



Factsheet: COVID-19 and Smoking: ongoing rapid assessment of the available evidence

(last update: 31.08.2020)

About this document:

We published a first version of this Factsheet on 23 April 2020. Since then more evidence has been made available, however on some aspects long-term well-designed studies are still lacking. However, we want to stress again that there is enough general evidence that smoke and nicotine consumption, in all their forms, is bad for health and there are no “safe” products. The negative impact of those products on the respiratory health is more than demonstrated. In some points regarding the negative impact of smoke and nicotine on Covid-19 infections and illness, absence of evidence can never be assumed to be evidence of absence.

In this document, we summarize and comment upon available evidence and make it available for scientific debate. Our objective is not to draw general conclusions or recommendations, but to make freely available the evidence and crucial arguments. We also summarize the recommendations and positions of the main health organizations, WHO, the FOPH, and other relevant public health organizations.

General considerations

Any kind of smoking is harmful and seriously affects the cardiovascular and respiratory systems. This well-established fact raises many questions about smoking (including vaping) and the respiratory disease COVID-19. This pandemic presents not only fundamental scientific questions but also questions about what public health responses are needed. Central to all are what we already know and what we need to know about the influence of tobacco or nicotine products consumption on COVID-19 infection risk, and smokers’ increased risk of severe complications in case of infection.

What is the influence of tobacco or nicotine products consumption on COVID-19 infection risk—is a smoker or ex-smoker at elevated risk of contracting COVID-19? How does a smoking or vaping habit influence the course of the infection? Is there anything that can be done to influence the risks? For each of these questions, what evidence already is available, and what new research is needed?

Given the rapid onset of the COVID-19 pandemic, risks related to the consumption of tobacco and nicotine products are not yet well understood, even if knowledge is progressively improving. The investigation has only begun as scientists and public health experts mobilize to publish articles, research results, opinions, and interpretations. Public health organizations are issuing recommendations on the basis of available evidence. Though direct evidence for the link between COVID-19 and smoking and vaping habits is still limited, we know that tobacco and nicotine consumption is a major risk factor for several non-communicable diseases, in particular respiratory and cardiovascular diseases. There are increasing indications that smoking and vaping can worsen the risk of being infected by COVID-19. At the same time, they increase the risk of more serious complications in case of infection.

Note on products: In addition to traditional cigarettes and tobacco products, in recent years electronic nicotine delivery systems (ENDS), also called vapers or e-cigarettes, and heated tobacco products (HTP) have appeared. HTP contain tobacco, and though the industry promotes them under the marketing term “heat not burn,” we reject that characterization. (Ruggia 2020) No product containing tobacco or its addictive component nicotine is safe for human consumption. Tobacco products have been studied for decades and the evidence of their

negative impact on health, especially pulmonary health, constantly expands. For ENDS and HTP, which arrived on the market only recently, not enough research has yet been conducted. HTP, which pyrolyze tobacco at elevated temperatures, are similar in their dangerousness to traditional tobacco products. Regarding the potential harm to pulmonary health of ENDS and HTP, particularly in the context of the very recent COVID-19 pandemic, we want to stress that absence of evidence can never be considered as evidence of absence.

Limitation: The opinions and comments expressed are those of the author of this document.

1. Smoking and vaping may increase the spread of Covid-19

The Covid-19 can be easily spread from hand-to mouth contact, which is common when using cigarettes or vaping devices. Social sharing of smoking and vaping products can also facilitate the spread of the virus, in particular we know of outbreaks of Covid-19 linked to Shisha-bars. The risk of Covid-19 linked to passive smoke cannot be excluded and should be better considered.

The risks of transmission linked to hookahs was immediately recognized in the early stages of the Covid-19 epidemic. (Shekhar and Hannah-Shmouni 2020) The water of the pipe could in itself be a favorable environment for the survival of the Covid-19 virus. Cleaning a water pipe is long and complicated and should be done after each use, but this is rarely the case. Because of the airborne transmission of the virus, the social consumption of hookah in closed public places could be a very favorable environment for infections to occur.

In May 2020, an outbreak of Covid-19 in Göttingen (Germany), in which 68 people were infected, was linked to a shisha bar : 310 people having been in contact with the infected people were identified, including 57 children and teenagers.¹ In Iran, where hookah consumption is a social tradition, the waterpipes also played an important role in the early transmission of the infections. (Mirsoleymani and Nekooghadam 2020)

Especially in the Middle East, several countries banned their use in public place, among them Iran, Turkey, Qatar, Saudi Arabia and the UAE. Egypt was the first to ban water pipes when they closed bars and coffee shops at mid-March². If bars have now reopened, the water pipes ban is still in place. South-Africa has also banned the sale of all tobacco and nicotine products, including water pipes. On 4 August, New Delhi, the Indian capital, banned the use of shishas in all public places because of the risk of Covid-19 transmission. In most western countries, hookah consumption is less common and this might explain why, despite the risk, action to ban hookah has not yet been taken.

Covid-19 is spread is through close contact with infected people via oral and nasal secretions, including saliva and respiratory droplets released from the mouth or nose when someone coughs, sneezes, speaks or sings. That is one of the main reasons why a principal measure to protect himself or herself and other from the spreading of the virus is wearing facial masks. But what about smoking? If you enter into contact with the smoke or vape cloud exhaled by another person, could this contains saliva and respiratory droplets and therefore putting you at risk? Yes, we consider this a very serious possibility. While there are no studies looking directly at secondhand smoke and the spread of the coronavirus, the same droplets people spray when they are coughing, sneezing, or talking are exhaled when they are smoking (and vaping).

¹ <https://www.welt.de/vermischtes/article208713717/Corona-Ausbruch-in-Goettingen-wegen-Shisha-Bar-und-Familienfeiern.html>

² <https://www.egypttoday.com/Article/1/82686/Hookahs-banned-at-Cairo%E2%80%99s-cafes-to-combat-Covid-19>

In Spain, two regions introduced a ban on smoking in all open public places because of the resurgence of Covid-19 and the fear of airborne transmission. First, the region of Galicia, followed a few days later by the Canary Islands, introduced a ban on smoking in open public places if a distance of 2 meters cannot be respected.³

2. Smoking, vaping and the risk of contracting COVID-19

Current evidence tends to indicate that smoking and vaping could potentially increase the risk of being infected by COVID-19. The exact infection risk for smokers and vapers in comparison to non-smokers or non-vapers is not exactly known. That would require well-designed population-based studies that control for age and relevant underlying risk factors.

Smoking is already known to be a risk-factor for many other respiratory infections, including colds, influenza, pneumonia and tuberculosis. (Centers for Disease Control and Prevention (US) 2014) The effects of smoking on the respiratory system makes it more likely that smokers contract these diseases, which could be more severe. Smoking is also associated with increased development of acute respiratory distress syndrome, a key complication for severe cases of COVID-19, among people with severe respiratory infections.⁴

Recent study also clearly point out at the adverse effects of ENDS on the disease-naïve oral microbiome. E-cigarettes stress the subgingival environment, as evidenced by significantly greater abundances of genes regulating stress response in the human metagenome, a brisk proinflammatory response, and robust, positive correlations between these cytokines and putative virulence factors. This study suggest that the risk-for-harm from e-cigarettes is different from, but not less than, conventional cigarettes. (Ganesan et al. 2020) Taking the conclusion of this study as a basis, we should also consider the hypothesis that, because of harm from tobacco and ENDS products, the Covid-19 virus could infiltrate the body more easily though the mouth. So far, to our knowledge this hypothesis has not been raised.

Smoking is known to weaken the immune system and the body's ability to fight infections. Smoking-related pathophysiologic changes occur also in the respiratory system of so-called "healthy smokers," including inflammation and immune changes, genetic alterations, structural changes, and pulmonary dysfunction. Even "healthy smokers" are not healthy. (Zhou et al. 2016)

Smoking doubles the risk of developing respiratory infections. In one study, 391 healthy volunteers were exposed to 1 of 5 different respiratory viruses, including a coronavirus, dropped via a liquid into their noses. The volunteers who smoked were twice as likely as those who did not smoke to develop an infection. (Cohen et al. 1993)

We already know that individuals exposed to cigarette smoke have a greater number and severity of viral infections, but the cellular mechanism of this is unknown. A study conducted in 2009 showed that cigarette smoke causes necrosis rather than apoptosis in viral infection, resulting in increased inflammation and enhanced viral replication. (Groskreutz et al. 2009) Subsequent research has confirmed that cigarette smoke decreases innate responses of epithelial cells to rhinovirus infection. (Eddleston et al. 2011)

The dangerous link between Middle East Respiratory Syndrome (MERS) and smoking has already been established. (Seys et al. 2018; Nam et al. 2017; Park et al. 2018)

³ <https://uk.reuters.com/article/uk-health-coronavirus-spain-smoking/spains-canary-islands-curb-smoking-amid-covid-19-worries-idUKKCN2592YV>

⁴ <https://www.who.int/publications/i/item/clinical-management-of-covid-19>

COVID-19 is predominantly a disease of the respiratory tract, with evidence emerging that cellular entry, viral replication, and virion shedding occur within the respiratory tract. (Zou et al. 2020)

Recent studies have found that SARS-CoV-1 and SARS-CoV-2 bind the same receptor, ACE2. Following recognition of this, an analysis of five large-scale bulk transcriptomic datasets of normal lung tissue and two single-cell transcriptomic datasets investigated disparities related to race, age, gender, and smoking status in ACE2 gene expression and its distribution among cell types. The study did not find significant disparities in ACE2 gene expression between racial groups (Asian vs Caucasian), age groups (>60 vs <60), or genders (male vs female). However, it observed significantly higher ACE2 gene expression in lung tissue of former smokers than nonsmokers. This study suggests that smokers, especially former smokers, may be more susceptible to SARS-CoV-2 and have infection paths different from nonsmokers. Smoking history may therefore provide valuable information for identifying susceptible populations and standardizing treatment regimens. (Cai 2020a) This susceptibility has been also highlighted by other studies. (Brake et al. 2020; Wang et al. 2020)

Vaping is linked to a substantially increased risk of COVID-19 among teenagers and young adults, according to a new study led by researchers at the Stanford University School of Medicine. The study, which was published online Aug. 11 in the *Journal of Adolescent Health*, is the first to examine connections between youth vaping and COVID-19 using U.S. population-based data collected during the pandemic. Among young people who were tested for the virus that causes COVID-19, the research found that those who vaped were five to seven times more likely to be infected than those who did not use e-cigarettes. “Teens and young adults need to know that if you use e-cigarettes, you are likely at immediate risk of COVID-19 because you are damaging your lungs,” said the study’s senior author, Bonnie Halpern-Felsher, PhD, professor of pediatrics.⁵ (Gaiha et al. 2020)

3. Smoking and the increased risk of COVID-19 complications

Smoking increases the risk of chronic lung disease, reduces lung capacity, and causes inflammation of the airways, which can increase the risk of developing pneumonia or a serious complication in COVID-19 patients. (Arcavi and Benowitz 2004; Liu et al. 2020)

One of the first studies to establish a link between the smoking history of patient and the severity of COVID-19 was conducted among patients admitted to three tertiary hospitals in Wuhan between December 30, 2019, and January 15, 2020. The study was conducted with 78 patients, and history of smoking (OR, 14.285; 95% CI: 1.577-25.000; P = 0.018) was considered as a risk factor along with age, among others. (Liu et al. 2020)

A second important article examined the clinical characteristics of coronavirus in China. In this larger study of 1099 people with COVID-19, people who smoke were 2.4 times more likely to get really sick and were admitted to an intensive care unit, needed mechanical ventilation, or died compared to those who did not smoke. This study also found that COVID-19 patients who suffered from a severe course of disease had certain pre-existing illnesses or were active or former smokers. (Guan et al. 2020)

Regarding the data of the early studies conducted in Wuhan, we feel that some caution should be exercised. On 17 April 2020, the Chinese city of Wuhan, where the coronavirus originated last year, has raised its official Covid-19 death toll by 50%, adding 1,290 fatalities. Wuhan officials attributed the new figure to updated reporting and deaths outside hospitals. China has insisted there was no cover-up. Whatever the reasons, we consider that conclusions in the initial studies of the impact smoking should be regarded with a measure of

⁵ <https://med.stanford.edu/news/all-news/2020/08/vaping-linked-to-covid-19-risk-in-teens-and-young-adults.html>

caution. Underrepresentation of smokers could be considered as a possibility in the previously reported Chinese data (<https://www.bbc.com/news/world-asia-china-52321529>).

In a study published on 9 April 2020 and conducted in Vancouver, the focus was on how SARS-CoV-2 uses the angiotensin converting enzyme II (ACE-2) as the cellular entry receptor. While the virus can infect individuals of any age, to date most of the severe cases have occurred in those over the age of 55 years and with significant comorbidities such as chronic obstructive pulmonary disease (COPD). The study determined whether patients with COPD had increased expression of ACE-2 in bronchial epithelial cells in the lower respiratory tract. In summary, active cigarette smoking and COPD up-regulate ACE-2 expression in lower airways, which in part may explain the increased risk of severe COVID-19 in these populations. These findings highlight the importance of smoking cessation for these individuals and increased surveillance of these risk subgroups for prevention and rapid diagnosis of this potentially deadly disease. (Leung et al. 2020)

A systematic review of smoking and influenza showed that smoking was consistently associated with higher risk of hospital admission after influenza infection, but the results for ICU admissions and deaths were less conclusive because of the limited number of studies. (Han et al. 2019)

A meta-analysis based on papers published until 28 April, showed a significant association between smoking and progression of COVID-19 (OR 1.91, 95% confidence interval [CI] 1.42-2.59, $p = 0.001$). Limitations in the 19 papers suggest that the actual risk of smoking may be higher. The authors in their conclusion stated that smoking is a risk factor for progression of COVID-19, with smokers having higher odds of COVID-19 progression than never smokers. (Patanavanich and Glantz 2020)

4. Vaping and lung health

Electronic nicotine delivery systems are rapidly increasing in popularity due to the perception that they may represent a safe alternative to conventional cigarettes. For this reason, ENDS are used to assist smoking cessation. But there is growing evidence that the aerosol from ENDS, also known as vaping devices, can harm lungs at both the cellular and organ level and reduce the body's ability to fight respiratory infections. A 2019 review of the evidence for the effects of e-cigarettes on respiratory health showed measurable adverse biologic effects on organ and cellular health in humans, animals, and in vitro. The effects of e-cigarettes are similar to and have important differences from those of cigarettes. But since decades of chronic smoking can precede the development of diseases such as lung cancer or chronic obstructive pulmonary disease, the population effects of e-cigarette use may not be apparent until the middle of this century. Current knowledge of these effects is insufficient to determine whether the respiratory health effects of e-cigarettes are less than those of combustible tobacco products. (Gotts et al. 2019)

However, vaping could weaken the immune system even more than traditional cigarettes. A 3-arm study of smokers, vapers, and total nonusers examined 594 genes known to aid in immune system support and fighting off infections. Smoking status was determined based on smoking history and a 3- to 4-week smoking diary, and was confirmed using serum cotinine and urine 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL) levels. Total RNA from nasal scrape biopsies and superficial scrape biopsies was analyzed to assess the expression of 597 human immunology-related genes. Both vapers and cigarette smokers showed signs of diminished gene activity. However, the vaping group exhibited decreased activity in 300 more genes than regular smokers. This suggests that compounds found in the liquid used to create the vapor has an immunosuppressive effect on the body. (Martin et al. 2016)

A growing body of evidence indicates that ENDS exposure can indeed disrupt maintenance of pulmonary immune homeostasis and antimicrobial immunity independently of nicotine. A mouse study found that ENDS exposure, independent of nicotine, altered lung lipid homeostasis in alveolar macrophages and epithelial cells. Comprehensive lipidomic and structural analyses of the lungs revealed aberrant phospholipids in alveolar macrophages and increased surfactant-associated phospholipids in the airway. In addition to ENDS-induced lipid deposition, chronic ENDS vapor exposure downregulated innate immunity against viral pathogens in resident macrophages. Independent of nicotine, ENDS-exposed mice infected with influenza demonstrated enhanced lung inflammation and tissue damage. These findings reveal that chronic e-cigarette vapor aberrantly alters the physiology of lung epithelial cells and resident immune cells and promotes poor response to infectious challenge. More extensive investigations of the solvent vehicles used in e-cigarettes is warranted. ENDS-exposed mice also displayed greater inflammation and tissue damage in response to influenza A. The implications of these previously unrecognized adverse effects of ENDS exposure on pulmonary lipid metabolism for long-term respiratory health requires future exploration. (Madison et al. 2019; Singanayagam and Snelgrove 2019)

The effects of ENDS on the inflammatory response and viability of COPD bronchial epithelial cells have also been studied. ENDS vaping extracts are toxic and reduce the antiviral response to polyinosinic:polycytidylic acid (poly I:C). This raises further concerns about the safety of ENDS use. Now, these findings should also heighten concern about the impact of severe COVID-19 upon ENDS users. (Higham et al. 2018)

ENDS also have specific unique negative impacts on health different than traditional cigarettes. They can cause a unique innate immune response in the lung, involving increased neutrophilic activation and altered mucin secretion. Results of 2018 study indicate that e-cigarette use alters the profile of innate defense proteins in airway secretions, inducing similar and unique changes relative to cigarette smoking. These data challenge the concept that e-cigarettes are a healthier alternative to cigarettes. (Reidel et al. 2018)

Given the limited evidence regarding ENDS impact on lung disease in general and on COVID-19 in particular, we cannot conclude that the products have no impact on the risk of COVID-19 infection or the severity of the infection. The precautionary principle does not allow the exclusion of danger; the burden of scientific proof is on those who would like to exclude such danger.

HTP are also being touted as reduced harm tobacco products by tobacco companies across the world despite limited scientific evidence supporting this claim. However, an assessment based on industry generated data concluded that Philip Morris's modified risk tobacco product (MRTP) application for I-Quit-Ordinary-Smoking (IQOS) shows that IQOS generates significant pulmonary and immunomodulatory harm, most notably in human studies, and that, with regards to pulmonary and immunomodulatory harm, based on the limited available data to date, IQOS use does not appear to significantly differ from conventional cigarettes. (Moazed et al. 2018)

5. Smoking and other COVID-19 risk factors

Several chronic conditions, including hypertension, diabetes, and cardiovascular disease are risk factors clearly associated with increased odds of death in Covid-19 patients. (Fried et al. 2020) For those chronic disease smoking and vaping is an established important major risk factor. (Johnson 2018; Kavousi et al. 2020; Lynch et al. 2020; Saffar Soflaei et al. 2018; Centers for Disease Control and Prevention (US) 2014)

Already in March, early research indicated that, compared to non-smokers, having a history of smoking may substantially increase the chance of adverse health outcomes for COVID-19 patients, including being admitted

to intensive care, requiring mechanical ventilation and suffering severe health consequences. (Vardavas and Nikitara 2020)

Studies of the biology of viral infection and clinical management of the disease have also demonstrated that differences in COVID-19 disease prevalence and severity are associated with sex, and that smoking is related to higher expression of ACE2, the cell surface receptor to which SARS-CoV-2 binds. (Cai 2020b)

Given the association between smoking and certain COVID-19 aggravating conditions like diabetes or cardiovascular diseases, more research and detailed data would be needed, especially to disaggregate the impact of the different factors.

Medical vulnerability was demonstrated not only in older populations with preexisting conditions, but also in younger populations. Smoking may boost severe COVID-19 risk among young adults. Close to one third of young U.S. adults appear to have an elevated risk for severe COVID-19, with smoking their strongest risk factor, according to survey data. Researchers looked at data from more than 8,000 participants, ages 18 to 25, in the nationally representative National Health Interview Survey for 2016 to 2018. They also looked at participants' medical conditions identified by the U.S. Centers for Disease Control and Prevention as making people of any age "medically vulnerable" to severe illness from the coronavirus. Among these are diabetes, heart disease, immune problems, smoking, poorly controlled HIV or AIDS, and respiratory diseases. Overall, 32% of the surveyed were seen as medically vulnerable to severe COVID-19. Among non-smoking young adults, however, only 16% were seen as medically vulnerable. The researchers said that "Efforts to reduce smoking and e-cigarette use among young adults would likely reduce their medical vulnerability to severe illness" and that "Our analysis suggests that risk from smoking and e-cigarette use is highest among young adults who are male, white, and lower income and who are fully or partially uninsured." (Adams et al. 2020)

6. Questionable evidence

The interpretation of data can be challenging even when data are not clearly manipulated to serve the interest of a specific group.

An article published on 17 March 2020 offers an example of questionable conclusions suggested at the outset by its title: "Active smoking is not associated with severity of coronavirus disease 2019 (COVID-19)." The article reported a meta-analysis of five studies of the association between active smoking and severity of COVID-19 illness. Its authors concluded that "the results of this preliminary meta-analysis based on Chinese patients suggest that active smoking does not apparently seem to be significantly [sic!] associated with enhanced risk of progressing towards severe disease in COVID-19". (Lippi and Henry 2020)

The article fails to be explicit about its own limitations and risks of error. We question whether it is sufficient to select only "active smokers." Past smokers and detailed smoking history of patients could also be relevant. We also doubt the consistency of the collection of such information from patients admitted to urgent care during a pandemic crisis. The selected studies were conducted under urgent and potentially stressful circumstances conditions, when COVID-19 was at his highest in China. Regardless, the conclusion suffers a major, classical flaw: the absence of evidence is not evidence of absence. While the data cannot demonstrate an association between active smoking and a significantly higher risk of severe COVID-19, the data equally cannot demonstrate that there is no such association. Nevertheless, the authors' affirmative title, "Active smoking is not associated with severity of coronavirus disease 2019 (COVID-19)," misrepresents an association that cannot be excluded. The article should not have been accepted for publication or at the least its title and conclusion should have been modified.

7. Tobacco industry influence and the COVID-19 crisis

COVID-19 attacks the lungs, and behaviors that weaken the lungs put individuals at greater risk. The harmful impact of smoking on the lungs is well documented, and the evidence is growing that e-cigarette use (vaping) can also harm lung health. Unsurprisingly there is mounting concern among leading public health organizations and experts that smokers and e-cigarette users may be at a higher risk for severe illness from COVID-19. In certain countries, this concern is already leading to the strengthening of tobacco and nicotine control measures. The industry clearly fears more such measures in future. (Hefler and Gartner 2020)

Big tobacco is continuing to influence the market and trying to counter the possible negative impact on sales, or even trying to profit from the current COVID-19 crisis through marketing, lobbying, spreading misinformation, and philanthropy. This industry behavior is being tracked and can be seen at <https://www.takeapart.org/campaigns/covid-19-activities> and <https://exposetobacco.org/news/covid-statement>. The focus of the industry during this crisis seems to have been on establishing a difference between tobacco and ENDS in order to promote the latter. And Riccardo Polosa, who is a well-known Italian scientist with strong historical ties to the tobacco and nicotine industry, has actively intervened to keep vape shops open during the COVID-19 crisis in Italy. (https://www.tobaccotactics.org/index.php/Riccardo_Polosa) (Redmond 2020)

An article that raises further concern was published online in late March. The systematic review by another well-known advocate of the vaping industry identified 7 studies examining the clinical characteristics of a total of 2352 hospitalized COVID-19 patients that presented data on smoking status (Farsalinos et al. 2020a). In an updated version of the article (consulted online on 15 April 2020), the study included 13 articles. The Farsalinos et al. article is published on Qeios, which is not a scientific journal, but an open publishing platform with no peer review. Changes to items posted to Qeios can be made anytime and the stability of website posts is not assured.

Farsalinos et al. conclude the online posting by saying that "No studies recording e-cigarette use status among hospitalized COVID-19 patients were identified. Thus, no recommendation can be made for e-cigarette users." The actual intent of this statement is to forestall any recommendation against the use of ENDS during the COVID-19 pandemic. But it is not the case that the evidence for such a recommendation is insufficient. Clear evidence on the general impact of ENDS on lung function already recommends against ENDS vaping in the midst of this pandemic of respiratory disease.

Moving to traditional cigarettes, given the low prevalence of smokers among hospitalized and ICU patients in China as well as the US, one could "raise a possible hypothesis that nicotine might reduce the risk for severe COVID-19. Hospitalization for COVID-19 will inevitably result in abrupt withdrawal of nicotine and its beneficial effect linked to this hypothesis in smokers or users of other nicotine products. This could, at least partly, explain the association between smoking and COVID-19 severity among hospitalized patients". (Farsalinos et al. 2020a)

In the second version of the article (04.04.2020), the authors go even further. Not only do they say that "no recommendation can be made for e-cigarette users" but they add "all the above-mentioned issues relevant to the hypothesis about the effects of nicotine and nicotine withdrawal on COVID-19 progression and severity are equally applicable to e-cigarette users." Thus, based mostly on the fact that in China smoking prevalence is higher (27%) than the prevalence of COVID-19 patients, Farsalinos wants to raise the hypothesis that nicotine may have beneficial effects on COVID-19. Farsalinos warrants "an urgent investigation of the clinical effects of

pharmaceutical nicotine on COVID-19 susceptibility, progression and severity.” Even if this does not go as far as saying it explicitly, it seems to suggest that nicotine and ENDS should be used as therapy for COVID-19. The article has been directly criticized online. (Sheltzer 2020)

In a post published on his own blog, Farsalinos explicitly promotes the idea that e-cigarettes could have a beneficial effect in the context of COVID-19: “There is no evidence on any effects of e-cigarettes on coronavirus infectivity and disease progression, and we cannot exclude the possibility that the use of propylene glycol might have some beneficial effects”. (Farsalinos 2020b)

Because the prevalence of ENDS usage appears to be very low in China, caution is clearly advised regarding any statement about the effects of ENDS on COVID-19 in Chinese patients. According to the China Adult Tobacco Survey in 2015, 40.5% of adults aged 15 years and older had heard of e-cigarettes, but only 3.1% had ever tried them. (Wang et al. 2019) The current lack of detailed stratified data does not justify doubting the possible harmful impact of ENDS on COVID-19, as Farsalinos tries to imply it does.

On 24 March 2020, an analysis titled COVID-19 and Tobacco Industry Interference, 2020 was posted on the page of Global Center for Good Governance on Tobacco Control (GGTC). In this article, a table summarizes the tobacco-industry-backed articles in relation to COVID-19. Farsalinos is among the authors cited in the industry-backed publications. (Global Center for Good Governance in Tobacco Control 2020)

On 17 April 2020, the French Alliance contre le Tabac published a press release warning against the hypothesis that tobacco and nicotine could have a protective effect against COVID-19 and any hasty conclusion that could be drawn. Any protective effect of nicotine remains to be proven, and even if there was such an effect the risk/benefit balance would still favor complete cessation. (Alliance contre le Tabac 4/17/2020)

On 22 April 2020, information was published that a new study wishing to test the hypothesis of the supposed preventive and therapeutic implication of nicotine was going to be launched in France. One of the main starting point of this study is that in COVID-19 a lower prevalence of smokers has been observed that in the general population, hence the “current smoking status appears to be a protective factor against the infection by SARS-CoV-2.” We consider that this is jumping some necessary steps. If a lower prevalence of smokers is observed (which is not the case in every available study), one should first analyze if this is due to any other bias. The obvious one appears to be that COVID-19 patients are older and that smoking prevalence in elderly populations is lower than in the general population. Comparing the prevalence of smokers in COVID-19 patients to the one in the general population is not sufficient, if not simply wrong. This study propose plan a therapeutic assay against Covid-19 with nicotine (and other nicotinic agents) patches or other delivery methods (like sniffing/chewing) in hospitalized patients and in the general population. Some methodological and ethical elements are still unclear, and the proposed study has already raised a debate. The cautions expressed by the French Alliance contre le Tabac just a few days earlier do not seems to have been considered here. (Changeux et al. 2020)

The Changeux article was heavily based on a study attempting to show a low incidence of daily active tobacco smoking in patients with symptomatic COVID-19 in France. In this study, the rate of current daily smokers was significantly lower in COVID-19 outpatients and inpatients (80.3% and 75.4%, respectively), as compared to that in the French general population prompting the authors to declare that suggests that daily smokers have a very much lower probability of developing symptomatic or severe SARS-CoV-2 infection as compared to the general population. (Miyara et al. 2020) This study, which was also a Qeios publication, therefore lacking a

peer-review process, was immediately criticized online in the Qeios platform as well by others.⁶ Fortunately, also the press criticized the study and showed how the industry tried to use the Covid-19 crisis to its benefit.⁷

Research should be remain free, but we could nevertheless ask if investigating the preventive and therapeutic hypothetical effect of nicotine is the most pressing topic that needs investigation at the high of the COVID-19 crisis. In any case, researcher formulating such controversial hypothesis should offer a full transparency on their motivations and on the links, they have with the tobacco industry. The duty of transparency is even higher for researcher that already have a past in this respect. The main investigator promoting the above mentioned study has received industry funding in the past. (https://www.lemonde.fr/sciences/article/2012/05/31/guerre-du-tabac-la-bataille-de-la-nicotine_1710837_1650684.html)

In France, very rapidly some key institutions reacted to the “nicotine hypothesis” of the Changeux article. The Haut Conseil de la Santé Publique (HCSP) quickly ordered a literature review and brought together a group of experts. On 9 May 2020, the HCSP published a clear and documented statement opposing the nicotine hypothesis. In its statement, the HCSP state clearly, that, to date, there are no reasons to suggest that smoking helps protect against infection by SARS-CoV-2 and call to reject the fake information presenting tobacco as having a possible protective effect against Covid-19 in any public communication. (Haut Conseil de la santé publique 2020)

8. Impact of the Covid-19 on smokers behaviors

On 15 July 2020, ASH UK announced that, based on their analysis, a million people have stopped smoking since the COVID pandemic hit Britain. According to a survey, a further 440,000 smokers tried to quit during this period.⁸

It is difficult to evaluate exactly what are the reasons for smokers to quit. Stress related to the COVID-19 pandemic appears to affect smokers in different ways; some smokers increase their smoking while others decrease it. While boredom and restrictions in movement might have stimulated smoking, the threat of contracting COVID-19 and becoming severely ill might have motivated others to improve their health by quitting smoking. In any case, available data highlight the importance of providing greater resources for cessation services and the importance of creating public campaigns to enhance cessation in this dramatic time. (Bommel  et al. 2020)

Certain campaigns to help people to stop smoking seems to be very effective, like the US CDC “Tips From Former Smokers” campaign, which led between 2012 and 2018 to 1 million American adults to successfully quit smoking and to 16 million quit attempts.⁹ Which the increased dangers consciousness of smokers linked to the Covid-19, it is necessary to find ways to use existing successful methods to help people to smoke while integrating better information on the risk of consumption of tobacco and nicotine products.

Currently, in Switzerland a study is being conducted, based on a survey among a sample of the smoker population, in order to better understand the behavior of smokers during the confinement. Results should be available towards the end of the year.

⁶ <https://exposetobacco.org/news/review-of-smoking-and-covid19/>

⁷ <https://www.tagesanzeiger.ch/wie-sich-tabakkonzerne-als-corona-bekaempfer-darstellen-848104582222>

⁸ <https://ash.org.uk/media-and-news/press-releases-media-and-news/pandemicmillion/>

⁹ <https://www.cdc.gov/media/releases/2020/p0824-tips-campaign-quit-smoking.html>



The principal resource to document and demonstrate how the industry is trying to exploit the Covid-19 crisis for its own agenda and interests is the page **Tobaccotactics**, of the University of Bath, is regularly updated and publish regular monitoring briefs: <https://tobaccotactics.org/wiki/covid-19/>

9. Systematic reviews

Only one article is available so far that attempts a systematic review of the evidence regarding COVID-19 and smoking. (Vardavas and Nikitara 2020). This review identified only 5 studies (Guan et al. 2020; Zhang et al. 2020; Liu et al. 2020; Zhou et al. 2020; Huang et al. 2020) and concluded that “smoking is most likely associated with negative progression and adverse outcomes of COVID-19.”

Current evidence has also been examined and summarized in one short analysis. (Berlin et al. 2020) Its main conclusion is that stronger evidence about the association of smoking with COVID-19 is needed, and that ongoing public health campaigns should mention the importance of smoking cessation during the pandemic.

The systematic literature review that we consider more actual and more pertinent is the one of the Center for Tobacco Control Research and Education published on 11 May. (Patanavanich and Glantz 2020)

10. References pages

Several online webpages provide regularly updated information about the links between COVID-19 and tobacco and nicotine consumption. We provide here the most important ones.

BMJ Tobacco Control. A blog regularly updated to provide information to health professionals and the general public, resources, research, and news reports about COVID19 and tobacco:

<https://blogs.bmj.com/tc/2020/03/26/covid-19-and-smoking-resources-research-and-news/>

Tobacco Free Initiative (WHO-EMRO). <http://www.emro.who.int/tfi/know-the-truth/tobacco-and-waterpipe-users-are-at-increased-risk-of-covid-19-infection.html> (available in English, French, and Arabic)

European Respiratory Society. The ERS also offers a page “ERS COVID-19 resource centre” that is regularly updated:

<https://www.ersnet.org/the-society/news/novel-coronavirus-outbreak--update-and-information-for-healthcare-professionals>

11. Stop smoking during the COVID-19 crisis

When someone stops smoking the health benefits are very rapid. Cessation not only increases blood circulation within 2 to 12 weeks but also increases oxygen levels and lowers inflammation—all of which give the immune system a boost; thus does it become easier to fight off colds and other illnesses. Within 1 to 9 months coughing and shortness of breath decrease, which indicates improvement of pulmonary function (<https://www.who.int/tobacco/quitting/benefits/en/>).

The **Cochrane Library** published a special collection on “Coronavirus (COVID-19): effective options for quitting smoking during the pandemic” (1 April 2020 and regularly updated):

<https://www.cochranelibrary.com/collections/doi/SC000042/full>



12. Current statements and other opinions

Several organizations and associations are taking positions concerning the COVID19 crisis and smoking.

In Switzerland, the **Federal Office of Public Health (FOPH)** maintains a page of Frequently Asked Questions (FAQs) about the new coronavirus (in four languages):

<https://www.bag.admin.ch/bag/de/home/krankheiten/ausbrueche-epidemien-pandemien/aktuelle-ausbrueche-epidemien/novel-cov/haeufig-gestellte-fragen.html#1813479246>

The FOPH states that smoking considerably increases the risk of becoming seriously ill with the novel coronavirus disease COVID-19. It also weakens the immune system in general. Smoking is therefore a risk factor for a COVID-19 infection. FOPH strongly recommends stopping smoking.

The **WHO** has a Questions&Answers page:

<https://www.who.int/news-room/q-a-detail/q-a-on-smoking-and-covid-19>

WHO warns that smokers are likely to be more vulnerable to COVID-19 as the act of smoking means that fingers and possibly contaminated cigarettes are in contact with lips, which increases the possibility of transmission of virus from hand to mouth. Smokers may also already have lung disease or reduced lung capacity, which would greatly increase risk of serious illness. WHO also stresses that 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.

The **Knowledge Hub of the WHO Framework Convention for Tobacco Control** also issued a statement on the increased risk of COVID-19 infection among smokers and water pipe users:

https://untobaccocontrol.org/kh/waterpipes/covid-19/#_edn2

In Germany, the **Robert Koch Institute** also runs a regularly updated page on COVID-19:

https://www.rki.de/DE/Content/InfAZ/N/Neuartiges_Coronavirus/Steckbrief.html

In a risk-group ranking, after elderly people, the Institute lists smokers as the second group, although it notes that the evidence is still weak.

On 3 April 2020, the **International Union against Pulmonary Diseases and Tuberculosis** published a statement warning of the risks of smoking in association with the COVID-19. For the Union's director, Dr. Gan Quan, this is the absolute best time to quit smoking. The Union urges countries to prioritize and implement proven, evidence-based policies from the WHO's Framework Convention on Tobacco Control, which has 181 parties. The Union is also deeply concerned that the tobacco industry is spreading misinformation through blog posts and social media, and denying the link between smoking and COVID-19. The industry, notes Dr. Gan Quan, is capitalizing on the crisis to improve its public relations by offering donations and partnership to governments. At the same time, tobacco companies continue to aggressively market their products, which, in addition to causing eight million deaths each year, are exacerbating the COVID-19 crisis. "With mounting evidence that smokers are at higher risk of severe illness from this disease, the best thing the tobacco industry can do to fight COVID-19 is to immediately stop producing, marketing and selling tobacco." (<https://www.theunion.org/news-centre/news/the-unions-statement-on-covid-19-and-smoking>)



The **US National Institute on Drug Abuse** also published a statement, COVID-19: Potential Implications for Individuals with Substance Use Disorders (6 April 2020), warning that “Because it attacks the lungs, the coronavirus that causes COVID-19 could be an especially serious threat to those who smoke tobacco or marijuana or who vape.” (<https://www.drugabuse.gov/about-nida/noras-blog/2020/04/covid-19-potential-implications-individuals-substance-use-disorders>)

The **European Network for Smoking and Tobacco Prevention (ENSP)** published a factsheet on COVID-19 pandemic and smoking behavior on 16 April 2020, in which ENSP summarized evidence related to smokers and novel tobacco users, and made recommendations to be followed in the context of COVID-19 pandemic. (<http://ensp.network/ensp-factsheet-series-1-2020-covid-19-pandemic-and-smoking-behaviour-2/>)

13. Conclusion

Our conclusion do not differ from the ones we draw in mid-April. If ever, the danger of smoking and vaping in relation with Covid-19 only appears stronger.

- Severity of COVID-19 very much depends upon pulmonary function.
- All smoked and vaped products in varying degrees affect the lungs. In the particular context the new COVID-19 infection, relative toxicity of the different products is not yet known.
- ENDS and HTP cannot be considered a “safe” option.
- Research that attempts to demonstrate that ENDS and/or HTP have no impact on COVID-19, or that nicotine could even have a “protective” effect should be approached with strong caution. So far no evidence is available to substantiate such views.
- Conflict of interest and the influence of the tobacco and nicotine industry in research and publications should be clearly examined and discussed.
- To prevent and fight all infections, including COVID-19, which affect the lung and pulmonary function, complete cessation of smoking and vaping should remain the ultimate aim of everyone.

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31 August 2020

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