COVID-19 and TOBACCO: THE UNION BI-WEEKLY BRIEF ISSUE #1 (18 May, revised 1 June 2020)

INTRODUCTION

The Union’s Tobacco Control Department will provide a bi-weekly scientific brief analysing the current science—and any related controversies—regarding COVID-19 and smoking. The briefs will include a short introduction—an overview of the latest science, enumerating trends, key findings and study flaws before delving into specific publications. This first brief synthesises several months of smoking and COVID-19 literature and seeks to summarise a number of important issues. A series of Frequently Asked Questions are presented for easy reference.

1. Are hospitalised smokers more likely to suffer worse outcomes from COVID-19?

Important findings to support this hypothesis appeared 28 February in The New England Journal of Medicine. The Guan et al study, “Clinical Characteristics of Coronavirus Disease 2019 in China”, as later analysed by Vardavas and Nikitara, shows that compared to non-smokers, smokers are 2.4 times more likely to be admitted to an intensive care unit, need mechanical ventilation or die.

The systematic review of five studies from China by Vardavas and Nikitara concluded “[A]lthough further research is warranted as the weight of the evidence increases, with the limited available data, and although the above results are unadjusted for other factors that may impact disease progression, smoking is most likely associated with the negative progression and adverse outcomes of COVID-19.”

Patanavanich and Glantz conducted a meta-analysis of 12 published papers to determine the association between smoking and COVID-19 progression. The authors focused on studies on smoking behaviour and COVID-19 disease progression published between 1 January and 6 April. In total, the meta-analysis reports on 9,025 COVID-19 patients, including 495 patients with a history of smoking. Of the patients with this history, a total of 88 (17.8%) experienced disease progression, compared with 9.3% of never smoking patients. The authors wrote: “[S]mokers have 2.25 times the odds of severe COVID-19 outcomes than never smokers.”

While most of the studies to date have consistently found smokers to be at a higher risk of developing severe outcomes from COVID-19, Petrilli et al. failed to observe such a relationship in a large study from New York City.

It is important to note that many studies suffer major flaws in design or by virtue of the fact that they are pending peer review. The current evidence does suggest hospitalised smokers with COVID-19 may have worse outcomes than non-smokers, but more evidence is needed to confirm this relationship. While acknowledging that research evolves rapidly and continues to raise new questions, logic should guide our thinking as should the well-established fact that smoking is the number one risk factor for preventable death and disease.

2. What are the French studies?

In late April, three studies—1) the “Pasteur Institute paper,” a retrospective study from a Oise high school; 2) a study from a Paris hospital, Low Incidence of Daily Active Tobacco Smoking in Patients with Symptomatic COVID-19; and 3) Jean-Pierre Changeux’s “A nicotinic hypothesis for COVID-19”—were released, garnering significant media attention for bold claims that nicotine use and/or smoking may have a protective effect against COVID-19 infection. The two French
researchers who authored the third paper with the “Nicotinic Hypothesis” also announced that they would begin a human trial on 1500 health professionals.

The studies (see chart below) occupied headlines, confused people, put tobacco control advocates on the defensive and even resulted in people panic buying nicotine. In response, France decided to limit nicotine sales between 26 April and 11 May for fear that nicotine gum and patches would be either misused or unavailable to those who needed them for smoking cessation.

These studies are fraught with a number of serious problems:

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<th>Study</th>
<th>Publication</th>
<th>Synopsis</th>
<th>Study and Design Flaws</th>
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<td>“Cluster of COVID-19 in northern France: A retrospective closed cohort study”</td>
<td>23 April, 2020 Medrxiv preprint</td>
<td>This retrospective, closed cohort study of a heavily impacted community in Oise, France involved a questionnaire that covered history of fever and respiratory systems and also examined blood, with collection from two centers, for anti-SARS-CoV-2 antibodies. The study involved 661 participants with a median age of 37 and the infection attack rate (IAR) was defined as “the proportion of participants with confirmed SARS-CoV-2 infection based on antibody detection.” The study concluded that smokers were less likely (7.2%) to be infected with the virus than non-smokers (28%).</td>
<td>This study involved a small sample size, likely involved selection bias, and a large number of participants who, because they were under the legal age for tobacco use, were likely inclined to not self-report its consumption. Tests used to report antibodies were not validated, increasing the likelihood that they produced results. And, key variables—attendance at the school where there was a COVID-19 outbreak—were conveniently ignored.</td>
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<td>“Low Incidence of Daily Active Tobacco Smoking in patients with Symptomatic COVID-19”</td>
<td>21 April, 2020 Qetios.com No peer review</td>
<td>Miyara et al. state that their objective was to “evaluate the correlation of daily smoking with the susceptibility to develop SARS-CoV-2 infection.” Their study examined both inpatients (343) and outpatients (139) with confirmed COVID-19 at a large French University Hospital in Paris. Because the proportion of daily smokers among the study group was significantly lower (5.3%) compared to the general population of France (25.4%), the authors conclude that “daily smokers have a very much lower probability of developing symptomatic or severe SARS-CoV-2 infection as compared the general public.”</td>
<td>The study has several significant limitations. The first involves sample bias and the fact that the studied group excluded patients in the intensive care unit, who would comprise the most seriously ill and who might present as smokers at much higher rates. Second, studies set in hospitals are far from ideal—they include very localised populations, including healthcare workers, who comprised a significant number of studied cases. This cohort is most likely to become infected in the hospital, which reveals minimal information about community infection. Finally, the study focuses on present smokers, emphasising that 22/482 COVID-19 patients were daily smokers—a lower proportion than...</td>
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### “A Nicotinic Hypothesis for COVID-19 with preventive and therapeutic implications”

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<tr>
<th>Date</th>
<th>Author(s)</th>
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<td>21 April, 2020</td>
<td>Changeux et al.</td>
<td>Qeios.com</td>
<td>No peer review</td>
<td>This paper does not actually test its hypothesis, nor does it offer any evidence to support it. In addition, as others, including STOP, have noted, the author Jean-Pierre Changeux has long-standing historical links to the tobacco industry.</td>
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**3. What do we know (and not know) about nicotine and COVID-19?**

The hypothesis that nicotine protects against SARS-Cov-2 infection draws from several studies in China, the US, and Europe, where the smoking rate was found to be lower among COVID-19 patients than in the general population. Besides the French studies analysed above, three studies from NYC all revealed a lower smoking rate of around 5% among COVID-19 patients, compared to 11% in the general population in NYC. The smoking rates among COVID-19 patients in the Chinese studies are generally lower than 15%, as compared to the 30% prevalence among the corresponding age group in the general population. Similar findings have also been reported from Switzerland and Italy.

Two studies from the US and UK tested hospital patients for COVID-19 and found that smokers were less likely to be positive. Another study from the UK with a sample size of 2.4 million, found smokers to be more likely to self-report COVID-19 symptoms. Interestingly, among a subset of the sample tested for COVID-19, smokers were less likely to be tested positive.

Several reviews attempted to analyse the evidence and propose hypotheses to shed light on this phenomenon. All noted the early stage of research and pointed out the many limitations the studies suffer, most noteworthy of which is the potential of underreporting of smoking history among COVID-19 patients. While the majority of the studies are from China, the possible underreporting and misreporting of smoking status among COVID-19 patients in China becomes highly relevant. According to GATS China (2018), only 58.3% of smokers who visited a healthcare provider during the past 12 months said they were asked about...
their smoking history. When hospitals are overwhelmed, as during the COVID-19 outbreak, it is likely that smoking history might not be recorded during admission. A New York City study revealed a similar problem, as hospital records proved to be an unreliable information source for patient smoking history. Benowitz et al also concluded that hospital records in the US under-reported the prevalence of smokers among patients. Realizing this limitation in previous research, a recent study from Italy made an effort to contact patients or their relatives to confirm smoking history. The authors didn’t report the extent of under-reporting of smoking from hospital records, but found similar lower smoking rate among patients than the general population.

Another general limitation of research published thus far is that the studied hospital patients may not represent the general population, thus making the smoking rates comparison problematic. The CDC study published in MMWR noted, as one of its limitations, that only 5.8% of the COVID-19 patient records were complete with patient information, including underlying conditions and smoking history. The study from a hospital in France, as another example, is based in a region that also has a lower smoking rate than France’s national average. In addition, it is speculated that smokers may conceal their tobacco consumption if they fear that hospitals would not provide resources to patients deemed to have low survival rates.

Clinical and laboratory data is also missing as part of the evidence base to support or reject the hypothesis that smoking or nicotine protects against SARS-CoV-2 infection. It is generally accepted that SARS-CoV-2, the virus that causes COVID-19, enters human cells through ACE2, the same receptor for SARS-CoV. Researchers are less in agreement about whether smoking and nicotine upregulates or downregulates the activity of ACE2, which presumably affects the chance that SARS-CoV-2 enters cells. French researcher Changeux argues that another receptor—nAchR—may play a key role in SARS-CoV-2 infection and that nicotine may compete with or even block the binding of SARS-CoV-2 to nAchR, thus lowering smokers’ chance of infection. It should be noted that there is little consensus regarding whether any tobacco smoke constituents, particularly nicotine, play a role in the SARS-CoV-2 infection mechanism. The hypotheses by Changeux and others are backed by either conflicting or very limited evidence.

The lower smoking rates observed among Covid-19 patients is an important finding, however, the evidence is presently far from conclusive to infer any relationship between SARS-CoV-2 infection and nicotine or any other tobacco smoke constituents. Precaution against smoking should be upheld as research has shown that smoking increases the risk of both viral and bacterial infections, including flu and TB. WHO’s caution on increased risk of infection among smokers from the hand-to-mouth of smoking is certainly warranted.

4. What do public health organisations say about smoking and COVID-19?

American Cancer Society: “There’s no direct evidence yet showing that a history of smoking makes a person more likely to get COVID-19, but there is evidence that smoking increases the risk of other types of viral lung infections. This increase in risk stems from changes in a person’s immune system, as well as damage to the cells lining the airways in the lungs.”

American Lung Association: “In addition to washing your hands thoroughly, staying home and maintaining social distancing, the American Lung Association urges smokers to quit which will immediately improve overall health and will help avoid the most serious symptoms of the new disease.”

Action on Smoking and Health (ASH): Smokers face a particular challenge as data “strongly suggests a significant co-morbidity between smoking and serious complications from exposure to the coronavirus.”
Centers for Disease Control and Prevention (CDC): While much remains to be determined about COVID-19 risk, "people of all ages with underlying medical conditions, particularly if not well controlled" might be at higher risk. Among high risk populations, the CDC includes those who are immunocompromised, noting that "many conditions can cause a person to be immunocompromised, including…smoking.” (emphasis added).

European Network for Smoking and Tobacco Prevention (ENSP): Makes a series of recommendations about smoking and COVID-19 and notes that “Smokers, as a vulnerable group, must be supported to quit.”

Food and Drug Administration (FDA): “Smoking cigarettes can leave you more vulnerable to respiratory illnesses, such as COVID-19. For example, smoking is known to cause lung disease and people with underlying lung problems may have increased risk for serious complications from COVID-19, a disease that primarily attacks the lungs. Smoking cigarettes can also cause inflammation and cell damage throughout the body, and can weaken your immune system, making it less able to fight off disease.”

The National Institutes of Drug Abuse (NIDA): “Patients with already compromised lung conditions may be at higher risk for more severe complications from COVID-19. Specifically, people who smoke or vape… While all people should be taking precautions to prevent exposure to COVID-19, this is particularly critical for higher risk groups, including people who smoke, vape, or use opioids or methamphetamine. Dr. Volkow urges clinicians to be alert to the possibility of increased risks for adverse COVID-19 outcomes in these patients.”

World Health Organization (WHO): “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. Smoking products such as water pipes often involve the sharing of mouth pieces and hoses, which could facilitate the transmission of COVID-19 in communal and social settings. 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.”

5. What are governments doing to address smoking and COVID-19?

Governments in countries across continents have taken a number of actions to limit tobacco sales— in person or online—ban tobacco imports, and deem selling tobacco non-essential.

- **Botswana:** A [tobacco sales and importation ban](#) was enacted for a period of 6 months (beginning April 30th). The government cited health concerns, noting that COVID-19 is a respiratory illness and tobacco could aggravate symptoms and worsen outcomes. The government was encouraged to take this action by the Anti-Tobacco Network Botswana.

- **France:** Tobacconists in France were categorised as essential businesses and have remained open throughout the pandemic. The government has since [banned the online sale of nicotine replacements](#) to prevent a run on these products resulting from media coverage around the link between smoking and COVID-19.

- **India:** A [tobacco sales ban](#) and a ban on the use of smokeless tobacco and Pan Masala was implemented by the Ministry of Home Affairs 15 April and extended until 3 May. Some states have [extended the ban](#), while others have resumed sale but with added [restrictions](#).
• **Israel**: Israel instituted a ban on all non-essential business operations. Tobacco and smoking products have not been included in the list of essential services.

• **South Africa**: A tobacco ban was implemented 27 March after the trade and industry minister said tobacco products were not essential goods. The industry began legal action against the government which announced that legal sales would be permitted during phase 2 of the lockdown (from 1 May).

• **The United Kingdom** launched the #QuitforCOVID campaign to encourage smokers to stop using tobacco. As of 4 May, nearly 300,000 smokers have quit; 500,000 people have attempted to quit; and 2.4 million people have cut down on smoking.

• **Vietnam**: Dedicated tobacconists were labelled non-essential and were closed. However, tobacco products were still available at grocery and convenience stores. Vietnam has since lifted restrictions.

6. **What is the tobacco industry doing during COVID-19?**

The tobacco industry has not kept a low profile during the COVID-19 pandemic despite strong evidence that its products exacerbate the disease. Instead, the industry makes significant efforts to ensure that smokers have easy, affordable access to tobacco; that governments view the industry favourably; and that profits remain intact—or improved. Altria has even reported a first-quarter revenue increase of 13.0%, primarily due to higher net revenues in its “smoke” segments, such as cigarettes and cigars, as well as its oral tobacco products segments.

A few examples from countries supported by The Union illustrate the scale and scope of TI activity—these vary from loud, splashy fiscal donations to social media promotional deals offering home-delivery so customers can quarantine and obtain tobacco.

• **India**: The ITC group donated both supplies and money to COVID-19 relief efforts. In early April, according to The Hindustan Times, the group partnered with several NGOs to deliver boxes of “hope” and “happiness” to both elderly populations and children under lockdown.

• **Indonesia**: PMI has lobbied for relaxed tax collection.

• **Turkey**: Both PMI and JTI made donations to the national COVID-19 help campaign—US $675,000 and $180,000, respectively. In response, The Union grantee, The Health Institute Association issued a press statement, noting that the donations defy FCTC and demanding that they be returned.

• **Ukraine**: In late March, PMI donated over US $350,000 to fight COVID-19. During the same time period, the company placed ads on Facebook, offering free, local delivery of iQOS. Glo also offered a similar promotion.

• **Vietnam**: Vinataba donated VND 300 million to Hanoi’s Bach Mai Hospital, 1,000 protective suits and 2 disinfection chambers to the Vietnam Heart Institute. PMI’s Marian Salzman issued a letter in Dong Nai newspaper, urging that COVID-19 might bring people together and subtly positioning the tobacco company as a corporate entity deeply concerned about humanity.
STOP is monitoring how tobacco companies are exploiting the pandemic to advance their agendas. A bi-weekly COVID-19 monitoring brief has been produced. STOP’s COVID-19 Action Center contains useful information and materials. Several materials detailing how the tobacco industry is exploiting the COVID-19 pandemic have already been published. These include:

- Press statements exposing industry behaviour:
  - Industry Watchdog Warns Governments of Tobacco Industry Attempts to Take Advantage of COVID-19 Pandemic
  - COVID-19 Related Deaths at Tobacco Factory in Indonesia Are Latest Example of Prioritizing Profits Over Workers

- Materials to refute the controversial French studies that hypothesis that smoking and nicotine products could reduce the risk of COVID-19.
  - Studies That Suggest Smoking and Nicotine Protect Against COVID-19 Are Flawed
  - Overview of Controversial French Studies on Link Between Smoking and COVID-19

- Resources detailing the Links Between Smoking and COVID-19

Please email Emma Green (emma.green@theunion.org) if you wish to receive the bi-weekly STOP monitoring briefs.

BI partner Tobacco Free Kids is also keeping tabs on tobacco and e-cigarette company activities during COVID-19. For example, the organization analyzed data in 28 countries and found extensive use of social media to market and promote products. Details about pandemic-themed promotions, appropriation of “stay at home” social media hashtags, special discounts, delivery services, and unproven and illegal health claims can be found here.

7. **What is The Union’s position on smoking during COVID-19?**

- The Union is deeply concerned about COVID-19’s impact on the world’s 1.3 billion smokers and the LMICs whose health systems are plagued by tobacco-related disease.
- Smoking is one of the leading causes of NCD’s; according to WHO, people with cardiovascular disease, chronic respiratory disease, and cancer, among other NCDs, are more likely to experience serious illness or death from COVID-19.
- Smokers with COVID-19 may have worse outcomes than non-smokers, such as ICU admission, use of mechanical ventilation and death.
- The Union warns against the purported protective effect of smoking or nicotine against Covid-19. Such hypothesis, which is yet to be substantiated with scientific evidence, has resulted in misinformation, confusion, and potentially enormous public health damage.
- Governments should run mass media campaigns to amplify the key message: smokers should quit tobacco now. Tobacco cessation resources—quit lines, mobile messaging, internet support—should be sufficiently staffed, even in the face of lockdowns.
- The Union continues to urge countries to prioritise and implement proven, evidence-based policies from the WHO’s Framework Convention on Tobacco Control (FCTC).
- The Union also remains gravely 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 is also capitalizing on the crisis—by offering donations and partnerships—to improve its public relations.
- If the tobacco industry truly wants to ameliorate the COVID-19 crisis, it will immediately stop producing, marketing and selling tobacco.
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INTERNATIONAL UNION AGAINST TUBERCULOSIS AND LUNG DISEASE (THE UNION)

Please contact Megan Quitkin (megan.quitkin@theunion.org) if you have any questions about this brief.

9 Petrelli C et al. “Factors associated with hospitalization and critical illness among 4,103 patients with COVID-19 disease in New York City.”
14 Regina J et al. “Epidemiology, risk factors and clinical course of SARS-CoV-2 infected patients in a Swiss university hospital: an observational retrospective study.” MedRxiv. doi: https://doi.org/10.1101/2020.05.11.20097741


Miyara M et al. "Low incidence of daily active tobacco smoking in patients with symptomatic COVID-19 infection."


Hopkinson et al. "Current tobacco smoking and risk from COVID-19: results from a population symptom app in over 2.4 million people."


