

S. O. Yastremska, O. M. Krekhovska-Lepiavko, B. A. Lokay, O. V. Bushtynska, S. V. Danchak

I. Horbachevsky Tenopil National Medical University

THE INFLUENCE OF CHRONIC DISEASES ON THE MANIFESTATION  
OF COVID-19 INFECTIONThe influence of chronic diseases on the manifestation  
of COVID-19 infectionS. O. Yastremska, O. M. Krekhovska-Lepiavko,  
B. A. Lokay, O. V. Bushtynska, S. V. Danchak

I. Horbachevsky Tenopil National Medical University

e-mail: yastremska@tdmu.edu.ua

**Summary.** The first known case of infection from the novel coronavirus was recorded almost one year ago, in China's Hubei province. The city of Wuhan was infamous the world over as the original virus epicenter, seeing more than half of China's reported cases and deaths. The outbreak of COVID-19 virus, as sickened more than 14.7 million people. At least 610,200 people have died.

**The aim of the study** – to analyze and systematize the literature data about the influence of chronic diseases on the manifestation of COVID-19 infection.

**Materials and Methods.** The study uses publications of the world scientific literature on COVID-19 infection, in particular the causes and mechanisms of its development, treatment, complications and its consequences as well as the influence of different chronic disorders on the course of COVID-19.

**Results.** A sample of patients hospitalized with COVID-19 across 14 states of the USA in March was analyzed by The Centers for Disease Control and Prevention. It was found that many (89 %) had underlying health problem and 94 % of patients were at the age 65 and older. The case fatality rate for those under age 60 was 1.4 percent. For those over age 60, the fatality rate jumps to 4.5 percent. The older the population, the higher the fatality rate. For those 80 and over, COVID-19 appears to have a 13.4 percent fatality rate. Moreover, it was recognized, that older adults don't present in a typical way of the course of different disorders, and we're seeing that with Covid-19 as well.

**Conclusions.** Chronic diseases and conditions are on the rise worldwide. COVID-19 became the most challenging pandemic influencing all countries worldwide. Chronic diseases are suggested to be one of the main causes of different life-threatening complications of COVID-19 infection and one of the main factors of poor prognosis for the patients.

**Key words:** COVID-19; viral infection; chronic disorders.

Вплив хронічних захворювань на перебіг  
COVID-19С. О. Ястремська, О. М. Креховська-Лепявко,  
Б. А. Локай, О. В. Буштинська, С. В. ДаньчакТернопільський національний медичний університет  
імені І. Я. Горбачевського МОЗ України

**Резюме.** Перший відомий випадок інфікування новим коронавірусом був зафіксований більше року тому в китайській провінції Хубей. Місто Ухань, в якому було зареєстровано більше половини випадків зараження та смерті в результаті COVID-19, стало відомим у всьому світі як оригінальний епіцентр вірусу. Під час спалаху вірусу COVID-19 захворіло понад 14,7 млн людей. Щонайменше 610 200 людей загинули.

**Мета дослідження** – проаналізувати та систематизувати літературні дані про вплив хронічних захворювань на прояви інфекції COVID-19.

**Матеріали і методи.** У дослідженні використані публікації світової наукової літератури про інфекцію COVID-19, зокрема про причини та механізми її розвитку, лікування, ускладнення та її наслідки, а також вплив різних хронічних розладів на перебіг COVID-19.

**Результати.** Центром контролю та профілактики захворювань США був проведений аналіз вибірки пацієнтів, госпіталізованих із COVID-19, у 14 штатах США в березні 2020 р. У ході даного аналізу було встановлено, що у більшості пацієнтів (89 %) мали місце супутні захворювання, а 94 % осіб були у віці 65 років і старше. Рівень летальних випадків у віці до 60 років становив 1,4 %. В осіб віком більше 60 років відмічалось підвищення рівня смертності до 4,5 %. Для людей у віці більше 80 років смертність від COVID-19 становить 13,4 %. Окрім того, було встановлено, що для людей похилого віку не характерний типовий перебіг COVID-19.

**Висновки.** Частота випадків хронічних захворювань зростає у всьому світі. Пандемія COVID-19 стала однією з найскладніших глобальних пандемій. Вважається, що хронічні захворювання є однією з основних причин різних загрозливих для життя ускладнень COVID-19 та одним з основних факторів несприятливого прогнозу для пацієнтів.

**Ключові слова:** COVID-19; вірусна інфекція; хронічні розлади.

**INTRODUCTION** After first appearing in Wuhan, China in December 2019, the novel coronavirus spread to at least 181 countries and regions. Nowadays, the coronavirus COVID-19 is affecting 222 countries and territories around the world [1].

The first confirmed coronavirus cases outside China occurred on January 20, in Japan, Thailand and South Korea [2]. On January 21, the first case in the U.S. was identified in Washington state.

On January 24, the first two European cases were confirmed in France. By February 1, eight European nations had confirmed cases of COVID-19, and a month later that count had risen to 24 countries with at least 2.200 cases, most of them in Italy. On March 11, Italy eclipsed 10.000 cases and the World Health Organization declared the outbreak a pandemic – the first since H1N1 in 2009. That's also when China, the original epicenter, began seeing drops in daily counts of new cases.

March also saw exponential spread of the virus throughout the U.S., with all 50 states reporting cases by March 17.

The disease was confirmed to reach Canada on January 27, 2020, after a man who had returned to Toronto from Wuhan, Hubei, China, tested positive.

The coronavirus pandemic was confirmed to spread to Ukraine when its first case was confirmed to be hospitalized in Chernivtsi Oblast on March 3, 2020, a man who had travelled from Italy to Romania by plane and then arrived in Ukraine by car [3].

Globally, as of 5:34pm CET, December 20, 2020, there were 75 479 471 confirmed cases of COVID-19, including 1 686 267 deaths, reported to WHO [4].

**The aim of the study** – to analyze and systematize the literature data about the influence of chronic diseases on the manifestation of COVID-19 infection.

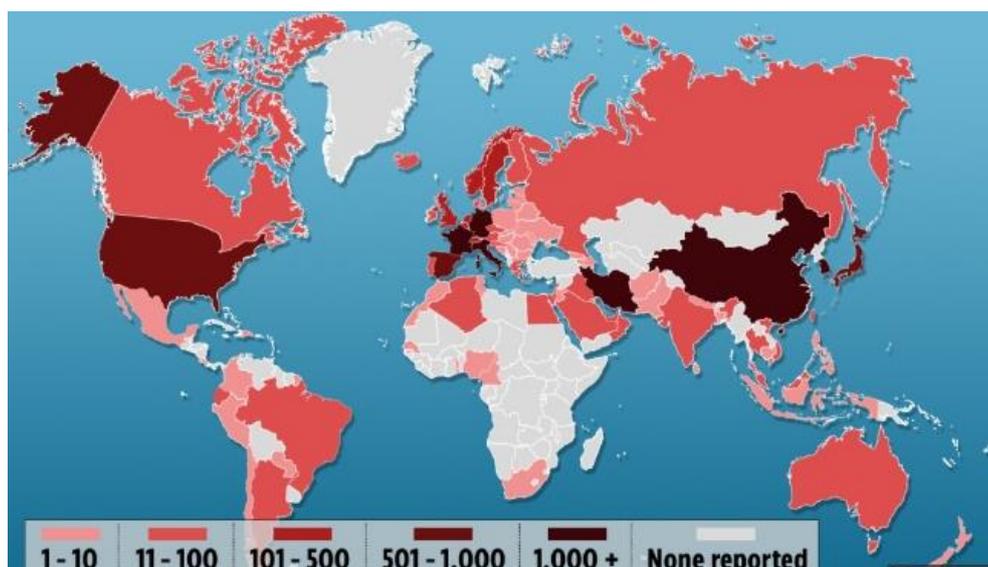
**MATERIALS AND METHODS.** The study uses publications of the world scientific literature on COVID-19 infection, in particular the causes and mechanisms of its development, treatment, complications and its consequences as well as the influence of different chronic disorders on the course of COVID-19.

### RESULTS AND DISCUSSION

The Centers for Disease Control and Prevention analyzed a sample of patients hospitalized with COVID-19 across 14 states of the USA in March and found that many had underlying health problems. It was recognized that 89 % of those hospitalized in March had underlying conditions [5]. 94 % of patients were at the age 65 and older.

Taking into account that the entering gates for COVID 19 are localized in the upper respiratory system and in the lungs, the results of CDC analyses demonstrate, that the percentage of COVID patients with underlying respiratory disorders is low, comparing to other diseases, for example, hypertension. As you can see from the diagram, the number of all patients with COPD is approximately 11 %, comparing to 50 % of all patients with hypertension, which is 5 fold higher. The diagram shows that almost 73 % and 23 % of COVID patients with hypertension and COPD, respectively, were at the age of 65 and older. At the same time, it is observed that obesity is a really important risk factor of COVID 19, because among 48 % of patients with that disorder 41 % were older adults (65+). Talking about diabetes, it is on the third place in the list of underlying conditions, associated with COVID 19 with the percentage of all patients equal to 28. It is necessary to point, that 31 % of them were at the age 65 years and older.

The journal Lancet Infectious Diseases published the latest estimates of the death rate of COVID-19.



Picture 1. Confirmed Cases of COVID-19 Worldwide.

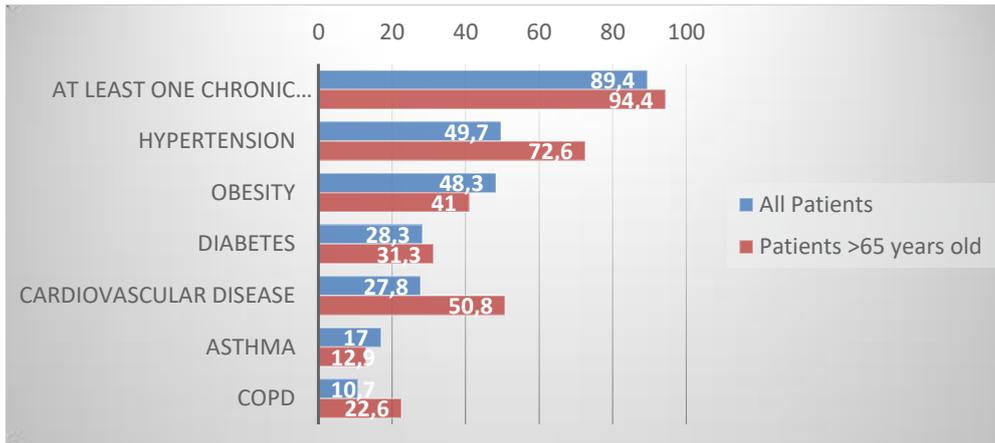


Diagram 1. Chronic Conditions in Patients Hospitalized with COVID-19 (Source: U.S. Centers for Disease Control and Prevention).

The paper found that globally, **the case fatality** rate for those under age 60 was 1.4 percent [6]. For those over age 60, the fatality rate jumps to 4.5 percent. The older the population, the higher the fatality rate. For those 80 and over, COVID-19 appears to have a 13.4 percent fatality rate.

In the US, the CDC reports, “overall, 31 % of cases, 45 % of hospitalizations, 53 % of ICU admissions, and 80 % of deaths associated with COVID-19” are among adults older than 65. “With the highest percentage of severe outcomes among persons aged ≥85 years.” (To note: This CDC data is compiled from February 12 to March 16, when there were just 4.226 confirmed cases in the United States.) [7].

In a Morbidity and Mortality Weekly Report published by the CDC on April 3, it was reported that, among 457 ICU hospital admissions and 1.037 non-ICU hospitalizations, 78 % and 71 % respectively occurred in

those with one or more reported underlying health conditions [8].

Another Chinese study published in the New England Journal of Medicine found that, of 1.099 hospitalized patients, coexisting illnesses were more common among those with severe disease (38.7 %) versus non-severe disease (21 %) [9].

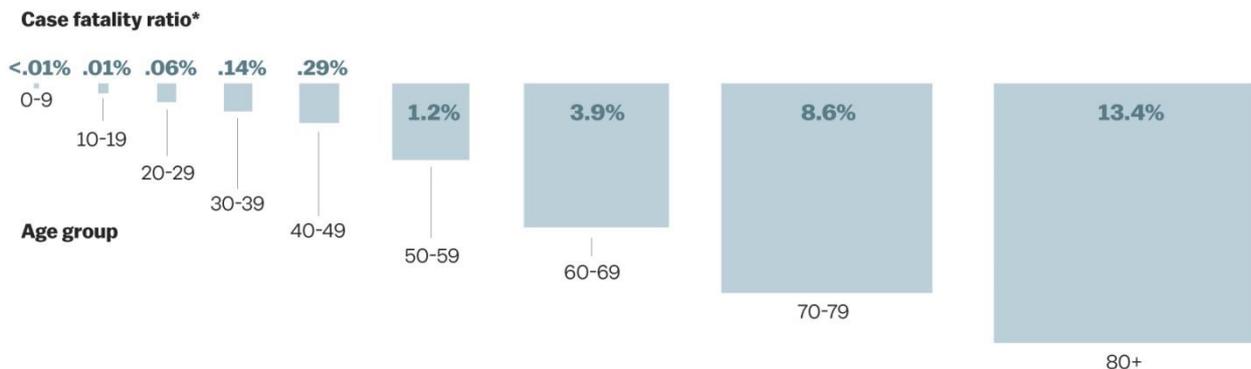
If you look at the data [10], older adults and those with chronic health problems who get COVID-19 are more likely to require hospitalization and admission to an intensive care unit. And so far in the US, 80% of the deaths from the new coronavirus virus have occurred in people who were older.

But this raises a number of questions:

- What do they mean by “older”?
- Which chronic diseases are most important?
- Why does older age and chronic disease increase the risk of COVID-19?

### Covid-19’s case fatality rate increases with age, according to China’s data

Case fatality ratios are estimated from aggregate data on cases and deaths in mainland China from January 1 to February 11, 2020.



\*Adjusted for incomplete data. Values are rounded down.

Source: Estimates of the severity of coronavirus disease 2019: a model-based analysis, The Lancet



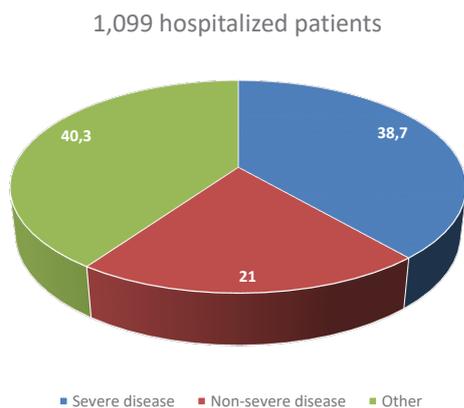


Diagram 2. Chinese study.

**“Older” is more than a number**

When it comes to coronavirus, the CDC’s magic number is now set at 65. That’s the age at which risk of severe disease, complications, and death from COVID-19 appears to rise.

**Which chronic diseases put people at higher risk from COVID-19?**

What do health experts mean when they talk about chronic diseases that put some people at increased risk of severe disease with COVID-19? It varies, but generally includes people who have

- heart disease
- high blood pressure
- diabetes
- asthma or other chronic lung diseases
- HIV
- a suppressed immune system due to a disease or a treatment

**Why do older age and chronic disease increase risk for severe illness if a person gets COVID-19?**

It’s not entirely clear, but here are some possibilities:

- **An immune system weakened by age or illness** is unable to fight off the virus, which could lead to an overwhelming infection.
- **The immune system “misfires” or has an exaggerated response** in some people, triggering so much inflammation and tissue damage that the immune reaction itself causes complications.
- **Organ damage due to existing or past illness** might make additional damage caused by the

virus more than a person can handle; one example is smoking-related lung disease complicated by respiratory infection from the new coronavirus.

- **The stress of a viral infection can increase demand** on already damaged or aging organs (such as the heart).

- **Medications taken to treat chronic conditions** could increase the severity of infection. One suggestion (unproven so far) is that a family of medicines called ACE inhibitors allows more viral organisms to enter cells. ACE inhibitors are commonly taken by people with diabetes and hypertension, perhaps explaining why these conditions are linked to more severe disease.

We need more research to understand whether one or more of these is most important, or whether there are other factors at play.

**Symptoms of COVID-19**

COVID-19 is typically signaled by three symptoms: a fever, an insistent cough and shortness of breath [11, 12, 13]. But older adults – the age group most at risk of severe complications or death from this condition – may have none of these characteristics.

Instead, seniors may seem “off” – not acting like themselves – early on after being infected by the coronavirus. They may sleep more than usual or stop eating. They may seem unusually apathetic or confused, losing orientation to their surroundings. They may become dizzy and fall. Sometimes, seniors stop speaking or simply collapse.

As an example, Dr. Quratulain Syed, an Atlanta geriatrician, describes a man in his 80s who she treated in mid-March. Over a period of days, this patient, who had heart disease, diabetes and moderate cognitive impairment, stopped walking and became incontinent and profoundly lethargic. But he didn’t have a fever or a cough. His only respiratory symptom: sneezing off and on.

The man’s elderly spouse called 911 twice. Both times, paramedics checked his vital signs and declared he was OK. After another worried call from the overwhelmed spouse, Syed insisted the patient be taken to the hospital, where he tested positive for COVID-19.

So, it is very important to remember, that with a lot of conditions, older adults don’t present in a typical way, and we’re seeing that with COVID-19 as well.

Table 2. Symptoms of COVID-19

Typical Symptoms	Atypical Symptoms Common for Older Adults
a fever	sleep more than usual
an insistent cough	stop eating
shortness of breath	unusually apathetic
	confused, losing orientation
	dizzy and fall
	stop speaking
	Collapse

**COVID-19 infection in people with diabetes**

The COVID-19 infection is a double challenge for people with diabetes [14]. Diabetes has been reported to be a risk factor for the severity of the disease and at the same time patients have to control glucose in a situation with a decreased and more variable food intake. Diabetes is a risk factor for hospitalisation and mortality of the COVID-19 infection. Diabetes was a comorbidity in 22 % of 32 non-survivors in a study of 52 intensive care patients. In another study of 173 patients with severe disease, 16.2 % had diabetes, and in further study of 140 hospitalised patients, 12 % had diabetes. When comparing intensive care and non-intensive care patients with COVID-19, there appears to be a twofold increase in the incidence of patients in intensive care having diabetes. Mortality seems to be about threefold higher in people with diabetes compared with the general mortality of COVID-19 in China.

**What explain the increase risk of diabetes?**

It is a fact that people with diabetes are at increased risk of infections including influenza and for related complications such as secondary bacterial pneumonia. Diabetes patients have impaired immuneresponse to infection both in relation to cytokine profile and to changes in immune-responses including T-cell and macrophage activation. Poor glycaemic control impairs several aspects of the immune response to viral infection and also to the potential bacterial secondary infection in the lungs. It is likely that many of the patients with diabetes in China have been in poor metabolic control when infected by COVID-19.

Many patients with type 2 diabetes are obese and obesity is also a risk factor for severe infection. It was illustrated during the influenza A H1N1 epidemic in 2009 that the disease was more severe and had a longer duration in about twofold more patients with obesity who were then treated in intensive care units compared with background population. Metabolic active abdominal obesity is associated with higher risk. The abnormal secretion of adipokines and cytokines like TNF-alfa and interferon characterise a chronic low-grade in abdominal obesity and may induce an impaired immune-response. People with severe abdominal obesity also have mechanical respiratory problems, with reduced ventilation of the basal lung sections increasing the risk of pneumonia as well as reduced oxygen saturation of blood. Obese subjects also have an increased asthma risk, and those patients with obesity and asthma have more symptoms, more frequent and severe exacerbations and reduced response to several asthma medications.

Lastly, late diabetic complications such as diabetic kidney disease and ischemic heart disease may complicate the situation for people with diabetes, making them frailer and further increasing the severity of COVID-19 disease and the need for care such as acute dialysis. Some findings indicate that COVID-19

could cause acute cardiac injury with heart failure, leading to deterioration of circulation.

**Role of angiotensin-converting enzymes in the development of COVID 19 infection**

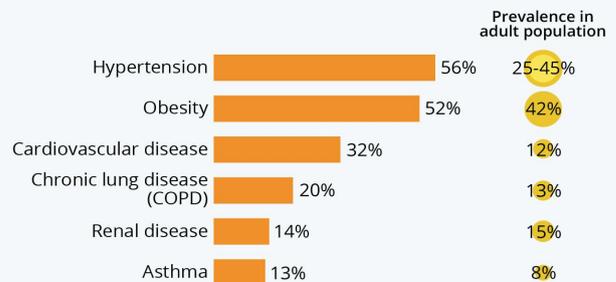
The most frequent comorbidities to COVID 19 are hypertension and diabetes. Both diseases are often treated with angiotensin-converting enzymes (ACE) inhibitors. According to one theory [15], coronavirus binds to target cells through angiotensin-converting enzyme 2 (ACE2), which expressed in the epithelial cells in the lungs, blood vessels and in the intestine. In patients treated with ACE and angiotensin II receptor blockers, expression of ACE2 is increased. Therefore, it has been suggested that ACE2 expression may be increased in these two groups of patients with hypertension and diabetes, which could facilitate infection with COVID-19 and increase the risk of severe disease and fatality.

**Do chronic respiratory diseases or their treatment affect the risk of COVID 19?**

Surprisingly, the prevalence of chronic respiratory disease among patients with COVID-19 appears to be lower than other underlying disorders among the general population. If you take a look on the results of analyses of preliminary hospitalizations of adult COVID 19 patients in US as of April 19, 2020, you will recognize that 56 % of them had hypertension, with the prevalence in adult population 25–45 %. It was also observed, that more then a half of hospitalized patients (52 %), which correspondes to 42 % of all adult population were, obese. And only 13 % of COVID patients had asthma. The results of this analysis are consistent with the results of the previuos CDC analyses of a sample of patients, hospitalized with COVID 19 in March [16]. This is not the case for other chronic diseases and leads us to hypothesise that lung disease, patients' behaviour or, more likely,

**Which Underlying Conditions Do COVID-19 Patients Have?**

Share of hospitalized adult COVID-19 patients in the U.S. which had the following underlying medical conditions



Preliminary hospitalizations as of April 18, 2020. U.S. adult prevalence latest available from CDC NHIS, NHANES or BRFSS (2016-2018)  
Source: CDC



their treatment may have some protective effective.

Sadly, patients with underlying lung disease who develop COVID-19 and are hospitalised have worse outcomes, with a case fatality rate of 6.3 % compared to 2.3 % overall in China. These individuals may have less reserve to cope with the pulmonary effects of severe infection or their immunopathological abnormalities may make them more susceptible to developing pulmonary inflammation and ARDS.

**FACTORS of lower reported prevalence of asthma and COPD in patients diagnosed with COVID-19**

The lower reported prevalence of asthma and COPD in patients diagnosed with COVID-19 might be due to one or a number of factors [17]. First, it is possible that, in contrast to the diagnosis of diabetes, there was substantial underdiagnosis or poor recognition of chronic respiratory disease in patients with COVID-19, particularly in China. However, this seems unlikely, as in very recent data (March 23, 2020) from Italy, among 355 patients dying with COVID-19 (mean age 79.5 years), diabetes was reported in 20.3 % of patients but COPD was not listed as a comorbidity for any patient.

A second possibility is that having a chronic respiratory disease protects against COVID-19, perhaps through a different immune response elicited by the chronic disease itself. However, this theory is not supported by the finding that among those with COVID-19 who have COPD as a comorbidity, mortality is increased, as would otherwise be expected.

A third possibility is that therapies used by patients with chronic respiratory diseases can reduce the risk of infection or of developing symptoms leading to diagnosis. It is important to note that, at most, only

around half of patients with COPD in China take treatments that are standard in Europe and North America, but up to 75 % of people in China with asthma use inhaled corticosteroids. Yet, the possibility that inhaled corticosteroids might prevent (at least partly) the development of symptomatic infection or severe presentations of COVID-19 cannot be ignored. By contrast, a systematic review on the use of systemic corticosteroids to treat SARS, once established, showed no benefit but possible harm.

**Coronavirus and smoking: What does the World Health Organization say?**

Given that tobacco use is thought to kill an estimated eight million people every year, a report that claimed that smokers were less likely to contract coronavirus raised eyebrows [18].

The preliminary study, by the Pitié-Salpêtrière Hospital in Paris, stated that "current smoking status appears to be a protective factor against the infection by SARS-CoV-2" [19].

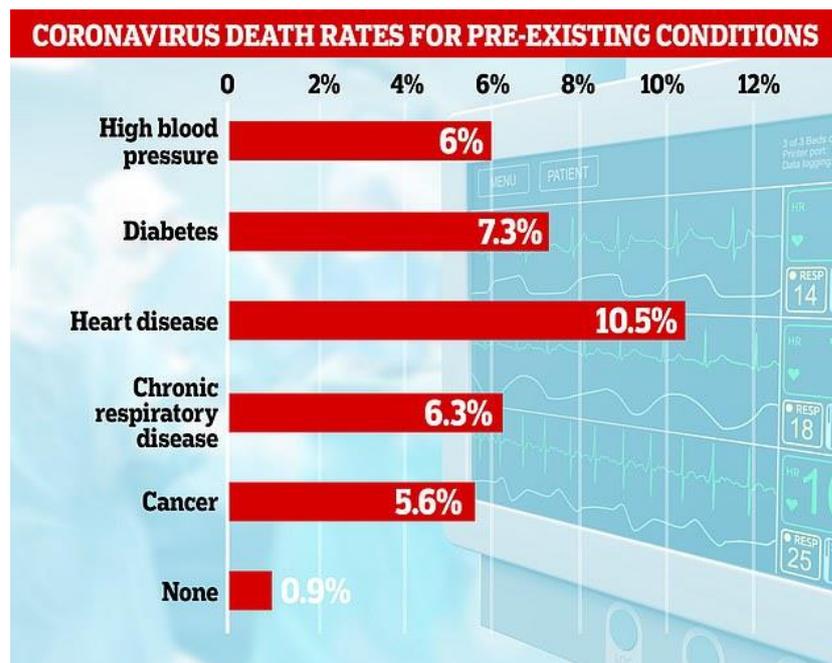
Pitié-Salpêtrière Hospital wrote that "nicotine may be suggested as a potential preventive agent against COVID-19 infection", based on scientific literature and the hospital's own observations.

But the study also warned that "nicotine is a drug of abuse responsible for smoking addiction

**So what do world health experts say? Are smokers less likely to contract the virus?**

No. According to the World Health Organization (WHO), those who smoke are likely to be more vulnerable to infection.

"The act of smoking means that fingers (and possibly contaminated cigarettes) are in contact with lips which increases the possibility of transmission of the virus from hand to mouth," said the WHO.



Smoking products such as water pipes often involve the sharing of mouthpieces and hoses, which could facilitate the transmission of COVID-19 in communal and social settings.

Smokers may also already have lung disease or reduced lung capacity which would greatly increase the risk of serious illness.

Conditions that increase oxygen needs or reduce the ability of the body to use it properly will put patients at higher risk of serious lung conditions such as pneumonia.

Studies also show that smokers were more likely to die than non-smokers during the Middle Eastern Respiratory Syndrome (MERS) outbreak in 2012.

In a further statement, the World Health Organization say they are currently reviewing research and studies concerning smoking and nicotine. The current evidence suggests that the severity of COVID is higher among smokers. The only people who should be using nicotine patches right now are people who need to use them to quit smoking.

A report in March by the European Centre for Disease Control (ECDC) has also identified smokers as a "vulnerable group" to infection from COVID-19.

#### REFERENCES

1. [https://www.who.int/emergencies/diseases/novel-coronavirus-2019?gclid=CjwKCAiArIH\\_BRB2EiwALfbH1P1AoShtJDKrJ0rAjR5n6U\\_f10\\_-LBblbRI3-mu9dluTHHdQKK8uMRoCKcYQAvD\\_BwE](https://www.who.int/emergencies/diseases/novel-coronavirus-2019?gclid=CjwKCAiArIH_BRB2EiwALfbH1P1AoShtJDKrJ0rAjR5n6U_f10_-LBblbRI3-mu9dluTHHdQKK8uMRoCKcYQAvD_BwE)
2. [https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200121-sitrep-1-2019-ncov.pdf?sfvrsn=20a99c10\\_4](https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200121-sitrep-1-2019-ncov.pdf?sfvrsn=20a99c10_4)
3. In Ukraine – the first case of coronavirus. *Ukrainska pravda*. March 3, 2020). Available from: <https://www.ppravda.com.ua/news/2020/03/3/7242332/> Ukrainian.
4. <https://covid19.who.int/>
5. Garg S, Kim L, Whitaker M. Hospitalization rates and characteristics of patients hospitalized with laboratory-confirmed coronavirus disease 2019 – COVID-NET, 14 States, March 1–30, 2020. *MMWR Morb Mortal Wkly Rep* 2020;69: 458-64.
6. Verity R, Okell LC, Dorigatti I, Winskill P, Whittaker C, Imai N, et al. Estimates of the severity of coronavirus disease 2019: a model-based analysis. *Lancet Infect Dis*. 2020 Mar 30.
7. Severe outcomes among patients with coronavirus disease 2019 (COVID-19) – United States, February 12–March 16, 2020. *MMWR Morb Mortal Wkly Rep* 2020;69: 343-6.
8. Preliminary estimates of the prevalence of selected underlying health conditions among patients with coronavirus disease 2019 –United States, February 12–March 28, 2020. *MMWR Morb Mortal Wkly Rep* 2020;69: 382-6.
9. [https://www.nejm.org/doi/full/10.1056/NEJMoa2002032?url\\_ver=Z39.88-2003&rfr\\_id=ori%3Arid%3Acrossref.org&rfr\\_dat=cr\\_pub%3Dpubmed](https://www.nejm.org/doi/full/10.1056/NEJMoa2002032?url_ver=Z39.88-2003&rfr_id=ori%3Arid%3Acrossref.org&rfr_dat=cr_pub%3Dpubmed)
10. [https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/older-adults.html?CDC\\_AA\\_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019-ncov%2Fspecific-groups%2Fhigh-risk-complications%2Folder-adults.html](https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/older-adults.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019-ncov%2Fspecific-groups%2Fhigh-risk-complications%2Folder-adults.html)
11. Guan WJ, Ni ZY, Hu Y. China medical treatment expert group for COVID-19. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med* 2020
12. COVID-19 Surveillance Group. Characteristics of COVID-19 patients dying in Italy: report based on available data on March 20th, 2020.
13. CDC COVID-19 Response Team. Severe outcomes among patients with coronavirus disease 2019 (COVID-19) –United States, February 12–March 16, 2020.
14. <https://www.idf.org/aboutdiabetes/what-is-diabetes/covid-19-and-diabetes/1-covid-19-and-diabetes.html>
15. [https://www.researchgate.net/publication/342901626\\_Role\\_of\\_angiotensin-converting\\_enzyme\\_2\\_ACE2\\_in\\_COVID-19](https://www.researchgate.net/publication/342901626_Role_of_angiotensin-converting_enzyme_2_ACE2_in_COVID-19)
16. World Health Organization. Coronavirus disease 2019 (COVID-19) situation report–57. Geneva, Switzerland: World Health Organization; 2020.
17. <https://www.sciencedirect.com/science/article/pii/S0306987720312007#bi005>
18. Miyara M, Tubach F, Martinez V, Panzini-Morelot C, Pernet J, Haroche J, Morawiec E, Gorochoff G, Caumes E, Hausfater P, Combes A, Similowski T, Amoura Z. Low incidence of daily active smokers in patients with symptomatic COVID19. *Qeios* 2020.
19. <https://www.qeios.com/read/FXGQSB>

Received 01.02.21