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Electronic Cigarettes and Public Health

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Executive Summary

Electronic cigarette (e-cigarettes, also known as Electronic Nicotine Delivery Systems or ENDS) use has grown rapidly within a few years and this rapid expansion of their use took public health professionals in tobacco control by surprise. The products are regulated to different extents in different jurisdictions and new products and forms are being manufactured constantly and added to the markets. Unlike other new tobacco-derived products that had limited sustained interest in them, e-cigarettes have become a major product used globally. E-cigarette use and acceptability vary by country making it a global health issue in terms of assessing the evidence and reaching consensus about harms versus benefits. The recent outbreak of lethal respiratory distress illnesses that are associated with e-cigarette use gained worldwide attention about serious risks these products may cause. There are major concerns and restrictions regarding e-cigarette use in many countries, largely because of the unknown consequences of epidemic nicotine use by youth; conversely, e-cigarettes are seen as part of the solution to reducing the harm from cigarette smoking in some jurisdictions. The WHO's report on the tobacco epidemic released in July 2019 concluded that e-cigarettes are not recommended for smoking cessation and the harm to health must be better evaluated, but that the evidence regarding their role in nicotine addiction among young people is convincing. This policy brief provides an overview and assessment of possible policy approaches to address this major public health issue.Although the United States is a rich source of data this should not imply that this policy brief is focused on the United States, nor is this brief meant to be a review article that covers every aspect of this phenomenon, especially given the uncertainty and rapidly changing situation with regard to harms or potential benefits attributable to e-cigarettes.

Context and Importance of the Problem

Origin and Current Use

The e-cigarette was not created by the tobacco industry but rather from small companies, starting with its inventor in China in 2007.This open market led to dramatic increase in the number of new products, some of which received wide acceptance and had a major share of the market, such as JUUL, that is being widely used by teens and apparently marketed for them (1). Most recently the tobacco industry invested billions to own a big share of JUUL. This adaptation of the tobacco industry to new products and global inconsistencies in the regulation of e-cigarette products are major concerns to the tobacco control community.

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The methods of using e-cigarettes include, in addition to the conventional 'vaping', non-traditional ways such as direct dripping of the e-liquid leading to much higher toxic aldehyde production (2), which is reportedly very popular among teens(3). Using other drugs of abuse or using mixtures of them instead of nicotine when vaping, as well as use of high doses of nicotine, are all related to the lack of effective regulation of e-cigarettes. Flavoring of e-cigarettes is serving to propagate their use among both youth and adults. Based on the existing data, almost all youth (96% of them in the PATH study from the United States) initiate use with flavored e-cigarettes, which are preferred over non-flavored types, which is why the large majority of youth continue to use the flavored type after initiation (4, 5). There are over 15,000 flavors, and menthol or mint flavored e-liquid is very popular, but the fruit and candy flavors are the most preferred (6). Further, these flavoring are approved for ingestion, but not for inhalation and there are several case reports indicating serious respiratory and cardiovascular health impacts associated with flavorings used in e-cigarettes (7, 8). In light of both the recent severe respiratory disease outbreak and other potential risks associated with e-cigarette use, there are now serious calls to ban flavored e-liquids and revisit regulations.

It should be noted that a minority of e-cigarettes contain no nicotine. These e-cigarettes are much less likely to be addictive, although the unquantified health risks of inhaled aerosol flavorings and excipients remain and might be linked to the respiratory disease outbreak recently reported, which was associated with the use of e-cigarettes.

Regarding the use among teens, there is no disagreement that use of e-cigarettes has become the number one product being used illegally at the present time by middle and high school students in the United States (9). United States national data also showed that in one year there has been a doubling of e-cigarette use among middle and high school students (9). There is evidence this is also the trend in the UK where there has been a doubling in ever use by teenagers, although no evidence to date of an increase in their regular use (10).But this is expected given nicotine, delivered by e-cigarettes as vapor, is highly addictive. To date, particularly before the evidence of e-cigarette associated respiratory diseases, the gateway to tobacco use is the most serious risk of e-cigarettes feared by most public health professionals for teens and young adults, who otherwise may not have tried nicotine in tobacco products nor become addicted to it. In the UK there is limited evidence that young people who have used e-cigarettes may be more likely to start smoking (11), a trend that must be closely monitored.

Harm

E-cigarettes are currently a public health controversy that requires careful consideration by health policy makers based on a growing research literature. The harm vs benefit assessment should take into consideration the risk of introduction of nicotine to nonsmokers and the risk of severe, potentially lethal, lung or other as yet unidentified diseases to users, and the benefits to smokers who are helped to quit combustion cigarettes. The concern of most public health professionals about e-cigarettes is that we are introducing a product that delivers nicotine, which is addictive, with a range of excipients and other additives, the nature and safety of which manufacturers were not required to disclose before putting them in the market.

Initiation of use or addiction to nicotine and then adopting or reverting to combustion cigarettes (12, 13), or for smokers to have difficulty in quitting because of higher nicotine consumption from their

combination of cigarettes and e-cigarettes (14), would be by all means and measures harmful to those individuals and the health of the public.

Prior to the severe respiratory distress cases linked to e-cigarettes, there was general agreement that e-cigarettes are less harmful than combustion cigarettes and smokers would reduce the serious long-term risks to their health by using them instead of conventional cigarettes. However, there is now serious reconsideration about safety of e-cigarettes because of the findings of consistent lung tissue damage, including inflammation and damage of alveoli causing severe respiratory distress (15) and a new cluster of an emerging respiratory syndrome across large geographical areas and population that was previously unrecognized. One recent peer reviewed article questions whether the respiratory health effects of e-cigarettes are less than those of combustible tobacco products (16). Due to the lack of consistent and long-term epidemiological or data about these products, there are differences in opinion about the harms and benefits in the long-term, since they are relatively recent products and it will take some years for them to have measurable impacts on the health of a population. Some products, such as the "JUUL" have clearly shifted the argument about risks of harms and benefits towards harms, because of the wide appeal and targeted marketing to teens and the very high nicotine concentration that in some products is more than double the levels of other products and each pod of e-liquid equivalent to 20 cigarettes (17). Further, there is growing evidence that short-term exposure to e-cigarette aerosols can cause acute endothelial cell dysfunction, DNA damage, and signs of oxidative stress, as well as temporarily increased heart rate (18), the potential health impacts of which are not yet understood. These factors should be reflected when promoting e-cigarettes as a less harmful product, which nevertheless is not entirely safe (18). Furthermore, another concern for both smokers and nonsmokers is new evidence that is emerging to show that e-cigarettes are more harmful than had been claimed, especially the health impact of flavoring, as well as nicotine, that causes DNA damage (International Agency for Research on Cancer), brain damage among teens (US Surgeon General), and the harm from liquid Propylene glycol, metals, silicate, ultrafine and nano-particles, and carcinogenic flavoring byproducts (18). Very recently it was found that e-cigarette flavor mint and menthol had 100-1000 higher concentrations of pulegone than what is considered safe by IARC, even though pulegone is a known animal carcinogen that causes hepatic and pulmonary and other cancers in animal feeding studies (19). It remains to be seen if an effectively regulated market would prevent exposure to harmful levels of these contents.

Risk of poisoning from e-liquid and burn from explosion and malfunctioning of e-cigarettes is another public health hazard that may be overlooked, although reported serious incidents are not uncommon. The American Association of Poison Control Centers reported 3000-4000 cases of poisoning from e-liquid and e-cigarettes every year since 2014, and between 2015 and 2017 there were over 2000 emergency visits in hospitals in the United States (20, 21). The majority of e-cigarette burns are severe and require skin grafting.

Smoking Cessation

The use of e-cigarettes is increasing rapidly among both smokers and nonsmokers, but according to independent reviews from Cochrane Review, The United States Surgeon General, The United States Institute of Medicine, United States Prevention Task Force, and other entities globally, there is so far insufficient consistent and clear evidence concerning their role in meaningfully helping the smokers who use them to quit, to recommend them universally as a cessation product, without careful and effective

regulation to restrict access to never-smokers. In the United States, e-cigarettes are not seen as a cessation product and it is believed that there is not enough evidence to support it as such. This is stated in the Surgeon General report (22), by the USFDA (23), and the National Academies of Sciences (22), which are three authoritative sources for policies in the United States. There are some studies that show benefit for smokers, but these studies are counterbalanced by studies that show there is harm from these products, insufficient evidence for achieving cessation and even encouraging higher levels of smoking because of the higher nicotine exposure according to the WHO (24). The WHO report reached these conclusions and warned that despite lack of conclusive evidence there is more indication of net harm from use of e-cigarettes than net benefit (24). Accordingly, the WHO's recent Framework for Tobacco Control Convention Treaty negotiations renewed the restrictions on e-cigarettes and other nicotine and tobacco delivery systems and there is limited evidence that e-cigarettes may be effective aids to promote smoking cessation (25). The exception to date is the review from Public Health England (PHE) that found e-cigarettes to be far safer than cigarettes and, as a result, PHE now recommends e-cigarettes for smokers as a smoking cessation product where all other methods have failed. The German Addiction Society also recommends e-cigarettes only when other cessation products are not effective or declined by the smoker.

Critique of Current Policy Options

Epidemiology is a unique science that can be used systematically to address major public health problems, from the 19th Century's cholera epidemics to major contemporary challenges such as Ebola and chronic non-communicable diseases. This approach should be applied to e-cigarettes to address the controversy surrounding their use. The recent outbreak of severe and sometimes lethal lung diseases in the United States associated with e-cigarettes use has led to calls by the Centers for Disease Control and Prevention to immediately stop the use of e-cigarettes until proper epidemiological investigation is carried out to determine the cause of this outbreak(26). The recent severe respiratory distress linked to using e-cigarette products is an added risk not previously accounted for and its sudden acute impact leading to deaths has brought to attention why proper evidence from epidemiological and clinical studies should guide the use of these products and the policies associated with their use.

Regulation

Inadequate regulation of these products in jurisdictions all over the world has led to manufacturers using chemicals in e-liquids that are a risk for human health and used by millions.

The USFDA has issued a ruling to regulate the manufacture of e-cigarettes, but has been slow in applying these regulations. They issued a warning about the widespread use of these products among youth in the past two years, attributed to advertisement campaigns targeting minors. There is widespread advertising for these products accessible to teens and youth as well as repeated evidence of targeting young people, by use of celebrity endorsement on social media, introduction of candy, dessert, and fruit flavors and even promotion by sex appeal.

Epidemiological data are needed to support development of evidence-based policies to limit use of e-cigarettes to those smokers who are likely to benefit from their use by switching and quitting combustion cigarettes.

This public health phenomenon has been spreading faster than the pace of research to provide solid evidence about its harms and benefits. Different rules and regulations exist across countries and jurisdictions. It has therefore become a controversial public health topic today, and requiring much more research. When there is no robust evidence about the balance of benefits and harms of a new product, this leads to the situation we have with e-cigarettes, where different players will use the evidence that supports their view, and especially when there is a vested interest. This difference in opinion may have contributed to a delay in regulation. The lack of policy and evidence and the delay in introducing consistent, effective regulation has left a void being filled in many jurisdictions and the media by inaccurate data, advertisement, inadequately regulated products, all encouraging the widespread and popular use of these products.

The precautionary principle invokes the notion that when there is uncertainty about a product or approach in terms of harm to the public, the precautionary approach will not support the widespread dissemination of such product. The burden of proof is then on the producers to demonstrate their product does not cause harm before making it widely available to the public. Health policy makers should have invoked the ethical precautionary principle before allowing the propagation, advertising, and large-scale consumer sales of e-cigarettes and related products. This would mean in any jurisdiction making accessible these products for smoking cessation in adults, only in the presence of consistent independent research evidence of benefit substantially outweighing harm, and ongoing evaluation to support such measure. Introducing policies with penalties regarding advertising, marketing, sponsorship and sale to underage individuals and prohibiting flavors that appeal to children would lead to restrictions similar to those covering cigarettes and other smoking tobacco products. Swift and effective regulation should be imposed to protect consumers and hold manufacturers legally responsible to prevent unregulated products from reaching markets. Following the precautionary principle, there is a need to prohibit the sale of any new forms before providing evidence of safety from comparative and large scale epidemiology studies by independent research and evaluation. Public health professionals need to promote short-term and long-term evidence-based policies to address the negative and harm reduction contribution of this product.

Lack of effective policies and regulations are allowing the production, advertising, and sale of e-cigarettes to continue with limited restrictions and often lack of enforcement in many countries. Even where national regulation is robust, the social media and internet market provides largely unregulated platforms for advertisement and promotion of the products.

Some countries, including Japan, Brazil, Australia, India, and Norway, have strict restrictions or bans on e-cigarettes, and severe sanctions for those found in possession. San Francisco, where JUUL has its HQ, has recently (25 June 2019) become the first city to ban e-cigarettes in the United States, but in the wake of the respiratory disease outbreak, the State of Michigan is planning a ban, Massachusetts is to ban e-cigarettes for 4 months, and Rhode Island and New York City are planning a ban on flavored e-liquid sales. In the State of California, in the United States, the Governor has applied policies to e-cigarette use and sales that are very similar to those applicable to cigarette use and sales.

In some countries, for example, Australia, nicotine-free e-cigarettes are excluded from the very stringent restrictions on sales of nicotine-containing e-cigarettes.

The recent rise in use of e-cigarettes among teens in the United States has prompted tobacco control entities such as the Centers for Disease Control & Prevention (CDC) and the Food and Drug

Administration (FDA) in the United States to focus on the impact of nicotine upon youth. The "Real Cost" media campaign is targeting 12-17-year olds through social media sites to make them aware of the risks of harm from e-cigarettes. However, without a robust e-cigarette cessation program to help the already addicted youth, education has historically not been effective in this age group (27). The estimated 2 million youth in the United States who have used or are using e-cigarettes at high nicotine concentration will need special attention and comprising cessation programs coupled with aggressive media campaigns and effective regulation. There were warning signs of this emerging epidemic among youth, but no serious prevention intervention was put in place. Notably, e-liquids and e-cigarettes are much more affordable than cigarettes in many jurisdictions, due in large part to much lower taxation, making it easier for youth, in particular, to get addicted to the often high levels of nicotine in this relatively unregulated market.

Policy Recommendations

1. Regulations for new products: Apply the precautionary principle to e-cigarette regulations and policies of requiring producers of e-cigarettes, e-liquids, as well as manufacturers of other new products, such as heat-not-burn products, to demonstrate that such products are not associated with harmful health impacts or new addictions, before being marketed, and then follow with mandatory post-marketing surveillance and reporting akin to those for medicinal products.

2. Regulations for existing products: regulation should be immediately introduced by each jurisdiction, regarding the content of nicotine and other constituents in existing e-cigarettes, including a ban on flavors and structural design features that make them particularly attractive to youth.
3. Enforcement of restrictions and regulations: There are likely a lot of unknown health impacts from e-cigarette use in the long-term, therefore:
    a. There is a need for effective enforcement of regulation to severely penalize advertising and sales of e-cigarettes to youth, especially online and through social media,
    b. Require vaping industry to highlight the known risks of harm of using e-cigarettes on packaging and advertisements and refrain from claiming they are safe.
4. Smoking cessation:
    a. Adults: Based on evidence, albeit inconsistent, that some individuals are assisted in quitting smoking cigarettes by the use of e-cigarettes, the use of e-cigarettes on a case-by-case basis can be advised by health care providers to assist people to quit smoking if other established cessation measures fail, as long as consumers are aware of the known, and as yet unknown, possible long term health risks of e-cigarettes and the known substantial risks of tobacco products.
    b. Youth: Providing easy access to cessation advice and support for those teens who become addicted to these products, comparable to the cigarette smoking cessation programs accessible to adult smokers of combustion cigarettes.
5. Research: Support policies to require local and national independently funded epidemiological studies, including large scale clinical trials, as well as long term longitudinal prospective observational studies in different countries with different experiences with e-cigarettes, to upgrade the evidence of all short- and long-term harms and benefits attributable to e-cigarettes.

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