

Recent exposure to inhaled nicotine and COVID-19

Online Appendix

This appendix was part of the submitted manuscript and has been peer reviewed. It is posted as supplied by the authors.

	Page
List of 27 retrieved case-series on COVID-19 published on major journals	Page 2
Supplementary Methods	Page 5
Supplementary Figure 1	Page 6
Supplementary Figure 2	Page 7
Supplementary Figure 3	Page 8
Supplementary References	Page 9

Reference for the 27 major case series retrieved on major journals

Borba MGS, Val FFA, Sampaio VS, et al; CloroCovid-19 Team. Effect of High vs Low Doses of Chloroquine Diphosphate as Adjunctive Therapy for Patients Hospitalized With Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Infection: A Randomized Clinical Trial. *JAMA Netw Open* 2020;3:e208857. doi: 10.1001/jamanetworkopen.2020.8857.

Mehra MR, Desai SS, Kuy S, Henry TD, Patel AN. Cardiovascular Disease, Drug Therapy, and Mortality in Covid-19. *N Engl J Med* 2020. doi: 10.1056/NEJMoa2007621. [Epub ahead of print]

Shen C, Wang Z, Zhao F, et al. Treatment of 5 Critically Ill Patients With COVID-19 With Convalescent Plasma. *JAMA* 2020. doi: 10.1001/jama.2020.4783. [Epub ahead of print]

Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet* 2020;395(10229):1054-1062. doi: 10.1016/S0140-6736(20)30566-3.

Guan WJ, Ni ZY, Hu Y, et al; China Medical Treatment Expert Group for Covid-9. Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med* 2020;382:1708-1720. doi: 10.1056/NEJMoa2002032.

Guo T, Fan Y, Chen M, et al. Cardiovascular Implications of Fatal Outcomes of Patients With Coronavirus Disease 2019 (COVID-19). *JAMA Cardiol* 2020. doi: 10.1001/jamacardio.2020.1017. [Epub ahead of print]

Yang X, Yu Y, Xu J, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *Lancet Respir Med* 2020;8:475-481. doi: 10.1016/S2213-2600(20)30079-5.

Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020;395:497-506. doi: 10.1016/S0140-6736(20)30183-5.

Arentz M, Yim E, Klaff L, et al. Characteristics and Outcomes of 21 Critically Ill Patients With COVID-19 in Washington State. *JAMA* 2020. doi: 10.1001/jama.2020.4326. [Epub ahead of print]

Bhatraju PK, Ghassemieh BJ, Nichols M, et al. Covid-19 in Critically Ill Patients in the Seattle Region - Case Series. *N Engl J Med* 2020. doi: 10.1056/NEJMoa2004500. [Epub ahead of print]

Cao B, Wang Y, Wen D, et al. A Trial of Lopinavir-Ritonavir in Adults Hospitalized with Severe Covid-19. *N Engl J Med* 2020;382:1787-1799. doi: 10.1056/NEJMoa2001282.

Chang D, Lin M, Wei L, et al. Epidemiologic and Clinical Characteristics of Novel Coronavirus Infections Involving 13 Patients Outside Wuhan, China. *JAMA* 2020. doi: 10.1001/jama.2020.1623. [Epub ahead of print]

Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* 2020;395(10223):507-513. doi: 10.1016/S0140-6736(20)30211-7.

Grasselli G, Zangrillo A, Zanella A, et al; COVID-19 Lombardy ICU Network. Baseline Characteristics and Outcomes of 1591 Patients Infected With SARS-CoV-2 Admitted to ICUs of the Lombardy Region, Italy. *JAMA* 2020. doi: 10.1001/jama.2020.5394. [Epub ahead of print]

Grein J, Ohmagari N, Shin D, et al. Compassionate Use of Remdesivir for Patients with Severe Covid-19. *N Engl J Med* 2020. doi: 10.1056/NEJMoa2007016. [Epub ahead of print]

Li Q, Guan X, Wu P, et al. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia. *N Engl J Med* 2020;382:1199-1207. doi: 10.1056/NEJMoa2001316.

Mao L, Jin H, Wang M, et al. Neurologic Manifestations of Hospitalized Patients With Coronavirus Disease 2019 in Wuhan, China. *JAMA Neurol* 2020. doi: 10.1001/jamaneurol.2020.1127. [Epub ahead of print]

Myers LC, Parodi SM, Escobar GJ, Liu VX. Characteristics of Hospitalized Adults With COVID-19 in an Integrated Health Care System in California. *JAMA* 2020. doi: 10.1001/jama.2020.7202. [Epub ahead of print]

Richardson S, Hirsch JS, Narasimhan M, et al. Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area. *JAMA* 2020. doi: 10.1001/jama.2020.6775. [Epub ahead of print]

Shi S, Qin M, Shen B, et al. Association of Cardiac Injury With Mortality in Hospitalized Patients With COVID-19 in Wuhan, China. *JAMA Cardiol* 2020. doi: 10.1001/jamacardio.2020.0950. [Epub ahead of print]

Wang D, Hu B, Hu C, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. *JAMA* 2020. doi: 10.1001/jama.2020.1585. [Epub ahead of print]

Wang Y, Zhang D, Du G, et al. Remdesivir in adults with severe COVID-19: a randomised, double-blind, placebo-controlled, multicentre trial. *Lancet* 2020. doi: 10.1016/S0140-6736(20)31022-9. In press. [Epub ahead of print]

Wu C, Chen X, Cai Y, et al. Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China. *JAMA Intern Med* 2020. doi: 10.1001/jamainternmed.2020.0994. [Epub ahead of print]

Wu P, Duan F, Luo C, et al. Characteristics of Ocular Findings of Patients With Coronavirus Disease 2019 (COVID-19) in Hubei Province, China. *JAMA Ophthalmol* 2020. doi: 10.1001/jamaophthalmol.2020.1291. [Epub ahead of print]

Xie J, Tong Z, Guan X, Du B, Qiu H. Clinical Characteristics of Patients Who Died of Coronavirus Disease 2019 in China. *JAMA Netw Open* 2020;3:e205619. doi: 10.1001/jamanetworkopen.2020.5619.

Young BE, Ong SWX, Kalimuddin S, et al; Singapore 2019 Novel Coronavirus Outbreak Research Team. Epidemiologic Features and Clinical Course of Patients Infected With SARS-CoV-2 in Singapore. *JAMA* 2020. doi: 10.1001/jama.2020.3204. [Epub ahead of print]

Zhang J, Litvinova M, Wang W, et al. Evolving epidemiology and transmission dynamics of coronavirus disease 2019 outside Hubei province, China: a descriptive and modelling study. *Lancet Infect Dis* 2020. doi: 10.1016/S1473-3099(20)30230-9. [Epub ahead of print]

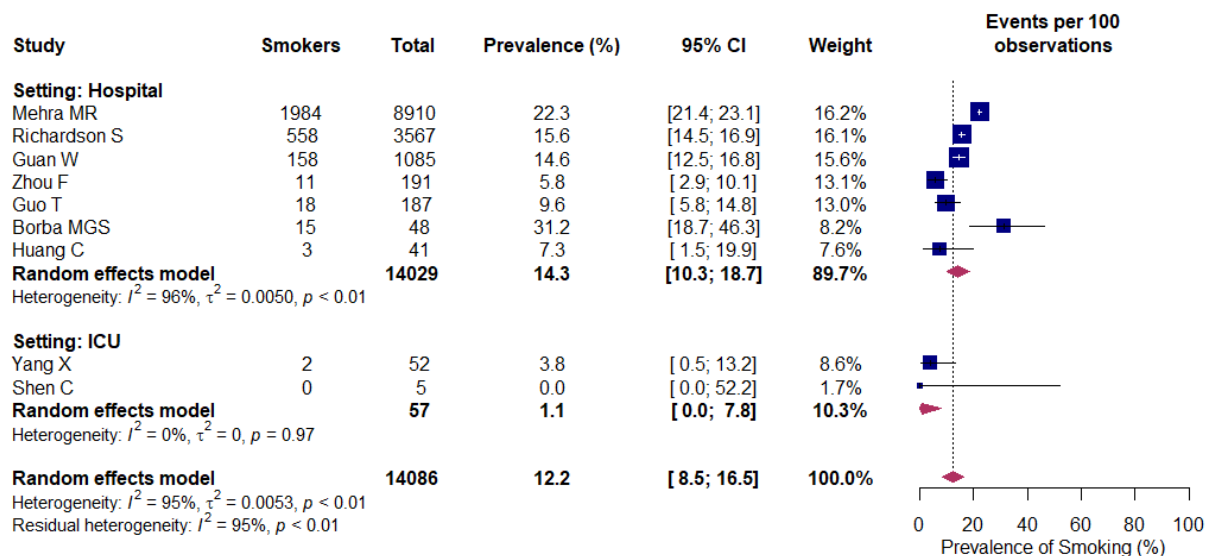
Supplementary Methods for Meta-Analysis and Meta-Regression

For each study, the prevalence of smoking was recorded and standard errors for the study-specific estimates were determined from the point estimate and the appropriate denominators, assuming a binominal distribution. A random-effect model was used to calculate the pooled prevalence and results are reported with 95% confidence interval, after stabilizing the variance of individual studies using the Freeman-Tukey double arcsine transformation.¹ Heterogeneity of studies was evaluated by the χ^2 test on Cochrane's Q statistic, quantified by I^2 values. In order to prevent misleading conclusions for the Freeman-Tukey double arcsine transformation, a sensitivity analysis using a logit transformation was used.² Mortality among the groups was compared in a random-effect meta-analysis using restricted maximum likelihood method. Only studies reporting mortality data on the basis of smoking status were included in the mortality analysis.

To check the stability of the findings and potential outliers influencing the results, a set of leave-one-out diagnostic tests were used. As sensitivity analysis, a random-effect meta-regression using restricted maximum likelihood method was used to assess the impact of the prevalence of smoking in the population on the prevalence of smokers in the studies.

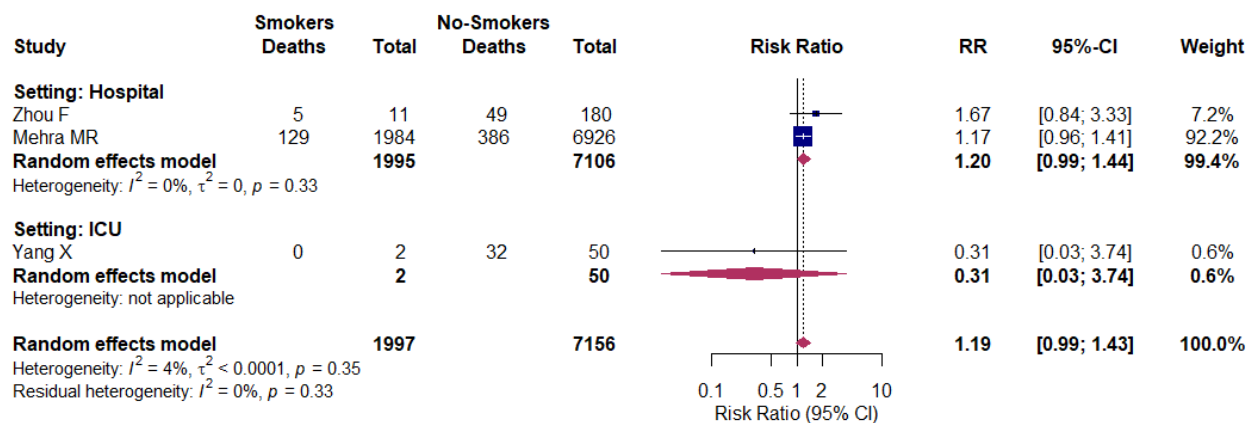
All analyses were performed in R v.3.6.3 using the package *meta*.

Supplementary Figure 1. Prevalence of smoking in the included studies. In this analysis, active and former smokers were grouped together where possible.



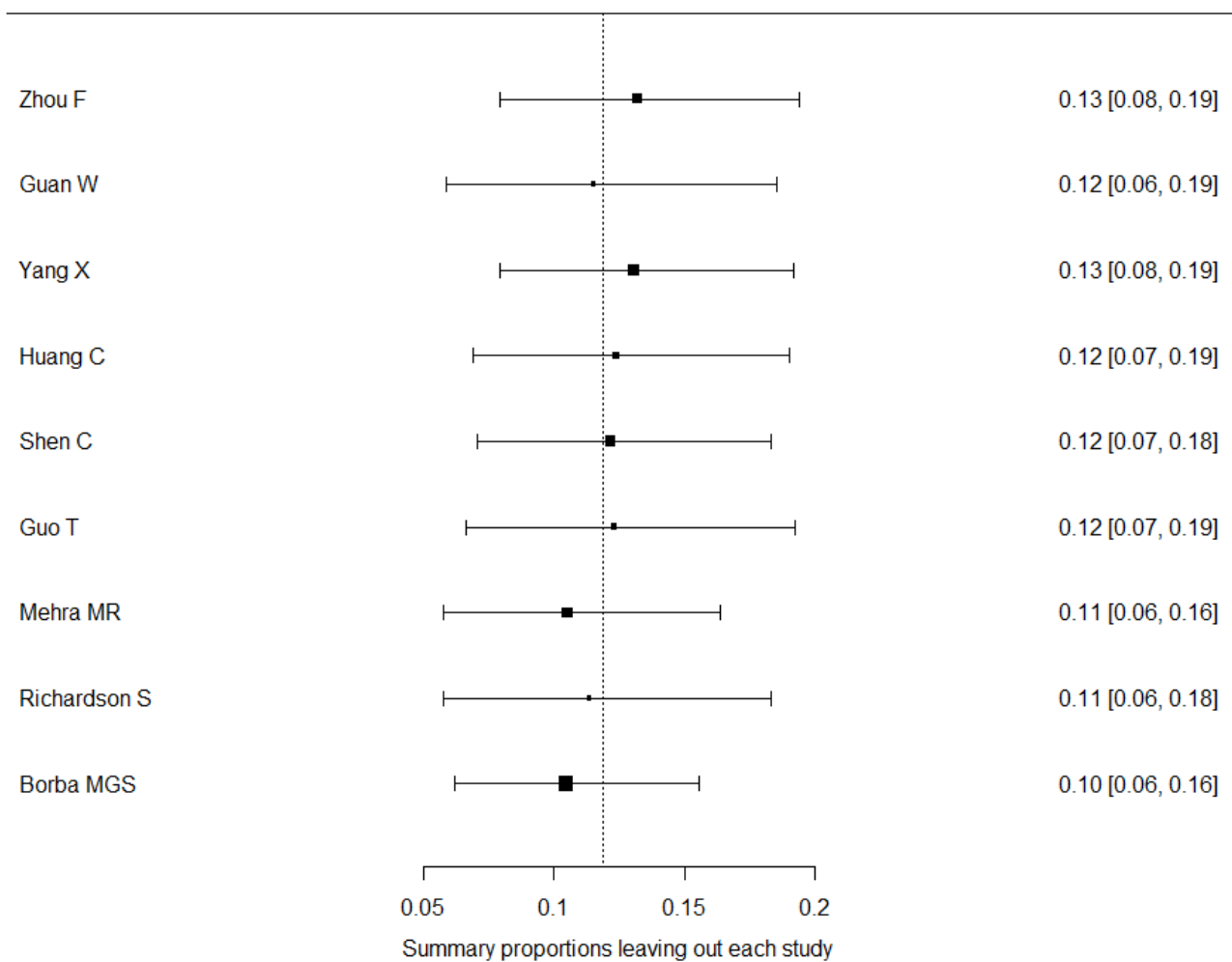
CI: confidence interval; ICU: intensive care unit

Supplementary Figure 2. Effect of active smoking on mortality in the studies included in the meta-analysis. Only studies reporting mortality data on the basis of smoking status were included in this analysis.



CI: confidence interval; ICU: intensive care unit; RR: risk ratio

Supplementary Figure 3. Results of the leave-one-out analysis



Supplementary References

1. Barendregt JJ , Doi SA , Lee YY , et al . Meta-analysis of prevalence. *J Epidemiol Community Health* 2013;67:974–8
2. Schwarzer G, Chemaitelly H, Abu-Raddad LJ, Rücker G. Seriously misleading results using inverse of Freeman-Tukey double arcsine transformation in meta-analysis of single proportions. *Res Synth Methods* 2019;10:476-483. doi: 10.1002/jrsm.1348.