



Smoking and Comorbidities in COVID-19: A Systematic Review

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Abstract

COVID-19 is highly contagious, causing pneumonia, respiratory failure, death, and becoming a pandemic. Patients with severe infections must be treated in the Intensive Care Unit (ICU) with a ventilator. Ventilator facilities in the ICU are limited; it must take precautions by knowing the characteristics of patients at high risk of severe disease in COVID-19, one of which was smoking or comorbidity. The purpose of this study was to assess the risk of comorbidity and smoking in COVID-19. This study used systematic review by searching for articles from the ScienceDirect and Medline databases with journals published on January 1, 2019 - March 31, 2020. The results of the study showed that there were 12 relevant articles full text in English and were analysed. The conclusion was that patients with COVID-19 who were smoking or had comorbidities were more susceptible to COVID-19 infection, more severe illness, and causing death.

INTRODUCTION

The coronavirus was a virus discovered by Tyrell and Bynoe in 1996. This virus enveloped in a large single-stranded positive RNA in the shape of a spherical virion like a ball with a core projection and a surface that resembled a solar corona (Latin: corona = crown) that could infect humans and various kinds of animals (Velavan & Meyer, 2020). Coronavirus causes respiratory disease in the form of pneumonia, which can result in death and is highly contagious (Panahi, et al., 2020). The World Health Organization on March 11, 2020, stated that there was a pandemic from a new strand of the coronavirus family associated with the severe acute respiratory syndrome (SARS-CoV 2) (Rio & Malani, 2020). The virus was first discovered in December

2019 in Wuhan City, Hubei Province, China, which allegedly originated from the seafood market, where the carrier of this new type of coronavirus originated from chrysanthemum head bat and was officially named coronavirus 2019 (COVID-19) (Zhu et al., 2020).

Every day, the number of people infected with COVID-19 continues to increase. Since it first appeared in China (Wuhan) until March 19, 2020, there were 234,073 people infected with COVID-19 and 9,840 people died (Panahi et al., 2020), and this virus has spread to 60 countries, including Indonesia (Adalja et al., 2020). At present, the COVID-19 virus infection is increasingly widespread, and the number of people infected is increasing so that the number of deaths is higher, which causes health care

problems, global economic losses, and becomes a pandemic (Basile et al., 2020) a disease caused by a novel coronavirus, is a major global human threat that has turned into a pandemic. This novel coronavirus has specifically high morbidity in the elderly and in comorbid populations. Uraemic patients on dialysis combine an intrinsic fragility and a very frequent burden of comorbidities with a specific setting in which many patients are repeatedly treated in the same area (haemodialysis centres. In Indonesia, as of March 31, 2020, 1,528 people were infected with COVID-19, and 136 people died (8%), which is the highest percentage of mortality in the world (Gugus Tugas Percepatan Penanganan COVID-19, 2020).

Huang et al. (2020) reported, 13 patients (32%) from 41 COVID-19 cases had comorbidities such as cardiovascular disease, diabetes, hypertension, and obstructive pulmonary disease (Huang et al., 2020). Another study found that from 138 COVID-19 cases, 64 patients (46.4%) had comorbidities in which patients treated in intensive care units (ICU) had a higher number (72.2%) than those not treated in ICU (37.3%). This study showed that comorbidities can be an adverse risk factor and cause

death (D. Wang et al., 2020).

Smoking is assumed to be a prognosis of the adverse disease, harms lung health, and causes various diseases such as cancer and respiratory diseases (Tonnesen et al., 2019). Smoking also damages immunity and its effectiveness in killing bacteria or viruses so that it can prevent infection. This study shows that smokers are more susceptible to infectious disease infections (Z. Zhou et al., 2016).

The available ICU facilities are not proportional to the increasing number of patients; it is necessary to know the characteristics of patients at high risk of severe disease in COVID-19. Smoking and comorbidities are the basis for reducing and preventing the risk of death in patients with COVID-19 infection.

This study aimed to get more reliable evidence through a systematic review to assess the risk of comorbidities and smoking in causing death in COVID-19 cases. The result is expected to provide overview guidance to perform responses and strategies to develop prioritizing procedure of ventilator utilization to prevent deaths in COVID-19 cases.

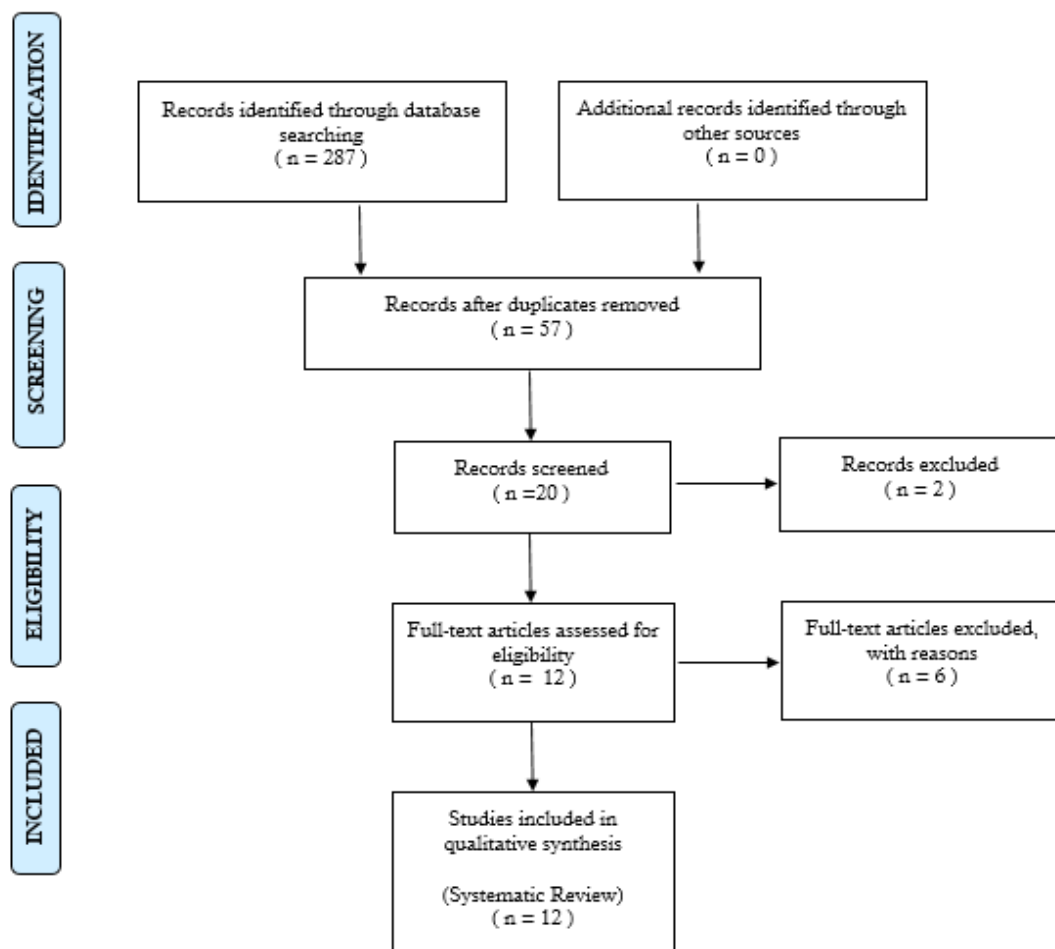


Figure 1. Systematic Review Steps

METHODS

The steps of this systematic review were carried out based on the PRISMA protocol (Moher et al., 2015). It can be seen in Figure 1. The articles used were articles in the ScienceDirect and Medline databases published on January 1, 2019 - March 31, 2020. Searching used the keywords of "COVID-19" AND "comorbidities" and "COVID-19" AND "smoking" by checking each article to prevent any discrepancies with the specified topic. Management of study data and duplicate data used Mendeley v1.19.4 and qualitative synthesis used NVIVO 12 Plus software. The inclusion criteria in this study, namely the article must explain the characteristics and prevalence of the disease of patients with COVID-19, and the exclusion criteria, namely the case of COVID-19 in animals with SARS (Severe Acute Respiratory Syndrome) and Middle East Respiratory Syndrome (MERS) that are not relevant to COVID-19.

RESULT AND DISCUSSION

Article search results obtained 287 sources (68 from PubMed and 219 from ScienceDirect). The articles obtained were selected which relevant according to the research topic and deleted duplicates. There were 12 related articles in full text in English, and it was analyzed. It can see in Table 1 for the results of the analysis.

COVID-19 is a virus that infects the respiratory system, with three classifications of signs and symptoms such as mild, severe, and critical (Driggin et al., 2020; Jordan et al., 2020). Sign and symptoms begin with the same mild symptoms like flu, fever, fatigue, and dry cough (Huang et al., 2020), while sign and symptoms of severe infections such as shortness of breath, diarrhea, pneumonia and high fever ($>39^{\circ}\text{C}$) (Giwa et al., 2020). The patient indicates severe show if they have pneumonia and dyspnea (W.J. Guan et al., 2020). The patient means critical, if they have respiratory failure, septic shock, and multi-organ failure, and it can cause death (Jordan et al., 2020).

Most people who are infected with COVID-19 in the elderly, whereas in children, it is infrequent, and the number of cases is fewer (Lai et al., 2020). The most infected patients in China are men because many men smoke and are older people (Zhang et al., 2020). Infected with COVID-19 signs and symptoms will appear depending on classification, such as mild cases: about two weeks, severe or critical illness: three to six weeks, time from onset to development of severe disease in one week. (World Health Organization (WHO), 2020). COVID-19 is estimated to be the incubation period for COVID-19 between 2 and

14 days (Lauer et al., 2020).

Factors causing COVID-19 patients to experience severe and critical symptoms are smoking and comorbidity (W. Guan et al., 2020; Jordan et al., 2020; Vardavas & Nikitara, 2020; Zhang et al., 2020), even COVID-19 patients who smoke can have chemicals in cigarettes contain hydrogen cyanide (HCN). If it enters the respiratory system, it becomes toxic to the ciliary cells lining the respiratory tract to function as the body's defense system to prevent the entry of foreign objects, including viruses and bacteria into the lungs so that COVID-19 can quickly enter the lung cells and damage the cells. Hence, the patient becomes short of breath and must be using a ventilator (Onor et al., 2017).

COVID-19 patients in China who experience severe symptoms are treated in the Intensive Care Unit (ICU) to cause death (W. Guan et al., 2020). COVID-19 patients who are smokers in critical rooms experience Pneumonia and Severe Acute Respiratory Distress Syndrome (ARDS) so that they must use a ventilator in the Intensive Care Unit (ICU) that can even cause death (W. Liu, et al., 2020). Another study found that the virus receptor of angiotensin-converting enzyme II (ACE2) is the medium for SARS-CoV 2 entry into the body's cells, and ACE2 expression is significantly higher in smokers than in nonsmokers. Severe and critical cases of COVID-19 are more likely to be in smokers (Du et al., 2020). A study on the effect of active or passive smokers, the number of cigarettes smoked every day, and the period of being a smoker is still unclear. No studies have been performed accurately on COVID-19 infection.

Patients with COVID-19 who experience severe disease symptoms and cause death not only occur in smokers but also in patients with comorbidities (W. Guan et al., 2020). History of Chronic diseases that often occur in COVID-19 are hypertension, cerebrovascular disease, hepatitis B infection chronic obstructive pulmonary disease, diabetes, coronary heart disease, cancer, chronic renal disease, and immunodeficiency (Huang et al., 2020; K Liu, et al., 2020). Comorbidities such as cardiovascular and endocrine are the most common causes of COVID-19 patients in China (W. Guan et al., 2020).

People who have comorbidities are more susceptible to COVID-19. If already infected with COVID-19, chronic disease will get worse so that more patients are treated in the ICU (K Liu et al., 2020b; Z. Wang et al., 2020)Journal of Infection (2020, especially older people with a history of chronic illness with a high risk of respiratory failure and has a worse prognosis (W. Guan et al., 2020) and can lead to death (Yang et al., 2020)2019, in Wuhan, China. Information about critically ill patients with

Table 1. The results of the studies on smoking and comorbidities

No	Author	Location	Population	Study Design	Result
1	Du et al., 2020	Wuhan, China	398 patients COVID-19	Analyzing transcriptomes and proteomes derived from databases and genetic analysis on the ACE2 pathway. The P-value is calculated from the t-test.	The receptor virus of angiotensin-converting enzyme II (ACE 2) mediates the entry of SARS-CoV 2 into the body's cells, and ACE2 expression is significantly higher in smokers than in nonsmokers. Severe cases of COVID-19 are more likely to have a history of smoking than non-severe COVID-19.
2	W Liu et al., 2020	Three tertiary hospitals in Wuhan	78 Patients COVID-19 with pneumonia and hospitalized for over two weeks in December 30, 2019, and January 15, 2020	Retrospective	Smoking is one of the factors that cause the development of pneumonia in COVID-19 patients.
3	W. Guan et al., 2020	Wuhan JinYinTan Hospital, China	1590 patients with COVID-19 in December 11th, 2019 and January 31st, 2020	Retrospective case study	Among the COVID-19 cases confirmed in the laboratory, patients with smoking produced worse clinical outcomes than those who did not.
4	F. Zhou et al., 2020	Jinyintan and Wuhan Pulmonary Hospital, China	191 patients All adult inpatients (aged ≥ 18 years) with COVID-19 on Jan 31, 2020	The retrospective multicenter cohort study	People who smoke increase the risk of death in COVID-19 patients.
5	Zhang et al., 2020	No. 7 Hospital of Wuhan, China	140 patients clinically COVID-19 with Pneumonia in 16 January to 3 February 2020	Retrospective	People who smoke aggravate COVID-19.

6	W.J. Guan et al., 2020	552 hospitals in 30 provinces, autonomous regions, and municipalities in mainland China	1099 patients. Patients with laboratory-confirmed COVID-19 in 29 January 2020	Retrospective	People who were smoking the higher risk of developing more severe COVID-19.
7	W.J. Guan et al., 2020	552 hospitals in 30 provinces, China	1099 patients. Patients with COVID-19 on 29 January 2020	Retrospective	Patients with COVID-19 and have a history of previous chronic diseases (chronic obstructive, lung disease, diabetes, Hypertension, Coronary heart disease, cerebrovascular disease, Hepatitis B infection, cancer, Chronic kidney disease, and immune deficiency). Making the disease worse and entering more ICUs.
8	Huang et al., 2020	Hospital in Wuhan	41 patients with COVID-19 on Dec 16, 2019, to Jan 2, 2020	Retrospective	COVID-19 patients are more susceptible to infections in patients who have a history of previous chronic diseases (Diabetes, Hypertension, Cardiovascular Disease, and Chronic obstructive).
9	K. Liu, et al., 2020	Hainan Provincial People's Hospital	56 patients had enrolled 18 elderly patients (32.14%), and 38 young and middle-aged patients (67.86%) with COVID-19 in January 15, 2020, to February 18, 2020	Retrospective study	Older people who have a history of chronic diseases are more susceptible to COVID-19 infection.

10	K Liu, et al., 2020	Nine tertiary hospitals in Hubei province	Clinical data from 137 2019-nCoV-infected patients in December 30, 2019, to January 24, 2020	Retrospectively	Older people with a history of chronic illness before being infected with COVID-19 are at high risk of experiencing respiratory failure and have a worse prognosis.
11	Y. Liu et al., 2020	Shenzhen Third People's Hospital in Shenzhen, China	12 COVID-19 infected patients.	Retrospectively	People who have a history of chronic diseases (chronic heart disease, renal diseases, and diabetes) are more prone to be infected with COVID-19.
12	Wang et al., 2020	Zhongnan Hospital of Wuhan University in Wuhan, China	The 138 consecutive hospitalized patients with confirmed COVID-19 in January 1 to January 28, 2020	Retrospective, single-center case series	People who have a history of chronic diseases (chronic heart disease, renal diseases, and diabetes) are more prone to be infected with COVID-19.
13	Yang et al., 2020	Wuhan Jin Yin-tan hospital Wuhan, China	52 critically ill adult patients with COVID-19 and pneumonia in an intensive care unit (ICU) in late December 2019, and Jan 26, 2020	Single-centered, retrospective, observational study	Patients treated in ICU and having a history of chronic illness before have a higher risk of dying.
14	Zhang et al., 2020	No. 7 Hospital of Wuhan, China	140 patients clinically COVID-19 with Pneumonia in 16 January to 3 February 2020	Retrospective	COVID-19 patients who have a history of chronic illness previously worsen the patient's disease condition.
15	F. Zhou et al., 2020	Jinyintan Hospital and Wuhan Pulmonary Hospital, Wuhan, China	191 patients All adult inpatients (aged ≥ 18 years) with COVID-19 on Jan 31, 2020	The retrospective multicenter cohort study	People who have a history of chronic disease before being infected with COVID-19 increase the risk of death in patients.

16	Guan et al., 2020	Wuhan JinYinTan Hospital	1590 patients with CO-VID-19 in December 11th, 2019 and January 31st, 2020	Retrospective case study	Older people with a history of chronic disease before being infected with COVID-19 have a worse prognosis.
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SARS-CoV-2 infection is scarce. We aimed to describe the clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia. Methods: In this single-centered, retrospective, observational study, we enrolled 52 critically ill adult patients with SARS-CoV-2 pneumonia who were admitted to the intensive care unit (ICU). Comorbidity assessment is an essential component in determining the prognosis of several diseases, especially pneumonia (W. Liu, et al., 2020) so that a comprehensive assessment of comorbidities can build risk classification of COVID-19 patients in the hospital (W. Guan et al., 2020). There are no studies on the effects of long periods of chronic disease with COVID-19 infection, drugs or COVID-19 vaccine do not yet exist, so it must prevent transmission of COVID-19 in patients who have a history of comorbidity.

COVID-19 is very contagious. Prevention of transmission of COVID-19 such as self-isolation or quarantine, using personal protective equipment such as masks, washing hands with soap or disinfectants, keeping social distance; Preparation of a health system for seriously ill patients who need isolation, oxygen, and ventilators; Clean and disinfect school buildings, classrooms and environmental sanitation, and especially surface areas that are often touched by many people, eat lots of highly nutritious foods or multivitamins, and exercise (Adhikari et al., 2020; Tingbo, 2020; World Health Organization (WHO), 2020).

CONCLUSION

This study showed that having condition of smoking or comorbidities on COVID-19 patients caused critical illness even death. This condition caused them to be cared in the ICU. Also, smoking people were more susceptible to COVID-19 infection, especially in older age. Children were slightly infected with COVID-19 with severe symptoms.

REFERENCES

- Adalja, A.A., Toner, E., & Inglesby, T.V. 2020. Priorities for the US Health Community Responding to COVID-19. *JAMA - Journal of the American Medical Association*, 323(14):1343-1344. DOI:10.1001/jama.2020.3413
- Adhikari, S. P., Meng, S., Wu, Y.J., Mao, Y.P., Ye, R.X., Wang, Q.Z., & Zhou, H. 2020. Epidemiology, causes, clinical manifestation and diagnosis, prevention and control of coronavirus disease (COVID-19) during the early outbreak period: a scoping review. *Infectious Diseases of Poverty*, 9: 29. DOI: 10.1186/s40249-020-00646-x
- Basile, C., Combe, C., Pizzarelli, F., Covic, A., Davenport, A., Kanbay, M., & Mitra, S. 2020. Recommendations for the prevention, mitigation and containment of the emerging SARS-CoV-2 (COVID-19) pandemic in haemodialysis centres. *Nephrology Dialysis Transplantation*, 35(5): 737-741. DOI: 10.1093/ndt/gfaa069
- Driggin, E., Madhavan, M.V, Bikdeli, B., Chuich, T., Laracy, J., Bondi-Zoccai, G., & Parikh, S.A. 2020. Cardiovascular Considerations for Patients, Health Care Workers, and Health Systems During the Coronavirus Disease 2019 (COVID-19) Pandemic. *Journal of the American College of Cardiology*, 75(18). DOI: 10.1016/j.jacc.2020.03.031
- Du, M., Cai, G., Chen, F., Christiani, D. C., Zhang, Z., & Wang, M. 2020. Multi-omics Evaluation of Gastrointestinal and Other Clinical Characteristics of SARS-CoV-2 and COVID-19. *Gastroenterology*, 158(8): 2298-2301. e7. DOI: 10.1053/j.gastro.2020.03.045
- Giwa, A., Desai, A., & Duca, A. 2020. Novel coronavirus COVID-19: an overview for emergency clinicians. *Emergency Medicine Practice*, 22(2), 1–21. Retrieved from www.ebmedicine.net/COVID-19
- Guan, W.J., Ni, Z.Y., Hu, Y., Liang, W.H., Ou, C.Q., & He, J.X. 2020. Clinical Characteristics of Coronavirus Disease 2019 in China. *The New England Journal of Medicine*, 382:1708-1720. DOI: 10.1056/NEJMoa2002032
- Guan, W., Liang, W., Zhao, Y., Liang, H., Chen, Z., Li, Y., & Liu, X. 2020. Comorbidity and its impact on 1590 patients with Covid-19 in China : A Nationwide Analysis. *Eur Respir J*, 56(1). DOI:10.1183/13993003.00547-2020
- Gugus Tugas Percepatan Penanganan COVID-19. 2020, March 31. Covid-19 di Indonesia. BNPB. Retrieved from <https://www.covid19.>

- go.id/
- Huang, C., Wang, Y., Li, X., Ren, L., Zhao, J., Hu, Y., & Gu, X. 2020. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *The Lancet*, 395(10223), 497–506.
- Jordan, R.E., Adab, P., & Cheng, K.K. 2020. Covid-19 : risk factors for severe disease and death. *BMJ Open*, 368:m1198. DOI:10.1136/bmj.m1198
- Lai, C.C., Liu, Y. H., Wang, C.Y., Wang, Y.H., Hsueh, S.C., Yen, M.Y., & Hsueh, P.R. 2020. Asymptomatic carrier state, acute respiratory disease, and pneumonia due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2): Facts and myths. *Journal of Microbiology, Immunology and Infection*, 53(3): 404–412. DOI: 10.1016/j.jmii.2020.02.012
- Lauer, S.A., Grantz, K.H., Bi, Q., Jones, F.K., Zheng, Q., Meredith, H. R., & Lessler, J. 2020. The incubation period of coronavirus disease 2019 (COVID-19) from publicly reported confirmed cases: estimation and application. *Annals of Internal Medicine*, 172(9): 577–582.
- Liu, K., Chen, Y., Lin, R., & Han, K. 2020a. Clinical feature of COVID-19 in elderly patients: a comparison with young and middle-aged patients. *Journal of Infection*, 80(6): E14–E18. DOI: 10.1016/j.jinf.2020.03.005
- Liu, K., Fang, Y.Y., Deng, Y., Liu, W., Wang, M.F., Ma, J.P., & Liu, H.G. 2020b. Clinical characteristics of novel coronavirus cases in tertiary hospitals in Hubei Province. *Chinese Medical Journal*, 133(9): 1025–1031. DOI: 10.1097/cm9.0000000000000744
- Liu, W., Tao, Z.W., Lei, W., Ming-Li, Y., Kui, L., Ling, Z., & Yi, H. 2020. Analysis of factors associated with disease outcomes in hospitalized patients with 2019 novel coronavirus disease. *Chinese Medical Journal*, 133(9): 1032–1038. DOI: 10.1097/cm9.0000000000000775
- Liu, Y., Yang, Y., Zhang, C., Huang, F., Wang, F., Yuan, J., & Liu, L. (2020). Clinical and biochemical indexes from 2019-nCoV infected patients linked to viral loads and lung injury. *Science China Life Sciences*, 63: 364–374. DOI: 10.1007/s11427-020-1643-8
- Moher, D., Shamseer, L., Clarke, M., Ghersi, D., Liberati, A., & Petticrew, M. 2015. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Systematic Reviews*, 4: 1(2015). DOI: 10.1186/2046-4053-4-1
- Onor, I. O., Stirling, D. L., Williams, S. R., Bediako, D., Borghol, A., Harris, M. B., & Sarpong, D. F. 2017. Clinical effects of cigarette smoking: epidemiologic impact and review of pharmacotherapy options. *International Journal of Environmental Research and Public Health*, 14(10), 1147.
- Panahi, L., Amiri, M., & Pouy, S. 2020. Risks of Novel Coronavirus Disease (COVID-19) in Pregnancy; a Narrative Review. *Archives of Academic Emergency Medicine*, 8(1): 1–5.
- Rio, C. del, & Malani, P. N. 2020. COVID-19—New Insights on a Rapidly Changing Epidemic. *JAMA - Journal of the American Medical Association*, 323(14): 1339–1340. DOI: 10.1001/jama.2020.3072
- Tingbo, L. 2020. *Handbook of COVID-19 Prevention and Treatment*. China: The First Zhejiang University School of Medicine.
- Tonnesen, P., Marott, J.L., Nordestgaard, B., Bojesen, S.E., & Lange, P. 2019. Secular trends in smoking in relation to prevalent and incident smoking-related disease: A prospective populationbased study. *Tobacco Induced Diseases*, 17(October): 72. DOI: 10.18332/tid/112459
- Vardavas, C.I., & Nikitara, K. 2020. COVID-19 and smoking: A systematic review of the evidence. *Tobacco Induced Diseases*, 18(March): 20. DOI: 10.18332/tid/119324
- Velavan, T.P., & Meyer, C.G. 2020. The COVID-19 epidemic. *Tropical Medicine and International Health*, 25(3), 278–280. DOI:10.1111/tmi.13383
- Wang, D., Hu, B., Hu, C., Zhu, F., Liu, X., Zhang, J., & Peng, Z. 2020. Clinical Characteristics of 138 Hospitalized Patients with 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. *JAMA - Journal of the American Medical Association*, 323(11), 1061–1069. DOI: 10.1001/jama.2020.1585
- Wang, Z., Yang, B., Li, Q., Wen, L., & Zhang, R. 2020. Clinical Features of 69 Cases with Coronavirus Disease 2019 in Wuhan, China. *Clinical Infectious Diseases*, XX(XX): 1–9. DOI: 10.1093/cid/ciaa272
- World Health Organization (WHO). 2020a. *Coronavirus disease [COVID-19] Technical Guidance: Infection Prevention and Control*. WHO. Retrieved from <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance-publications>
- World Health Organization (WHO). 2020b. *Report of the who-china joint mission on coronavirus disease 2019 (Covid-19)*. Geneva: World Health Organization.
- Yang, X., Yu, Y., Xu, J., Shu, H., Xia, J., Liu, H., & Shang, Y. 2020. Clinical course and outcomes of critically ill patients with SARS-CoV-2

- pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *The Lancet Respiratory Medicine*, 2600(20): 1–7. DOI: 10.1016/S2213-2600(20)30079-5
- Zhang, J.J, Dong, X., Cao, Y.Y., Yuan, Y.D., Yang, Y.B., Yan, Y.Q., & Gao, Y.D. 2020. Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China. *Allergy: European Journal of Allergy and Clinical Immunology*, 75(7): 1730-1741. DOI: 10.1111/all.14238
- Zhou, F., Yu, T., Du, R., Fan, G., Liu, Y., Liu, Z., & Cao, B. 2020. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *The Lancet*, 395(10229), 1054–1062. DOI: 10.1016/S0140-6736(20)30566-3
- Zhou, Z., Chen, P., & Peng, H. 2016. Are healthy smokers really healthy? *Tobacco Induced Diseases*, 14(1), 1–12. DOI: 10.1186/s12971-016-0101-z
- Zhu, N., Zhang, D., Wang, W., Li, X., Yang, B., Song, J., & Tan, W. 2020. A Novel Coronavirus from Patients with Pneumonia in China, 2019. *New England Journal of Medicine*, 382(8): 727–733. DOI: 10.1056/NEJMoa2001017