: Data are available upon reasonable request. Technical appendix, statistical code, and dataset available from CLG.

References

1. Wu F, Zhao S, Yu B, et al. A new coronavirus associated with human respiratory disease in China. *Nature.* 2020;579(7798):265-269.
2. Worldometers. Coronavirus Update (Live). 2020; https://www.worldometers.info/coronavirus/.
3. *New coronavirus pneumonia prevention and control program (6th ed)(in Chinese). 2020. http://www.nhc.gov.cn/yzygj/s7653p/202002/8334a8326dd94d329df351d7da8aefc2/files/b218cfeb1bc54639af227f922bf6b817.pdf.*
4. BBC News. 'Window of opportunity' to stop coronavirus: @BBCNews; 2020. Available from: https://www.bbc.com/news/world-asia-china-51368873.
5. Sun K, Chen J, Viboud C. Early epidemiological analysis of the coronavirus disease 2019 outbreak based on crowdsourced data: a population-level observational study. *Lancet.* 2020;2(4):PE201-E208.
6. Guan WJ, Liang WH, Zhao Y, et al. Comorbidity and its impact on 1590 patients with Covid-19 in China: A Nationwide Analysis. *Eur Respir J.* 2020.
7. Chen T, Wu D, Chen H, et al. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. *BMJ.* 2020;368:m1091.
8. Adams JG, Walls RM. Supporting the Health Care Workforce During the COVID-19 Global Epidemic. *JAMA.* 2020.
9. Emami A, Javanmardi F, Pirbonyeh N, Akbari A. Prevalence of Underlying Diseases in Hospitalized Patients with COVID-19: a Systematic Review and Meta-Analysis. *Arch Acad Emerg Med.* 2020;8(1):e35.
10. Yang J, Zheng Y, Gou X, et al. Prevalence of comorbidities in the novel Wuhan coronavirus (COVID-19) infection: a systematic review and meta-analysis. *Int J Infect Dis.* 2020.
11. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *PLoS Med.* 2009;6(7):e1000100.
12. Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. *JAMA.* 2000;283(15):2008-2012.
13. https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov. Accessed 23 April 2020.
14. Stang A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. *Eur J Epidemiol.* 2010;25(9):603-605.
15. Higgins JPT GS. *Cochrane Handbook for Systematic Reviews of Interventions.* 2011.
16. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Stat Med.* 2002;21(11):1539-1558.
17. Carpenter CJ. A Trim and Fill Examination of the Extent of Publication Bias in Communication Research. *Communication Methods and Measures.* 2012;6(1):41-55.
18. Bhatraju PK, Ghassemieh BJ, Nichols M, et al. Covid-19 in Critically Ill Patients in the Seattle Region - Case Series. *N Engl J Med.* 2020.
19. Cao J, Tu WJ, Cheng W, et al. Clinical Features and Short-term Outcomes of 102 Patients with Corona Virus Disease 2019 in Wuhan, China. *Clinical Infectious Diseases.* 2020;02:02.
20. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet.* 2020;395(10223):507-513.

21. Deng Y, Liu W, Liu K, et al. Clinical characteristics of fatal and recovered cases of coronavirus disease 2019 (COVID-19) in Wuhan, China: a retrospective study. *Chinese Medical Journal.* 2020;20:20.
22. Li X, Xu S, Yu M, et al. Risk factors for severity and mortality in adult COVID-19 inpatients in Wuhan. *Journal of Allergy & Clinical Immunology.* 2020;12:12.
23. McMichael TM, Currie DW, Clark S, et al. Epidemiology of Covid-19 in a Long-Term Care Facility in King County, Washington. *N Engl J Med.* 2020.
24. Richardson S, Hirsch JS, Narasimhan M, et al. Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area. *JAMA.* 2020.
25. 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.
26. 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(10229):1054-1062.
27. Garg S, Kim L, Whitaker M, et al. Hospitalization Rates and Characteristics of Patients Hospitalized with Laboratory-Confirmed Coronavirus Disease 2019 - COVID-NET, 14 States, March 1-30, 2020. *MMWR - Morbidity & Mortality Weekly Report.* 2020;69(15):458-464.
28. Chen T, 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. *Journals of Gerontology Series A Biological Sciences & Medical Sciences.* 2020;11:11.
29. Cheng Y, Luo R, Wang K, et al. Kidney disease is associated with in-hospital death of patients with COVID-19. *Kidney International.* 2020;20:20.
30. CDC COVID-19 Response Team. Preliminary Estimates of the Prevalence of Selected Underlying Health Conditions Among Patients with Coronavirus Disease 2019 - United States, February 12-March 28, 2020. *MMWR Morb Mortal Wkly Rep.* 2020;Apr 3(13):382-386.
31. Feng Y, Ling Y, Bai T, et al. COVID-19 with Different Severity: A Multi-center Study of Clinical Features. *American Journal of Respiratory & Critical Care Medicine.* 2020;10:10.
32. 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;06:06.
33. Guo T, Fan Y, Chen M, et al. Cardiovascular Implications of Fatal Outcomes of Patients With Coronavirus Disease 2019 (COVID-19). *JAMA Cardiol.* 2020.
34. Guo W, Li M, Dong Y, et al. Diabetes is a risk factor for the progression and prognosis of COVID-19. *Diabetes/Metabolism Research Reviews.* 2020:e3319.
35. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet.* 2020;395(10223):497-506.
36. Lian J, Jin X, Hao S, et al. Analysis of Epidemiological and Clinical features in older patients with Corona Virus Disease 2019 (COVID-19) out of Wuhan. *Clinical Infectious Diseases.* 2020;25:25.
37. Liang WH, Guan WJ, Li CC, et al. Clinical characteristics and outcomes of hospitalised patients with COVID-19 treated in Hubei (epicenter) and outside Hubei (non-epicenter): A Nationwide Analysis of China. *European Respiratory Journal.* 2020;08:08.
38. Liu K, Fang YY, Deng Y, et al. Clinical characteristics of novel coronavirus cases in tertiary hospitals in Hubei Province. *Chin Med J (Engl).* 2020.
39. Wan S, Xiang Y, Fang W, et al. Clinical features and treatment of COVID-19 patients in northeast Chongqing. *Journal of Medical Virology.* 2020;21:21.
40. 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.

41. Wang Z, Yang B, Li Q, Wen L, Zhang R. Clinical Features of 69 Cases with Coronavirus Disease 2019 in Wuhan, China. *Clinical Infectious Diseases.* 2020;16:16.
42. Guan WJ, Ni ZY, Hu Y, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med.* 2020.
43. 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.
44. Zhang JJ, Dong X, Cao YY, et al. Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China. *Allergy.* 2020.
45. https://www.icnarc.org/About/Latest-News/2020/04/04/Report-On-2249-Patients-Critically-Ill-With-Covid-19 (Accessed 9th April 2020).
46. Simonnet A, Chetboun M, Poissy J, et al. High prevalence of obesity in severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) requiring invasive mechanical ventilation. *Obesity (Silver Spring).* 2020.
47. Chen YM, Gong X, Wang L, Guo J. Effects of hypertension, diabetes and coronary heart disease on COVID-19 diseases severity: a systematic review and meta-analysis. *medRxiv.* 2020;Preprint.
48. Jain V, Yuan JM. Systematic review and meta-analysis of predictive symptoms and comorbidities for severe COVID-19 infection. *medRxiv.* 2020;Pre-print.
49. Li B, Yang J, Zhao F, et al. Prevalence and impact of cardiovascular metabolic diseases on COVID-19 in China. *Clin Res Cardiol.* 2020.

Table 1: Characteristics of Included Studies

Study Name	Dates cases identified	Location (study design)	N	Age (yr) (mean (SD))	Male	Hypertension	Diabetes	CVD	COPD	Chronic kidney disease	Cerebrovascular disease	Cancer
CDC USA[30]	12 Feb – 28 Mar	Laboratory confirmed cases reported to CDC, USA	7,162^	-	-	-	784 (10.9)	647 (9.0)	656 (9.2)	213 (3.0)	-	-
Chen T[7]	13 Jan – 12 Feb	Tongji Hospital, Wuhan, China	274	<40 53(19) 40-59 68 (25) >60 153 (56)	171 (62.4)	93 (33.9)	47 (17.2)	23 (8.4)	18 (6.6)	4 (1.5)	4 (1.5)	7 (2.6)
Chen TL[28]	01 Jan – 10 Feb	Zhongnan Hospital, Wuhan University, China	203	54 (41-68)*	108 (53.2)	43 (21.2)	16 (7.9)	16 (7.9)	8 (3.9)	8 (3.9)	9 (4.4)	7 (3.4)
Cheng[29]	28 Jan – 11 Feb	3 branches of the Tongji Hospital, Wuhan, China	701	63 (50-71)*	367 (52.4)	233 (33.4)	100 (14.3)	-	13 (1.9)	14 (2)	-	32 (4.6)
Feng[31]	01 Jan – 15 Feb	Jinyintan Hospital, Wuhan, and Tongling People's Hospital, Anhui Province, China	476	53 (40-64)*	271 (56.9)	113 (23.7)	49 (10.3)	38 (8)	22 (4.6)	-	17 (3.6)	12 (2.5)
Grasselli[32]	20 Feb – 18 Mar	72 hospitals, Lombardy Region, Italy	1043^	63 (56-70)*	1304 (82.0)	509 (48.8)	180 (17.3)	223 (21.4)	42 (4.0)	36 (3.5)	-	81 (7.8)
Guan[6]	11 Dec – 29 Jan	552 hospitals, China	1099	47 (35-58)*	640 (58.2)	165 (15.0)	81 (7.4)	27 (2.5)	12 (1.1)	8 (0.7)	15 (1.4)	10 (0.9)
Guo T[33]	23 Jan – 23 Feb	Seventh Hospital, Wuhan City, China	187	58.5 (14.7)	91 (48.7)	61 (32.6)	28 (15.0)	21 (11.3)	4 (2.1)	6 (3.2)	-	13 (7.0)

Guo W[34]	10 Feb – 29 Feb	Union Hospital, Wuhan, China	174	59 (49-67)*	76 (43.7)	43 (24.7)	37 (21.3)	32 (18.4)	-	13 (7.5)	13 (7.5)	17 (4.6)
Huang[35]	01 Dec – 02 Jan	Jinyintan Hospital, Wuhan, China	41	49 (41-58)*	30 (73.2)	6 (14.6)	8 (19.5)	6 (14.6)	1 (2.4)	-	-	1 (2.4)
Lian[36]	17 Jan – 12 Feb	Zhejiang province, China	788	-	407 (51.6)	126 (16.0)	57 (7.2)	11 (1.4)	3 (0.4)	7 (0.9)	-	6 (0.8)
Liang[37]	Nov 21 - 31 Jan	575 hospitals, China	1590	48.9 (16.3)	904 (57.3)	269 (16.9)	130 (8.2)	59 (3.7)	24 (1.5)	21 (1.3)	30 (1.9)	18 (1.1)
Liu Kui[38]	30 Dec – 24 Jan	Nine tertiary hospitals, China	137	57 (20-83)†	61 (44.5)	13 (9.5)	14 (10.2)	10 (7.3)	2 (1.5)	-	-	2 (1.5)
Wan[39]	23 Jan – 08 Feb	Chongqing University Three Gorges Hospital	135	47 (36-55)*	72 (53.3)	13 (9.6)	12 (8.9)	7 (5.2)	1 (0.7)	-	-	4 (3.0)
Wang D[40]	01 Jan – 03 Feb	Zhongnan Hospital, Wuhan, China	138	56 (42-68)*	75 (54.3)	43 (31.2)	14 (10.1)	20 (14.5)	4 (2.9)	4 (2.9)	7 (5.1)	10 (7.2)
Wang Z[41]	16 Jan - 29 Jan	Union hospital, Wuhan, China	69	42 (35-62)*	32 (46.4)	9 (13.0)	7 (10.1)	8 (11.6)	4 (5.8)	-	-	4 (5.8)
Wu[43]	25 Dec – 26 Jan	Jinyintan Hospital, Wuhan, China	201	51 (43-60)*	128 (63.7)	39 (19.4)	22 (10.9)	8 (4.0)	5 (2.5)	2 (1.0)	-	1 (0.5)
Zhang[44]	16 Jan – 03 Feb	Seventh Hospital, Wuhan City, China	140	57 (25-87)†	71 (50.7)	42 (30.0)	17 (12.1)	7 (5.0)	2 (1.4)	2 (1.4)	3 (2.1)	

Values are n(%) unless otherwise stated, *median (IQR), † median (range), ^N reporting co-morbidities

Table 2: Summary of meta-analyses results for prevalance of co-morbidities, and increased risk of mortality and severity of disease by co-morbidities, in COVID-19 patients

Comorbidities	N studies	Pooled effect size (95% CI), p-value	I^2 (%), p-value	Egger's (p-value)
Estimated pooled prevalences (%) of co-morbidities in COVID-19 patients				
Hypertension	13	22.9 (15.8, 29.9), <0.001	97.3, <0.001	0.524
Diabetes	14	11.5 (9.7, 13.4), <0.001	81.2, <0.001	0.573
CVD	14	9.7 (6.8, 12.6), <0.001	96.6, <0.001	0.724
COPD	13	3.1 (1.0, 5.2), <0.004	97.4, <0.001	0.018*
CKD	10	2.4 (1.5, 3.2), <0.001	81.8, <0.001	0.996
Cerebrovascular disease	7	3.0 (1.8, 4.2), <0.001	56.3, 0.033	0.114
Cancer	13	3.9 (2.5, 5.4), <0.001	88.2, 0.001	0.400
Estimated pooled RR of suffering severe COVID-19 if you have a comorbidity compared to if you do not				
Hypertension	6	1.66 (1.32, 2.09), <0.001	30.9, 0.204	0.819
Diabetes	7	2.11 (1.40, 3.19), <0.001	84.6, 0.001	0.030*
CVD	7	2.55 (1.85, 3.51), <0.001	72.5, 0.001	0.031*
COPD	6	2.62 (2.31, 2.97), <0.001	0.0, 0.830	0.015*
CKD	2	3.86 (2.32, 6.40), <0.001	38.5, 0.202	-
Cerebrovascular disease	1	1.73 (0.74, 4.05), 0.208	-	-
Cancer	2	2.48 (1.46, 4.19), 0.001	0.0, 0.544	-
Estimated pooled RR of mortality from COVID-19 if you have a comorbidity compared to if you do not				
Hypertension	3	1.52 (0.86, 2.71), 0.151	92.2, 0.001	0.251
Diabetes	2	1.83 (0.89, 3.73), 0.100	81.9, 0.019	-
CVD	2	1.88 (1.41, 2.51), <0.001	0.0, 0.478	-
COPD	1	1.53 (1.03, 2.28), 0.035	-	-
CKD	1	1.84 (1.03, 3.30), 0.040	-	-
Cerebrovascular disease	1	2.48 (2.14, 2.86), <0.001	-	-
Cancer	1	1.77 (1.08, 2.88), 0.023	-	-

*Where publication bias was significant trim and fill analyses were carried out (details reported in supplementary material)