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## RESEARCH INTEGRITY

# Covid 19: How harm reduction advocates and the tobacco industry capitalised on the pandemic to promote nicotine

Scientific papers suggesting that smokers are less likely to fall ill with covid-19 are being discredited as links to the tobacco industry are revealed, report **Stéphane Horel** and **Ties Keyzer**

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In the early days of the pandemic, media outlets around the world reported that smokers seemed to be under-represented among patients seriously ill with covid-19 in China and France. The headlines asked, does nicotine protect against covid-19?

The origins of this hype were two preprints published in quick succession in April 2020 by a team at the Pitié-Salpêtrière Hospital in Paris, led by Zahir Amoura. The first found that only 5% of patients with covid-19 were smokers.<sup>1</sup> Their second study hypothesised that nicotine might act on ACE2, the virus's entry receptor. "Nicotine substitutes may provide an effective treatment for acute infections such as covid-19," the authors argued.<sup>2</sup>

The stories made headlines worldwide. They were also picked up by libertarian media outlets such as the British online magazine *Spiked*. "Smoke fags, save lives," encouraged Christopher Snowden, director of lifestyle economics at the Institute of Economic Affairs, an industry sponsored think tank supported by the tobacco industry.

The World Health Organization worried that decades of tobacco control could be undermined. "Smoking is responsible for eight million deaths each year from cardiovascular and lung diseases, cancer, diabetes, and hypertension," WHO stated in response to the French studies, explaining that "available evidence suggests that smoking is associated with increased disease severity and mortality among hospitalized covid-19 patients."

It has since been roundly disproved that smoking protects against covid-19. Among other studies,<sup>3-5</sup> the OpenSafely dataset, based on the primary care records of 17.3 million adults in the UK, found that smoking, when adjusted for age and sex, was associated with a 14% increased chance of covid-19 related death.<sup>6</sup>

The *BMJ* can today also report on undisclosed financial links between certain scientific authors and the tobacco and e-cigarette industry in a number of covid research papers. This follows the high profile retraction of one such paper in the *European Respiratory Journal* last month,<sup>7</sup> after two authors failed to disclose conflicts of interest.

## Early concern

Tobacco watchdogs first became concerned after the publication of one of the Paris preprints, which floated the hypothesis that nicotine might have a

protective effect against covid-19.<sup>2</sup> The name of one of the coauthors rang alarm bells. A neuroscience celebrity and specialist in nicotine receptors, the retired Collège de France professor Jean-Pierre Changeux has a history of receiving funding from the most infamous tobacco industry front group, the Council for Tobacco Research, whose purpose was to fund research that would cast doubt on the dangers of smoking and focus on the positive effects of nicotine.<sup>8</sup> From 1995 to 1998, tobacco industry documents show that Changeux's laboratory received \$220 000 (£155 000; €180 000) from the Council for Tobacco Research.

This is a "sensitive issue [that] has unfortunately given rise to 'fake news' about me," wrote Changeux in an email to the authors of this *BMJ* article. He has not received any funding linked "directly or indirectly with the tobacco industry" since the 1990s, he assured us.

Even before the Paris preprints a Greek researcher, Konstantinos Farsalinos, was the first to publish a preprint on this subject, noting "the relatively low prevalence of current smoking" in patients admitted to hospital with covid-19 and relating it to ACE2 receptors.<sup>9</sup> In the absence of data on e-cigarettes he suggested that the potential protective effects of nicotine were "equally applicable" to them. Since then Farsalinos has championed the "nicotine hypothesis" in a dozen preprints and articles, as well as in tobacco industry circles such as the Global Tobacco and Nicotine Forum. In September 2020 he was a speaker in a panel on "the role of nicotine in the fight against covid-19" alongside the director of scientific research for British American Tobacco, which manufactures Lucky Strike cigarettes.

Farsalinos, a cardiologist affiliated to the universities of Patras and West Attica in Greece, is "one of the most prominent researchers in the field of electronic cigarettes," his own blog states. "Dr F", as he is known in the very active online vaping community, started publishing on e-cigarettes in 2011 and has published almost 100 scientific articles on the subject since.

## Tobacco harm reduction

For almost a decade Farsalinos has also been at the heart of a small, seemingly hyperactive network of scientists and consultants who advocate for vaping and tobacco harm reduction (THR) through initiatives sometimes akin to lobbying. Writing letters to WHO,

the European Parliament, the European Commission, and national governments, these advocates urge policy makers to “embrace harm reduction.” Stemming from treatment for drug addiction, the THR approach recognises that some smokers are unable to quit and should rather switch to non-combustible nicotine delivery products, positioned as “reduced risk products.”

THR is a complex concept, advocated by individuals with ties to the tobacco industry or to e-cigarette manufacturers, as well as by public health experts and consumers who are convinced that it is a solution. In the UK, for example, the basic principle of harm reduction in tobacco control is accepted as having a place in smoking cessation by the National Institute for Health and Care Excellence and the Royal College of Physicians, among others. Nick Hopkinson, reader in respiratory medicine at Imperial College and chair of Action on Smoking and Health, says, “There are staunchly anti-tobacco industry groups that acknowledge tobacco harm reduction among other approaches based on what we know about the safety [or] effectiveness of e-cigarettes.”

Ruth Malone, editor in chief of *Tobacco Control*, wrote in a recent editorial that “different countries already take very different approaches” to newer and novel nicotine and tobacco products (NNTPs), which “keep popping up like Whack-A-Mole,” and that “it can be hard to find a place to stand together on shifting sands.” She added, “The proliferation of new NNTPs creates much instability, with resources potentially diverted from work to advance basic tobacco control policies to studying, sorting, arguing about and addressing the wide range” of those products.<sup>10</sup>

WHO, which does not endorse THR, warns policy makers that electronic devices also pose a health risk. It has said of e-cigarettes, “There is insufficient data to understand the full breadth of their impact on health, as devices have not been on the market long enough.”<sup>11 12</sup>

However, tobacco companies redeployed THR as a marketing strategy to sell their new products: e-cigarettes and heated tobacco products. Philip Morris International, the largest cigarette manufacturer, began the staggered launches of IQOS, its stylishly designed heated tobacco product, in 2014. Smokeless products now account for nearly 19% of the company’s sales—nearly €5bn (£4.3bn; \$6.1bn) in 2019.

Although his preprint on the Qeios website<sup>7</sup> had gone largely unnoticed, Farsalinos was the first to publish the “nicotine hypothesis” formally in a journal, in the form of an editorial in *Toxicology Reports* in late April 2020.<sup>13</sup> The journal’s editor in chief, Aristidis Tsatsakis, whose name was not present in the preprint, featured as a coauthor. Another coauthor, A Wallace Hayes, was a member of Philip Morris International’s scientific advisory board in 2013 and has served as a paid consultant to the tobacco company.<sup>14 15</sup>

## University conflicts

Another coauthor on the *Toxicology Reports* editorial on the nicotine hypothesis is Konstantinos Poulas, head of the Molecular Biology and Immunology Laboratory at the University of Patras, where Farsalinos is affiliated.<sup>16</sup> The laboratory has received funding from Nobacco, the market leader in Greek e-cigarettes.<sup>17</sup> Their partnership included the development of “nicotine e-liquids” through funding of up to €75 000 a year, Greek accounting documents show.<sup>18 -20</sup> Nobacco has been the exclusive distributor of British American Tobacco’s nicotine delivery systems since 2018.<sup>21</sup>

Neither Farsalinos nor Poulas has ever declared this Nobacco funding in their published scientific articles. Both authors attended the press conference launching the Nobacco project in 2014.<sup>22</sup>

Poulas has not responded to multiple requests for comment for this article. In an email response Farsalinos said that he was unaware of the relations between Nobacco and Patras University and was therefore unable to mention it. “I have never participated in any project funded by a commercial entity,” he added, accusing us of “witch hunting.” Nobacco took the webpage mentioning their collaboration offline shortly after being contacted.

## Research funding

Farsalinos nonetheless received a fee<sup>23</sup> from the American E-Liquid Manufacturing Standards Association, in connection with two studies<sup>24</sup> and his presence as an expert at a meeting with US regulators in 2014. In declarations of interest through the years across journals, he also disclosed funding from the Tennessee Smoke Free Association,<sup>25</sup> FlavourArt,<sup>26</sup> and Nobacco for an earlier study in 2013.<sup>26</sup>

Poulas, for his part, declared in a 2019 paper “a scoping grant by the Foundation for a Smoke Free World,”<sup>27</sup> a non-profit established by Philip Morris International in 2017, with a funding commitment of \$1bn over 12 years to promote “harm reduction science.” Four years later, Philip Morris International is still the foundation’s only funder. Claiming “to end smoking in this generation” and distributing grants worth millions, the foundation is in other respects similar to the many front groups that the tobacco industry has set up in the course of the last century to manufacture doubt about the harmful effects of smoking.<sup>28</sup> In the days following its creation, WHO’s Framework Convention on Tobacco Control secretariat warned against what it considered “a clear attempt to breach the [Convention] by interfering in public policy.” More than 400 organisations, including 17 leading North American schools of public health, have since committed to refuse any funding from the Foundation for a Smoke Free World.

Two grants were in fact attributed in 2018 by the foundation to “Patras Science Park” for the “development of an Institute for Research and Innovation” on THR.<sup>29 30</sup> Tax documents filed in the US show that the grants, whose amounts are not disclosed on the foundation’s website, came close to €83 000.<sup>31</sup> The money went to NOSMOKE, a university start-up incubator headed by Poulas, which markets an “organic” vaping product.

## Retraction

This March the *European Respiratory Journal* issued a retraction notice for a July 2020 publication<sup>32</sup> cowritten by Poulas and Farsalinos, among others. “Two of the authors had failed to disclose potential conflicts of interest at the time of the manuscript’s submission,” the notice stated. Poulas did not declare his role at NOSMOKE (funded by the Foundation for a Smoke Free World); nor had José M Mier disclosed his activities as a harm reduction consultant to the tobacco industry. The retracted article had found that “current smoking was not associated with adverse outcome” in patients admitted to hospital with covid, and it claimed that smokers had a significantly lower risk of acquiring the virus.<sup>32</sup>

The foundation has invested heavily in the covid-19/nicotine hypothesis. In June 2020 it set aside €900 000 for research “to better understand the associations between smoking and/or nicotine use, and covid-19 infection and outcome.” Its request stated that the pandemic offered “both an opportunity and a challenge for individuals to quit smoking or transition to reduced risk nicotine

products.” In March 2021 the foundation named the US based consultancy BOTEC Analysis as the benefactor of the grant.<sup>33</sup>

“If anyone is going to take away our business it should be us,” wrote a British American Tobacco executive as early as 1992, in a correspondence unearthed by Dorie Apollonio and Stanton Glantz, researchers at the University of California, San Francisco. In 2021, amid a global lung disease pandemic, tobacco industry figures are increasingly pushing the narrative of nicotine as the solution to an addiction that they themselves created, with the aim of persuading policy makers to give them ample room to market their “smoke-free” products. This makes studies on the hypothetical virtues of nicotine most welcome indeed.

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