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COVID-19 and Tobacco



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Caused by a novel coronavirus (SARS-CoV-2), COVID-19 is an infectious disease that was first identified by the World Health Organization in late December 2019. There is significant range on the COVID-19 disease spectrum—from completely asymptomatic or mild infection to advanced disease progression that results in death. Much remains to be determined about the disease—and movement along its various stages—but there is strong evidence that certain populations are particularly vulnerable to adverse consequences and that certain underlying medical conditions exacerbate it. Smokers and smoking fall into these respective categories.

This factsheet provides the most up-to-date information on what is presently known about smoking and COVID-19 during various inflection points; clarifies misinformation; and summarizes biochemical research on tobacco, ACE2 receptors, and SARS-CoV-2.

Smoking and Infection with SARS-CoV-2

In May 2020, the World Health Organization noted that the act of bringing fingers to the lips could increase “the possibility of transmission of viruses from hand to mouth.”¹ To date, however, there are limited studies examining the relationship between smoking and SARS-CoV-2 infection. Two are notable. A non-peer reviewed case-control study from Israel² found that both current and former smokers were at significantly lower infection risk than non-smokers. A study from Kuwait³ —it is limited in failing to clearly define smoking—also found that smokers were at lower infection risk. Clarifying the relationship between smoking and infection with SARS-CoV-2 would require testing large samples of the population to locate asymptomatic cases as well as mild ones that do not require hospitalization.

There is presently insufficient information to draw any conclusions about smoking risk and infection.

Smoking and Emergence of COVID-19 symptoms that require an outpatient hospital visit or hospitalization of 24+ hours

Several studies—from the US⁴, the UK⁵, Denmark⁶ and Mexico (none were peer reviewed)^{7 8 9 10 11 12}—found that smokers are less likely to develop significant COVID-19 symptoms. Because all four include positive and negative patients and compare the two groups for smoking risk, they support the hypothesis that smoking is less prevalent among confirmed COVID-19 cases. At the same time, however, the studies demonstrate two significant limitations—major misclassification of smokers and reliance on hospital records to determine smoking status—that might skew the findings in significant ways.

Additional research is critical to understanding the relationship between smoking and hospitalization (in or outpatient) from COVID-19.

¹ <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/question-and-answers-hub/q-a-detail/coronavirus-disease-covid-19-tobacco>

² Israel, A.F., Elan et al. *Smoking and the Risk of COVID-19 in a large observational study.* MedRxiv, 2020.

³ Almazzeedi, S., et al., *Characteristics, risk factors and outcomes among the first consecutive 1096 patients diagnosed with COVID-19 in Kuwait.* EClinicalMedicine, 2020; p. 100448.

⁴ Rentsch, C.K.-K., Farah; et al., *Covid-19 Testing, Hospital Admission, and Intensive Care Among 2,026,227.* MedRxiv, 2020.

⁵ De Lusignan, S., et al., *Risk factors for SARS-CoV-2 among patients in the Oxford Royal College of General Practitioners Research and Surveillance Centre primary care network: a cross-sectional study.* The Lancet Infectious Diseases, 2020.

⁶ Eugen-Olsen, J.A., Izzet; et al., *Low levels of the prognostic biomarker suPAR are predictive of mild outcome in patients with symptoms of COVID-19 - a prospective cohort study.* MedRxiv, 2020.

⁷ Gutierrez, J.P.M., Stefano M., *Non-communicable diseases and inequalities increase risk of death among COVID-19 patients in Mexico.* MedRxiv, 2020.

⁸ Giannouchos, T.V.S., Roberto A.; et al., *Characteristics and risk factors for COVID-19 diagnosis and adverse outcomes in Mexico: an analysis of 89,756 laboratory-confirmed COVID-19 cases.* MedRxiv, 2020.

⁹ Carrillo-Vega, M.F.S.-E., Guillermo; et al., *Early estimation of the risk factors for hospitalisation and mortality by COVID-19 in México.* MedRxiv, 2020.

¹⁰ Solis, P.C., Hiram, *COVID-19 Fatality and Comorbidity Risk Factors among Diagnosed Patients in Mexico.* MedRxiv, 2020.

¹¹ Berumen, J.S., Max; et al., *Risk of infection and hospitalization by Covid-19 in Mexico: A case-control study.* MedRxiv, 2020.

¹² Petrilli, C.M.J., Simon A.; et al., *Factors associated with hospitalization and critical illness*

Smoking and Advanced COVID-19 Disease Progression: ICU Admission, Mechanical Ventilation and Mortality

There is sufficient evidence to conclude that the world's 1.3 billion smokers—eighty percent of whom live in low- and middle- income countries—are at increased risk of advanced COVID-19 disease progression that results in grave consequences.

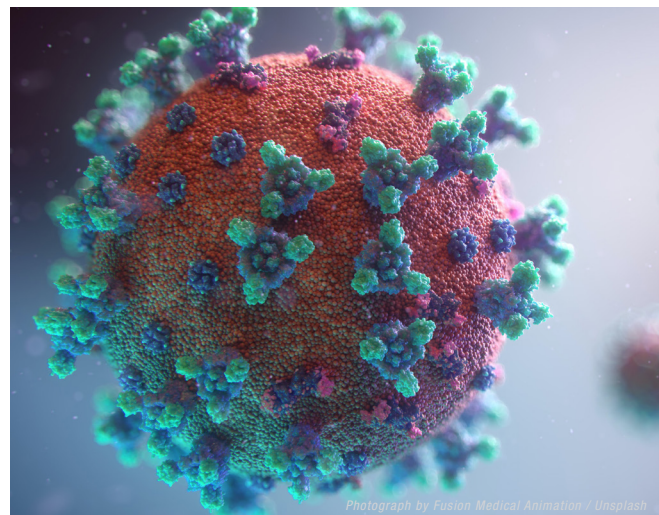
Data regarding advanced disease progression first emerged in February 2020, with a seminal piece of research¹³ providing the first indication that smokers were disproportionately affected by COVID-19. Study authors noted that when compared to non-smokers, infected smokers were 2.4 times more likely to be admitted to an intensive care unit, need mechanical ventilation, or die. Several weeks later, a second study out of China¹⁴ found that while smokers accounted for just 8 percent of total cases, they comprised 12 percent of severe cases.

A subsequent systematic review¹⁵ and six meta-analyses also determined that smoking (past or present) was associated with elevated risk of severe COVID-19 outcomes.^{16 17 18 19 20} And, the U.S. Centers for Disease Control cautions that smoking—present or past—predisposes adults of all ages to “increased risk of severe illness from the virus that causes COVID-19.”²¹

Smokers are at increased risk of the worst outcomes associated with COVID-19.



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Nicotine and COVID-19

In April 2020, three studies^{22 23 24} garnered significant attention for bold claims that nicotine use and/or smoking might have a protective effect against COVID-19. Collectively referred to as the “French studies,” they occupied headlines, confused people, and put tobacco control advocates on the defensive. As desperate people engaged in panic-induced purchase of nicotine replacement therapies, the French government temporarily limited product sales.²⁵ As noted by the World Health Organization²⁶ and STOP²⁷ these studies are fraught with problems.

Nicotine should not be consumed in the hopes that it will prevent COVID-19.

Biochemistry, Smoking and COVID-19

Biochemists are in general agreement that SARS-CoV-2, the virus that causes COVID-19, enters human cells through the ACE2 receptor. They are, however, divided on whether smoking and nicotine upregulates or downregulates ACE2 activity, which could affect the chance of SARS-CoV-2 entering cells. Upregulation might, as certain researchers have proposed,²⁸ create a cytokine storm, which would exacerbate COVID-19 outcomes.

The relationship between smoking and ACE2 receptors is unclear; additional research is critical.

¹³ Guan, et al., Clinical Characteristics of Coronavirus Disease 2019 in China. *New England Journal of Medicine*, 2020. 382(18): p. 1708-1720.

¹⁴ Shi, Y., Yu, X., Zhao, H. et al. Host susceptibility to severe COVID-19 and establishment of a host risk score: findings of 487 cases outside Wuhan. *Crit Care* 24, 108 (2020). <https://doi.org/10.1186/s13054-020-2833-7>

¹⁵ Yavdas, C.I.N., Katerina. COVID-19 and Smoking: A systematic review of the evidence. *Tobacco Induced Diseases*, 2020. 18 (20).

¹⁶ Alqahitani, J.S., et al., Prevalence, Severity and Mortality associated with COPD and Smoking in patients with COVID-19: A Rapid Systematic Review and Meta-Analysis. *PLOS ONE*, 2020. 15(5): p. e0233147.

¹⁷ Del Sole, F., et al., Features of severe COVID-19: a systematic review and meta-analysis. *European Journal of Clinical Investigation*, 2020.

¹⁸ Reddy, R.K., et al., The effect of smoking on COVID-19 severity: A systematic review and meta-analysis. *Journal of Medical Virology*, 2020.

¹⁹ Zhao, Q., et al., The impact of COPD and smoking history on the severity of COVID-19: A systemic review and meta-analysis. *Journal of Medical Virology*, 2020.

²⁰ Zheng, Z., et al., Risk factors of critical & mortal COVID-19 cases: A systematic literature review and meta-analysis. *Journal of Infection*, 2020. 81(2): p. e16-e25.

²¹ <https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html>

²² Fontanet, A.T., Laura; et al., Cluster of COVID-19 in northern France: A retrospective closed cohort study. *MedRxiv*, 2020.

²³ Miyara, M., et al., Low incidence of daily active tobacco smoking in patients with symptomatic COVID-19. *Qeios*, 2020.

²⁴ Changeux, J.-P., et al., A nicotinic hypothesis for Covid-19 with preventive and therapeutic implications. *Qeios*, 2020.

²⁵ <https://www.bbc.com/news/world-europe-52415793>

²⁶ <https://www.who.int/news-room/detail/11-05-2020-who-statement-tobacco-use-and-covid-19#XrJGqqsEvs.email>

²⁷ <https://exposetobacco.org/news/flawed-covid19-studies/>

²⁸ Kashyap, V.K., et al., Smoking and COVID-19: Adding Fuel to the Flame. *International Journal of Molecular Sciences*, 2020. 21(18): p. 6581.