

A network meta-analysis assessing the association between cardiometabolic risk factors and
coronavirus disease 2019 (COVID-19) -related outcomes

By

Alina Binbin Li

B.S., Emory University, 2018

Thesis

Submitted in partial fulfillment of the requirements for the
Degree of Master of Public Health in the Brown University School of Public Health

PROVIDENCE, RHODE ISLAND
OCTOBER 2021

This thesis by ***Alina Binbin Li*** is accepted in its present form
by the Brown University School of Public Health as satisfying the
thesis requirements for the degree of Master of Public Health.

Date _____

Simin Liu, MD, ScD, Advisor

Date _____

Andrew Zullo, PharmD, PhD, Reader

Date _____

Annie Gjelsvik, PhD
Director, Master of Public Health Program

Approved by the Graduate Council

Date _____

Andrew G. Campbell, Dean of the Graduate School

Preface and Acknowledgements

Written during the COVID-19 pandemic, this thesis reflects the unforgettable, once-in-a-lifetime experiences in both light and pain. There is not enough gratitude one can extend during this unique period. I have learned so much about the intersections of COVID-19, health equity, and the already prominent cardiometabolic epidemic. Friends, families, and people globally took a collaborative, emotional toll from lockdown to political tensions. As such, the prevalence of COVID-19 and cardiometabolic comorbidities of this academic work affected many personally. I spent an additional year from my thesis to serve Rhode Island, a generous state of public health initiatives and yet inequities. Thank you to the Rhode Island Department of Health for the informative experience working directly on COVID-19 pandemic through contact tracing and applied epidemiology. The leadership of the COVID-19 EPI-OPS taught me about public health management and collaboration. The RIDOH Health Equity Team reinforced an important social justice lens, allowing me to teach and inform others of integrating compassion into our work.

Thank you to my friends and family in their emotional and academic support, particularly Jackson McMahon and my father Shiqun Li. I must thank Joann Barao and Diane Schlacter for forwarding the opportunity to work at RIDOH and updating students on the MPH process. Dr. Annie Gjelsvik has also compassionately extended her advice and support when I was lost in the progress of my degree. Thank you to the invaluable input of my advisor, Dr. Simin Liu who seeded the original hypothesis and arranged the scientific and analytical resource at the Center for Global Cardiometabolic Health (CGCH) in support of this work. Bo Yang assisted in much of the data analysis and writing of the Introduction of this paper. I am also grateful to Dr. Andrew Zullo, Dr. Kenneth Lo, and Dr. Jie Li at the CGCH who directly contributed much of the database development, analysis, and interpretation of the paper.

Table of Contents

RESEARCH PAPER – A NETWORK META-ANALYSIS ASSESSING THE ASSOCIATION BETWEEN CARDIOMETABOLIC RISK FACTORS AND COVID-19 RELATED OUTCOMES

Abstract.....	1
Introduction	3
Methods	4
<i>Search Strategy and Study Selection Criteria</i>	4
<i>Data Extraction and Quality Assessment</i>	5
<i>Data Analysis</i>	6
Results	7
<i>Fixed Effect Models from Early Pandemic (May 14, 2020 to July 28, 2020)</i>	7
<i>Fixed Effect Models from Recent Pandemic (July 29, 2020 to May 19, 2021)</i>	8
<i>Network Analysis</i>	8
Discussion.....	9
Conclusion and Recommendations	11
Table 1: Main Characteristics of included studies with highest Newcastle-Ottawa Scale (NOS) scores in first half of pandemic (May 14, 2020 to July 28, 2020).....	12
Table 2a: Studies Included in Meta-Analysis from Early Pandemic (March 30, 2020 to July 28, 2020).....	14
Table 2b: Studies Included in Meta-Analysis from Recent Pandemic (July 29, 2020 to May 19, 2021).....	41
Table 3a: Fixed Effect Models of Cardiometabolic Risk Factors and COVID-19 Outcomes During Early Pandemic (May 14, 2020 to July 28, 2020).....	51
Table 3b: Fixed Effect Models of Cardiometabolic Risk Factors and COVID-19 Outcomes During Recent Pandemic (July 29, 2020 to May 19, 2021)	52
Figure 1: Search and selection process by timeframe according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses checklist.	53
Figure 2: Network Line Graph of Cardiometabolic Comparisons Included from all Studies During COVID-19 Pandemic Timeframe	54
Figure 3: Network Analysis Forest Plot of Cardiovascular Comorbidities Fixed Effect Models from full Pandemic Timeframe.	55
Figure 4: Comparison-adjusted Funnel Plot of Publication Bias in Relations of COVID-19 composite outcome incidence in any cardiometabolic comorbidity	56
Appendix 1: Search Strategy	57
References	59

List of Tables

Table 1: Main Characteristics of included studies with highest Newcastle-Ottawa Scale (NOS) scores in first half of pandemic (May 14, 2020 to July 28, 2020).....	12
---	----

Table 2a: Studies Included in Meta-Analysis from Early Pandemic (March 30, 2020 to July 28, 2020).....	14
--	----

Table 2b: Studies Included in Meta-Analysis from Recent Pandemic (July 29, 2020 to May 19, 2021).....	41
---	----

Table 3a: Fixed Effect Models of Cardiometabolic Risk Factors and COVID-19 Outcomes During Early Pandemic	51
---	----

Table 3b: Fixed Effect Models of Cardiometabolic Risk Factors and COVID-19 Outcomes During Recent Pandemic	52
--	----

List of Figures

Figure 1: Search and selection process by timeframe according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist.	53
Figure 2: Network Line Graph of Cardiometabolic Comparisons Included from all Studies During COVID-19 Pandemic Timeframe	54
Figure 3: Network Analysis Forest Plot of Cardiovascular Comorbidities Fixed Effect Models from full Pandemic Timeframe.	55
Figure 4: Multiple Comparison-adjusted Funnel Plot of Publication Bias in Relations of COVID-19 composite outcome incidence in any cardiometabolic comorbidity ...	56

Abstract of A network meta-analysis assessing the association between cardiometabolic risk factors and COVID-19-related outcomes, by Alina Binbin Li, Degree M.P.H, Brown University, May 2022 –

Importance: Cardiometabolic comorbidities have been associated with a higher risk of COVID-19 severity and mortality and are prevalent among COVID-19 patients.

Objective: Synthesize evidence regarding cardiometabolic risk factors for COVID-19 outcome severity using a network analysis.

Data Sources: Embase 1910, Ovid Emcare 1995, and MEDLINE® 1946 to May 19, 2021 were searched for prospective and retrospective studies related to cardiometabolic risk factors when infected by COVID-19. English and Chinese studies were included.

Study Selection: Search criteria were on primary studies on cardiometabolic risk factors among COVID-19 diagnosed patients. Studies with insufficient data were excluded. Initially, 6,081 studies were identified, and 146 studies qualified from early pandemic timeframe up to July 28, 2020. Additional 20,580 were screened and finalized as 181 studies from July 29, 2020 to May 19, 2021.

Data Extraction and Synthesis: Two investigators who performed literature screening, extracted data separately, and pooled data using a fixed-effect model. The assessment of literature quality was performed independently following the Newcastle-Ottawa Scale (NOS).

Main Outcome(s) and Measure(s): Before data collection, a hypothesis of greater risk and increasing severity between cardiometabolic risk and all COVID-19 outcomes was formulated. Study outcomes were hospitalization, severe outcomes of COVID-19, and mortality.

Results: During first year of pandemic, the presence of all cardiometabolic risk factors except for myocardial infarction were associated with a higher risk of risk of disease severity. Patients with heart failure (OR 2.73, 95% CI: 2.37 to 3.16) and overweight status (OR 1.89, 95% CI: 1.46 to 2.45) had greatest association with severe outcomes. During recent pandemic, patients with diabetes (OR 1.46, 95% CI: 1.45 to 1.47) were most likely to be hospitalized, and obese patients had highest risk for severe COVID-19 outcomes. Network analysis for any COVID-19 outcome was led by cerebrovascular disease as an individual risk factor at 1.69 (95% CI: 1.65 to 1.73) and CVD and DM combined (OR 6.98, 95% CI: 5.28 to 9.22).

Conclusions and Relevance: By accounting for heterogeneity, this meta-analysis and network analysis strengthened existing evidence on increased risk of COVID-19 hospitalization, severity, and mortality among those with cardiometabolic comorbidities. Considering the high prevalence of cardiometabolic comorbidities and risk of all severe outcomes, patients with cardiometabolic should be prioritized in vaccination and treatment development of COVID-19.

Introduction

Coronavirus disease 2019 (COVID-19) caused by novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first reported in December 2019 [1] and spread worldwide rapidly, leading to an ongoing pandemic. The impact of this disease on human health, society functioning, and the global economy are unprecedented. COVID-19 can infect people of all age groups, although severe symptoms are more common in older adults [2]. Infected patients present a wide range of clinical manifestations and outcomes including subclinical infections, organ dysfunction, hospitalization, and death [3].

Nearly half of the patients with COVID-19 [2-4] have co-morbidities, including obesity, hypertension, diabetes, and cardiovascular diseases (CVDs) [5, 6]. Patients with underlying cardiometabolic comorbidities are more likely to have severe symptoms and get admitted to ICU [4]. Moreover, the percentages of patients with cardiometabolic comorbidities are much higher among the fatality cases than survival cases [7]. Much of the prior research conducted has revealed associations between single underlying comorbidities and COVID-19 outcomes [8-17]. Studies have also been done to analyze the effects of combinations of comorbidities towards the adverse outcomes of COVID-19 [18-22]. Inconsistencies in the associations were observed among the publications and definitive conclusions have yet to be made. A rapid increase in systematic reviews and meta-analyses have provided a great summary of the published papers [23-27]; however, due to the methodological restrictions of meta-analysis [28], different cardiometabolic risk factors of the COVID-19 cannot be compared with one another because of the heterogeneity among the studies.

To compare and systematically evaluate the associations of cardiometabolic risk factors with COVID-19 incidence and adverse outcomes, we conducted a quantitative network meta-analysis treating multiple risk factors simultaneously as if they were from a network of randomized controlled intervention trials by means of direct and indirect evidence [29-30]. Specifically, we first treated cardiometabolic risk factors as if they were interventions for COVID-19 analogous to randomized clinical trials with direct and indirect associations that form into a net. The impact of individual and combined cardiometabolic risk factors was subsequently assessed to rank the relative importance of these influential risk factors.

Methods

Search strategy and selection criteria

The meta-analysis was conducted following the Preferred Reporting Items for Systematic reviews and Meta-analysis (PRISMA) Statement. Two consecutive timeframes were compared using the same search strategy. According to our predetermined protocol, the search of eligible literature was initially performed by two researchers (K. Lo and S Liu) in three databases with a language restriction of English and Chinese: 1) Embase 1910 to July 28, 2020; 2) Ovid Emcare 1995 to 2020 Week 30; 3) Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations 1946 to July 28, 2020. The second set used the same search strategy for publications subsequent to the first timeframe of each corresponding dataset up to May 19, 2021. Eligible non-experimental reports were those that provided information on the association between cardiometabolic risk factors and COVID-19 related outcomes. The risk factors were atrial fibrillation (AF), coronary artery disease (CAD), cerebrovascular disease (CBD), coronary heart disease (CHD), cardiovascular disease (CVD), diabetes mellitus (DM), heart failure (HF),

hypertension (HTN), myocardial infarction (MI), obesity (OBS), overweight (OW), and stroke (STK). Severe outcomes of COVID-19 included ICU admission, respiratory failure, in-hospital complications, ARDS, disease progression, invasive mechanical ventilation (IMV), radiographic exacerbation, acute kidney injury, ventricular arrhythmias during hospitalization, high flow nasal cannula, or a combined adverse endpoint. Studies that were (a) literature reviews, letters, and abstracts from conference proceedings, (b) providing insufficient data information, or (c) duplicate publications were excluded. Detailed search terms are listed in Appendix 1.

We did not restrict the study types during the literature searching stage considering the phenomenon that a proportion of articles related to COVID-19 were not assigned their study types in the databases timely. All literature information was downloaded into Microsoft Excel. After the removal of duplicates, two researchers performed abstract screening and full-text screening for each set (B. Yang and Y. Li for set one, B. Yang and A. Li for set two). Disagreements were resolved with discussions with the senior investigators or by consensus. Only primary studies that provided the required association information were included in our study. A total number of 146 and 181 studies were included for early and later pandemic timeframes, respectively (Figure 1).

Data extraction and quality assessment

The two investigators who performed the literature screening also extracted the data from included studies separately. We extracted the following variables: author, date, country, number of males, age, sample size, comorbidities, basis of disease severity, and the effect size estimates. The assessment of literature quality was performed by four investigators (B. Yang, Y. Li, S. Shim, and R. Huynh) independently following the Newcastle-Ottawa Scales (NOS). Disagreements were resolved with discussions with the senior investigators or by consensus. NOS were used to evaluate

the quality of a study in three aspects: selection, outcome, and comparability. NOS scores can be given a maximum of nine while higher NOS scores represent higher literature quality. Information of all included studies can be found in Tables 1a and 1b.

Data analysis

All data analyses were performed using R version 3.6.2. The relative risk (RR) and relevant 95% confidence intervals (CI) were used to estimate the pooled results from studies. Odds ratios (OR) and hazard ratios (HR) were also pooled. The heterogeneities across studies or different characteristics were then assessed via scatterplots and formal statistical tests. A result of $P \leq 0.05$ or $I^2 \geq 50\%$ indicated the existence of heterogeneity, and $I^2 \geq 75\%$ was considered high heterogeneity.

Evaluation of the combined and independent effects of cardiometabolic factors towards COVID-19 related outcomes was done through the network meta-analysis approach. Using network plots, the geometry of the evidence network was summarized to visualize the network geometry and node connectivity. A network meta-analysis of the comparative effects was conducted using a multivariate fixed effect meta-analysis model. Estimates for relative risks, odds ratios, and hazard ratios and 95% CIs were calculated for all effect comparisons. The risk factor ranking was computed for all cardiometabolic risk factors by means of the P-scores, which measure the certainty that one risk factor is more influential than another. Q statistics were calculated both within-designs and between-designs to assess the homogeneity. Network analysis was conducted using all data until May 19, 2021.

Results

Fixed effect models from early pandemic (until July 28, 2020)

In the earlier set, 146 studies were evaluated for cardiometabolic risk factors for COVID-19 outcomes of hospitalization, severe COVID-19 outcomes, and mortality. Largely, most studies reported severe outcomes (n=217) and mortality (n=180) for any cardiometabolic exposure due to COVID-19. Among the highest NOS scored studies (n=12), two-thirds focused on mortality as an outcome and were 44.8% to 61.9% men (Table 1). Risk of COVID-19 hospitalization, severity, and mortality for those with any cardiometabolic condition was 1.62 (1.37 to 1.91), 1.29 (1.25 to 1.32), and 1.31 (1.29 to 1.32) times greater than those without, respectively.

COVID-19 patients with either diabetes or obesity were also at significantly increased risk of hospitalization, disease severity, and mortality than those COVID-19 patients without (Table 2a). Hospitalization was 1.64 (1.44 to 1.87) and 1.66 (1.53 to 1.81) times higher among COVID-19 patients with diabetes and obesity, respectively. Moreover, having any cardiometabolic factors also increased risk of hospitalization (RR 1.48, 95% CI: 1.40 to 1.56). Risk of disease severity was positively associated with all cardiometabolic risk factors. Patients with heart failure (2.73: 2.37 to 3.16) and overweight status (1.89: 1.46 to 2.45) were the most likely to have severity of disease. Compared to those without coronary artery disease, risk of severe COVID-19 outcomes and mortality were 1.76 (1.58 to 1.95) and 1.19 (1.14 to 1.24) times greater among those with coronary artery disease. Patients who had stroke, cerebrovascular disease, heart failure, and cardiovascular disease were at least 65% more likely to have mortality.

Fixed effect models from recent pandemic (July 2020 to May 2021)

From the more recent half of the pandemic, 181 papers were included in our analysis. Any

cardiometabolic risk factor increased hospitalization risk by 1.48 (1.40 to 1.56) times. Risk of severity (1.29: 1.25 to 1.32) and mortality (1.31: 1.29 to 1.32) were lower than hospitalization risk. Patients with DM consistently had significant risk for hospitalization, severity, and mortality (Table 2b). DM patients (1.46: 1.45 to 1.47) were most likely to be hospitalized, whereas obese and stroke patients were more likely to have severe COVID-19 outcomes. HF and CBD patients had 1.72 (1.67 to 1.77) and 1.65 (1.62 to 1.69) times the mortality risk of non-cardiometabolic patients, respectively. While the early set did not have enough studies on AF, five recent studies on AF reflected 1.23 (1.05 to 1.45) times the risk of mortality compared to those without. Risk of mortality due to COVID-19 among those with prior myocardial infarction did not change from the first year of the COVID-19 pandemic. Risk of severity and mortality decreased in models for CBD, CVD, and HF. While risk of severe COVID-19 outcomes remained similar among diabetic and CHD patients, risk of mortality increased. Obese patients had increased risk of severe outcomes and death from COVID-19 whereas hospitalization risk decreased compared to the earlier timeframe. In fact, obese patients had the greatest effect size for severe COVID-19 outcomes out of all cardiometabolic exposures (1.82: 1.77 to 1.87). In contrast, overweight patients decreased in risk of severe COVID-19 compared to early pandemic.

Network Analyses

A composite outcome of hospitalization, severe outcomes, or mortality due to COVID-19 was studied in an analysis of all data accrued (n=327). DM, HTN, and OBS had the greatest number of studies on risk of COVID-19 outcomes (Figure 2). The ranking of any cardiometabolic risk factor affecting hospitalization, severe outcomes, or mortality was led by CBD at 1.69 (1.65 to 1.73). DM, HF, and OBS individually had at least 35% greater risk of the composite of any COVID-19 outcome (Figure 3). Combined outcomes were all ranked higher than individual

outcomes, at a minimum of 1.66. CVD and DM had the greatest RR estimates of 6.98 (5.28 to 9.22).

In network analyses stratified by the two time periods (early vs. recent), all cardiometabolic risk factors were significantly associated with COVID-19 outcomes compared to having no risk factors. In the early pandemic analysis, MI (95% CI: 2.41 to 4.99) and STK (2.03 to 2.23) had the highest association with having any level of COVID-19 outcome; however, CBD was ranked the highest individual risk factor during recent timeframe (1.64 to 1.73) with DM, HF, and OBS following. Little to no chance of publication bias was indicated by the funnel plot (Figure 4, $p > 0.05$), although a moderate amount of heterogeneity was suggested across studies likely due to the varied methodology and exposures studied ($T^2 < 0.05$).

Discussion

In this systematic and quantitative assessment of all published literature concerning COVID-19 and CMD risk factors, we observed strong positive associations between CMD risk factors and COVID-19 outcome severity. The significant associations of CBD, DM, OBS, HTN, STK, and HF with hospitalization, severity, and mortality were consistent with prior reports. This network meta-analysis is most comprehensive and up-to-date including 747 prospective and retrospective studies of 73,928,213 COVID-19 patients and evaluating multiple CMD comorbidities. By segregating data by two phases, we attempted to elucidate potential effect modification accounted by changing priorities of treatment regimens/programs, resource distribution, and vaccination during the pandemic. At the time of publication, this analysis uniquely compares combinations of 12 cardiometabolic risk factors individually or in combination through network analyses. Since CMDs are frequently clustered, the network meta-analysis accounts for comorbidities, study

heterogeneity, and indirect associations. Previously, a meta-analysis including 24 studies on diabetes, hypertension, chronic pulmonary diseases and CVD found similar [32] association patterns with COVID-19 adverse outcomes. There were also two studies attempting to rank CMD risk factors and reported different relative ranking of CMD risk factors than our network analysis [33,34]. Although heterogeneities exist across studies, CHD, CAD, and CVD appeared to have the largest impact on COVID-19 mortality and severity, followed by HTN and DM (32, 35, 36). Cardiac injury, stress, and other complications indicated by biomarkers are particularly prevalent among individuals with cardiometabolic disorders, possibly leading to an increased risk of mortality [31]. Like the strong associations for obesity found in network analysis, one genome wide association study (GWAS) also has determined BMI to be strongly associated with COVID-19 hospitalization [36]. Underlying genotypic and phenotypic factors related to Angiotensin I Converting Enzyme 2 (ACE2) are associated with OBS and DM, and may be involved in the mechanisms of COVID-19 pathogenesis [37].

Limitations

We considered -- both qualitatively and quantitatively -- the heterogeneity of the methods, sample population, and model adjustments used by the individual studies identified. Differences in treatments [38, 39, 40], genetics, ethnicity [41], and location [13, 41] may impact consistency of results. While heterogeneity was increased in the generic meta-analysis, the network analysis adjusted for such variables. As the COVID-19 pandemic continues to rage on, additional or unanticipated factors may affect the co-morbidity—COVID-19 outcome severity, including the recent recognition of the Delta SARS-CoV-2 variant projections and vaccination status that affect COVID-19 severity [42, 43].

Conclusion and Recommendations

this meta-analysis and network analysis strengthened existing evidence on increased risk of COVID-19 hospitalization, severity, and mortality among those with cardiometabolic comorbidities. The high prevalence and risk of cardiometabolic comorbidities should be accounted for when predicting prospects and programs of the COVID-19 pandemic.

Tables

Table 1. Main Characteristics of included studies with highest Newcastle-Ottawa Scale (NOS) scores in first half of pandemic (May 14, 2020 to July 28, 2020).

Author	Month, Year	Country of Sample	Sample Size	Male (%)	Age Mean (range or SD)	Level of disease severity and outcomes	NOS
Soares, et al.	Sep, 2020	Brazil	10,713	44.8	-	Mortality, hospitalization	9
Lala, et al.	Aug, 2020	USA	2,736	59.6	66.4 (18-100)	Mortality	9
Poblador-Plou, et al.	Jul, 2020	Spain	4,412	41.2	67.7 (20.7)	Mortality	9
Santos, et al.	Jul, 2020	Spain	3711	47	75.3	Mortality	9
Atkins, et al.	Jul, 2020	UK	507	61.3	74.3 (4.5)	Mortality	9
Wang, et al.	Jun, 2020	China	605	53.2	59 (47-68)	Mortality	9
Lee, et al.	May, 2020	UK	800	56	69 (59-76)	Mortality	9

<i>Rastad, et al.</i>	July, 2020	Iran	2957	53.7	54.8 (16.9)	Mortality	9
<i>Golpe, et al.</i>	Jun, 2020	Spain	539	45.8	70.4 (12.3)	Hospitalization	9
<i>Hur, et al.</i>	May, 2020	USA	486	55.8	59 (19-101)	Intubation	9
<i>Cai, et al.</i>	Apr, 2020	China	383	47.8	61 (52-65)	Progression to severe	9
<i>Busetto, et al.</i>	May, 2020	Italy	92	61.9	70.5 (13.3)	Need for IMV and NIV	9

Abbreviations: NOS, Newcastle-Ottawa Scale; IMV, invasive mechanical ventilation; NIV, non-invasive assisted ventilation.

Percentage of male was calculated based on the whole population. Age was expressed as mean (standard deviation) or median (range).

Table 2a. Studies Included in Meta-Analysis from Early Pandemic (March 30, 2020 to July 28, 2020).

<i>Author, year</i>	<i>Publication Title</i>
<i>Albitar, 2020</i>	Risk factors for mortality among COVID-19 patients.
<i>Al-Salameh, 2020</i>	Characteristics and outcomes of COVID-19 in hospitalized patients with and without diabetes.
<i>Atkins, 2020</i>	Preexisting Comorbidities Predicting COVID-19 and Mortality in the UK Biobank Community Cohort.
<i>Bello-Chavolla, 2020</i>	Predicting Mortality Due to SARS-CoV-2: A Mechanistic Score Relating Obesity and Diabetes to COVID-19 Outcomes in Mexico.
<i>Bello-Chavolla, 2020</i>	Unequal impact of structural health determinants and comorbidity on COVID-19 severity and lethality in older Mexican adults: Considerations beyond chronological aging.
<i>Benussi, 2020</i>	Clinical characteristics and outcomes of inpatients with neurologic disease and COVID-19 in Brescia, Lombardy, Italy.
<i>Bravi, 2020</i>	Predictors of severe or lethal COVID-19, including angiotensin converting enzyme inhibitors and angiotensin II receptor blockers, in a sample of infected Italian citizens.
<i>Cabezudo-Garcia, 2020</i>	Incidence and case fatality rate of COVID-19 in patients with active epilepsy.
<i>Cai, 2020</i>	Obesity and COVID-19 Severity in a Designated Hospital in Shenzhen, China.
<i>Cai, 2020</i>	Association between obesity and clinical prognosis in patients infected with SARS-CoV-2.
<i>Cariou, 2020</i>	Phenotypic characteristics and prognosis of inpatients with COVID-19 and diabetes: the CORONADO study.
<i>Cecconi, 2020</i>	Early predictors of clinical deterioration in a cohort of 239 patients hospitalized for Covid-19 infection in Lombardy, Italy.
<i>Cen, 2020</i>	Risk factors for disease progression in patients with mild to moderate coronavirus disease 2019-a multi-centre observational study.
<i>Chang, 2020</i>	Risk factors for disease progression in COVID-19 patients.
<i>Chung, 2020</i>	The Risk of Diabetes on Clinical Outcomes in Patients with Coronavirus Disease 2019: A Retrospective Cohort Study.
<i>Cummings, 2020</i>	Epidemiology, clinical course, and outcomes of critically ill adults with COVID-19 in New York City: a prospective cohort study.
<i>Deng, 2020</i>	Obesity as a Potential Predictor of Disease Severity in Young COVID-19 Patients: A Retrospective Study.
<i>Deng, 2020</i>	The diagnostic and prognostic role of myocardial injury biomarkers in hospitalized patients with COVID-19.
<i>Denova-Gutiérrez, 2020</i>	The association between obesity, type 2 diabetes, and hypertension with severe COVID-19 on admission among Mexicans.

<i>Docherty, 2020</i>	Features of 20 133 UK patients in hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: Prospective observational cohort study.
<i>Ebinger, 2020</i>	Pre-existing traits associated with Covid-19 illness severity.
<i>Ferrante, 2020</i>	Risk factors for myocardial injury and death in patients with COVID-19: insights from a cohort study with chest computed tomography.
<i>Galloway, 2020</i>	A clinical risk score to identify patients with COVID-19 at high risk of critical care admission or death: An observational cohort study.
<i>Grasseli, 2020</i>	Risk Factors Associated With Mortality Among Patients With COVID-19 in Intensive Care Units in Lombardy, Italy.
<i>Claudia, 2020</i>	Characteristics, predictors and outcomes among 99 patients hospitalised with COVID-19 in a tertiary care centre in Switzerland: an observational analysis.
<i>Hajifathalian, 2020</i>	Obesity is associated with worse outcomes in COVID-19: Analysis of Early Data From New York City.
<i>Hamer, 2020</i>	Lifestyle risk factors, inflammatory mechanisms, and COVID-19 hospitalization: A community-based cohort study of 387,109 adults in UK.
<i>Hashemi, 2020</i>	Impact of chronic liver disease on outcomes of hospitalized patients with COVID-19: A multicentre United States experience.
<i>Hu, 2020</i>	Logistic regression analysis of death risk factors of patients with severe and critical coronavirus disease 2019 and their predictive value. [Chinese]
<i>Hu, 2020</i>	Clinical epidemiological analyses of overweight/obesity and abnormal liver function contributing to prolonged hospitalization in patients infected with COVID-19.
<i>Huang, 2020</i>	Clinical findings of patients with coronavirus disease 2019 in Jiangsu Province, China: A retrospective, multi-center study.
<i>Huang, 2020</i>	COVID-19 patients with hypertension have more severe disease: a multicenter retrospective observational study.
<i>Hur, 2020</i>	Factors Associated With Intubation and Prolonged Intubation in Hospitalized Patients With COVID-19.
<i>Hwang, 2020</i>	Neurological diseases as mortality predictive factors for patients with COVID-19: a retrospective cohort study.
<i>Imam, 2020</i>	Older age and comorbidity are independent mortality predictors in a large cohort of 1305 COVID-19 patients in Michigan, United States.
<i>Jang, 2020</i>	Prognostic Factors for Severe Coronavirus Disease 2019 in Daegu, Korea.
<i>Ji, 2020</i>	Effect of Underlying Comorbidities on the Infection and Severity of COVID-19 in Korea: a Nationwide Case-Control Study.
<i>Kim, 2020</i>	The Correlation of Comorbidities on the Mortality in Patients with COVID-19: an Observational Study Based on the Korean National Health Insurance Big Data.
<i>Kim, 2020</i>	Risk Factors for Intensive Care Unit Admission and In-hospital Mortality among Hospitalized Adults Identified through the U.S. Coronavirus Disease 2019 (COVID-19)-Associated Hospitalization Surveillance Network (COVID-NET).
<i>Klang, 2020</i>	Morbid Obesity as an Independent Risk Factor for COVID-19 Mortality in Hospitalized Patients Younger than 50.

<i>Kuderer, 2020</i>	Clinical impact of COVID-19 on patients with cancer (CCC19): a cohort study.
<i>Lala, 2020</i>	Prevalence and Impact of Myocardial Injury in Patients Hospitalized With COVID-19 Infection.
<i>Lee, 2020</i>	Risk Factors for Mortality and Respiratory Support in Elderly Patients Hospitalized with COVID-19 in Korea.
<i>Lee, 2020</i>	COVID-19 mortality in patients with cancer on chemotherapy or other anticancer treatments: a prospective cohort study.
<i>Li, 2020</i>	Newly diagnosed diabetes is associated with a higher risk of mortality than known diabetes in hospitalized patients with COVID-19.
<i>Li, 2020</i>	Clinical features and short-term outcomes of elderly patients with COVID-19.
<i>Li, 2020</i>	Risk factors for severity and mortality in adult COVID-19 inpatients in Wuhan.
<i>Li, 2020</i>	Baseline characteristics and risk factors for short-term outcomes in 132 COVID-19 patients with diabetes in Wuhan China: A retrospective study.
<i>Louapre, 2020</i>	Clinical Characteristics and Outcomes in Patients With Coronavirus Disease 2019 and Multiple Sclerosis.
<i>Perez, 2020</i>	Comorbidity and prognostic factors on admission in a COVID-19 cohort of a general hospital.
<i>Mccullough, 2020</i>	Electrocardiographic Findings in Coronavirus Disease-19: Insights on Mortality and Underlying Myocardial Processes.
<i>Mehra, 2020</i>	Cardiovascular disease, drug therapy, and mortality in COVID-19.
<i>Nie, 2020</i>	Epidemiological and clinical characteristics of 671 COVID-19 patients in Henan Province, China.
<i>Petersen, 2020</i>	The role of visceral adiposity in the severity of COVID-19: highlights from a unicenter cross-sectional pilot study in Germany.
<i>Pettit, 2020</i>	Obesity is Associated with Increased Risk for Mortality Among Hospitalized Patients with COVID-19.
<i>Poblador-Plou, 2020</i>	Baseline chronic comorbidity and mortality in laboratory-confirmed COVID-19 cases: Results from the PRECOVID study in Spain.
<i>Price-Haywood, 2020</i>	Hospitalization and mortality among black patients and white patients with Covid-19.
<i>Rastad, 2020</i>	Risk and predictors of in-hospital mortality from COVID-19 in patients with diabetes and cardiovascular disease.
<i>Rivera-Izquierdo, 2020</i>	Sociodemographic, clinical and laboratory factors on admission associated with COVID-19 mortality in hospitalized patients: A retrospective observational study.
<i>Salacup, 2020</i>	Characteristics and clinical outcomes of COVID-19 patients in an underserved-inner city population: A single tertiary center cohort.
<i>Shah, 2020</i>	Demographics, comorbidities and outcomes in hospitalized Covid-19 patients in rural southwest Georgia.
<i>Shang, 2020</i>	The Relationship between Diabetes Mellitus and COVID-19 Prognosis: A Retrospective Cohort Study in Wuhan, China.
<i>Shi, 2020</i>	Lactate dehydrogenase and susceptibility to deterioration of mild COVID-19 patients: A multicenter nested case-control study.

<i>Shi, 2020</i>	Clinical Characteristics and Risk Factors for Mortality of COVID-19 Patients With Diabetes in Wuhan, China: A Two-Center, Retrospective Study.
<i>Shi, 2020</i>	Association of Cardiac Injury with Mortality in Hospitalized Patients with COVID-19 in Wuhan, China.
<i>Simonnet, 2020</i>	High Prevalence of Obesity in Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) Requiring Invasive Mechanical Ventilation.
<i>Wang, 2020</i>	A tertiary center experience of multiple myeloma patients with COVID-19: Lessons learned and the path forward.
<i>Wang, 2020</i>	Coronavirus disease 2019 in elderly patients: Characteristics and prognostic factors based on 4-week follow-up.
<i>Wang, 2020</i>	Fasting blood glucose at admission is an independent predictor for 28-day mortality in patients with COVID-19 without previous diagnosis of diabetes: a multi-centre retrospective study.
<i>Wei, 2020</i>	Acute myocardial injury is common in patients with COVID-19 and impairs their prognosis.
<i>Williamson, 2020</i>	OpenSAFELY: factors associated with COVID-19 death in 17 million patients.
<i>Wu, 2020</i>	Risk Factors Associated with Acute Respiratory Distress Syndrome and Death in Patients with Coronavirus Disease 2019 Pneumonia in Wuhan, China.
<i>Wu, 2020</i>	Influence of diabetes mellitus on the severity and fatality of SARS-CoV-2 (COVID-19) infection.
<i>Wu, 2020</i>	Early antiviral treatment contributes to alleviate the severity and improve the prognosis of patients with novel coronavirus disease (COVID-19).
<i>Xie, 2020</i>	Association Between Hypoxemia and Mortality in Patients With COVID-19.
<i>Yan, 2020</i>	Clinical characteristics and outcomes of patients with severe covid-19 with diabetes.
<i>Yang, 2020</i>	Visceral Adiposity and High Intramuscular Fat Deposition Independently Predict Critical Illness in Patients with Sars-COV-2.
<i>Ye, 2020</i>	Impact of comorbidities on patients with COVID-19: A large retrospective study in Zhejiang, China.
<i>Yip, 2020</i>	Liver injury is independently associated with adverse clinical outcomes in patients with COVID-19.
<i>Yu, 2020</i>	Clinical Characteristics, Associated Factors, and Predicting COVID-19 Mortality Risk: A Retrospective Study in Wuhan, China.
<i>Zeng, 2020</i>	Simple nomogram based on initial laboratory data for predicting the probability of ICU transfer of COVID-19 patients: Multicenter retrospective study.
<i>Zhang, 2020</i>	Obesity predisposes to the risk of higher mortality in young COVID-19 patients.
<i>Zhang, 2020</i>	Do underlying cardiovascular diseases have any impact on hospitalised patients with COVID-19?.
<i>Zhang, 2020</i>	Clinical characteristics of different subtypes and risk factors for the severity of illness in patients with COVID-19 in Zhejiang, China.
<i>Zhang, 2020</i>	Association of diabetes mellitus with disease severity and prognosis in COVID-19: A retrospective cohort study.

<i>Zhao, 2020</i>	Comparison of clinical characteristics and outcomes of patients with coronavirus disease 2019 at different ages.
<i>Zhou, 2020</i>	Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study.
<i>Zhu, 2020</i>	Clinical value of immune-inflammatory parameters to assess the severity of coronavirus disease 2019.
<i>Giacomelli, 2020</i>	30-day mortality in patients hospitalized with COVID-19 during the first wave of the Italian epidemic: A prospective cohort study.
<i>Kayem, 2020</i>	A snapshot of the Covid-19 pandemic among pregnant women in France.
<i>Hirsch, 2020</i>	Acute kidney injury in patients hospitalized with COVID-19.
<i>Phipps, 2020</i>	Acute Liver Injury in COVID-19: Prevalence and Association with Clinical Outcomes in a Large US Cohort.
<i>Xia, 2020</i>	An increased neutrophil/lymphocyte ratio is an early warning signal of severe COVID-19
<i>Han, 2020</i>	Analysis of factors affecting the prognosis of COVID-19 patients and viral shedding duration.
<i>Chen, 2020</i>	Analysis of myocardial injury in patients with COVID-19 and association between concomitant cardiovascular diseases and severity of COVID-19.
<i>Gao, 2020</i>	Association of hypertension and antihypertensive treatment with COVID-19 mortality: a retrospective observational study.
<i>Kalligeros, 2020</i>	Association of Obesity with Disease Severity Among Patients with Coronavirus Disease 2019.
<i>Chen, 2020</i>	Cardiovascular manifestations in severe and critical patients with COVID-19.
<i>Inciardi, 2020</i>	Characteristics and outcomes of patients hospitalized for COVID-19 and cardiac disease in Northern Italy.
<i>Killerby, 2020</i>	Characteristics Associated with Hospitalization Among Patients with COVID-19 - Metropolitan Atlanta, Georgia, March-April 2020.
<i>Toussie, 2020</i>	Clinical and Chest Radiography Features Determine Patient Outcomes In Young and Middle Age Adults with COVID-19.
<i>Chen, 2020</i>	Clinical Characteristics and Outcomes of Patients With Diabetes and COVID-19 in Association With Glucose-Lowering Medication.
<i>Suleyman, 2020</i>	Clinical Characteristics and Morbidity Associated with Coronavirus Disease 2019 in a Series of Patients in Metropolitan Detroit.
<i>Pan, 2020</i>	Clinical Features of COVID-19 in Patients With Essential Hypertension and the Impacts of Renin-angiotensin-aldosterone System Inhibitors on the Prognosis of COVID-19 Patients.
<i>Zhang, 2020</i>	Clinical outcomes of COVID-19 cases and influencing factors in Guangdong province.
<i>Guan, 2020</i>	Comorbidity and its impact on 1590 patients with COVID-19 in China: a nationwide analysis.
<i>Bhatla, 2020</i>	COVID-19 and Cardiac Arrhythmias.
<i>Garassino, 2020</i>	COVID-19 in patients with thoracic malignancies (TERAVOLT): first results of an international, registry-based, cohort study.
<i>Hultcrantz, 2020</i>	COVID-19 infections and outcomes in patients with multiple myeloma in New York City: a cohort study from five academic centers.

<i>Deiana, 2020</i>	Deaths in SARS-CoV-2 positive patients in Italy: The influence of underlying health conditions on lethality.
<i>Santos, 2020</i>	Determinants of COVID-19 disease severity in patients with underlying rheumatic disease.
<i>Zhou, 2020</i>	Development and validation a nomogram for predicting the risk of severe COVID-19: A multi-center study in Sichuan, China.
<i>Dong, 2020</i>	Development and Validation of a Nomogram for Assessing Survival in Patients with COVID-19 Pneumonia.
<i>Xiao, 2020</i>	Development and validation of the HNC-LL score for predicting the severity of coronavirus disease 2019.
<i>Ciceri, 2020</i>	Early predictors of clinical outcomes of COVID-19 outbreak in Milan, Italy.
<i>Yang, 2020</i>	Effect of hypertension on outcomes of adult inpatients with COVID-19 in Wuhan, China: a propensity score-matching analysis.
<i>Mendy, 2020</i>	Factors Associated with Hospitalization and Disease Severity in a Racially and Ethnically Diverse Population of COVID-19 Patients.
<i>Xu, 2020</i>	Factors Associated With Prolonged Viral RNA Shedding in Patients with Coronavirus Disease 2019 (COVID-19).
<i>Rottoli, 2020</i>	How important is obesity as a risk factor for respiratory failure, intensive care admission and death in hospitalised COVID-19 patients? Results from a single Italian centre.
<i>Liu, 2020</i>	Hyperglycemia is a strong predictor of poor prognosis in COVID-19.
<i>Xiong, 2020</i>	Hypertension is a risk factor for adverse outcomes in patients with coronavirus disease 2019: a cohort study.
<i>Wu, 2020</i>	Influence of diabetes mellitus on the severity and fatality of SARS-CoV-2 infection.
<i>Harmouch, 2020</i>	Is it all in the heart? Myocardial injury as major predictor of mortality among hospitalized COVID-19 patients.
<i>Hamer, 2020</i>	Lifestyle Risk Factors for Cardiovascular Disease in Relation to COVID-19 Hospitalization: A Community-Based Cohort Study of 387,109 Adults in UK.
<i>García-Azorín, 2020</i>	Neurological Comorbidity Is a Predictor of Death in Covid-19 Disease: A Cohort Study on 576 Patients.
<i>Sabri, 2020</i>	Novel coronavirus disease 2019: predicting prognosis by using a computed tomography severity score and clinicolaboratory data.
<i>Busetto, 2020</i>	Obesity and COVID-19: an Italian snapshot.
<i>Bhargava, 2020</i>	Predictors for Severe COVID-19 Infection.
<i>Wang, 2020</i>	Prognostic value of myocardial injury in patients with COVID-19.
<i>Fang, 2020</i>	Relationship between clinical types and radiological subgroups defined by latent class analysis in 2019 novel coronavirus pneumonia caused by SARS-CoV-2.
<i>Mehra, 2020</i>	RETRACTED:Hydroxychloroquine or chloroquine with or without a macrolide for treatment of COVID-19: a multinational registry analysis.
<i>Hu, 2020</i>	Risk Factors Associated with Clinical Outcomes in 323 COVID-19 Hospitalized Patients in Wuhan, China.
<i>Soares, 2020</i>	Risk Factors for Hospitalization and Mortality due to COVID-19 in Espirito Santo State, Brazil.

<i>Escalera-Antezana, 2020</i>	Risk factors for mortality in patients with Coronavirus Disease 2019 (COVID-19) in Bolivia: An analysis of the first 107 confirmed cases.
<i>Chen, 2020</i>	Risk Factors of Fatal Outcome in Hospitalized Subjects With Coronavirus Disease 2019 From a Nationwide Analysis in China.
<i>Golpe, 2020</i>	Risk of severe COVID-19 in hypertensive patients treated with renin-angiotensin-aldosterone system inhibitors.
<i>Yang, 2020</i>	Risks factors for death among COVID-19 patients combined with hypertension, coronary heart disease or diabetes. [Chinese]
<i>Palaiodimos, 2020</i>	Severe obesity is associated with higher in-hospital mortality in a cohort of patients with COVID-19 in the Bronx, New York.
<i>Palaiodimos, 2020</i>	Severe obesity, increasing age and male sex are independently associated with worse in-hospital outcomes, and higher in-hospital mortality, in a cohort of patients with COVID-19 in the Bronx, New York.
<i>Zeuschner, 2020</i>	Should We Perform Old-for-Old Kidney Transplantation during the COVID-19 Pandemic? The Risk for Post-Operative Intensive Stay.
<i>Chen, 2020</i>	The characteristics and outcomes of 681 severe cases with COVID-19 in China.
<i>Nakeshbandi, 2020</i>	The impact of obesity on COVID-19 complications: a retrospective cohort study.
<i>Watanabe, 2020</i>	Visceral fat shows the strongest association with the need of intensive Care in Patients with COVID-19.

Table 2b. Studies Included in Meta-Analysis from Recent Pandemic (July 29, 2020 to May 29, 2021).

<i>Author, year</i>	<i>Publication Title</i>
<i>Abbas, 2020</i>	Presenting the characteristics, smoking versus diabetes, and outcome among patients hospitalized with COVID-19.
<i>Abohamr, 2020</i>	Clinical characteristics and in-hospital mortality of covid-19 adult patients in saudi arabia.
<i>Abraha, 2021</i>	Clinical features and risk factors associated with morbidity and mortality among patients with COVID-19 in northern Ethiopia.
<i>Agarwal, 2020</i>	Cardiovascular Disease in Hospitalized Patients With a Diagnosis of Coronavirus From the Pre-COVID-19 Era in United States: National Analysis From 2016-2017.
<i>Aghaaliakbari, 2020</i>	Angiotensin converting enzyme inhibitors, a risk factor of poor outcome in diabetic patients with COVID-19 infection.
<i>Aidaoui, 2020</i>	Predictors of Severity in Covid-19 Patients in Casablanca, Morocco.
<i>Akpinar, 2021</i>	Comparison of Clinical, Laboratory and Demographic Characteristics of Patients Diagnosed with COVID-19 as Symptomatic and Atypical Symptoms
<i>Andreano, 2021</i>	Development of a multivariable model predicting mortality risk from comorbidities in an Italian cohort of 18,286 confirmed COVID-19 cases aged 40 years or older.
<i>Aslaner, 2021</i>	The effect of chronic diseases, age and gender on morbidity and mortality of covid-19 infection.
<i>Ayten, 2020</i>	Retrospective analysis of severe covid-19 pneumonia patients treated with lopinavir/ritonavir: A comparison with survivor and non-survivor patients.
<i>Barbu, 2020</i>	The Impact of SARS-CoV-2 on the Most Common Comorbidities-A Retrospective Study on 814 COVID-19 Deaths in Romania.
<i>Barman, 2020</i>	The effect of the severity COVID-19 infection on electrocardiography.
<i>Barron, 2020</i>	Associations of type 1 and type 2 diabetes with COVID-19-related mortality in England: a whole-population study.
<i>Bepouka, 2020</i>	Predictors of mortality in covid-19 patients at Kinshasa University Hospital, Democratic Republic of the Congo, from March to June 2020.
<i>Bergman, 2021</i>	Risk factors for COVID-19 diagnosis, hospitalization, and subsequent all-cause mortality in Sweden: a nationwide study.
<i>Bhatt, 2021</i>	Clinical Outcomes in Patients With Heart Failure Hospitalized With COVID-19.
<i>Bonifazi, 2021</i>	Predictors of worse prognosis in young and middle-aged adults hospitalized with covid-19 pneumonia: A multi-center italian study (covid-under50).
<i>Burrell, 2020</i>	Outcomes for patients with COVID-19 admitted to Australian intensive care units during the first four months of the pandemic.
<i>Byeon, 2021</i>	Factors affecting the survival of early COVID-19 patients in South Korea: An observational study based on the Korean National Health Insurance big data.
<i>Cao, 2021</i>	Obesity and COVID-19 in Adult Patients With Diabetes.
<i>Carrillo-Vega, 2020</i>	Early estimation of the risk factors for hospitalization and mortality by COVID-19 in Mexico.

<i>Castelnuovo, 2020</i>	Common cardiovascular risk factors and in-hospital mortality in 3,894 patients with COVID-19: survival analysis and machine learning-based findings from the multicentre Italian CORIST Study.
<i>Cervantes, 2021</i>	Factors associated with COVID-19 severity and mortality among Hispanic patients living on the USA-Mexico border.
<i>Chan, 2021</i>	COVID-19 in the New York City Jail System: Epidemiology and Health Care Response, March-April 2020.
<i>Chang, 2020</i>	COVID-19 Hospitalization by Race and Ethnicity: Association with Chronic Conditions Among Medicare Beneficiaries, January 1-September 30, 2020.
<i>Chatrath, 2020</i>	The effect of concomitant COVID-19 infection on outcomes in patients hospitalized with heart failure.
<i>Chen, 2020</i>	Coagulopathy is a major extrapulmonary risk factor for mortality in hospitalized patients with COVID-19 with type 2 diabetes.
<i>Cheng, 2020</i>	Clinical characteristics and fatal outcomes of hypertension in patients with severe COVID-19.
<i>Chetboun, 2021</i>	BMI and pneumonia outcomes in critically ill COVID-19 patients: an international multicenter study.
<i>Chishinga, 2020</i>	Characteristics and Risk Factors for Hospitalization and Mortality among Persons with COVID-19 in Atlanta Metropolitan Area.
<i>Cho, 2021</i>	Impact of comorbidity burden on mortality in patients with COVID-19 using the Korean health insurance database.
<i>Ciardullo, 2021</i>	Impact of diabetes on COVID-19-related in-hospital mortality: a retrospective study from Northern Italy.
<i>Cottini, 2021</i>	Obesity is a Major Risk Factor for Hospitalization in Community-Managed COVID-19 Pneumonia.
<i>Crouse, 2021</i>	Metformin Use Is Associated With Reduced Mortality in a Diverse Population With COVID-19 and Diabetes.
<i>Cummins, 2021</i>	Factors associated with COVID-19 related hospitalisation, critical care admission and mortality using linked primary and secondary care data.
<i>Dennis, 2021</i>	Type 2 diabetes and covid-19- related mortality in the critical care setting: A national cohort study in england, march-july 2020.
<i>Denova-Gutiérrez, 2020</i>	The Association of Obesity, Type 2 Diabetes, and Hypertension with Severe Coronavirus Disease 2019 on Admission Among Mexican Patients.
<i>Desai, 2021</i>	The role of anti-hypertensive treatment, comorbidities and early introduction of LMWH in the setting of COVID-19: A retrospective, observational study in Northern Italy.
<i>El-Jawahri, 2021</i>	Clinical Outcomes of Patients Hospitalized with Coronavirus Disease 2019 (COVID-19) in Boston.
<i>Eshrati, 2020</i>	Investigating the factors affecting the survival rate in patients with COVID-19: A retrospective cohort study.
<i>Esme, 2021</i>	Older Adults With Coronavirus Disease 2019: A Nationwide Study in Turkey.
<i>Fang, 2021</i>	Impact of comorbidities on clinical prognosis in 1280 patients with different types of COVID-19.

<i>Fresán, 2021</i>	Hypertension and related comorbidities as potential risk factors for covid-19 hospitalization and severity: A prospective population-based cohort study.
<i>Gao, 2021</i>	Associations between body-mass index and COVID-19 severity in 6.9 million people in England: a prospective, community-based, cohort study.
<i>Geng, 2021</i>	Risk factors for developing severe COVID-19 in China: an analysis of disease surveillance data.
<i>Geteneh, 2021</i>	Clinical characteristics of patients infected with sars-cov-2 in north wollo zone, north-east ethiopia.
<i>Girardin, 2021</i>	Contribution of pulmonary diseases to COVID-19 mortality in a diverse urban community of New York.
<i>Gobbato, 2020</i>	Clinical characteristics and risk factors associated with severe COVID-19: prospective analysis of 1,045 hospitalised cases in North-Eastern France, March 2020.
<i>Goodman, 2020</i>	Impact of Sex and Metabolic Comorbidities on COVID-19 Mortality Risk Across Age Groups: 66,646 Inpatients Across 613 U.S. Hospitals.
<i>Görgülü, 2020</i>	Effects of Comorbid Factors on Prognosis of Three Different Geriatric Groups with COVID-19 Diagnosis.
<i>Gottlieb, 2020</i>	Clinical Course and Factors Associated With Hospitalization and Critical Illness Among COVID-19 Patients in Chicago, Illinois.
<i>Gray, 2021</i>	Changes in COVID-19 in-hospital mortality in hospitalised adults in England over the first seven months of the pandemic: An observational study using administrative data.
<i>Gregory, 2021</i>	COVID-19 severity is tripled in the diabetes community: A prospective analysis of the pandemic's impact in type 1 and type 2 diabetes.
<i>Gu, 2020</i>	Characteristics Associated with Racial/Ethnic Disparities in COVID-19 Outcomes in an Academic Health Care System.
<i>Gude-Sampedro, 2021</i>	Development and validation of a prognostic model based on comorbidities to predict COVID-19 severity: a population-based study.
<i>Gupta, 2021</i>	Diabetes Mellitus and Hypertension Increase Risk of Death in Novel Corona Virus Patients Irrespective of Age: a Prospective Observational Study of Comorbidities and COVID-19 from India.
<i>Hagg, 2020</i>	Age, Frailty, and Comorbidity as Prognostic Factors for Short-Term Outcomes in Patients With Coronavirus Disease 2019 in Geriatric Care.
<i>Harrison, 2020</i>	Comorbidities associated with mortality in 31,461 adults with COVID-19 in the United States: A federated electronic medical record analysis.
<i>He, 2021</i>	The Prognostic Value of Myocardial Injury in COVID-19 Patients and Associated Characteristics.
<i>Heberto, 2020</i>	Implications of myocardial injury in Mexican hospitalized patients with coronavirus disease 2019 (COVID-19).
<i>Henein, 2021</i>	Combined cardiac risk factors predict covid-19 related mortality and the need for mechanical ventilation in coptic clergy.
<i>Hernández-Galdamez, 2020</i>	Increased Risk of Hospitalization and Death in Patients with COVID-19 and Pre-existing Noncommunicable Diseases and Modifiable Risk Factors in Mexico.

<i>Ho, 2020</i>	Modifiable and non-modifiable risk factors for COVID-19, and comparison to risk factors for influenza and pneumonia: Results from a UK Biobank prospective cohort study.
<i>Hobbs, 2021</i>	Risk factors for mortality and progression to severe covid-19 disease in the Southeast United States (US): A report from the SEUS study Group.
<i>Hu, 2020</i>	Risk Factors Associated with Clinical Outcomes in 323 Coronavirus Disease 2019 (COVID-19) Hospitalized Patients in Wuhan, China.
<i>Huang, 2020</i>	A novel risk score to predict cardiovascular complications in patients with coronavirus disease 2019 (COVID-19): A retrospective, multicenter, observational study.
<i>Ilic, 2021</i>	Pneumonia in healthcare workers during a COVID-19 outbreak at a cardiovascular hospitals.
<i>Ioannou, 2021</i>	Development of COVIDVax Model to Estimate the Risk of SARS-CoV-2-Related Death Among 7.6 Million US Veterans for Use in Vaccination Prioritization.
<i>Islam, 2020</i>	Risk factors associated with morbidity and mortality outcomes of COVID-19 patients on the 28th day of the disease course: A retrospective cohort study in Bangladesh.
<i>Jackson, 2020</i>	Predictors at admission of mechanical ventilation and death in an observational cohort of adults hospitalized with COVID-19.
<i>Jain, 2020</i>	A retrospective observational study to determine the early predictors of in-hospital mortality at admission with covid-19.
<i>Jakob, 2021</i>	First results of the "Lean European Open Survey on SARS-CoV-2-Infected Patients (LEOSS)".
<i>Jaspard, 2021</i>	Clinical presentation, outcomes and factors associated with mortality: a prospective study from three COVID-19 referral care centers in West Africa.
<i>Javanian, 2020</i>	Risk factors for mortality of 557 adult patients with COVID 19 in Babol, Northern Iran: a retrospective cohort study.
<i>Jayanama, 2021</i>	The association between body mass index and severity of Coronavirus Disease 2019 (COVID-19): A cohort study.
<i>Jimeno, 2020</i>	Prognostic implications of neutrophil-lymphocyte ratio in COVID-19.
<i>Kaeuffer, 2020</i>	Survival and predictors of deaths of patients hospitalised due to COVID-19 from a retrospective and multicentre cohort study in Brazil.
<i>Kang, 202</i>	Clinical characteristics of coronavirus disease 2019 patients with diarrhea in Daegu.
<i>Ken-Dror, 2020</i>	COVID-19 outcomes in UK centre within highest health and wealth band: A prospective cohort study.
<i>Keski, 2021</i>	Hematological and Inflammatory Parameters to Predict the Prognosis in COVID-19.
<i>Khan, 2021</i>	Clinical characteristics and outcomes of patients with Corona Virus Disease 2019 (COVID-19) at Mercy Health Hospitals, Toledo, Ohio.
<i>Khawaja, 2020</i>	COVID-19 and its impact on the cardiovascular system.
<i>Kim, 2020</i>	Analysis of mortality and morbidity in covid-19 patients with obesity using clinical epidemiological data from the korean center for disease control & prevention.

<i>Kim, 2020</i>	Clinical Characteristics and Outcomes of COVID-19 Cohort Patients in Daegu Metropolitan City Outbreak in 2020.
<i>Kim, 2020</i>	Risk factors on the progression to clinical outcomes of covid-19 patients in south korea: Using national data.
<i>Kim, 2021</i>	Evaluation of the prognosis of covid-19 patients according to the presence of underlying diseases and drug treatment.
<i>Kim, 2021</i>	Risk Factors for Intensive Care Unit Admission and In-hospital Mortality Among Hospitalized Adults Identified through the US Coronavirus Disease 2019 (COVID-19)-Associated Hospitalization Surveillance Network (COVID-NET).
<i>Koh, 2021</i>	Diabetes predicts severity of COVID-19 infection in a retrospective cohort: A mediatory role of the inflammatory biomarker C-reactive protein.
<i>Kolhe, 2020</i>	Acute kidney injury associated with COVID-19: A retrospective cohort study.
<i>Laake, 2021</i>	Characteristics, management and survival of ICU patients with coronavirus disease-19 in Norway, March-June 2020. A prospective observational study.
<i>Lampasona, 2020</i>	Antibody response to multiple antigens of SARS-CoV-2 in patients with diabetes: an observational cohort study.
<i>Lanini, 2020</i>	COVID-19 disease - Temporal analyses of complete blood count parameters over course of illness, and relationship to patient demographics and management outcomes in survivors and non-survivors: A longitudinal descriptive cohort study.
<i>León-Pedroza, 2021</i>	Impact of metabolic syndrome in the clinical outcome of disease by SARS-COV-2 in Mexican population.
<i>Lian, 2020</i>	High neutrophil-to-lymphocyte ratio associated with progression to critical illness in older patients with COVID-19: a multicenter retrospective study.
<i>Liu, 2021</i>	Diabetes, even newly defined by HbA1c testing, is associated with an increased risk of in-hospital death in adults with COVID-19.
<i>Liu, 2021</i>	Clinical characteristics and related risk factors of disease severity in 101 COVID-19 patients hospitalized in Wuhan, China.
<i>Loannou, 2020</i>	Risk Factors for Hospitalization, Mechanical Ventilation, or Death among 10131 US Veterans with SARS-CoV-2 Infection.
<i>Loffi, 2020</i>	Coronary artery disease in patients hospitalised with Coronavirus disease 2019 (COVID-19) infection.
<i>Lucar, 2021</i>	Epidemiology, Clinical Features, and Outcomes of Hospitalized Adults with COVID-19: Early Experience from an Academic Medical Center in Mississippi.
<i>Ma, 2020</i>	A nomogram model based on clinical and laboratory parameters at admission for predicting the survival of COVID-19 patients.
<i>Maddaloni, 2020</i>	Cardiometabolic multimorbidity is associated with a worse Covid-19 prognosis than individual cardiometabolic risk factors: A multicentre retrospective study (CoViDiab II).
<i>Magro, 2021</i>	Predicting in-hospital mortality from Coronavirus Disease 2019: A simple validated app for clinical use.
<i>Mallow, 2020</i>	Outcomes of hospitalized COVID-19 patients by risk factors: Results from a United States hospital claims database.

<i>Manohar, 2021</i>	Social and Clinical Determinants of COVID-19 Outcomes: Modeling Real-World Data from a Pandemic Epicenter.
<i>Marcedo, 2020</i>	Correlation between hospitalized patients' demographics, symptoms, comorbidities, and COVID-19 pandemic in Bahia, Brazil.
<i>Marcolino, 2021</i>	Clinical characteristics and outcomes of patients hospitalized with COVID-19 in Brazil: Results from the Brazilian COVID-19 registry.
<i>Martins-Filho, 2020</i>	Factors associated with mortality among hospitalized patients with covid-19: A retrospective cohort study.
<i>Mbarga, 2021</i>	Clinical profile and factors associated with COVID-19 in Yaounde, Cameroon: A prospective cohort study.
<i>McCarty, 2020</i>	How Do Presenting Symptoms and Outcomes Differ by Race/Ethnicity Among Hospitalized Patients with COVID-19 Infection? Experience in Massachusetts.
<i>Mendes, 2021</i>	Incidence, characteristics and clinical relevance of acute stroke in old patients hospitalized with COVID-19.
<i>Minhas, 2021</i>	The role of sex and inflammation in cardiovascular outcomes and mortality in COVID-19.
<i>Mirani, 2020</i>	Impact of comorbidities and glycemia at admission and dipeptidyl peptidase 4 inhibitors in patients with type 2 diabetes with covid-19: A case series from an academic hospital in lombardy, italy.
<i>Moon, 2020</i>	Independent impact of diabetes on the severity of coronavirus disease 2019 in 5,307 patients in South Korea: A nationwide cohort study.
<i>Morys, 2021</i>	Poor Metabolic Health Increases COVID-19-Related Mortality in the UK Biobank Sample.
<i>Motaib, 2021</i>	Obesity and Disease Severity Among Patients With COVID-19.
<i>Munblit, 2020</i>	StopCOVID cohort: An observational study of 3,480 patients admitted to the Sechenov University hospital network in Moscow city for suspected COVID-19 infection.
<i>Najera, 2021</i>	Health and Institutional Risk Factors of COVID-19 Mortality in Mexico, 2020.
<i>Nascimento, 2021</i>	COVID-19 and Myocardial Injury in a Brazilian ICU: High Incidence and Higher Risk of In-Hospital Mortality. [Portuguese, English]
<i>Ngiam, 2021</i>	Demographic shift in COVID-19 patients in Singapore from an aged, at-risk population to young migrant workers with reduced risk of severe disease.
<i>Nguyen, 2021</i>	Community Characteristics and COVID-19 Outcomes: A Study of 159 Counties in Georgia, United States.
<i>Nijman, 2021</i>	Risk factors for in-hospital mortality in laboratory-confirmed COVID-19 patients in the Netherlands: A competing risk survival analysis.
<i>Nimkar, 2020</i>	Incidence and Risk Factors for Acute Kidney Injury and Its Effect on Mortality in Patients Hospitalized From COVID-19.
<i>Niu, 2021</i>	Development of a predictive model for mortality in hospitalized patients with COVID-19.
<i>Núñez-Gil, 2020</i>	Underlying heart diseases and acute COVID-19 outcomes.
<i>Oetjens, 2020</i>	Electronic health record analysis identifies kidney disease as the leading risk factor for hospitalization in confirmed COVID-19 patients.

<i>Olivas-Martinez A., 2020</i>	In-hospital mortality from severe COVID-19 in a tertiary care center in Mexico City; causes of death, risk factors and the impact of hospital saturation.
<i>Omrani, 2020</i>	The first consecutive 5000 patients with Coronavirus Disease 2019 from Qatar; a nation-wide cohort study.
<i>Osibogun, 2021</i>	Outcomes of COVID-19 patients with comorbidities in southwest Nigeria.
<i>Panagiotou, 2021</i>	Risk Factors Associated with All-Cause 30-Day Mortality in Nursing Home Residents with COVID-19.
<i>Paranjape, 2021</i>	Development and validation of a predictive model for critical illness in adult patients requiring hospitalization for COVID-19.
<i>Park, 2020</i>	Impact of Cardiovascular Risk Factors and Cardiovascular Diseases on Outcomes in Patients Hospitalized with COVID-19 in Daegu Metropolitan City.
<i>Peng, 2020</i>	Clinical characteristics and prognosis of 244 cardiovascular patients suffering from coronavirus disease in Wuhan, China.
<i>Peterson, 2021</i>	The relationship between coronary artery disease and clinical outcomes in COVID-19: a single-center retrospective analysis.
<i>Pettrone, 2021</i>	Characteristics and risk factors of hospitalized and nonhospitalized COVID-19 patients, Atlanta, Georgia, USA, March-April 2020.
<i>Pishgahi, 2021</i>	Echocardiographic Abnormalities as Independent Prognostic Factors of In-Hospital Mortality among COVID-19 Patients.
<i>Polverino, 2020</i>	Comorbidities, cardiovascular therapies, and COVID-19 mortality: A nationwide, italian observational study (ItaliCO).
<i>Redondo-Bravo, 2020</i>	The first wave of the COVID-19 pandemic in Spain: Characterisation of cases and risk factors for severe outcomes, as at 27 April 2020.
<i>Reilev, 2020</i>	Characteristics and predictors of hospitalization and death in the first 11 122 cases with a positive RT-PCR test for SARS-CoV-2 in Denmark: A nationwide cohort.
<i>Ricchio, 2021</i>	Characteristics, Management, and Outcomes of Elderly Patients with Diabetes in a Covid-19 Unit: Lessons Learned from a Pilot Study.
<i>Rodriguez-Gonzalez, 2021</i>	COVID-19 in hospitalised patients in Spain: a cohort study in Madrid.
<i>Romagnolo, 2020</i>	Neurological comorbidity and severity of COVID-19.
<i>Rossi, 2020</i>	Characteristics and outcomes of a cohort of COVID-19 patients in the Province of Reggio Emilia, Italy.
<i>Rossi, 2021</i>	Obesity as a risk factor for unfavourable outcomes in critically ill patients affected by Covid 19.
<i>Rozaliyani, 2020</i>	Factors Associated with Death in COVID-19 Patients in Jakarta, Indonesia: An Epidemiological Study.
<i>Rumery, 2021</i>	Outcomes of coronavirus disease-2019 among veterans with pre-existing diagnosis of heart failure.
<i>Saleh, 2020</i>	The association between cardiac injury and outcomes in hospitalized patients with COVID-19.

<i>Sands, 2020</i>	Patient characteristics and admitting vital signs associated with coronavirus disease 2019 (COVID-19)-related mortality among patients admitted with noncritical illness.
<i>Santos, 2020</i>	Clinical, demographical characteristics and hospitalisation of 3,010 patients with Covid-19 in Friuli Venezia Giulia Region (Northern Italy). A multivariate, population-based, statistical analysis.
<i>Satman, 2021</i>	Unexpectedly lower mortality rates in COVID-19 patients with and without type 2 diabetes in Istanbul.
<i>Seiglie, 2020</i>	Diabetes as a risk factor for poor early outcomes in patients hospitalized with covid-19.
<i>Shah, 2020</i>	Factors associated with increased mortality in hospitalized COVID-19 patients.
<i>Sharif, 2021</i>	Prevalence and impact of diabetes and cardiovascular disease on clinical outcome among patients with COVID-19 in Bangladesh.
<i>Shin, 2021</i>	Anatomy of comorbidity complexity of COVID-19: the case of hospitalized South Korean patients.
<i>Shrestha, 2021</i>	Type 2 diabetes is associated with increased risk of critical respiratory illness in patients COVID-19 in a community hospital.
<i>Silva, 2021</i>	Risk factors for critical illness and death among adult Brazilians with COVID-19.
<i>Silverii, 2021</i>	Are diabetes and its medications risk factors for the development of COVID-19? Data from a population-based study in Sicily.
<i>Sonmez, 2021</i>	Clinical characteristics and outcomes of COVID-19 in patients with type 2 diabetes in Turkey: A nationwide study (TurCoviDia).
<i>Sousa, 2020</i>	Mortality and survival of COVID-19.
<i>Souza, 2021</i>	Clinical course and outcome of patients with COVID-19 in Mumbai City: An observational study.
<i>Sun, 2020</i>	Independent and combined effects of hypertension and diabetes on clinical outcomes in patients with COVID-19: A retrospective cohort study of Huoshen Mountain Hospital and Guanggu Fangcang Shelter Hospital.
<i>Surendra, 2021</i>	Clinical characteristics and mortality associated with COVID-19 in Jakarta, Indonesia: A hospital-based retrospective cohort study.
<i>Suresh, 2021</i>	Association of obesity with illness severity in hospitalized patients with COVID-19: A retrospective cohort study.
<i>Sutter, 2020</i>	Association of diabetes and outcomes in patients with COVID-19: Propensity score-matched analyses from a French retrospective cohort.
<i>Tang, 2021</i>	A comprehensive evaluation of early potential risk factors for disease aggravation in patients with COVID-19.
<i>Tchang, 2021</i>	The Independent Risk of Obesity and Diabetes and Their Interaction in COVID-19: A Retrospective Cohort Study.
<i>Terlecki, 2021</i>	Association between cardiovascular disease, cardiovascular drug therapy, and in-hospital outcomes in patients with COVID-19: data from a large single-center registry in Poland.
<i>Tessitore, 2021</i>	Mortality and high risk of major adverse events in patients with COVID-19 and history of cardiovascular disease.

<i>Thompson, 2020</i>	Patient characteristics and predictors of mortality in 470 adults admitted to a district general hospital in England with Covid-19.
<i>Toh, 2021</i>	Outcomes for the first wave of hospitalised patients with COVID-19 in the South Australian context: a retrospective audit.
<i>Toprak, 2021</i>	Do age, hypertension, coronary artery disease, ace-i, ARB or beta-blockers therapy increase the risk of mortality in COVID 19 patients? The results of a tertiary center in Turkey.
<i>Toussie, 2020</i>	Clinical and chest radiography features determine patient outcomes in young and middle-aged adults with COVID-19.
<i>Tsai, 2021</i>	COVID-19 associated mortality and cardiovascular disease outcomes among US women veterans.
<i>Turcotte, 2020</i>	Risk factors for severe illness in hospitalized Covid-19 patients at a regional hospital.
<i>Vaughan, 2021</i>	Relationship of socio-demographics, comorbidities, symptoms and healthcare access with early COVID-19 presentation and disease severity.
<i>Vena, 2020</i>	Clinical characteristics, management and in-hospital mortality of patients with coronavirus disease 2019 in Genoa, Italy.
<i>Vera-Zertuche, 2021</i>	Obesity is a strong risk factor for short-term mortality and adverse outcomes in Mexican patients with COVID-19: A national observational study.
<i>Vergara, 2021</i>	Role of comorbidities on the mortality in patients with SARS-CoV-2 infection: an Italian cohort study.
<i>Villalba, 2021</i>	Impact of the presence of heart disease, cardiovascular medications and cardiac events on outcome in COVID-19.
<i>Wang, 2020</i>	Clinical Features of COVID-19 Patients with Different Outcomes in Wuhan: A Retrospective Observational Study.
<i>Wang, 2020</i>	Overweight and Obesity are Risk Factors of Severe Illness in Patients with COVID-19.
<i>Wang, 2020</i>	Epidemiological characteristics of patients with severe COVID-19 infection in Wuhan, China: evidence from a retrospective observational study.
<i>Wollenstein-Betech, 2020</i>	Physiological and socioeconomic characteristics predict COVID-19 mortality and resource utilization in Brazil.
<i>Woolcott, 2021</i>	The effect of age on the association between diabetes and mortality in adult patients with COVID-19 in Mexico.
<i>Xu, 2020</i>	Diabetic patients with COVID-19 need more attention and better glycemic control.
<i>Yan, 2020</i>	Association of Overlapped and Un-overlapped Comorbidities with COVID-19 Severity and Treatment Outcomes: A Retrospective Cohort Study from Nine Provinces in China.
<i>Yazdanpanah, 2020</i>	Impact on disease mortality of clinical, biological, and virological characteristics at hospital admission and overtime in COVID-19 patients.
<i>Yoshida, 2021</i>	Clinical characteristics and outcomes in women and men hospitalized for coronavirus disease 2019 in New Orleans.
<i>You, 2020</i>	Clinical outcomes of COVID-19 patients with type 2 diabetes: A population-based study in Korea.

<i>Yun, 2020</i>	Severe COVID-19 Illness: Risk Factors and Its Burden on Critical Care Resources.
<i>Zamanian, 2020</i>	Association of underlying diseases and clinical characteristics with mortality in patients with 2019 novel coronavirus in Iran.
<i>Zandkarimi, 2020</i>	The Prognostic Factors Affecting the Survival of Kurdistan Province COVID-19 Patients: A Cross-sectional Study From February to May 2020.
<i>Zhang, 2020</i>	Clinical Course and Mortality of Stroke Patients with Coronavirus Disease 2019 in Wuhan, China.
<i>Zhang, 2021</i>	The association between obesity and severity in patients with coronavirus disease 2019: A retrospective, single-center study, Wuhan.
<i>Zhang, 2021</i>	Risk factors associated with the progression of COVID-19 in elderly diabetes patients.
<i>Zhong R., 2021</i>	Which Factors, Smoking, Drinking Alcohol, Betel Quid Chewing, or Underlying Diseases, Are More Likely to Influence the Severity of COVID-19?.
<i>Zhu, 2020</i>	Association of obesity and its genetic predisposition with the risk of severe COVID-19: Analysis of population-based cohort data.

Table 3a. Fixed Effect Models of Cardiometabolic Risk Factors and COVID-19 outcomes during early pandemic (first publication to July 28, 2020). AF, atrial fibrillation; CAD, coronary artery disease; CBD, cerebrovascular disease; CHD, coronary heart disease; CVD, cardiovascular disease; DM, diabetes mellitus; HF, heart failure; HTN, hypertension

	Hospitalization	Severity	Mortality
	OR (95% CI)	OR (95% CI)	OR (95% CI)
AF	N/A	N/A	N/A
CAD	N/A	1.76 (1.58 – 1.95)	1.19 (1.14 – 1.24)
CBD	N/A	1.54 (1.17 – 2.02)	1.88 (1.47 – 2.39)
CHD	N/A	N/A	1.17 (1.22 – 1.28)
CVD	N/A	1.76 (1.52 – 2.04)	1.68 (1.45 – 1.98)
DM	1.64 (1.44 – 1.87)	1.45 (1.36 – 1.54)	1.36 (1.33 – 1.39)
HF	N/A	2.73 (2.37 – 3.16)	1.75 (1.62 – 1.89)
HTN	N/A	1.28 (1.21 – 1.35)	1.14 (1.11 – 1.17)
MI	N/A	0.84 (0.61 – 1.18)	1.18 (1.13 – 1.23)
OBS	1.66 (1.53 – 1.81)	1.13 (1.09 – 1.17)	1.25 (1.21 – 1.29)
OW	N/A	1.89 (1.46 – 2.45)	N/A
STK	N/A	N/A	2.15 (2.05 – 2.26)

*Estimates based on fewer than 3 studies were not included.

Table 3b. Fixed Effect Models of Cardiometabolic Risk Factors and COVID-19 outcomes during recent pandemic (July 29, 2020 to May 19, 2021). AF, atrial fibrillation; CAD, coronary artery disease; CBD, cerebrovascular disease; CHD, coronary heart disease; CVD, cardiovascular disease; DM, diabetes mellitus; HF, heart failure; HTN, hypertension

	Hospitalization	Severity	Mortality
	OR (95% CI)	OR (95% CI)	OR (95% CI)
AF	N/A	N/A	1.23 (1.05 – 1.45)
CAD	1.08 (1.00 – 1.17)	1.14 (0.99 – 1.31)	1.27 (1.24 – 1.31)
CBD	1.17 (1.03 – 1.34)	1.10 (0.94 – 1.30)	1.72 (1.67 – 1.77)
CHD	N/A	1.14 (0.99 – 1.31)	1.27 (1.24 – 1.31)
CVD	1.23 (1.22 – 1.24)	1.33 (1.30 – 1.36)	1.19 (1.16 – 1.22)
DM	1.46 (1.45 – 1.47)	1.42 (1.38 – 1.45)	1.52 (1.51 – 1.54)
HF	1.43 (1.41 – 1.44)	1.34 (1.18 – 1.53)	1.52 (1.51 – 1.54)
HTN	1.24 (1.23 – 1.26)	1.25 (1.20 – 1.31)	1.28 (1.26 – 1.30)
MI	N/A	N/A	1.19 (1.14 – 1.24)
OBS	1.35 (1.34 – 1.37)	1.82 (1.77 – 1.87)	1.44 (1.42 – 1.46)
OW	N/A	1.27 (1.16 – 1.39)	0.82 (0.74 – 0.92)
STK	1.13 (1.11 – 1.15)	1.63 (1.21 – 2.21)	1.15 (1.01 – 1.31)

*Models including fewer than 3 studies were not included.

Figures

Figure 1. Search and selection process by timeframe according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist.

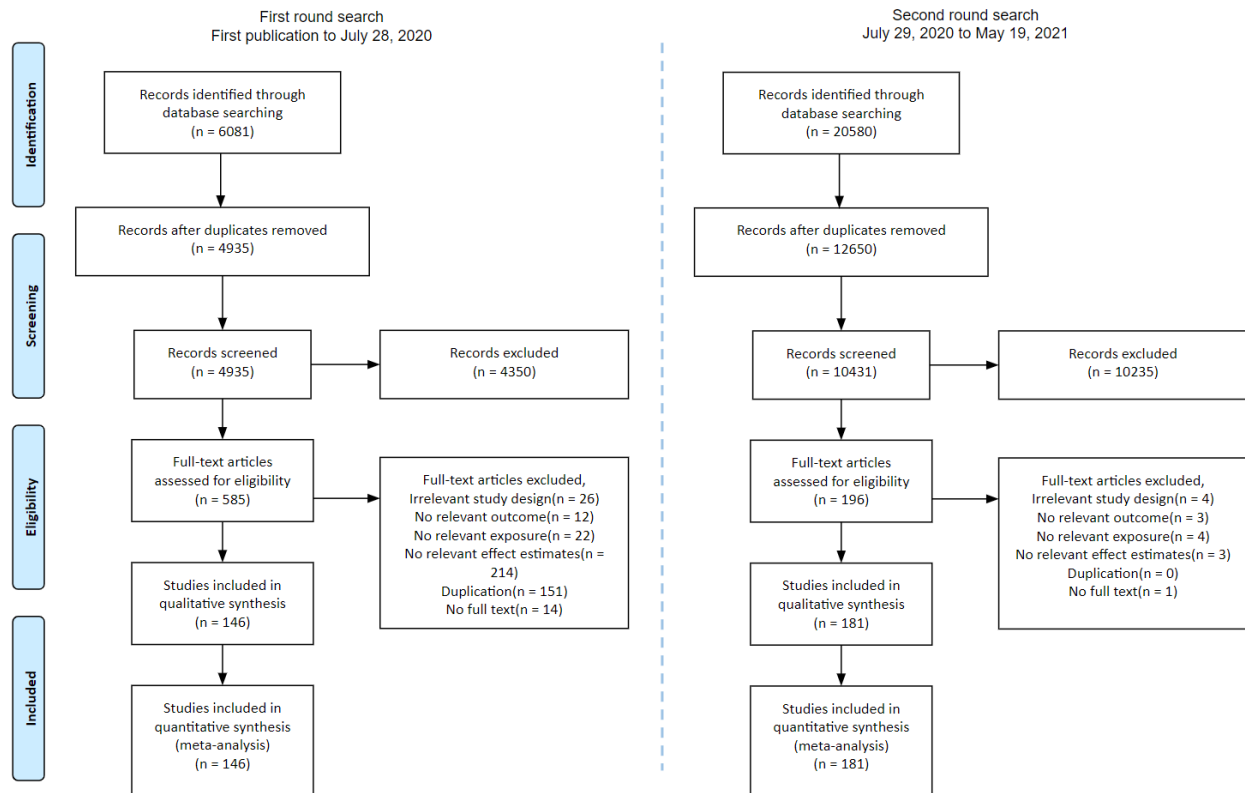


Figure 2. Network Line Graph of Cardiometabolic Comparisons Included from all Studies During COVID-19 Pandemic Timeframe. Cardiometabolic factors were compared to a non-comorbid category of having none of the cardiometabolic risk factors studied. AF, atrial fibrillation; CAD, coronary artery disease; CBD, cerebrovascular disease; CHD, coronary heart disease; CVD, cardiovascular disease; DM, diabetes mellitus; HF, heart failure; HTN, hypertension; MI, myocardial infarction; OBS, obesity; OW, overweight; STK, stroke.

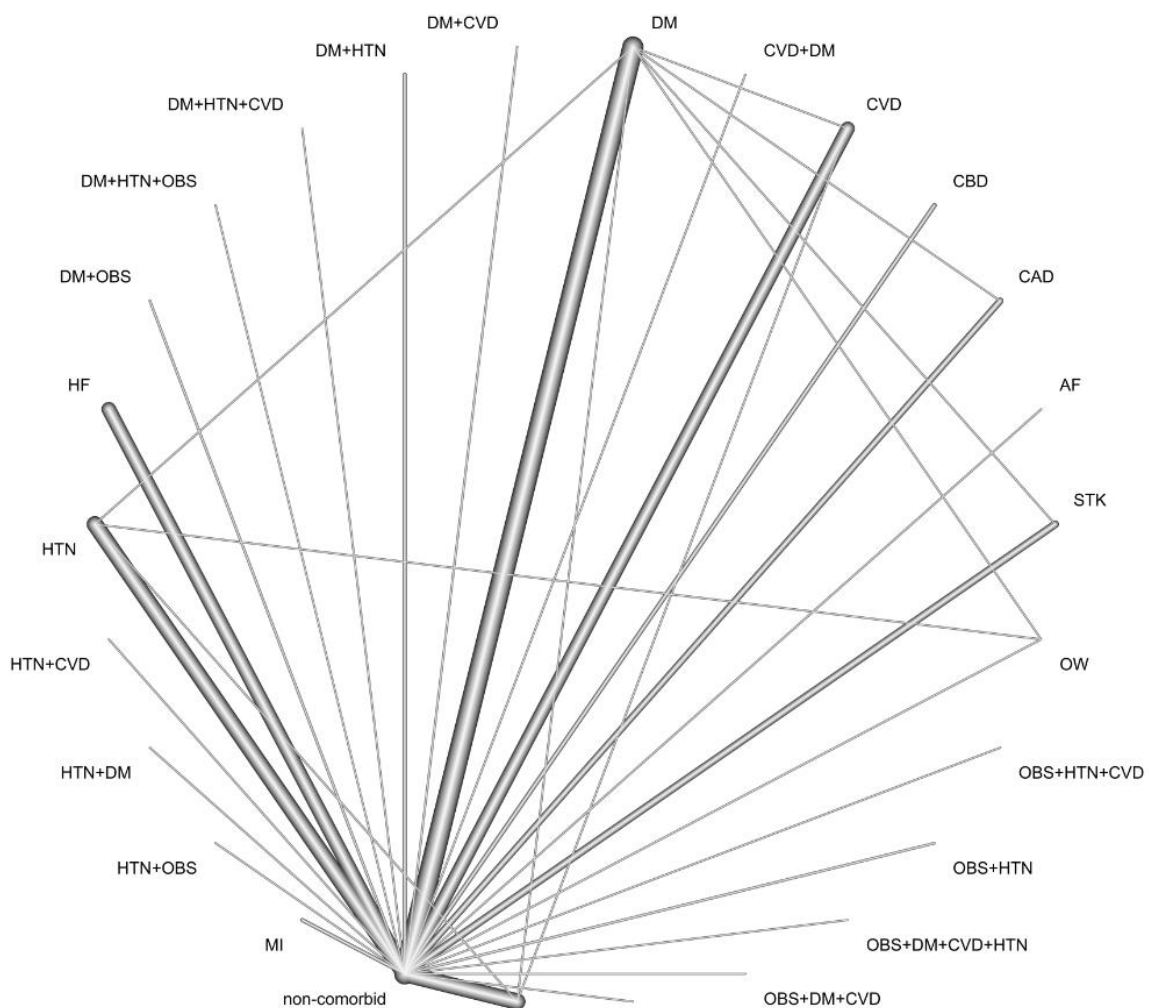


Figure 3. Network Analysis Forest Plot of Cardiovascular Comorbidities Fixed Effect

Models from full Pandemic Timeframe. AF, atrial fibrillation; CAD, coronary artery disease;

CBD, cerebrovascular disease; CHD, coronary heart disease; CVD, cardiovascular disease; DM,

diabetes mellitus; HF, heart failure; HTN, hypertension.

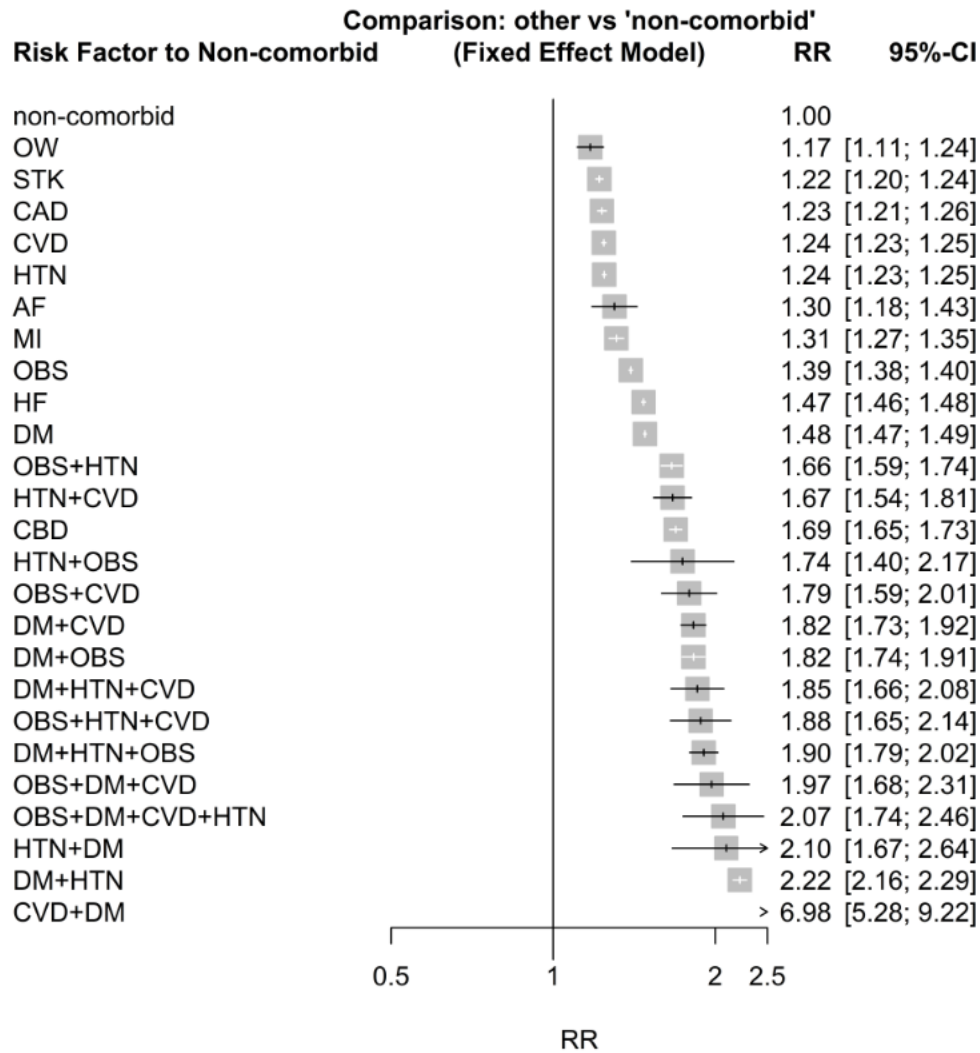


Figure 4. Comparison-adjusted Funnel Plot of Publication Bias in Relations of COVID-19 composite outcome incidence in any cardiometabolic comorbidity.



Appendix 1

Search strategy

The following search strategy was used for each of the databases.

Databases:

1. Embase 1910 to Present
2. Ovid Emcare 1995 to 2020 Week 30
3. Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations
1946 to July 28, 2020

Exposure:

cardiometabolic OR cardiovascular disease OR CVD OR coronary heart disease OR CHD OR
stroke OR cerebrovascular disease OR myocardial OR ischemic heart disease OR hyperten*

OR obes* OR overweight

OR diab* OR glucose intoleran* OR insulin resistance OR hyperglycem*

OR metabolic syndrome OR MetS OR Syndrome X OR insulin resistance syndrome OR
dysmetabolic syndrome

OR dyslipidemia OR hyperlipidemia OR hypercholesterolemia OR hyperglyceridemia OR
hyperlipoproteinemia

OR dyslipidaemia OR hyperlipidaemia OR hypercholesterolaemia OR hyperglyceridaemia OR
hyperlipoproteinaemia

Study population:

severe acute respiratory syndrome coronavirus 2 OR 2019 ncov OR 2019nCoV OR sars cov 2
virus OR COVID-19 OR coronavirus disease 2019 virus OR SARS-CoV-2 OR SARS2 OR
2019-nCoV OR 2019 novel coronavirus

Inclusion criteria:

- Primary studies with a cross-sectional, prospective, or retrospective design
- All diagnosed patients with COVID-19
- Studies that provided information on the association between cardiometabolic risk factors and outcomes related to COVID-19 (Hospitalization and length of stay; Disease progression as measured by days in ER, days in ICU, and days on ventilator; and Complications - Blood clots (e.g., stroke, heart attacks, pulmonary embolism, deep vein thrombosis), Kidney failure/dialysis, and mortality)
- Studies that provided effect estimates on the association between cardiometabolic risk factors and outcomes related to COVID-19, including odds ratio, relative risk, rate ratio, hazard ratio

Exclusion criteria:

- Intervention studies, literature reviews, letters, or abstracts from conference proceedings
- Studies that only reported prevalence of cardiometabolic comorbidities
- Insufficient data information provided

Reasons for exclusion:

1. Review articles
2. Irrelevant study design
3. No relevant exposure
4. No relevant effect estimates
5. Duplication

References

- 1 Report of clustering pneumonia of unknown etiology in Wuhan City. Wuhan Municipal Health Commission, 2019. (<http://wjw.wuhan.gov.cn/front/web/showDetail/2019123108989>).
- 2 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; 395:507–13.
- 3 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.
- 4 Wang D, Hu B, Hu C, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China [published correction appears in *JAMA*. 2021 Mar 16;325(11):1113]. *JAMA*. 2020;323(11):1061-1069.
doi:10.1001/jama.2020.1585
- 5 Li B, Yang J, Zhao F, et al. Prevalence and impact of cardiovascular metabolic diseases on COVID-19 in China. *Clinical research in cardiology : official journal of the German Cardiac Society*. 2020.
- 6 Wang B, Li R, Lu Z, Huang Y. Does comorbidity increase the risk of patients with COVID-19: evidence from meta-analysis. *Aging*. 2020;12.
- 7 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. *The Lancet Respiratory Medicine*. 2020;8(5):475-481.
- 8 Hernández-Garduño E. Obesity is the comorbidity more strongly associated for Covid-19 in Mexico. A case-control study. *Obes Res Clin Pract*. 2020 Jul-Aug;14(4):375-379.

- 9 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;55(5):2000547. Published 2020 May 14.
- 10 Grasselli G, Greco M, Zanella A, et al. Risk Factors Associated With Mortality Among Patients With COVID-19 in Intensive Care Units in Lombardy, Italy [published correction appears in *JAMA Intern Med*. 2021 Jul 1;181(7):1021]. *JAMA Intern Med*. 2020;180(10):1345-1355.
- 11 Price-Haywood EG, Burton J, Fort D, Seoane L. Hospitalization and Mortality among Black Patients and White Patients with Covid-19. *N Engl J Med*. 2020;382(26):2534-2543.
- 12 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*. 2020;369:m1985. Published 2020 May 22.
- 13 Barron E, Bakhai C, Kar P, et al. Associations of type 1 and type 2 diabetes with COVID-19-related mortality in England: a whole-population study. *Lancet Diabetes Endocrinol*. 2020;8(10):813-822.
- 14 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 [published correction appears in *Lancet Respir Med*. 2020 Apr;8(4):e26]. *Lancet Respir Med*. 2020;8(5):475-481.
- 15 Iaccarino G, Grassi G, Borghi C, et al. Age and Multimorbidity Predict Death Among COVID-19 Patients: Results of the SARS-RAS Study of the Italian Society of Hypertension. *Hypertension*. 2020;76(2):366-372.

- 16 Berenguer J, Ryan P, Rodríguez-Baño J, et al. Characteristics and predictors of death among 4035 consecutively hospitalized patients with COVID-19 in Spain. *Clin Microbiol Infect.* 2020;26(11):1525-1536.
- 17 Xu PP, Tian RH, Luo S, et al. Risk factors for adverse clinical outcomes with COVID-19 in China: a multicenter, retrospective, observational study. *Theranostics.* 2020;10(14):6372-6383. Published 2020 May 15.
- 18 Bezzio C, Saibeni S, Variola A, et al. Outcomes of COVID-19 in 79 patients with IBD in Italy: an IG-IBD study. *Gut.* 2020;69(7):1213-1217.
- 19 Williamson EJ, Walker AJ, Bhaskaran K, et al. Factors associated with COVID-19-related death using OpenSAFELY. *Nature.* 2020;584(7821):430-436.
- 20 Ebinger JE, Achamallah N, Ji H, et al. Pre-existing traits associated with Covid-19 illness severity. *PLoS One.* 2020;15(7):e0236240. Published 2020 Jul 23.
- 21 Owen RK, Conroy SP, Taub N, et al. Comparing associations between frailty and mortality in hospitalised older adults with or without COVID-19 infection: a retrospective observational study using electronic health records. *Age Ageing.* 2021;50(2):307-316.
- 22 Du H, Pan X, Liu N, et al. The effect of vascular risk factor burden on the severity of COVID-19 illness, a retrospective cohort study. *Respir Res.* 2020;21(1):241. Published 2020 Sep 21.
- 23 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;81(2):e16-e25.
- 24 Fang X, Li S, Yu H, et al. Epidemiological, comorbidity factors with severity and prognosis of COVID-19: a systematic review and meta-analysis. *Aging (Albany NY).* 2020;12(13):12493-12503.

- 25 Li J, Huang DQ, Zou B, et al. Epidemiology of COVID-19: A systematic review and meta-analysis of clinical characteristics, risk factors, and outcomes. *J Med Virol*. 2021;93(3):1449-1458.
- 26 Yang J, Zheng Y, Gou X, et al. Prevalence of comorbidities and its effects in patients infected with SARS-CoV-2: a systematic review and meta-analysis. *Int J Infect Dis*. 2020;94:91-95.
- 27 Allotey J, Stallings E, Bonet M, et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. *BMJ*. 2020;370:m3320. Published 2020 Sep 1.
- 28 Egger M, Smith GD, Phillips AN. Meta-analysis: principles and procedures. *BMJ*. 1997;315(7121):1533-1537.
- 29 Rouse B, Chaimani A, Li T. Network meta-analysis: an introduction for clinicians. *Intern Emerg Med*. 2017;12(1):103-111.
- 30 Xu Y, Amiche MA, Tadrous M. Network meta-analysis: an introduction for pharmacists. *Int J Clin Pharm*. 2018;40(5):942-947.
- 31 Pellicori P, Doolub G, Wong CM, et al. COVID-19 and its cardiovascular effects: a systematic review of prevalence studies. *Cochrane Database Syst Rev*. 2021;3(3):CD013879. Published 2021 Mar 11. doi:10.1002/14651858.CD013879
- 32 Liu H, Chen S, Liu M, Nie H, Lu H. Comorbid Chronic Diseases are Strongly Correlated with Disease Severity among COVID-19 Patients: A Systematic Review and Meta-Analysis. *Aging Dis*. 2020;11(3):668-678. Published 2020 May 9. doi:10.14336/AD.2020.0502

- 33 Ioannou GN, Green P, Fan VS, et al. Development of COVIDVax Model to Estimate the Risk of SARS-CoV-2–Related Death Among 7.6 Million US Veterans for Use in Vaccination Prioritization. *JAMA Network Open*. 2021;4(4):e214347.
doi:10.1001/jamanetworkopen.2021.4347
- 34 Gude-Sampedro F, Fernández-Merino C, Ferreiro L, et al. Development and validation of a prognostic model based on comorbidities to predict COVID-19 severity: a population-based study. *Int J Epidemiol*. 2021;50(1):64-74. doi:10.1093/ije/dyaa209
- 35 Tian W, Jiang W, Yao J, et al. Predictors of mortality in hospitalized COVID-19 patients: A systematic review and meta-analysis. *J Med Virol*. 2020;92(10):1875-1883.
doi:10.1002/jmv.26050
- 36 Leong A, Cole JB, Brenner LN, Meigs JB, Florez JC, Mercader JM. Cardiometabolic risk factors for COVID-19 susceptibility and severity: A Mendelian randomization analysis. *PLoS Med*. 2021;18(3):e1003553. Published 2021 Mar 4.
doi:10.1371/journal.pmed.1003553
- 37 El-Sayed Moustafa JS, Jackson AU, Brotman SM, et al. ACE2 expression in adipose tissue is associated with COVID-19 cardio-metabolic risk factors and cell type composition. Preprint. *medRxiv*. 2020;2020.08.11.20171108. Published 2020 Aug 14.
doi:10.1101/2020.08.11.20171108
- 38 Awortwe C, Cascorbi I. Meta-analysis on outcome-worsening comorbidities of COVID-19 and related potential drug-drug interactions. *Pharmacol Res*. 2020;161:105250.
doi:10.1016/j.phrs.2020.105250

- 39 Chen, Chaolei, et al. "Relations of Treatments for Cardiometabolic Co-Morbidities with Critical Outcomes and Mortality in Hospitalized Patients with Coronavirus Disease 2019 (COVID-19): A Retrospective Cohort Study." *Available at SSRN 3696829* (2020).
- 40 Kaur U, Chakrabarti SS, Patel TK. Renin-angiotensin-aldosterone system blockers and region-specific variations in COVID-19 outcomes: findings from a systematic review and meta-analysis. *Ther Adv Drug Saf.* 2021;12:20420986211011345. Published 2021 May 14. doi:10.1177/20420986211011345
- 41 Manohar J, Abedian S, Martini R, et al. Social and Clinical Determinants of COVID-19 Outcomes: Modeling Real-World Data from a Pandemic Epicenter. Preprint. *medRxiv.* 2021;2021.04.06.21254728. Published 2021 Apr 7. doi:10.1101/2021.04.06.21254728
- 42 Yang W, Shaman J. COVID-19 pandemic dynamics in India and impact of the SARS-CoV-2 Delta (B.1.617.2) variant. *medRxiv.* June 2021. doi:10.1101/2021.06.21.21259268
- 43 Lopez Bernal J, Andrews N, Gower C, et al. Effectiveness of Covid-19 vaccines against the B.1.617.2 (delta) Variant. *New England Journal of Medicine.* 2021;385(7):585-594. doi:10.1056/nejmoa2108891