Electronic cigarettes: a harm reduction option for smokers?

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Dear Editor,

An electronic cigarette (EC) or electronic nicotine delivery system is a tobacco-free device powered by a battery. It usually contains a solution of nicotine, flavorings, and various chemicals, some of which may carry potential risks. The amount of nicotine in an individual EC can vary, ranging from 0 to as high as 50 mg/mL. However, it is important to note that some countries, such as the U.S. and Canada, have imposed bans on the maximum concentration of nicotine in e-liquids, limiting it to 20 mg/mL. ECs are grouped by generations: first-generation as cig-a-likes, which closely resemble traditional cigarettes and are disposable or non-rechargeable, second-generation as tank models or 'vape pens', which feature refillable tanks and rechargeable batteries, and third-generation as adjustable power tank models. Newer fourth-generation 'pod' devices like Juul use nicotine salt formulations for higher concentrations and have a compact design. These are the most commonly used devices nowadays [1] (Figure 1). ECs are believed to aid in smoking cessation. EC aerosols have fewer damaging toxins related to the thousands of toxic compounds in tobacco smoke. The production of carcinogenic substances is unmistakably reduced by the lack of combustion in ECs. The severity of the respiratory and cardiovascular damage also seems to be less noticeable with ECs than with regular tobacco cigarettes [2].

Cigarette smoke delivers nicotine by combusting tobacco and has been found to be 33% more harmful than using ECs [3]. EC aerosols contain approximately 80 chemicals [4], whereas cigarette smoke contains around 7000 chemicals and 70 carcinogens [5]. EC comes with some distinct potential risks in contrast to cigarette smoking, including the possibility of fractures, burns, and bleeding due to battery bursts. The leakage of e-liquid can result in contact dermatitis, rashes, and allergic reactions. Alarmingly, there have been reports of e-liquid misuse in suicidal attempts through injection or oral ingestion. Moreover, the attractive taste of ECs has led to their widespread use indoors. Users of EC have reported higher usage of sleep medication compared to combustible cigarette users [6]. The combination of high wattage, elevated nicotine levels (up to 50 mg/mL, while a cigarette contains 20mg/mL of nicotine) [7], and low coil resistance in ECs may lead to increased nicotine exposure compared to tobacco cigarettes [6]. Acute effects of EC aerosol with nicotine include a significant increase in heart rate, an increase in blood pressure, and arterial stiffness. It also causes a sudden increase in flow resistance, indicating obstruction of the conducting airways. Increased arterial stiffness is a blood pressure-independent risk factor for cardiovascular events such as myocardial infarctions and stroke [8]. Butt *et al*., in a recent study, described a wide spectrum of histopathological findings seen in EC or vaping product use-associated lung injury, including acute fibrinous pneumonitis, diffuse alveolar damage, or organizing pneumonia, usually bronchiolocentric and accompanied by bronchiolitis [9]. Recent literature has also reported a strong correlation between the use of ECs and the development of pulmonary injury, thereby giving rise to respiratory symptoms and chronic obstructive pulmonary disease (COPD). Thus, chronic usage may lead to long-term adverse health effects [10,11].

EC liquids come in both nicotine and nicotine-free variants. Among the chemicals in ECs, nicotine is the most addictive [12]. Hence, nicotine-free ECs are much less addictive. A systematic review of 78 studies, involving over 22,000 participants, provides strong evidence that ECs with nicotine are more effective for smoking cessation compared to both nicotine-free ECs and nicotine replacement therapy (NRT). For every 100 individuals using nicotine ECs to quit smoking, around 10 to 11 individuals succeed, whereas only 6 out of 100 using NRT or nicotine-free ECs achieve the same outcome [1]. However, the involvement of nicotine in tumor promotion and progression with antiapoptotic and indirect mitogenic properties has also been reported [13]. In four cross-sectional surveys conducted in Connecticut in 2014, a considerable

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Key words: electronic cigarette, nicotine, tobacco, ENDS, cigarette.

Contributions: HamA, conceptualization and visualization; both authors contribute to data curation, writing of the original draft, review, and editing.

Conflict of interest: the authors declare no potential conflict of interest.

Ethics approval and consent to participate: no approval was required as this study is solely based on the author's observations and literature review and does not involve human subjects.

Informed consent: not applicable.

Patient consent for publication: not applicable.

Availability of data and materials: data available from the corresponding author upon request.

Funding: none.

Received: 23 February 2024.
Accepted: 26 August 2024.
Early view: 25 September 2024.

Monaldi Archives for Chest Disease 2025; 95:2965
doi: 10.4081/monaldi.2024.2965

percentage of youth (34.1%) were unaware of the nicotine concentration in their ECs [14]. Also, nicotine was detected in certain products that were marketed as nicotine-free [12].

While ECs have been promoted as a potential harm reduction tool for smokers looking to quit, it is essential to recognize that they are not without health consequences. Based on the available evidence and the lack of knowledge about the long-term effects of ECs on respiratory health, the Global Initiative for Obstructive Lung Disease (GOLD) also revised its stance on the possibility that ECs may help as a bridge for smoking cessation, and GOLD 2024 does not recommend this intervention for smoking cessation in patients with COPD as it can worsen the progression of the disease [15]. The American Heart Association (AHA) and the Spanish Society of Pulmonology and Thoracic Surgery (SEPAR) share concerns about the rise in EC use, particularly among young non-smokers. While the AHA acknowledges that ECs might serve as a harm reduction tool for smokers [16], both societies prioritize the potential dangers of initiation in non-smokers. SEPAR advocates the use of proven and effective treatments for smoking cessation, such as varenicline, NRT, bupropion, and psychological counseling, over ECs [17]. This suggests a need to establish clear, careful, and balanced policies that consider both harm reduction for current smokers and the prevention of initiation in non-smokers.

While experimental human studies show that ECs have acute cardiovascular effects consistent with stimulants, the long-term effects of ECs are not well understood because they have not been used long enough to observe chronic impacts. Most EC users are former or current smokers, complicating causation. Therefore, conclusions on the long-term effects of the use of ECs are currently unavailable. More longitudinal, methodologically sound studies are needed to understand the potential long-term impacts of EC use [18]. The popularity of ECs among youth, coupled with limited awareness of nicotine content, underscores the need for targeted education and rigorous oversight. Enforcing legislation to protect passive smokers from EC aerosols is of the utmost importance [2]. Additional clinical and animal exposure model research is critically needed as the use of EC products continues to grow. To work towards a smoking-free world, we should prioritize evidence-based tobacco control policies, effective cessation programs, and comprehensive public awareness campaigns [16].

Figure 1. The evolution of e-cigarettes.

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