Updated evidence on vaping: a report from the ENDS repository

UPDATED EVIDENCE ON VAPING:

A REPORT FROM THE ENDS REPOSITORY

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Presentation

In this XXI century, the global technological innovation has reached the tobacco industry, which through the combination of high-level engineering continues to manipulate the tobacco leaf to deliver nicotine to its users in a more efficient way; through combustion-free and sophisticated electronic systems that aim to reduce exposure to tobacco smoke among non-users. With these arguments, the tobacco industry seeks to reposition itself in the society while continuing with its last century millionaire profits, using new and old marketing tactics with specific objectives aimed at retaining current smokers of combustible cigarettes, persuading them to make a change towards the new non-combustible electronic products, but relevantly recruiting the new generations in the powerful nicotine addiction.

During this last decade of market repositioning, they continue to deny the conclusive scientific evidence regarding the nicotine addiction and the harmful health effects to both users and those unintentionally exposed. Similarly, they have dedicated themselves to manipulate scientific information with the incorrect argument of "harm reduction" while implemented along with an aggressive marketing strategy aimed at young people, women, and groups of influence in a digital world connected through social networks, which is practically unattainable with the current global tobacco regulation.

Mexico, immersed in this globalized reality, is home to 15 million smokers of combustible cigarettes, with an epidemic that has focused on men, but which maintains a growing trend of consumption among women, young people, and low-income groups. Although in 2004, the World Health Organization Framework for Tobacco Control (WHO-FCTC) was signed and ratified, and the General Law for Tobacco Control (LGCT) has been implementing health warnings with pictograms and an increase in taxes; the tobacco industry has boosted its marketing strategies to position its new products despite being prohibited by law.

Considering the evolution of the tobacco epidemic at a global and local level, the project "The Repository of electronic nicotine administration systems (SEAN) - "The Repository SEAN-" was carried out, which aimed to analyze the current scientific literature (2017-2019) related to the SEAN aiming to inform both, decision makers and society in general about the scientific evidence, free of conflict of interest, that allows answering questions of interest in the field of public health. This report compiles a review of the state of the art, the information containd here allows readers to argue with a scientific base in academic and public policy debates related to the legislation and regulation of new tobacco products and vaping. This updated information has methodological validity, is reliable, accessible, and systematically describes the sources of original information, and the conflict of interest of the authors.

This current review of the scientific literature concludes that nicotine is a powerful addictive substance, and it is a very hard addiction to give up, so making it accessible to the adolescent population will trap the new generation of consumers of the 21st century, who will not only use these new products, but will also use combustible cigarettes. Since the supply of nicotine will continue for smokers of combustible cigarettes, they will not have the opportunity for complete cessation and instead will continue as dual users. The health damage from its repeated use already occurs among youth populations, the EVALI (lung injury due to the use of new tobacco products) outbreak has been underestimated by the tobacco and vaping industry, but the negative effects at the population level of this new driver of the tobacco epidemic are yet to come.

The report invites us not to lose sight of the dimension and magnitude of the tobacco epidemic and to continue with the full implementation of the WHO-FCTC and with the guidelines of the Conference of the Parties COP 6 and 7 related to the regulation of new products, defending the perspective of article 5.3 of the WHO-FCTC that allows public health decisions to be made with total independence from the tobacco and vaping industry, prioritizing the health of the population and future generations, beyond commercial and economic interests that this industry could generate for the economic development of this century.

Luz Myriam Reynales Shigematsu

Executive summary

Tobacco use is the number one preventable cause of disease and death worldwide. In addition to the potential harm that it causes to the health of its consumers, it is also a problem for the tobacco industry (TI) since, when it is used correctly, cigarettes kill more than a third of its consumers. This means that the TI must constantly renew its consumer base and fight against regulations that seek to discourage tobacco use. To deal with these situations, the TI is constantly promoting technological innovations that appear to reduce the risks caused by smoking. Its most recent attempt are the electronic nicotine delivery systems (ENDS) also known as vapers or vaping devices. ENDS have been advertised as devices that promise to be a safer consumption option than combustible cigarettes. However, to date, the existing scientific evidence is not enough to determine whether, in fact, ENDS are a safer consumption option. The objective of this project was to analyze the current scientific ENDS literature (2017-2019), to document the discussion about these devices through informative materials that disclose accurate information in an accessible way. To inform decision-making on the matter, relevant themes such as: conflict of interest, cessation, recruitment, physical harm, dual use, flavorings, toxic components, nicotine, marijuana use, alcohol consumption, and advertising were analyzed. In general, it was found that ENDS research has a limited amount of good quality information, and that conflict of interest plays an important role by increasing the probability of having positive results towards ENDS by 21 times if the research conducted was related to TI or the vaping industry. In addition, the results showed that although ENDS have been promoted or advertised, as devices to help quit smoking, their unique characteristics such as customization, flavors, and designs, makes them more attractive among adolescents and young people, encouraging nicotine consumption and other toxic components from very early ages. The tobacco and vaping industries commercialize their products even in countries where they are prohibited and have managed to penetrate the psyche of people, making them believe that vaping is a low-risk activity, bringing serious consequences for public health in countries that are still struggling against the ongoing tobacco epidemic. A first step to advance in the study of vaping is stopping the comparative with combustible cigarettes. With a product as harmful as combustible cigarettes, vaping seems like a better option, but we need to ask ourselves if vaping is preferable than to not consume any tobacco product?

Introduction

After dozens of years of evidence and arguments, currently no one doubts that tobacco use is one of the biggest global public health problems. It is the first route for nicotine consumption (being one of the most addictive substances in existence) and its use is widespread. With more than 7.1 million attributable deaths per year,[1] it is the worldwide leading preventable cause of disease and death. In addition to a public health problem, the potential of harm caused by tobacco is also a "challenge" for the tobacco industry (TI) since it is the only legal product that, when used as indicated by the manufacturer, kills between a third and a half of people who consume it.[2] This implies that TI has to constantly renew its consumer base, in addition to fight the information and regulations that seek to discourage nicotine consumption. To deal with these situations, since the invention of roasted tobacco in 1916, the TI has developed and promoted technological innovations that appear to reduce the risk of disease caused by smoking.

The acetate filter in 1954, the menthol cigarette in 1960, light cigarettes in 1966 or low tar cigarettes in 1970, are part of this continuum of innovations[3]. At the time, all these products were advertised as a solution to the health hazards caused by smoking. Some of these innovations had been backed up with allegedly scientific information, usually paid for by the TI itself, supporting the claims of being healthier. Unfortunately for public health, none of these products reduce the risk cause by smoking.

The latest iterations in this continuum of innovation and renewal for nicotine consumption are represented both by vaping devices, also known as electronic nicotine delivery systems (ENDS), and heated tobacco products (HTP). Both, ENDS and HTP, claim to be a less harmful way of nicotine delivery for the user and those around them, however, these products work in different ways:

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1 ENDS, originally called electronic cigarettes, are made up of a resistor, a battery and a liquid storage or transport system. These devices function by aerosolizing a liquid consistent of a base, flavorings, and nicotine.

2 HTP consist of a lancet connected to a battery for heating a tobacco cartridge specially prepared with humectants. In this way, an aerosol loaded with nicotine is obtained which is consumed by the user.

These products have entered the markets of many countries, often illegally, and have been promoted as an alternative for nicotine consumption, 95% less harmful than combustible cigarettes.* and as products that help quit smoking. These ideas have been used as banners for consumer groups and their producers, as well as the TI, although without clear scientific support.**

In Mexico, these products have been prohibited since 2008 based on the interpretation of to the section VI of article 16 of the General Law for Tobacco Control (LGCT) made by the Federal Commission for Protection Against Sanitary Risks (COFEPRIS for its name in Spanish).[4] This prohibition was reinforced in February 2020 through a presidential decree that prohibited the import of these products.[5] However, this ban has not been free of controversy, several appeals have been filed against it, with both negative and positive results. On the other hand, more than a dozen proposals to modify the LGCT to regulate, or more clearly ban these products had been presented in both the Deputies and Senators chambers, however, until the date of publication of this report none has progressed. Despite its prohibition, the consumption of these products has proliferated in the country. The 2015 Global Adult Tobacco Survey (GATS) reported 557,104 e-cigarette users, between the ages 15 to 65 years in Mexico.[6] However, by 2016, this number had increased to 931 thousand according to the National Survey of Drugs, Alcohol and Tobacco consumption (ENCODAT for its name in Spanish).[7] In this same survey, it was found that 33.9% of non-smoking adults, 54.3% of adult smokers, and 45.3% of adolescents knew or had information about e-cigarettes. Similarly, among non-smoking adults, 2.6% have tried e-cigarettes and 0.3% were current consumers. Among smokers these numbers increase to 18.2% who have tried and 4.5% were currently consuming them. Finally, among adolescents, 6.5% have tried and 1.1% were current consumers.[7]

In a representative survey conducted in 2015 among more than 10,000 public middle school students in the cities of Mexico City, Guadalajara, and Monterrey, results showed that 51% of the students had heard of vaping, 19% believed that it was less harmful than smoking, and 10% had tried them. In 2016, in this same population of students, who were already in 3rd grade of middle school, the prevalence of vaping (12%) was higher than the prevalence of combustible cigarette consumption. (11%).[8,9]

This increase requires an informed discussion about nicotine consumption through these new devices to know if they really represent an advantage for public health in Mexico. Currently, there is a lack of knowledge about the consensus, discoveries, and scientific data surrounding these products and their consumption, beyond the conflicts of interest and the information selected to support a specific stance. Scientific knowledge, as part of an ongoing process, revises and rewrites its results from new information and new discoveries, especially in a new and changing phenomenon such as e-cigarettes.

Due to the things above mentioned, the SEAN Repository Project was designed aiming to analyze the current scientific literature (2017-2019) related to SEAN and to inform the discussion regarding these devices through accessible information materials. This report is the sum of what was found during a standardized methodological review, that will be explained in the following section, to provide an overview of the topic, reflecting as much as possible, the current scientific landscape without bias. The report is presented as a review of the state of the art, which seeks to document the debate regarding vaping with recent, free of conflict of interest, reliable, and accessible scientific information.

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* 95% is perhaps one of the most powerful messages in this regard, as it sounds good, is memorable, and is easy to get across. It is also one of the most misleading. Emerged from the article published by David Nutt and co-authors in 2014,[145] and subsequently taken up by other studies (mainly in the United Kingdom), it has been used as a measure of physical damage. However, this article talks about a comparative measure between 12 products, created from the opinion of 12 people on 14 damage criteria (including environmental and economic damage). In addition to having been harshly criticized at the time for the methodology used, this article does not measure what it has been used for, and has been widely surpassed by the information produced on the subject from 2014 to date. However, the number is still used.

**Although vape activists and vaping companies have tried to distance themselves from the TI, tobacco companies are in control of the vaping market: British American Tobacco (BAT) dominates with 11% of the market, followed by Juul Labs with 4% (partially owned by Altria Group which also owns Philip Morris USA), and Imperial Brands (4%, formerly called Imperial Tobacco Group and owner of brands such as Winston, Kool and Davidoff) according to data from the same industry (Global Trends in Nicotine Report, prepared by the Foundation for a Smoke-Free World 2018)

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Study design

General aim

This study aims to generate a repository about electronic nicotine delivery systems (ENDS) based on scientific evidence that reflects the current state of the art. With the purpose of informing decision makers, state holders, non-governmental organizations (NGOs), and the population, about the characteristics, advantages, risks, and needs for regulation of these products, including the prohibition, to protect the populations health.

Methods

To carry out the ENDS repository project, a collection of information was generated through a systematic review of the regional, national, and international literature, which included all information related to ENDS from mid-2017 to early 2020. The starting date of the review was mid 2017, because that was the immediate period covered by the consensus report of the Academies of Sciences, Engineering and Medicine (NASEM) of the United States (*Public Health Consequences of E-Cigarette*).

Inclusion criteria

The report included observational studies (ecological, cohort or longitudinal studies, systematic reviews, and meta-analyses) published from the second half of 2017 to the first months of 2020, which evaluated the consumption of ENDS, or any other health outcome related to its consumption. Scientific manuscripts written in English or Spanish, published in peer-reviewed journals, and indexed in the PUBMED database of the National Library of Medicine of the United States National Institutes of Health (https://pubmed.ncbi.nlm.nih.gov) were included.

Search

The literature search was conducted using a systematic review methodology, which as a first step, included the development of the MESH (Medical Subject Heading) term. MESH terms are a controlled vocabulary that uses a biomedical database such as Medline and PUBMED to process the information entered. Currently, there are more than 33 thousand terms arranged in hierarchical structures called "trees", which are reviewed annually to ensure that they are a true reflection of current medical practice and terminology.[10,11] As the main objective of this project was to carry out a review and analysis of the most recent literature on the topic of SEAN, the term MESH was built on the Medline platform (Annex 1). The main terms used were:

ENDS (Electronic Nicotine Delivery System) and vaping, for each of these terms subtopics such as: adverse effects, epidemiology, cessation, mortality, legislation, etc., were included and the search was limited from mid-2017 onwards. The MESH term was used to explore the Medline platform, which yielded a total of 1,304 articles. The complete database was downloaded and, subsequently, in an initial review of the titles and their abstracts, two researchers reviewed each of the articles independently, to decide if they met the inclusion criteria. After this initial review was completed, a new one was carried out to see the articles on which both researchers agreed to add or to left out. In case of discrepancy, the articles were downloaded to read its complete content and decide whether to include it in the study or not.

Instrument design and system programming

To extract data from each article, a data entry form that consisted of a questionnaire with 86 categories was designed. The questionnaire was divided into two parts; first, the information related to the article, such as the name of the authors, title, year, journal of publication, reported conflict of interest, among others; second, general and specific vaping topics. The programming of the questionnaire was done in AirTable (https://airtable.com), which is a programming system store in the cloud that allows collaborative work between several people. All coders had access to the data entry form, which allowed the responses to be compiled into the database. The research team had access to the complete database through personalized links.

For the creation of the database, a random distribution of the articles was carried out. Packages of five articles were formed, which were randomly distributed among coders with the only condition that the same item was not assigned twice to the same coder. Subsequently, three concordance correlation analyzes between coders were performed using the Kappa test. This statistical test adjusts for the effect of chance, measuring how much two coders agreed when analyzing the same article. The kappa coefficient adopts values ranging from -1 to 1, with 1 being the perfect correlation value. A concordance coefficient greater than 0.7 was considered adequate. Based on these analyses, the coders of the articles with low concordance were identified and virtual meetings were held to agree on the responses based on the information contained in the articles. In addition, to maintain the quality of the database continuous monitoring and training was provided to the coders.

Once the articles were coded, the final database was cleaned, duplicated articles were identified and eliminated, and the consistency of the coding was analyzed by reviewing key variables (design and type of study, form of data collection, main result, positive or negative conclusions towards vaping, etc.).

When the database was finalized, the articles were classified based on the topics covered, generating 11 thematic sub-bases (conflict of interest, cessation, recruitment, physical damage, dual use, flavorings, toxic components, nicotine, marijuana use, alcohol consumption and advertising) that allowed an analysis of specific and relevant topics for the study. Within each of the sub-bases, the articles were evaluated according to the type of study, methodological design, sample size, limitations, and conflict of interest. Articles were classified according to their good, regular, or poor quality, this last category related, mainly, with the existence of conflict of interest among its authors.

Main findings

Conflict of interest

The conflict of interest involves a clash between the functions that a person must fulfill and their private interests. This happens, when there is some secondary interest (work, personal, professional, family, or business related) that affects their impartial and objective performance.* The secondary interest does not have to be illegitimate, what is questionable is the relative weight of these interests with respect to the base interest, or function. In this review, 80 articles that reported conflict of interest were identified.

The TI has a long history of interfering and creating conflict of interest in scientific research, they do so by preventing the existence of evidence opposing its interests. This conflict has spilled over to vaping products. This study found that if any of the authors reported having ties, in the form of contracts, grants, fellowships, research grants, etc., with the tobacco or vaping industry the probability of having a conclusion favorable to vaping increases in 21-fold. Furthermore, compared to scientific articles where the authors reported no conflict of interest, those that had a conflict of interest with the pharmaceutical industry were twice as likely to support vaping.

Conclusion

It is necessary to remember that Mexico is part of the WHO Framework Convention for Tobacco Control (WHO FCTC), which mentions in its article 5.3 that, when establishing and applying tobacco control-related public health policies, they must be protected against the commercial and other TI interests. The latter applies to all employees, representatives, and public officials of any institution or body at all levels.[12] In addition, both researchers and public functionaries must analyze the sources from which the data they use comes from, being able to recognize those authors or institutions that have or have had conflicts of interest in the past. Specific to new tobacco or nicotine products, given that the favorable results towards vaping seem to be associated with having a conflict of interest (declared or not), it is necessary to analyze the data sources and proceed with caution before using them as evidence for generating public policies.

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Cessation

Quitting smoking improves the quality of life by reducing the risk of developing cardiovascular diseases, chronic obstructive pulmonary disease (COPD), and different types of cancer; while increasing life expectancy by up to 10 years.[13] Currently, pro-vaping support groups, the vaping industry, and tobacco companies present vaping as a real alternative for quitting.[14] Among the reasons reported to start e-cigarette use is the to help with the quitting journey, however, there is no conclusive evidence that this occurs.[15] In this review, 74 articles were found that analyzed vaping as a cessation method. This review identified 25 articles advocating for vaping as a cessation alternative, the most famous being the one written by Hajek et al., that found that at one year of follow-up the cessation rate was 18% for those who used vaping as a method for quitting smoking cigarettes, compared with 9.9% of those who used nicotine replacement therapy (NRT). However, after 12 months, 80% of people who used vaping to quit smoking were still vaping; while only 9% of those who used NRT continued to use it.[16] Besides this article, there is little good-quality evidence to conclude that vaping is a more effective method for smoking cessation than alternatives such as NRT.[17,18] In addition, no evidence has been found comparing vaping with other more effective cessation alternatives such as pharmacological therapy. Most of the articles included in this review (49, that is, about 75%) were not favorable to the idea of considering vaping as a cessation method.

A longitudinal study found that smokers who intended to quit at baseline were 30% less likely to quit if they vaped.[19] Among former smokers who had quitted 12 months ago or more, only 1.8% of never vapers restarted smoking, compared with the 10.4%, 9.6%, and 15% of former, occasional, and regular vapers, that resumed smoking, respectively.[18] Another study that investigated factors associated with successful cessation found that never having vaped increases six times the likelihood of not relapsing.[17]

Conclusion

Although there are articles that showed positive results about the use of vaping as a form of cessation, most of them do not support this idea. In addition, there are concerns that must be considered. The Hajek article,[16] for example, was a randomized clinical trial, which is undoubtedly one of the best pieces of evidence to test medical treatments, but not consumer products. Randomized clinical trials occur under specific conditions (selection among people who actively seek to quit smoking, psychological accompaniment, one-year follow-up, etc.) that do not apply for the commercial use of vaping devices. Epidemiological studies, on the other hand, showed opposite trends for vaping as a cessation tool: less likely to achieve complete cessation and more likely to relapse to combustible tobacco use.

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* Definition adapted from: http://www.contraloria.cdmx.gob.mx/conflicto/

Gateway

For decision-making in public health, it is important be clear whether vaping attracts more people, especially young people, to nicotine addiction. That is, to analyze whether these products are a gateway to the consumption of tobacco products and nicotine addiction. Especially since vaping seems more appealing to the younger sector of the population: children, adolescents, and young adults. In the reviewed articles, 59 investigated vaping as a gateway to the nicotine addiction.

Among the adolescent population, the likelihood of start smoking was higher among those who had recently vaped. Several articles focused on the adolescent population (12 to 17 years old) finding between 80% and 700% higher probability of start smoking among those who vaped.[20–28] Furthermore, the likelihood and willingness to try[29,30] or experiment with combustible cigarettes is higher among those who vape.[31] These results are similar for adolescents who are susceptible to smoke and for those who are not susceptible.[32]

In young adult population, it was observed that those who had vaped in the past 30 days prior to the survey were four times more likely to start smoking compared to the ones that had not vaped.[21,28] However, an article carried out in young people, between 19 and 24 years old, found no significant association between vaping and subsequent smoking, but did find that smoking was associated with starting to vape.[27] The effect, however, is not limited to the younger segments of the population. The likelihood of starting smoking is also increased in non-smoking adults who decide to try vaping.[33,34]

Conclusion

According to the evidence found, among adolescents and young adults, being a vaper or having tried vaping increases the probability of start smoking. However, its effects also extend to non-smoking adults. Vaping products cause curiosity among adolescents, young people, and adults[35] so it is possible that in all cases they serve as a gateway to nicotine addiction. In the best-case scenario, people remain only as vapers, however, it's likely they'll eventually look for more efficient ways to consume nicotine, via combustible tobacco.

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Dual use

Dual use refers to the use of vaping and combustible cigarettes concurrently, which can result in higher health risks than just smoking or just vaping. The review found 90 articles dealing with dual use.

Among adolescents, prevalence of dual use ranges from 1.6 to 9.4%,[36–39] these rates are higher than the rates of exclusive smokers.[37, 40] Among adolescents, experimenting with vaping or living with a smoker increases the probability of becoming a dual user between 3 and 8 times more.[37, 40] Some of the risk factors associated with dual use in adolescents are:[36, 41]

- Being male
- Have greater economic accessibility
- Currently use, or had ever used tobacco products
- Parents or friends that smoke

In addition, among adolescents and young people dual use has been linked to risk behaviors, and consumption of other substances. Compared with adolescents who do not use any tobacco products, dual users were three times more likely to experiment with marijuana and engage in risky sexual behaviors; additionally, dual use has been associated with a higher probability of excessive alcohol consumption and greater involvement in violent acts.[42–47]

Among the reviewed articles, the prevalence of dual use among adults ranged between 12.8% and 62% of the population studied.[48–50] Those with higher education had less dual use, while higher dual use was found in men and urban areas.[51–53] One of the most reported reasons for starting or trying vaping was to cut down or quit tobacco use. Some studies reported that among dual users there were twice as many quit attempts, greater reduced of the number of cigarettes samoked,[51,54–57], and greater self-perceived ability to quit.[55] However, other studies reported that the probability of quitting tobacco use among dual users is not maintained in the long term (12 and 18 months),[58] it was even observed that those who had started vaping as a mean to quit smoking cigarettes continued being dual users and some had even increased the number of smoked cigarettes.[58–60]

Conclusion

Dual use is increasing among the population. There are personal and sociodemographic characteristics associated with greater dual use, these characteristics could be explored to create specific interventions to target these population groups. Among adults, one of the most reported motivations to initiate dual use is the desire to quit smoking. However, there is no conclusive evidence that vaping helps for this purpose, in addition, a high percentage of users who do not quit cigarette smoking remain as dual users, which increases their risk of tobacco and nicotine-related diseases.

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Flavors

Nowadays there are thousands of e-liquids flavor options available on the market. These flavors range from tobacco flavor to pancake, desserts, or commercial sweets, going through menthols, sweet or alcoholic drinks, and fruits -alone or combined. The variety of flavors is part of the discussion about the appeal and impact of vaping. While its defenders promote flavors as an essential component for adults to quit smoking, detractors point them out (especially sweet and fruity ones) as a reason why children and adolescents can be hooked on nicotine addiction. 54 of the reviewed articles analyzed the impact of flavors on vaping development.

The articles concluded that for teens and young adults, flavored e-liquids are one of the most important factors in trying vaping, and for many it is the main reason to start vaping.[47,61–63] About 70% of teens vape exclusively e-liquids with flavors different to tobacco flavor.[62,63] However, curiosity about e-liquids with different flavors than tobacco is not exclusive to adolescents and young smokers, as adults also reported it as a reason to try vaping.[61]

The tobacco and vaping industry, as well as pro-vaping groups, have reported that ENDS are an alternative created for adult smokers,[64] however, vaping e-liquids with fruity or candy flavors are the most attractive and the most consumed among adolescents and young people.[61,63,65] These types of e-liquids are consumed much more frequently among adolescents who have never smoked than among adults who want to quit smoking.[61] Liquids with sweet or fruity flavors facilitate the initiation of nicotine consumption, removing the bad taste produced by smoking tobacco.[47,63,65] Compared to adults, is three times more likely that an adolescent or young people consume non-tobacco flavored liquids, with and without nicotine.[62] Although adults also mention that the variety of flavors offered for vaping is among the main reasons why they try or start vaping,[66] in general, the e-liquids most frequently consumed by this population are tobacco or menthol flavors.[62]

Conclusion

One of the most attractive features of vaping is the variety of flavors available. Although the tobacco and vaping industry mention that their products are focused on adults who want to reduce their risk from smoking, the curiosity to try the different flavors occurs mainly among adolescents and young smokers and non-smokers. Adults also mention that the variety of flavors is a motivation to try vaping, however, they consume more tobacco- or menthol-flavored e-liquids than sweet and fruity. The existence of thousands of flavors seems to be one more a tactic to attract consumers, unfortunately the most susceptible to this are young people, smokers, and non-smokers. This can lead non-smokers to become vapers and nicotine addicts.

Physical damage

Nowadays there is no doubt about the physical damage caused by the consumption of cigarettes, and in an attempt to quit tobacco and reduce the impact on their health, some people have replaced it with vaping devices. However, evidence shows that, similar to combustible cigarettes, e-cigarette devices have health effects. Within the sample, we found 100 articles that studied the impact of vaping on health.

Of the articles reviewed for physical damage, most of them mentioned damage to the respiratory system. Two experimental studies were among the best quality articles, these studies found that vaping with and without nicotine causes alterations and injuries in the airway tissue and oxygen depletion in young smokers and on those who were non-smokers and vaped.[67,68] Dual use (the use of combustible cigarettes and e-cigarettes) was associated with progression of COPD (prolonged severity status, bronchitis, and decreased lung function).[69] Three articles based on systematic reviews that include experimental animal studies, clinical trials, observational studies, and news reports, concluded that vaping affects the physiology and function of the lungs, causing cough, asthma, COPD, and inflammation.[15,70,71]

Within the evidence found of health damage due to vaping, the second most reported consequences were heart and circulatory systema damage. Three studies reported that the use of e-cigarettes can cause more health damage than the use of combustible cigarettes. On the other hand, three experimental studies conducted in humans found an increase in systolic blood pressure, heart rate, and arterial stiffness; all the above related to the use of e-cigarettes with nicotine.[72–74] Other studies attribute the characteristics of metabolic syndrome with insulin resistance[75] and a decreased blood insulin to vaping.[76]

Vaping can also affect the nervous system as both the nicotine contained in combustible cigarette nicotine and in the e-liquids decrease the functional interaction between different brain regions (medial cortex, thalamus, and brainstem).[77] Intrauterine exposure to e-cigarette aerosols can affect brain development,[78] and the exposure during childhood can cause intoxication and seizures.[79] In addition to this, exposure to nicotine modifies the area of the brain that is responsible for the processes of reward, motivation, learning, and execution; it is associated with anxiety, depressive symptoms, decreased sleep, and increased wakefulness.[80,81]

Vaping can also cause damage to the immune system and genetic damage.[82] Other physical damages mentioned are damage to the skin, digestive, and reproductive system. Vaping has been associated with the presence of abdominal pain, diarrhea, injuries, and illnesses in the mouth and throat in adolescents and adults.[83–87] Regarding reproductive health, two studies made in rats found testicular damage and alterations in sperm production.[88,89] In humans, it is associated with erectile dysfunction and altered sperm production;[76] in women, it could cause spontaneous abortions and premature births,[76,90] as well as newborn death due to postnatal exposure to e-cigarette substances.[91] On the other hand, the use of e-cigarettes can cause skin damage such as burns, dermatitis, and lesions in the oral mucosa, due to overheating, fire or explosion of the devices.[92] In addition, it can affect wound healing.[93]

Conclusion

Beyond the comparison against combustible tobacco, the use of e-cigarettes can affect the health of different systems: respiratory, nervous, circulatory, digestive, reproductive, immune, genetic, and integumentary. Its consumption carries potential risks, both for the consumer and for the people around, especially children and adolescents.

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Toxic contents

Among the main arguments in favor of vaping is that it is less toxic than combustible tobacco. Given the enormous toxic potential of combustible cigarettes, this is not difficult. However, that does not exempt vaping from having its own toxic potential. In this search, 69 articles addressed the topic of toxic content in vapers.

Vaping liquids contain acetaldehyde, formaldehyde (compounds classified as group 1 carcinogenic, carcinogenic to humans, and 2B, possibly carcinogenic to humans, respectively),† [94] glycerin, propylene glycol, and ethanol.[95] Additionally, aerosols produced by vaping devices have high concentrations of silver, iron, nickel, aluminum, and silicon, as well as nanoparticles (<100nm) of tin, chromium, and nickel.[70,94,96,97] However, it should be considered that voltage variations associated with vaping can result in excessive degradation of propylene glycol and formaldehyde, suggesting five to 15 times higher metal exposure from these devices compared to combustible cigarettes.[96]

Conclusion

The reviewed evidence indicates that e-liquids components have lower toxicity compared to combustible cigarettes. Beyond the comparison, the existence of a potential for harm in the consumption of the aerosol emitted by vaping devices is shown, for which it is necessary to evaluate the toxicological potential of e-cigarettes and the effects they may have on health, both of those who consume and those who are exposed.

† The nine priority toxic groups refer to those listed in the "Tobacco Products Regulation" and the 18 listed components refer to those listed by the United States Food and Drug Administration (FDA).

Social media

The prevalence of vaping has increased in the last decade, mainly in adolescents. This popularity may be associated with the novelty of the product and its features. However, the marketing from the vaping industry also plays an important role. In particular, the use of paid campaigns on social media, the hiring of influencers, and the promotion based oncontent generated by the users themselves have helped the popularity of the product. In this review, 19 articles were found that dealt with the subject of advertising and social media.

Social media impacts the life of the population and this, along with the lack of regulation of advertising on them, has made them ideal platforms for promoting vaping products. The diversity of content created, both by companies and by the users, greatly impact on the decisions of the people who are exposed to these contents, especially if this exposure is not made in a critical way.[98–102] Generally, this content is accompanied by unproven claims related to harm reduction and presenting alleged evidence, which may increase the intent to try and use e-cigarettes.[102,103] Currently, brands are seeking to put their products in more places, an example of this is the use of celebrities who endorse or promote the use of their products in their personal profiles. The fact that a celebrity endorses vaping significantly increases the positive attitudes towards it and the intentions to use it, compared to not having celebrities endorsing them or to presents the products alone.[104]

A study that followed 1,742 adolescents for a year, reported that at the beginning of the study, 9.6% of the participants who said they had never vaped, a year later had already started. These people reported seeing vaping ads on social media, convenience stores, and tobacco shops at a higher rate than those who did not started vaping. The study concluded that exposure to Facebook advertising reported in the first measurement, increased the risk of vaping in the follow-up.[98] In addition, another study found that with higher presence of vaping products on social media, people tend to generate more positive expectations regarding their use, increasing the probability of consumption.[99]

Conclusion

Social media advertisements can represent vaping in a positive way, creating the perception that is normal to use them and, therefore, predispose the initiation of consumption, especially among adolescents who trust social media to obtain their information. Given that social media can affect attitudes and behaviors through social influence, it is imperative that tobacco control efforts carry out public health approaches in these platforms, including the regulation of its commercialization through social media.

Advertising

Advertising related to combustible tobacco products is prohibited in most part of the world, there have been agreements formulated to limit advertising even on the internet. However, it is interesting to know if the same is true for vaping products and what effect has on the population. Since vaping promotes the consumption of nicotine, which is a highly addictive substance, its advertising should be regulated. This literature review found 34 articles that addressed the subject of advertising.

The Internet is the most popular way to advertise vaping products, however direct-to-email, point-of-sale, or television advertising still exists.[15,105,106] Being exposed to this type of advertising is related to an increase in general curiosity about vaping, in the intention to use, consumption, and sales among smokers and non-smokers of all ages.[15,98,106–117] More than 40% of smokers of all ages reported seeing advertising for tobacco and vaping products in the past 12 months.[109]

When adolescents and young adults are exposed to advertising related to vaping, the curiosity to experiment increases around 25%, and the probability of vaping increases between 1.7 and 9 times more.[15,98,106–117] Advertising mentioning that vaping is effective for cessation or that it is a healthier alternative to nicotine consumption, has an overall impact on adolescents and young people, increasing between six and nine times the probability of being attracted to vaping.[111,118] In contrast, when exposed to informative advertising about health risks, the intention to try decreases.[15,119,120]

Conclusion

Exposure to advertising increases curiosity, intention to use, consumption and sale of vaping products. Stronger regulations are needed to force marketers to specify the health risks of vaping and find ways to make advertising for these products unavailable to teens and young adults. In addition, it is necessary to consider within the restrictions for vaping not to weaken other efforts for the control of combustible tobacco, such as those established in article 13 of the WHO FCTC, referring to the total prohibition of advertising, promotion, and sponsorship by the TI.

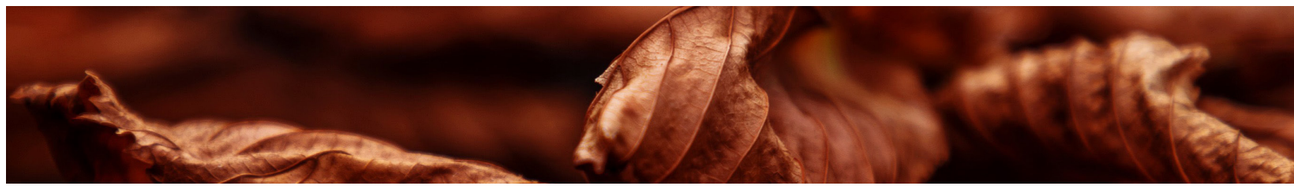
Alcohol

Among high school students, lifetime vaping use was correlated with greater likelihood of excessive alcohol consumption.[121,122] Age is an important risk factor, the younger people start using e-cigarettes, the probability of consuming alcohol increases. For example, adolescents that started vaping during their third year of middle school or before had between 70 to 80 times higher probability of start consuming alcohol, while those who had started in the third year of high school had six times the probability.[28,123–127] Adolescents who reported alcohol abuse were twice as likely to have vaped in the 30-day period prior to the survey.[121,125,128] This association has also been found inverted, that is, among adolescents who had never smoked or vaped, those who used alcohol were more likely to initiate their cigarette or e-cigarette consumption.[45,127,129,130] This could imply that there are social mechanisms that drive to the consumption of both products. Similarly, any of the two works as gateway for the other and, later, for the consumption of other substances. Among dual users, there was an 11-fold greater probability of using, consuming, and binge drinking compared to adolescents who neither smoked nor vaped.[47]

Among the adult population, we also found an increase in alcohol consumption among tobacco and e-cigarette users.[43,124,131] Compared with non-smoking and non-vaping adults, exclusive vapers consumed three times as much alcohol; exclusive smokers 4.3 more, and dual users 7.3 times more alcohol.[124] Compared with non-vapers, daily and occasional vapers were twice as likely to have monthly, weekly, and daily binge drinking episodes.[43]

Conclusion

In general, vaping is associated with other addictive behaviors such as the use of alcohol and other substances. We found an association between smoking, vaping, or dual use, and alcohol use among adolescents and adults. Among adolescents, vaping increases two times the probability of consuming alcohol, however, this probability increases up to 80 times more if they reported started vaping before the age of 15. Among adults, exclusive vapers and dual users have three to seven times higher alcohol consumption compared to non-smokers and non-vapers. In addition, the probability of consuming alcohol excessively increases two times more.



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Nicotine

Nicotine is an alkaloid derived from the leaves of tobacco plants and is the main addictive component in tobacco products.[132] Reducing the amount of nicotine could help people who want to quit smoking. Since 2018, the United States Food and Drug Administration (FDA) has tried to regulate the concentrations of nicotine contained in conventional cigarettes at a level that is not addictive.[133] Nowadays, vaping liquids have concentrations ranging from 0 to 60 mg/ml; the concentration of nicotine available in vape e-liquids has been found to be an important factor in choosing which vape device to use.

This is related to the fact that the concentration of nicotine increases the "hit" so having control over the nicotine level is an attractive feature of e-cigarettes. The preference for nicotine strength also differs according to individual characteristics such as gender, smoking status, and vaping history.[61] For example, inexperienced smokers or non-smokers prefer e-liquids without nicotine or with low concentrations, while more experienced smokers prefer high concentrations.[61]

We found that in adolescents, those who reported vaping e-liquids with higher concentrations of nicotine were twice as likely to increase the frequency of cigarette consumption and vaping, compared to those who vaped e-liquids without nicotine.[134] Among adults who vaped e-liquids with nicotine, a decrease in the number of cigarettes smoked was observed in less than three months; however, there is no long-term evidence that indicates those who vape continue to consume fewer cigarettes. Results reported that people who consume e-liquids with nicotine showed a decrease in the craving and desire to smoke conventional cigarettes, and an alleviation of withdrawal symptoms.[135,136] This may be associated to the fact that nicotine content in e-liquids is similar, and sometimes higher than, combustible cigarettes.

The evidence of health damage caused by nicotine consumption varies between body systems. One study found that when people vaped only e-liquid base, that is, e-liquids without nicotine (only propylene glycol and glycerol), there was no damage to the cardiovascular system. However, when nicotine-containing e-liquids are vaped at high temperatures, toxic effects on micro- and macrovascular functions had been observed.[137] There is evidence that both vaping and smoking affect the elasticity of the arteries and generate more acute oxidative stress. However, vaping e-liquids without nicotine produced a slight increase in the stiffness of the arteries, while, at one month follow-up, a decrease in central and brachial systolic blood pressure and oxidative stress was observed when substituting conventional cigarettes for vaping.[73]

Conclusions

There are several factors, such as gender, smoking status, and vaping history, that determine the preference for nicotine concentrations. Among adolescents, it was found that vaping e-liquids with high nicotine concentrations increases the frequency of cigarette and e-cigarette consumption. In adults, it was found that in the short term, vaping e-liquids with nicotine was associated with a decrease in the desire to smoke, and an improvement in stress markers and blood pressure when switching from cigarettes to e-cigarettes. However, more studies that focus on the health damage of nicotine and the benefit from stopping its consumption are needed.

Other substances: Marijuana

Some vaping devices have the feature that the tank can be removed to add or mix liquids. The use of these devices, with or without nicotine, to vape marijuana extract is becoming more common every day. From 62 articles that approached the topic of vaping other substances, 5 of them analyzed marijuana vaping.

The practice of vaping with active ingredients other than nicotine is becoming more common every day. It has been found that cocaine, ecstasy, crack, heroin, ketamine, and other substances are being vaped. The most common of these substances is marijuana.[138] This is because vaping is perceived as less harmful than traditional combustible methods. In addition, marijuana vaping is considered more convenient among users, since it helps reducing the odor and lower throat irritation when vaped.[28,46,139]

On the other hand, the use of alternative nicotine consumption systems has been associated with an increase in marijuana consumption and a decrease in the perception of harm in marijuana use.[140,141] Among adolescents, it has been observed that they are more likely to initiate or try marijuana if they have previously smoked or vaped.[46]

Conclusion

There is a growing trend in the use of marijuana in parallel with the increase in the use of vaping devices. Vaping has caused a decrease in the risk perception of tobacco and marijuana consumption, and it also facilitates its consumption due to the ease and discretion provided by the devices, eliminating drawbacks such as throat irritation and odor. Marijuana vaping has been related to an increased risk to the users health and the potential risk of a e-cigarette system where any mixture of components can be consumed with these devices.

Regulation

No consensus has been reached on how to regulate e-cigarettes. One of the strengths to properly regulate them is knowing their potential risk, that is, how dangerous they are. Not only in comparison to other products such as combustible tobacco, but with a clear idea of how much damage they can do. This harm can and should be looked at on two levels: first, how much people recruits into the nicotine addiction; second, how much damage does it do to its users and the people around them. The first part has already been examined, now we will be discussed the second one related to the implications of its regulation. Of 69 articles found that addressed toxic content, eight focused on the regulatory impact.

It has been observed that the content of harmful components present in vaping aerosol is potentially less than the content present in the smoke from combustible cigarettes, and that vaping-related toxicological consequences depend on many interrelated factors: voltage, temperature, flavoring, nicotine content, behavior of the vaper regarding its consumption, among others; therefore, the study of the possible results of aerosolization and its impact is complex and still partial.[70,142,143] However, some studies indicate that none of the e-liquids analyzed were free of toxic components,[70] and that their components are above the limits of detection allowed in conventional cigarette.[143]
The design and materials of e-cigarettes expose its users to toxic and potentially carcinogenic metals such as nickel, chromium, cadmium, tin, aluminum, and lead.[96] In addition, due to their action mechanism, which consists in heating a metallic resistance, these devices produce a greater number of toxic metals during the aerosolization process, compared to combustible cigarettes.[94,96]

Finally, there are reports that suggest that both, the nicotine levels, and other contents of e-liquids vary depending on the brands and flavors, in addition to the fact that the labels of these products are misleading and inaccurate. The latter shows the need to maintain its prohibition or, if the current prohibition in Mexico is lifted, the implementation of extremely strict regulatory measures in the manufacture, packaging, and sales of these products.[70,95] It is necessary to inform consumers, but also inform future regulatory policies related to product standards, accurate, and understandable labeling of e-cigarette and e-liquids.[144]

Conclusion

To properly regulate vaping devices, it is necessary to know their harm potential, beyond comparisons or other products. Regulation presents more challenges as there is so much lack of knowledge about the components and operation of e-cigarettes. It has been shown that during the process of hydrolyzing e-liquids there is a release of substances that are harmful to the body. Unfortunately, the large number of possible combinations between the thousands of e-liquids and e-cigarettes means that the progress made in this task is still partial. Given this, it is necessary to carry out future studies that allow knowing the health impact due to the use of these devices. In the meantime, it is recommended that any legislation considered be cautions and consider the potential risk of these products. Given the uncertainty of the potential risks or benefits of these products, it is preferable to use the precautionary principle and, as established by the World Health Organization, to strictly regulate or prohibit the use of these devices until there is enough information to create an adequate regulation.

Photo from Freepik

* Formally enunciated for the first time at the Wingspread Conference in 1988, the precautionary principle establishes that "when an activity represents a threat or harm to human health or the environment, precautionary measures must be taken even when the cause-effect relationship has not been scientifically proven".

General conclusions

Tobacco consumption is a public health problem that causes numerous health damages to those who consume it and to the people around them. That is why governments have regulated its sale, limiting its commercialization, and have emphasized the numerous benefits that quitting smoking brings. Due to the great danger it imposes, even tobacco sales had been subjected to the WHO-FCTC, which is the largest health treaty that exists, and Mexico is a Partee. To combat tobacco, the WHO-FCTC obliges the undertaking of a series of measures (MPOWER). It is important not to start smoking and, if you do, you must immediately cease its consumption. Fortunately, most people, even those who smoke, are at least partially aware of the harm tobacco causes. In this context, vaping devices had emerged as a new way of nicotine consumption, posing new challenges.

From the beginning, vaping devices have been promoted as a low-risk product that helps adult smokers to quit. However, due to its novelty, and the highly variable and customizable characteristics of e-cigarettes, there is no conclusive evidence to confirm that, in effect, these products are safer alternatives or that they help people to effectively achieve cessation, not only of cigarettes, but nicotine. Is highly possible that the harms or benefits of vaping will be seen many years after it hits the market. It is necessary to remember that, although lung cancer related to tobacco consumption had been identified since 1930, and by 1950 there was irrefutable scientific evidence of the damage caused by its consumption, but it was not until 1978 that there was a scientific consensus in this matter. Largely due to TI interference. Even in 1995, Directors of big tobacco companies testified in court that, as far as they knew, tobacco was neither addictive nor harmful. Not more than a cup of coffee.

This story seems to be repeating itself with vaping. The arguments and mechanisms are similar. As it happened with combustible tobacco, the scientific arm of the industry supports its products. Researchers who have found vaping to be superior to other cessation therapies or to have fewer health risks, generally report links to the tobacco or vaping industries; which represents a conflict of interest that cannot be ignored, making difficult to find neutral and good quality evidence.

As a marketable product e-cigarette, and the act of vaping, are attractive in many ways. They have a new design which in many cases can be fully customizable by the user. You can choose the color, the flavor, and even the nicotine concentration, making the initiation on nicotine consumption easier and more pleasant. Despite that TI promotes e-cigarettes as a product for adults, evidence shows that all the customizable features are more attractive to adolescents and young people than to adults who want to quit smoking. This impacts the countries' public health and the burden of disease, since it will be easier to have increasingly younger populations addicted to nicotine and exposed to the toxic components associated with vaping.

The tobacco and vaping industries have managed to get their product even in countries where there is a current ban, such as Mexico. In addition, they have managed to infiltrate peoples' psyche, making them believe that vaping is a low-risk activity. This brings serious public health consequences for countries like Mexico that are still struggling against the tobacco epidemic and the health damages caused by its consumption. Nowadays, there are generations that start consuming these products from very early ages, or that due to failure in cessation will remain as dual users, further increasing their health risks. A first step to advance in the study of vaping is to stop comparing then to the combustible cigarettes. With a product as harmful as combustible cigarette, vaping seems like a better option, but is it preferable to not consuming any tobacco product?

† In addition to the WHO, which in the Decision on Electronic Nicotine Administration Systems of the sixth Conference of the Parties (COP6), invited the member states to ban or regulate these devices, other international organizations have positioned themselves in favor of the ban. The International Union Against Tuberculosis and Respiratory Diseases (The Union) presented the position paper When to ban is best, supporting prohibition based on the use of the precautionary principle in public health, where it states: "Public health professionals and those responsible in policy making they should follow the precautionary principle and evidence-based approach to policy making. These fundamental public health concepts urge preventive action where the science is inconclusive. Given the potential harms of e-cigarettes and PTCs, plus the fact that long-term health effects are unknown because insufficient time has elapsed to demonstrate them, governments must commit to preventing an impending epidemic."[146]

‡ MPOWER is the WHO tobacco control strategy. It is based on six key measures: Monitor (tobacco consumption), Protect (the population from tobacco smoke), Offer (help to quit tobacco), Warn (about the dangers of tobacco), Enforce (bans on advertising, promotion, and sponsorship), and Raise (tobacco taxes).[147]

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Apéndice 1.1 Término de búsqueda

Final MeSH term:
(("Electronic Nicotine Delivery Systems/adverse effects"[Mesh] OR "Electronic Nicotine Delivery Systems/classification"[Mesh] OR "Electronic Nicotine Delivery Systems/epidemiology"[Mesh] OR "Electronic Nicotine Delivery Systems/ethics"[Mesh] OR "Electronic Nicotine Delivery Systems/history"[Mesh] OR "Electronic Nicotine Delivery Systems/instrumentation"[Mesh] OR "Electronic Nicotine Delivery Systems/legislation and jurisprudence"[Mesh] OR "Electronic Nicotine Delivery Systems/methods"[Mesh] OR "Electronic Nicotine Delivery Systems/mortality"[Mesh] OR "Electronic Nicotine Delivery Systems/pharmacology"[Mesh] OR "Electronic Nicotine Delivery Systems/psychology"[Mesh] OR "Electronic Nicotine Delivery Systems/standards"[Mesh] OR "Electronic Nicotine Delivery Systems/statistics and numerical data"[Mesh] OR "Electronic Nicotine Delivery Systems/therapeutic use"[Mesh] OR "Electronic Nicotine Delivery Systems/therapy"[Mesh] OR "Electronic Nicotine Delivery Systems/trends"[Mesh])) OR ("Vaping/adverse effects"[Mesh] OR "Vaping/analysis"[Mesh] OR "Vaping/epidemiology"[Mesh] OR "Vaping/ethics"[Mesh] OR "Vaping/legislation and jurisprudence"[Mesh] OR "Vaping/metabolism"[Mesh] OR "Vaping/mortality"[Mesh] OR "Vaping/pharmacology"[Mesh] OR "Vaping/physiology"[Mesh] OR "Vaping/physiopathology"[Mesh] OR "Vaping/prevention and control"[Mesh] OR "Vaping/psychology"[Mesh] OR "Vaping/statistics and numerical data"[Mesh] OR "Vaping/therapeutic use"[Mesh] OR "Vaping/therapy"[Mesh] OR "Vaping/trends"[Mesh])