



Health practitioners should caution about misinformation and association of adverse effects of electronic cigarette use and COVID-19

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COVID-19, the deadly infectious respiratory disease caused by a coronavirus (SARS-CoV-2) that reached pandemic levels in early 2020, continues to impact many around the world. Many efforts to control COVID-19's spread have focused on preventing SARS-CoV-2 infection among those particularly vulnerable to the disease, such as people over the age of 60 and/or with underlying medical conditions. However, there may be other factors that increase SARS-CoV-2 infection and resulting morbidity and mortality, including the use of electronic cigarettes or electronic nicotine delivery systems (ENDS), also known as "vaping."

1. The effects of ENDS use: preclinical data

Pre-clinical studies suggest a mechanism by which chronic ENDS use could impact COVID-19 outcomes: ENDS aerosol, independent of nicotine, disrupts alveolar surfactant homeostasis (Madison et al., 2019). Notably, ENDS-induced disruption in surfactant homeostasis along with aberrant lung macrophage responses to viral infection increased morbidity and mortality in mice exposed to influenza (Madison et al., 2019). Human studies also demonstrate that ENDS use is associated with life-threatening lipoid pneumonia (McCauley et al., 2012; Thota and Latham, 2014; Atkins and Drescher, 2015; Modi et al., 2015; Itoh et al., 2018; Viswam et al., 2018). Thus, ENDS users may be at greater risk for negative outcomes associated with SARS-CoV-2 infection. Indeed, lung surfactant disruption and lung inflammation may represent a major concern regarding COVID-19 outcomes. The receptor for coronavirus is expressed on airway epithelial cells including the distal alveolar type II (AT-II) cells, a specialized type of stem cells in the lungs that make surfactant (Smith et al., 2020). This substance helps the alveoli in the lungs stay open between breaths and is critical to normal lung function. As the inflammation from COVID-19 pneumonia progresses, it causes

atelectasis (alveolar collapse), and hypoxemia, which are associated with loss of surfactant (Ainsworth and Milligan, 2002). Further, previous research found that lung cell samples from patients whose cause of death was SARS-CoV infection failed to express surfactant (Chen et al., 2007). The authors concluded that acute viral infection of AT-II cells could promote disruption of lung repair and induce acute respiratory distress syndrome (ARDS), a hallmark of novel coronavirus infection (Hu et al., 2020). Together, these findings suggest that disruption of lung surfactant production, as ENDS aerosol exposure does in mice, may exacerbate COVID-19 health risks. Research in clinical or population settings is needed to examine the relationship between ENDS use and COVID-19 further, though recent epidemiological research suggests an association between ENDS use and COVID-19 (Gaiha et al., 2020).

2. Public perception of ENDS use and COVID-19

Despite scientific evidence to the contrary, some ENDS users believe that ENDS use is *protective* against COVID-19. In a recent study that used a mixed-method approach to examine self-reports of how COVID-19 has impacted ENDS users from across the United States (Soule et al., 2020), some ENDS users reported that they believed: i) the heat generated from their ENDS device may kill the coronavirus, ii) ENDS use may increase immune system response, and iii) ENDS use may provide a protective layer to prevent COVID-19. The extent to which these beliefs are common is uncertain, though similar messages are being spread online. Indeed, at one website related to ENDS use and COVID-19 under the heading "Will vaping protect you from bacteria and viruses?", the text reads "So, does PG [propylene glycol] stop vapers from getting sick? We still don't know. Bottom line: it might. It definitely can kill bacteria and viruses. The trick, it seems, might be hitting the microbes at just the right moment with the right amount of PG..." (Vaping and Coronavirus,

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2020). This website refers to blogs, Twitter posts, and other media sources to support the text, and also includes references to empirical reports that appear to be related to the topic of ENDS use and COVID-19. For example, one blog post (Farsalinos, 2020) that is quoted at the website includes the erroneous text: "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." This blog cites research from the 1940s examining the possible anti-bacterial and anti-viral properties of propylene glycol gas (as opposed to aerosol generated from ENDS devices).

However, one of the empirical reports to which the text refers is from a 1980 U.S. Environmental Protection Agency document that predates COVID-19 by three decades and describes the effectiveness of aerosolized propylene glycol for reducing the number of airborne bacteria. The document concludes that "adequate experimental data is available to show that air sanitizers do not sterilize, disinfect, act as a germicide, or protect experimental animals from infections by airborne bacteria or viruses. Thus, claims of value in preventing or treating diseases, or providing any other health protection, whether expressed or implied, are not acceptable" (Sanitizers, 2020). However, the online text continues to cite a blog and a hypothesis generated from a case study (Miller and Hajek, 2017) in which the authors speculate that propylene glycol from ENDS use may have a beneficial antimicrobial effect.

3. Impacts of misinformation from health professionals, researchers, and media outlets

Further research is needed to examine what impact speculations that ENDS use may be protective for COVID-19 outcomes may have, especially when they are spread widely and rapidly online. However, recent events demonstrate how unsubstantiated suggestions regarding putative methods of reducing COVID-19 morbidity and mortality are of great concern because of their potential for influencing behavior. One example of this potential influence was documented recently when shortages of the drug hydroxychloroquine were observed after suggestions, made without supporting scientific data, that it could be used to prevent or treat COVID-19 (U.S. Food and Drug Administration, 2020). Similarly, after claims that nicotine might be effective for COVID-19 prevention or treatment, limits had to be set on nicotine replacement therapy products sold in France due to a spike in demand (France limits nicotine sales after researchers say it may protect against coronavirus, 2020). In these two scenarios, unsubstantiated suggestions may have caused drug shortages while increasing the potential for unintended consequences among individuals who self-administered these medications that were not proven to prevent or treat COVID-19.

Similarly, suggestions that ENDS use may be protective for COVID-19 made online, in popular media, or by researchers, have the potential to cause major negative impacts on public health. While very preliminary results (Farsalinos, 2020), based on minimal data of uncertain quality (Polubriaginof et al., 2017; Schofield and Hill, 1999) suggest that nicotine may play a protective role in COVID-19 based on reduced incidence of COVID-19 among cigarette smokers, much more research is needed before that hypothesis is addressed definitively. Indeed, data supporting this "smoker's paradox" are "limited and questionable" (Usman et al., 2020). Conversely, a meta-analysis and systematic review suggest that progression to severe forms of COVID-19 is more likely among smokers than non-smokers (Patanavanich and Glantz, 2020; Vardavas and Nikitara, 2020). There are still many unanswered questions regarding whether cigarette smoking plays a role in reduced incidence of COVID-19, and if any potential effects can be linked to nicotine or ENDS use. For example, cigarette smoking may have effects on squamous metaplasia that reduce viral binding (Farsalinos et al., 2020), or have other effects that are not dependent on nicotine. Furthermore, the long-term health effects of administering nicotine by inhalation of ENDS aerosol remain uncertain (Eissenberg et al., 2020), and current evidence suggests that chronic ENDS use increases the

morbidity and mortality associated with viral infection (Madison et al., 2019). Until more is known, health practitioners should continue to follow Centers for Disease Control guidelines regarding ENDS use. Specifically, while ENDS may benefit some cigarette smokers looking to quit smoking, ENDS are not safe for youth, young adults, pregnant women, or non-tobacco users (CDCTobaccoFree, 2020). There are currently no available data that indicate ENDS use is protective for COVID-19, and health professionals should share this message widely.

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Declaration of Competing Interest

The following authors report specific relationships that could be interpreted as implying a conflict (name author, nature of the relationship, and company or organization): E. Soule and T. Eissenberg are named on a patent application for a smartphone app that determines electronic cigarette device and liquid characteristics. T. Eissenberg is a paid consultant in litigation against the tobacco industry and are named on a patent for a device that measures the puffing behavior of electronic cigarette users. In addition, as of September 2019, T. Eissenberg is a consultant in litigation against the electronic cigarette industry.

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