

Table S1. Medline Search Strategy.

#	Searches
1	exp Comorbidity/
2	comorbidit*.tw.
3	exp Cardiovascular Diseases/
4	exp Cardiology/
5	((heart or cardiovascular) adj (disease* or illness* or anomal* or infection* or abnormalit*)) or CVD or cardio* or cardiac*).tw.
6	1 or 2 or 3 or 4 or 5
7	exp Coronavirus/
8	exp Coronavirus Infections/
9	((corona* or corono*) adj1 (virus* or viral* or virinae*)).tw.
10	(coronavirus* or coronovirus* or coronavirinae* or Coronavirus* or Coronovirus*).tw.
11	(Wuhan* or Hubei* or Huanan or "2019-nCoV" or 2019nCoV or nCoV2019 or "nCoV-2019").tw.
12	(COVID-19 or COVID19).tw.
13	(SARS-CoV-2 or SARSCoV-2 or SARSCoV2 or SARS-CoV2 or SARSCov19 or SARS-Cov19 or SARSCov-19 or SARS-Cov-19).tw.
14	((respiratory* adj2 (symptom* or disease* or illness* or condition*)) or "seafood market*" or "food market*") adj10 (Wuhan* or Hubei* or China* or Chinese* or Huanan*).tw.
15	((outbreak* or wildlife* or pandemic* or epidemic*) adj1 (China* or Chinese* or Huanan*)).tw.
16	"severe acute respiratory syndrome".tw.
17	("long covid" or "long covid-19" or "long covid19" or "long coronav*" or "post acute covid" or "post acute coronav*").tw.
18	7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17
19	exp Smoking/
20	smoking.tw.
21	exp Hypertension/
22	hypertens*.tw.
23	"high blood pressure".tw.
24	exp Obesity/
25	obes*.tw.
26	exp Sedentary Behavior/
27	("sedentary behavio?r*" or "physical inactiv*").tw.
28	exp Alcohol-Induced Disorders/
29	alcohol.tw.
30	exp Diet/
31	diet*.tw.
32	exp Cholesterol/
33	cholesterol.tw.
34	19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33
35	exp Atrial Fibrillation/
36	"atrial fibrillation".tw.
37	exp Hyperlipoproteinemia Type II/
38	hyperlipoproteinemia*.tw.
39	"familial hypercholesterolemia".tw.
40	exp Dementia/
41	dementia.tw.
42	exp Hyperglycemia/

43	hyperglycemia.tw.
44	exp Prediabetic State/
45	("prediabetic state" or "pre diabetic state" or "pre diabet*").tw.
46	exp Renal Insufficiency/
47	exp Kidney Diseases/
48	((kidney or renal) adj diseas*).tw.
49	exp Liver Diseases/
50	liver disease*.tw.
51	exp Fibrosis/
52	fibrosis.tw.
53	cirrhosis*.tw.
54	exp Stroke/
55	stroke*.tw.
56	35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55
57	(((comprehensive* or systematic*) adj3 (bibliographic* or review* or literature)) or (meta-analy* or metaanaly* or "research synthesis" or ((information or data) adj3 synthesis) or (data adj2 extract*))).ti,ab. or (cinahl or (cochrane adj3 trial*) or embase or medline or psyclit or (psycinfo not "psycinfo database") or pubmed or scopus or "sociological abstracts" or "web of science").ab. or "cochrane database of systematic reviews".jn. or ((review adj5 (rationale or evidence)).ti,ab. and review.pt.) or meta-analysis as topic/ or Meta-Analysis.pt.
58	exp "Systematic Review"/
59	57 or 58
60	6 and 18 and 34 and 56 and 59
61	limit 60 to (english language and humans and yr="2020 - 2021")

Study first and second author	AMSTAR 2 Rating	1		2		3		4			5		6		7			8			9			10		11		12		13		14		15		16			
		Y	N	Y	P	Y	N	Y	N	Y	P	Y	N	Y	N	Y	P	Y	N	Y	P	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N		
Wu, Zuo ⁷⁶	Critically low quality	X			X		X			X		X				X		X		X		X		X		X		X		X		X		X		X			
Xu, Mao ⁷⁷	Critically low quality	X			X		X			X		X				X		X		X		X		X		X		X		X		X		X		X			
Youssef, Hussein ⁷⁸	Moderate quality	X		X			X			X		X				X		X		X		X		X		X		X		X		X		X		X			
Yu, Wu ⁷⁹	Moderate quality	X		X			X			X		X				X		X		X		X		X		X		X		X		X		X		X			
Zhang, Shen ⁸⁰	Moderate quality	X		X			X			X		X			X		X		X		X		X		X		X		X		X		X		X		X		
Zhang, Wu ⁸¹	Critically low quality	X			X		X				X		X			X		X		X		X		X		X		X		X		X		X		X		X	
Zhao, Meng ⁸²	Critically low quality	X		X			X				X		X			X		X		X		X		X		X		X		X		X		X		X		X	
Zheng, Peng ⁸³	Low quality	X		X			X			X		X			X		X		X		X		X		X		X		X		X		X		X		X		
Zuin, Rigatelli ⁸⁴	Low quality	X		X			X			X		X			X		X		X		X		X		X		X		X		X		X		X		X		

NA: not applicable (meta-analysis not performed to score this category)

Table S3. Characteristics and results of all included reviews.

Study characteristics	Exposures examined	Outcomes examined	Systematic review/ meta-analysis results
<p>First and second author surname</p> <p>Search dates</p> <p>N=studies (n=patients) Primary study countries</p> <p>Study designs of included primary studies</p> <p>Quality assessment of primary studies</p> <p>AMSTAR2 grade</p>	<p>COVID-19 patients and cardiovascular condition(s) reported in primary data</p>	<p>Severe COVID* Mortality Mortality in severe disease</p> <p>*Composite outcome of (1) Respiratory distress, respiratory rate ≥ 30 per minute; (2) Oxygen saturation at rest $\leq 93\%$; (3) Partial pressure of oxygen in arterial blood/fraction of inspired oxygen ≤ 300 mmhg; (4) Patients requiring mechanical ventilation/vital life support/intensive care unit admission; (5) Death.</p>	<p>Results of meta-analyses are presented unless otherwise stated, such as narrative review findings from a systematic review without meta-analysis.</p> <p>OR (95% CI)</p> <p>CVD and Severe COVID 3.14 (2.32-4.24) $I^2=0\%$</p> <p>CVD and mortality 11.08 (2.59-47.32) $I^2=55\%$</p> <p>CVD and mortality in severe disease 1.72 (0.97-3.06) $I^2=0\%$</p> <p>Meta-regression of odds of severe disease with CVD: The age of patients in the severe group had no significant influence ($P=0.34$). As the percentage of women in the severe group increased, so did the odds ratio of severe disease and CVD association ($P=0.02$).</p>
<p>Aggarwal, Cheruiyot¹</p> <p>November 1, 2019 to April 20, 2020</p> <p>N=18 studies (4,858 patients) 16 China, 2 US</p> <p>Case-control/cohort Newcastle-Ottawa Scale, range 6-9</p> <p>AMSTAR2: Low quality</p>	<p>CVD defined as any cardiac pathology with the exception of hypertension</p>	<p>Mechanical ventilation Mortality</p>	<p>Systematic review findings:</p> <p>One study demonstrated 25% patients required mechanical ventilation (n=52).</p> <p>In one study, 60% of patients with elevated Troponin required mechanical ventilation compared to 10% with normal Troponin.</p> <p>In one study (n=416), patients with cardiac injury 22% (18/82) required mechanical ventilation compared to 4.2% in those without cardiac injury (14/334).</p>
<p>Almeshari, Alobaidi²</p> <p>December 1, 2019 to April 23, 2020</p> <p>N=16 studies; 2 cardiac injury (9,988 patients; 603 cardiac injury) 12 China, 3 USA, 1 Italy</p> <p>Case-control/Cohort NIH quality assessment tool: Good quality</p> <p>AMSTAR2: Low quality</p>	<p>Cardiac injury</p>	<p>Severe COVID (those who were admitted to ICU, had severe, oxygenation,</p>	<p>RR (95% CI)</p> <p>Current smoking vs ex/never smoked 1.45 (1.03–2.04) $I^2=92\%$</p>
<p>Alqahtani, Oyelade³</p> <p>Inception to March 24, 2020</p>	<p>Current/ex-smoker</p>	<p>Severe COVID (those who were admitted to ICU, had severe, oxygenation,</p>	<p>RR (95% CI)</p> <p>Current smoking vs ex/never smoked 1.45 (1.03–2.04) $I^2=92\%$</p>

<p>N=15 studies; 8 smoking (2,473 patients; 221 smoking studies) 14 China, 1 USA</p> <p>Case-control/cohort, case-series, Modified Newcastle-Ottawa Scale, range: 0.4 to 2.7 (9 studies >2, indicating low risk of bias)</p> <p>AMSTAR2: Low quality</p>		<p>needed mechanical ventilation or death)</p>	
<p>Bajgain, Badal⁴</p> <p>Inception to May 15, 2020.</p> <p>N=27 studies (22,753 patients) 18 China, 2 South Korea, 2 Italy, 2 USA, 1 Mexico, 1 UK, 1 Iran</p> <p>Study design NR Newcastle-Ottawa Scale, range 6-10</p> <p>AMSTAR2: Critically low quality</p>	<p>Hypertension</p>	<p>Mortality</p>	<p>OR (95% CI)</p> <p>Hypertension 1.65 (1.01-1.85)</p>
<p>Barrera, Shekhar⁵</p> <p>December 1, 2019 to April 6, 2020</p> <p>N=65 studies (15,794 patients) 46 China, 5 USA, 3 Singapore, 2 Italy, 2 Republic of Korea, 2 Hong Kong, 1 Australia, 1 Bolivia, 1 France, 1 Iran, 1 Japan</p> <p>Case-control/cohort, case-series GRADE, 18 low risk of bias, 3 some concerns, 44 high risk of bias. Overall confidence was low.</p> <p>AMSTAR2: Low quality</p>	<p>Hypertension Diabetes mellitus Hypertension and diabetes mellitus</p>	<p>Severe COVID* Mortality ICU admission</p> <p>*ICU admission or mortality</p>	<p>RR (95% CI)</p> <p>Diabetes and severe COVID N=6 studies (1,991 patients) 1.50 (0.90-2.50) I²=74%</p> <p>Diabetes and ICU admission N=3 studies (8,890 patients) 1.96 (1.19-3.22) I²=80%</p> <p>Diabetes and mortality N=4 studies (2,058 patients) 2.78 (1.39-5.58) I²=75%</p> <p>Hypertension and severe COVID N=8 studies (2,023 patients) 1.48 (0.99-2.23) I²=69%</p> <p>Hypertension and ICU admission N=4 studies (1,737 patients) 2.95 (2.18-3.99) I²=0%</p> <p>Hypertension and mortality N=8 studies (3,107 patients) 2.39 (1.54-3.73) I²=66%</p>
<p>Bennett, Tafuro⁶</p>	<p>COVID-19</p>	<p>Acute cardiac injury</p>	<p>Prevalence of acute cardiac injury</p>

<p>January 1, 2019 to April 26, 2020</p> <p>N=45 studies (14,358 patients) 42 China, 2 USA, 1 Europe Case-control/cohort, cross-sectional</p> <p>Newcastle-Ottawa Scale, range 4-6 (out of 7)</p> <p>AMSTAR2: Low quality</p>			<p>N studies=4 (1,096 patients) 16.2%</p>
<p>Bhatia, Pedapati⁷</p> <p>Inception to May 22, 2020</p> <p>N=30 studies (115 patients) Primary study origin NR</p> <p>Case-reports, case-series, case-control/cohort Oxford Centre for Evidence-based Medicine's Levels of Evidence and Grades of Recommendation "The risk of bias was not assessed systematically but was likely to be high in all studies since most were case reports, case series, and retrospective observational studies."</p> <p>AMSTAR2: Critically low quality</p>	<p>For stroke patients: Type of stroke Hypertension Diabetes Smoking Dyslipidaemia CAD</p>	<p>Mortality</p>	<p>OR (95% CI)</p> <p>Ischaemic vs. Non-ischaemic stroke N=73 patients 1.1 (0.3-4.1)</p> <p>NIH stroke scale (NIHSS) N=13 patients 1 (0.9-1.2)</p> <p>TOAST criteria N=52 patients Large artery disease 0.5 (0.1-2.3) Small vessel disease 0.16 (0.01-1.9) Cardioembolic 1.3 (0.3-4.7) Cryptogenic 1.5 (0.3-7.6)</p> <p>Hypertension N=72 patients 1.5 (0.6-3.9)</p> <p>Diabetes N=72 patients 2.1 (0.7-6.3)</p> <p>Old stroke N=72 patients 2.3 (0.2-2.7)</p> <p>Smoking N=47 patients 6 (1.1-33.9)</p> <p>Atrial fibrillation N=72 patients 1.1 (0.3-4.9)</p> <p>Dyslipidaemia N=65 patients</p>

			3 (0.96-9.7) CAD N=72 patients 6.4 (0.7-58)
Biswas, Rahaman ⁸ Inception to March 25, 2020 N=21 studies (47,807 patients) 19 China, 1 South Korea, 1 Singapore Case-control/cohort, RCT Newcastle-Ottawa Scale, range 5-8 AMSTAR2: Moderate quality	Hypertension Diabetes mellitus Cardio-cerebrovascular disease Renal disease CHD	Mortality	RR (95% CI) Hypertension N=4 studies (44,975 patients) 2.63 (2.32–2.98) I ² =0% Diabetes mellitus N=5 studies (44,995 patients) 3.34 (2.79–4.0) I ² =0% Cardio-cerebrovascular disease N=3 studies (44,701 patients) 5.06 (4.13–6.20) I ² =0% Renal disease N=3 studies (1,189 patients) 3.59 (1.49–8.67) I ² =0% CHD N=4 studies (1,346 patients) 3.84 (1.64–8.99) I ² =54%
Chang, Elhousseiny ⁹ Inception to May 1, 2020 N=28 studies (12,437 patients) 13 China, 9 USA, 2 UK, 1 Mexico, 1 Italy, 1 Spain, 1 France Case-control/cohort NIH quality assessment tool, 15 Good, 13 Fair AMSTAR2: Moderate quality	Hypertension Diabetes mellitus CVD Smoking Cerebrovascular disease	ICU Mortality	OR (95% CI) Hypertension N=6 studies (1,327 patients) 2.02 (1.37-2.98) I ² =52% Diabetes mellitus N=5 studies (677 patients) 1.78 (1.19-2.65) I ² =42% CVD N=6 studies (858 patients) 2.77 (1.76-4.37) I ² =45% Smoking N=3 studies (318 patients) 1.19 (0.48-2.92) I ² =42% Cerebrovascular diseases N=2 studies (67 patients) 3.84 (0.48-30.89) I ² =17%
Chen, Gong ¹⁰ Inception to March 6, 2020 N=9 studies (1,936 patients) 9 China Case-control/cohort	Hypertension Diabetes mellitus CHD	Severe COVID (severe vs. Non-severe; or intensive care unit (ICU) vs. Non-ICU; or progression and improvement/stabilization)	OR (95% CI) Hypertension N=9 studies (1,936 patients) 2.30 (1.76-3.00) I ² =50% Diabetes mellitus N=9 studies (1,936 patients)

<p>Newcastle-Ottawa Scale, range 6-7</p> <p>AMSTAR2: Low quality</p>			<p>2.67 (1.91-3.74) I²=42%</p> <p>CHD N=6 studies (1,720 patients) 2.85 (1.68-4.84) I²=0%</p>
<p>Chidambaram, Tun¹¹</p> <p>Inception to May 7, 2020</p> <p>N=109 studies (20,296 patients in the comparison of died and survived, 17,992 in the comparison of severe and non-severe) Comparison of died and survived: 32 China, 6 USA, 2 Spain, 1 UK, 1 Italy 1 Iran, 1 International Comparison of severe vs. Non-severe: 71 China, 1 Italy</p> <p>Case-control/cohort, cross-sectional, case-series Newcastle-Ottawa Scale, range 4-9 (1 scored 9, 54 scored 8, 39 scored 7, 6 scored 6, 6 scored 5, 3 scored 4)</p> <p>AMSTAR2: Low quality</p>	<p>Ever smoker Diabetes mellitus Hypertension CVD Heart failure Cerebrovascular disease Renal disease Chronic liver disease Acute cardiac injury Acute cardiac failure</p>	<p>Mortality Severe COVID*</p> <p>*Respiratory rate ≥30 breaths/minute, oxygen saturation ≤93% at rest, arterial oxygen tension (pao2) over inspiratory oxygen fraction (fio2) ratio ≤300 mm Hg or patients with >50% lesions progression within 24 to 48 hours in pulmonary imaging' or having 'evidence of respiratory failure and/or a need for mechanical ventilation, or shock or organ failure that requires intensive care monitoring.</p>	<p>OR (95% CI)</p> <p>Ever smoked Mortality: N=7 studies (10,419 patients) 1.43 (1.09-1.87) I²=0% Severe COVID: N=10 studies (4,511 patients) 1.51 (1.06-2.14) I²=62%</p> <p>Diabetes mellitus Mortality: N=27 studies (16,263 patients) 1.59 (1.41-1.78) I²=23% Severe COVID: N=36 studies (7,552 patients) 2.09 (1.66-2.64) I²=40%</p> <p>Hypertension Mortality: N=26 studies (15,947 patients) 1.90 (1.69-2.15) I²=28% Severe COVID: N=33 studies (7,002 patients) 2.63 (2.08-3.33) I²=64%</p> <p>CVD Mortality: N=25 studies (16,576 patients) 2.27 (1.88-2.79) I²=71% Severe COVID: N=31 studies (6,932 patients) 2.83 (2.21-3.63) I²=23%</p> <p>Heart failure Mortality: N=5 studies (9,910 patients) 2.08 (1.54-2.80) I²=0% Severe COVID: N=3 studies (558 patients) 4.76 (1.34-17.0) I²=0%</p> <p>Cerebrovascular disease Mortality: N=15 studies (2,437 patients) 2.63 (1.97-3.51) I²=75% Severe COVID: N=13 studies (4,246 patients) 2.62 (1.76-3.90) I²=7%</p> <p>Renal disease Mortality: N=15 studies (6,556 patients) 2.24 (1.78-2.81) I²=20% Severe COVID: N=14 studies (4,442 patients)</p>

			<p>2.62 (1.46-4.71) I²=27%</p> <p>Chronic liver disease Mortality: N=6 studies (3,672 patients) 2.18 (1.40-3.40) I²=20% Severe COVID: N=17 studies (8,869 patients) 1.56 (1.12-2.17) I²=0%</p> <p>Acute cardiac injury Mortality: N=14 studies (2,860 patients) 5.42 (3.79-7.77) I²=86% Severe COVID: N=3 studies (495 patients) 3.10 (2.55-3.77) I²=0%</p>
<p>De Lorenzo, Kasal¹²</p> <p>February 4, 2020 OR April 2, 2020</p> <p>N=8 studies (1,229 patients) 8 China</p> <p>Case-control/cohort, case-series Newcastle-Ottawa Scale, 1 Good, 7 Fair</p> <p>AMSTAR2: Moderate quality</p>	COVID-19	Prevalence of acute cardiac injury in hospitalised patients	<p>Proportion (95%CI)</p> <p>Acute cardiac injury N=8 studies (1,229 patients) 0.16 (0.09-0.27) I²=92%</p>
<p>Fang, Li¹³</p> <p>April 5, 2020</p> <p>N=69 studies (15,071 patients) 67 China, 1 Japan, 1 Singapore</p> <p>Case-control/cohort Newcastle-Ottawa Scale, range 5-7</p> <p>AMSTAR2: Moderate quality</p>	<p>Comorbidity</p> <p>Hypertension</p> <p>Diabetes mellitus</p> <p>CVD</p> <p>CHD</p> <p>Cerebrovascular disease</p> <p>Renal disease</p>	<p>Severe COVID* Mortality</p> <p>Admission to ICU</p> <p>*a. Respiratory distress, respiratory rate ≥ 30/min; b. Oxygen saturation of finger ≤ 93% in resting condition; c. Arterial partial pressure of oxygen (pao₂) /oxygen concentration (fio₂) ≤ 300 mmhg (1 mmhg = 0.133 kpa); including critical patients a. Respiratory failure requiring mechanical ventilation; b. Shock; c. Concomitant failure of other organs and requirement for ICU.</p>	<p>RR (95% CI)</p> <p>Comorbidity</p> <p>Severe COVID: N=16 studies 1.72 (1.44-2.06) I²=83% Mortality: N=8 studies 1.68 (1.32-2.12) I²=89% ICU: N=5 studies 1.82 (1.44-2.29) I²=61%</p> <p>Hypertension</p> <p>Severe COVID: N=23 studies 2.09 (1.73-2.52) I²=75% Mortality: N=11 studies 1.74 (1.31-2.30) I²=84% ICU: N=5 studies 2.31 (1.99-2.69) I²=0%</p> <p>Diabetes mellitus</p> <p>Severe COVID: N=23 studies 1.94 (1.6-2.36) I²=43% Mortality: N=10 studies 1.75 (1.27-2.41) I²=67% ICU: N=5 studies 1.88 (1.10-3.23) I²=51%</p> <p>CVD</p>

			<p>Severe COVID: N=18 studies 2.74 (2.03-3.70) I²=46% Mortality: N=11 studies 2.66 (1.60-4.43) I²=76% ICU: N=5 studies 2.83 (1.98-4.05) I²=0%</p> <p>CHD Severe COVID: N=8 studies 2.03 (1.39-2.97) I²=44% Mortality: N=5 studies 3.16 (1.45-6.91) I²=88% ICU: NR</p> <p>Cerebrovascular disease Severe COVID: N=12 studies 2.77 (1.70-4.52) I²=40% Mortality: N=6 studies 4.55 (2.60-7.94) I²=0% ICU: N=3 studies 4.52 (2.48-8.25) I²=5%</p> <p>Renal disease Severe COVID: N=15 studies 2.38 (1.43-3.97) I²=26% Mortality: N=5 studies 7.45 (3.5-15.86) I²=0% ICU: N=2 studies 1.50 (0.37-5.99) I²=0%</p>
<p>Figliozzi, Masci¹⁴</p> <p>April 24, 2020</p> <p>N=49 studies (20,211 patients) Primary study origin NR</p> <p>Case-control/cohort, cross-sectional Newcastle-Ottawa Scale, range 7-8</p> <p>AMSTAR2: Moderate quality</p>	<p>Diabetes mellitus Hypertension CVD Acute cardiac injury</p>	<p>Composite adverse outcome (mortality, mechanical ventilation, and severe COVID-19)</p>	<p>OR (95% CI)</p> <p>Diabetes mellitus N=34 studies (15,953 patients) 2.34 (1.64–3.33) I²=80%</p> <p>Hypertension N=35 studies (9,360 patients) 2.25 (1.80–2.82) I²=50%</p> <p>CVD N=19 studies (12,717 patients) 3.15 (2.26–4.41) I²=40%</p> <p>Acute cardiac injury N=12 studies (2,069 patients) 10.58 (5.00–22.40) I²=59%</p>
<p>Flook, Jackson¹⁵</p> <p>November 1, 2019 to April 29, 2020</p> <p>N=33 studies (153,003 patients) 29 China, 1 France, 1 Italy, 1 Singapore, 1 UK</p> <p>Case-control/cohort</p>	<p>Comorbidity</p>	<p>Mortality</p>	<p>Five (out of 33) studies presented evidence for the presence of any comorbidity being a risk factor for mortality in patients with COVID-19.</p> <p>No studies demonstrated evidence against.</p>

<p>The quality of included studies was assessed using an adapted checklist. Included studies were generally too small to detect a 10% increase in risk of disease, disease severity, or mortality. 3 were well power, 26 were descriptive or presented univariable analysis only.</p> <p>AMSTAR2: Critically low quality</p>			
<p>Florez-Perdomo, Serrato-Vargas¹⁶</p> <p>Inception to May 2020</p> <p>N=7 studies (3,244 patients) 6 China, 1 Italy</p> <p>Case-control/cohort Newcastle-Ottawa Scale, range 5-6</p> <p>AMSTAR2: Moderate quality</p>	<p>Cerebrovascular disease</p>	<p>Mortality</p>	<p>OR (95% CI)</p> <p>Cerebrovascular disease N=7 studies (3,244 patients) 2.78 (1.42-5.46) I²=49%</p>
<p>Fridman, Bullrich¹⁷</p> <p>November 1, 2019 to May 29, 2020</p> <p>N=10 studies (8,628 patients) Primary data origin NR</p> <p>Case-control/cohort, case-series, reports ROBINS-I tool, overall risk of bias was moderate.</p> <p>AMSTAR2: Critically low quality</p>	<p>COVID-19</p>	<p>Prevalence of new-onset stroke following COVID-19 diagnosis</p>	<p>Proportion (95% CI)</p> <p>Any stroke N=9 studies (3,306 patients) 0.02 (0.01-0.04) I²=84%</p> <p>Ischemic stroke N=9 studies (5,322 patients) 0.02 (0.01-0.03) I²=82%</p>
<p>Fu, Wang¹⁸</p> <p>Inception to March 2, 2020</p> <p>N=43 studies (3,600 patients) 43 China</p> <p>Case-control/cohort, case-series NIH quality assessment tool, range 2-7 (9 low risk, 30 moderate, 4 high risk)</p> <p>AMSTAR2: Moderate quality</p>	<p>COVID-19</p>	<p>Cardiac failure</p>	<p>Prevalence % (95% CI)</p> <p>Cardiac failure N=4 studies (245 patients) 6.5 (2.2-12.2) I²=78%</p>

<p>Gu, Zhang¹⁹</p> <p>April 24, 2020</p> <p>N=53 studies (7,679 patients) 52 China, 1 USA</p> <p>Case-control/cohort, case-series, cross-sectional The methodological quality of included rcts was evaluated according to Cochrane Collaboration Risk of Bias Tool. The methodological quality included observational studies was assessed according to the Newcastle-Ottawa Scale. All 53 studies were rated as relatively good quality, range 5-8.</p> <p>AMSTAR2: Moderate quality</p>	<p>COVID-19</p>	<p>Myocardial injury</p>	<p>Incidence (95% CI)</p> <p>Myocardial injury N=53 studies (7,679 patients) 0.21 (0.17-0.25) I²=97%</p> <p>Myocardial injury in non-survivors N=8 studies (380 patients) 0.66 (0.54-0.78) I²=86%</p> <p>RR (95% CI)</p> <p>Myocardial injury in severe vs non-severe COVID cases N=29 studies (4,233 patients) 5.74 (3.74-8.79) I²=87%</p>
<p>Gulsen, Yigitbas²⁰</p> <p>December 2019 to April 15, 2020</p> <p>N=16 studies (11,322 patients) in quantitative analyses 14 China, 1 USA, 1 CDC report (unknown)</p> <p>Case-control/cohort, cross-sectional Newcastle-Ottawa scale, range 5-8 (out of 9)</p> <p>AMSTAR2: Moderate quality</p>	<p>Smoking</p>	<p>Prevalence of smokers stratified for severity</p> <p>(Studies classified COVID-19 cases broadly as follows: (i) mild to moderate: mild, non-severe, common type, did not require ICU care, and COVID-19 survivors and (ii) severe: severe, critical, required ICU care, and non-survivors.)</p>	<p>OR (95% CI)</p> <p>History of smoking Severe vs non-severe COVID N=16 studies (10,797 patients) 2.17 (1.37-3.46) I²=71%</p> <p>Severe COVID Current smoker vs non-smoker N=10 studies (9,372 patients) 1.51 (1.11-2.05) I²=49%</p>
<p>Hamam, Goda²¹</p> <p>Search dates NR</p> <p>N=9 studies (1,445 patients) 8 China, 1 USA</p> <p>Case-control/cohort Newcastle-Ottawa scale, range 7-8 (out of 9)</p> <p>AMSTAR2: Moderate quality</p>	<p>COVID-19</p>	<p>Incidence of arrhythmia</p>	<p>Incidence (95% CI)</p> <p>N=9 studies (1,445 patients) 0.20 (0.12-0.28) I²=95%</p>
<p>Hammoud, Bendari²²</p>	<p>COVID-19 mortality</p>	<p>Histopathologies of the heart</p>	<p>In the 23 articles that described cardiac pathology, the most reported pathology was myocardial hypertrophy (87 cases,</p>

<p>December 2019 to August 15, 2020</p> <p>N=50 studies (430 patients) 16 USA, 10 China, 6 Germany, 5 Italy, 2 Switzerland, 1 Iran, 1 Finland, 1 Austria, 1 Belgium, 1 Japan, 1 Spain, 1 Netherlands, 1 UK, 1 Romania, 1 Austria, 1 Denmark</p> <p>Case-control/cohort, cross-sectional, case report Newcastle-Ottawa Scale (modified) 4 Fair (26-50%) 26 Good (51-75%) 20 Excellent (>76%)</p> <p>AMSTAR2: Critically low quality</p>			<p>51%), followed by myocardial fibrosis (85 cases, 50%), coronary small vessel disease (44 cases, 26%) myocardial cell infiltrate (27 cases, 16%), cardiac amyloidosis (10 cases, 6%), and myocardial necrosis (9 cases, 5%).</p>
<p>Han, Diao²³</p> <p>Inception to March 7, 2020</p> <p>N=14 studies (1,800 patients) 14 China</p> <p>Case-control/cohort, case-series</p> <p>Newcastle-Ottawa Scale (0-8 points) and CARE statement (0-8 points), all high quality (≥ 5)</p> <p>AMSTAR2: Critically low quality</p>	<p>Hypertension CVD Diabetes Cerebrovascular disease Chronic renal disease</p>	<p>Severe COVID (mechanical ventilation, ICU admission or mortality)</p>	<p>OR (95% CI)</p> <p>Hypertension N=6 studies (655 patients) 2.86 (1.83-4.47) $I^2=1\%$</p> <p>CVD N=5 studies (539 patients) 3.53 (1.89-6.58) $I^2=0\%$</p> <p>Diabetes mellitus N=6 studies (655 patients) 3.10 (0.79-12.07) $I^2=78\%$</p> <p>Cerebrovascular disease N=2 studies (254 patients) 2.53 (0.87-7.41) $I^2=0\%$</p> <p>Chronic renal disease N=5 studies (505 patients) 2.29 (0.84-6.25) $I^2=0\%$</p>
<p>Hessami, Shamshirian²⁴</p> <p>Inception to May 27, 2020</p> <p>N=56 studies (29,056 patients) Primary study origin NR</p> <p>Case-control/cohort, case series</p> <p>Newcastle-Ottawa Scale, all low risk of bias for selection and outcome</p>	<p>Acute cardiac injury Heart failure Arrhythmia Hypertension CVD CHD</p>	<p>Mortality</p>	<p>OR (95% CI)</p> <p>Acute cardiac injury N=12 studies 13.29 (7.35-24.0) $I^2=74\%$</p> <p>Heart failure N=8 studies 6.72 (3.34-13.52) $I^2=87\%$</p> <p>Arrhythmia N=3 studies 2.75 (1.43-5.25) $I^2=0\%$</p>

<p>AMSTAR2: Low quality</p>			<p>Hypertension N=31 studies 2.60 (2.11-3.19) I²=74%</p> <p>CVD N=14 studies 2.61 (1.89-3.62) I²=56%</p> <p>CHD N=16 studies 3.78 (2.42-5.90) I²=76%</p> <p>Prevalence of acute cardiac injury in ICU N=8 studies 0.33 (0.24-0.43) I²=51%</p>
<p>Hu, Sun²⁵</p> <p>Inception to March 10, 2020</p> <p>N=21 studies (47,344 patients) 20 China, 1 Singapore</p> <p>Case-control/cohort Newcastle-Ottawa Scale, range 5-8 (out of 9)</p> <p>AMSTAR2: Moderate quality</p>	<p>COVID-19</p>	<p>Acute cardiac injury</p> <p>Severe COVID</p>	<p>Incidence (95% CI)</p> <p>Acute cardiac injury N=4 studies 0.06 (0.01-0.11) I²=72%</p>
<p>Islam, Barek²⁶</p> <p>January 1, 2020, to May 17, 2020</p> <p>N=85 studies (67,299 patients) 69 China, 8 USA, 6 Italy, 1 South Korea, 1 Iran</p> <p>Case-control/cohort Newcastle-Ottawa scale, range 5-8 (out of 9) 83 High quality (6-8), 2 Moderate (5)</p> <p>AMSTAR2: Moderate quality</p>	<p>Comorbidity</p> <p>Hypertension</p> <p>CVD</p> <p>Diabetes mellitus</p> <p>Cerebrovascular disease</p> <p>Renal disease</p> <p>Liver disease</p>	<p>Mortality</p>	<p>OR (95% CI)</p> <p>Any comorbidity N=6 studies (927 patients) 3.46 (2.56-4.67) I²=0%</p> <p>Hypertension N=19 studies (47,797 patients) 3.16 (2.51-3.97) I²=44%</p> <p>CVD N=20 studies (47,685 patients) 4.67 (3.22-6.77) I²=54%</p> <p>Diabetes mellitus N=21 studies (47,864 patients) 2.45 (1.82-3.30) I²=49%</p> <p>Cerebrovascular disease N=13 studies (2,183 patients) 5.84 (3.63-9.39) I²=8%</p> <p>Renal disease N=9 studies (1,977 patients) 5.62 (3.34-9.46) I²=0%</p> <p>Liver disease N=8 studies (1,350 patients) 2.81 (1.31-6.01) I²=0%</p>

<p>Izcovich, Ragusa²⁷</p> <p>Inception to April 28, 2020</p> <p>N=207 studies (75,607 patients) China, USA, Canada, Spain, France, Turkey, Korea, Japan, Italy, Germany, India and Singapore</p> <p>Primary study design NR Quality in Prognosis Studies tool (QUIPS) Risk of bias was high across most identified studies. Only 7 were low risk of bias. The remaining presented important limitations in at least one domain or item.</p> <p>AMSTAR2: Low quality</p>	<p>Smoking</p> <p>Any chronic condition or comorbidity</p> <p>Cerebrovascular disease</p> <p>Chronic kidney disease (Renal disease)</p> <p>CVD (CHD or Heart failure)</p> <p>Cardiac arrhythmia</p> <p>Arterial hypertension</p> <p>Diabetes mellitus</p> <p>Obesity</p> <p>Dyslipidaemia</p>	<p>Mortality</p> <p>Severe COVID-19*</p> <p>*based on primary study definitions</p>	<p>OR (95% CI)</p> <p>Current smoker Mortality: N=16 studies (12,025 patients) 1.57 (1.19-2.07) Severe COVID-19: N=45 studies (9,147 patients) 1.65 (1.25-2.17)</p> <p>Comorbidity Mortality: N=16 studies (4,406 patients) 3.3 (2.18 to 5) Severe COVID-19: N=40 studies (6,640 patients) 3.16 (2.71-3.68)</p> <p>Cerebrovascular disease Mortality: N=26 studies (15,294 patients) 2.85 (2.02 to 4.01) Severe COVID-19: N=42 studies (11,050 patients) 2.67 (1.84-3.87)</p> <p>Renal disease Mortality: N=28 studies (23,448 patients) 2.27 (1.69 to 3.05) Severe COVID-19: N=42 studies (12,056 patients) 2.21 (1.51-3.24)</p> <p>CVD (CHD or Heart failure) Mortality: N=51 studies (37,156 patients) 2.12 (1.77 to 2.56) Severe COVID-19: N=73 studies (16,679 patients) 3.34 (2.71-4.1)</p> <p>Cardiac arrhythmia Mortality: N=6 studies (37,156 patients) 2.13 (1.72 to 2.65) Severe COVID-19: N=4 studies (747 patients) 16.51 (6.69-40.77)</p> <p>Arterial hypertension Mortality: N=52 studies (31,341 patients) 2.02 (1.71 to 2.38) Severe COVID-19: N=94 studies (20,817 patients) 2.5 (2.21- 2.92)</p> <p>Diabetes mellitus</p>
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			<p>Mortality: N=52 studies (31,341 patients) 1.84 (1.61 to 2.1) Severe COVID-19: N=97 studies (21,381 patients) 2.51 (2.2-2.87)</p> <p>Obesity Mortality: N=3 studies (8,922 patients) 1.41 (1.15-1.74) Severe COVID-19: N=8 studies (1,140 patients) 3.74 (2.37-5.89)</p> <p>Dyslipidaemia Mortality: N=4 studies (11,273 patients) 1.26 (1.06-1.5) Severe COVID-19: N=4 studies (559 patients) 0.63 (0.22-1.83)</p>
<p>Jain, Yuan²⁸</p> <p>January 1, 2019, to March 5, 2020</p> <p>N=7 studies (1,813 patients) 7 China</p> <p>Case-control/cohort STROBE Checklist: 1 Study <55% criteria met 4 studies 55-65% criteria met 2 studies >65% criteria met</p> <p>AMSTAR2: Low quality</p>	<p>CVD Hypertension Diabetes mellitus</p>	<p>Severe COVID ICU admission</p>	<p>OR (95% CI)</p> <p>CVD Severe COVID-19: N=3 studies (53 patients) 2.70 (1.52–4.80) ICU: N=3 studies (75 patients) 4.44 (2.64–7.47)</p> <p>Hypertension Severe COVID-19: N=3 studies (212 patients) 1.97 (1.40–2.77) ICU: N=3 studies (214 patients) 3.65 (2.22–5.99)</p> <p>Diabetes mellitus Severe COVID-19: N=3 studies (105 patients) 3.12 (1.00–9.75) ICU: N=3 studies (103 patients) 2.72 (0.70–10.6)</p>
<p>Khan, Khan²⁹</p> <p>December 1, 2019 to April 31, 2020</p> <p>N=41 studies (27,670 patients) 29 China, 4 Italy, 3 USA, 1 Australia, 1 Mexico, 1 Iran, 1 UK, 1 Korea</p> <p>Case-control/cohort Newcastle-Ottawa Scale, range 5-8</p> <p>AMSTAR2: Low quality</p>	<p>CVD Cerebrovascular disease Renal disease Liver diseases Hypertension Heart failure Arrhythmia</p>	<p>Mortality</p>	<p>OR (95% CI)</p> <p>Cerebrovascular disease N=15 studies 4.12 (3.04-5.58) I²=26%</p> <p>Renal disease N=21 studies 3.02 (2.60-3.51) I²=56%</p> <p>Liver diseases N=13 studies 2.35 (1.50-3.69) I²=0%</p> <p>CVD N=32 studies</p>

			<p>3.42 (2.86-4.09) I²=84%</p> <p>Hypertension 3.36 (2.64-4.28)</p> <p>Heart failure 4.72 (3.19-6.97)</p> <p>Arrhythmia 3.89 (2.51-6.02)</p>
<p>Kumar, Arora, Clinical Features³⁰</p> <p>January 1, 2020 and March 17, 2020</p> <p>N=58 studies; 21 in meta-analyses (6,892 patients; 3,496 in meta-analyses) 53 China, 1 Hong Kong, 1 Singapore, 1 South Korea, 1 Australia, 1 Europe</p> <p>Case-control/cohort NIH tool, range 6-9 (50 good quality, 8 f fair quality, 0 poor quality).</p> <p>AMSTAR2: Critically low quality</p>	<p>Comorbidity Diabetes mellitus Hypertension CVD</p>	<p>Severe clinical course</p> <p>(Patients in the primary studies with severe COVID-19, ICU, and/or mortality are labelled severe clinical course)</p>	<p>OR (95% CI)</p> <p>Comorbidity N=12 studies 3.16 (2.32-4.29) I²=29%</p> <p>Diabetes mellitus N=14 studies 3.11 (1.99-4.88) I²=48%</p> <p>Hypertension N=13 studies 2.30 (1.84-2.89) I²= 3%</p> <p>CVD N=13 studies 3.88 (2.30-6.54) I²=26%</p>
<p>Kumar, Arora, Diabetes³¹</p> <p>January 01, 2020 to April 22, 2020</p> <p>N=33 studies (16,003 patients) 30 China, 2 USA, 1 France</p> <p>Case-control/cohort NIH tool, range 7-9 (out of 12); 32 good quality, 1 study fair quality.</p> <p>AMSTAR2: Low quality</p>	<p>Diabetes mellitus</p>	<p>Severe clinical course*</p> <p>Severe COVID as labelled in primary studies</p> <p>Mortality</p> <p>*Patients in the primary studies with severe COVID-19, ICU, and/or mortality are labelled severe clinical course.</p>	<p>OR (95% CI)</p> <p>Diabetes mellitus and severe clinical course N=33 studies 2.49 (1.98-3.14) I²=63%</p> <p>Diabetes mellitus and severe COVID N=24 studies 2.75 (2.09-3.62) I²=63%</p> <p>Diabetes mellitus and mortality N=9 studies 1.90 (1.98-3.14) I²=32%</p>
<p>Li, Guan³²</p> <p>January 01, 2020 to April 14, 2020</p> <p>N=10 studies (3,118 patients) 10 China</p> <p>Case-control/cohort, case-series</p>	<p>CVD Acute cardiac injury</p>	<p>In-hospital mortality</p>	<p>OR (95% CI)</p> <p>CVD N=8 studies 4.85 (3.06-7.70) I²=29%</p> <p>Acute cardiac injury N=8 studies 21.15 (10.19-43.94) I²=71%</p>

Newcastle-Ottawa scale, range 6-8 AMSTAR2: Low quality			
Li, He ³³ January 01, 2020 to April 14, 2020 N=12 studies (2,445 patients) 12 China Case-control/cohort Newcastle-Ottawa scale, range 6-8 AMSTAR2: Low quality	Smoking Acute cardiac injury	Severe COVID (ICU vs No ICU)	OR (95% CI) Smoking history Fixed effect N=5 studies 1.70 (1.20-2.41) I ² =43% Random effect N=5 studies 1.62 (0.79-3.36) I ² =43% Acute cardiac injury Fixed effect N=3 studies 3.38 (1.50-7.60) I ² =78% Random effect N=3 studies 4.35 (0.47-40.00) I ² =78%
Li, Huang ³⁴ January 01, 2020 to April 6, 2020 N=212 studies (281,461 patients) 180 China, 8 USA, 6 South Korea, 3 Singapore, 3 Italy, 3 Taiwan, 2 UK, 2 Hong Kong, 1 Canada, 1 Japan, 1 Vietnam, 2 multi-country Case-control/cohort, case-series Newcastle-Ottawa Scale, range 4-9 (average 7) AMSTAR2: Low quality	Diabetes mellitus Smoking Cerebrovascular disease CVD Hypertension Cardiac failure	Severe COVID* Mortality *Severe COVID-19 disease definition based on the WHO Interim Guidance Report or IDSA/ATS criteria for severe pneumonia	Meta-regression coefficient (95% CI) Diabetes mellitus and severe COVID 23.4 (14.99-31.7) P<0.0001 Smoking severe COVID -1.4 (9.7-6.9) P=0.7 Cerebrovascular disease severe COVID 19.6 (2.6-36.6) P=0.02 CVD and severe COVID 2.0 (3.4-7.4) P=0.5 Hypertension and severe COVID 5.1 (1.1-9.1) P=0.01 Cardiac failure and severe COVID -37.2 (-81.2-6.7) P=0.1 Diabetes mellitus and mortality 8.2 (2.4-13.99) P=0.006 Smoking and mortality -10.3 (29.7-9.2) P=0.3 Cerebrovascular disease and mortality 0.8 (6.0-7.7) P=0.8 Chronic heart disease and mortality 3.7 (0.96-8.4) P=0.1 Hypertension and mortality 6.99 (3.3-10.7) P=0.0002

			Cardiac failure and mortality 6.2 (2.3-10.1) P=0.002
<p>Liu, Chen³⁵</p> <p>April 5, 2020</p> <p>N=24 studies (10,948 patients) 20 China, 2 USA, 1 Italy, 1 France</p> <p>Primary study design NR Newcastle-Ottawa Scale, range 6-8</p> <p>AMSTAR2: Low quality</p>	<p>Diabetes mellitus Hypertension CVD/CAD</p>	<p>Severe COVID* ICU admittance Mortality</p> <p>*as defined in primary studies</p>	<p>OR (95% CI)</p> <p>Comorbidity and Severe COVID 3.50 (1.78-6.90) I²=61%</p> <p>Comorbidity and ICU 3.36 (1.67-6.76) I²=36%</p> <p>Comorbidity and mortality 2.09 (0.26 to 16.67)</p> <p>Diabetes mellitus and severe COVID N=10 studies 2.61 (1.93-3.52) I²=27%</p> <p>Hypertension and severe COVID N=9 studies 2.84 (2.22-3.63) I²=37%</p> <p>CVD and severe COVID N=8 studies 4.18 (2.87-6.09) I²=32%</p>
<p>Liu, Zhang³⁶</p> <p>Inception to April 13, 2020</p> <p>N=36 studies (6,395 patients) 36 China</p> <p>Case-control/cohort, case series Newcastle-Ottawa scale, range 4-6 (31 studies =5, 4 studies=6, 1 study=4)</p> <p>AMSTAR2: Critically low quality</p>	<p>Renal disease</p>	<p>Severe COVID</p>	<p>OR (95% CI)</p> <p>Renal disease 3.28 (2.00-5.37) I²=0% N=13 studies (3,325 patients)</p>
<p>Lu, Zhong³⁷</p> <p>April 11, 2020</p> <p>N=10 studies (11,818 patients) 7 China, 1 Italy, 1 Korea, 1 USA</p> <p>Case-control/cohort, case-series Newcastle-Ottawa Scale, range 5-9</p> <p>AMSTAR2: Moderate quality</p>	<p>Comorbidity Hypertension Diabetes mellitus</p>	<p>Mortality</p>	<p>OR (95% CI)</p> <p>Comorbidity N=7 studies (2,517 patients) 3.50 (2.35-5.20) I²=45%</p> <p>Hypertension N=6 studies (3,342 patients) 3.25 (2.15-4.91) I²=69%</p> <p>Diabetes mellitus N=5 studies (2,307 patients) 2.63 (1.45-4.76) I²=64%</p>

<p>Luo, Fu³⁸</p> <p>December 2019 to July 2020</p> <p>N=124 studies 86 China, 10 USA, 7 Italy, 5 Korea, 2 Spain, 2 Switzerland, 2 Iran, 1 UK, 1 France, 1 Bolivia, 1 Egypt, 1 Greece, 1 Israel, 1 Netherlands, 1 Asia, EU, and USA, 1 Poland, 1 Japan</p> <p>Primary study design NR Newcastle-Ottawa scale, range 5-8 (out of 9)</p> <p>AMSTAR2: Moderate quality</p>	<p>Hypertension Diabetes mellitus CVD Renal disease Acute cardiac injury</p>	<p>Severe COVID* Mortality</p> <p>*as defined in primary studies</p>	<p>OR (95% CI)</p> <p>Hypertension Severe COVID: N=55 studies 2.56 (2.12-3.11) I²=83% Mortality: N=58 studies 2.50 (2.02-3.11) I²=93%</p> <p>Diabetes mellitus Severe COVID: N=58 studies 2.54 (1.89-3.41) I²=89% Mortality: N=63 studies 2.50 (2.02-3.11) I²=93%</p> <p>CVD Severe COVID: N=29 studies 3.86 (2.70-5.52) I²=63% Mortality: N=30 studies 2.65 (1.86-3.78) I²=86%</p> <p>Renal disease Severe COVID: N=28 studies 2.20 (1.26-3.85) I²=77% Mortality: N=35 studies 3.07 (2.43-3.88) I²=73%</p> <p>Acute cardiac injury Severe COVID: N=11 studies 6.57 (3.70-11.65) I²=75% Mortality: N=14 studies 16.97 (7.87-36.57) I²=89%</p>
<p>Ma, Gu³⁹</p> <p>Inception to February 25, 2020</p> <p>N=30 studies (53,000 patients) 27 China, 1 USA, 1 Australia, 1 South Korea</p> <p>Case-control/cohort Agency for Healthcare Research and Quality, range 5-10</p> <p>AMSTAR2: Low quality</p>	<p>Hypertension Diabetes mellitus CVD Cerebrovascular disease Renal disease</p>	<p>Severe COVID Mortality</p>	<p>OR (95% CI)</p> <p>Hypertension Severe COVID: N=10 studies (2,511 patients) 2.06 (1.61-2.62) I²=36% Mortality: 4.48 (3.69-5.45)</p> <p>Diabetes mellitus Severe COVID: N=10 studies (2,511 patients) 2.49 (1.82-3.40) I²=44% Mortality: 4.43 (3.49-5.62)</p> <p>CVD Mortality: 6.75 (5.40-8.43)</p> <p>Cerebrovascular disease Severe COVID: N=5 studies (2,197 patients) 3.22 (1.49-6.97) I²=0% Mortality: 5.34 (2.34-12.16)</p>

			Renal disease Severe COVID: N=4 studies (1,620 patients) 6.02 (2.19-16.51) I ² =0% Mortality: 9.02 (3.81-21.36)
Mantovani, Byrne ⁴⁰ January 1, 2020 to May 15, 2020 N=83 studies (78,874 patients) 62 Asia, 21 Europe, Australia, USA Case-control/cohort Newcastle-Ottawa scale, range 5-6 AMSTAR2: Moderate quality	Diabetes mellitus	Severe COVID* In-hospital mortality *as defined in primary studies	OR (95% CI) Diabetes mellitus and severe COVID N=22 studies 2.10 (1.71-2.57) I ² =42% Diabetes mellitus and mortality N=15 studies 2.68 (2.09-3.44) I ² =47%
Mao, Lin ⁴¹ October 1, 2019 to July 26, 2020 N=17 studies (1,310 patients) 13 China, 1 England, 1 France, 1 South Korea, 1 Turkey Case-control/cohort Newcastle-Ottawa Study for cohort studies (12 moderate quality and 4 high quality) and AHRQ for cross-sectional studies (1 moderate quality) AMSTAR2: Critically low quality	Amongst patients with COVID-19 and diabetes mellitus: Hypertension CVD Cerebrovascular disease For all patients: Diabetes mellitus	Mortality Severe COVID Cardiac injury	OR (95% CI) Patients with COVID-19 and diabetes mellitus: Hypertension and mortality N=3 studies (288 patients) 0.60 (0.12-3.11) I ² =47% CVD and mortality N=3 studies (288 patients) 0.44 (0.17-1.19) I ² =52% Cerebrovascular disease and mortality N=2 studies (201 patients) 0.32 (0.10-1.02) I ² =0% All patients: Diabetes mellitus and mortality N=14 studies (3,699 patients) 2.52 (1.77-3.58) I ² =58% Diabetes mellitus and severe COVID N=9 studies (2,366 patients) 2.66 (2.12-3.32) I ² =33% Diabetes mellitus and cardiac injury N=7 studies (2,154 patients) 2.13 (1.66-2.73) I ² =47%
Matsushita, Ding ⁴² December 1, 2019 to April 3, 2020	Smoking Hypertension Diabetes mellitus CVD	Severe COVID (all-cause mortality, ICU admission, ARDS, or the need for mechanical ventilation)	OR (95% CI) Current vs. never smoking N=3 studies 1.82 (0.83-3.96) I ² =58%

<p>N=25 studies (76,638 patients) 21 China, 3 USA, 1 Italy</p> <p>Case-control/cohort, cross-sectional Newcastle-Ottawa Scale, range 5-9</p> <p>AMSTAR2: Moderate quality</p>			<p>Former vs. never smoking N=3 studies 2.95 (1.15-7.53) I²=65%</p> <p>Hypertension N=8 studies 3.08 (2.33-4.07) I²=41%</p> <p>Diabetes mellitus N=9 studies 3.55 (2.56-4.93) I²=61%</p> <p>CVD N=10 studies 5.05 (4.36-5.85) I²=0%</p>
<p>Momtazmanesh, Shobeiri⁴³</p> <p>Inception to April 21, 2020</p> <p>N=54 studies Primary data origin NR</p> <p>Case-control/cohort, case-series, case-reports Newcastle-Ottawa scale, range 5-8</p> <p>AMSTAR2: Moderate quality</p>	<p>Diabetes mellitus Hypertension CVD Acute cardiac injury</p>	<p>Prevalence of new-onset CV conditions - Acute cardiac injury - Arrhythmia - Heart failure</p> <p>Mortality</p>	<p>Prevalence % (95% CI)</p> <p>Acute cardiac injury N=16 studies (2,647 patients) 25.3 (19.5-31.1) I²=93%</p> <p>Arrhythmia N=4 studies (444 patients) 26.1 (5.9-46.1) I²=97%</p> <p>Heart failure N=2 studies (367 patients) 23.7 (19.3-28.0) I²=0%</p> <p>OR (95% CI)</p> <p>Acute cardiac injury and mortality N=7 studies (1,046 patients) 19.64 (10.28-37.53) I²=64%</p> <p>CVD and mortality N=6 studies (550 patients) 7.87 (2.117-28.57) I²=54%</p> <p>Hypertension and mortality N=8 studies (1,033 patients) 2.49 (2.02-3.07) I²=25%</p> <p>Diabetes mellitus and mortality N=6 studies (682 patients) 1.66 (1.20-2.29) I²=0%</p>
<p>Moula, Micali⁴⁴</p> <p>December 1, 2019 to May 18, 2020</p> <p>N=26 studies (8,497 patients) 20 China, 2 Italy, 2 Korea, 1 Iran, 1 USA</p> <p>Case-control/cohort, case-series</p>	<p>CVD and CAD Hypertension Cerebrovascular disease Diabetes mellitus</p>	<p>Mortality</p>	<p>RR (95% CI)</p> <p>CVD/CAD N=26 studies 1.96 (1.51-2.54)</p> <p>Hypertension N=24 studies 1.73 (1.37-2.19)</p>

<p>ROBINS-I tool, overall bias ratings were: 10 Critical, 6 Serious, 11 Moderate (one paper split into two cohorts = '27 studies')</p> <p>AMSTAR2: Low quality</p>			<p>Cerebrovascular disease N=15 studies 1.76 (1.25-2.50)</p> <p>Diabetes mellitus N=26 studies 1.59 (1.25-2.02)</p>
<p>Nannoni, de Groot⁴⁵</p> <p>December 1, 2019 to September 14, 2020</p> <p>N=145 studies (108,571 patients) 12 North America, 6 EU, 6 Asia</p> <p>Case-control/cohort, case-series, case-reports Newcastle-Ottawa Scale, 14 High quality, 19 Moderate quality.</p> <p>AMSTAR2: Critically low quality</p>	<p>Severe COVID-19 Hypertension Diabetes mellitus CAD</p>	<p>Acute cerebrovascular disease</p>	<p>Proportion % (95% CI)</p> <p>Acute cerebrovascular disease N=24 studies (108,571 patients) 1.4 (1.0–1.9) I²=95%</p> <p>OR (95% CI)</p> <p>Hypertension and acute cerebrovascular disease N=4 studies (11,683 patients) 7.35 (1.94-27.87) I²=76%</p> <p>Diabetes mellitus and acute cerebrovascular disease N=4 studies (11,683 patients) 5.56 (3.34-9.24) I²=22%</p> <p>CAD and acute cerebrovascular disease N=2 studies (2,181 patients) 3.12 (1.61-6.02) I²=0%</p> <p>Severe COVID and acute cerebrovascular disease N=3 (2,389) 5.10 (2.72-9.54) I²=0%</p>
<p>Nasiri, Haddadi⁴⁶</p> <p>January 1, 2019 to May 29, 2020</p> <p>N=34 studies (5,057 patients) 32 China, 1 Germany, 1 Norway</p> <p>Case-control/cohort, case-series, case-reports, cross-sectional Joanna Briggs Institute (JBI) checklist, all classified as low risk of bias.</p> <p>AMSTAR2: Moderate quality</p>	<p>COVID-19</p>	<p>Acute cardiac injury</p>	<p>Pooled frequency (95%CI)</p> <p>Acute cardiac injury N=243 patients 12.4 (6.2-23.2) I²=65%</p>
<p>Noor, Islam⁴⁷</p> <p>January 1, 2020 to August 11, 2020</p>	<p>Obesity Smoking Hypertension Diabetes mellitus CVD Cerebrovascular</p>	<p>Mortality</p>	<p>RR (95% CI)</p> <p>Obesity N=7 studies (13,477 patients) 2.18 (1.10–4.34) I²=99%</p>

<p>N=58 studies (122,191 patients) 26 China, 8 USA, 7 Italy, 4 Spain, 2 South Korea, 2 Mexico, 1 Bangladesh, 1 Brazil, 1 UK, 1 Greece, 1 Iran, 1 Kuwait, 1 Switzerland, 1 Turkey, 1 EU</p> <p>Case-control/cohort Newcastle-Ottawa scale, range 6-9</p> <p>AMSTAR2: Moderate quality</p>	<p>disease CHD Renal disease Liver disease</p>		<p>Smoking N=10 studies (13,598 patients) 1.81 (0.99–3.33) I²=99%</p> <p>Hypertension N=38 studies (37,785 patients) 2.08 (1.79–2.43) I²=98%</p> <p>Diabetes mellitus N=35 studies (35,411 patients) 1.87 (1.23–2.84) I²=100%</p> <p>CVD N=16 studies (8,925 patients) 2.51 (1.20–5.26) I²=100%</p> <p>Cerebrovascular disease N=11 studies (6,069 patients) 2.75 (1.54–4.89) I²=99%</p> <p>CHD N=11 studies (10,851 patients) 3.63 (1.52–8.65) I²=100%</p> <p>Renal disease N=16 studies (24,450 patients) 2.11 (1.72–2.58) I²=97%</p> <p>Liver disease N=8 studies (7,090 patients) 2.02 (1.16–3.50) I²=95%</p>
<p>Palaiodimos, Chamorro-Pareja⁴⁸</p> <p>May 10, 2020</p> <p>N=14 studies (18,506 patients) 5 Asia, 5 USA, 4 EU</p> <p>Case-control/cohort Quality in Prognosis Studies (QUIPS) tool, all low risk of bias</p> <p>AMSTAR2: Moderate quality</p>	<p>Diabetes mellitus</p>	<p>Mortality</p>	<p>OR (95% CI)</p> <p>Diabetes mellitus N=14 studies (18,506 patients) 1.65 (1.35-1.96) I²=77%</p>
<p>Parohan, Yaghoubi⁴⁹</p> <p>Inception to May 1, 2020</p> <p>N=14 studies (29,909 patients) 12 China, 1 Italy, 1 Iran</p> <p>Case-control/cohort Newcastle-Ottawa scale, range 5-8</p>	<p>Hypertension CVD Diabetes mellitus</p>	<p>Mortality</p>	<p>OR (95% CI)</p> <p>Hypertension N=8 studies 2.70 (1.40-5.24) I²=93%</p> <p>CVD N=9 studies 3.72 (1.77-7.83) I²=89%</p>

AMSTAR2: Critically low quality			Diabetes mellitus N=7 studies 2.41 (1.05-5.51) I ² =94%
Parveen, Sehar ⁵⁰ Inception to March 31, 2020 N=7 studies (2,018 patients) 7 China Case-control/cohort, case-series NIH Quality Assessment tool, 4 Good, 3 Fair AMSTAR2: Critically low quality	Diabetes mellitus Hypertension	Prevalence in of diabetes mellitus/hypertension	OR (95% CI) Diabetes mellitus in non-survivors vs. survivors N=2 studies 0.56 (0.35-0.90) I ² =0% Diabetes mellitus in ICU vs non-ICU N=2 studies 0.78 (0.06-9.34) I ² =76% Hypertension in non-survivors vs survivors N=2 studies 0.50 (0.34-0.73) I ² =0% Hypertension in ICU vs non-ICU N=2 studies 0.42 (0.22-0.81) I ² =0%
Patanavanich, Glantz ⁵¹ January 1, 2020 to May 25, 2020 N=47 studies (31,871 patients) 33 China, 8 USA, 3 Italy, 1 UK, 1 South Korea, 1 International Case-control/cohort, case- series Modified ACROBAT-NRSI tool, range 0-1.6 AMSTAR2: Moderate quality	Smoking	Severe COVID* Mortality *Respiratory distress with respiratory rate ≥30/min, or oxygen saturation ≤93% at rest, or oxygenation index ≤300 mmhg.	OR (95% CI) Smoking and severe COVID N=47 studies 1.56 (1.32-1.83) I ² =45% Smoking and mortality N=8 studies 1.19 (1.05-1.34) I ² =0%
Patel, Malik, Shah ⁵² December 1, 2019 to April 30, 2020 N=11 studies (4,987 patients) Primary study origin NR Case-control/cohort Newcastle-Ottawa Scale, range 4-6 Cochrane's Collaboration Tool (3 high risk of bias, 8 moderate risk of bias) AMSTAR2: Critically low quality	Cerebrovascular disease	ICU admission Mechanical ventilation Mortality Composite outcome	OR (95% CI) ICU admission unadjusted N=7 studies (3,901 patients) 1.54 (1.25-1.62) I ² =95% ICU admission age-adjusted N=7 studies (3,901 patients) 1.82 (1.25-2.69) I ² =94% Mechanical ventilation unadjusted N=8 studies (2,196 patients) 1.32 (1.13-1.55) I ² =91% Mechanical ventilation age-adjusted N=8 studies (2,196 patients)

			<p>1.33 (1.09-1.63) I²=93%</p> <p>Mortality unadjusted N=8 studies (4,240 patients) 1.45 (1.22-1.72) I²=96%</p> <p>Mortality age-adjusted N=8 studies (4,240 patients) 1.42 (1.14-1.77) I²=96%</p> <p>Composite outcome 2.67 (1.75-4.06) I²=12%</p>
<p>Patel, Malik, Usman⁵³</p> <p>December 1, 2019 to May 31, 2020</p> <p>N=29 studies (12,258 patients) 19 China, 5 USA, 2 Singapore, 1 Australia, 1 Europe, 1 South Korea</p> <p>Case-control/cohort Newcastle-Ottawa Scale, 12 high risk of bias, 17 moderate risk of bias</p> <p>AMSTAR2: Critically low quality</p>	<p>Smoking Diabetes mellitus Hypertension Cerebrovascular disease Chronic liver disease CVD Cardiac complications</p>	<p>Mortality Mechanical ventilation</p>	<p>OR (95% CI)</p> <p>Smoking Mechanical ventilation 0.9 (0.88-0.97) I²=94% Mortality 0.95 (0.93-0.98) I²=81%</p> <p>Diabetes mellitus Mechanical ventilation 1.02 (0.94-1.11) I²=96% Mortality 1.02 (0.93-1.12) I²=96%</p> <p>Hypertension Mechanical ventilation 1 (0.94-1.11) I²=96% Mortality 1.01 (0.93-1.09) I²=96%</p> <p>Cerebrovascular disease Mechanical ventilation 1.42 (1.14-1.77) I²=96% Mortality 1.34 (1.09-1.63) I²=93%</p> <p>Chronic liver disease Mechanical ventilation 1.08 (1.01-1.17) I²=96% Mortality 1.08 (1.03-1.17) I²=94%</p> <p>CVD Mechanical ventilation 0.99 (0.88-1.12) I²=96% Mortality 1.32 (1.1-1.58) I²=90%</p> <p>Cardiac complications Mechanical ventilation 1.01 (0.92-1.11) I²=95% Mortality 0.98 (0.9-1.06) I²=95%</p>
<p>Porto, Iamonti⁵⁴</p>	<p>Diabetes mellitus</p>	<p>Mortality</p>	<p>OR (95% CI)</p>

<p>Inception to April 2020</p> <p>N=5 studies (1,453 patients) 5 China</p> <p>Primary study design NR Jedad scale, only studies scoring ≥ 2 points were included and considered high quality</p> <p>AMSTAR2: Critically low quality</p>			<p>Diabetes mellitus 8.9 (4.5-17.4)</p>
<p>Reddy, Charles⁵⁵</p> <p>December 1, 2019 to June 2, 2020</p> <p>N=47 studies (32,849 patients) 32 China, 10 USA, 2 International, 1 UK, 2 Italy</p> <p>Case-control/cohort Newcastle-Ottawa scale, 22 Good quality, 6 Fair quality, 19 Poor quality</p> <p>AMSTAR2: High quality</p>	<p>Current smoking vs. Former/never Smoking history vs. Never</p>	<p>Severe or critical COVID Mortality Disease progression ICU admission Mechanical ventilation</p>	<p>RR (95% CI)</p> <p>Current smoking Severe/critical COVID: N=8 studies (2,100 patients) 1.98 (1.16-3.38) $I^2=87\%$ Mortality: N=7 studies (14,741) 1.46 (0.83-2.60) $I^2=81\%$ N=7 (14,741 patients) Disease progression: N=3 studies (458 patients) 1.54 (0.52-4.58) $I^2=81\%$ ICU admission: N=6 studies (2,368 patients) 0.72 (0.42-1.24) $I^2=40\%$ Mechanical ventilation: N=5 studies (1,585 patients) 1.13 (0.75-1.72) $I^2=32\%$</p> <p>Smoking history Severe/critical COVID: N=15 studies (4,007 patients) 1.35 (1.19-1.53) $I^2=19\%$ Mortality: N=9 studies (14,105 patients) 1.26 (1.20-1.32) $I^2=0\%$ Disease progression: N=5 studies (468 patients) 2.18 (1.06-4.49) $I^2=69\%$ ICU admission: N=4 studies (1,802 patients) 1.12 (0.96-1.31) $I^2=0\%$ Mechanical ventilation: N=4 studies (917 patients) 1.20 (1.01-1.42) $I^2=0\%$</p>
<p>Rhim, Park⁵⁶</p> <p>Inception to May 1, 2020</p> <p>N=23 studies (227,856 patients) 19 China, 1 Italy, 1 Spain, 1 USA, 1 Korea</p>	<p>Diabetes mellitus Hypertension CVD Cerebrovascular disease Chronic liver disease Renal disease Acute cardiac injury</p>	<p>Mortality</p>	<p>OR (95% CI)</p> <p>Diabetes mellitus 2.53 (1.77-3.61) $I^2=66\%$ N=15 studies (206,488 patients)</p> <p>Hypertension 2.88 (2.22-3.73) $I^2=7\%$ N=11 studies (1,246 patients)</p>

<p>Case-control/cohort, cross-sectional, case series Newcastle-Ottawa Scale, range 7-9</p> <p>AMSTAR2: Low quality</p>			<p>CVD 5.06 (3.54-7.24) I²=46% N=14 studies (206,287 patients)</p> <p>Cerebrovascular disease 4.83 (2.61-8.93) I²=34% N=9 studies (1,306 patients)</p> <p>Chronic liver disease 1.36 (0.68-2.74) I²=1% N=6 studies (812 patients)</p> <p>Renal disease 6.32 (3.62-11.03) I²=0% N=8 studies (1,500 patients)</p> <p>Acute cardiac injury Cases: 43% 22.7 (4.81-107.2) I²=81% N=4 studies (582 patients)</p>
<p>Roncon, Zuin⁵⁷</p> <p>Inception to March 25, 2020</p> <p>N=8 studies (1,382 patients) Primary study origin NR</p> <p>Primary study design NR Newcastle-Ottawa Scale, 7 high quality (>7 stars), 1 moderate quality (5-7 stars)</p> <p>AMSTAR2: Critically low quality</p>	<p>Diabetes mellitus</p>	<p>ICU admission Mortality</p>	<p>OR (95% CI)</p> <p>Diabetes mellitus and ICU admission N=4 studies (114 patients) 2.79 (1.85-4.22), I²=46%</p> <p>Diabetes mellitus and mortality N=4 (354 patients) 3.21 (1.82, 5.64) I²=16%</p>
<p>Sabatino, De Rosa⁵⁸</p> <p>December 1, 2019 to June 11, 2020</p> <p>N=21 studies (77,317 patients)</p> <p>11 China, 5 USA, 1 Italy, 1 UK, 1 Singapore, 1 Korea, 1 Iran</p> <p>Primary study design NR Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies (QAT-OC/CSS) of the NIH, overall quality rating was judged as Fair</p> <p>AMSTAR2: Moderate quality</p>	<p>COVID-19</p> <p>Cardiovascular co-morbidity/risk factor Cardiovascular complications</p>	<p>Angina Arrhythmias Myocardial injury Acute Heart failure Myocardial infarction CV complications</p> <p>Mortality</p>	<p>Prevalence % (95% CI)</p> <p>Angina 10.2 (3.2-20.5)</p> <p>Arrhythmias 18.4 (7.8-32.3)</p> <p>Myocardial injury 10.3 (6.7-14.6)</p> <p>Acute Heart failure 2.0 (0.94-3.35)</p> <p>Myocardial infarction 3.5 (2.1-5.3)</p> <p>Cardiovascular complications 14.1 (10.3-20.2)</p> <p>Associations with mortality, regression coefficient 95%CI</p>

			<p>Cardiovascular comorbidity 0.004 (0.003-0.005) p<0.001</p> <p>Cardiovascular complications 0.001 (0.000-0.003) p=0.038</p>
<p>Sales-Peres, Azevedo-Silva⁵⁹</p> <p>Inception to April 27, 2020</p> <p>N=9 studies (6,577 patients) 3 USA, 2 China, 2 France, 1 Spain, 1 Italy</p> <p>Case-control/cohort, cross-sectional, case series Newcastle-Ottawa Scale, range 6-8</p> <p>AMSTAR2: Critically low quality</p>	<p>Obesity</p>	<p>Severe complications</p>	<p>RR (95% CI)</p> <p>Obesity N=3 studies (463 patients) 1.40 (0.91-2.17) I²=38%</p>
<p>Sepandi, Taghdir⁶⁰</p> <p>January 1, 2020 to March 23, 2020</p> <p>N=13 studies (12,044 patients)</p> <p>13 China Case-control/cohort Newcastle-Ottawa Scale, 2 Fair, 11 Good</p> <p>AMSTAR2: Critically low quality</p>	<p>Diabetes mellitus Hypertension Renal disease CVD Smoking</p>	<p>Mortality</p>	<p>OR (95% CI)</p> <p>Diabetes mellitus N=9 studies 2.42 (1.06-5.52) I²=90%</p> <p>Hypertension N=8 studies 2.54 (1.21-5.32) I²=91%</p> <p>Renal disease N=7 studies 2.61 (1.22-5.60) I²=78%</p> <p>CVD N=6 studies 4.37 (1.13-16.9) I²=88%</p> <p>Smoking N=3 studies 1.70 (0.53-5.35) I²=43%</p>
<p>Shafi, Shaikh⁶¹</p> <p>Search dates NR</p> <p>N=61 studies 33 China, 10 USA, 5 Italy, 3 Spain, 2 Germany, 1 International, 1 France and Switzerland, 1 South Korea, 1 France, 1 Belgium, 1 Iran, 1 Trinidad, 1 Brazil</p> <p>Case-control/cohort, case series, case report, RCT</p>	<p>COVID-19</p>	<p>Cardiovascular and cardiac manifestations</p>	<p>Patients with hypertension or any other cardiovascular comorbidity were more likely to develop a cardiovascular complication due to SARS-CoV-2 infection, with a higher proportion of hypertensive patients developing acute heart injury and heart failure.</p> <p>Patients affected with COVID-19 are at an increased risk of arrhythmias due to underlying comorbidities, polypharmacy, and disease progression.</p>

<p>Newcastle-Ottawa Scale, range 5-9</p> <p>AMSTAR2: Low quality</p>			<p>Myocardial injury in COVID-19 is a recognized phenomenon. Case series include reports of myocarditis, ACS, and spontaneous coronary artery dissection. Cardiac biomarkers are important in recognizing patients that might be presenting with early signs of myocardial injury secondary to COVID-19.</p>
<p>Shao, Shang⁶²</p> <p>Inception to March 31, 2020</p> <p>N=9 studies (1,470 patients) 9 China</p> <p>Primary study design NR Newcastle-Ottawa Scale, range 7-8 (7 studies scored 8 and 2 studies scored 7)</p> <p>AMSTAR2: Low quality</p>	<p>Myocardial injury</p>	<p>Mortality</p>	<p>OR (95% CI)</p> <p>Myocardial injury 13.7 (9.8-19.1) I²=52%</p>
<p>Shi, Wang⁶³</p> <p>December 1, 2019 to April 29, 2020</p> <p>N=27 studies 24 China, 2 USA, 1 Italy</p> <p>Case-control/cohort</p> <p>Quality in Prognostic Factor Studies (QUIPS) tool, range low risk in all categories-high risk in 3 categories</p> <p>AMSTAR2: Low quality</p>	<p>Current smoking Renal disease Cerebrovascular disease CVD Diabetes mellitus Hypertension Chronic liver disease Acute cardiac injury</p>	<p>Mortality</p>	<p>RR (95% CI)</p> <p>Current smoking N=5 studies (2,761 patients) 2.95 (1.32-6.58) I²=30%</p> <p>Renal disease N=4 studies (2,111 patients) 8.37 (3.94-17.77) I²=0%</p> <p>Cerebrovascular disease N=4 studies (2,071 patients) 7.66 (3.87-15.2) I²=0%</p> <p>CVD N=5 studies (2,258 patients) 3.16 (2.19-4.56) I²=17%</p> <p>Diabetes mellitus N=5 studies (2,689 patients) 2.21 (1.37-3.56) I²=45%</p> <p>Hypertension N=6 studies (2,880 patients) 2.11 (1.49-2.99) I²=82%</p> <p>Chronic liver disease N=3 studies (2,109 patients) 1.47 (0.63-3.42) I²=0%</p> <p>Acute cardiac injury N=6 studies (1,207 patients) 8.22 (4.95-13.7) I²=72%</p>
<p>Sinclair, Zhu⁶⁴</p>	<p>COVID-19</p>	<p>Cardiac complications</p>	<p>Cardiac complications - prevalence</p>

<p>December 1, 2019 to May 11, 2020</p> <p>N=5 studies (1,053 patients) 4 China, 1 USA</p> <p>Primary study design NR Newcastle Ottawa Scale, all 7 (high quality)</p> <p>AMSTAR2: Moderate quality</p>	<p>CVD Hypertension Diabetes mellitus</p>		<p>17%</p> <p>OR (95% CI) – cardiac complications</p> <p>CVD Fixed-effect: 5.12 (3.09-8.48) Random-effect: 3.82 (1.44-10.15) I²=33%</p> <p>Hypertension Fixed-effect: 4.37 (2.99-6.39) Random-effect: 4.35 (2.96-6.38) I²=0%</p> <p>Diabetes mellitus Fixed-effects: 2.61 (1.67-4.09) Random-effects: 2.40 (1.51-3.82) I²=0%</p>
<p>Sreenivasan, Khan⁶⁵</p> <p>November 30, 2019 to March 30, 2019</p> <p>N=10 studies (1,427 patients) 8 China, 1 Singapore, 1 USA</p> <p>Case-control/cohort Newcastle-Ottawa Scale, range 3-7</p> <p>AMSTAR2: Critically low quality</p>	<p>COVID-19</p> <p>Renal disease Chronic liver disease Smoking CVD Cerebrovascular disease Diabetes mellitus Hypertension</p>	<p>Acute myocardial infarction/injury Arrhythmia</p> <p>Complicated hospital course*</p> <p>*Mortality, ICU admission, acute respiratory distress syndrome, or need for invasive mechanical ventilation.</p>	<p>Event rate (95% CI)</p> <p>Acute myocardial infarction/injury 0.079 (0.029-0.197, p<0.001) N=441 patients</p> <p>Arrhythmia 0.167 (0.113-0.238, p<0.001) N=138 patients</p> <p>OR (95% CI) – Complicated hospital course</p> <p>Renal disease N=3 studies 5.12 (1.18-22.19) I²=0%</p> <p>Chronic liver disease N=2 studies 1.07 (0.30-3.87)</p> <p>Smoking N=2 studies 2.54 (1.00-6.46)</p> <p>CVD N=6 studies 5.82 (2.44-13.85) I²=28%</p> <p>Cerebrovascular disease N=2 studies 8.30 (1.24-55.4) I²=0%</p> <p>Diabetes mellitus N=6 studies 2.46 (1.37-4.42) I²=23%</p> <p>Hypertension N=6 studies 2.09 (1.02-4.27) I²=74%</p>

<p>Ssentongo, Ssentongo⁶⁶</p> <p>December 1, 2019 to July 9, 2020</p> <p>N=25 studies (65,484 patients) 19 China, 3 USA, 1 Italy, 1 Africa, 1 International</p> <p>Case-control/cohort, case series Newcastle-Ottawa Scale, range 5-9 (mean 7)</p> <p>AMSTAR2: Moderate quality</p>	<p>CVD Hypertension Cerebral vascular disease Diabetes mellitus Renal disease Chronic liver disease Heart failure</p>	<p>Mortality</p>	<p>RR (95% CI)</p> <p>CVD N=14 studies 2.25 (1.60-3.17) I²=49%</p> <p>Hypertension N=13 studies 1.82 (1.43-2.32) I²=70%</p> <p>Cerebral vascular disease N=4 studies 2.16 (0.97-4.80) I²=64%</p> <p>Diabetes mellitus N=16 studies 1.48 (1.02-2.15) I²=84%</p> <p>Renal disease N=9 studies 3.25 (1.13-9.28) I²=99%</p> <p>Chronic liver disease N=3 studies 1.73 (0.86-3.46) I²=0%</p> <p>Heart failure N=3 studies 2.03 (1.28-3.21) I²=0%</p>
<p>Tabrizi, Lankarani⁶⁷</p> <p>Inception to March 12, 2020</p> <p>N=17 studies (3,189 patients) 16 China, 1 Singapore</p> <p>Case-control/cohort Newcastle Ottawa Scale, range 3-8</p> <p>AMSTAR2: Critically low quality</p>	<p>Diabetes mellitus Hypertension CVD Renal disease Cerebrovascular accident Liver disease</p>	<p>Severe COVID (as measured by disease severity criteria as severe/critical disease type or admitted to ICU or the use of mechanical ventilation)</p>	<p>OR (95% CI)</p> <p>Diabetes mellitus N=9 studies 3.54 (1.79-7.01) I²=58%</p> <p>Hypertension N=10 studies 2.35 (1.83-3.02) I²=0%</p> <p>CVD N=9 studies 2.44 (1.64-3.63) I²=0%</p> <p>Renal disease N=6 studies 6.38 (3.23-12.59) I²=0%</p> <p>Cerebrovascular accident N=4 studies 3.94 (0.88-17.59) I²=53%</p> <p>Liver disease N=6 studies 1.25 (0.35-4.41) I²=40%</p>
<p>Tamara, Tahapary⁶⁸</p>	<p>Obesity (BMI >25 or 30 kg/m²)</p>	<p>In-hospital critical care</p>	<p>One study demonstrated that COVID-19 patients with obesity grade II had 7.36</p>

<p>Inception to April 14, 2020</p> <p>N=3 studies (806 patients) 1 China, 1 USA, 1 France</p> <p>Case-control/cohort Newcastle Ottawa Scale, range 7-9</p> <p>AMSTAR2: Moderate quality</p>			<p>(1.63-33.14; p= 0.021) times increased risk of having invasive mechanical ventilation during in-hospital care, compared to non-obese patients with COVID-19.</p> <p>One study stratified patients by age, <60 years and >60 years. Compared to healthy weight and over-weight groups, the rate of hospitalization increased by 2.0 (1.6-2.6; p<0.0001) and 2.2 (1.7-2.9; p< 0.0001) times in the younger patient group with obesity grade I and II, respectively.</p> <p>Another study reported an increased risk of 1.30 (1.09-1.54; p<0.003) times in COVID-19 patients with a BMI higher than 25 kg/m² to develop severe COVID-19 compared to healthy weight and over-weight patients, however, this was attenuated in multivariate analyses.</p>
<p>Taylor, Hofmeyr⁶⁹</p> <p>January 1, 2020 to April 7, 2020</p> <p>N=9 studies (1,823 patients) 7 China, 1 USA, 1 Italy</p> <p>Case-control/cohort Newcastle-Ottawa Scale, range 4-6</p> <p>AMSTAR2: Critically low quality</p>	<p>Hypertension</p>	<p>Mortality in intensive care</p>	<p>OR (95% CI)</p> <p>Hypertension N=3 studies 4.17 (2.90-5.99) I²=0%</p>
<p>Tian, Jiang⁷⁰</p> <p>January 1, 2020 to April 24, 2020</p> <p>N=14 studies (4,659 patients) 13 China, 1 USA</p> <p>Primary study design NR Agency for Healthcare Research and Quality (AHRQ) score checklist, 1 low quality, 5 moderate quality, 8 high quality</p> <p>AMSTAR2: Critically low quality</p>	<p>Hypertension CVD Cerebrovascular disease Diabetes mellitus Smoking Renal disease</p>	<p>Mortality</p>	<p>OR (95% CI)</p> <p>Hypertension N=11 studies (4,263 patients) 2.53 (2.07-3.09) I²=15%</p> <p>CVD N=12 studies (1,842 patients) 3.81 (2.11-6.85) I²=61%</p> <p>Cerebrovascular disease N=6 studies (948 patients) 4.92 (1.54-15.68) I²=51%</p> <p>Diabetes mellitus N=12 studies (4,315 patients) 1.97 (1.67-2.31) I²=0%</p> <p>Smoking N=4 studies (678 patients) 1.77 (0.83-3.81) I²=8%</p>

			Renal disease N=6 studies (1,087 patients) 9.41 (3.23-27.40) I ² =0%
Villalobos, Ott ⁷¹ Inception to April 29, 2020 N=75 studies 66 China, 5 USA, 2 UK, 1 Iran, 1 France Primary study design NR ROBINS-I tool 45 high risk of bias, only few had overall low risk of bias in all categories. AMSTAR2: Moderate quality	CVD Cerebrovascular disease Renal disease Diabetes mellitus Liver disease Hypertension Myocardial infarction	ICU admission Mortality	RR (95% CI) CVD ICU: N=8 studies 2.1 (1.3-3.2) I ² =86% Mortality: N=15 studies 3.3 (2.3-4.5) I ² =86% Cerebrovascular disease ICU: N=4 studies 1.9 (0.9-4.0) I ² =92% Mortality: N=7 studies 2.6 (1.7-4.1) I ² =61% Renal disease ICU: N=4 studies 2.1 (0.9-4.9) I ² =90% Mortality: N=3 studies 2.5 (1.8-3.4) I ² =0% Diabetes mellitus ICU: N=12 studies 1.9 (1.4-2.6) I ² =90% Mortality: N=18 studies 2.2 (1.7-2.9) I ² =83% Hypertension ICU: N=9 studies 1.4 (1.1-1.7) I ² =53% Mortality: N=17 studies 2.7 (2.1-3.4) I ² =80% Liver disease Mortality: N=3 studies 1.9 (0.6-6.4) I ² =30% Myocardial infarction Mortality: N=5 studies 3.9 (1.5-8.6) I ² =89%
Wang, Deng ⁷² December, 2019 to March 16, 2020 N=25 studies (4,881 patients) 25 China Case-control/cohort, cross- sectional Newcastle-Ottawa scale, range 3-7	Diabetes mellitus Hypertension CVD Chronic liver disease	Severe COVID	RR (95% CI) Diabetes mellitus N=12 studies (1,740 patients) 1.53 (1.29-1.82) Hypertension N=13 studies (1,781 patients) 1.40 (1.22-1.60) CVD N=12 studies (1,412 patients) 1.79 (1.50-2.13)

AMSTAR2: Critically low quality			Chronic liver disease N=8 studies (1,312 patients) 0.93 (0.62-1.42)
<p>Wang, Li⁷³</p> <p>Inception to March 1, 2020</p> <p>N=6 studies (1,558 patients) 6 China</p> <p>Case-control/cohort Newcastle-Ottawa Scale, range 6-8</p> <p>AMSTAR2: Critically low quality</p>	<p>Hypertension Diabetes Liver disease Renal disease CVD Cerebrovascular disease</p>	Severe COVID	<p>OR (95% CI)</p> <p>Hypertension N=6 studies 2.29 (1.69-3.10) I²=4%</p> <p>Diabetes N=6 studies 2.47 (1.67-3.66) I²=39%</p> <p>Liver disease N=5 studies 0.67 (0.30-1.49) I²=0%</p> <p>Renal disease N=4 studies 2.51 (0.93-6.78) I²=0%</p> <p>CVD N=4 studies 2.93 (1.73-4.96) I²=0%</p> <p>Cerebrovascular disease N=3 studies 3.89 (1.64-9.22) I²=45%</p>
<p>Wu, Liu⁷⁴</p> <p>Inception to April 1, 2020</p> <p>N=41 studies (5,064 patients) 41 China</p> <p>Case-control/cohort Newcastle-Ottawa Scale, range 7-8 (2 studies =7, 39 studies =8)</p> <p>AMSTAR2: Moderate quality</p>	<p>Smoking Alcohol Diabetes mellitus CVD Cerebrovascular disease Hypertension Chronic liver disease BMI</p>	Severe COVID	<p>OR (95% CI)</p> <p>Smoking N=7 studies (1,484 patients) 1.26 (0.69-2.32)</p> <p>Diabetes mellitus N=17 studies (2,476 patients) 2.38 (1.59-3.57)</p> <p>CVD N=13 studies (2,089 patients) 3.16 (2.19-4.56)</p> <p>Cerebrovascular disease N=7 studies (1,213 patients) 3.34 (1.29-8.69)</p> <p>Hypertension N=18 studies (2,510 patients) 2.63 (1.79-3.88)</p> <p>Chronic liver disease N=11 studies (1,982 patients) 0.81 (0.47-1.40)</p> <p>SMD (95% CI)</p> <p>BMI</p>

			N=4 studies (221 patients) 1.27 (-0.88-3.42)
<p>Wu, Tang⁷⁵</p> <p>Inception to April 14, 2020</p> <p>N=9 studies (926 patients) 9 China</p> <p>Primary study origin NR Newcastle-Ottawa scale, range 7-8 (9 studies=7 and 1 study =8)</p> <p>AMSTAR2: Moderate quality</p>	Diabetes mellitus	Mortality	<p>OR (95% CI)</p> <p>Diabetes mellitus 1.75 (1.31-2.36) I²=5%</p> <p>Diabetes mellitus (Age ≥70 years) 1.33 (0.78-2.28) I²=0%</p> <p>Diabetes mellitus (Age <70 years) 2.05 (1.44-2.94) I²=32%</p>
<p>Wu, Zuo⁷⁶</p> <p>Inception to May 13, 2020</p> <p>N=73 studies (171,108 patients) 54 China, 4 Italy, 2 USA, 2 UK, 2 France, 2 Spain, 6 'other'</p> <p>Case-control/cohort</p> <p>Agency for Healthcare Research and Quality, 31 high quality, 41 moderate, 1 low</p> <p>AMSTAR2: Critically low quality</p>	Hypertension CVD Arrhythmia Renal disease Smoker Acute cardiac injury	Severe COVID	<p>OR (95% CI)</p> <p>Hypertension N=22 studies 2.40 (2.08-2.78) I²=39%</p> <p>CVD N=15 studies 3.54 (2.68-4.68) I²=37%</p> <p>Arrhythmia N=3 studies 14.8 (8.9-24.6) I²=49%</p> <p>Renal disease N=15 studies 1.84 (1.47-2.30) I²=26%</p> <p>Smoker N=10 studies 1.61 (1.28-2.02) I²=0%</p> <p>Acute cardiac injury N=7 studies 11.9 (7.64-18.46) I²=0%</p> <p>Incidence of acute cardiac injury 6% (3%-9%)</p>
<p>Xu, Mao⁷⁷</p> <p>Inception to March 8, 2020</p> <p>N=20 studies (4,602 patients) 20 China</p> <p>Cross-sectional American Agency for Healthcare Research and Quality, range 3-7</p>	BMI Smoker Diabetes mellitus Hypertension CVD	Severe COVID	<p>SMD (95% CI)</p> <p>BMI 3.38 (0.07-6.69)</p> <p>OR (95% CI)</p> <p>Smoker N=3 studies (412 patients) 1.40 (0.65-3.01) I²=0%</p> <p>Diabetes mellitus N=10 studies (1,083 patients)</p>

<p>AMSTAR2: Critically low quality</p>			<p>3.04 (2.01-4.60) I²=20%</p> <p>Hypertension N=10 studies (1,083 patients) 2.31 (1.68-3.18) I²=47%</p> <p>CVD N=7 studies (906 patients) 2.76 (1.39-5.45) I²=26%</p>
<p>Youssef, Hussein⁷⁸</p> <p>Inception to April 16, 2020</p> <p>N=20 studies (3,428 patients) 20 China</p> <p>Case-control/cohort Newcastle-Ottawa scale, 2-8 (1 study =2, 2 studies =3, 6 studies =5, 2 studies =6, 4 studies =7, 5 studies =8)</p> <p>AMSTAR2: Moderate quality</p>	<p>Hypertension Renal disease Diabetes mellitus CVD Chronic liver disease Cerebrovascular disease Myocardial injury</p>	<p>Severe COVID</p>	<p>OR (95% CI)</p> <p>Hypertension 2.36 (1.86-3.01) I²=14% N=13 studies (2,141 patients)</p> <p>Renal disease 7.28 (3.25-16.16) I²=0% N=7 studies (1,675 patients)</p> <p>Diabetes mellitus 2.72 (2.05-3.60) I²=42% N=14 studies (2,193 patients)</p> <p>CVD 5.11 (2.03-12.83) I²=77% N=12 studies (2,327 patients)</p> <p>Chronic liver disease 1.17 (0.66-2.06) I²=0% N=9 studies (1,629 patients)</p> <p>Cerebrovascular disease 5.73 (2.52-13.04) I²=33% N=5 studies (769 patients)</p> <p>Myocardial injury 11.2 (0.44-285.9) I²=90% N=3 studies (464 patients)</p>
<p>Yu, Wu⁷⁹</p> <p>December 2019 to July 25, 2020</p> <p>N=31 studies (23,632 patients) 20 China, 4 USA, 2 Brazil, 1 Greece, 1 Iran, 1 Italy, 1 Spain, 1 Oman</p> <p>Case-control/cohort Newcastle-Ottawa scale, range 6-8 (5 studies =6, 19 studies =7, 7 studies =8)</p> <p>AMSTAR2: Moderate quality</p>	<p>Cardio-cerebrovascular disease</p>	<p>Severe COVID Mortality</p>	<p>OR (95% CI)</p> <p>Cardio-cerebrovascular disease and severe COVID N=20 studies 3.00 (2.10-4.30) I²=65%</p> <p>Cardio-cerebrovascular disease and mortality N=16 studies 5.59 (2.81-11.11) I²=94%</p>

<p>Zhang, Shen⁸⁰</p> <p>Inception to May 8, 2020</p> <p>N=17 studies (1,913 patients) 6 China, 5 France, 3 Italy, 3 Netherlands</p> <p>Case-control/cohort Newcastle-Ottawa scale, range 5-8 (2 studies =5, 1 study =6, 8 studies =7, 6 studies =8)</p> <p>AMSTAR2: Moderate quality</p>	<p>COVID-19</p> <p>Venous thromboembolism</p>	<p>Incident:</p> <ul style="list-style-type: none"> - Venous thromboembolism - Pulmonary embolism - Deep vein thrombosis <p>Severe COVID</p>	<p>Incidence (95% CI)</p> <p>Venous thromboembolism 0.25 (0.19-0.31) I²=96%</p> <p>Pulmonary embolism 0.19 (0.13-0.25) I²=93%</p> <p>Deep vein thrombosis 0.07 (0.04-0.10) I²=88%</p> <p>RR (95% CI)</p> <p>Venous thromboembolism and severe COVID 4.76 (2.66-8.50) I²=47%</p>
<p>Zhang, Wu⁸¹</p> <p>Inception to March 20, 2020</p> <p>N=12 studies (2,389 patients) 12 China</p> <p>Case-control/cohort Newcastle-Ottawa scale and STROBE, range 6-8 (6 studies =6, 7 studies =7, 5 studies =8)</p> <p>AMSTAR2: Critically low quality</p>	<p>Hypertension</p>	<p>Severe COVID Mortality</p>	<p>OR 95%CI</p> <p>Hypertension and severe COVID 2.27 (1.80-2.86) I²=8%</p> <p>Stratified by age:</p> <p><50 years 2.21 (1.58-3.10) I²=0%</p> <p>≥50 years 2.32 (1.70-3.17) I²=42%</p> <p>Hypertension and mortality 3.48 (1.72-7.08) I²=56%</p>
<p>Zhao, Meng⁸²</p> <p>December 2019 to March 22, 2020</p> <p>N=11 studies (2,002 patients) 11 China</p> <p>Case series Methodological index non-randomized studies (MINORS) statement, rangre10-13 (overall quality moderate)</p> <p>AMSTAR2: Critically low quality</p>	<p>Smoking history</p>	<p>Severe COVID</p>	<p>OR (95% CI)</p> <p>Smoking history 1.98 (1.29-3.05) I²=44%</p>
<p>Zheng, Peng⁸³</p> <p>January 1, 2020 to Mar 20, 2020</p> <p>N=13 studies (3,027 patients) 13 China</p> <p>Case-control/cohort</p>	<p>Current smoking Diabetes mellitus CVD Hypertension</p>	<p>Composite outcome of severe COVID/mortality</p>	<p>OR (95% CI)</p> <p>Current smoking N=5 studies (1,980 patients) 2.04 (1.32-3.25) I²=0%</p> <p>Diabetes mellitus N=11 studies (2,579 patients)</p>

<p>MINORS statement, range 18-21 (all low risk)</p> <p>AMSTAR2: Low quality</p>			<p>3.68 (2.68-5.03) I²=45%</p> <p>CVD N=10 studies (2,422 patients) 5.19 (3.25-8.29) I²=37%</p> <p>Hypertension N=10 studies (2,527 patients) 2.72 (1.60-4.64) I²=72%</p>
<p>Zuin, Rigatelli⁸⁴</p> <p>Inception to April 10, 2020</p> <p>N=9 studies (1,686 patients) Primary study origin NR</p> <p>Primary study design NR Newcastle-Ottawa Scale, 7 high quality</p> <p>AMSTAR2: Low quality</p>	<p>COVID-19</p> <p>Acute cardiac injury</p>	<p>Acute cardiac injury</p> <p>Mortality</p>	<p>Incidence of acute cardiac injury 24%</p> <p>OR (95% CI)</p> <p>Acute cardiac injury and mortality 21.65 (8.60-54.52) I²=82%</p>
<p>OR; Odds ratio, RR; Relative risk, SMD; Standardised mean difference, CI; Confidence interval, I²; I-squared test for heterogeneity, AMSTAR2; a critical appraisal tool for systematic reviews, BMI; Body mass index, CVD; Cardiovascular disease, CAD; Coronary artery disease, CHD; Coronary heart disease, ICU; Intensive care unit, NR; not reported. N=studies included in meta-analysis (n=patients) Severe COVID-19 (as described in primary systematic reviews)</p>			

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