

Smoking is associated with worse outcomes of COVID-19 particularly among younger adults: A systematic review and meta-analysis

ADDITIONAL FILE

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Risk of Bias Assessment

We evaluated the quality of studies using a modification of the ACROBAT-NRSI[7] tool on 5 domains: study population, exposure measurement, outcome assessment, measurement of confounders, and adequate follow-up. Each one of these domains was scored 0 for low risk of bias, 1 for moderate risk of bias, and 2 for high risk of bias and the average score of each study was computed and discussed among both authors. Studies with the average score higher than 1 were considered high risk and excluded in a sensitivity analysis.

Study population

- Low risk: studies included at least 50 patients
- Moderate risk: studies included at least 20 patients
- High risk: studies included less than 20 patients

Exposure measurement

- Low risk: studies reported 3 categories of smoking status: current, former, and never smokers
- Moderate risk: studies reported 2 categories of smoking status
- High risk: studies reported only 1 category of smoking status

Outcome assessment

- Low risk: studies reported a clear definition of outcomes
- High risk: studies did not report specific outcomes

Measurement of confounders

- Low risk: adjustment for confounders
- High risk: unadjusted analyses

Adequate follow-up

- Low risk: identify duration of data collection
- High risk: duration of data collection is unclear

References

References are the same as cited in the main text.

Table A1 Summary of Studies													
Author	Setting	Study type	Time of data collection	Population	Definition of disease progression	Smoking status	Odds of disease progression (95%CI)		Adjustment	Smoking prevalence			Patients' mean age
							Unadjusted	Adjusted		Overall	More severe group	Less severe group	
Beyrouti et al [8]	UK National Hospital for Neurology and Neurosurgery, Queen Square, London	Case series	1 Apr 2020-16 Apr 2020	6 confirmed COVID-19 patients with acute ischemic stroke	ICU admission	Smoking	0.47 (0.01, 16.89)	N/A	N/A	16.7%	N/A	25.0%	70
Buckner et al [9]	US University of Washington affiliated hospitals	Retrospective	2 Mar 2020-26 Mar 2020	105 hospitalized patients with laboratory confirmed COVID-19	A composite endpoint of admission to an intensive care unit (ICU) or death	Smoking (ever)	0.89 (0.34, 2.35)	N/A	N/A	25.6%	24.4%	26.7%	69
CDC COVID-19 Response Team [10]	US	Retrospective	12 Feb 2020-28 Mar 2020	7,162 confirmed COVID-19 patients with completed information*	ICU admission	Current and former smoker	Current smoker: 0.86 (0.35-2.13) Former smoker: 3.76 (2.53-5.59) Current/former: 2.60 (1.82-3.73)	N/A	N/A	Current smoker: 1.3% Former smoker: 2.3% Current/former: 3.6%	Current smoker: 0.5% Former smoker: 3.1% Current/former: 3.6%	Current smoker: 1.3% Former smoker: 2.0% Current/former: 3.4%	N/A
Chen Q et al [11]	China Taizhou Public Health Medical Center, Zhejiang	Retrospective	1 Jan 2020- 11 Mar 2020	145 hospitalized patients with laboratory confirmed COVID-19	Respiratory distress with respiratory rate ≥ 30 /min, or oxygen saturation $\leq 93\%$ at rest, or oxygenation index ≤ 300 mmHg	Smoking history	0.56 (0.15-2.10)	N/A	N/A	10.3%	7.0%	11.8%	48
Chen T et al [12]	China Tongji Hospital	Retrospective	13 Jan 2020-13 Feb 2020	799 moderately to severely ill or critically ill patients with confirmed covid-19	Death	Current and former smoker	Current smoker: 2.03 (0.63-6.58) Former smoker: 0.58 (0.11-3.05) Current/former: 1.31 (0.51-3.33)	N/A	N/A	Current smoker: 4.4% Former smoker: 2.6% Current/former: 6.9%	Current smoker: 6.2% Former smoker: 1.8% Current/former: 8.0%	Current smoker: 3.1% Former smoker: 3.1% Current/former: 6.2%	62

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							Unadjusted	Adjusted		Overall	More severe group	Less severe group	
Dong et al [13]	China Zhongnan Hospital of Wuhan University, No. 7 hospital of Wuhan, and Wuhan Children's Hospital	Case series	20 Jan 2020-3 Mar 2020	9 adults hospitalized patients with laboratory confirmed COVID-19**	Bilateral pneumonia, respiratory distress, required mechanical ventilation, ICU care, or hospitalized > 10 days.	Current smoker	1.15 (0.03-38.88)	N/A	N/A	11.1%	14.3%	0.0%	44
Feng et al [14]	Jinyintan Hospital in Wuhan, Shanghai Public Health Clinical Center in Shanghai and Tongling People's Hospital in Anhui Province	Retrospective	1 Jan 2020-15 Feb 2020	476 hospitalized patients with laboratory confirmed COVID-19	Severe (respiratory distress with respiratory rate ≥ 30 /min, or oxygen saturation $\leq 93\%$ at rest, or oxygenation index ≤ 300 mmHg), or critical (respiratory failure, shock, or organ dysfunction)	Smoking	1.85 (0.97-3.54)	N/A	N/A	9.7%	14.0%	8.1%	53
Gayam et al [15]	Interfaith Medical Center, Brooklyn, New York	Case series	1 Mar 2020-15 April 2020	6 confirmed hospitalized COVID-19 patients coinfecting with Mycoplasma pneumoniae	Required intensive mechanical ventilator	Current smoker	0.47 (0.01-16.89)	N/A	N/A	33.3%	0.0%	40.0%	57
Giacomelliet al [16]	Infectious Diseases and Intensive Care units of Luigi Sacco Hospital, Milan	Prospective cohort	21 Feb 2020-19 Mar 2020	233 hospitalized patients with laboratory confirmed COVID-19	Death	History of smoking	1.37 (0.70-2.68)	N/A	N/A	30.0%	35.4%	28.6%	61

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Goyal et al [17]	US 862-bed quaternary referral center and an affiliated 180-bed nonteaching community hospital in Manhattan, New York	Retrospective	3 Mar 2020-27 Mar 2020	393 hospitalized patients with COVID-19 diagnosis	Required intensive mechanical ventilator	Current smoker	0.86 (0.32-2.29)	N/A	N/A	5.1%	4.6%	5.3%	62
Guan et al [18]	552 hospitals in 30 provinces, autonomous regions, and municipalities	Retrospective	11 Dec 2019-29 Jan 2020	1,099 patients (both hospitalized and outpatient) with laboratory confirmed COVID-19	ICU admission, the use of mechanical ventilation, or death	Current, former and never	Current smoker: 2.84 (1.57-5.14) Former smoker: 6.27 (2.20-17.90) Current/former: 3.25 (1.89-5.59)	N/A	N/A	Current smoker: 12.6% Former smoker: 1.9% Current/former: 14.6%	Current smoker : 25.8% Former smoker : 7.6% Current /former : 33.3%	Current smoker : 11.8% Former smoker : 1.6% Current /former : 13.3%	47
Guo et al [19]	Seventh Hospital of Wuhan City	Retrospective	23 Jan 2020-23 Feb 2020	187 hospitalized patients with laboratory confirmed COVID-19	Acute myocardial injury	Smoking	1.75 (0.64-4.80)	N/A	N/A	9.6%	13.5%	8.1%	59

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							Unadjusted	Adjusted		Overall	More severe group	Less severe group	
Hu et al [20]	China Tianyou Hospital in Wuhan	Retrospective	8 Jan 2020- 20 Feb 2020	323 hospitalized patients with COVID-19 diagnosis	Death, progression from non-severe to severe (patients showed features of nonsevere patients plus respiratory distress with RR ≥ 30 breaths/min, oxygen saturation $\leq 93\%$, arterial partial pressure of oxygen/oxygen concentration ≤ 300 mmHg) or critical (patients showed respiratory failure requiring ventilatory support, as well as shock and organ dysfunction requiring intensive care) or severe to critical status, and/or maintenance of severe or critical status	Smoking history	2.12 (1.00-4.47)	3.46 (1.18-10.17)	Age, hypnotics, diagnosis at critical status, diabetes, hypertensive troponin I, white blood cell count, neutrophil count	11.8%	15.1%	7.9%	61
Huang C et al [21]	China Jin Yin-tan Hospital in Wuhan	Retrospective	16 Dec 2019-2 Jan 2020	41 hospitalized patients with laboratory confirmed COVID-19	ICU admission	Current smoking	0.27 (0.01-5.62)	N/A	N/A	7.3%	0.0%	10.7%	49
Huang R et al [22]	China 8 designated hospitals in 8 cities of Jiangsu Province	Retrospective	22 Jan 2020- 10 Feb 2020	202 hospitalized patients with laboratory confirmed COVID-19	Severe (respiratory distress with respiratory rate ≥ 30 /min, or oxygen saturation $\leq 93\%$ at rest, or oxygenation index ≤ 300 mmHg), or critical (respiratory failure, shock, or organ dysfunction)	Smoking history	1.12 (0.24, 5.22)	N/A	N/A	7.9%	8.7%	7.8%	44

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Hur et al [23]	US 10 hospitals in the Chicago metropolitan area	Retrospective	1 Mar 2020- 8 April 2020	486 hospitalized patients with laboratory confirmed COVID-19	Intubation and prolonged intubation for acute respiratory failure	Current/former smoker	1.47 (0.98-2.22)	N/A	N/A	33.5%	39.9%	31.0%	59
Ji et al [24]	China Fuyang Second People's Hospital and the Fifth Medical Center of Chinese PLA General Hospital	Retrospective	20 Jan 2020-22 Feb 2020	208 hospitalized patients with laboratory confirmed COVID-19	Progression to respiratory distress with respiratory rate ≥ 30 /min, or oxygen saturation $\leq 93\%$ at rest, or oxygenation index ≤ 300 mmHg, or requirement of mechanical ventilator	Smoke	2.10 (0.75-5.93)	N/A	N/A	9.1%	15.0%	7.7%	44
Kim et al [25]	Korea	Retrospective	19 Jan 2020-17 Feb 2020	28 confirmed COVID-10 cases nationwide	Required oxygen supplement	Smoking	2.25 (0.30-16.85)	N/A	N/A	21.4%	33.3%	18.2%	43
Klang et al [26]	US 5 hospital campuses of the Mount Sinai hospital, New York	Retrospective	1 Mar 2020- 17 May 2020	3,406 hospitalized patients with laboratory confirmed COVID-19	Death	Smoking	age ≤ 50 : 1.97 (1.01-3.85) age > 50 : 1.13 (0.95-1.35)	age ≤ 50 : 1.7 (0.8-1.2) age > 50 : 1.0 (0.8-1.2)	Age, sex, coronary arterial disease, congestive heart failure, hypertension, diabetes, hyperlipidemia, chronic kidney disease, cancer, intubation, BMI, and race	age ≤ 50 : 13.3% age > 50 : 25.3%	age ≤ 50 : 21.7% age > 50 : 26.8%	age ≤ 50 : 12.3% age > 50 : 24.4%	age ≤ 50 : 41 age > 50 : 71

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Li X et al[27]	China Tongji Hospital	Retrospective	26 Jan 2020-5 Feb 2020	548 hospitalized patients with laboratory confirmed COVID-19	Respiratory distress with respiratory rate ≥ 30 /min, or breaths per minute, PaO ₂ /FIO ₂ ratio lower than 250, multilobar infiltrates confusion, or disorientation, or respiratory failure, or required mechanical ventilation, or septic shock	Current, former and never	Current smoker: 0.87 (0.46-1.66) Former smoker: 2.04 (1.12-3.73) Current/former: 1.38 (0.88-2.17)	N/A	N/A	Current smoker: 7.5% Former smoker: 9.4% Current/former: 16.9%	Current smoker : 6.8% Former smoker : 12.5% Current /former : 19.2%	Current smoker : 8.2% Former smoker : 6.5% Current /former : 14.7%	60
Li YK et al[28]	China Department of Thoracic Surgery of Tongji Hospital affiliated with Tongji Medical College of Huazhong University of Science and Technology	Retrospective	1 Jan 2020- 20 Feb 2020	25 hospitalized patients with laboratory confirmed COVID-19	Severe (respiratory distress with respiratory rate ≥ 30 /min, or oxygen saturation $\leq 93\%$ at rest, or oxygenation index ≤ 300 mmHg), or critical (respiratory failure, shock, or organ dysfunction)	Smoking	8.75 (1.21-63.43)	N/A	N/A	28.0%	55.6%	12.5%	51
Liang et al [29]	China 575 hospitals in 31 provincial administrative regions	Retrospective	21 Nov 2019- 31 Jan 2020	1,590 hospitalized patients with laboratory confirmed COVID-19	Admission to the intensive care unit (ICU), invasive ventilation, or death	Current/former and never	2.34 (1.36-4.02)	N/A	N/A	7.0%	13.7%	6.4%	49

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Liu et al [30]	China Three tertiary hospitals in Wuhan	Retrospective	30 Dec 2019-15 Jan 2020	78 hospitalized patients with laboratory confirmed COVID-19	Respiratory distress, respiratory failure, required mechanical ventilation and ICU care, or death	History of smoking	12.19 (1.76-84.31)	14.29 (1.58-25.0)	Age, maximum temperature at admission, respiratory failure, severe illness, albumin, creatinine, procalcitonin, and C-reactive protein level	6.4%	27.3%	3.0%	38
Mo et al [32]	China Zhongnan hospital of Wuhan University	Retrospective	1 Jan 2020-5 Feb 2020	155 hospitalized patients with laboratory confirmed COVID-19	Did not improve after treatment, status changed to severe, or hospitalized > 10 days	Current smoking	1.68 (0.30-9.45)	N/A	N/A	3.9%	4.7%	2.9%	54
Morassi et al [33]	Italy Fondazione Poliambulanza Hospital, Brescia, Italy and Udine University Hospital, Udine	Case series	16 Mar 2020- 5 Apr 2020	6 hospitalized patients with laboratory confirmed COVID-19 who developed clinical and neuroimaging evidence of acute stroke	Death	Smoker	1.00 (0.03-40.28)	N/A	N/A	16.7%	20.0%	0.0%	69

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Palaiodimos et al [34]	US Montefiore Medical Center, Bronx, New York	Retrospective	9 Mar 2020- 22 Mar 2020	200 hospitalized patients with laboratory confirmed COVID-19	Increasing oxygen requirement*** Intubation In-hospital mortality	Current/former smoker	Increasing oxygen requirement: 1.86 (1.02-3.39) Intubation: 1.56 (0.77-3.15) In-hospital mortality: 1.19 (0.60-2.36)	Increasing oxygen requirement: 2.1 (1.07-4.1) Intubation : 1.66 (0.76-3.62) In-hospital mortality: 0.83 (0.37-1.87)	N/A	32.5%	N/A	N/A	64
Petrilli et al [35]	US NYU Langone Health with more than 260 outpatient office sites and four acute care hospitals in New York	Prospective cohort	1 Mar 2020- 8 Apr 2020	5,279 patients with laboratory confirmed COVID-19	Admission to intensive care unit, use of mechanical ventilation, discharge to hospice, or death	Current, former and never	Current smoker: 0.94 (0.65-1.36) Former smoker: 1.49 (1.22-1.82) Current/former: 1.37 (1.14-1.65)	Current smoker: 0.77 (0.52-1.20) Former smoker: 1.06 (0.85-1.30)	Age, sex, race, BMI, coronary arterial disease, heart failure, hyperlipidemia, hypertension, diabetes, asthma, COPD, chronic kidney disease, cancer, week of admission	Current smoker: 5.2% Former smoker: 20.6% Current/former: 25.7%	Current smoker : 4.4% Former smoker : 23.8% Current /former : 28.3%	Current smoker : 5.6% Former smoker : 18.7% Current /former : 24.3%	63
Qin et al [36]	China Tongji Hospital	Retrospective	10 Jan 2020- 12 Feb 2020	452 hospitalized patients with laboratory confirmed COVID-19	Respiratory distress with respiratory rate ≥ 30 /min, or oxygen saturation $\leq 93\%$ at rest, or oxygenation index ≤ 300 mmHg	Smoking	0.43 (0.10-1.94)	N/A	N/A	1.5%	1.0%	2.4%	58

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Rastrelli et al [37]	Italy Carlo Poma Hospital in Mantua	Case series	No information	31 male patients with laboratory confirmed COVID-19 in the respiratory intensive care unit	Transferred to ICU for intubation, or death	Current and former smoker	Current smoker: 2.33 (0.07-74.55) Former smoker: 1.89 (0.23-15.74) Current/former: 1.70 (0.21-14.02)	N/A	N/A	Current smoker: 3.2% Former smoker: 35.5% Current/former: 38.7%	Current smoker: 0% Former smoker: 50% Current/former: 50%	Current smoker: 4.8% Former smoker: 42.9% Current/former: 47.7%	65
Ren et al [38]	Third People's Hospital of Shenzhen	Retrospective	11 Jan 2020- 12 Feb 2020	150 hospitalized patients with laboratory confirmed COVID-19	Development of sepsis	Smoking history	15.28 (0.77-301.86)	N/A	N/A	2.0%	6.1%	0.0%	54
Shi et al [39]	China Zhejiang Province	Retrospective	Up to 02/17/2020	487 hospitalized patients with laboratory confirmed COVID-19	Severe disease (without precisely defining it) or death	Smoking history	1.61 (0.64-4.04)	N/A	N/A	8.2%	12.2%	7.8%	46
Wan et al [40]	China Chongqing University Three Gorges hospital, in northeast Chongqing	Retrospective	23 Jan 2020-8 Feb 2020	135 hospitalized patients with laboratory confirmed COVID-19	Respiratory distress with respiratory rate ≥ 30 /min, or oxygen saturation $\leq 93\%$ at rest, or oxygenation index ≤ 300 mmHg	Current smoking	0.28 (0.03-2.31)	N/A	N/A	6.7%	2.5%	8.4%	47
Wang et al [41]	NO.2 People's Hospital of Fuyang City	Retrospective	20 Jan 2020-9 Feb 2020	125 hospitalized patients with laboratory confirmed COVID-19	Severe (respiratory distress with respiratory rate ≥ 30 /min, or oxygen saturation $\leq 93\%$ at rest, or oxygenation index ≤ 300 mmHg), or critical (respiratory failure, shock, or organ dysfunction)	Current smoking	3.93 (1.30-11.93)	N/A	N/A	12.8%	28.0%	9.0%	39

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							Unadjusted	Adjusted		Overall	More severe group	Less severe group	
Xiong et al [42]	China Wuhan Hemodialysis Quality Control Center	Retrospective	1 Jan 2020- 10 Mar 2020	131 hospitalized patients with laboratory confirmed COVID-19 who received maintenance hemodialysis at 65 centers in Wuhan, China	Severe (respiratory distress with respiratory rate ≥ 30 /min, or oxygen saturation $\leq 93\%$ at rest, or oxygenation index ≤ 300 mmHg), or critical (respiratory failure, shock, or organ dysfunction)	Current smoker	0.66 (0.26-1.69)	N/A	N/A	29.8%	23.3%	31.7%	63
Xu et al [43]	China First Affiliated Hospital, School of Medicine, Zhejiang University and Shenzhen Third People's Hospital	Retrospective	13 Jan 2020- 19 Feb 2020	113 hospitalized patients with laboratory confirmed COVID-19	Prolonged viral RNA shedding	Current smoker	0.80 (0.18-3.54)	N/A	N/A	7.1%	6.6%	8.1%	52
Yan et al [44]	China No.3 People's Hospital of Hubei Province	Retrospective	31 Jan 2020- 9 Mar 2020	168 hospitalized patients with laboratory confirmed COVID-19	Prolonged viral RNA shedding	Current smoker	0.86 (0.23-3.18)	N/A	N/A	10.0%	11.9%	8.2%	52
Yang et al [45]	China Wuhan Jin Yin-tan Hospital, Wuhan	Retrospective	24 Dec 2019-26 Jan 2020	52 critically ill hospitalized patients with laboratory confirmed COVID-19	Death	Smoking	0.11 (0.01-2.50)	N/A	N/A	3.8%	0.0%	10.0%	60

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Yao et al [46]	China Dabieshan Medical Center 19 in Huanggang city, Hubei Province	Retrospective	30 Jan 2020-11 Feb 2020	108 hospitalized patients with laboratory confirmed COVID-19	Respiratory distress with respiratory rate ≥ 30 /min, or breaths per minute, PaO ₂ /FIO ₂ ratio lower than 250, multilobar infiltrates confusion, or disorientation, or respiratory failure, or required mechanical ventilation, or shock, or organ dysfunction, or death	Current smoker	11.18 (1.11-112.83)	N/A	N/A	3.7%	12.0%	1.2%	52
Yu Q et al [47]	24 designated hospitals in Jiangsu province	Retrospective	10 Jan 2020- 18 Feb 2020	421 hospitalized patients with laboratory confirmed COVID-19	Admission to ICU, acute respiratory failure occurrence, or shock	Current smoker	0.20 (0.01-3.37)	N/A	N/A	3.1%	0.0%	3.6%	47
Yu T et al [48]	China Dongguan People's Hospital and Nanfang Hospital, Southern Medical University	Retrospective	Jan 2020-Feb 2020	95 hospitalized patients with laboratory confirmed COVID-19	Pneumonia exacerbation	Tobacco smoking	6.67 (1.11-40.04)	16.13 (1.28-204.16)	Age, sex, blood pressure, BMI, serum lactic acid, neutrophil count, lymphocyte count, hemoglobin, platelet count, creatinine, ALT, AST, and LDH	7.1%	21.1%	2.0%	43

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Yu X et al [49]	Shanghai	Retrospective	1 Jan 2020- 19 Feb 2020	323 hospitalized patients with laboratory confirmed COVID-19	Severe (dyspnoea, and respiratory rate \geq 30/min, blood oxygen saturation \leq 93%, PaO ₂ / FiO ₂ ratio \leq 300 mmHg); Critical (respiratory failure, or septic shock, or multiple organ dysfunction/ failure)	Smoking history	0.89 (0.20-4.01)	N/A	N/A	8.1%	8.0%	8.9%	50
Zhang J et al [50]	China No.7 Hospital of Wuhan	Retrospective	16 Jan 2020-3 Feb 2020	140 hospitalized patients with laboratory confirmed COVID-19	Respiratory distress with respiratory rate \geq 30/min, or oxygen saturation \leq 93% at rest, or oxygenation index \leq 300 mmHg	Current and past smoker	Current smoker: 7.57 (0.35-160.88) Former smoker: 2.03 (0.44-9.42) Current/former: 3.04 (0.73-12.69)	N/A	N/A	Current smoker: 1.4% Former smoker: 5% Current/former: 6.4%	Current smoker : 3.4% Former smoker : 6.9% Current /former : 10.3%	Current smoker : 0% Former smoker : 3.7% Current /former : 3.7%	57
Zhang R et al [51]	China Renmin Hospital of Wuhan University	Retrospective	10 Jan 2020- 10 Feb 2020	120 hospitalized patients with laboratory confirmed COVID-19	Respiratory distress with respiratory rate \geq 30/min, or oxygen saturation \leq 93% at rest, or oxygenation index \leq 300 mmHg, or respiratory failure requiring mechanical ventilation, shock, or organ dysfunction requiring ICU treatment	Current smoking	48.02 (2.61-882.27)	N/A	N/A	5.0%	20.0%	0.0%	45
Zhang X et al [52]	China Zhejiang Province	Retrospective	17 Jan 2020-8 Feb 2020	645 patients confirmed with SARSCoV-2 infection	Abnormal imaging findings (CT scan or Chest X-ray)	Current smoker	1.17 (0.41-3.39)	N/A	N/A	6.4%	6.5%	5.6%	47

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Zheng Y et al [53]	China Taihe Hospital at Shiyan	Retrospective	16 Jan 2020- 4 Feb 2020	73 hospitalized patients with laboratory confirmed COVID-19	Severe (dyspnoea, and respiratory rate \geq 30/min, blood oxygen saturation \leq 93%, PaO ₂ / FiO ₂ ratio \leq 300 mmHg); Critical (respiratory failure, or septic shock, or multiple organ dysfunction/ failure)	Smoker	0.44 (0.08-2.35)	N/A	N/A	11.0%	6.7%	14.3%	43
Zhou et al [54]	China Jin Yin-tan Hospital and Wuhan Pulmonary Hospital in Wuhan	Retrospective	29 Dec 2019-31 Jan 2020	191 hospitalized patients with laboratory confirmed COVID-19	Death	Current smoker	2.23 (0.65-7.63)	N/A	N/A	5.8%	4.4%	9.3%	56

* Hospitalization status unknown was excluded from the analysis.
** Two children were excluded from the analysis.
*** Increasing oxygen requirement was used in the analysis.

Table A2 Risk of Bias of Studies (2=high risk, 1=intermediate risk, 0=low risk)						
Study	Study population	Exposure measurement	Outcome assessment	Measurement of confounders	Adequate follow-up	Average score
Beyrouti et al [8]	2	2	0	2	0	1.2
Buckner et al [9]	0	2	0	2	0	0.8
CDC COVID-19 [10]	0	0	0	2	0	0.4
Chen Q et al [11]	0	2	0	2	0	0.8
Chen T et al [12]	0	0	0	2	0	0.4
Dong et al [13]	2	2	2	2	0	1.6
Feng et al [14]	0	2	0	2	0	0.8
Gayam et al [15]	2	2	0	2	0	1.2
Giacomelli et al [16]	0	2	0	2	0	0.8
Goyal et al [17]	0	2	0	2	0	0.8
Guan et al [18]	0	0	0	2	0	0.4
Guo et al [19]	0	2	0	2	0	0.8
Hu et al [20]	0	2	0	0	0	0.4
Huang C et al [21]	1	2	0	2	0	1
Huang R et al [22]	0	2	0	2	0	0.8
Hur et al [23]	0	1	0	2	0	0.6
Ji Dong et al [24]	0	2	0	2	0	0.8
Kim et al [25]	1	2	0	2	0	1
Klang et al [26]	0	2	0	0	0	0.4
Li X et al [27]	0	0	0	2	0	0.4
Li YK et al [28]	1	2	0	2	0	1
Liang et al [29]	0	1	0	2	0	0.6
Liu et al [30]	0	2	0	0	0	0.4
Mo et al [32]	0	2	0	2	0	0.8
Morassi et al [33]	2	2	0	2	0	1.2
Palaiodimos et al [34]	0	1	0	0	0	0.2
Petrilli et al [35]	0	0	0	0	0	0
Qin et al [36]	0	2	0	2	0	0.8
Rastrelli et al [37]	1	0	0	2	2	1
Ren et al [38]	0	2	0	2	0	0.8
Shi et al [39]	0	2	0	2	2	1.2
Wan et al [40]	0	2	0	2	0	0.8
Wang et al [41]	0	2	0	2	0	0.8
Xiong et al [42]	0	2	0	2	0	0.8
Xu et al [43]	0	2	0	2	0	0.8
Yan et al [44]	0	2	0	2	0	0.8

Table A2 Risk of Bias of Studies (2=high risk, 1=intermediate risk, 0=low risk)						
Study	Study population	Exposure measurement	Outcome assessment	Measurement of confounders	Adequate follow-up	Average score
Yang et al [45]	0	2	0	2	0	0.8
Yao et al [46]	0	2	0	2	0	0.8
Yu Q et al [47]	0	2	0	2	0	0.8
Yu T et al [48]	0	2	0	0	2	0.8
Yu X et al [49]	0	2	0	2	0	0.8
Zhang J et al [50]	0	0	0	2	0	0.4
Zhang R et al [51]	0	2	0	2	0	0.8
Zhang X et al [52]	0	2	0	2	0	0.8
Zheng Y et al [53]	0	2	0	2	0	0.8
Zhou et al [54]	0	2	0	2	0	0.8

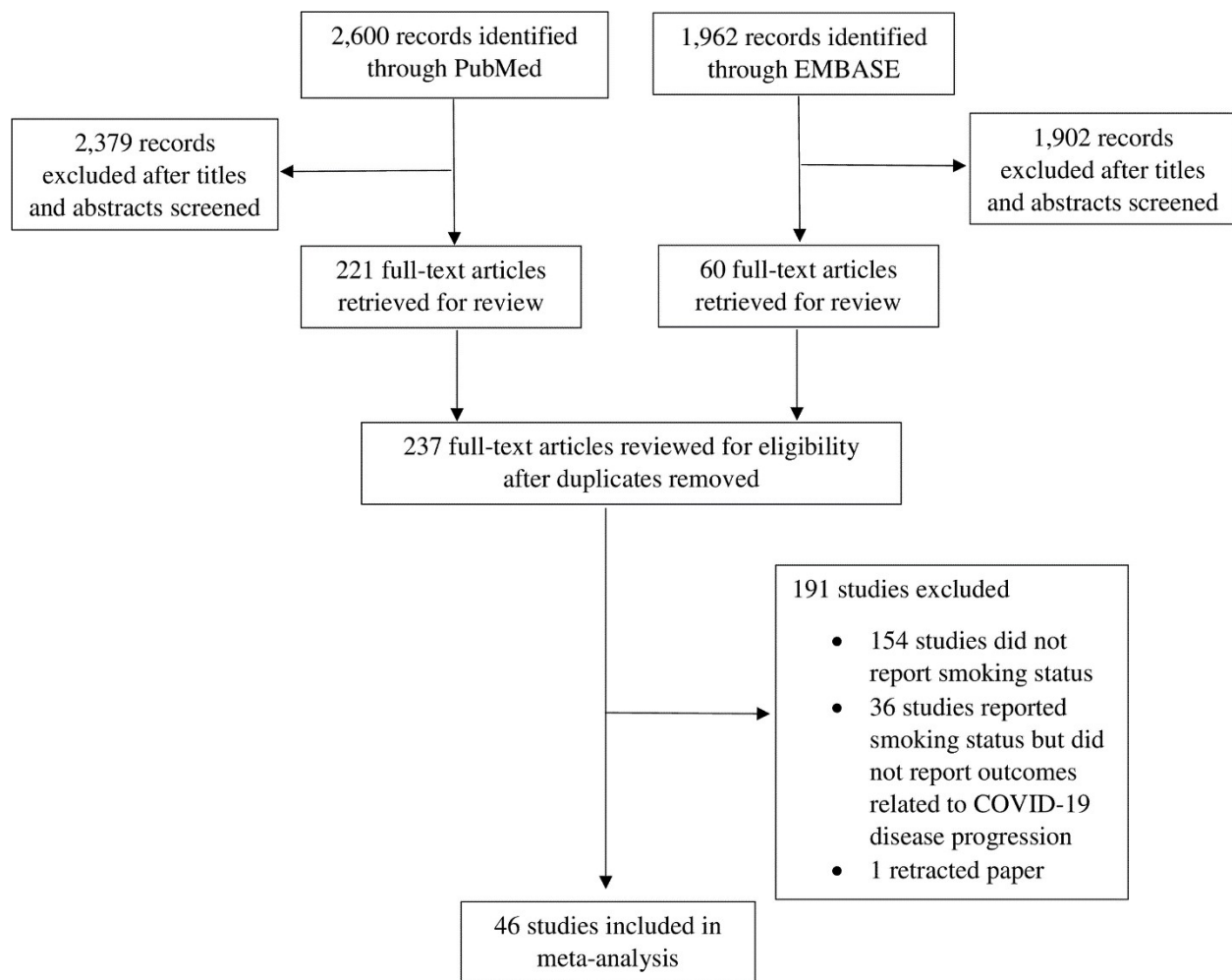


Figure A1. PRISMA diagram

Ever (current and former) smoking and COVID-19 disease progression (exclude 5 high-risk studies)

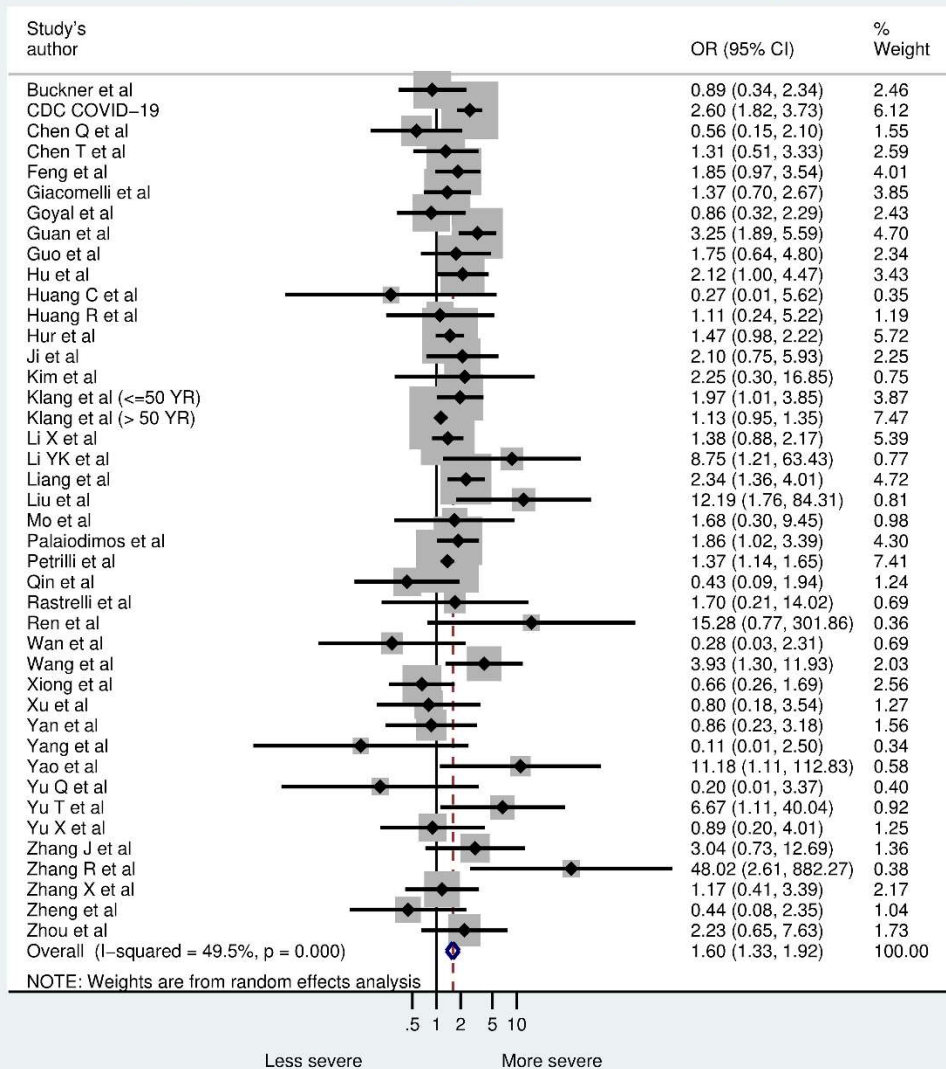


Figure A2. Ever (current and former) smoking and COVID-19 disease progression, dropping 5 studies with high risk of bias scores.

Ever (current and former) smoking and COVID-19 mortality

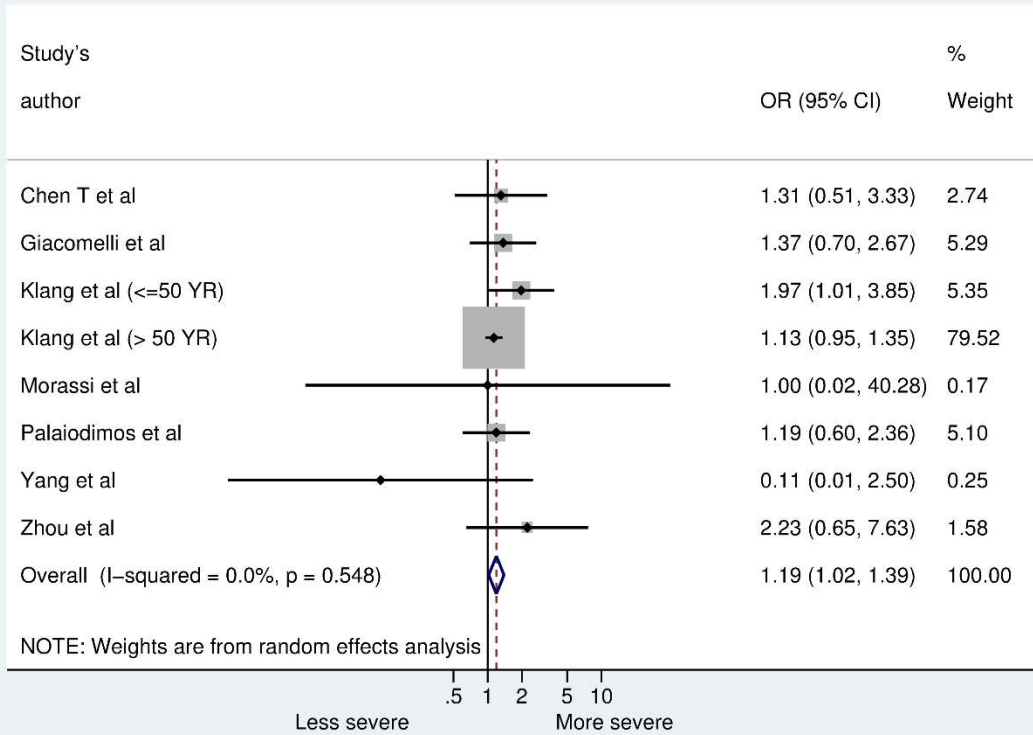


Figure A3. Ever (current and former) smoking and COVID-19 mortality

Current smoker and COVID-19 disease progression

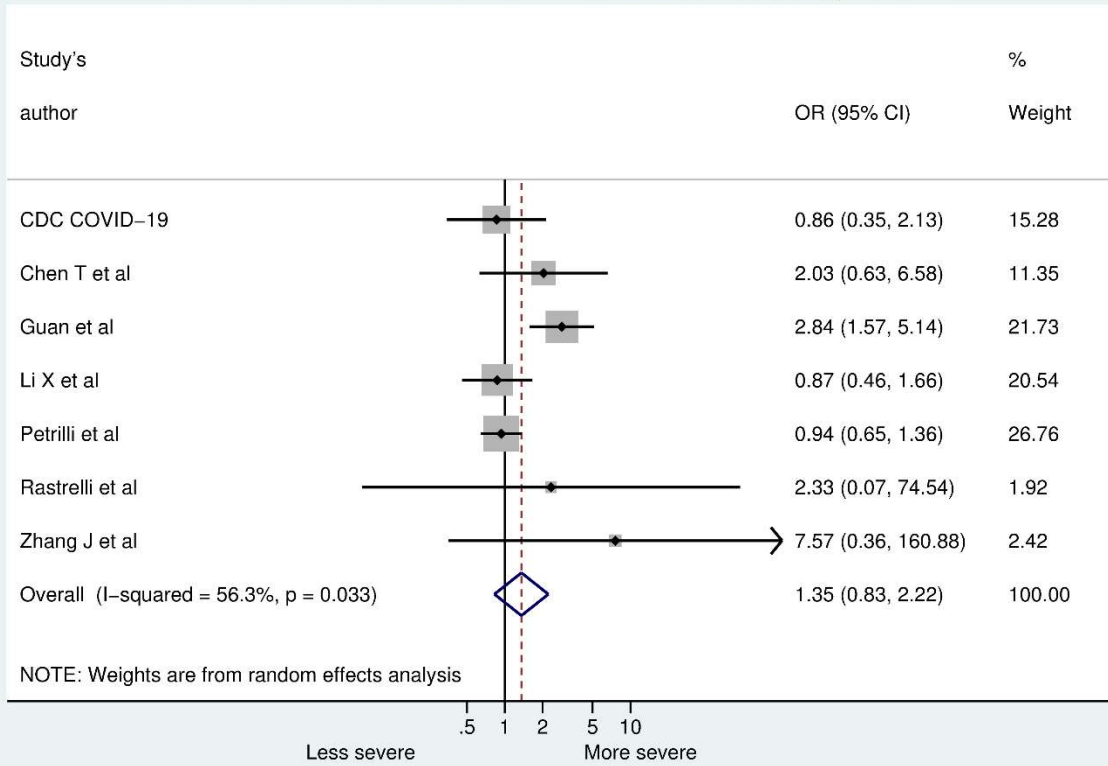
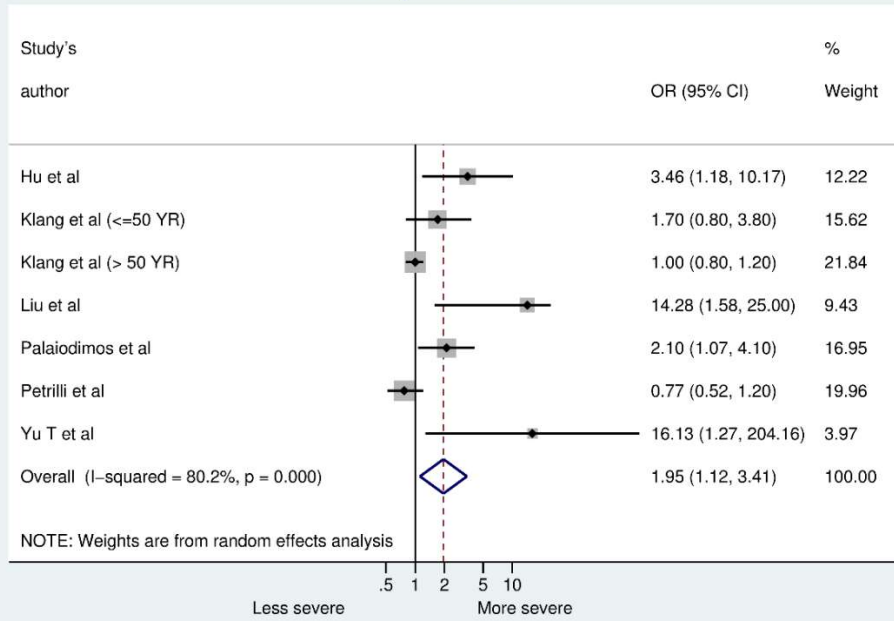


Figure A4. Current smokers vs. never smokers and COVID-19 disease progression.

Ever (current and former) smoking and
COVID-19 disease progression
Adjusted ORs



Ever (current and former) smoking and
COVID-19 disease progression
Unadjusted ORs

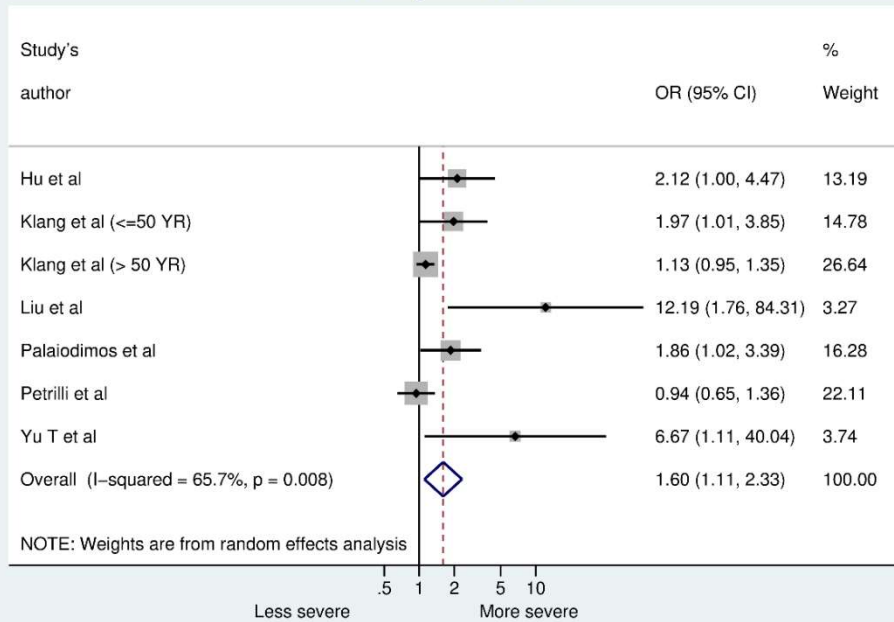


Figure A5. Ever (current and former) smoking and disease progression in models that adjusted (top) and did not adjust (bottom) ORs for confounding variables.