

Electronic cigarettes: achieving a balanced perspective

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ABSTRACT

Concerns have been raised that the advent of electronic cigarettes (e-cigarettes) may be harmful to public health, and smokers have been advised by important agencies such as the US Food and Drug Administration not to use them. This paper argues that, while more research is needed on the cost–benefit equation of these products and the appropriate level and type of regulation for them, the harms have tended thus far to be overstated relative to the potential benefits. In particular: concern over repeated inhalation of propylene glycol is not borne out by toxicity studies with this compound; risk of accidental poisoning is no different from many household devices and chemicals available in supermarkets; concern that e-cigarettes may promote continued smoking by allowing smokers to cope with no-smoking environments is countered by the observation that most smokers use these products to try to quit and their use appears to enhance quitting motivation; concerns over low nicotine delivery are countered by evidence that the products provide significant craving reduction despite this in some cases; and e-cigarettes may help reduce toxin exposure to non-smokers.

Keywords Electronic cigarette, harm reduction, nicotine.

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Electronic cigarettes, or 'e-cigarettes', look and feel like regular cigarettes but do not contain tobacco, require combustion or produce smoke. To date, they have not been manufactured by tobacco or pharmaceutical companies. e-Cigarettes are marketed to smokers as an alternative to regular cigarettes, offering the 'freedom to smoke anywhere'. e-Cigarettes are becoming increasingly popular, especially in locations with stronger tobacco control regulations [1]. The e-cigarette has been the cause of significant debate both in the United States and around the world. Although there are many staunch supporters of e-cigarettes, there appears to be even stronger and more powerful opposition from the US Food and Drug Administration (FDA) and many individuals in the tobacco control community who would prefer that e-cigarettes be regulated as drug-delivery devices or banned entirely from the market. In recent months, several commentaries on electronic cigarettes have been presented [2,3]. One recent paper [4] by Cobb & Abrams in the *New England Journal of Medicine* reviews many of the strongly held concerns of regulators and those in the tobacco control community regarding the potential perils

of e-cigarettes, but does little to examine the evidence of the potential promise of e-cigarettes.

The concerns of Cobb & Abrams focus on the limited evidence regarding both the safety and cessation benefit of e-cigarettes. They question the quality control standards of e-cigarette manufacturers, the impact of repeated propylene glycol (a major chemical component of some e-cigarettes) inhalation by humans, and the possibility of children (or adults) being harmed by inadvertently consuming large refill bottles or cartridges of e-cigarette liquid. Regarding quality control standards, Cobb & Abrams are correct, as the current standards of e-cigarette manufacturers have been quite variable, which could be a significant public safety concern. However, the impact of repeated propylene glycol vapor inhalation by humans, as it may be a throat irritant, though understandable, does not seem to be reason enough to remove these products from the market. Furthermore, animal studies on repeated propylene glycol vapor exposure indicate no deleterious effects [5], and the nicotine inhaler has similar side effects [6]. Finally, their concern regarding the possibility of accidental child

poisonings is also something that should be investigated and monitored. Currently, e-cigarette companies label their products with warnings to keep cartridges out of the reach of children. However, it is important to put this concern into context. Many household products are potentially dangerous to children if consumed, yet we do not ban these products. For example, if a child consumed a large bottle of cherry-flavored liquid acetaminophen, this too would be dangerous—if not deadly. Similar to e-cigarette labels, for consumer products that are hazardous to children we simply warn adults to keep them out of their reach.

On the topic of cessation benefit, Cobb & Abrams argue that there is no evidence that e-cigarettes are beneficial for cessation, and that there may be a risk that e-cigarettes will be used only in places where smoking is prohibited by current smokers (i.e. 'bridge products') or function as attractive starter products for young non-smokers. We agree that these concerns need to be addressed through continued thoughtful, rigorous scientific investigations. Current research investigating these concerns is limited, although not non-existent. Moreover, the research indicates some promising effects. For example, Cobb & Abrams argue that e-cigarettes are unlikely to be useful for smoking cessation because of ineffective nicotine delivery, as evidenced by low plasma levels of nicotine by the smokers who used them. However, the study [7] that they cite to support this argument actually showed that one e-cigarette brand was able to significantly reduce subjective craving for cigarettes *despite* low plasma levels of nicotine. Another study [8], not mentioned by Cobb & Abrams, found that e-cigarettes not only deliver nicotine effectively (more rapidly than a nicotine inhaler), but that they significantly reduce cigarette craving and number of cigarettes smoked at a level similar to that of nicotine replacement products. Furthermore, a recent clinical trial [9] published after the Cobb & Abrams article showed that e-cigarette use may motivate quitting. Among 40 smokers who were initially not interested in quitting but who were asked to use the e-cigarette *ad libitum*, 22.5% achieved sustained smoking abstinence (biochemically verified) at 6-month follow-up [9]. Furthermore, an additional 12.5% and 32.5% reduced their smoking by $\geq 80\%$ and $\geq 50\%$, respectively [9]. Several survey studies support these findings. In a large international survey of current, former or never users of e-cigarettes, 72% of users reported that e-cigarettes helped them to deal with cravings and withdrawal symptoms, 92% reported reductions in their smoking when using e-cigarettes, and only 10% reported that they experienced the urge to smoke tobacco cigarettes when using the e-cigarette [10]. Moreover, of more than 2000 former smokers in this survey, 96% reported that the e-cigarette helped them to stop smoking, and 79% reported fearing

that they would start smoking again if they stopped using it [10]. Consequently, removing e-cigarettes from the market or discouraging their use could harm public health by depriving smokers of a potentially important option for smoking cessation.

Although larger trials are needed to help answer questions regarding the possibility of dual use (i.e. smokers maintain current smoking levels and add e-cigarettes), the available evidence suggests that this is not the case. Research indicates that the vast majority of e-cigarette users use e-cigarettes for either complete (79%) or partial replacement (17%) of tobacco cigarettes [10]. In addition, fears that smokers will forego traditional cessation methods in favor of e-cigarettes has not been substantiated. A substantial number of current e-cigarette users report having tried to quit previously using nicotine replacement therapies (70%), bupropion (29%) and/or varenicline (18.6%) [10]. This finding, taken together with the Bullen *et al.* [8] finding that placebo e-cigarettes also reduced craving, withdrawal symptoms and number of cigarettes per day, suggests that e-cigarettes address an additional behavioral component (e.g. hand to mouth gesture, 'throat hit' of the vapor, exhaling visible vapor) beyond the pharmacological effect of nicotine provided by current FDA-approved therapies. As a result, for smokers who have failed to quit with current approved therapies, e-cigarettes offer an alternative method of quitting, or a method of supplementing these currently approved therapies. Moreover, withdrawing e-cigarettes from the market or discouraging ex-smokers who have quit by using these devices to discontinue their use and switch to approved forms of therapy is unlikely to be a boon for public health, as the current evidence suggests that e-cigarette users often have high levels of nicotine dependence and have tried and failed to quit smoking with multiple forms of approved cessation therapies [10]. It seems misguided to ask people to discontinue an approach that is working in favor of an approach that has already been ineffective for them.

Finally, an often unconsidered advantage of e-cigarettes is that they do not require combustion and therefore produce no second-hand smoke exposure (SHSe) to the user or to individuals in the smoker's environment. Second-hand smoke, especially in homes with children, poses a serious public health risk increasing the incidence of sudden infant death syndrome, respiratory illness, middle-ear disease and asthma [11,12]. Children aged between 3 and 11 years have the highest levels of SHSe, probably because they spend a majority of their time in close proximity to a caregiver who smokes [13–15]. Despite the strong national effort of introducing smoking bans in public spaces, children living with smokers have not experienced any reduction in their SHSe, as evidenced by serum cotinine levels [16].

Furthermore, clinical interventions aimed at reducing children's SHSe by targeting caregiver smoking behavior (i.e. cessation and/or smoking outside) often fail to produce long-term cessation and result in minimal to no reduction in SHSe for children, as measured by objective indicators such as urinary or serum cotinine or a child-worn passive smoke monitor [17]. A significant majority of parents return to smoking or do not maintain consistently smoke-free homes. As such, the current methods of reducing caregiver smoking behavior cannot be relied upon as the sole means of reducing children's SHSe. The use of e-cigarettes by caregivers who smoke and who are unable or unwilling to quit smoking by more traditional means may be a viable alternative method to reduce children's SHSe.

We contend that the initial evidence suggests that e-cigarettes offer more promise than peril, but more research needs to be conducted. The debate over e-cigarettes will no doubt continue. It is our hope that those participating in this debate report all sides of the issue, considering both the potential harm e-cigarettes could cause the user and the potential harm the tobacco control community could cause by dismissing the e-cigarette prematurely as a viable alternative for smoking cessation and second-hand smoke reduction. We also encourage e-cigarette investigators to draw conclusions within the appropriate context to prevent misleading conclusions. For example, the FDA held a press conference during which it warned consumers not to use e-cigarettes because of the presence of toxic chemicals, including diethylene glycol and carcinogens (tobacco-specific nitrosamines) [18]. What the FDA did not report was that it detected only trace levels of carcinogens (0.07–0.2% of the corresponding levels in cigarettes) [19,20] at levels similar to the nicotine patch and nicotine gum, and found diethylene glycol in only one of the 18 samples tested (a chemical that has not been found in any other brand since) [20]. Viewed in this context, instead of warning consumers not to use e-cigarettes we would argue that these data suggest that e-cigarettes may pose much lower carcinogenicity than regular cigarettes and are probably similar in carcinogenicity to FDA-approved nicotine replacement products. However, we recognize that stronger quality control standards need to be utilized by e-cigarette manufacturers to prevent human exposure to toxic chemicals, such as diethylene glycol. Indeed, some e-cigarette manufacturers are attending to safety concerns by making their products safer, such as using distilled water and glycerine instead of propylene glycol vapor. Overall, we hope that continued discussion about the promise and perils of e-cigarettes is based on a balanced view of the available science, rather than an ideology that opposes harm reduction without consideration of both sides of the issue, including potential public health benefits.

Declarations of interest

None.

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